Patients' Health Related Quality of Life after Coronary Revascularization: a Longitudinal Mixed Method Study

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Dedication

To my lovely daughters and the Angel of my life

Acknowledgments

This thesis would not have been feasible without the participation of the individuals who agreed to participate to the research studies, and I would like to express my sincerest thanks for their contribution. I would also like to offer my deepest thanks to my supervisors Dr Nikolas Troop and Dr Stefanie Schmeer for the encouragement, guidance and support provided during this journey. Furthermore, I would like to express my appreciation to Dr Irene Manaras for her encouragement to start the present research. Also, I would like to thank Dr Eirini Kampriani and Dr Dimitrio Fouskaki for their guidance and support. Finally, I would like to express my gratitude to my family for their patience as well as their practical and emotional support.

Abstract

Aims: Coronary Revascularization (CR) has increased patients' survival rate globally. However, the lack of a consensus definition of Health Related Quality of Life (HRQoL) and the different methodological and conceptual approaches adopted by researchers in the cardio-revascularization field create an incomplete picture of the influence of CR on individuals' HRQoL. By using mixed methodology, the current research aimed to explore Greek CHD patients' perspectives of their HRQoL after CR (Coronary Artery Bypass Grafting (CABG) or Percutaneous Coronary Interventions (PCI)), as well as detect and explain individual disparities.

Method: Two studies were conducted with a total sample of 487 individuals: (1) The translation and validation of the Coronary Revascularization Outcome Questionnaire (CROQ) into Greek and (2) The longitudinal mixed methods study, the main study of the thesis, following a sequential explanatory design with two research components: a) the longitudinal quantitative component aimed to detect changes in patients' HRQoL (both overall and its subdomains) following CR over a 12-month period based on individuals' subjective evaluation as captured by the CROQ, detect the influence of CR type on the outcome and to explore potential predictors (individuals' demographic, clinical and behavioural features). Data were analysed using multilevel modelling; b) the qualitative component aimed to capture individuals' lived experience, their view and understanding of themselves and their life approximately 12 months after treatment using Interpretive Phenomenological Analysis (IPA).

Results/findings: Based on participants' subjective evaluations as captured by the validated Greek version of the CROQ, one year after CR Greek Coronary Heart Disease (CHD) patients experience an increase in their HRQoL level compared to prior to CR. The pattern of change though is not constant; initially HRQoL increases with time, and then decreases again, however, remaining much greater compared to prior to CR one year after CR. Regarding the influence of the CR type of treatment on patients' HRQoL level, a year after CR mixed findings are revealed. In the *symptoms* and *physical functioning* subdomain, patients treated with CABG demonstrate a greater increase compared to patients treated with PCI. In the *psychosocial functioning* subdomain no difference is found. In the *cognitive functioning* subdomain, patients treated with CABG demonstrate a decline compared to their cognitive functioning prior to the CR. Various demographic, clinical and behavioural features are demonstrated to be predictors of the outcome though not consistent for all subdomains. The main predictors associated with larger positive changes following CR seem to be sex, BMI and smoking; females with low BMI that do not smoke tend to demonstrate a greater increase in HRQoL after CR.

According to individuals' lived experience, participants, reflecting on their experience one year after treatment, perceive CR as a simple process and their negative experience is mostly related to medical care. Many participants with no symptoms or adverse effects tend to misperceive CHD, viewing their health condition as an acute disease treated with CR. Trying to understand disease causality they tend to adopt medical discourse especially in relation to stress as a factor that can be controlled by themselves and reflect on their own responsibility as a causal factor. Feeling grateful for being alive, sensing a different body, a "revitalized body" as many participants suggest, as well as a fear of re-occurrence or disease progression motivate individuals to work on aspects of the self related to the CHD development in an effort to regain control over their life which has been reduced after the CHD diagnosis. In effect a dramatic change in how the self and life are viewed is reported, highlighting a positive growth; a greater appreciation of life, a personal growth and effort to build more meaningful relationships. Challenges that participants face in modification of their lifestyle are attributed to both external and internal factors. Concerning smoking participants' accounts point to a lack of knowledge regarding the relationship between smoking and CHD, a lack of support (by experts or family members) and conscious denial as a way to cope with every day anxiety and stress, but also a pleasure in everyday life.

The findings provide a complementary insight into perceptions of individuals with CHD about their quality of life one year after CR, suggesting that other factors beyond CR may influence their perspectives.

Conclusions/implications: This study highlights the benefits of using a mixed methods longitudinal design in exploring HRQoL. Both the quantitative and qualitative findings support the notion that HRQoL is a multidimensional, continuously changing concept, providing support for the Wold Health Organization's definition. Also, the findings suggest that CR has a positive influence on individuals' HRQoL. The effect of the CR type needs further investigation as mixed findings are observed in the present thesis. Moreover, it seems difficult to investigate the pure effect of CR on individuals' HRQoL without taking into consideration individuals' adjustment processes and positive growth triggered by the CR.

The self regulation model (SRM) might be considered a useful theoretical framework for developing theory-based interventions aiming to alter patients' false beliefs since individuals' making-meaning process seems to be aligned with it. Finally, the complementary insights

concerning smoking may help health care providers to develop smoking cessation interventions tailored to cardiac patients.

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List of abbreviations

BMS = Bare Metal Stent

CABG = Coronary Artery Bypass Grafting

CAD = Coronary Artery Disease

CAT = Cognitive Adaptation Theory

CCT = Cardiac Computed Tomography

CHD = Coronary Heart Disease

CMR = Cardiac Magnetic Resonance

CR = Coronary Revascularization

CROQ = Coronary Revascularisation Outcome Questionnaire

CRP = Sublingual Glyceryltrinitrate

CVD = Cardiovascular Disease

DA = Discourse analysis

DES = Drug Eluting Stent

E = Ethnography

ECG = Electrocardiogram

EQ-5D = EUROQOL – 5D

ES = Effect Size
ETT = Exercise Tolerance Test

GT = Grounded Theory

HF = Heart Failure

HRQoL= Health Related Quality of Life

IPA = Interpretative Phenomenological Analysis

QUAN= Quantitative

QUAL= Qualitative

MACE= Major Adverse Cardiac Events

MCS =Mental Component Summary

MI = Myocardial Infarction

MLM = Multilevel Linear Modelling

MED = Medical Therapy
NHP = Nottingham Health Profile

PCI = Percutaneous Coronary Interventions

PCS = Physical Component Summary

PTCA = Percutaneous Transluminal Coronary Angioplasty

PTG = Post-Traumatic Growth

QoL = Quality of Life

SAQ = Seattle Angina Questionnaire

SF-36 = Short Form -36

RS = Response shift

SRM = Self-Regulatory Model

TA = Thematic Analysis

TABP = Type A Behaviour Pattern

TAP = Type A Personality

WHO = World Health Organization

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Chapter One

Introduction to Coronary Heart Disease and its clinical treatment

1.1.Introduction

This thesis focuses on patients with coronary heart disease (CHD) and the impact of Coronary Revascularization (CR) on their Health Related Quality of Life (HRQoL) over a one-year period, by using a mixed methods approach. The scope of this chapter is to introduce essential concepts related to CHD as well as to present a rationale for conducting this study in Greece. Issues presented address the following questions: 1) What is the nature and the burden of CHD? 2) What are the symptoms and how can a diagnosis be made? 3) Which are the risk factors for CHD development? 4) What are the most common ways of treatment as well as what may be the pros and cons of each type of treatment regarding clinical outcomes? 5) What does research evidence indicate about the incidence of CHD and its treatment in Greece and why is it important to investigate the HRQoL of individuals who have undergone CR in the Greek context?

1.2.Coronary Heart Disease

Coronary heart disease or coronary artery disease is a non-communicable chronic disease caused by the atherosclerosis of the coronary arteries. Atherosclerosis refers to the hardening and narrowing of the blood vessels (coronary arteries) due to fat deposits known as plaques in the walls of the arteries. Atherosclerosis reduces the normal flow of blood towards the heart and, as a result, the oxygen and energy supply reaching the heart muscle are insufficient for its normal functioning (Fuster, Moreno, Fayad, Corti, & Badimon, 2005). The common medical term for a condition where the heart does not get enough oxygen is ischemia.

Long lasting ischemia due to atherosclerosis may result in a myocardial infarction (MI– that is, heart attack) and sudden cardiac death. A heart attack causes damage to the heart muscle from the blood supply being completely cut off due to a spasm or blood clot in the coronary arteries. Heart attacks and angina can cause electrical disturbances in the heart which can result in abnormal heart rhythms (arrhythmias) such as ventricular fibrillation, which is a fatal condition. Repeated heart attacks where substantial parts of the heart muscle have died can lead to heart failure (HF). In turn, heart failure may provoke various conditions such as paroxysmal nocturnal dyspnea (PND), that is shortness of breath during sleep at night (Ju Young, Martin, & Bryant Howren, 2009). CHD cannot be cured, but the appropriate treatment can improve the functioning of the heart muscle providing a relief of symptoms (these will be discussed in the next section) and diminish the risk of further problems, such as MI or HF (Fuster et al., 2005).

According to reports by the World Health Organization (The Whoqol Group, 2011a, 2011b, 2011c) in 2008 17.3 million individuals died from cardiovascular disease representing 30% of total deaths in the world. Of these deaths, approximately 7.3 million were due to coronary heart disease, making this disease one of the leading causes of global deaths. Moreover, based on a recent report (Nichols, Townsend, Scarborough, & Rayner, 2013), CHD is the most common cause of death in Europe, representing 1.8 million deaths in the most recent year for which the data were available; approximately 22% of females and 20% of males. Furthermore, in 2009 the total health care costs for CHD in European countries was approximately 19.9 million EUROS

(2% of the total health care expenditure) while the non-healthcare cost of CHD was 40.3 million EUROS (informal care, productivity losses due to morbidity and mortality).

Moreover, the life of people with CHD may be dramatically affected. CHD symptoms can cause great discomfort and/or pain resulting in a reduction of performance of daily activities and even absence from work. These can lead to a loss of income, which may affect health care (inability to buy medicines, undergo mandatory re-examination and support a healthy diet) and may negatively influence individuals' lives.

1.3.Symptoms and diagnosis

1.3.1. Symptoms

The common symptoms of CHD are angina pectoris (chest pain) and shortness of breath during various daily activities or low/moderate exercise (Mittal, 2005). However, the manifestations of CHD may be experienced differently by different individuals. For instance, research evidence demonstrates that females may have different or additional CHD manifestations compared to males. They may experience fuzzy symptoms, such as extreme fatigue, discomfort in the shoulder blades, shortness of breath, nausea, and a burning sensation in the chest or upper abdomen (Young et al., 2009; Kumar, Kaur, & Devi, 2011; O'Keefe-McCarthy, 2008). Additionally, some studies maintain that females experience greater levels of chest pain resulting from angina compared to males (Ghezeljeh et al., 2010). At this point it is important to mention that there are cases, less common but still existing, where individuals do not experience any symptoms (Lindsay & Gaw, 2004).

Angina pectoris is the medical term for chest pain, which can appear at exertion or at rest. It is usually described as pain in the chest or as a radiating pain in arms, shoulders, neck, back, epigastrium (upper central part of the abdomen) and jaw (Lindsay & Gaw, 2004). In some cases, the angina is not perceived as pain, but as a sensation of discomfort, squeezing, pressure, strangling, bursting in the chest (Lindsay & Gaw, 2004; Sangareddi et al., 2004). The experience of angina pectoris is the condition that typically leads individuals to seek medical help. There are three main types of angina pectoris caused by coronary heart disease: a) *stable angina*, which is experienced during a state of physical exertion or emotional or mental stress, b) *unstable angina*, which is experienced at rest when chest pain is unexpected and c) *variant angina pectoris* which is more rare and mostly experienced at rest (during sleep) due to a coronary artery spasm.

Researchers point out that the levels of angina may be influenced by the weather and food consumption. In fact, there are a number of studies supporting that angina is worse when there is cold (Ezekowitz et al., 2013) or windy weather and after heavy meals (Bhowmik, Das, & Dutta, 2011).

1.3.2. Diagnosis

The diagnosis of CHD and angina is made partly on the basis of the medical history and assessment of risk factors for artherosclerosis and partly on the basis of a clinical test. Three different types of clinical assessment usually take place: an initial assessment consisting of blood tests and measurement of blood pressure, a functional and an anatomic assessment (Kantor, Nagel, Schoenhagen, Barkhausen, & Gerber, 2009).

An initial assessment is made in order to detect the level of certain fats, cholesterol, glucose and low levels of proteins (e.g. C-reactive protein (CRP) and Hemoglobin, an iron-rich protein) in the blood. Additionally, blood pressure is measured. Abnormal levels may suggest existing risk factors for CHD.

A functional assessment is made in order to find support for the diagnosis of CHD by recording heart rhythm and electrical function. The most common functional assessment is an electrocardiogram (ECG). However, an ECG is usually obtained not at rest, but during exercise on a treadmill or on an exercise bicycle in order to identify an irregular heart rhythm; this procedure is known as stress ECG or stress test or exercise tolerance test (ETT (Aaronson & Ward, 2007).

An anatomic assessment is made in order to detect narrowing in the arteries. Cardiac catheterization is the most accurate test, however, it is mostly employed in cases where there are severe CHD symptoms or where intervention treatment is being considered, because there is a small possibility of creating arrhythmia or a myocardial infarction (Aaronson, & Ward, 2007). The cardiac catheterization procedure involves a catheter being inserted into an arm or leg artery, which is then threaded through to the coronary arteries affected. Then an X-ray liquid is injected to show the blood supplies from the arteries to the heart while X-ray filming (a coronary angiogram) takes place in order to identify any blockages of the coronary arteries. In the last decade more noninvasive tests have been used for anatomic and functional imaging of CHD: cardiac computed tomography (CCT) and cardiac magnetic resonance (CMR). According to researchers (Kantor et al., 2009), these tests can demonstrate the degree of coronary artery blockage and the presence of ischemia while avoiding the risk of plaque rupture during the test which may lead to MI.

1.4. Risk factors

Since both prevention and treatment of CHD involve consideration of risk factors, it is essential to present these briefly. Risk factors may broadly be separated into two categories: the conventional (behavioural and medical) and the non-conventional (psychosocial) risk factors related to CHD.

1.4.1. Conventional risk factors

Researchers have identified several environmental and biochemical factors that can account for pathogenesis and progression of coronary heart disease. A family history of premature coronary artery disease (Lloyd-Jones et al., 2004), especially if it is associated with coronary artery calcification (Nasir et al., 2007), smoking (Al-Nozha et al., 2009; Khot et al., 2003), high blood pressure (Khot et al., 2003), diabetes (Khot et al., 2003), high cholesterol levels (Khot, et al., 2003; Roeters van Lennep, Westerveld, Erkelens, & van der Wall, 2002), obesity (Roeters van Lennep, et al., 2002), physical inactivity, diet and stress are the most common factors that can increase the risk of CHD (Mittal, 2005; Schenck-Gustafsson, 2009). A large cross-national study demonstrated that eating fruit and vegetables, moderate exercising, and avoiding smoking could lead to an about 80% lower relative risk for a heart attack (Yusuf, et al., 2004). These findings are supported by the WHO (2011) report on noncommunicable diseases indicating that 80% of coronary heart disease deaths are related to behavioural risk factors such as an unhealthy diet, physical inactivity and tobacco use.

Additionally, recent research findings point out some additional risk factors as being associated with CHD, such as periodontal infections (Bahekar, Singh, Saha, Molnar, & Arora, 2007; Berent et al., 2011; Spahr et al., 2006) and polycystic ovary syndrome in females

(Alexander, Tangchitnob, & Lepor, 2009; Christian et al., 2003). Furthermore, age is also a risk factor for developing CHD. Researchers maintain that atherosclerosis begins in childhood and develops over adolescence and adulthood and, if left untreated, can lead to CHD in middle or older age (McGill & McMahan, 2003; McMahan et al., 2006) Finally, there are contradictory findings regarding sex as a risk factor, a recent review points out that sex could be considered a risk factor but only in interaction with age. Based on Tan, Gast and van der Schouw (2010), young and early middle-aged males are at greater risk compared to females. However, the risk of CHD in females increases dramatically after menopause. In fact, the earlier menopause occurs, the greater the risk becomes (Tan et al., 2010).

1.4.2. Non-conventional risk factors

According to literature, traditional or conventional risk factors (e.g. smoking, hypertension, hypercholesterolemia, diabetes) do not completely explain the presence of CHD. A plethora of studies have investigated the role of psychological factors such as personality type (please see appendix 1.1), negative affect (hostility and anger, depression, anxiety) and social factors such as social support, social isolation not only as possible risk factors for the development and progression of CHD, but also as predictors for treatment outcome.

Regarding the influence of anger and hostility in the development and progress of CHD, the literature demonstrates contradictory findings (Siegman & Smith, 2013). Based on a recent systematic review, the harmful effects of anger and hostility on CHD are not significant after fully controlling for conventional risk factors such as smoking, physical activity and obesity (Chida & Steptoe, 2009). This could be explained by the fact that these two traits could lead to the development of biochemical disturbances. For instance, hostility level has been associated with the level of hypertension (Yan et al., 2003) while anger has been associated with high blood pressure (Steffen, McNeilly, Anderson, & Sherwood, 2003), and especially diastolic blood pressure (Schum, Jorgensen, Verhaeghen, Sauro, & Thibodeau, 2003), which is significantly associated with coronary heart disease (D'Agostino, Belanger, Kannel, & Cruickshank, 1991). In fact, inhibition of anger expression is strongly associated with increased risk of CHD, especially in males (Davidson & Mostofsky, 2010), major cardiac events (Denollet, Gidron, Vrints, & Conraads, 2009) and adverse effects after coronary revascularization (Denollet, Gidron, Vrints, & Conraads, 2010). Furthermore, the conflicting finding may be explained by the fact that specific types of anger expression (constructive anger, destructive anger justification and destructive anger rumination) may account for different levels of risk and many researchers do not differentiate between these (Siegman & Smith, 2013). Constructive anger refers to anger expression motivated by constructive reasons (e.g. to solve a problem). This type of anger expression is considered to make individuals more creative. An example of constructive anger expression might be a director who is angry due to rumors suggesting that s/he is not a good team leader and as a result s/he is motivated to take actions to increase team bonding and interaction. Destructive anger justification refers to anger expression to justify one’s current feelings by blaming others. For instance, using the same example, the director expressing this type of anger will defend her/himself by minimizing own fault and by blaming the staff. Destructive anger rumination refers to the tendency to repetitively think about the situation that provoked anger. During angry rumination, anger is re-provoked by the repeated focus on the cause and consequences of the anger trigger. Angry rumination results in increasing and maintaining anger levels and aggressive response (Siegman & Smith, 2013). Following on with the same example, the director will repetitively think about the event that elicited her/his anger, developing increased levels of anger. Based on research findings, reduced constructive anger in males and increased destructive anger justification in both sexes are associated with increased risk of CHD (Davidson & Mostofsky, 2010), while destructive anger rumination is related to increased acute coronary events (Fernandez, et al., 2010).

Concerning depression, there is established research evidence that it is a compelling risk factor for CHD incidence (Bunker et al., 2003; Ferketich, Schwartzbaum, Frid, & Moeschberger, 2000; Wulsin & Singal, 2003), progression (Lett et al., 2004) and treatment (Parissis et al., 2007). While a number of reviewers maintain that studies vary in the assessment methodology, leading to an inability to conclude on the exact degree to which depression accounts for CHD development and progression (Goldston, & Baillie, 2008; Van der Kooy et al., 2007; Wulsin & Singal, 2003), more recently reviewers have demonstrated that the prevalence of depression in the cardiac population is high (Celano & Huffman, 2011). In fact, 31-41% of patients with coronary artery disease (CAD; including those with stable CAD, unstable angina, or myocardial infarction) show depressive symptoms (Celano & Huffman, 2011). Moreover, the findings of a recent study conducted by Mcguire, Eastwood, Hays, Macabasco-O'Connell & Doering (2014) who aimed to assess depression in a sample of 323 patients hospitalized with coronary heart disease revealed that approximately 31% experienced depressive symptoms. Compared with patients who were not depressed, patients who were depressed had higher scores for dysphoria, loss of appetite, sleep disturbance, fatigue, loss of libido, and irritability ($p < .001$). Interestingly patients with acute coronary syndrome were less likely to have depressive symptoms than those who had not experienced ACS ($p = .02$). The incidence of depression among Greek patients with CHD seems to be high as well. The findings of a recent Greek study with a sample of 702 heart patients suggest that approximately 40% of patients experience depression (19.1% moderate and 20% high levels of depression; Polikandrioti et al, 2012). Furthermore, a number of behavioural factors may affect the relationship between depression and heart disease. Patients with depressive symptoms are less likely to be engaged in health-promoting behaviours (e.g. following a healthy diet, regular physical activity (Whooley et al., 2008), adherence to prescribed medicines (Gehi et al., 2007) and completion of cardiac rehabilitation programs (Casey et al., 2008; Gehi et al., 2007). CHD patients with depressive symptoms tend to have greater difficulty with lowering other conventional risk factors (e.g. cholesterol level) related to the development, progression and recurrence of cardiac events (Gehi et al., 2007).

A plethora of research findings has demonstrated that anxiety is significantly associated with the development and progression of CHD (Sirois & Burg, 2003). Anxious individuals are at higher risk of experiencing cardiac episodes independently of demographic variables, biological risk factors and health behaviours (Olafiranye, Jean-Louis, Zizi, Nunes & Vincent, 2011; Roest, Martens, De Jonge & Denollet, 2011). Prevalence of anxiety in patients with stable CHD seems to range from 16% to 42% (Polykandrioti & Olympios, 2014). However, there are a number of researchers maintaining that anxiety is not a significant predictor of the development of CHD for both males and females. For example, Nabi, and his colleagues (Nabi et al., 2010) found that none of the measured components of anxiety (psychological and physiological symptoms) were associated with an increased risk of CHD in males after adjusting for socio-demographic characteristics, behavioral risk factors, and clinically significant symptoms of depression. On the other hand, in females, only somatic symptoms of anxiety were associated with an increased risk of CHD after adjustments (Nabi et al., 2010). The prevalence of anxiety in Greek patients with CHD in Polikandrioti et al.'s (2012) study seems to be quite high. In a sample of 702 cardiac patients (from four public hospitals in Attica and two provincial hospitals), almost half experienced moderate or high levels of anxiety (26% and 32.7% respectively; Polikandrioti et al., 2012).

Research evidence demonstrates that anxiety is associated not only with the onset and progression of CHD but also with the treatment outcome both directly and indirectly. Anxiety directly influences physiological functioning (e.g. activation of the sympathetic nervous system results in increased heart rate, elevated levels of hypercortisolemia and recurrent ischemia, which impede recovery; Moser, 2007; Olafiranye et al., 2011). Anxiety also indirectly affects treatment outcome by impairing levels of energy and cognition; CHD patients tend to demonstrate poor psychological functioning (e.g. intense worry about future cardiac events or disease progression, restriction of pleasure activities (Karimi-Moonaghi, Mojalli, & Khosravan, 2014)), self-care behaviour (e.g. low adherence to lifestyle change recommendations and medicines (Olafiranye et al., 2011)) and psychosocial functioning (e.g. low sense of emotional control (Lionis et al., 2010), low levels of positive adjustment and interpersonal conflicts (Moser, 2007; Olafiranye et al., 2011), and early retirement (Glozier et al., 2013)) .

Regarding psychosocial issues, the literature (e.g. Bunker et al., 2003; Karimi-Moonaghi et al., 2014). Rosengren et al., 2004; Lett et al., 2005) reveals that the experience of major life events and lack of social support are strongly related to the development and progression of CHD and recurrent adverse cardiac events. A number of studies suggest that major life events during the last year (e.g. death within family, divorce, unemployment; Lett et al., 2005) as well as financial problems, job satisfaction (Glozier et al., 2013; Panagiotakos et al., 2007), severe intra-family conflicts (Karimi-Moonaghi et al., 2014) increase the risk and progression of CHD (Colquhoun et al., 2013) in both sexes (Rosengren et al., 2004). For females only another psychosocial aspect associated with the development and progress of CHD is responsibilities at home (Low, Thurston & Matthews, 2010). Another psychosocial factor that is associated with CHD is social support. A literature review conducted by different independent investigators on 57 prospective studies (Bunker et al., 2003) proposes that there is a strong association between social isolation or lack of social support and CHD. Based on Heaney and Israel (2008) social supports refers to having a social network, i.e. individuals have people around them that understand their needs and are willing to help them by providing either emotional (e.g. by listening and empathic understanding) or instrumental support (e.g. by offering physical or financial assistance). Social isolation refers to a lack of social network (e.g. living alone with no friends or no participation in group activities). This "lack" of social interaction could lead to reduced access to information that can influence one's lifestyle and health related behaviours on the one hand, and absence of emotional support in stressful situations, on the other (Lett et al., 2005). At this point it is essential to mention that both lack of social support or exaggerated support may lead to social isolation as the individuals may either lose their trust in others or confidence in themselves (Karimi-Moonaghi et al., 2014).

1.5. Treatment

CHD prevention is a challenging issue. However, this thesis focuses only on QoL following treatments for established CHD. Therefore, only treatment will be discussed. Treatment for CHD involves attention to biopsychosocial risk factors, medicine therapy (MED) and coronary revascularization (CR) which includes two main types: interventional procedures (Percutaneous Coronary Intervention - PCI) and surgical procedures (Coronary Artery Bypass Graft Surgery-CABG). Both types of CR deal directly with artery blockage. Briefly, PCI, widely known as balloon angioplasty or stent, is used in order to open any blocked arteries during cardiac catheterization; the insertion of a fine tube into a vein in the groin or sometimes in the arm, reaching the coronary artery and then the blocked section (Holmes & Williams, 2008). CABG, widely known as bypass, involves an opening in the chest bone (sternoctomy), which gives the cardiac surgeon adequate access to the heart in order to bypass the blockage with a new vein (usually from the patient's leg or arm which is used as a graft; Peterson et al., 2002). Usually, CABG takes place when the coronary artery is too small, there is a complete blockage or more than two arteries are narrowed (NICE team guidelines, 2012). For further information about medical therapy and CR treatment please see Appendix 1.2

1.5.1 Clinical outcomes: Comparing PCI, CABG and MED

Regarding PCI vs CABG mortality rates, Bravata et al. (2007), based on 13 RCTs with 9,963 patients of whom 5,019 were randomly assigned to PCI and 4,944 to CABG treatment, with a range of 6 months to 13 years follow-up after initial treatment, conclude that the mortality rates of patients treated either with PCI or CABG are less than 1%. Comparing the pros and cons of the two procedures is rather hard due to many changes and ongoing technical improvements.

In general terms, the advantages of PCI over CABG are a brief hospital stay, less discomfort from an operation, more rapid recovery (Hong et al., 2005) and return to work (Sellier, 2007). The most essential long-term disadvantage of PCI (balloon or with stent) is restenosis. Comparing the two procedures, it is very important to consider the exact technique used (e.g. balloon angioplasty vs off-pump bypass or drug stenting vs MIDCAB) and the severity of coronary artery disease (single vs multiples vessels). There have been a number of trials comparing percutaneous coronary interventions vs coronary artery graft bypass surgery.

However, the results should be viewed with caution due to the fact that there is great heterogeneity of methodology among studies. Comparative meta-analyses and systematic reviews give various insights. For instance, some investigators suggests that the overall mortality and myocardial infarction rates are similar for bare metal stents and MIDCAB patients (Jaffery, Kowalski, Weaver, & Khanal, 2007), or PCI and CABG patients (Bravata, et al., 2007; Hlatky et al., 2009), but surgical approaches are associated with fewer repeated revascularizations (Edelman, Yan, Padang, Bannon, & Vallely, 2010). Others point out that off-pump surgery significantly reduces major adverse cardiac events compared to PCI and the only disadvantage is the longer hospital stay (Bainbridge, Cheng, Martin, & Novick, 2007). Similar findings have been demonstrated by Serruys and his colleagues (2009) who have compared CABG with PCI (with a drug eluting stent) for severe CHD (three-vessel or left main coronary artery disease). Based on this meta-analysis, CABG may be a more favourable procedure for severe CHD because of fewer major adverse cardiac events (MACE) after one year. Other meta-analysts claim that there is no difference between CABG and PCI patients with unprotected left main coronary artery stenosis in terms of MACE (Lee, Yang, Dhoot, & Liao, 2010). Nevertheless, due to the great heterogeneity of trials and limitations in the methodology of each study, firm conclusion cannot be drawn. Moreover, many issues are left uninvestigated. For example, it is unknown if these findings are equally applicable to males and females or if they apply long term.

Regarding Coronary Revascularization (CR) vs medical treatment (MED), Jeremias, et al. (2009) carried out a meta-analysis based on 28 RCTs with 13,121 patients of whom 6,476 were revascularized and 6,645 treated with medicines, with a median of 3 years after initial treatment follow-up. These authors conclude that these two procedures successfully reduce the mortality rate. Actually, patients treated with CABG and PCI have greater survival rates (OR= 0.62 (95%

CI, 0.50-0.77) and 0.82 (95% CI, 0.68-0.99) respectively) compared to medical treatment. A more recent meta–analysis (Pursnani et al., 2012), however, based on 12 RCTS with 7,182 patients comparing PCI and medical treatment did not find evidence for the superiority of PCI. However, the same review highlighted that PCI is related to fewer angina symptoms compared to medical treatment. In another study (Hueb et al., 2010) comparing CABG, PCI and MED in terms of morbidity rates, 10 years after treatment, the authors concluded that MED compared to CABG was related to a significantly higher incidence of subsequent myocardial infarction, and a higher incidence of cardiac death.

1.6. Assessing the outcome of coronary revascularization

As pointed out earlier, the majority of clinicians treat their patients with the aim of increasing longevity, preventing future morbidity and making them feel better (Guyatt et al., 2007), by reducing various symptoms such as chest pain and discomfort which affect their physical functioning and make them distressed. Therefore, a plethora of randomised controlled trials have been conducted in order to evaluate the effectiveness of treatments for CHD and many are still ongoing as new procedures are being developed. In the literature, various trials have been reported which explore the impact of intervention on the full spectrum of coronary revascularization outcomes. A number of them focus on mortality and morbidity rates and others also consider patients' health related quality of life (HRQoL), viewing illness as having a pervasive effect on various aspects of life (Guyatt, Feeny, & Patrick, 1993).

In previous decades, postoperative clinical outcomes after coronary revascularisation were initially measured on the basis of clinical events (e.g. mortality, myocardial infarction, stroke) and complications (such as arrhythmias, atrial fibrillation, infections). Having achieved the goals of raising patients' survival rate (Guru, Fremes, Austin, Blackstone, & Tu, 2006; Singh et al., 2008), especially among male patients (Kim, Redberg, Pavlic, & Eagle, 2007; Tillmanns et al., 2005; Vaccarino, Abramson, Veledar, & Weintraub, 2002) and reducing MACE due to the procedures via the advances in revascularization techniques, the focus of attention has shifted onto the improvement of patients' symptomatic and functional status.

Assessment of treatment outcomes has turned to symptom alleviation and improvement of physical functioning (Hlatky et al., 1989), assuming that physiological improvement is strongly associated with functional improvement and well-being (Guyatt, et al., 2007). Actually, research has shown that coronary revascularisation improves patients' functional status and successfully reduces chest pain (Hlatky, 2004). However, physiological/objective measures provide essential information to the clinician, but they do not fully capture what is of interest to patients themselves (Guyatt, et al., 1993). For patients, objective measures sometimes represent just values that may not be comprehensible or even meaningful. For example, the treadmill exercise test which is an attempt to reproduce patients' daily exercise in a controlled environment, cannot take into account the realities of life, and thus it cannot be an adequate measure of everyday activities. Hence, self-reported activity may be a better predictor than treadmill exercise where patients' functional capacity is concerned (Asakuma, Ohyanagi, & Iwasaki, 2000). Investigators that incorporate this aspect tend to conduct more patient-oriented trials. In other words, a growing number of trials assess subjective measures focusing on patients' point of view alongside with objective measures in order to address the basic question of how patients may experience treatment and how they perceive treatment to influence their HRQoL. Such information, along with patient characteristics (e.g. demographics and existing comorbidities), may help doctors to gain a deeper understanding, to draw conclusions about the benefits of treatment and help them in deciding what is the most appropriate treatment (Jokinen, Hippelainen, Turpeinen, Pitkanen, & Hartikainen, 2010). In fact, HRQoL data from CABG and PCI research could play a key role in identifying which patient groups (concerning e.g. age) benefit mostly from each revascularization procedure. This will be discussed over the next two chapters.

1.7.CHD in Greece

Until the late 1970s, coronary heart disease (CHD) was of low prevalence in Greece compared to other European countries (WHO, 1983 in Kalandidi et al., 1992; Gigkas, Soriropoulos, Panagiotakos & Papas, 2004). Forty years later, Greece has turned into a country with a high prevalence of CHD among European nations (Mennotti & Puddu, 2013). The results of a recent epidemiological study (ATTICA; Panagiotakos et al., 2015) demonstrated that the incidence of CHD has increased 9% between 2001 and 2006 (Panagiotakos, Pitsavos, Chrisohoou, Skoumas, & Stefanadis, 2008) and approximately another 7% between 2006 and 2012 (Panagiotakos et al., 2015). Consequently, this increase raised the risk of mortality from CHD. Based on Nichols et al.'s (2013) report, in 2009 CHD was the third most likely cause of mortality in Greece. Recent reports suggest that there is a decline in CHD mortality, especially among urban citizens, due to developments in CHD treatment, but there is still an ongoing increase in non-fatal CHD incidence, in both sexes (Panagiotakos et al., 2009).

Some researchers suggest that the increased incidence of CHD in the Greek population reflects the lack of adherence to a Mediterranean diet (which used to be followed in the past; Trichopoulou, Lagiou, & Trichopoulos, 1994; Vlismas et al., 2011) as well as an aging population (Panagiotakos et al., 2008). Also, researchers maintain that beyond these factors, the continuing increased rates of CHD may be explained by the altered modern life style which has increased the prevalence of various risk factors in the Greek population, both biological (e.g. hypertension, diabetes mellitus, hypercholesterolemia; Karalis et al., 2007; Kiritsi, Tsiou, Gouvelou-Deligianni & Stamou, 2008) and behavioural (e.g. physical inactivity, smoking, unhealthy diet; Gigkas et al., 2004; Panagiotakos et al., 2008; Sbarouni et al., 2014). Other researchers refer to additional psychological factors such depression (Athanasiadou, Tzotzi, Eumorfia, Alevizopoulos, & Kallergis, 2015) and anxiety (Polikandrioti et al., 2012).

Another factor related to the increased incidence of CHD in the Greek population seems to be the financial crisis experienced since 2009 (Simou & Koutsogeorgou, 2014). A number of studies demonstrated that during these years the prevalence of various biopsychosocial risk factors increased (e.g. diabetes mellitus (Panagiotakos et al., 2013a), depression (Efthimiou, Argalia, Kaskaba & Makri, 2013), unemployment and work loss anxiety (Drydakis, 2015)). Moreover, a recent study reports that adherence to medication is lessening due to financial constraints which in turn increase the risk of acute coronary syndromes (Notara et al., 2015).

All these issues might explain the worse profile of Greeks with CHD compared to their counterparts in Western Europe. A study by Sbarouni et al. (2014) revealed that Greek patients with CHD tend to be younger, have a higher body mass index (BMI) and higher prevalence of hyperlipidemia and smoking.

Regarding treatment, although no national statistics are available at the current moment, the findings of Sbarouni and colleagues (2014) suggest that Greek CHD patients are treated with coronary revascularization (CR) more often compared to their counterparts in other Western European countries, while medication is used to an equal degree.

Taking into consideration: a) differences in the CHD profile and CR rates between Greeks and Western Europeans, b) the increasing survival rates in the Greek population (which can be viewed as an additional economical burden not only for Greece and its inhabitants but for all Europeans and c) the limited research on CR treatment in Greece regarding individuals' evaluation and lived experience (issues that will be discussed at the following chapter) compared to other Western European countries and the US, a Greek study could be very useful. A longitudinal study in Greece in this area may provide further information about the profile of individuals who undergo CR, throw light on essential factors that influence individuals' perceptions of the impact of CR on their life and help the development of tailored cost-effective policies and practice guidelines.

1.8.Conclusion

Coronary heart disease (CHD) is a leading cause of mortality. The most common way to treat coronary heart disease is through coronary revascularization (PCI or CABG). Those types of CR have prolonged the life expectancy of people with CHD. However, a lot of questions still remain to be addressed, such as why CHD is still a leading cause of mortality and how good survivors' quality of life is after CR. Regarding the first question, a possible answer could be that revascularization may save someone's life temporarily, but if biological factors such as diabetes mellitus remain unregulated, behavioural (e.g. smoking) and psychological (e.g. overwhelming anxiety) risk factors remain unchanged, then the problem is ongoing. The factors that led to the development of CHD in the first place may lead to a recurrence. So it is important to investigate if survivors make appropriate changes in their everyday life and, if not, explore the reasons why.

Concerning the question about patients' well-being and quality of life, a systematic literature review (Chapter 3) has been conducted to address this, focusing on global literature since very few studies have been published in this area with Greek patients. However, before presenting this review, it is essential to comprehend the notions of QoL, HRQoL as well as to highlight related issues such as major factors that influence HRQoL and concerns when measuring HRQoL, as will be discussed in the following chapter (Chapter 2).

Chapter two

Introduction to HRQoL and its measurement

2.1.Introduction

The previous chapter introduced essential concepts related to coronary heart disease (CHD) and its treatment as well as presented reasons for conducting such a study in Greece. As discussed, the main evaluation of treatment outcomes is based on biomedical aspects. However there is a growing body of researchers who espouse the notion that health is not solely a biomedical issue but rather a biopsychosocial one which is linked with the concept of the health related quality of life (HRQoL) as defined by the World Health Organization (WHO, 1948). Therefore, the scope of this chapter is to introduce the biopsychosocial model of health and disease, the conceptual framework of HRQoL and to discuss the importance of its adequate evaluation in health care. Various theoretical issues and methodological approaches that should be taken into consideration when aiming to investigate patients' subjective perspectives will be discussed. The challenge of selecting the most appropriate instrument for measuring HRQoL after coronary revascularization (CR) and the main instruments used in this research arena will be presented. Finally, the approach to HRQoL adopted in this thesis as well as the thesis rationale will be outlined in the final section of the chapter.

2.2.Defining the Biopsychosocial (BPS) model of health and disease

For many decades the biomedical model guided the notions of health and disease and clinical practice (Engel, 1980). However, this approach was challenged by many established professionals such as Lazare (1973), suggesting that the biomedical model focused on: "…etiology, pathogenesis, signs and symptoms, differential diagnosis, treatment and prognosis. Knowing the syndrome or disease determines the treatment"(p. 346) leaving aside many other influential aspects such as psychological and social issues that influence physical state and functioning.

Engel (1977), in response to the shortcomings of the biomedical model, acknowledging both the huge advantages of the biomedical approach but also the necessity of an extensive model, developed the well-known Biopsychosocial (BPS) model (Engel, 1980). Based on this model the patient should be viewed as a person with an individual lifestyle and not simply as a patient with a disease who has deviated from "normal" physical functioning. As Engel (1980) argued, ignoring other important and interconnected aspects of a disease such as psychological, social and cultural aspects and disregarding the individual's experience and focusing solely on biological factors provides a poor understanding of disease and clinical practice; a holistic conceptualization of disease should take into account the individual and the environment too (Butler, Evans, Greaves, & Simpson, 2004; Engel, 1980).

In short, the BPS model examines three aspects of a disease; the "bio", the "psycho" and the "social". The "bio" component refers to aspects of biology that influence health such as genetics, functioning of body organs (e.g. heart, liver, the kidneys), and body biochemistry. The "psycho" component refers to psychological components such as thoughts, emotions, or behaviours. The "social" component refers to social factors such as interactions with others, culture and economic status. At this point it is essential to highlight that these components are interconnected. Biology can affect psychology, which can affect social well-being, which can further affect biology, and so on. For example, a heavy smoker after prolonged work stress may experience angina which may raise feelings of fears of sudden death which may produce overwhelming anxiety and depression which may prevent the person from making life style changes, e.g. to quit smoking or go out (leaving the safety of the house) making him/her unable to fulfill his/her social role which might trigger problems with existing friends which, in turn, may influence the progression of his/her disease. The power of the BPS model is its holistic view, examining a symptom or disease from different perspectives and trying to find out how the interaction of different factors leads to specific issues for an individual.

Thus, the utilization of the model in healthcare settings allows clinicians to explore various aspects of a disease before making a diagnosis and being able to make tailored recommendations about how an individual may adjust his/her lifestyle in order to have a better quality of life (Havelka, Despot, & Lučanin, 2009). For instance, in relation to the previous example, the individual's doctors may incorporate medical therapy to deal with the angina, psychological therapy (e.g. cognitive behavioural therapy (CBT; Lichtman et al., 2008) to help individuals to cope with anxiety and depression and may suggest smoking cessation group therapy in order to both quit smoking and increase their social network.

There is a growing body of evidence demonstrating that the use of model has helped in the art of good communication and understanding of an individual's disease (Frankel & McDaniel, 2003; Weiner, 2008) which in turn has led to advances in the treatment of disease. As has been demonstrated in the previous chapter, research in coronary heart disease (CHD) has found not only biomedical but also psychological and social components to its development and progression.

The World Health Organization (WHOQOL group, 1993) seems to agree with Engel's perspective in that it defines an individual’s well-being as an overall state of health and well-being in biological, psychological and social aspects.

2.3.Defining QoL and HRQoL

The term Quality of Life (QoL) can be perceived as a multi-dimensional though elusive concept. Many different definitions can be found in the published literature (Barcaccia et al., 2013; Moons, Budts, & De Geest, 2006), so that, as Gasper (2010) suggests, QoL can be understood as an “umbrella term” covering various definitions. QoL may portray the notion of a “good life”, but its “ingredients” vary dramatically among scholars (Moons, Budts, & De Geest, 2006). Overall, Feinstein (1987) states that QoL is a multidimensional concept, which involves functioning, health status, perceptions, life conditions, behaviour, happiness, lifestyle, and symptoms.

Over the last decades, it was believed that the QoL definition was related to both objective and subjective aspects. For instance, Felce and Perry (1995) suggested that QoL should be defined as the overall well-being that encompasses objective descriptors as well as subjective evaluations of physical, material, social, and emotional well-being along with the extent of individual development and purposeful activity, assessed by a personal set of values. Similarly, Haas (1999) concurs that the definition of QoL should include both objective indicators as well as a subjective evaluation, arguing that if only the subjective point of view is assessed then well-being rather than QoL is captured. Gradually, the objective aspect tended to be left aside, leading to a more concrete view that QoL refers to subjective perceptions of well-being although the factors that are assumed to influence subjective perceptions may vary. The World Health Organisation (Kuyken & Orley, 1995; WHOQOL Group, 1993) proposes a broad definition according to which QoL refers to:

> *"individuals' perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations and standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment" (p. 1403).*

Similarly, Costanza et al. (2007) claim that QoL should be defined with reference to the extent that individual needs (e.g. security, affection, understanding, participation, spirituality, identity, freedom) are fulfilled in relation to perceived subjective well-being, which in turn is evaluated based on one's sense of happiness, life satisfaction, utility, or welfare. The relation between specific individual needs and perceived satisfaction is affected partially by elements like mental capacity, cultural context, information, educational level and temperament and partially by the weights that individuals or cultures may give to reaching each of the individual's needs compared to the others. Malkina-Pykh and Pykh (2008) suggest that QoL should be perceived as individual appraisal of well-being, that is the positive or negative subjective perception of one's life consisting of three basic aspects: the built environment (e.g. house, facilities), the social environment (e.g. friends, family, entertainment, health and education) and the economic environment (employment, money). They place particular emphasis on the notion that QoL is a subjective concept strongly dependent on cultural perspectives and values.

Since there is no consensus definition of QoL, factors that may influence it vary in accordance to the model adopted. According to the WHOQOL Group (1996) factors that influence QoL can be clustered under four pillars: *physical health* (e.g. activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility, pain and discomfort, sleep, work capacity), *psychological state* (e.g. body image and appearance, negative feelings (such as anxiety, depression, anger, self-esteem, spirituality, thinking, learning, memory and concentration) *social relationships* (e.g. personal relationships, social support, social isolation, sexual activity), and *environment* (e.g. financial resources, freedom/independence, physical safety and security, health and social care including both accessibility and quality, home environment, opportunities for acquiring new information and skills, participation in leisure activities, physical environment such as pollution noise, traffic, climate), transport. Individual indicators (e.g. age; Hansen, Slagsvold, & Moum, 2008), however, can also influence perception of QoL as the four pillars are strongly influenced by an individual' value system which varies across cultures, context and stage of life. For example, various studies have revealed that old people are more satisfied with their finances than young people with similar income levels (George, 1992; Hansen et al., 2008).

The terms Quality of Life (QoL) and Health Related Quality of Life (HRQoL) are often used interchangeably in the literature. However, there is a major difference between these two concepts (Crosby, Kolotkin, & Williams, 2003; Revicki et al., 2000). HRQoL refers to the effect of a medical condition and/or its treatment on patients' subjective perspective of QoL (Schipper, Clinch, & Olweny, 1990). In other words, HRQoL is a narrowed concept of QoL. Consequently, there is no consensus about the definition of HRQoL too. The most widely accepted definition of HRQoL is based on the World Health Organization's (WHO, 1948) definition of health suggesting that health is not only a biomedical issue, but rather as “a state of complete physical, mental and social well-being” (WHOQOL group, 1993). Moreover, many scholars agree upon the subjective nature of HRQoL maintaining that its evaluation should be based on patients’ reflection on the impact of disease and treatment across the physical (e.g. daily activities [ranging from activities of daily living (ADL) such as bathing and grooming to more demanding instrumental activities of daily living (IADL) such as cleaning, laundry], exercise [physical activity], energy and fatigue, mobility), psychological (e.g. anxiety, depression, frustration) and social aspects (e.g. support of family and friends, social isolation, employment, sexual activity) of their life, as well as their overall well-being (Bowling, 2001; Duits, Boeke, Taams, Passchier, & Erdman, 1997; Hawthorne, Richardson, & Osborne, 1999; Szygula-Jurkiewicz, Zembala, Wilczek, Wojnicz, & Polonski, 2005). Furthermore, many researchers in the field aiming to evaluate people’s HRQoL include additional components such as disease-related somatic domains (Revicki et al., 2000), cognitive functioning (Ford et al., 2008), and sexual satisfaction (Lukkarinen & Lukkarinen, 2007; Przewlocki et al., 2000).

In the field of coronary heart disease, research evidence demonstrates various factors that influence patients HRQoL. A critical review (Pragodpol, & Ryan, 2013) on factors that can predict HRQoL in newly diagnosed individuals with CHD carried out on studies published between 1997 and 2009 suggested that these factors can be divided into three main categories; sociodemographic (education level, marital status and sex), clinical (angina and physical functioning) and psychological (anxiety, depression, social support). More recent research evidence provides further support for the factors associated with poor HRQoL indicating factors such as depression (Hsu, Tsao, Chen, & Chou, 2014; León-Pérez, Wallston, Goggins, Poppendeck, & Kripalani, 2015; Middel et al., 2014), anxiety (Hsu, Tsao, Chen, & Chou, 2014;

Middel et al., 2014), lack of social support (León-Pérez, Wallston, Goggins, Poppendeck, & Kripalani, 2015), low income (Wang et al., 2015) restriction of daily activities (Sin, Yaffe, & Whooley, 2015) including sexual activity (Steinke, 2015), fatigue (Eckhardt, DeVon, Piano, Ryan, & Zerwic, 2014) chest or bodily pain (Chiou, Hsu, & Hung, 2016), and diabetes (Uchmanowicz, Loboz-Grudzien, Jankowska-Polanska, & Sokalski, 2013; Wang et al., 2015) that interfere with physical, psychological and social aspects of HRQoL (Sin, Yaffe, & Whooley, 2015; Uchmanowicz, Loboz-Grudzien, Jankowska-Polanska, & Sokalski, 2013).

2.4. Benefits of evaluating HRQoL

HRQoL evaluation can have several benefits for patients, physicians and associated health professionals both in routine practice and clinical trials.

For patients, assessing HRQoL can be beneficial because they have the opportunity to express themselves and identify those aspects of their health condition that are critical for them. At the same time, HRQoL assessment may facilitate doctor-patient communication, allowing doctors to become aware of the problems that affect their patients (Varni, Burwinkle, & Lane, 2005; Walters, 2009). Moreover, for medical doctors, the evaluation of patients HRQoL can provide additional input to clinical information. As they focus not only on prolonging patient life and reducing morbidity, but also on improving their patients' well-being (Guyatt et al., 2007), information about patients' HRQoL at each crucial time point (e.g. prior to intervention and after intervention) can help them form a complete picture of patients' subjective experience and therefore apply the best therapeutic regimen in daily practice (Walters, 2009). The assessment of patients' HRQoL on average as provided by clinical trials can also facilitate clinicians in many ways: drawing conclusions about the pros and cons of a specific treatment; being aware about the efficiency of different aspects of therapeutic management; recognizing any negative effects of treatment; and, thus, being more confident in making decisions on the most appropriate medical treatment for their patients (Efficace et al., 2007; Parameswaran et al., 2008; Rumsfeld et al., 2003; Singh & Dixit, 2010). Furthermore, the assessment of HRQoL can reveal individuals' level of functioning after treatment, allowing other health professionals (e.g. psychologists) to facilitate patients' transition, provide additional care (if needed) and tailor interventions (Kugler et al., 2010; Singh & Dixit, 2010) during rehabilitation. Moreover, the longitudinal assessment of HRQoL can provide both clinicians and the wider scientific community with knowledge about the long-lasting effects of treatment or disease status and associated symptoms such as pain, discomfort and fatigue and capture shifts in patients' subjective perceptions concerning the impact of disease on their QoL (Singh & Dixit, 2010; Varni, et al., 2005). However, what is essential to mention at this point is that there is no consensus on whether all domains incorporated in a definition should be considered when drawing inferences about the effect of a treatment on patients' HRQoL. For instance, if there is improvement in physical functioning, can improvement in overall HRQoL be claimed? Based on Coons, Rao, Keininger and Hays (2000), claiming improvement in HRQoL implies that all core domains should be improved. Thus, the authors suggest that whatever definition is adopted, conclusions about the effect of the treatment on QoL should be established on the basis of an overall picture.

In summary, the evaluation of HRQoL is an essential aspect of health care assessment and health intervention programmes. Due to the fact that it reflects patients' subjective experiences of their daily functioning and well-being concerning their disease, HRQoL data enhances understanding, facilitates communication, guides therapeutic management and aids transition as well as increases the ability to establish the effectiveness of rehabilitation.

2.5.Considerations in exploring HRQoL

As the concept of HRQoL lacks a consensus definition, HRQoL evaluation has been conducted by using various approaches. The literature indicates that the more widely used methods are quantitative, with an increasing advocacy for mixed methods. Still, in the field of HRQoL research, especially when measuring changes in HRQoL level as a result of a treatment, various considerations and debates exist regarding a) the influence of adjustment and post-traumatic growth, b) the most appropriate methodological approach (qualitative vs quantitative), and c) type of patient-based instrument (generic vs specific) that should be used if the quantitative approach is selected. These issues are discussed below.

2.5.1. Adjustment and Post-Traumatic Growth

As HRQoL is a dynamic concept and may change over time, longitudinal assessment should be made. However, when the aim is to detect the influence of a treatment on changes in HRQoL level, the pure effect is hard to measure due to individual adjustment to the disease as well as potential emotional growth (Tedeschi & Calhoun, 1996). In fact, as the literature highlights, human beings tend to adjust to their life conditions due to changes in their internal standards, expectations, needs, reprioritization of values, and/or general re-conceptualizations of their HRQoL (Beeken, Eiser, & Dalley, 2011; Sprangers & Schwartz, 1999). Research evidence provides support for various adjustment theories (e.g. Response Shift (Sprangers & Schwartz, 1999) and Cognitive Adaptation Theory (Taylor, 1983)) in people with chronic disease

(Pierobon, Giardini, Callegari, & Majani, 2011) such as spinal cord injuries (e.g. Dibb, Ellis-Hill, Donovan-Hall, Burridge, & Rushton, 2014), cancer (e.g. Christianson, Weis, & Fouad, 2013), arthritis (Arends, Bode, Taal, & Van de Laar, 2013), CHD (Helgeson, 2003) or other chronic health conditions such as HIV (Dibb & Kamalesh, 2012).

According to the theoretical model known as Response Shift (RS) of Sprangers and Schwartz (1999) on QoL, the "meaning" of an individual's self-assessment can alter with time as a result of three things: a) an alternation in the individual's internal standards (known as recalibration, i.e. changes in how the individual evaluates what is good or bad), b) a change in the components that comprise QoL (known as reprioritization, i.e. changes on what the individual assesses as important), and c) redefinition of QoL (known as reconceptualization, i.e. changes in what the individual evaluates as meaningful; Schwartz et al., 2007; Sprangers & Schwartz, 1999; Schwartz & Sprangers, 1999; Visser et al., 2013). Ring, Höfer, Heuston, Harris and O'Boyle (2005) suggest that these cognitive changes, i.e., response shift, in internal standards of measurement, values, and definition may be due to various adopted strategies such as coping strategies and observations of others who are in a better and worse conditions than themselves, but may also be due to external factors such as a treatment effect. Thus, the response shift can be present in any pre-post or longitudinal study challenging the interpretation of changes in QoL over time (Visser et al., 2013). Therefore, a consideration of the RS would be helpful. In the literature, various ways for evaluating response shift have been suggested (Visser et al., 2013). The most widely documented technique is "The Then Test" (Visser et al., 2013). This approach consists of asking individuals to provide a re-evaluation on their pre-treatment level of functioning. As Schwartz and Sprangers (1999) note:

> *The conventional posttest and Then Test measures are presumed to be completed with the same internal standard of measurement since they are collected at the same time. Consequently, comparison of posttest and Then Test scores would eliminate treatment-induced response-shift effects ... The Then Test can be implemented on entire measures or on selected items (p. 1539).*

The *Then Test* has been used by many researchers in order to detect RS effects showing contradictory results; some researchers concluded that the treatment effect was underestimated, some others that it was overestimated while others did not detect any RS effect in level of change of HRQoL (Hamidou, Dabakuyo, & Bonnetain, 2011). This diversity in findings might be explained by the fact that this approach has been criticized for recall biases, i.e. that memory can affect the then-test evaluation (Ahmed, Mayo, Wood-Dauphinee, Hanley, & Cohen, 2004). In the field of heart disease, response shift in HRQoL assessment is very limited. Nagl, & Farin, (2012), using the *Then Test*, found a recalibration effect (changes in the individual's internal standards) which may have led, they suggest, to an underestimation of the actual effects of the treatment on change. However, when they used structural equation modelling (SEM) to evaluate the RS effect on change in QoL they did not detect any essential influence. Thus, RS detection is an ongoing challenge. As a number of researchers suggest, the evaluation of response shift is an important element and has to be considered in order to identify "true" change. However, further research should be conducted in order to identify the most accurate way to capture RS impact when measuring change in QoL (Hamidou, Dabakuyo, & Bonnetain, 2011).

According to the Cognitive Adaptation Theory (CAT; Taylor, 1983), after experiencing a negative event individuals experience a decline in self-esteem as well as a loss of control. Therefore, as this theory suggests, the adjustment process is related to three major issues: (1)

search for meaning in the experience, (2) effort to regain mastery (i.e. control) over the situation and life overall and (3) effort to restore self-esteem through self-enhancement. In other words, individuals develop a need to make sense of the condition (e.g. why has this happened to me?), make efforts to regain control (e.g. what can I do to prevent recurrence?) and enhance the self (i.e. compare themselves with others of the same condition) in order to restore self-esteem. The limited research in the field of CHD provides support for CAT (Helgeson, 2003; Helgeson, 1999, Helgeson, & Fritz, 1999). In fact, based on Helgeson (2003) CAT factors can predict positive adjustment and individuals with positive adjustment are less likely to experience recurrent cardiac events.

Furthermore, the Post Traumatic Growth model (PTG; Tedeschi & Calhoun, 1996) suggests that individuals experience positive changes and emotional growth as a response to challenging traumatic events or life crises. PTG is an ongoing process influenced by life span wisdom (Tedeschi & Calhoun, 1996). It is not the traumatic event itself, but rather the experience that motivates individuals to “re-build” their lives (Tedeschi & Calhoun, 2004). PTG’s most evident manifestations are related to increased life appreciation, increased sense of personal strength, changing priorities, more meaningful interpersonal relationships, and a richer spiritual life (Tedeschi & Calhoun, 2004). Research evidence indicates that PTG is related to better HRQoL in various diseases (Kahana, Feeny, Youngstrom, & Drotar, 2006) such as cancer (Arpawong, Richeimer, Weinstein, Elghamrawy, & Milam, 2013; Tomich & Helgeson, 2012), HIV (Sawyer, Ayers, & Field, 2010) and rheumatoid arthritis (Minkin, 2014). Regarding perceived benefits and PTG in the heart disease field, the limited research, mostly carried out on patients after a heart attack (Affleck, Tennen, Croog, & Levine, 1987; Garnefski, Kraaij, Schroevers, & Somsen, 2008; Hassani, Afrasiabifar, Khoshknab, & Yaqhmaei, 2009; Petrie, Buick, Weinman, & Booth, 1999; Bluvstein, Moravchick, Sheps, Schreiber, & Bloch, 2013; Leung et al., 2010; Sheikh, 2004), reveals that individuals experience positive changes after the challenging event. However, findings are inconsistent regarding the relationship between PTG and HRQoL. For instance, Leung et al. (2010) found that predictors of PTG were younger age, non-smoking status, high physical dysfunction and greater psychological functioning. Ai, Hall, Pargament, and Tice's (2013) findings demonstrated that CABG survivors showing an increased spirituality (one aspect of PTG) had better HRQoL. On the other hand, interestingly, Bluvstein and colleagues (2013) found that the psychological aspects of HRQoL (the mental compotent summary of the Short Form-12; Ware, Keller, Gandek, Brazier, & Sullivan, 1995) is negatively correlated with PTG. Another recent qualitative study (Waight, Strodl, Sheridan, & Tesar, 2015) exploring posttraumatic growth in post-surgical coronary artery bypass graft patients (CABG) revealed that patients experienced two types of cognitive growth following CABG; 'greater appreciation of life' (living in the moment instead of focusing on what the future may bring) and 'new possibilities' as they view surgery as the event that helped them to improve their physical functioning as well as provided the motivation to adopt healthy behaviours to control the risk of recurrence.

Moreover, the Self-Regulation Model of illness (SRM; Leventhal, 1992) provides a framework for understanding how individual symptoms and emotions experienced during a health threat or diagnosis can influence illness perception (illness beliefs) and guide subsequent coping behaviour. This model suggests that individuals go through three major stages: 1) Interpretation (i.e. identify illness (diagnosis), causality, consequences, time line, cure /control), 2) Coping (i.e. dealing with the problem in order to regain a state of equilibrium either by approaching, e.g. taking pills, or by avoiding e.g. not taking the pill, minimize the severity of the disease and so on) and 3) Evaluation of coping (i.e. self evaluation regarding the effectiveness of coping adopted). Specifically, the model suggests that when a threatening event is present individuals' "status quo" becomes unbalanced and, therefore, they are internally motivated to undergo a problem-focused process in order to regain a sense of balance. Interpretation is very important because, based on this, individuals develop approach or avoidance coping strategies aiming to regain control over their lives and a sense of equilibrium. Individuals are involved with a continuous evaluation of their coping strategies in order to maintain it or adopt a different strategy (Cameron, & Leventhal, 2003; Leventhal, Leventhal, & Contrada, 1998). The literature in the field of CR and HRQoL demonstrates that patients' illness perceptions are significantly correlated with the level of HRQoL experienced; negative illness beliefs predict a decline in HRQoL (Foxwell, Morley, & Frizelle, 2013). Moreover, research evidence (Lin, Wang, Tung, & Furze, 2012) shows that there are many cardiac patients who hold misconceptions (inaccurate beliefs) while others may hold accurate illness beliefs but intentionally minimize the problem in order to reduce distress level. In any case, they adopt maladaptive coping strategies (e.g. low adherence to medication and doctors' recommendations for a healthy lifestyle; Platt, Green, Jayasinghe, & Morrissey, 2014). As a result, their health condition and overall well-being may be affected by recurrent events for instance. Such elements may influence the assessment of the true impact of a treatment in HRQoL level over time.

Thus, when researchers focus on detecting the influence of a treatment on individuals' HRQoL over time, adjustment and emotional growth should be considered. Efforts to detect positive adjustment, post-traumatic growth but also illness self-management pattern (including illness beliefs) may allow the researcher to draw more plausible conclusions about the true impact of the treatment.

2.5.2. The methodological approach: Quantitative vs qualitative methodology

First of all, there is a plethora of research that has assessed subjective HRQoL with the use of valid and reliable patient-based or patient-reported outcome (PRO) instruments, aiming to elicit patients' subjective perceptions regarding the impact of treatment on QoL. However, the majority of instruments used have been developed on the basis of researchers' definitions of QoL or HRQoL and associated theoretical frameworks (Taillefer, Dupuis, Roberge, & LeMay, 2003) rather than on the basis of points of view about QoL of the individuals concerned. Also, many instruments used have been based on rigorous statistical analysis (e.g. factor analysis); yet, this procedure may reduce content validity as those items that are less often reported are eventually excluded (Carr & Higginson, 2001; Lasch et al., 2010; Patrick et al., 2011). Thus, it could be claimed that those instruments may have limited validity in terms of content. There are some instruments though (e.g. the CROQ, discussed below) that deal with such issues by adding an open-ended question in order to capture other issues experienced by respondents as relevant or significant.

Moreover, through the use of structured quantitative instruments confounding variables such as major life events (death of a close relative, job loss, divorce) that can influence someone's perception and experience remain undetected. Pre-existing or different confounding variables at different points in time of testing may produce false negative levels of HRQoL. Research evidence shows that stressful negative events may affect dramatically psychological functioning (Pagano et al., 2004) and overall HRQoL level (Eastwood, Doering, Roper, & Hays, 2008; Le Grande et al., 2006). Thus, the results of quantitative research, when such confounders cannot be detected, might be doubtful.

Furthermore, a number of researchers suggest that, in some cases, the effect size of a treatment on HRQoL levels might be underestimated when solely conventional psychometric testing is used (Ring, Hofer, Heuston, Harris, & O'Boyle, 2005). Some others argue that it is an oxymoron to try to quantify quality (Hammell, 2004; Murray & Chamberlain, 1999) without a deeper understanding.

Many of these points concerning under-represented or undetected aspects related to QoL may be addressed by qualitative approaches. On the other hand, limitations of qualitative methodology (QUAL) may be addressed by the strengths of quantitative (QUAN) methodology (Yilmaz, 2013). Specifically, the major pros of QUAN research are in relation to its contribution to the body of knowledge. It addresses questions through valid and reliable instruments and is theoretically driven. Valid conclusions can be drawn about the causation or predictability of the phenomenon under investigation with a potential for generalizability. These conclusions are viewed as valid due to robust methods employed (e.g. rigorous sampling, large sample size, valid and reliable measurements, sophisticated statistical analysis). On the other hand, QUAN research has been severely criticized for not recognizing the individuality of human beings and grouping individuals into set of categories that can be "easily" analyzed resulting in an oversimplification of both human nature and experience. A reduction of data to numbers may result in lost information. Many types of information are difficult to be obtained through structured data collection instruments, particularly on sensitive topics (e.g. domestic violence). Also, a large sample size might not be possible for certain conditions (e.g. drug users, patients with rare health conditions). Self-reported information obtained from questionnaires may be inaccurate (e.g. due to social desirability biases) or incomplete (i.e. missing data; Streiner and Norman, 2008; Ogden, 2007). Moreover, due to the complexity of human experience, controlling for all related variables is not feasible, meaning that other uncontrolled variables can influence the outcome (Creswell, 2014; Gelo, Braakmann, & Benetka, 2008; Yilmaz, 2013).

The major pros of QUAL research are that it provides a in-depth understanding of subjective experience as data collection is less structured as well as an opportunity to explore sensitive topics and rare conditions. QUAL research, however, has been severely criticized for its lack of “validity” and “reliability” as conventional standards cannot be employed. Data collection and analysis is rather demanding and requires researchers with specialist skills. Furthermore, its findings are subject to researchers’ interpretations, which can be influenced by their personal biases and idiosyncrasies. It is almost impossible to identify predictors and findings cannot be generalized to the wider population or other settings (Creswell, 2014; Gelo, Braakmann, & Benetka, 2008; Yilmaz, 2013).

Therefore, many researchers in HRQoL research endorse mixed methods to address their research question(s) (Creswell & Clark, 2007). The mixed methods approach, acknowledging both the advantages and the disadvantages of each methodology, suggests a combination of qualitative and quantitative methods; a “triangulation of method” in order to gain a better understanding and draw insightful conclusions on the topic under investigation with fewer possible biases and confounding (Bentahar, & Cameron, 2015; Dunning, Williams, Abonyi, & Crooks, 2008). In fact, an ongoing body of researchers suggest that the present dualism between qualitative and quantitative research approaches should be abandoned and an emphasis should be placed on mixed methods (Tashakkori & Teddlie, 2003).

According to Johnson, Onwuegbuzie, and Turner (2007), based on a synthesis of 19 definitions, mixed methods research is:

> *... the type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration. (p. 123)*

However, a number of researchers, especially those espousing the philosophical dualism in research (e.g. in social and behavioural sciences post-positivism vs constructivism or interpretivism; Guba & Lincoln, 2005) have challenged whether it is possible to reconcile the two methodological approaches as they differ fundamentally in their epistemological and ontological assumptions (Hathcoat, & Meixner, 2015; Howe, 1988). Some others have argued that the reconciliation of the two worldviews in a mixed methods approach is nothing more than a "bastardization of positivism" (Giddings & Grant, 2007 in De Lisle, 2011, p.90). As Giddings (2006) stated:

> *... mixed methods could serve as a cover for the continuing hegemony of positivism, and maintain the marginalisation of non-positivist research methodologies. I argue here that mixed methods as it is currently promoted is not a methodological movement, but a pragmatic research approach that fits most comfortably within a post-positivist epistemology (p. 195)*

Even researchers espousing the mixed methods approach (e.g. Yardley, 2001) have developed doubts about this reconciliation of quantitative and qualitative approaches. As various scholars have highlighted, the design and evaluation of research is influenced by its philosophical stance; a simple integration of techniques without maintaining the integrity of each one (i.e. underpinning epistemological assumptions about knowledge and its legitimate sources) cannot optimize contribution to knowledge (e.g. Bishop, 2016). Furthermore, many scholars (e.g. Giddings, & Grant, 2007; Greene, Caracelli, & Graham, 1989, in Bryman, 2007) have raised concerns about mixed methods approach employed in many studies. Some have observed many instances where the term mixed methods is misused as what was actually mixed were methods (often only a part of them) rather than methodologies, and often the role of the qualitative part was inferior (Tashakkori & Creswell, 2007). Greene and colleagues (1989, in Bryman, 2007) in their review paper highlighted that only five articles among a sample of 57 claiming that their study followed a mixed methods approach, carried out the final step of interpretation to integrate the quantitative and qualitative findings. Tashakkori and Creswell (2007) through a search in academic databases identified several studies where their authors considered their research as ‘‘mixed’’ because they had utilized qualitative or quantitative approaches in only some aspect(s) of their research. For instance, they may have used both approaches e.g. on developing different kind of research questions (qualitative and quantitative); and/or two types of sampling procedures (e.g. probability and purposive), and/or two types of data collection procedures (e.g. surveys and focus groups), and/or two types of data (e.g. numerical and textual), and/or two types of data analysis (statistical and thematic), and two types of conclusions (arising from the results of the quantitative study and from the findings of the qualitative study). However, those claims somewhat violate a major tenet of the mixed methods approach, that of the integration of results/findings in interpretation (Tashakkori and Creswell, 2007). Similarly many researchers (e.g. Bryman, 2007; De Lisle, 2011) raise concerns about the “genuine” integration of findings in mixed methods studies. As Bryman (2007) states, the main aim for conducting a mixed method study is to maximize knowledge and understanding of the research problem and complex phenomena at hand and thus “the end product” should not simply be a summary of findings of the individual quantitative and qualitative studies within a research project, but rather integrate quantitative and qualitative findings in order to offer insights that could not otherwise be gained .

In response to all these concerns, various paradigms have been proposed and adopted by mixed methods researchers (Teddlie & Tashakkori, 2003). The three most frequently discussed paradigms in the mixed methods literature are: a) the a-paradigmatic stance (which bypass the paradigm issue claiming that methodology is independent of epistemology; Patton, 1990 in Hall, 2012), b) the dialectic stance (which suggests multiple paradigms in a single study as they can contribute to a better understanding; Greene, 2007) and c) the single paradigm stance (which proposes that the two research approaches, quantitative and qualitative, can be combined into one paradigm; Johnson & Onwuegbuzie, 2004).

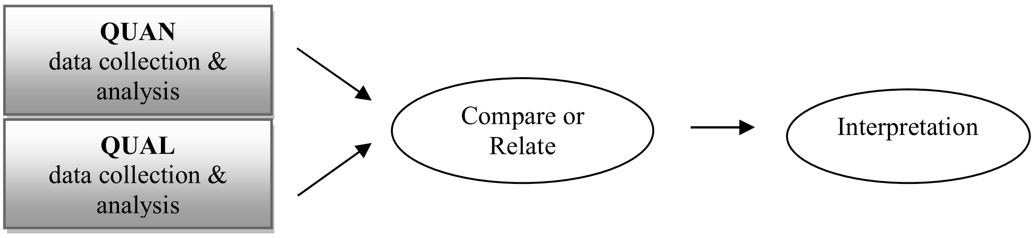
Regarding the latter case, three diverse positions have been developed and espoused: the pragmatism, the critical realism and the transformative paradigm (Creswell, 2014; Greene, 2007; Teddlie & Tashakkori, 2003. Among them, the most recognized and adopted paradigm in mixed methods research is that of pragmatism (Teddlie & Tashakkori, 2003; Creswell, 2014). Pragmatism refers to a paradigm that focuses on the use of mixed methods in research, putting aside the debatable issues of truth and reality (Feilzer, 2010), focusing on 'what works' for addressing the research questions (Tashakkori & Teddlie, 2003). Pragmatism "accepts, philosophically that there are singular and multiple realities that are open to empirical inquiry and orients itself toward solving practical problems in the 'real world' " (p. 8, Feilzer, 2010). In other words, pragmatist approaches acknowledge the epistemological differences between qualitative and quantitative approaches but perceive the different forms of inquiry as commensurable and sharing a common goal, namely that of producing positive change in the world (Bishop, 2015).

According to Owuegbuzie and Leech (2005), pragmatism, as a paradigm, is driven by "consequences". For instance, for a health psychologist such consequences could be related to increased levels of HRQoL of individuals with a health problem (e.g. heart disease) or more effective health care services targeting specific behaviours (e.g. smoking cessation).

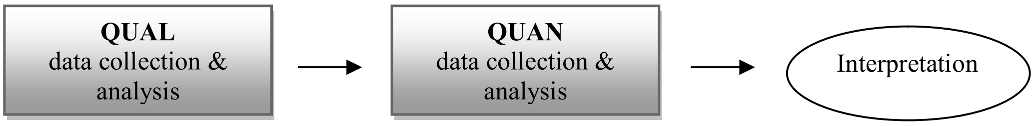
For pragmatism it is essential that the "right questions" are asked by the research. For instance, with a research question such as "Does treatment x result in changes in depression levels and how does individual experience influence these" the quantitative component (quantitative study) will address the descriptive and/or comparative part (e.g. the influence of the treatment on depression level) while the qualitative component (qualitative study) will address "what" might be those experiences and "how" may they interfere with the phenomenon under investigation. These questions will guide researchers to choose the most appropriate design (e.g. explanatory), sampling type (e.g. sub-group sampling), sample size, material of data collection (e.g. the most appropriate questionnaire), data analysis techniques per sub-study as well as the way that the interpretation of results and findings could be integrated in the discussion (Owuegbuzie & Leech, 2006).

The particular mixed methods design adopted plays a crucial role for the pragmatic epistemological stance; a good and suitable design will allow researchers to achieve their desired external consequences (Bishop, 2015). Creswell and Plato-Clark (2011) proposed two mixed methods design typologies; concurrent (when both quantitative and qualitative studies are carried out simultaneously) and sequential (when either the quantitative or qualitative study is carried out first and after completion the second begins). These two typologies based on timing and emphasis are clustered into six types (Figure 2.1); Sequential: explanatory (QUAN-QUAL-interpretation) and exploratory (QUAL-QUAN-interpretation). Concurrent: convergent parallel (QUAN and QUAL-compare-interpretation). Concurrent or sequential: transformative (many combinations of methods), multiphase (QUAL-QUAN-Mixed methods) and embedded (multiple combinations).

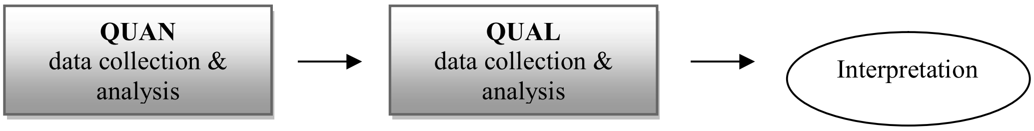
1. Concurrent design (convergent pararell)



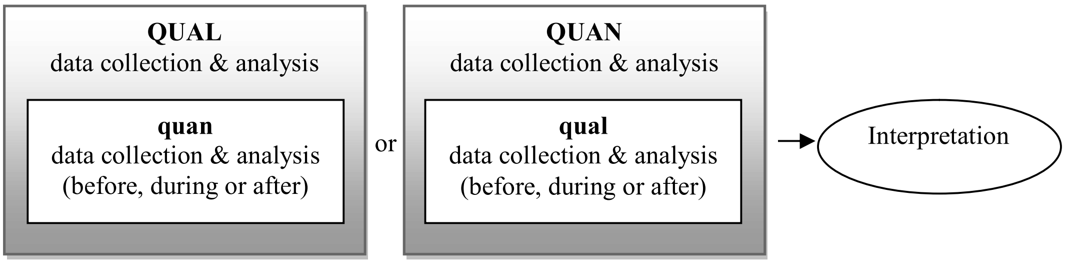
2. Exploratory Sequential design



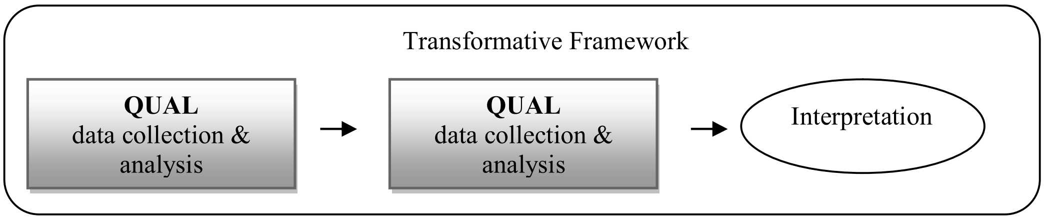
3. Explanatory Sequential design



4. Embedded design (concurrent or sequential)



5. Transformative design



6. Multiphase design (concurrent or sequential)

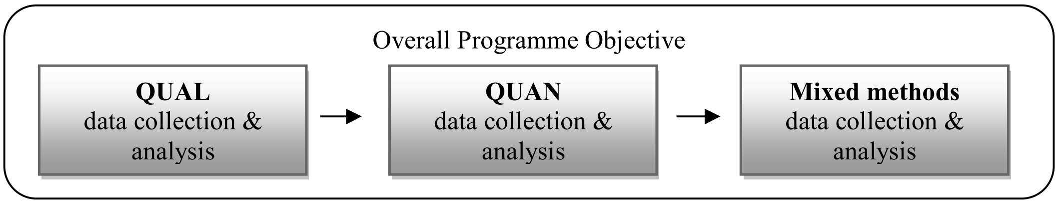


Figure 2.1 Mixed methods research designs. Adapted from Creswell and Plato Clark (2011).

At this point, it should be mentioned that many other scholars have proposed other typologies (e.g. Morgan, 1998; Jonson & Onwuegbuzie, 2004; Van Ness, Fried, & Gill, 2011) especially in relation to timing. For example, Van Ness, Fried, and Gill (2011) have proposed another classification based on "priority" and "sequence" of data collection: prospective (qualitative data collection once at the beginning of the study prior to repeated quantitative data collection), retrospective (qualitative data collection once at the end of the study after repeated quantitative data collection) and fully longitudinal (qualitative and quantitative data collection at all time points).

Another fundamental issue is related to the way in which interpretation of results and findings is integrated in order to enlighten the phenomenon of interest. Based on Creswell and Plato-Clark (2011) with the pragmatic stance this usually takes place in the discussion where the results of the quantitative components are integrated with the findings of any qualitative components. The limited literature in this area (e.g. O'Cathain, Murphy, & Nicholl, 2010) suggests three main types: triangulation (in particular following a triangulation protocol), following a thread and theoretical explanatory integration.

The triangulation protocol suggests triangulating findings after both data sets have been analyzed separately. Researchers (e.g. Farmer, Robinson, Elliott, & Eyles, 2006; Sampson, O'Cathain, & Goodacre, 2010) typically list the findings from each componenton the same page and consider where findings from each study agree (convergence), offer complementary information on the same issue (complementarity), or appear to contradict each other (discrepancy or dissonance), producing a “convergence coding matrix”. This allows them to develop meta-themes that contribute to shedding light on the phenomenon of interest (O’Cathain, Murphy, & Nicholl, 2010). The ‘following a thread’ approach (Moran-Ellis et al.*,* 2006) for integrating the findings suggests that integration takes place at the analysis stage. It starts with an initial analysis of each component to identify key themes and questions needing further exploration. Then the researchers choose a question or theme from one component and follow it across the other component(s). Finally, theoretical explanatory interpretation refers to the fact that data generated by different components may be integrated by bringing them together into one explanatory framework. This means that contradictions, divergences and convergences in the findings produced by each analysis are reconciled at the point of interpretation and explanation (Green, 2003).

The contribution of mixed methods is widely recognized in various fields, particularly in health care research (Curry, 2010). Researchers and clinicians interested in the study of QoL find mixed methods useful (either in cross-sectional or longitudinal studies depending on the aim of the study), as they are helping them to gain a greater understanding not only of what and how often, but also of why, and thus to be able to draw more confident conclusions based on “total evidence” (Dunning, Williams, Abonyi, & Crooks, 2008; Ring, Gross, & McColl, 2010). However, as mentioned earlier, researchers often do not directly refer to the paradigm adopted or to the particular design employed to address their research questions (Bishop, 2015; Bryman, 2007; Klassen, Creswell, Plano Clark, Smith, & Meissner, 2012) which in turn, challenges the quality of their research (Bryam, 2006; De Lisle, 2011; Heyvaert, Hannes, Maes, & Onghena, 2013).

For example, in a recent cross-sectional mixed methods study (Chan & Wang, 2013) exploring the impact of obesity on children's QoL, the quantitative results demonstrated that children with normal weight and increased weight did not significantly differ in physical functioning. However, the qualitative findings based on some children's accounts revealed that overweight children experienced difficulties with playing activities. Furthermore, in the same research study, quantitative analysis indicated that overweight children experienced lower social functioning but not emotional functioning compared to normal weight children. The qualitative findings, on the other hand, showed that obese children were severely unhappy and experienced various worries. However, neither the philosophical stance nor particular mixed methods design adopted was mentioned. Also, no clarification of how the final interpretation based on integration of the findings was arrived at was presented. Thus, the validity of the conclusions might be challenged.

Another study focusing on exploring individuals' QoL after allogeneic haematopoietic stem cell transplantation (HSCT; Niederbacher, Them, Pinna, Vittadello, & Mantovan, 2012) supports the complementarity of insights gained through a sequential mixed methods research design. The study involved 44 patients and applied a disease-specific instrument for measuring QoL over a 3-month period after treatment. The quantitative results demonstrated that individuals perceived their QoL as quite good. On the other hand, the qualitative findings revealed that although those individuals had experienced many changes in their life (e.g. loss of independence), their medical experience led them to a re-prioritization and for many of them "a new world has opened up". The researchers concluded that individuals' physical functioning might have been dramatically affected, but they started to appreciate life, focus on and appreciate the things that they could do instead of things that they could not do anymore. Thus, they experienced a sense of psychological and interpersonal growth which affected their perception of well-being positively. This kind of insight is very helpful for medical doctors who tend to overestimate the influence of the treatment on their patients' QoL (Pidala, Anasetti, & Jim, 2009).

Moreover, many researchers aiming to detect the influence of a factor (e.g. treatment or activity) on QoL or HRQoL change over time conduct longitudinal mixed methods studies. A recent longitudinal mixed methods study (Bath-Hextall et al., 2013) on 77 patients with non-melanoma skin cancer explored patients' needs, knowledge and experiences over one year by employing a fully longitudinal design at four time points. The researchers used a disease-specific instrument for measuring QoL as well as other questionnaires for measuring anxiety, depression and emotions regarding appearance, and interviewed a sub-sample of participants. The quantitative results demonstrated that individuals' QoL increased at 8 weeks and 12 months post treatment while the qualitative findings showed that people experienced relief from the fact that the lesion(s) had been removed, but many of them still worried about new lesions resulting in constant skin checking. Another essential issue revealed was the lack of information on skin checking even one year after treatment, especially among older individuals who might delay treatment due to the misconception that the spot was a mark due to old age. This understanding offered important insights for promoting best practice and designing tailored interventions for both primary and secondary prevention. However, again the researchers did not discuss clearly either their philosophical stance or how final interpretation was guided.

Another mixed methods study (with a pre-post quantitative component; Ray, & Verhoef, 2013) on 100 female breast cancer survivors examined the influence of a team-based activity (dragon boat racing) on survivors' HRQOL. Researchers employed a sequential explanatory design (first the quantitative part was conducted and data were analyzed, then the qualitative part took place and data were analyzed). The quantitative and qualitative findings were combined afterwards during the interpretation of the data, where qualitative themes were used to better explain and elaborate on the quantitative results. The researchers used a disease-specific instrument for measuring HRQoL and other instruments for measuring spiritual well-being and fatigue. The quantitative results demonstrated that a positive significant change was experienced by participants in most areas examined in relation to HRQoL; social /family well-being was almost significant (p=0.059). The findings of the qualitative part supported the quantitative results by highlighting and explaining why this positive chance may have occurred. For instance, the positive evaluation of emotional well-being was explained by individuals' experiences with regard to emotional strength and reduced anxiety, while the non-significant change on social well-being was explained by the fact that positive aspects of the dragon boat experiences were reduced through differences in competitive drive, commitment level as well as personality conflicts. In this case, researchers provided their readers with many details about the methods employed including the "genuine" interpretation (Bryman, 2006), increasing the quality of the mixed methods study (Heyvaert, Hannes, Maes, & Onghena, 2013).

In the field of coronary heart disease (CHD) or coronary revascularization (CR) in relation to individuals' HRQoL only limited mixed methods research has been carried out; either cross-sectional (e.g. Dantas, Rossi, Costa, & Vila, 2010) or longitudinal (e.g. Lukkarinen, 2005).

Lukkarinen (2005) conducted a longitudinal mixed methods study on 280 patients with CHD aiming to explore individuals' perceptions of their HRQoL employing methodological triangulation. She followed the patients from the onset of treatment (medication, percutaneous coronary interventions (PCI) or coronary artery bypass grafting (CABG)) throughout 12 months initially through the quantitative and then the qualitative part of the study. The quantitative analysis (based on data collected through a HRQoL generic instrument) revealed that one year after bypass surgery or angioplasty, individuals' HRQoL was significantly better on the dimensions of energy, pain and mobility, but poorer, especially in the younger age group (34-55 years), on the dimensions of social isolation and emotional reactions. Moreover, divorced and widowed individuals, individuals with poor financial status, smokers, and those with a history of traumatic life experiences had more psychosocial problems. The qualitative analysis (based on phenomenology) revealed that individuals with a passive attitude towards treatment tended to maintain their lifestyle previous to the CHD diagnosis, typically developed CHD in early adulthood and tended to have a pessimistic view of the future, while females suffered from a lack of emotional support more often than male participants. On the other hand, individuals with an active attitude towards treatment and re-orientation of their life course typically developed CHD in middle adulthood. Individuals with an active approach felt their surviving a serious disease to be a new opportunity in life, and tried to build stronger bonds with family members. Lukkarinen, in her interpretation integrating the findings of both components according to the triangulation protocol, concluded that both the quantitative and the qualitative findings revealed that the psychosocial component of HRQoL of the youngest CHD patients was poorest (confirmative triangulation). Moreover, she concluded that a poor psychosocial state is related to acute onset of illness at a young age, financial problems, concern for one's family and a lack of emotional support, which was a specific challenge for females with CHD (complementary triangulation). Still, although the author of the present thesis acknowledges Lukkarinen's major contribution in the field, it should be noted that she made used of a generic disease instrument to capture individuals' perceptions and her type of qualitative data collection and analysis neither permitted her to capture CR patients' specific concerns nor individuals' in-depth experience.

All the above examples highlight the beneficial impact of mixed-methods research on knowledge in the HRQoL field. Longitudinal mixed methods studies in addition to cross-sectional studies can capture individuals' perspectives of their HRQoL over various time points allowing researchers both to detect changes on HRQoL level related to a factor of interest (e.g. treatment) through the quantitative component of their study as well as to explore individuals' experience through the qualitative component. At the final interpretation stage where findings of both components are integrated, depending on the type of the integration espoused, convergent, complementary and/or contradictory meta-themes and/or exploratory or explanatory models can be revealed and presented. However, in order to draw upon the advantages of a mixed-methods approach, researchers should be cautious with regard to design selection and final interpretation (integration of findings from each sub-study) which should be based on their research questions and intended "consequences" (e.g. how individuals' HRQoL level can be increased).

2.5.3. Patient-based instruments for measuring HRQoL: Generic vs specific measurement

Hundreds of patient-based measures aiming to detect patients' HRQoL have been established over recent decades (Coons et al., 2000). The vast majority are aligned with the perspective that HRQoL should capture patients' points of view about the effects of disease on their physical, psychological (including emotional and cognitive), and social functioning (Patrick et al., 2007). Most of them are established in line with rigid criteria and scientific standards (Schroter & Lamping, 2004) in order to be able to provide accurate and meaningful results (Streiner &

Norman, 2008), while also acknowledging that measures with poor psychometric properties may produce misleading results.

These instruments are divided into two main categories: generic and specific. Generic instruments, such as the Medical Outcomes Study 36-Item Short Form (SF-36 (Ware, 2008; Ware & Gandek, 1998)), and the Nottingham Health Profile (NHP (Hunt, McKenna, McEwen, Williams, & Papp, 1981)), are designed to capture subjective perceptions of a wide range of populations regarding a wide range of interventions. Specific instruments, such as the Coronary Revascularization Outcome Questionnaire (CROQ (Schroter & Lamping, 2004)) and the MacNew (Hofer, Lim, Guyatt, & Oldridge, 2004), are designed to measure the individual perceptions of a specific subgroup of the population (e.g. cancer patients, heart disease patients) and/or with regard to specific interventions (Coons et al., 2000). A large library of generic and specific HRQoL instruments can be found on the Mapi Research Trust -PROQOLID website.

The essential difference between these two categories is that a generic tool may be less sensitive to particular domains in relation to a disease than a specific one (Chen, Li, & Kochen, 2005). The generic instrument may only superficially cover each HRQoL domain and it may fail to detect the impact of adverse effects. Specific pains (e.g. pain in a groin wound), for example, that are common and influence HRQoL in CR patients (Schroter & Lamping, 2006) cannot be investigated by those instruments. On the other hand, generic measures are very helpful to build a clearer picture about patients' QoL, especially in the long-term when individuals have adjusted to a new way of life and have temporally moved from the experience of a certain treatment or condition. For instance, severe anxiety due to coronary revascularization (identified by a specific measure) might not be present, but anxiety due to work problems might be detected. This aspect of QoL can be identified only through generic measures (Chen, Li, & Kochen, 2005).

In short, patient-based instruments are widely used in order to capture patients' subjective perspectives about their HRQoL. A great number of instruments focus on capturing the general perception of HRQoL whereas others focus on the perception of HRQoL in relation to a particular disease. However, due to the fact that there is no single established and accepted definition, researchers investigating HRQoL include various dimensions perceived as being strongly connected with the concept under investigation. For a presentation and brief discussion of HRQoL instruments more commonly used in the CR field please see appendix 2.1.

2.6.Approach to HRQoL in this thesis

In this thesis, HRQoL is defined drawing on the WHO definition (1948;1996) linked to the Biopsychosocial model of health and disease (Engel, 1980) which states that HRQoL refers to the individuals' perception of health status (related to disease symptoms and/or treatment side effects), physical, psychosocial and mental functioning. Furthermore, based on the general agreement in the literature that HRQoL is not static but rather a dynamic concept which can change over time a longitudinal design has been employed to capture changes over a one year period. As this thesis focuses on the influence of coronary revascularization (CR) on patients' HRQoL, a disease-specific self-rated measure has been chosen to capture individuals' subjective evaluations, the Coronary Revascularization Outcome Questionnaire (CROQ) as it measures dimensions consistent with the adopted definition. Also, as the author endorses the pragmatic stance in research, it was assumed that HRQoL could be better explored by employing a mixed methods study. Thus, in order to explore individuals' perceptions of their HRQoL after CR and to measure changes over a 12-month period, a longitudinal mixed methods study with two components, a quantitative and a qualitative, was carried out. This allowed the author to capture individuals' perspectives based on both CR specific items related to HRQoL and additional issues via the open- ended question (e.g. financial issues) not investigated through the structured questionnaires (quantitative component) as well as individuals' lived experience (qualitative component). The integration of the findings of each component at the end, at the interpretation stage, employing a narrative explanatory synthesis, allowed to present support, convergence and complementary insights (both in terms of new issues and explanation of other findings). This in turn allowed to identify individuals' conceptualization of HRQOL as well as understand their individual perspectives.

2.7.Rationale of the present thesis

Based on World Health Organization reports Coronary Heart Disease (CHD) can be viewed as a leading cause of morbidity and mortality globally (WHO, 2014). Coronary revascularization (CR), consisting of two types, percutaneous coronary intervention (PCI) and coronary bypass graft surgery (CABG), is one of the main treatment of CHD. Research evidence indicates that CR results in prolonged life expectancy (Bravata et al., 2007; Jeremias et al., 2009) and has reduced morbidity rates through increasing the physical functioning of patients with coronary diseases (Jeremias et al., 2009). While physical functioning is an important factor in the treatment of CHD, there is growing evidence that non-clinical variables such as psychological and social factors have great influence on the life of CHD patients (Funder, Steinmetz & Rasmussen, 2009; Herlizt et al., 2005; Hofer, Doering, Rumpold, Oldridge & Benzer, 2006; Lett et al., 2004, 2005; Mallik et al., 2005), which have received less attention compared to biomedical ones (Lett et al., 2004; 2005).

Therefore, over the last decades, due to the general acceptance that a health issue like CHD can be more efficiently understood if viewed in a holistic, biopsychosocial manner, an ongoing body of research has been devoted to investigating the impact of CHD and its treatment on patients' HRQoL. However, the lack of a consensus definition of HRQoL and the different methodological and conceptual approaches adopted by researchers in the cardio-revascularization field, create an incomplete picture about the influence of CR on patients' HRQoL. The few recent reviews in the field are aligned with this claim (Abah et al., 2015; Blankenship et al., 2013; Jokinen et al., 2010; Noyez, de Jager, & Markou, 2011).

Undoubtedly, the insight provided by the few reviews in this area is essential. Still a number of issues remain to be explored; for instance, the extent of the effect size (ES) of CR on CHD patients' HRQoL as measured by self-rating instruments or related influential factors (issues that will be discussed in chapter 3).

Against this background, the present thesis aims to develop a more holistic and deep insight into the influence of CR on CHD patients' HRQoL. Initially, a systematic review employing meta-analytic techniques (Chapter 3) has been conducted aiming primarily to summarize research evidence and evaluate the impact of coronary revascularization (CR; including CR types (CABG and PCI)), on patients' HRQoL. The findings helped in establishing conclusions about the influence on CR on patients' HRQoL, detecting possible factors that may be related to the outcome, as well as revealing possible methodological problems in quantitative research that should be addressed. The main research questions addressed were:

1. What does the research evidence suggest concerning the effect of type of treatment for CHD on patients' HRQoL?

2. What does the research evidence indicate concerning factors that influence the effect size (ES) of CR on patients' HRQoL?
3. What does the research evidence demonstrate regarding the influence of CR or its types (PCI and CABG) on the main subdomains of patients' HRQoL (i.e. physical and psychosocial aspects)?

Taking into consideration: a) the findings of the systematic review (part of it already in press; Takousi et al., 2016); b) the author's adopted definition of the HRQoL concept (i.e. the WHO's definition (WHOQoL, 1993) linked to the Biopsychosocial model (BPS; Engel, 1980)); c) the author's endorsed mixed methods pragmatic stance (where quantitative and qualitative research methods are combined to generate a clearer picture; Creswell, 2014); d) the extremely limited research in this field in Greece (where the incidence of CHD has been constantly increasing over the last decades, and where CR treatment is mostly applied, as discussed in section 1.7), two studies have been carried out:

(1) The translation, adaptation and validation of the Coronary Revascularization Outcome Questionnaire (CROQ) into Greek (presented in Chapter 5; part of it has been already published; Takousi et al., 2015) since the study would be conducted with Greek patients. The selection of the particular instrument was made based on the fact that it is currently the only disease/treatment specific instrument which captures individuals' subjective evaluation of their HRQoL and health outcomes following CR and it is developed based on the WHO's definition (Schroter, 2001).

(2) The longitudinal mixed methods study, the main study of the thesis, following a sequential explanatory design, refers to a 3-part study consisting of two research components:

a) Part 1 (presented in Chapter 6), the longitudinal quantitative component, aimed to detect changes in patients' HRQoL (both overall and in its subdomains) following CR over a 12-month period based on individuals' subjective evaluation as captured by the CROQ, exploring various clinical, behavioural and demographic predictors as well.

b) Part 2 (presented in Chapter 7), the qualitative component aimed to capture individuals' lived experience, their view and understanding of themselves and their life approximately 12 months after treatment as well as explore in depth and explain aspects of the quantitative findings (e.g. individual differences related to the type of CR treatment, smoking).

c) Part 3 (presented within Chapter 8), the integration of the findings of both components (interpretation and explanation) aimed to address the following questions:

1) How do Greek individuals with CHD conceptualize HRQoL?
2) How do aspects of the disease experience after CR and meaning-making processes inform individuals' perspectives on their HRQoL?

Thus, it is expected that this thesis will contribute to the field in various ways:

- The systematic review will be the first to include literature on both CR types (PCI and CABG) in relation to HRQoL.
- The Greek version of the CROQ will fill a gap in the Greek literature, since there is no scientifically valid and reliable instrument detecting HRQoL and health outcomes after coronary revascularization.
- The longitudinal quantitative study will reveal changes in HRQoL over time and its predictors more accurately than previous studies since it makes use of a disease-specific instrument with a 12-month follow-up.

- The qualitative study will be the first to explore lived experience and subjective meanings of quality of life and lifestyle modifications after intervention/surgery in CHD patients employing Interpretive Phenomenological Analysis.
- The mixed methods approach employed in the main study will facilitate the development of research-based theoretical considerations of the concept of HRQoL, with specific emphasis on aspects related to coronary revascularization.
- The final discussion based on the integration of findings will build the overall picture of CHD patients' subjective perspectives on their life following CR and identifying needs that should be addressed by tailored interventions.

Chapter three

Health Related Quality of Life after Coronary Revascularization: A systematic review with a meta-analysis

3.1.Introduction

The two previous chapters introduced essential concepts related to coronary heart disease (CHD), its treatment focusing mainly on coronary revascularization (CR) and its two types, percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG), including a rationale for conducting this study in Greece. In addition, the concept of health related quality of life (HRQoL) was introduced as well as the benefit of exploring it and ways to do so. Since there is a general acceptance that a health issue like CHD can be more efficiently understood using a holistic, biopsychosocial approach, an ongoing body of research has been devoted to investigating the impact of CHD and its treatment on patients' HRQoL. This chapter aims primarily to: a) explore research evidence approximately over the last two decades (1996-2012, where great advances in CR treatment have been made) in order to establish the effect size (ES) of CR on patients' HRQoL as well as examining the influence of the different CR types on the extent of the ES, and b) explore whether various individual characteristics (e.g. age), and various methodological issues (e.g. quality of the study) are associated with the ES. The secondary aim is to develop recommendations, especially for future research that in turn will guide the quantitative part of the mixed methods study. In order to fulfill these aims, the use of rigorous search, screening and meta-analytic techniques are employed in order to address the following research questions:

1. What does the research evidence suggest concerning the effect of type of treatment for CHD on patients' HRQoL?
2. What does the research evidence indicate concerning factors that influence the effect size (ES) of CR on patients' HRQoL?
3. What does the research evidence demonstrate regarding the influence of CR or its types (PCI and CABG) on the main subdomains of patients' HRQoL (i.e. physical and psychosocial aspects)?

3.1.1. Overview of systematic reviews and meta-analyses

The field of coronary heart disease has advanced considerably in the last decade. Coronary procedures, either interventional (percutaneous coronary interventions; PCI) or surgical (coronary artery bypass graft surgery; CABG), have been used in treating coronary heart disease and have increased the survival rate globally (Jeremias et al., 2009). However, it is important to mention that the comparative effectiveness of CABG and PCI remains poorly understood for patients that are eligible for either procedure (Bravata et al., 2007). A recent review, conducted by Hlatky and colleagues (2009) suggests that only diabetes and age may be related to the effect of type of CR on the survival rate of patients with multi-vessel coronary disease. Specifically, older patients and those with diabetes have lower mortality rates when treated with CABG than with PCI, but younger and non-diabetic patients demonstrate similar rates.

Apart from the survival benefit and relief of symptoms, patients' health-related quality of life (HRQoL) is a critical issue (Sawatzky & Naimark, 2009). As discussed in chapter 2, although no consensus definition exists, HRQoL includes aspects of physical, psychological and social well-being (Bowling, 2001; Patrick et al., 2007). Enhancing coronary patients' HRQoL should be among the priorities of the medical team.

A search of the literature shows that few systematic reviews have been carried out over the past ten years on the effect of coronary interventions on HRQoL. In fact, in relation to HRQoL, only one review of randomized controlled trials focusing on CABG (Jokinen et al., 2010), one review focusing on cardiac surgery (Noyez, de Jager, & Markou, 2011), two meta-analyses on cognitive functioning (one aspect of HRQoL) following coronary heart surgery (Cormack et al., 2012; Sun, Wu, Wang, & Jin, 2012) and one review centered on coronary interventions (PCI; (Blankenship et al., 2013)) have been reported. More specifically, Jokinen and colleagues (2010) reviewed 21 randomized controlled trials using CABG. They concluded that post-surgically patients experience improved HRQoL regardless of the procedure followed (on- vs off-pump CABG), especially when performed by experienced surgeons. Furthermore, Jokinen and colleagues (2010) suggest that pre-operative HRQoL predicted post-treatment HRQoL in an RCT and the beneficial effect is long lasting and comparable to that of the general population. Noyez et al. (2011) reviewed 29 articles on the effect of cardiac surgery. They concluded that many studies do not present preoperative QoL data, only postoperative QoL data, which limits conclusions concerning the beneficial effect of heart surgery on QoL. Furthermore, they highlighted the need for good clinical trials with a longer follow up (greater than one year). Sun et al. (2012) and Cormack et al. (2012) reviewed 13 RCTs and 28 longitudinal studies respectively using CABG. Both reviews concluded that CABG patients may experience a decline in cognitive functioning during the first weeks after treatment but that this reverses at twelve months post surgery. Finally, Blankenship et al. (2013) reviewed 25 studies and concluded that the effect of PCI on QoL is greater than medical treatment (drug treatment), however this benefit decreased over time. Moreover, the findings of the same review highlight that PCI’s effect on QoL in the first months post treatment is greater than that of CABG but, in the longer term, the effect of both procedures leads to similar improvements. Also, Blankenship et al.’s (2013) findings suggest that all ages benefit equally regardless of which revascularization procedure is performed although females report lower HRQoL than males following PCI. Unemployment status, smoking and medical co-morbidities after PCI are related to lower QoL experience (Blankenship et al., 2013). Soo Hoo, Gallagher, and Elliott (2014) reviewed 18 studies using PCI and supported Blankenship et al.’s (2013) suggestion that all individuals, regardless of their age, report improvements in their HRQoL and that age, therefore, cannot be considered a moderator, especially when other co-morbidities are taken into consideration. Abah and colleagues (2015) reviewed 44 studies (mostly retrospective) on the influence of heart surgery (CABG, PCI, Valve) on older patients’ HRQoL. Results show that the majority of patients demonstrated improvement following heart surgery while 8-19% demonstrated a decline.

Although these reviews provide insight regarding the effect of CR on cardiac patients’ HRQoL, a number of issues need to be addressed in order to draw a clear picture and be able to make suggestions for clinical practice. For instance, Sun et al. (2012) and Cormack et al. (2012) focus only on one aspect of HRQoL, cognitive functioning, thus, a clear conclusion about the effect of CR on HRQoL cannot be drawn. Blankenship et al.’s study (2013) while of good standard, is actually a literature review, implying a lack of rigorous systematic methodology (e.g. many studies included are of low quality and/or provide only post treatment data for the effect of CR on HRQoL), thus, the results may be biased. Noyez et al.’s (2011) and Abah et al.’s (2015) work focuses on surgical treatment of various heart problems (e.g. aortic or mitral valve surgery) not only on coronary artery disease. Hence, a clear conclusion about the effect of CR requires further investigation. Jokinen et al.'s (2010) review was limited to RCTs published in English as their main aim was to compare on- vs off-pump CABG effects on patients' HRQoL. As a result, they excluded a number of studies that may influence conclusions. Finally, it should be mentioned that none of the above reviews provide the effect size of CR on HRQoL as they did not use meta-analytic techniques to calculate the effect size and identify its moderators. Thus, a systematic review with a meta-analysis would update the literature and at the same time, due to the nature of its methodology, allow for conclusions based on quantitatively integrated results about the impact of CR on patients' HRQoL and its possible moderators.

3.2.Methods

The methodology used in the present study follows the guidelines of the Centre for Reviews and Dissemination (CRD (University of York, 2008) for undertaking systematic reviews, the Cochrane Collaboration (Higgins & Green, 2011) and Field and Gillett's (2010) suggestions for systematic reviews with meta-analysis.

3.2.1. Systematic literature search

The literature search was carried out from December 2012 to January 2013 making use of five online databases: Medline (PubMed), EMBASE, Cochrane Library, Sciverse (Science Direct and Scopus) and PsycInfo. Key words used in all searches were:

"Quality of life"

"QoL"

“Health related quality of life”

“HRQoL”

“Health status”

“Heart surgery”

“Coronary Revascularization”

“Coronary bypass”

“CABG”

“PCI”

“PTCA”

“Coronary angioplasty”

“Coronary percutaneous interventions”

Those terms were searched in combination (and/or (e.g. Quality of life or HRQoL and Coronary Revascularization)) with only one restriction “not adolescent not children”. Furthermore, they were searched for in the title, abstract and keywords. The search included studies published in the 13 years between January 2000 and December, 2012. In addition, “snowball” techniques (Greenhalgh & Peacock, 2005) were used in order to detect more studies. In line with this technique, reference lists of studies and reviews published from 2000-2012 were searched manually in order to detect studies that may fulfill the eligibility criteria for inclusion. Moreover, abstracts written in English were considered as well, even if the research paper was written in another language. When an abstract seemed relevant to the topic under investigation, and the paper was published in a language other than English, Greek, French, German, or Spanish the authors were contacted in order to ask whether a full English version, or results section, were available. Authors were also contacted when their papers seemed eligible for inclusion, but not all information needed for the analysis was presented.

Studies were included when fulfilling the follow criteria: (1) participants should be ≥ 18 years of age, (2) HRQoL was the primary outcome (dependent) variable in order to be the variable of greatest importance and values were provided either for total HRQoL or all its subdomains per measured time-point as assessed by the instrument used, (3) the design of the study was randomised, non-randomised or observational, (4) reported at least two interval times, pre treatment (baseline) and after intervention, (5) data collection after 1996, (6) published in a peer reviewed journal, (7) published in various language in which the present authors were proficient (i.e. English, Greek, French, Spanish, German) or the author(s) of the articles provided/sent an English translation following a request.

The cut-off point of 1996 was set in order to reduce heterogeneity in outcome caused by "old" medical procedures, that are less applied nowadays. According to the cardiology literature, in the last fifteen years new methods have been developed in the field of both interventional and surgical coronary revascularization (Holmes & Williams, 2008; Thanikachalam, Lombardi, Tehrani, Katariya, & Salerno, 2004).

Studies were excluded when (1) they used a questionnaire that did not measure all subdomains of HRQoL (based on the WHO definition) or that had poor/unknown psychometric properties. As the literature suggests that meta-analysts should pay attention to the constructs being tested and responsiveness of instruments in order to decide on the appropriateness for inclusion (Puhan, Soesilo, Guyatt, & Schunemann, 2006), (2) studies were excluded if they were case reports, (3) the available data were not sufficient for effect size estimation (e.g. only graphs without *SD*, only post data, no scores for all subdomains) even after contacting the corresponding author, (4) only norm based summary scores were presented (these two summary scores represent scores related to the US population (Taft, Karlsson, & Sullivan, 2001; Ware, 2007)) and (5) they were psychometric studies testing the properties of a QoL instrument.

3.2.2. Screening identified studies

A total of 1123 citations were identified from the searches; snowball techniques did not reveal any additional studies based on the inclusion criteria. Details about the exclusion procedure are shown in the flow diagram below (Figure 3.1). After reading the title or abstract a vast number of studies (901) were excluded as either irrelevant or lacking emphasis on CR. Of the remaining 222 studies, after entering them in the Endnote® software (X3), 11 studies were duplications (the same article was retrieved from both of the databases). Moreover, 14 papers referred to the same study examining different predictors of QoL after revascularization (Gjeilo, Wahba, Klepstad, Lydersen, & Stenseth, 2008, 2012; Jarvinen, Julkunen, Saarinen, Laurikka, & Tarkka, 2005; Jarvinen, Julkunen, & Tarkka, 2007; Järvinen, Saarinen, Julkunen, Huhtala, & Tarkka, 2003; Jarvinen et al., 2004; Peric et al., 2010; Peric, Borzanovic, Stolic, Jovanovic, & Sovtic, 2006). Moreover, 126 were excluded as reporting only post-CR HRQoL (e.g. focusing on rehabilitation or comparison with other heart operations and/or populations, follow up design). From the remaining 71 papers, three studies were excluded based on the instrument used for measuring HRQoL. Eleven studies were excluded as providing data earlier to 1996. Furthermore, four papers were excluded due to the fact that they presented only norm based scoring and not the total raw score for each subscale. For instance, some authors presented only the Mental Component Summary (MCS) and Physical Component Summary (PCS) of the SF-36 (Ware, 2008).

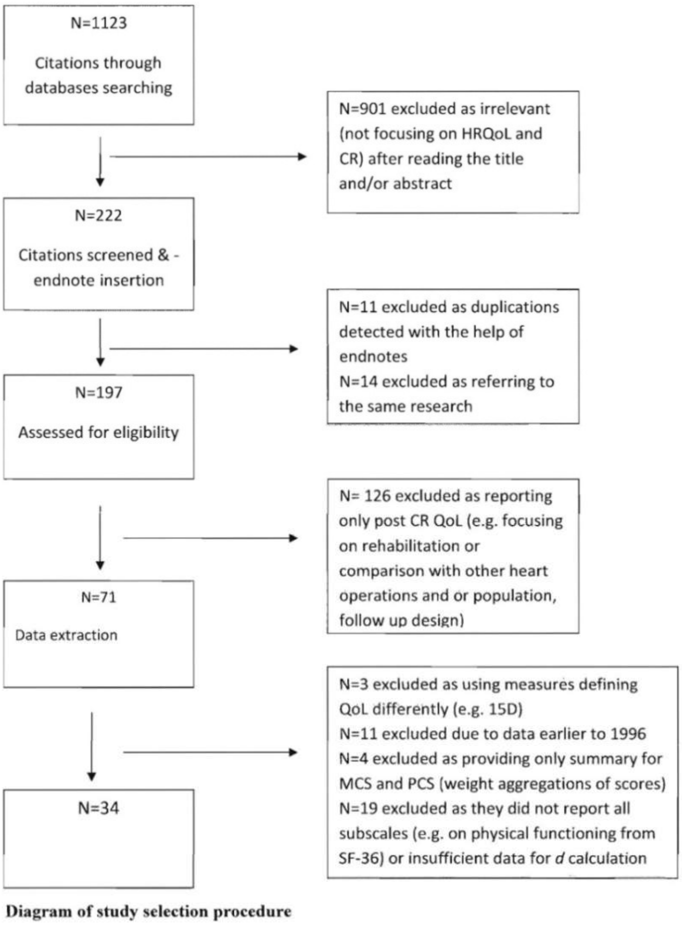


Figure 3.1 Flow diagram illustrating the study selection procedure

Actually, some meta-analysts conduct a separate analysis for papers that report only those two scores (Trevisol, Moreira, Kerkhoff, Fuchs, & Fuchs, 2011), or transform all subdomain scores into such scores with the use of the SAS programme following a three step procedure (Kuspinar, Rodriguez, & Mayo, 2012). Finally, 19 papers were excluded as providing inadequate data for effect size calculation of HRQoL after CR. In order to reduce systematic biases from the main reviewer, a second reviewer (Dr Manaras, the external supervisor) was involved from the beginning of the study, following the same steps as described above. In the final step, regarding inclusion of studies, there was only one disagreement (concerning Zwoliński et al.'s [2013] study). After discussion it was decided to exclude the study on the basis of the data being collected prior to 1996.

After the overview of remaining papers, the number of eligible studies was dramatically reduced. Only 34 papers were identified as fulfilling the criteria for inclusion in this review. From these articles, five articles were written in a language other than English (2 were in German, 2 in Spanish, 1 in Greek). Therefore, the help of other psychologists who were proficient in the particular language was requested. Appendix 3.1 gives the reason for exclusion of each of the 34 papers excluded through the last screening.

3.2.3. Data extraction

Studies were coded for: year of publication, country, type of CR, study design, sample size at baseline and at the follow ups, participants' mean age, sex distribution, percentage who smoked, percentage with hypertension, percentage with diabetes (I or II) as displayed at Table 3.2. Intervention duration, numbers of follow up assessments, HRQoL measurement tool, HRQoL pre- and/or post-intervention score (raw means score for total HRQoL or each subscale at baseline and for the last follow up and their standard deviations (or effect size if directly reported) and authors' main findings. In some cases where the standard deviation (SD) was missing confidence intervals (CI) and/or standard error (SE), were extracted in order to calculate SD (as suggested by Higgins & Green, 2011). An SPSS data sheet was created for each included study in order to facilitate *d* conversions avoiding hand calculation errors. Table 3.4 summarizes studies' intervention duration, numbers of follow up assessments, effect size, and authors' main findings.

3.2.4. Quality assessment of the included studies

Studies were assessed for quality using a combination of the Downs and Black (1998) checklist focusing on methodological quality (e.g. reporting, validity), Noyez et al.'s (2011) suggestions about characteristics of a good study, and the Critical Appraisal Skills Programme (CASP, 2013) for cohort studies, focusing on the overall quality of studies. There were 10 criteria in total; listed in Table 3.1). Answers were scored 0 when the criterion was not met, 0.5 when partially met and 1 when totally met. Scores could therefore range from 0 to 10.

Table 3.1 Quality criteria of the primary studies

	Criteria	Source
1	Did the study address a clearly focused issue?	CASP[*], 2013& Downs and Black, 1998
2	Are patient characteristics clearly described?	Downs and Black, 1998
3	Was the outcome accurately measured (valid and reliable instrument)?	CASP , 2013 & Downs and Black, 1998
4	Were confounding factors taken into consideration?	CASP, 2013 & Downs and Black, 1998
5	Have the characteristics of patients lost to follow-up been described?	Downs and Black, 1998
6	Were losses of patients to follow-up taken into account?	Downs and Black, 1998
7	Is the procedure fully described?	Noyez, de Jager, and Markou, 2011
8	Were the statistical tests used to assess the main outcomes appropriate?	Downs and Black, 1998
9	Are the main findings of the study clearly described?	Downs and Black, 1998
10	Was the follow-up of participants long enough[**]	Noyez, de Jager, and Markou, 2011

[*] CASP= Critical Appraisal Skills Programme

[**] No specific guidelines are given for this thus the author set that point to 12 months (a yearly follow up)

3.2.5. Methodological considerations in the meta-analysis

3.2.5.1. Effect size

The effect size reveals the impact that an intervention may have in a quantitative way (Puhan, et al., 2006). There are various ways to calculate effect size.

Among the most widely used are Person's *r* and Cohen's *d*. Pearson's correlation coefficient *r* is calculated by using the following formula $\sqrt{t^2}/\sqrt{(t^2+df)}$. An effect size of 0.10 is viewed as small, 0.30 as medium and 0.50 as large (Field, 2005). Cohen's *d* is calculated by dividing the mean change (post treatment mean-pre treatment mean) by the standard deviation (Kinnear & Gray, 2008). Based on Cohen an effect size of 0.20 is defined as small, 0.50 as moderate and 0.80 or greater as large (Cohen, 1988). For the present study, Cohen's *d* was selected.

3.2.5.2. Fixed vs random effects models

For systematic reviews with meta-analysis, the effect size of each study should be established and these effect sizes are then combined in order to estimate overall effect size. However, due to the fact that not all studies are identical, a simple mean of effect sizes might be misleading. In order to resolve this problem, a weighted mean should be computed giving some studies more weight and some less weight (Borenstein, Hedges, & Rothstein, 2007). Based on the literature, there are two ways to calculate the overall effect size: the fixed and the random effects models. These two approaches differ in their assumptions concerning the nature of each study. The fixed effect model (Hedges & Vevea, 1998) suggests that there is only "one true effect size" (Borenstein, Hedges, Higgins, & Rothstein, 2009) which is represented by the overall effect. In this model, it is accepted that all factors affecting the effect size are the same and that any variation observed is due to random error. Therefore, the sample size of the study (regarding information) strongly affects its weight in the calculation of the overall effect.

On the other hand, the random effect model (Hunter & Schmidt, 2004) suggests that the “true” effect could dramatically differ from study to study due to design, sample (Borenstein et al., 2007), cultural differences and so on. Thus, the overall effect size is assumed to be the mean of the distribution of true effect sizes. In this model, it is accepted that there is not only one true effect, not only because of random error, but also due to the variation of true effect size among studies as each study represents the scores of a “unique” population. Therefore, the size of the study should not be overemphasised because it underestimates the findings of small studies that may reveal important and interesting aspects of the topic under study. The aim in this model is to summarize the range of various effect sizes.

In short, the fixed effect model assumes homogeneity in the studies under investigation. Thus, one true effect size exists and any variation in the effect sizes is due to random error. Large studies are weighted more heavily when calculating the average effect. Conversely, the random effect model assumes heterogeneity among studies, giving equal importance to all studies regardless of sample size. The mean effect size represents the sum of effect ranges.

3.2.5.3. ***Quantifying heterogeneity between studies***

The heterogeneity/homogeneity notions refer to the level of consistency in results of the studies included in the meta-analysis. When the effect sizes of the included studies have poor overlap heterogeneity is present. The presence of heterogeneity provides less rigorous results and thus, weaker conclusions. When heterogeneity is present, an investigation of the source of this phenomenon should be made, usually by employing both a moderator and subgroup analysis (Higgins et al., 2011).

A conventional heterogeneity statistical test, widely used in meta-analysis, is the *Q-test* (Cochran Q statistics; Cochran (1954)). The Q index presents the summary of the squared deviations of each study's effect estimate from the overall effect estimate, weighting the contribution of each by its inverse variance and it is influenced positively by the number of studies (k) included in the meta-analysis (Rucker, Schwarzer, Carpenter, & Schumacher, 2008). If the test reveals a non-significant result homogeneity is assumed whereas if the significance of Q is $p<0.05$, heterogeneity is assumed (Field & Gillett, 2010). However, the Q index should not be used in order to decide the appropriate model, random or fixed, that is employed in the meta-analysis. This method is useful just for conceptualizing results. Based on the literature, the Q test has poor power to detect true heterogeneity (especially when the number of studies included is small) and it does not reliably demonstrate the extent to which heterogeneity is present (Huedo-Medina, Sanchez-Meca, Marin-Martinez, & Botella, 2006).

A more sophisticated way to detect heterogeneity in meta-analysis is the I^2 index suggested by Higgins, Thompson, Deeks, and Altman (2002). The I^2 index represents the percentage of total variation in study outcomes regarding effect sizes. It calculates the extent of the heterogeneity by dividing the difference between the result of the Q test and its degrees of freedom by the Q value itself, and then, multiply it by 100. Based on the Cochrane Collaboration guidelines, percentages of I^2 between 0 and 40% count as having non important heterogeneity, around 50% ($I^2 = 50$) as having medium, and 75% ($I^2 = 75$) as having considerable heterogeneity. However, the I^2 index has been severely criticized for its use in interpreting heterogeneity and, in turn, for deciding whether to include studies or not, especially when continuous data are involved (Rucker et al., 2008). Based on research findings, authors argue that the I^2 index might be misleading, as it emphasizes precision (size of k included) and does not acknowledge sampling error. Researchers have suggested that as precision increases, the I^2 index increases accordingly, becoming nearly 100%. This phenomenon was present in 157 meta-analyses (Rucker et al., 2008). In order to resolve this problem, the τ^2 index (Tau squared; (DerSimonian & Laird, 1986)) can be used.

The τ^2 index assesses the between-study variance without being influenced by the number of studies included in the meta-analysis. When $\tau^2 > 1$, then substantial heterogeneity can be assumed.

3.2.6. Sensitivity analysis

Based on Higgins and Green (2011), the aim of a sensitivity analysis is to detect whether the studies included in the meta-analysis or the method used (fixed vs random) to obtain the combined effect may dramatically influence the findings. The literature suggests a number of ways of dealing with such concerns (Bartolucci & Hillegass, 2010; Walker, Hernandez, & Kattan, 2008). Some of them are: a) employing both fixed and random effects models and compare the outcomes, b) excluding studies that seem to be outliers (their results differ from the other studies) and then compare the results of both methods of analysis (all vs remaining after exclusion of outliers) and c) examining the presence or absence of publication biases.

3.2.7. Publication bias

A basic concern shared by the majority of meta-analysts refers to publication bias. This concern is based on the fact that many meta-analyses are based only on published papers, usually written in the English language. Published papers generally reveal a positive effect. Thus, papers with negative or inconclusive findings are unrepresented because they are less like to be found in journals or other published sources. Th literature (Field & Gillett, 2010; Thornton & Lee, 2000) suggests various ways to detect publications biases: *funnel plots, Begg's z* index and *Egger's t* index.

The funnel plot is an easy way to determine publication bias through a graphical representation (Sterne & Egger, 2001). A funnel plot demonstrates effect sizes against the sample size or standard error. A symmetrical distribution indicates little publications bias while an asymmetrical distribution indicates the presence of publication bias.

Begg's rank correlation test demonstrates the rank correlation between the standardized mean differences in effect size and their variances, assuming that selective distribution will result a correlation between them (Begg & Mazumdar, 1994). This test should result in a significant *a* (alpha) value ($p<0.05$) and should include a range of effect sizes in order to allow clear conclusions about the absence of publication bias (Borenstein, 2005).

Egger's regression model, similar to Begg's, aims at detecting publication bias, but makes use of the actual effect sizes and not the ranks. Again, clear conclusions can be drawn when a range of effect sizes is included (Sterne, Egger, & Smith, 2001).

3.2.8. Moderators of effects

Reviewers highlight various factors as potential moderators of effect sizes such as study quality, study design, outcome measure (instrument) and length of the study (Conn, Ruppar, Phillips, & Chase, 2012). Furthermore, based on the CR literature a number of factors may affect the outcome (e.g. proportion of each sex, smokers; Soo Hoo, Gallagher, & Elliott, 2014). Therefore, as will be shown in the analysis section, an analysis of possible moderators will be carried out.

3.2.9. Calculations

For the analysis of the present study, calculations and conversion have been made. The mean difference was computed as the mean change before and after intervention (last follow-up). The effect size was computed based on Cohen's *d* formula, by dividing the mean change by the pre-intervention standard deviation, as appropriate for repeated measures design studies (Field, & Gillett, 2010b). Afterwards, conversion of *d* to Hedge's *g* was employed in order to correct small sample size bias.

Where Cohen's *d* was not directly provided, the appropriate formula was employed, revealing a *d* for each subscale and then, calculating the mean of *d*s. Where the standard deviation (*SD)* was not reported, it was calculated based on other indices provided. For instance, where the standard error was given the *SD* was computed by multiplying the standard error by the square root of the number of participants ($SD=SE \times \sqrt{n}$; (Higgins & Green, 2011)). Where confidence intervals were given, the following formula $SD=\sqrt{n} \times (\text{upper - lower limit}) / 3.92$ was applied (Higgins, & Green, 2011). For conversion of *d* to Hedge's *g* (for reducing sample bias) the following formula was employed Hedge's *g*=*d**(SQRT((n1+n2-2)/(n1+n2))).

3.3. Analysis

Cohen’s *d* formula was used to compute effect size (ES) for each study in accordance with the guidelines of many experts (Field & Gillett, 2010; Olive & Smith, 2005).

Forest plot diagrams were created in order to show graphically the effect size for each study as well as the average (combined) effect size produced by all studies. The overall effect size is indicated by a “diamond” while a zero effect is marked with a line for easy interpretation.

Sensitivity analysis was conducted by excluding outliers (studies with very different results) and poorer quality studies (Higgins et al., 2011).

Moderator analysis on mean difference (md; last follow up- prior to revascularization) was obtained by running a multiple linear regression weighted by mean difference inverse variance. Design and type of instrument variables, as these are categorical, were converted to dummy variables in order to fulfill regression assumptions regarding data type.

Univariate Analysis of Variance was conducted to detect differences between treatment types and weighted multiple comparisons (using Bonferroni post hoc tests) were carried out in order to compare the effect of CABG vs MED, PCI vs MED and CABG vs PCI.

Finally, a subgroup analysis was carried out for the two basic subdomains involved in HRQoL (physical and psychosocial) per CR type for studies using the SF-36 (Ware, 2008) as this instrument was most used and there were no other measures used sufficiently often to do a subgroup analysis. The subgroup analysis was conducted based on the average difference (md; last follow up- prior to revascularization) of the physical and psychosocial component summary respectively. Component summaries were calculated with the use of the Health Outcomes Scoring Software 3.0.

Analyses were performed using MIX 2.0 Pro (Bax, Yu, Ikeda, & Moons, 2007; Bax, Yu, Ikeda, Tsuruta, & Moons, 2006), Excel (MS office Excel, 2007) and SPSS 20 (IBM, 2011).

3.4.Results

A total of 34 prospective longitudinal studies published between 2000 and 2012 were included in the present systematic review (see flow diagram). Figure 3.2 presents the exact number of the studies included per procedure.

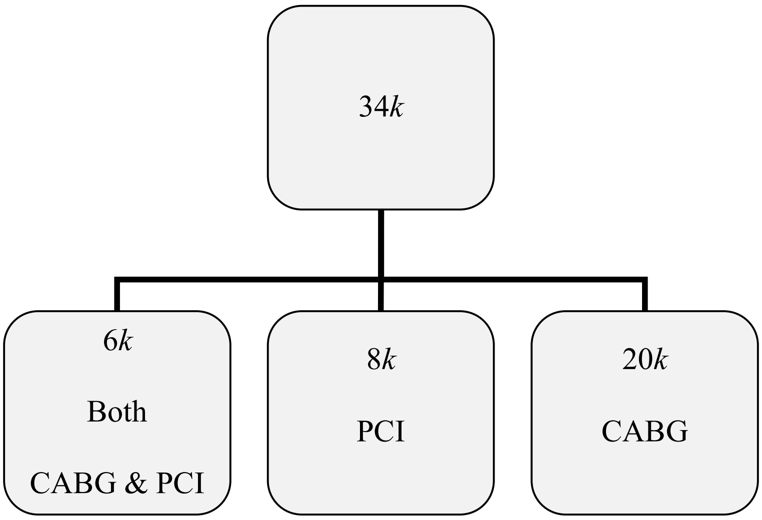


Figure 3.2 Diagram for studies included in the meta-analysis per CR type

Data for the PCI procedure were extracted partially from studies focusing mainly on PCI and partially from studies including both procedures (*k*=14), whereas data for the CABG procedure were extracted from studies focusing mainly on CABG and partially from studies including both procedures (*k*=26).

In total, 15,992 patients were included in the present systematic review and meta-analysis (8,027 underwent PCI, 6,348 underwent CABG and 1,617 received medication treatment). Patients' demographic and clinical characteristics per study are summarized in Table 3.2.

Table 3.2 Characteristics of participants in studies included in the systematic review and meta-analysis

	Study (year)	Country	sample size (T1)		Instrument†	Female %	Mean age	Smoking %	Hyper-tension %	Diabetes %
			PCI	CABG						
1	Benzer (2003)	Austria	64	33	MAcNew	35.3	64.5	44.3	NR	NR
2	Cohen (2011)	USA	903	897	SF-36 †	22.5	65.2	18.5/21.9	NR	38.1/28.9
3	Hofer (2006;2005)	Austria	60	121	MAcNew†	24.1	61.8	28.3/33.9	50/69.4	15/19.8
4	Lukkarinen (2006)	Finland	100	100	NHP	32.5	57.2/61.8	4	NR	NR
5	Škodová (2011)	Slovakia	37	41	SF-36	15.1	55.8/59.4	NR	NR	NR
6	Zang(2003)	Eur& can.	488	500	SAQ†	21	61.4	NR	45.2	14.4
7	de Quadros (2011)	Brazil	110		SAQ	38	62.8	24	90	32
8	Denvir (2006)	UK	1346		EQ-5D	32.5	60.9	38.6	32.5	11.1
9	Melberg (2010)	Norway	427		SF-36	20.3	58.4	29.9	23.9	6.1
10	Li (2010)	China	287		SF-36	26.2	64	31	58	30
11	Viswanathan (2011)	UK	2935		NHP	29.3	58.1	26.7	30.7	6.4
12	Weilu (2011)	China	223		SF-36	14.3	60.6	51.6	52.9	13.9
13	Weintraub (2008)	USA & Can	969		RAND-36	15	62	29	67	34
14	Wong (2007)	Hong Kong	78		SF-36	24.6	66	15.4	42.9	29.2
15	Azzopardi (2009)	Australia		87	SF-36	14.6	66.6	24.2	97.9	42
16	Barolia (2012)	Pakistan		65	WHOQOL-Bref	15.3	59.7	20.0	72.0	51.0
17	Colak (2008)	Coatia		111	SF-36	12.6	61.1	NR	87	28.2
18	Damgaard (2011)	Denmark		331	SF-36	11.8	59	46.5	47.6	25.3
19	Gjeilo (2008;2012)	Norway		534	SF-36	22.7	NR	NR	NR	NR
20	Houlind (2012)	Denmark		900	SF-36	23.0	75	25.5	71.0	20.0
21	Hunt (2000)	Australia		123	SF-36	22	64	NR	NR	NR

Table 3.2 Characteristics of participants in studies included in the systematic review and meta-analysis (continued)

	Study (year)	Country	sample size (T1)		Instrument†	Female %	Mean age	Smoking %	Hyper-tension %	Diabetes %
			PCI	CABG						
22	Jensen (2006)	Denmark		120	SF-36	40	76	18.3	60.8	18.3
23	Kiebzak (2002)	USA		85	SF-36	21.2	62	NR	NR	NR
24	Krecki, (2010)	Poland		55	SF-36	25	61.5	36	96	49
25	Krannich (2007)	Germany		142	SF-36	19.0	65.1	NR	NR	NR
26	Lie (2009)	Norway		185	SF-36	10.3	62	29	NR	16.2
27	Martin (2012)	USA		495	SF-12	17.1	63.9	44.0	78.0	32.0
28	Mathisen (2005)	Norway		120	SF-36	21.6	64.4	NR	40	14.2
29	Merkouris (2009)	Greece		63	MAcNew	23.8	72.9	64	62	35
30	Peric (2010; 2006)	Serbia		243	NHP	20	58.7	43	70	19
31	Pfaffenberger(2010)	German		55	SF-36	14.8	64.8	35.2	66.7	NR
32	Pirraglia (2003)	USA		590	SF-36	28	65.1	68.3	52.4	25.6
33	Puskas (2004)	USA		200	SF-36	22.5	62.3	29.4	63.8	33
34	Rothenhäusler(2010)	German		147	SF-36	16.5	60.8	NR	NR	NR

†The instrument used for ES calculations

Most studies (*k*=15) assessed HRQoL after CR up to year (Benzer, Hofer, & Oldridge, 2003; Cohen et al., 2011; Colak et al., 2008; Damgaard et al., 2011; de Quadros et al., 2011; Denvir et al., 2006; Gjeilo, et al., 2008; Hunt, Hendrata, & Myles, 2000; Kiebzak, Pierson, Campbell, & Cook, 2002; Krannich, Lueger, Weyers, & Elert, 2007; Krecki et al., 2010; Mathisen et al., 2005; Merkouris, et al., 2009; Puskas et al., 2004; Zhang et al., 2003). Fourteen studies (*k*=14) had outcome assessment(s) less than 12 months, ranging from 1 to 6 months (Barolia, Ali, & Jaffar, 2012; Hofer, Doering, Rumpold, Oldridge, & Benzer, 2006; Houlind et al., 2012; Jensen, Hughes, Rasmussen, Pedersen, & Steinbrüchel, 2006; Li, et al., 2010; Lie, Arnesen, Sandvik, Hamilton, & Bunch, 2009; Martin, et al., 2012; Melberg, Nordrehaug, & Nilsen, 2010; Peric, et al., 2010; Pfaffenberger et al., 2010; Pirraglia, Peterson, Williams-Russo, & Charlson, 2003; Rothenhausler, Stepan, Hetterle, & Trantina-Yates, 2010; Weilu et al., 2011; Wong & Chair, 2007) and only five (*k*=5) had additional outcome assessments that were longer than 12 months, ranging from 24 to 96 months (Azzopardi & Lee, 2009; Lukkarinen & Hentinen, 2006; Škodová et al., 2011; Viswanathan, Mayurathan, Hildreth, Worthley, & Zaman, 2011; Weintraub et al., 2008).

The majority of studies (*k*=24) used the SF-36 to measure HRQoL. Other measures used were the SAQ (*k*=2), the NHP (*k*=3), the WHOQoL (*k*=1), the MacNew (*k*=3) and the EQ-5D (*k*=1). Table 3.3 displays additional characteristics, such as the main focus of the study and the main finding of each study in plain English.

The majority of studies (*k*=26) had a moderate to good quality ranging from 5 to 7.5 points while the remaining studies (*k*=8) had a low quality ranging from 3.5 to 4.5. Appendix 3.2 displays the analytical scoring per study.

Table 3.3. Additional characteristics and main findings of studies included in the review

ID	Author	QoL Focus	N(prior to treatment)	*N* FU	Main findings
Both interventions					
1	Benzer, 2003	PCI vs CABG vs MED	64 33 109	1(12m)	Greater improvement in QoL 1 year after CABG or PCI compared to medical therapy.
2	Cohen, 2011	PCI vs CABG	903 897	3(1,6,12m)	PCI group score higher in physical aspects of QoL compared to CABG, but NS differences among treatment group at 12 months.
3	Hofer, 2006	PCI vs CABG vs MED	60 121 96	2(1,3m)	CR groups demonstrate greater change compared to MED groups. PCI group experience a significant increase 1 month post treatment with a little further increase at 3months. CABG group experience a significant increase at 3m. Depression & anxiety score accounted for most of the change in HRQoL (64-69%) whereas treatment accounted for less than 1% in HRQoL changes at 3m post treatment.
4	Lukkarinen, 2006	PCI vs CABG vs MED	100 100 80	2(12,96m)	PCI & CABG pts have greater QoL after 12 & 96 months compared to MED pts. CABG pts score significantly better on mobility, energy & pain. PCI pts had a sign. better HRQoL on emotional reactions, pain, mobility & energy at 96 months post.

NFU= Number of Follow Ups, PCI=Percutaneous Coronary Intervention, CABG=Coronary Bypass Graft Surgery, MED=Pharmacotherapy, d=days, w=weeks, m= months, pts= patients, NS= not significant, PTSD=post traumatic stress disorder

Table 3.3. Additional characteristics and main findings of studies included in the review

ID	Author	QoL Focus	N(prior to treatment)	*N* FU	Main findings
5	Škodová, 2011	PCI vs CABG vs MED	37 41 28	2(12,24m)	Significantly better QoL after all types of treatment. PCI and CABG groups demonstrate significantly greater mean change at physical aspects compared to MED, while CABG and MED groups demonstrate significantly greater mean change at mental aspects.
6	Zang, 2003	PCI vs CABG	488 500	2(6,12m)	Both CABG and PCI group demonstrate improvement in cardiac-related health status.
7	de Quadros, 2011	PCI predictors	110	2(6,12m)	Pts demonstrate a significant improvement after treatment. Male gender and QoL at baseline are significant predictors of post QoL level.
8	Denvir, 2006	PCI High vs low SES	1346	1(12m)	Pts demonstrate a significant improvement after treatment. Pts with low SES demonstrate significantly lower mean HRQoL score at baseline and 12 months post treatment compared to those with high SES.
9	Melberg, 2010	PCI non surg vs surg hospital	427	1(6m)	Significant improvement of QoL after treatment. Similar improvement in both types of hospitals.

NFU= Number of Follow Ups, PCI=Percutaneous Coronary Intervention, CABG=Coronary Bypass Graft Surgery, MED=Pharmacotherapy, d=days, w=weeks, m= months, pts= patients, NS= not significant, PTSD=post traumatic stress disorder

Table 3.3. Additional characteristics and main findings of studies included in the review

ID	Author	QoL Focus	N(prior to treatment)	*N* FU	Main findings
10	Li, 2012	PCI vs MED	287 298	1(6m)	PCI pts score higher in QOL 6 months post treatment compared to MED. PCI elderly patients, especially those ≥80 years of age, experienced the greatest benefit in QoL 6 months post treatment.
11	Viswanathan, 2011	PCI with & without prior CABG	2935	3(3,12,24,m)	Patients with previous CABG had less improvement in HRQOL after PCI. 24 months patients with prior CABG demonstrate worse physical functioning than at baseline.
12	Weilu, 2011	PCI stent effect	223	1(6m)	6 months after intervention, HRQOL increased in all 8 domains. Factors negatively related to 6 month scores seem to be: gender, age and activity with bodily pain; activity with physical functioning; age and activity with mental health, and general health.
13	Weintraub, 2008	PCI vs MED	969 958	7(1,3,6,12, 24,36m)	12 months after treatment pts underwent PCI demonstrate greater mean change compared to those with medication. 36 months after treatment NS difference between groups exists.
14	Wong, 2007	PCI	78	2(1,3m)	Increased scores after treatment. NS change at physical and social functioning.

NFU= Number of Follow Ups, PCI=Percutaneous Coronary Intervention, CABG=Coronary Bypass Graft Surgery, MED=Pharmacotherapy, d=days, w=weeks, m= months, pts= patients, NS= not significant, PTSD=post traumatic stress disorder

Table 3.3. Additional characteristics and main findings of studies included in the review

ID	Author	QoL Focus	N(prior to treatment)	*N* FU	Main findings
CABG interventions					
15	Azzopardi, 2009	CABG	87	3(6, 12, 24m)	Increased scores at 24 months-NS difference between pts and normative Australian individuals.
16	Barolia, 2011	CABG gender & age dif	65	1(1m)	Significant improvement in all domains. 1month post surgery females indicated significantly lower psychological health, while patients>60 yrs show significantly greatly social satisfaction.
17	Colak, 2008	CABG & comparison with norm	111	1(12m)	12m post treatment pts demonstrate improvement in all 6 domains of QoL. NS mean change to all subdomains.
18	Damgaard, 2011	CABQ vs CABG	170 161	2(3,11m)	Significant improvement 11months after treatment. NS differences between the two groups.
19	Gjeilo, 2012	CABG Gender & age effect	413	2(6,12m)	Female pts score lower compared to male at all measured time. Pts ≥75 years demonstrate lower general health, physical, social functioning and role emotional compared to younger patients. 12 months pts have almost equal HRQoL with non-cardiac population with an exemption to Role physical where ≥75 score rather lower.

NFU= Number of Follow Ups, PCI=Percutaneous Coronary Intervention, CABG=Coronary Bypass Graft Surgery, MED=Pharmacotherapy, d=days, w=weeks, m= months, pts= patients, NS= not significant, PTSD=post traumatic stress disorder

Table 3.3. Additional characteristics and main findings of studies included in the review

ID	Author	QoL Focus	N(prior to treatment)	*N* FU	Main findings
20	Houlind, 2012	CABG on vs off	900	1(6m)	Pts demonstrate a significant improvement in all domains. NS differences between groups.
21	Hunt, 2000	CABG	123	1(12m)	Pts demonstrate a significant improvement. NS gender differences.
22	Jensen, 2006	CABG on vs off	120	1(3m)	Pts demonstrate a significant improvement in all domains NS difference between groups.
23	Kiebzak, 2002	CABG	85	1(12m)	Improvement at 1yr. NS change in role emotional and general health subscales.
24	Krannich, 2007	CABG	142	2(10d,12m)	Pts demonstrate a significant improvement in all domains. At 1yr post GABG, pts demonstrate almost equal HRQoL with non-cardiac population.
25	Krecki, 2010	CABG vs MED	55 52	1(12m)	CABG pts demonstrate a significant improvement in all domains while MED pts demonstrate a significant improvement only to pain and limitation due to emotional problems.

NFU= Number of Follow Ups, PCI=Percutaneous Coronary Intervention, CABG=Coronary Bypass Graft Surgery, MED=Pharmacotherapy, d=days, w=weeks, m= months, pts= patients, NS= not significant, PTSD=post traumatic stress disorder

Table 3.3. Additional characteristics and main findings of studies included in the review

ID	Author	QoL Focus	N(prior to treatment)	*N* FU	Main findings
26	Lie, 2009	CABG Rehabilitation effects	185	2(6w,6m)	Improvement in QoL level. NS differences between groups.
27	Martin, 2012	CABG gender effect	495	1(6m)	Improvement in all domains. Women significantly score lower in baseline and 6 month post treatment compared to men.
28	Mathisen, 2005	CABG on vs off	120	3(3,6,12m)	QoL improved in both groups. NS differences between groups.
29	Merkouris, 2009	CABG age effect	63	2(4,12m)	Pts demonstrate a significant improvement in all domains except cognitive. Almost 1/3 of pts report cognitive decline. 12 months post treatment women significantly score lower compared to men.
30	Peric, 2010	CABG gender effect	243	1(6m)	Pts demonstrate improvement after treatment women score worse preoperative and postoperative compared to men.

NFU= Number of Follow Ups, PCI=Percutaneous Coronary Intervention, CABG=Coronary Bypass Graft Surgery, MED=Pharmacotherapy, d=days, w=weeks, m= months, pts= patients, NS= not significant, PTSD=post traumatic stress disorder

Table 3.3. Additional characteristics and main findings of studies included in the review

ID	Author	QoL Focus	N(prior to treatment)	*N* FU	Main findings
31	Pfaffenberger 2010	CABG anxiety, depression effect	54	2(4w,3m)	Pts demonstrate sig improvement after treatment Anxiety is a sig predictor of all QoL subdomains when MacNew is used as outcome measure, but only of Mental Health if SF-36 is used. Depression is a significant predictor of mental health only.
32	Pirraglia, 2003	CABG	590	1(6m)	Pts demonstrate a significant improvement after treatment.
33	Puskas, 2004	CABG on vs off	200	4(4,6w,6,12m)	Pts demonstrate a significant improvement after treatment. NS differences between groups.
34	Rothenhäusler 2010	CABG depression, PTSD	147	1(6m)	Pts demonstrate a significant improvement after treatment. Clinical depression and PTSD are related to lower improvement.

NFU= Number of Follow Ups, PCI=Percutaneous Coronary Intervention, CABG=Coronary Bypass Graft Surgery, MED=Pharmacotherapy, d=days, w=weeks, m= months, pts= patients, NS= not significant, PTSD=post traumatic stress disorder

3.4.1. The Overall Effect of CR on HRQoL

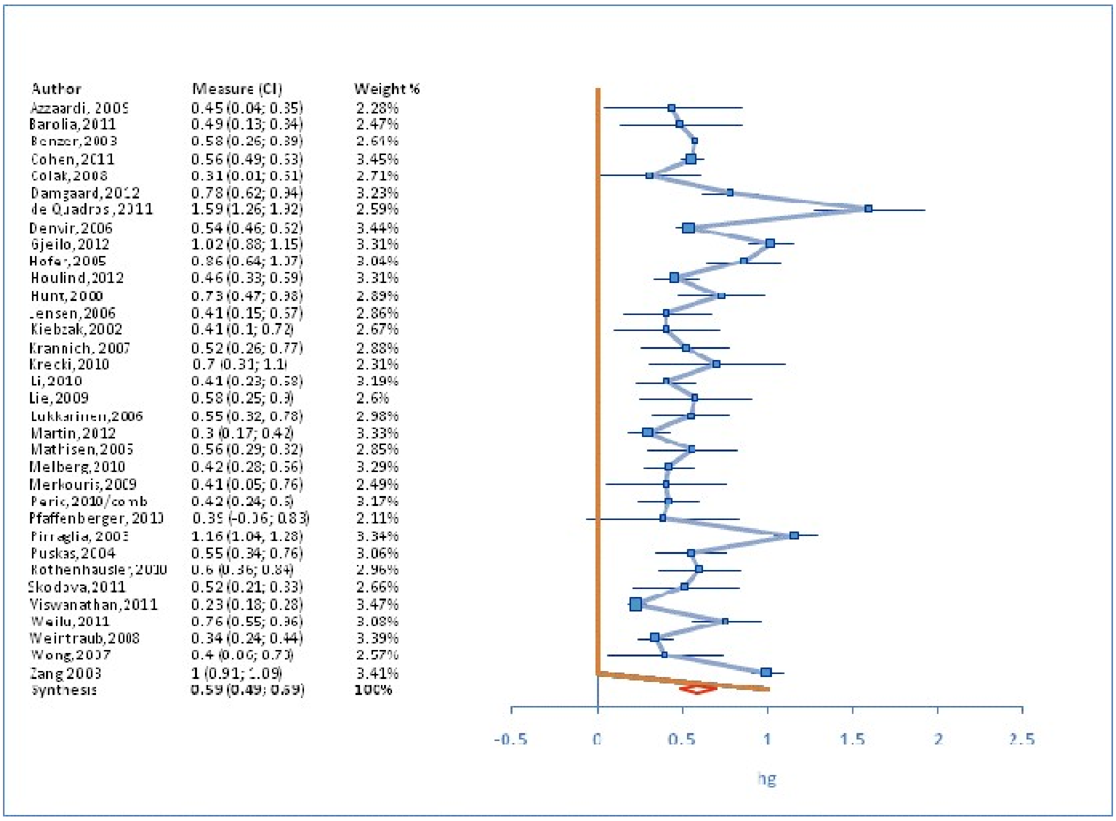
The overall effect size of CR on HRQoL after treatment, both for random and fixed effects models, is displayed in Table 3.4. Results suggested a moderate to low improvement on HRQoL after all types of treatments even after controlling for the length of study.

Table 3.4 Central tendency and variability in the impact of coronary treatment on Health Related Quality of Life

Groups	k	N (pre/last f-up)	Hedge’s g (95% CI)		Homogeneity of effect sizes	
			Fixed-effects assumptions	Random-effects assumptions	$I^{2\dagger}$	$\tau^{2\ddagger}$
Prior to sensitivity analysis						
All studies (CR)	34	14375/12502	0.53 (0.51, 0.56)	0.59 (0.48, 0.69)	93.02 (91.21, 94.45)	0.08
PCI groups	14	8027/6857	0.43 (0.39, 0.46)	0.55 (0.40, 0.69)	93.01 (89.93, 95.15)	0.06
CABG groups	26	6348/5645	0.67 (0.64, 0.71)	0.60 (0.48, 0.72)	89.95 (86.59, 92.47)	0.08
MED groups	7	1617/1039	0.25 (0.18, 0.33)	0.25 (0.18, 0.33)	0.00 (0.00, 70.81)	0.00
After exclusions of outliers						
All studies (CR)	19	5431/4656	0.54 (0.49, 0.57)	0.53 (0.47, 0.59)	29.92 (0.00, 59.85)	0.01
PCI groups	6	1955/1742	0.50 (0.44, 0.57)	0.48 (0.38, 0.59)	52.02 (0.00, 79.58)	0.01
CABG groups	15	3476/2914	0.54 (0.49, 0.59)	0.54 (0.47, 0.60)	25.42 (0.00, 0.45)	0.01
MED groups	3	390/290	0.32(0.17,0.43)	0.32(0.17,0.43)	0.00 (0.00, 89.60)	0.00

†based on precision ‡based on variance
I^2 = 25 accounts as having minor heterogeneity, I^2 = 50 moderate, and I^2 = 75 as having considerable heterogeneity)
$\tau^2 > 1$, considerable heterogeneity is present

The exact contribution per study on the overall effect of coronary revascularization (using random effects assumptions) on patients' HRQoL can been seen in Figure 3.3.



Author	Measure (CI)	Weight %
Azzaardi, 2005	0.45 (0.04; 0.85)	2.28%
Barolia,2011	0.49 (0.13; 0.84)	2.47%
Benzer,2003	0.58 (0.26; 0.89)	2.61%
Cohen,2011	0.56 (0.49; 0.63)	3.45%
Colak,2008	0.31 (0.01; 0.61)	2.71%
Damgaard,2012	0.78 (0.62; 0.94)	3.23%
de Quadros,2011	1.59 (1.26; 1.92)	2.59%
Denvir,2006	0.54 (0.46; 0.62)	3.44%
Gjeilo,2012	1.02 (0.88; 1.15)	3.31%
Hofer,2005	0.86 (0.64; 1.07)	3.04%
Houlind,2012	0.46 (0.33; 0.59)	3.31%
Hunt,2000	0.73 (0.47; 0.98)	2.89%
Jensen,2006	0.41 (0.15; 0.67)	2.86%
Kiebzak,2002	0.41 (0.1; 0.72)	2.67%
Krannich, 2007	0.52 (0.26; 0.77)	2.88%
Krecki,2010	0.7 (0.31; 1.1)	2.31%
Li,2010	0.41 (0.23; 0.58)	3.19%
Lie,2009	0.58 (0.25; 0.9)	2.6%
Lukkarinen,2006	0.55 (0.32, 0.78)	2.98%
Martin,2012	0.3 (0.17; 0.42)	3.33%
Mathisen,2005	0.56 (0.29; 0.82)	2.85%
Melberg,2010	0.42 (0.28; 0.56)	3.29%
Merkouris,2009	0.41 (0.05; 0.76)	2.49%
Paric,2010/comb	0.42 (0.24; 0.6)	3.17%
Pfaffenberger,2010	0.39 (-0.06; 0.83)	2.11%
Pirraglia,2003	1.16 (1.04, 1.28)	3.34%
Puskas,2004	0.55 (0.34; 0.76)	3.06%
Rothenhausler,2010	0.6 (0.36; 0.84)	2.96%
Skodova,2011	0.52 (0.21; 0.83)	2.66%
Viswanathan,2011	0.23 (0.18; 0.28)	3.47%
Weilu,2011	0.76 (0.55; 0.96)	3.08%
Weintraub,2008	0.34 (0.24; 0.44)	3.39%
Wong,2007	0.4 (0.06; 0.73)	2.57%
Zang 2003	1 (0.91; 1.09)	3.41%
Synthesis	0.59 (0.49; 0.69)	100%

Figure 3.3. Forest plot diagram showing the effect (hg) of CR within each study and the overall effect (k=34) after synthesis. CI= confidence interval. Q=472.67, p<0.005, I^2=93.02%

Univariate Analysis of Variance showed a significant difference among treatment types ($F(2, 44) = 4.57$, p<.05). The weighted multiple comparisons (using a Bonferroni post hoc test) revealed that patients who underwent CABG or PCI experienced a significantly greater improvement of HRQoL compared to patients treated with MED while patients treated with PCI and CABG did not differ significantly from each other (CABG>MED, mean difference (md)= 0.35, p<.005; PCI>MED, md=0.32, p<.05; CABG>PCI, md=0.03, p= 0.72).

Furthermore, when the τ^2 index is used to detect the level of heterogeneity on CR effect size, all studies seem to be homogeneous (τ^2=0.08), while when the I^2 estimate is used a high level of heterogeneity (I^2 = 93%) is present, suggesting there are studies that should be excluded as outliers.

When examining for publications biases, the trim-and fill method identified only one study as being necessary to be added to normalize effect size distribution. The results of a Begg's test (z=0.03, p=0.98) and Egger's test [t=4.98 (CI=0.25,0.61), p=0.19] rejected the probability of a significant publication bias.

Sensitivity analysis demonstrated that 15 studies should be excluded as outliers (Table 3.4). Even after exclusion, the combined effect size remained moderate for both coronary revascularization and low for MED. Overall the mean difference became slightly lower but no essential changes were detected, [F(2, 32) =10.42, p<0.001, CABG>MED, md= 0.27, p<0.001; PCI>MED, md=0.20, p<0.001, CABG>PCI, md=0.07, p= 0.28).

The forest plots (Figure 3.4) show a graphical representation of effects sizes and CI after sensitivity analysis.

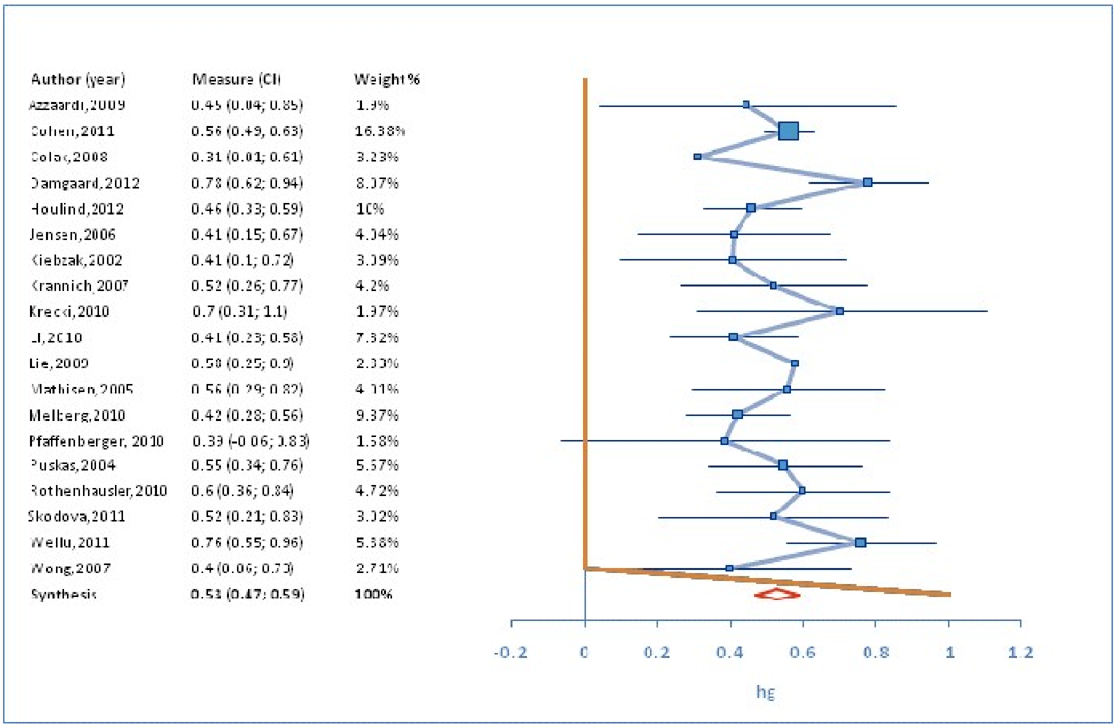


Figure 3.4 Forest plot diagram showing the effect (hg) of CR within each study and the overall effect (*k*=19) after excluding outliers. CI= confidence interval. *Q*=40.35, *p*<0.005, I^2=50.44%

3.4.2. Moderator analysis

Including all 34 studies, three factors were associated with the outcome: the type of instrument, length of the study (time) and study quality. Factors examined apart from the three presented were study design (single vs two or more treatments), demographic factors (mean age, proportion of female participants), and proportion of smokers; these factors were not associated with the outcome (p>0.05). The multiple linear regression of mean difference weighted by the inverse variance demonstrated that these moderators accounted for 93.4% of the variability in the outcome. In fact, 19.4% of the variance can be accounted by quality of study [*F*(1, 31) = 7.43, *p*<0.05], 73% by type of instrument [*F*(7, 25) = 49.62, *p*<0.001], while time (study duration) accounts for a tiny but significant 1% of the variance [$F(1, 24) = 8.21$, $p<0.05$]. Specifically, the analysis indicated that there is a larger effect for lower quality studies (b=-2.69, $t(33) = -2.36$, p=0.025) and short term follow-ups (b=-0.52, $t(33) = -2.87$, p=0.007) and that the effect size depends on the measure used; a larger effect was obtained for disease-specific measures (e.g. larger effect for the disease-specific measure SAQ (b=20.83, $t(33)$= 10.25, $p<0.001$) than for the generic SF-36 (b=11.91, $t(33)$= 14.66, $p<0.001$)).

When the analysis was repeated with 19 studies (after excluding outliers and poorer quality studies), the effect of CR on HRQoL was significant. Quality of study emerged as a significant predictor. The effect of time could not be detected as the pooled variance was reduced considerably. Also, measurement type could be not analysed as the majority of remaining studies (89%) used the SF-36.

3.4.2.1. *Subgroup analysis: Psychosocial vs Physical domains*

The subgroup analysis was conducted with studies using the SF-36 as an instrument for capturing patients' HRQoL after CR to detect any differences in the effect of CR on HRQoL between psychosocial and physical subdomains. Overall, in 21 studies (participants n=5,232) findings revealed that CR has a greater impact on the physical than on the psychosocial domain (md= 4.45, 95% CI, 3.93 to 5.20; $p<0.001$; τ^2=5.98).

The mean difference between physical and psychosocial domain was significant for CABG ($p<0.001$) but not for PCI (p= 0. 173; Figure 3.5). Meta-regression analysis for possible moderators in this difference in CABG effect between the physical and psychosocial dimensions did not reveal any significant result suggesting that the effect of CABG is not moderated by any of the variables measured. In short, results suggest that PCI impacts on both patients' physical and psychosocial functioning equally, whereas CABG has a greater effect on the physical functioning compared to psychosocial functioning.

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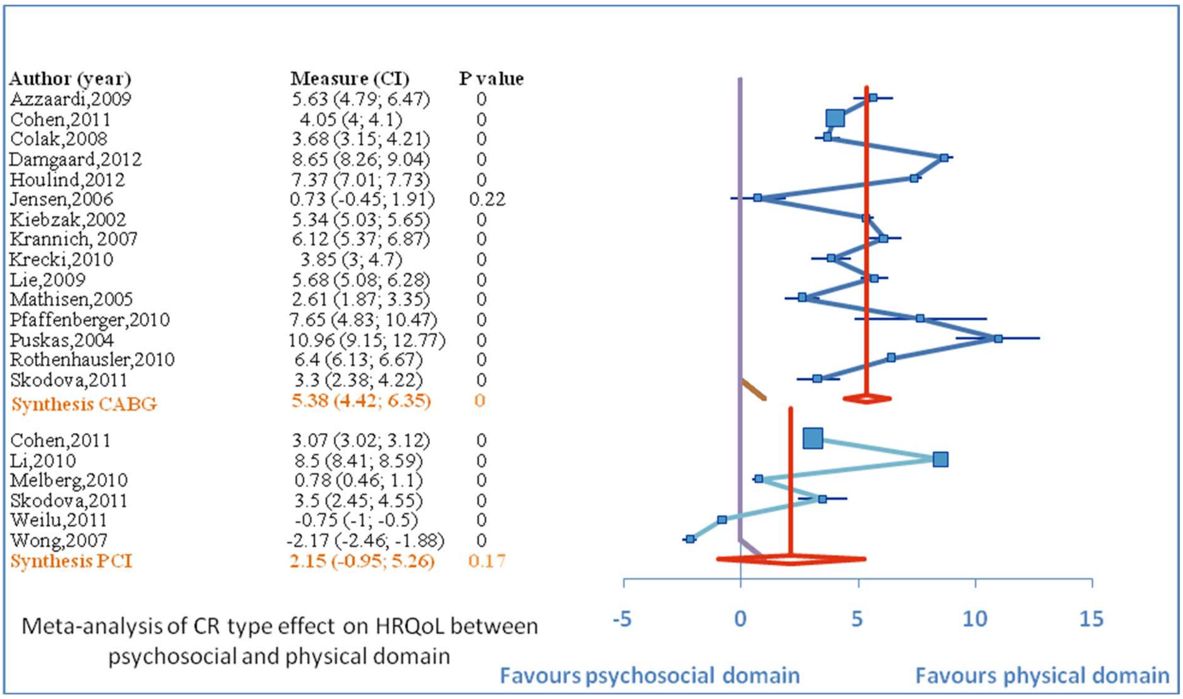

Author (year)	Measure (CI)	P value
Azzaardi,2009	5.63 (4.79; 6.47)	0
Cohen,2011	4.05 (4; 4.1)	0
Colak,2008	3.68 (3.15; 4.21)	0
Damgaard,2012	8.65 (8.26; 9.04)	0
Houlind,2012	7.37 (7.01; 7.73)	0
Jensen,2006	0.73 (-0.45; 1.91)	0.22
Kiebzak,2002	5.34 (5.03; 5.65)	0
Krannich, 2007	6.12 (5.37; 6.87)	0
Krecki,2010	3.85 (3; 4.7)	0
Lie,2009	5.68 (5.08; 6.28)	0
Mathisen,2005	2.61 (1.87; 3.35)	0
Pfaffenberger,2010	7.65 (4.83; 10.47)	0
Puskas,2004	10.96 (9.15; 12.77)	0
Rothenhausler,2010	6.4 (6.13; 6.67)	0
Skodova,2011	3.3 (2.38; 4.22)	0
Synthesis CABG	5.38 (4.42; 6.35)	0
Cohen,2011	3.07 (3.02; 3.12)	0
Li,2010	8.5 (8.41; 8.59)	0
Melberg,2010	0.78 (0.46; 1.1)	0
Skodova,2011	3.5 (2.45; 4.55)	0
Weilu,2011	-0.75 (-1; -0.5)	0
Wong,2007	-2.17 (-2.46; -1.88)	0
Synthesis PCI	2.15 (-0.95; 5.26)	0.17

Meta-analysis of CR type effect on HRQoL between psychosocial and physical domain

Figure 3.5 Forest plots for graphical representation of mean difference and CI between psychosocial and physical domains per CR type

3.5. Discussion

3.5.1. Overview of the results

The present study reviewed 34 primary studies, identified as suitable based on the inclusion criteria. Strong evidence of the positive influence of the treatment on CHD patients' HRQoL emerged from the meta-analysis. Results showed that there was a significant increase from pre to post HRQoL level; a moderate effect size was revealed for both CR types (PCI and CABG) and a low effect size was revealed for MED. These findings are partially in line with Blankenship, et al.'s (2013) conclusions who highlighted the superiority of PCI over medical treatment, and partially consistent with Jokinen et al. (2010) who highlighted the superiority of CABG over drug treatment. The CR procedures did not differ significantly in their effect on HRQoL which is consistent with Blankenship et al.'s (2013) and Jokinen et al.'s (2010) conclusions.

Regarding the maintenance of improved HRQoL most studies suggest that the positive effect of CR is long lasting, but decreases a little over years. This evidence is in line with Blankenship et al.'s (2013) conclusions.

Concerning moderators, from all the variables examined, for both CR procedures only type of instrument used and study quality were strong moderators of the outcome. A discussion can be found in the literature about the instruments used in HRQoL research. In the current analysis all studies used valid and reliable measures but the majority used generic rather than disease-specific measures. Most studies using a disease-specific instrument reported a greater effect size than studies using generic measures. As there is no consensus definition of QoL, results produced by various measurements may vary significantly as each instrument may include common as well as different domains based on the authors' theoretical concepts (Kendel, 2009). While generic measures like the SF-36 (Ware & Sherbourne, 1992) are valid and reliable, some items are likely to be less sensitive in detecting treatment effects (Guyatt et al., 2007; Wiebe, Guyatt, Weaver, Matijevic, & Sidwell, 2003) for specific health conditions (Jordan-Marsh, 2002).

Neither mean age nor the proportion of female participants was associated with the level of the effect size of CR on patients' HRQoL. These findings are in line with Lansky et al.'s (2005) and Hartman et al.'s (2014) conclusions, namely that females' worse outcome compared to males may lie in the higher risk profile of females referred to CR and that the difference in mortality or health outcomes that appears in some studies is related to risk factors other than sex. In short, the findings of the present study imply that both age and sex might be not considered risk factors when treatment decisions about coronary artery disease are made, at least in relation to HRQoL.

Subgroups analysis showed a greater effect for CABG on physical functioning compared to psychosocial functioning, but not for PCI. This finding implies that PCI may have a more "universal" effect on HRQoL than CABG. The literature supports these results (e.g. Abdallah et al., 2013). It should be mentioned, however, that research evidence indicates that this difference diminishes over time (Abdallah et al., 2013). Moreover, this result may suggest that when the overall effect is calculated (i.e. incorporating both physical and psychocial aspects of HRQoL) the PCI effect may not be influenced but the CABG effect may be dramatically reduced, providing potentially misleading results. Thus, one the one hand, subgroup analysis should be considered as an essential part of a researcher's analysis in order to highlight differences in subdomains effects as well as to avoid oversimplicity. On the other hand, the presence of difference in the mean change between the two subdomains in CABG treatment or the absence in the mean change between the two subdomains in PCI treatment might be related to the outcome measure used. As discussed earlier, the SF-36 (Ware & Sherbourne, 1992) is a generic measure meaning that it may leave disease/treatment-specific factors (e.g. adverse effects) underestimated (Chen, Li, & Kochen, 2005). Furthermore, other influential psychosocial aspects may remain unexplored as they cannot be captured solely by quantitative approaches (Mitchell, Benito-León, González, & Rivera-Navarro, 2005).

A large literature focuses on a debate about the appropriate index for detecting heterogeneity level in continuous data. Findings may change dramatically depending on the index chosen. The findings in the present study highlight this difference. When the τ^2 index is used, homogeneity among studies is suggested and type of instrument as well as female sex appear to have a moderating effect on the effect of CR on improvements in HRQoL. However, when the I^2 index is chosen, 15 studies would have to be excluded as outliers to increase homogeneity. With the subsequent decrease in heterogeneity, the effect of CABG and PCI on improvement in HRQoL was maintained but none of the variables examined had a significant moderating effect. This highlights two basic issues: a) that statisticians should focus on resolving this issue to allow researcher to detect the authentic heterogeneity level and b) that findings from heterogeneous studies should be considered carefully before any recommendations are made.

3.5.2. Limitations and Strengths

Several limitations are present in this study. First of all, only a few studies examined the severity of angina prior to treatment, or provided data on complex coronary lesions. As a result such important variables were not included in the analysis, raising questions about the precision of the estimation of the effect of CR on HRQoL. Similarly, stressful events, changes in lifestyle, adherence to medical advice and other potentially relevant factors are not considered since these were not routinely measured in the studies reviewed. Secondly, the majority of studies do not include control groups or alternative treatment. Only 30% of the studies reviewed presented comparisons between types of CR treatment, which may result in a misleading conclusion. According to the literature, studies using between-group designs demonstrate lower effect sizes in the change in HRQoL compared to single group designs due to the way effect size is estimated (Morris & DeShon, 2002). Thirdly, as this review focused on CR treatment of CHD, a comparison with medical treatment was made only via studies investigating this type of treatment thus conclusions might be doubtful. Furthermore, in the studies included in many cases the type of medication patients used was not systematically reported. Even if it was described, it differed dramatically between medical treatment groups, suggesting methodological biases that could not be controlled.

The strengths of this study are the efforts to adopt a rigorous methodology. Papers included were not limited to having been written in English or by cultural constraints. Furthermore, it placed emphasis on the last decade of research evidence highlighting that various factors, such as age, identified in the past as moderators, do not influence the beneficial effect of CR on patients' HRQoL. Thus, decision making regarding treatment is enhanced. To our knowledge, this is the first systematic review with meta-analysis that summarizes, evaluates and synthesizes research-based evidence concerning coronary patients' HRQoL following CR.

3.5.3. Recommendations

Measurement of HRQoL should be included in the routine assessment of coronary patients in order to have a complete picture as well as enhance conclusions about the effectiveness of treatment. Cardiothoracic surgeons should pay attention to their patients' psychosocial functioning too and if necessary advise them to seek professional guidance and support in order to maximize well-being.

Further high quality research should be developed in order to enable the scientific community to establish rigorous conclusions about factors that influence the effect of CR on patients' HRQoL. Specifically, more RCTs and Cohort studies (including patients with different treatment types, i.e. MED, PCI, CABG) are needed in order to inform health care professionals about the beneficial aspects of each treatment. More variables should be included in each study examining additional issues such as medical (e.g. angina), behavioural (e.g. adherence to medication, diabetes management, obesity) and psychological (e.g. stressful life events, emotional distress, personality) in order to identify relevant predictors. Studies should also include multiple time points in measuring HRQoL. More studies using disease-specific HRQoL instruments should also be conducted as the literature suggests disease-specific instruments allow clearer and more accurate conclusions than those derived from general instruments. Studies should also report all HRQoL subdomains, not just totals, and all relevant indices should be presented (e.g. including pre-post mean scores and *p* values) in order to avoid transformations and calculations by reviewers that might lead to misleading results (Higgins & Green, 2008; Higgins et al., 2011).

3.6.Conclusion

This systematic review with a meta-analysis provides evidence about the beneficial impact of coronary interventions and operations on patients' HRQoL. These results may help medical doctors to not only to justify their decision to operate but also to be able to inform their patients about the pros and cons of each CR type in terms of HRQoL, a need partially highlighted by many researchers (Creswell & Clark, 2007; Koch, Khandwala, & Blackstone, 2008). Best practice in research requires careful methodological design to maximize the quality of studies to produce trustworthy conclusions. Researchers should carefully select the QoL instrument because it plays an important role in the effect estimation and in detecting moderators and it may affect the results and, thus, conclusions. Despite the gains that have been accomplished, considerable challenges and questions remain to be addressed. Further rigorous research should be developed to illuminate the dark spots in this area.

Regarding the present thesis, these findings have guided the research to identify a disease/treatment specific instrument for assessing CHD individuals' subjective evaluations of their HRQoL following CR as well as to design and conduct a longitudinal mixed methods study to investigate the influence of various clinical, demographic, and behavioural features on the outcome in terms of statistical associations (of overall HRQoL and its subdomains) and the lived experience.

Chapter Four

Method

4.1.Introduction

This thesis has set out to explore individuals' perspectives on their HRQoL prior to coronary revascularization (CR), 3 and 12 months after (CR). Building on the knowledge acquired by a) the overview of the literature on coronary heart disease (CHD) and CR treatment (chapter 1), b) the overview of theoretical and research considerations on the concept of Health Related Quality of Life (HRQoL) (chapter 2) as well as c) the results of the systematic review with a meta-analysis guided the researcher to adopt a mixed methods approach for achieving the main aim of the study.

This chapter initially presents a short discussion of philosophical and methodological issues in research that led to the decision to use a mixed methods design (introduced in chapter 2, section 2.5.2). Then, it outlines the overall research design that involves two studies: a) the translation, adaptation and validation of the CROQ instrument into Greek, since the study was conducted in Greece and b) a longitudinal mixed methods study with two research components; the first is the quantitative component (the longitudinal, quantitative part of the study) aimed mainly to detect changes in CHD patients' HRQoL over a one-year period following CR and potential predictors of the outcome, and the second is the qualitative component (qualitative part of the study) aimed at capturing the lived experience of CHD individuals one year after CR, placing particular emphasis on a deeper understanding of some of the quantitative results.

Methods of data collection and data analysis employed in each study and issues related to research ethics and research quality assurance will be presented in the following sections.

4.1.1.The choice of a mixed methods research design

4.1.1.1. Paradigm considerations in research

According to the literature (e.g. Bryman, 2015; Creswell, 2014; Hussain, Elyas, & Nasseef, 2013) research is defined as a systematic enquiry that aims to produce and expand knowledge. However, the way that researchers try to address their questions and contribute to the body of knowledge is guided by the paradigm they adopt. Paradigm refers to a set of assumptions which underpins the researcher's worldview and thus guides their work in terms of *ontology*, i.e., their position on what constitutes reality, what is the nature of reality; *epistemology,* their assumption about what constitutes valid knowledge; *methodology*, the theory that underpins the principles of the research, how can the researcher go about obtaining the desired knowledge and understanding; and *methods*, the specific techniques and procedures that are used to collect and analyze data (Guba & Lincoln, 2005). The literature suggests that the two traditional paradigms that guide researchers are positivism and interpretivism (Creswell, 2013; Mackenzie, & Knipe, 2006). This categorization can be criticized as very simplistic (Reichardt and Rallis, 1994) as many more paradigms exist in the field of psychological research (e.g. critical realism, constructivism (which occasionally is used interchangeably with interpretivism; Creswell, 2013)). However, the presentation of such a simplistic approach is mainly for introducing the main paradigms that underpin quantitative and qualitative approaches to research in the social and behavioural sciences.

Briefly, the positivist ontological position is close to realism i.e. "reality is out there in the world and driven by permanent natural laws" (Guba & Lincoln, 2005, p. 201) while the epistemology of positivism stresses the assumption that the knowledge is objective and value free and can be obtained solely through the application of a scientific method. In other words, the social world can be studied in the same way that the natural world is studied. The aims of positivism are description, prediction, control, and explanation while the goal of positivism is to discover universal laws (Mackenzie & Knipe, 2006; Hussain, Elyas, & Nasseef, 2013). The positivist view restrics research to what can be observed, leaving areas such as subjective perceptions, feelings, thinking underinvestigated. This led to the rejection of the narrow positivist view and to the development of postpositivism. Post-positivists maintain the assumption of theory verification, i.e. hold the belief that laws and theories can explain various realities remaining though open to the verification establishing the "truth" by talking about "supporting" rather than "proving" hypotheses. The role of evidence is to establish a high degree of probability, rather than certainty, that something is "true" (Guba & Lincoln, 2005; Polit, 2001 in Giddings & Grant, 2007). Also, post-positivists, although maintaining that it is important to establish generalizability, acknowledge that is rather hard as they accept that other factors such as culture may influence the phenomenon under investigation. Post-positivism is linked with quantitative research methods (Creswell, 2014; Howe, 1988; Scotland, 2012).

On the other hand, ontological position of interpretivism is close to relativism, i.e. "reality is constructed and interpreted by individuals according to their ideological and cultural positions" (p.2376, Hussain, Elyas, & Nasseef, 2013), while its epistemological position is that of subjectivism, i.e. knowledge is personal and unique (Cohen, Manion, & Morrison, 2013). The role of the researcher is not limited to demonstrating how individuals or social groups interpret the world around them. Interpretation of an individual's understanding in relation to existing theories is an essential concept (Bryman, 2015; Cohen, Manion, & Morrison, 2013). The aims of interpretivism are to explore and understand not only the complexity of individual experience or social phenomena but also to give meaning (Hussain, Elyas, & Nasseef, 2013). Interpretivism is linked with qualitative research methods (Creswell, 2013; Howe, 1988; Scotland, 2012).

These differences in researchers' worldview have led to an ongoing debate between quantitative and qualitative researchers; the well-known war of paradigms. However, as has been discussed in section 2.5.2, both research approaches (quantitative and qualitative) have strengths and limitations (Yilmaz, 2013; Creswell & Plano-Clark, 2007). A growing number of researchers (e.g. Bryman, 2006; Hall, 2012; Teddlie and Tashakkori, 2003; Greene, 2007, Creswell & Plano-Clark, 2007) have challenged this dichotomous view arguing that quantitative and qualitative research can be combined leading to the maximization of the knowledge; this stance led to the development of mixed methods research and various paradigms encompassing mixed methods (e.g. pragmatism; Teddlie & Tashakkori, 2003).

Many researchers have challenged the mixed methods stance suggesting that these two dominant paradigms are incompatible as they hold different points of view and fundamentally differ in epistemological and ontological assumptions; the incompatibility thesis (Howe, 1988). As discussed earlier, Reichardt and Rallis (1994) among many others (e.g. Howe, 1988; Creswell & Plano-Clark, 2007) are opposed to the incompatibility thesis based on the "paradigm-method fit" suggesting that different philosophical paradigms and methods can be compatible and that paradigms and methods are not "inherently linked".

One of the most widely recognized and adopted paradigms in mixed methods research is that of pragmatism (Teddlie & Tashakkori, 2003; Creswell, 2014). Pragmatism refers to a "deconstructive" paradigm (Teddlie & Tashakkori, 2003) that focuses on the use of mixed methods in research, "sidesteps the contentious issues of truth and reality" (p. 8, Feilzer, 2010), and “focuses instead on ‘what works’ as the truth regarding the research questions under investigation” (p. 713, Tashakkori & Teddlie 2003,). Pragmatism “accepts, philosophically that there are singular and multiple realities that are open to empirical inquiry and orients itself toward solving practical problems in the ‘real world’ ”(p. 8, Feilzer, 2010).

4.1.1.2. Choosing a mixed methods longitudinal sequential explanatory research design

As mentioned elsewhere, pragmatism underpins the worldview of the author of this thesis. She adopts the definition by Creswell and colleagues (2003) that a mixed methods study refers to the collection and analysis of both quantitative and qualitative data in a single study in which the data can be collected concurrently or sequentially (based on aims and research questions) and involves the integration of the data at the final stage of research. By employing a mixed methods approach a more comprehensive understanding of the research area can be established as level of change can be detected, various predictors can be explored and the richness of subjective experience can be captured.

A mixed methods longitudinal sequential explanatory research design was selected for the main research study. This design is perceived as the most suitable design for the particular study for several reasons. Firstly, the longitudinal aspect was chosen based on the notion that HRQoL is a dynamic concept that changes over time, thus repeated measures would allow a greater understanding of the pattern of change. Secondly, the sequential explanatory aspects, where priority is given to quantitative data (the quantitative repeated data collection and analysis are carried out first and then qualitative data are collected and analysed) was chosen based on the assumption that quantitative data and their analysis would provide a general understanding of the research questions (e.g. trends in HRQoL change) while the qualitative data and analysis using the Interpretative Phenomenological Analysis (IPA) approach could refine and provide a deeper understanding by exploring participants' point of view and experience. Thirdly, the approach allows the integration of the findings from each part (quantitative and qualitative) at the end, at the interpretation stage, allowing the presentation of converging, diverging and complementary insights (in terms both of new, additional issues and explanation; Creswell & Plano-Clark, 2011).

For example, the quantitative results may reveal an improvement in HRQoL post treatment while the qualitative analysis may suggest *how* individuals define HRQoL one year later and whether individuals actually experience the degree of improvement suggested by the quantitative results as well as reveal other related concepts (e.g. post traumatic growth that may influence evaluation of quality of life, as discussed in Chapter 2).

At this point it is essential to explain the methodological approach chosen for the qualitative study; the Interpretative Phenomenological Analysis (IPA; Pietkiewicz & Smith, 2014; Smith, Flowers, & Larkin, 2009). IPA was chosen after considering four main issues. First of all, IPA best suits the research aims as it has been developed in order to explore individuals' understanding and sense-making of various phenomena as experienced in participants' own words. Secondly, it is interpretative with a double hermeneutic heuristic (Smith, 2004). In other words, the researcher makes an effort to understand and make sense of individuals' points of view and experience, with an emphasis on psychological interpretation, i.e., to extract meaning beyond individuals' direct claims. As Smith and colleagues (2009) argue, a good IPA should reveal more about the individuals than the individuals are aware of themselves. Thirdly, IPA is idiographic in nature. It treats each case as a case study and afterwards explores convergence and divergence across themes from the analysis of different interviews (Smith et al., 2009). This approach suggests that a phenomenon is experienced by an individual in a particular and unique way and allows the researcher to detect and illustrate important theme(s) even if they are only produced by one participant (Smith, et al., 2009). As Smith and Osborn (2003) state "The resulting analysis respects both theoretical convergence but also, within that, individual idiosyncrasy" (p.75). This facility for highlighting unique perspectives as well as shared experiences is one of the cornerstones of IPA (Smith, 2010; Smith and Osborn, 2003). The two latter aspects (i.e. idiography and interpretation) differentiate IPA from thematic analysis. This is important to be highlighted because there is a general misapprehension that IPA is a form of thematic analysis (Hefferon & Gil-Rodriguez, 2011). Idiography and interpretation guide researchers who endorse the IPA approach to recruit small purposeful samples (four to ten), have short interview schedules and starting with a generic question giving participants the opportunity to set the parameters of interest. This in turn allows researchers to explore in depth these parameters in addition to specified open-ended questions of the research schedule to gain a greater and deeper understanding (Hefferon & Gil-Rodriguez, 2011; Smith et al., 2009). Fourthly, findings from IPA studies can influence and contribute not only to theory but also to best health care services. Regarding theory, analysis can offer the development of an explanatory model, or elements that might be added to an existing theoretical framework. Concerning best health care services the better understanding of lived experiences regarding a health topic and health care can improve service provision as it can guide health care providers in their understanding of, for example, what behaviour should be targeted and how healthy lifestyles can be promoted (Fade, 2004; Pringle, Drummond, McLafferty, & Hendy, 2011).

As stated earlier IPA was found more suitable compared to other qualitative approaches, e.g. Thematic Analysis (TA; Braun & Clark, 2006), Grounded Theory (GT; Strauss, & Corbin, 2015), Discourse Analysis (DA; Jorgensen, & Phillips, 2002), Ethnography (E; Atkinson, & Pugsley, 2005).

TA as stated above often seems very similar to IPA, especially if it is guided by the phenomenological stance. It focuses on capturing commonly recurring themes (Braun & Wilkinson, 2003), on patterning meaning across the dataset that may answer the research question(s). In other words this approach places emphasis on predominant themes across participants' accounts, it does not aim to capture ideographic aspects (Braun & Clark, 2006; 2013). This makes TA and IPA differ markedly (Braun & Clark, 2006), both in sample size required and in the analysis steps. Briefly, the TA needs a larger sample compared to IPA (Smith et al., 2009), since the focus of TA is on patterning meaning, whereas IPA needs a smaller sample size (1-10) in order to maintain a more idiographic focus (Pietkiewicz & Smith, 2014; Smith et al., 2009). As Smith et al. (2009) suggest "less is more". Furthermore, IPA focuses on developing each stage of the analysis for each data item (case by case), before moving to the next in order to capture even the less frequent themes, whereas TA involves developing each stage of analysis across the whole dataset (Braun & Clark, 2006; Pietkiewicz & Smith, 2014; Smith et al., 2009).

GT (Strauss, & Corbin, 2015) was excluded due to the fact that it aims to detect factors that may explain the phenomenon experienced, usually rooted sociologically, not to understand the essence and meaning of the experience per se. It focuses on exploring common experiences to inductively develop a theory based usually on a large sample (10-30) and by using triangulation both in data collection (more than one type, e.g. interviews and focus group) and analysis (more than one analyst). On the other hand, IPA is more psychologically rooted focusing on the personal experience of a small sample (1-10) (Smith et al., 2009).

DA (Jorgensen & Phillips, 2002) was excluded as it aims to explore the language that people use and how it relates to the dominant discourses that influence individuals' ways of thinking, speaking and acting; which is far from the study's aim.

Finally, Ethnography (Atkinson & Pugsley, 2005; Mackenzie, 1994) was ruled out as it focuses on exploring the shared culture (e.g. values, beliefs, behaviours) of a group of people via the viewpoint of an insider; which again is rather dissimilar to the study's aim.

4.1.2.Overall research design and research questions

As discussed in the rationale for the thesis in Chapter 2, taking into consideration the findings of the systematic review, the author's endorsement of a mixed methods (pragmatic) stance and the extremely limited research in this field in Greece, two studies have been carried out (see Figure 4.1 for a graphical illustration of the studies and their procedure):

(1) The translation, adaptation and validation of the Coronary Revascularization Outcome Questionnaire (CROQ) into Greek, since the study would be conducted with Greek patients. This study addresses the following research questions:

1. Does the Coronary Revascularization Outcome Questionnaire Greek version (CROQ-Gr) seem straightforward and relevant to Greek patients?
2. Is there evidence to support the reliability of the CROQ-Gr?
3. Is there evidence to support the validity (both internal and external) of the CROQ-Gr?
4. Is there evidence to support that the CROQ-Gr is sensitive to change?

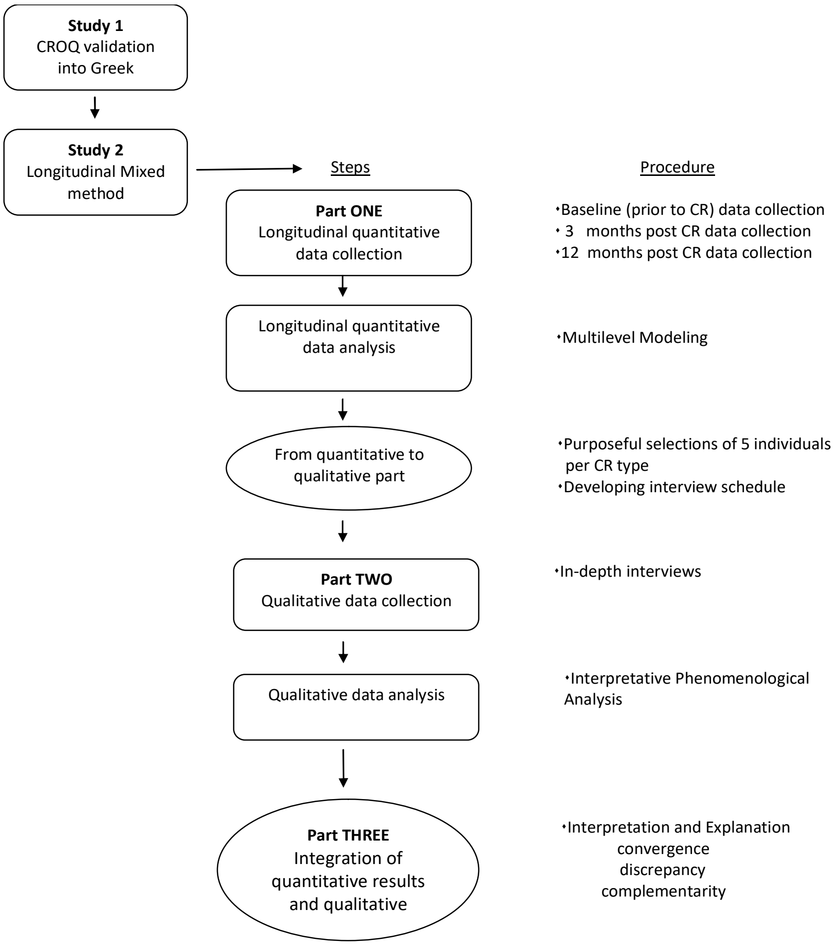

Figure 4.1 Graphical illustration of the study conducted and mixed methods steps and procedure.

(2) The longitudinal mixed methods study, the main study of this thesis, which consists of three main parts with two research components. In particular,

a) ***Part 1*** (presented in Chapter 6), the longitudinal quantitative component aimed to detect changes in patients' HRQoL (both overall and its subdomains) following CR over a 12-month period based on individuals' subjective evaluation as captured by the CROQ-Gr, exploring as well as various behavioural, clinical and demographic predictors. Also this study, on the basis of the recommendations of the meta-analysis, incorporates a number of features in order to improve issues and problems identified in the design of previous studies. This component addresses the following research questions:

1) What is the trajectory of change in HRQoL over a one-year period post CR?
2) Does the type of CR influence the level of change?
3) What are the predictors of change in HRQoL over a one-year period?
4) What is the trajectory of change in HRQoL specific aspects (symptoms, physical, psychosocial, cognitive function) and what are the predictors of change in each subdomain?

b) ***Part 2*** (presented in Chapter 7), the qualitative component aimed to capture individuals' lived experience, their view and understanding of themselves and their life approximately 12 months after treatment as well as to explain individual differences highlighted by the quantitative results. This component focused on "How do individuals make sense of HRQoL after CR?" Consequently, the following research questions are addressed:

1) How does having been diagnosed with CHD and undergone CR influence CHD patients' perspectives regarding QoL?
2) How do CHD individuals experience life changes after CR and what might be the adjustment process that follows?
3) What concerns do CHD individuals have about life style modifications, in particular smoking cessation?

c) ***Part 3*** (presented within Chapter 8), the integration of the findings of both components (interpretation) aimed to address the following research questions:

1) How do Greek individuals with CHD conceptualize HRQoL?
2) How do aspects of the disease experience after CR and meaning-making processes inform individuals' perspectives on their HRQoL?

4.1.3. Participants and recruitment

All participating patients were recruited at the Cardiology departments of three general hospitals: Metropolitan (private hospital), Attiko (public hospital), Thriasio (public hospital), in the prefecture of Attica, Greece. The main inclusion criteria for potential participants were five: a) they are scheduled to undergo coronary catheterization or CABG, b) individuals have no previous experience of a CR, c) are aged 18 and above, d) have an adequate knowledge and comprehension of the Greek language, e) do not experience another serious threatening disease (e.g. cancer).

A total of 487 patients were recruited between March 2010 and September 2012. All patients underwent either CABG or PCI and were over 18 years old.

Fifteen participants were recruited to assist with the translation validity (e.g. clarity of questions and items) of the CROQ (study 1). 405 participants were recruited prior to CR, 321 of whom completed the 3 month follow-up (response rate 79.26%) and 291 completed the 12 month follow-up (response rate 71.85 %). Additionally, 67 participants were recruited who had had their CR 3 months prior to recruitment in order to increase the sample size for the validation study of the CROQ-Gr. Out of these individuals 38 completed the 12 month follow-up (response rate for this subsample 56.72%) . The data collected from 472 participants (i.e. 405+67 please see Figure 4.2) were used both in the validation study of the CROQ-Gr as well as the quantitative component of the mixed methods study (Part 1). A subset of 10 participants was interviewed for the purposes of the qualitative component (Part 2). According to Ivankova and Creswell (2006), the sample for Part 2, should be purposively selected in order to explain aspects of the quantitative findings. Therefore, the subset of these 10 participants were five typical cases of each type of CR treatment who had participated at all three time points measured in the quantitative component (Part 1) of the mixed methods study in order to understand and explain differences in the HRQoL level of change.

This information is shown graphically in Figure 4.2 which demonstrates the exact number of participants in each part of study.

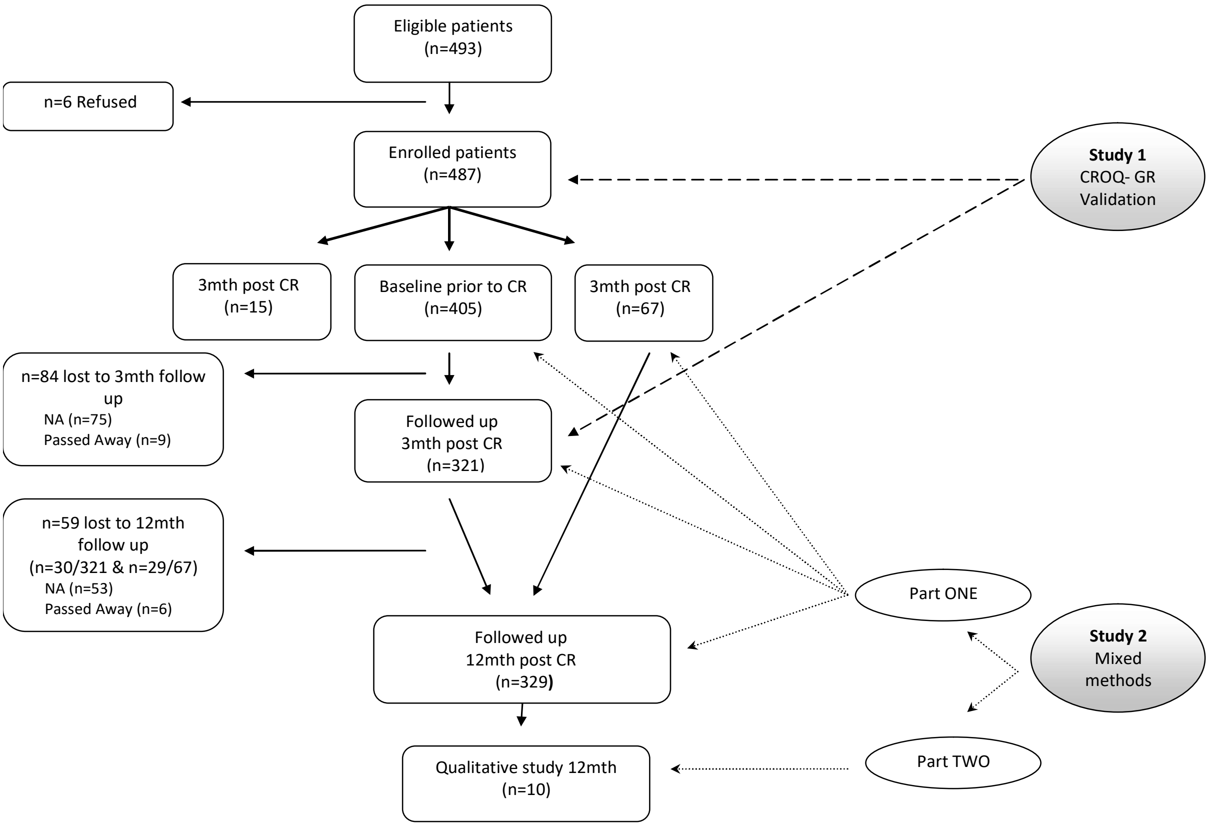

Figure 4.2 Flow diagram of research participants (mth=months)

The demographic and medical information for all participants in the sample per CR type is given in Table 4.1. The majority of participants were male (n=371) representing 76.1% of the total sample. Furthermore, the vast majority lived in Athens, were married and retired from work. Furthermore, half of the participants had a CHD family history and almost half of them were smokers. Interestingly, the vast majority were slightly overweight.

Table 4.1 Demographic and medical characteristics of the study participants per CR type (n=487)

	N(%)/Mean(SD) (n=487)	**N(%)/Mean(SD) PCI* (n=307)**	**N(%)/Mean(SD) CABG** (n=180)**
Age (yr)	60.59(10.9)	59.68(11.44)	62.16(9.64)
Sex (female %)	116(23.9)	72(23.5)	44(24.4)
Place of residence (%)			
Athens	379(77.8)	261(85.0)	118(65.6)
Other big city	31(6.4)	12(11.1)	19(10.5)
Rural areas	77(15.8)	34(3.9)	43(23.9)
Marital status(%)			
Unmarried/living alone	399(81.9)	62(20.2)	26(14.4)
Married	88(18.1)	245(79.8)	154(85.6)
Educational status(%)			
6 years or less	122(25.2)	82(26.7)	41(22.4)
7-12 years (high school	234(48.2)	150(48.9)	84(46.9)
12^{+} years	129(26.6)	74(24.1)	55(30.7)
Occupational status			
Unemployed	71(14.6)	47(15.3)	24(13.3)
Public/Private servant	127(26.1)	89(29.0)	38(21.1)
Freelance	102(20.9)	56(18.2)	46(25.6)
Pensioner	187(38.4)	115(37.5)	72(40.0)
Risk factors (%)			
CHD family history	243(50.0)	154(50.3)	89(49.4)
Hypertension	187(38.8)	114(37.6)	73(40.5)
Cholesterol	162(33.7)	92(30.4)	70(38.8)
Diabetes	143(29.7)	76(25.1)	67(37.2)
Smoking	234(48.3)	161(53.0)	73(40.5)
BMI*(kg/m^{2})**	28.59(4.44)	28.44(4.9)	28.84(4.67)

* PCI= Percutaneous Coronary Interventions **Coronary Artery Bypass Grafting
***BMI Categories:** Underweight = <18.5, Normal weight = 18.5–24.9, Overweight = 25–29.9, Obesity = BMI of 30 or greater

The clinical profile of participants followed over twelve months and those lost at some point in the research process (dropped out or passed away) did not significantly differ (*p* values range from 0.12 to 0.75; see Appendix 4.1). Regarding demographic characteristics, individuals differed only in marital and occupational status (Appendix 4.1). The majority of individuals lost at follow-ups lived alone (p<0.01) and were pensioners (p=0.02). Also, concerning the type of coronary revascularization, the majority of individuals lost at follow-ups had undergone PCI (*p*=0.01; Appendix 4.1).

Furthermore, it is worth mentioning that a final call two months prior to thesis submission (November 2014) was made to the 128 (please see Figure 4.2) patients lost at follow-ups. The aim of this communication was not to ask them to complete the questionnaires but rather to find out about their current status. Information on 71 individuals was obtained either directly from them or by their relatives. Out of those contacted, 11 had passed away. Thus, from the total of 472 individuals (excluding those 15 patients who participated only in the examination of translation validity for the CROQ-Gr) recruited for the main study, 26 individuals had passed away, nine had been treated with PCI (M_{age}=70.22, *SD*=6.44) and seventeen had been treated with CABG (M_{age}=69.94, *SD*= 11.39).

4.1.4. Material

4.1.4.1.Measures

<u>Study 1 & 2 (Part 1- quantitative component)</u>

Coronary Revascularization Outcome Questionnaire (CROQ; Schroter & Lamping, 2004)

The CROQ was selected based on the fact that, at the current moment, it is the only CR-specific measurement with satisfactory psychometric properties. All versions of the original English version (Appendix 4.2) have a good level of acceptability (missing data per subscale ranges from 1 to 5%; floor effects from 0 to 2%, ceiling effects from 7 to 62% and increased ceiling effects are related to absence of adverse effects), reliability (internal consistency, Cronbach's α ranging from 0.81 to 0.96; interclass correlation coefficient (ICC) ranging from 0.80 to 0.93 for all scales and subscales; Schroter, 2001) and both internal validity (principal axis factoring and inter-item correlations provide evidence for the proposed structure) and external validity (high and positive correlations between the CROQ and other measures of HRQoL such as the SF-36 and SAC (Schroter & Lamping, 2004)). Moreover, the CROQ has been shown to be more sensitive than other generic or disease specific measures of HRQoL (Schroter, & Lamping, 2006). Also it has been validated in other languages (e.g. Italian; Pintor et al., 2002) and Japanese (Seki et al., 2011) indicating that it may retain its properties in cross-cultural validation. Thus, it might not be severely influenced by Greek cultural discrepancies.

The CROQ developed by Schroter and Lamping (2004) is a patient-based, self-report instrument, specified for measuring HRQoL and health outcomes of patients undergoing CR. The CROQ consists of four versions (Table 4.2); one pre-PCI, one post- PCI, one pre-CABG and one post-CABG. The two pre-operative versions (pre-PCI and pre-CABG) are identical for the two procedures and capture four domains containing 32 core evaluative items and one descriptive item, the latter of which is not taken into account for scoring. More specifically, the four domains refer to: *symptoms* (7 items) "*During the past 4 weeks, how much were you bothered by each of the following problems related to your heart condition?*" e.g. *"pain due to angina"*; *physical functioning* (8 items) "*During the past 4 weeks, has your heart condition limited you in your usual daily activities?*" e.g. *"Lifting or carrying groceries"*); *psychosocial functioning* (14 items: a) *social functioning* (4 items) "*During the past 4 weeks, how often have you experienced the following as a result of your heart condition*" e.g. *"family or friends being overprotective toward you?"b) psychological functioning* (10 items) *"During the past 4 weeks, how often have you felt"* e.g. *"Worried about your heart condition?"*, and *cognitive functioning* (3 items) *"During the past 4 weeks, how much of the time did you"* e.g. *"Forget, for example things that happened recently, where you put things or appointments?"*

Table 4.2 CROQ- Subdomains and Number of Items per scale		
Subdomain	Number of items	
Common items in pre & post - versions	***PCI***[†]	***CABG***[‡]
Symptoms	7	7
Physical functioning	8	8
Psychosocial functioning	14	14
Cognitive functioning	3	3
Not classified	1	1
Additional items in post - version		
Satisfaction	6	6
Adverse effects	6	11
Not classified	2	2
Total	47	52
[†]PCI= percutaneous coronary interventions [‡]CABG= coronary artery bypass graft surgery		

The two post-operative versions contain the same 33 items as the pre-PCI/CABG versions as well as two more domains calculated from 12 (post-PCI version) or 17 (post-CABG version) core evaluative items. In addition, they include two items that are not taken into account when calculating scale scores; for example, "*Since your heart operation, have you been readmitted to hospital for an overnight stay for any reason to do with your heart condition or heart operation?*". The two additional domains are *adverse effects* ("*During the past 4 weeks, how much were you bothered by the following problems?"*; 6 items for the post-PTCA version e.g. *"pain in your groin wound"* and 11 for the post-CABG version e.g. "*pain in your chest wound"*) and *satisfaction with outcome* (6 items for both versions "*How satisfied are you with the"* e.g. *"Results of your heart operation?"*). The CROQ subscale items are measured on 3 to 6-point Likert scales and then transformed into 0-100 score. Furthermore, at the end of all versions there is an open-ended question: "*Is there anything else you would like to tell us about your heart condition or heart operation that is not covered in this questionnaire? If so please write bellow*".

A more detailed description of items included can be seen either in Chapter 5 where the translation, adaption and validation of the CROQ's Greek version will be presented or in Appendix 4.2. What is important to mention, by way of avoiding confusion of terms, is that the non-surgical procedure originally named as PTCA was changed to PCI with the developers' consent in order to be in line with the scientific term widely used for non-surgical coronary revascularization.

Short Form 36 (SF-36v2; Ware, Keller, Gandek, Brazier, & Sullivan, 1995)

The SF-36v2 (Appendix 4.3) consists of 36 questions that are combined in eight subscales. Moreover, it can be combined into two component summary scales; the physical component summary (PCS) and the mental component summary (MCS) (Ware, 2008). It was chosen for six reasons. Firstly, it is a valid and reliable generic measure of HRQoL that has already been translated into Greek and validated (Anagnostopoulos, et al., 2005; Pappa, Kontodimopoulos, & Niakas, 2006). The Greek version has a good level of acceptability (missing data per subscale varies from 0.1 to 1.3%; floor effects from 0.6 to 16%, ceiling effects from 3 to 77%), reliability (internal consistency, Cronbach's α ranging from 0.83 to 0.93 (Pappa, Kontodimopoulos, & Niakas, 2005)) and validity (Anagnostopoulos, Niakas, & Pappa, 2005). Secondly, as the literature indicates, it can be used for examining the external validity of the CROQ for two reasons: a) the SF-36 is a measure that has been widely used for measuring individuals' subjective evaluation of HRQoL and also, has been used in examining the external validity of other measures (Guermazi et al., 2012; Usta et al., 2013) and b) the SF-36 has already been used for testing CROQ external validity and responsiveness (Schroter & Lamping, 2006). Thirdly, the CROQ's developers borrowed items from the SF-36 (especially for the physical functioning subdomain) indicating some similarity between the SF-36 and CROQ. In addition the developers adopted the SF-36 scoring system, making these two instruments straightforward to compare. Forthly, the SF-36 totals and summary scores can be calculated using a computer program meaning that the results are more trustworthy since they are free from errors in calculation. Fifthly, it has been used by the majority of researchers interested in patients' HRQoL in the field of CR (e.g. Damgaard et al., 2011; Houlind et al., 2012; Hunt et al., 2000; Kendel, 2009; Lie et al., 2009; Mallik et al., 2005; Mathisen et al., 2005; Pfaffenberger et al., 2010; Rothenhäusler, 2010; Seto et al., 2000). This is important as it facilitates comparison of the present thesis results and the wider literature, leading to a clearer picture about the influence of the measure used. Sixthly, the SF-36 as a generic measure can highlight differences in long-term patients' HRQoL after CR, in a way that complements that of a disease-specific one (e.g. due to patients' adjustment).

Both instruments (CROQ and SF-36v2) measure their subscales on 3 to 6-point Likert scales. The total of each subscale ranges from 0 to 100 with higher scores indicating better status.

Demographic information

The demographic information questionnaire consisted of 6 questions: date of birth, sex, place of residence, family, educational and occupational status (Appendix 4.4). The specific questions were incorporated based on the literature that highlights these as the typical demographic questions that should be included in a survey (Wentworth & Chell, 2005).

Clinical and behavioural information

The self-reported clinical and behavioural record consisted of 5 dichotomous questions (yes/no) and 2 descriptive questions. This record was developed based on the literature review (chapters 1 and 2) and expert suggestions about behavioural and biological conditions related to CHD. The questions asked patients to indicate whether they had a family history of CHD and if they were on medication for hypertension, cholesterol, and/or diabetes. Also, there were questions on smoking, participants' weight and height (in order to calculate their BMI), and finally it investigated if they knew the number of arteries that would be revascularized as well as the kind of revascularization that they would undergo (Appendix 4.5). As a number of participants did not know the answers to the two last questions, such information was also retrieved and/or cross checked with clinical records. At this point it is essential to mention that time since diagnosis was not captured, mainly for consistency reasons, meaning that it would have only been possible to measure this variable for patients who had undergone CABG, not for patients who underwent PCI, as the majority of PCI individuals firstly underwent coronary catheterization as a screening process for a coronary heart disease. If a problem is detected doctors decide at hoc to proceed to a coronary revascularization through the implantation of a stent (as mentioned in Chapter 1).

At the post-CR measurement four questions were asked. Patients were asked to state the exact CR procedure that they underwent (e.g. off-pump CABG, on-pump CABG, PCI with Metal Stent, PCI with Drug Eluting Stent) and the number of arteries revascularized. They were also asked if they smoked and what their weight status was.

4.1.4.1.1. ***Semi-structured interview (Study 2, Part 2- qualitative component)***

For study 2, part 2, a semi-structured interview plan was developed following Smith et al's (Smith et al., 2009; Smith & Osborn, 2003) guidelines for qualitative interview. It consisted of thirteen open-ended questions (Appendix 4.6), developed to explore patients' perceptions in five key areas: a) HRQoL in general; b) symptoms and physical functioning; c) psychosocial functioning; d) changes in attitude towards self and life; and e) changes in lifestyle/behavioural changes and how these areas might "guide" patients in making sense of their experience. Table 4.2 displays the main questions of the topic guide. These questions were developed based on the theoretical framework of the definition of HRQoL adopted in the present thesis as well as on the longitudinal research findings. The topics were confirmed after discussion with the supervisors.

Table 4.3 Main questions of the Topic Guide

Opening questions	*How would you describe your life during the last year?* *What do you think caused coronary disease?* *How would you describe yourself now?*
HRQoL in general	*What does "quality of life" mean to you?*
HRQoL, symptoms and physical functioning area	*How do you feel about your body after CR?*
HRQoL psychosocial functioning area	*How do you experience your social life after CR?* *How do you feel about your heart condition?*
Changes in attitude towards self and life	*Have you observed any changes regarding the way you perceive life after CR?Have there been any life events (apart from CR) that have affected the way you perceive yourself and your life?*
Changes in lifestyle/behavioural changes	*Can you describe any changes in aspects of your lifestyle and habits that you made/had to make/intended to make after CR? How did you feel about changing (then and now)/having to change these aspects?*
Ending	*What would you say to an individual who now faces CR? (e.g. about what to expect, what life changes they may experience, how to deal with these)* *Is there something else that you would like to add in relation to your experience of CR?*

4.1.5. Procedure

After obtaining Dr Schroter's (the CROQ author's) written permission for adapting the CROQ into Greek, ethical approval to carry out the research studies was obtained from the University of Hertfordshire relevant institutional ethics committee, formerly the School of Psychology Ethics Committee with Devolved Authority (ECDA; Appendix 4.7). Afterwards the research protocol was submitted to five different general hospitals for consideration. Unfortunately, two out of the five hospitals approached denied access to their patients; both were private hospitals. Thus, approval from scientific committees of three hospitals located in Attica was obtained: Thriassio, Metropolitan and Attiko (Appendix 4.8).

Before describing the whole procedure it should be clarified that of the 487 individuals recruited, 307 participants underwent PCI and 180 underwent CABG. Excluding 15 patients who had undergone CABG and took part solely in study 1 (the CROQ translation validity), the same sample of 472 participants participated in studies 1 and 2. Different subsets of the same 472 individuals (307 who had undergone PCI and 165 who had undergone CABG) participated in different phases and completed different scales. The following paragraphs present a detail description.

Data collection of patients recruited prior to CR

Two set of patients was recruited prior to CR (n=405 either PCI (n=244) or CABG (n=161)). Recruitment of patients scheduled to undergo CABG was made one to two days before treatment, in their hospital rooms, as these patients enter the hospital for clinical examination 24-48 hours prior to CR. The patients' name and room number was provided by the clinic's registrar office.

Recruitment of patients scheduled to undergo PCI or coronary angiography was carried out in the hemodynamic waiting room early on the same day prior to intervention. At this point it is essential to mention that often the PCI is administered ad hoc during coronary angiography. Thus patient recruitment was carried out mostly prior to the coronary angiography without the researcher being aware which patients would have a PCI until the evening when the head of the coronary intervention office would let the researcher know the name of patients who had undergone PCI.

In both cases, a general call was made initially. This announcement included an introduction to the researcher, the aim of the study and the request for volunteers. It was highlighted that the decision regarding participation to the study would not affect medical care. Patients willing to participate were escorted to a private room provided by each hospital. There, the researcher both orally and in writing (Appendix 4.9.1) informed potential participants about the details and aim of the study, what was expected from them and the duration of their participation (both duration of the instrument administration and duration of participation in the overall studies). An information sheet was then given to each participant. Participants agreeing to participate signed the consent form (Appendix 4.10.1), being reminded that they could withdraw at any time without the need for providing an explanation and that this would not affect their medical care in any way. After that, the appropriate booklet was administered to participant. A 6-page booklet was administered as the vast majority of patients enrolled prior to treatment which consisted of the CROQ PCI or CABG pre-revascularization version, demographic and clinical information.

A subset of patients was administered instead of the 6-page booklet, a 12-page booklet. This larger booklet included also the Short Form-36 (SF-36v2 Greek version).

The data of all these participants were used both in Study 1 and Study 2 (quantitative component).

Data collection of patients recruited 2-5 months post CR

Fifteen patients who had undergone CR 2-5 months earlier were recruited for the CROQ preliminary translation validity of Study 1. Patients were met prior to their follow-up meeting with their doctors. After providing introductory details, information and obtaining consent, data collection was carried out via face to face interviews. These individuals were required solely for that purpose and they were not contacted again (details for this part are presented in chapter 5).

Data collection of patients recruited 3 months post CR

Sixty-seven patients were recruited 3 months post treatment (PCI (n=63), CABG (n=4)), to increase the sample of post-CR versions. Patients were met prior to their follow-up meeting with their doctors. After providing introductory details, information and obtaining consent, they completed the 3-month post revascularization CROQ-Gr version (either PCI or CABG). The administration procedure was similar to the one mentioned for the procedure of patients recruited prior to CR.

Data collection of patients followed up for Study 1 and Study 2 (Part 1)

The follow-up was made 3 months and 12 months after treatment through telephone calls. An 8-page booklet was administered both times which consisted of the CROQ PCI or CABG post-revascularization version, and the four items of clinical information mentioned earlier (in the

Materials section p.120). The subset of patients recruited at 3 months post treatment was followed up at 12 months as well.

The subset of patients who had completed both the CROQ and SF-36v2 Greek version prior to the coronary revascularization at 3 months follow up was administered a 14-page booklet which included again both questionnaires, at 12 months follow up only post CR revascularizations versions were administered.

Also, another subset of patients, the first 20 patients (excluding those administered both the CROQ and SF-36v2) of each CR type (PCI or CABG) were recalled two weeks after the 3-month phone call in order to collect data needed for CROQ-Gr validation (e.g. assessing reliability; an issue that will be discussed in chapter 5)

At this point it is essential to clarify that the 3-month follow up data were used for both Study 1 (the CROQ-Gr validation) and Study 2 (Part 1, quantitative component) while the 12 months follow up data were used only for Study 2.

Also, it should be mentioned that the three-month post revascularization follow-up interval was selected based on the suggestions of the CROQ author who maintains that a three-month period is generally considered an average recovery period for the procedure. At this point only a minority of patients will still be experiencing adverse effects from the particular procedure (Schroter, & Lamping, 2004).

Questionnaire administrations for Study 1 and Study 2 (Part 1)

Sessions lasted approximately 15-30 minutes, depending on the booklet being administered and whether participants completed the SF-36v2 or not. The booklet with the SF-36v2 was administered 60 times. Initially, this was administered to every 10th patient recruited but due to the amount of missing data and fear of not collecting the appropriate number in time, the SF-36v2 was then administered to every 2nd patient. Moreover, in order to minimize order bias, half of the booklets first presented the CROQ and then the SF-36v2 while the other half presented the SF-36v2 first and then the CROQ. Furthermore, the majority of patients completed the questionnaire by themselves except for a few participants who asked the researcher to help them due to sight problems.

All sessions were carried out by the same researcher using a standard procedure and standardised instructions. After the completion of the booklet, debriefing was provided both orally and in writing (Appendix 4.11.1), explaining the importance of the study and giving participants the opportunity to ask any relevant questions. All booklets were stored in a locked cupboard at the researcher's office, except for the booklets completed by patients who, having completed the questionnaires, did not subsequently undergo PCI; these were destroyed the same evening after the meeting with the doctors.

The follow up (3 and/or 12 months post treatment) of patients, as stated earlier, was made through telephone calls. Participants had been asked to provide their telephone number and suitable contact days and hours on the initial consent form. The follow-up calls were made to the phone number provided by the patients by a "call display" phone number where individuals could be aware of who is calling them, based on suggestions concerning telephone surveys (Streiner & Norman, 2008).

Depending of the follow up (3 or 12 months) participants were debriefed and either were reminded that there would be a final telephone contact, approximately 9 months later (i.e. 12 months post-CR), or if the call was the final one (12 months call) they were thanked for their participation.

Data collection for Study 2 (Part 2)

Of those participating at all three time points (study 2, Part 1, quantitative component), 10 participants were re-contacted to participate in Study 2, Part 2 (qualitative component). These were the first 5 CABG and the first 5 PCI patients that agreed to participate in the qualitative study. The main inclusion criteria were the time after revascularization, being current or ex-smokers and the absence of other serious life threatening co-morbidities (e.g. cancer). Patients asked to participate should have undergone CR 12-15 months before the interview. At the scheduled appointment, either at the patient's house or at the researcher's office, patients were given a brief overview about the aims of the study, both orally and in writing (Appendix 4.9.2), and written consent was obtained (Appendix 4.10.2). All interviews were recorded upon participants' approval and lasted from 45 minutes to 2 ½ hours. At the end of the interview patients were asked to comment on the interview (Appendix 4.12). After this, debriefing followed during which an information leaflet listing psychological support services (Appendices 4.11.2 & 4.13) was given to the participants in case they felt distressed at any time. Finally, participants were thanked for their time, participation and willingness to share with the researcher their thoughts and opinions.

4.2.Analysis

Various analyses were for the purposes of the two studies. In the following sections, a brief overview of the strategies and methods of data analysis for each study will be presented.

4.2.1. Study 1 – Translation, adaptation and validation of the CROQ into Greek

Concerning the translation stage a series of forward and backward translations of the questionnaire were conducted. Then, an expert panel revised the preliminary CROQ-Greek version. Afterwards, a preliminary draft of the CROQ - post CABG Greek version was piloted at two different hospitals prior to its wider use (details for this stage are presented in chapter 5). To evaluate the validity and reliability of the CROQ-Gr version, a range of analyses were performed following suggestions in the literature (Field, 2005). Briefly, a descriptive analysis was carried out in order to estimate instrument acceptability (missing data and response frequencies; ceiling and floor effects) and item variance. The reliability analysis was performed with the use of Cronbach's α to estimate internal consistency and intraclass correlation coefficients (ICC) to estimate test-retest reliability. In order to check sample sufficiency, the Kaiser-Meyer-Olkin measure of sampling adequacy was used. Bartlett's test of sphericity was carried out to determine whether the correlation matrix differed from the identity matrix (i.e. to check whether the correlations between items were non-zero and that therefore a factor analysis was feasible). A four-factor Principal Axis Factoring (PAF) extraction, set *a priori*, with Varimax rotation and coefficient suppression at 0.35 (appropriate criterion for a sample greater than 200 (Field, 2005)) was carried out for assessing instrument (internal) construct validity, as suggested by the CROQ developers (Schroter & Lamping, 2004). Zero-order correlation coefficients were calculated in order to test the equality of item-scale correlations and item discriminant validity. Correlations (Spearman's *rho*) between the CROQ and SF-36 scale scores were calculated for assessing the CROQ's external validity. The scoring of the SF-36 was carried out with the use of the Health

Outcomes Scoring Software 3.0. Statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM, 2011).

4.2.2. Study 2 – Part 1: Quantitative Component

For the 2nd study, analysis was conducted with the use of mixed models and in particular, conditional growth models, a type of multilevel modeling (MLM) for longitudinal or repeated measures, in order to detect the effect of the type of CR treatment at the different time points on Health Related Quality of Life (HRQoL) as measured with the coronary revascularization outcome questionnaire (CROQ), controlling for several demographic, clinical and behavioural variables. Mixed models were selected because they permit detecting changes over a period of time (repeated measures) both within and between individuals without being affected by missing data in a longitudinal study due to loss of follow up or dropouts; unequal data per participant over time can be treated by flexible specification of the time variable and to produce aggregate-level as well as individual-level growth curves (Kwok et al., 2008; Ntoumanis, 2014). Also, by treating “time” as a continuous variable instead of a discrete one can increase the statistical power for the detection of growth effects (Kwok et al., 2008).

As suggested by Chen and Peace (2011) and Singer and Willett (2003) a series of models were tested to determine the best fitting model. All models were computed with maximum likelihood estimation (ML) and AR(1) (first-order autoregressive structure) where it is assumed that the data are continuous and the relationship between changes in variances is systematic) following experts guidelines (Curran, Obeidat, & Losardo, 2010; Kwok et al., 2008; Singer & Willett, 2003). Also, for comparative reasons, to detect the best fitting model, the Schwarz’s

Bayesian Information Criterion (BIC) was used (Schwarz, 1978). The BIC was selected as the most appropriate compared to the -2LL (negative log likelihood) criterion as it takes into consideration both the statistical goodness of fit and the number of parameters to estimate the degree of fit. When fitting models, it is possible to increase the likelihood by adding parameters, resulting in an overfitting model. BIC resolves this problem by introducing a penalty term for the number of parameters in the model (Nishii, 1984), so the conclusion based on the BIC index about the model fit is more conservative. The smaller BIC value is the better the fit.

The initial steps followed (prior to the analysis) was to calculate the Body Mass Index (BMI; weight/height^2), restructure the data (discrete time points to become continuous; Field, 2013) and then change the coding of the time variable due to unequal time spacing (from 1-3 to 0-4 where 0 represented baseline data (Time0), 1 represented 3-month follow-up (Time1) and 4 represented the 12-month follow-up (Time2)). To test the quadratic (nonlinear) trend over the measurement time points, the time variable was generated by squaring the linear term (i.e. time^2=0 (baseline), time^2=1 (3-month), time^2=16 (12-month)).

Concerning the statistical analysis, the first step was to determine the best fit for the time trend; time (level 1 variable) as predictor nested within individuals (level 2 variable) and within the response variable, CROQ Total scores. Thus, a series of mixed models were computed (this issue is discussed further in the quantitative study's statistical section). The second step was to detect the CR type of treatment effects. The best fitted model for the Time trend was further investigated by adding the effect of the CR type (PCI, CABG; level 3 variable). Again a series of mixed models were computed to determine the best fitting model. The third step was to investigate further the best fitting model of step two by adding potential predictors, meaning all individual level covariates (time-invariant (e.g. gender, education, diabetes representing individuals' demographic and medical characteristics (as measured at a single time point) and time-varying (i.e. smoking and BMI representing individuals' behavioural characteristics that have been updated in all three time points) with random intercept, linear and time terms. Included in the model were also all the two way interaction terms between those potential predictors with time and CR type of treatment.

Next, the same analysis was repeated for each CROQ subdomain (symptoms, physical, psychosocial, cognitive functioning) as response variable. For adverse effects and satisfaction, as these were measured only at 3 months and 12 months post treatment, two new variables were created indicating the difference of each. Then multiple linear regression models were developed with response variables of difference in adverse effects and difference in satisfaction respectively in order to examine the fixed effects of all individual level covariates (time-invariant and time-varying potential predictors).

The level of significance was set at 0.05. Analyses were performed using SPSS 20.00 (IBM, 2011) and the R package nlme (Baayen, 2008; Baayen, Davidson, Bates, 2008; Pinheiro & Bates 2000; Pinheiro et al., 2016). R's popularity has increased substantially in recent years especially for its graphic capability and utility for nonlinear mixed models analyses (Muenchen, 2016; Revelle, 2016).

4.2.3. Study 2 – Part 2: Qualitative Component

Regarding the 2nd study Part 2, the qualitative data were analysed using Interpretative Phenomenological Analysis (Smith et al., 2009). After the verbatim transcription of interviews, a four step procedure took place. The first step involved reading and re-reading the transcribed interviews, creating a list of words, ideas and comments in the left hand margin. The second step focused on identifying emerging themes using a higher level of abstraction. At the right hand margin, extracted words and comments were transformed into themes. The third step involved listing the themes and then clustering themes that were similar or connected. At this stage, quotes related to each theme were attached to guarantee that the original meaning was not lost. The fourth step aimed to formulate super-ordinate themes that emerged from the clustering of themes. Then, a table of super-ordinate (master) themes was developed, followed by keywords from interview transcripts. After the analysis of the first interview, this process was repeated with data from all interviews (see in Appendix 4.14 the table of themes developed from analysis of the first interview). The tables of themes resulting from each transcript analysis were then compared and considered together for the development of an integrated table of themes (i.e. a Master table of themes). What is important to mention is that although all interviews were conducted in Greek, all analyses were conducted in English and relevant quotes have been translated as well.

4.2.4. Study 2 – Part 3: Interpretation (Integration of Part 1 and 2 findings)

In line with experts' guidelines for mixed methods research (e.g. Hanson, Creswell, Plano Clark, Petska, & Creswell, 2005; Ivankova, Creswell, & Stick 2006; Onwuegbuzie & Teddlie, 2003; Tashakkori & Teddlie 2003), the mixing occurred in two ways. The first occurred at the stage where quantitative results shaped the qualitative part (as shown in Figure 4.1) in terms of purposive selection of participants for the second part (a purposive subset of the sample) and of investigating in greater depth various issues that the researcher wanted to gain a greater understanding of. The second occurred at the integration of both quantitative and qualitative findings in part 3, the interpretation part, permitting to present converging, diverging and complementary insights (both in terms both new additional issues as well as explanation). The interpretation of findings is organized in a way to address the Study 2 main research questions. Findings are presented within a set of themes addressing key aspects.

4.3. Ethics

4.3.1. Thesis

Ethical approval was granted for the studies by the University of Hertfordshire Ethics Committee (ethics approval forms are presented in Appendix 4.7), and by the allied Hospitals (Attikon, Thriasio, Metropolitan; approval forms are presented in Appendix 4.8). This thesis has therefore considered and followed research ethics standards. Studies have been designed and conducted so as to respect participants' dignity, privacy and autonomy and the researcher has followed specific steps for to protect participants' identity, confidentiality, safety and kept the promises and agreements as stated both orally and in writing during the information phase. Patients were in no way misinformed nor was there any misconduct. The researcher has fully respected their right to refuse participation or to withdraw their participation without explanation and has shown due consideration to minimizing/dealing with patients' potential distress or discomfort and avoiding sex and race discrimination. Data protection and transparency in all scientific communication (e.g. methods and procedures, data analysis, data report) has been handled in a rigorous manner.

4.3.2. Participant information, consent and debriefing

The first step for ensuring informed consent was made by informing potential participants about the aims and objectives of the research both orally and in written form by providing a Participant Information Sheet (Appendix 4.9). This information also included what taking part would involve, for how long, for how many times, how data would be stored and who would have access to it. This information was provided as the basis for inviting participants to take part in the studies. After ensuring that participants had understood the contents of the information sheet, and agreed to participate they were given the consent form to read (Appendix 4.10). If they wanted to continue they were asked to give their written consent before the questionnaire pack was given. A signed copy of the consent form was given to the participant.

To ensure that participants did not feel obliged to take part in the research, it was emphasized that they were under no obligation to do so and that, whether or not they decided to participate, it would not affect their treatment or quality of care. Participants were also informed that they could withdraw from the study at any point, without needing to provide reasons for doing so. Individuals unwilling to give informed consent were excluded from the study. Finally, they were reminded that any concerns they might have about their medical condition should be discussed with their doctor.

At the end of data collection, debrief information regarding the research was provided, explaining the importance of the study and giving the opportunity to participants to ask any relevant questions. A debriefing sheet was also given in face-to-face administrations (Appendices 4.11). In cases of telephone contact, the standard debriefing was read.

4.3.3. Confidentiality and safe storage of data

Participants were fully informed about confidentiality and its limits. They were aware that their anonymised data (with pseudonyms), would be used in the write-up of the present thesis and journal publications. In particular, those participating in the qualitative study were informed that quotes of their utterances (translated versions) might be used. Moreover, they were informed that my supervisors would read the anonymised transcripts (with pseudonyms). Participants were also informed of the limits of confidentiality, that is, that I would share information with their doctors if their scores indicated that they were at risk of significant distress.

Also, participants were fully orally informed about the steps that would be taken to protect their data from third party access. All data were stored on a computer with restricted access protected by an 8-digit password at the researcher's office. Any hard copies (consent forms or transcriptions) were locked separately in a cupboard at the researcher's office accessible to the researcher only, with the key secured in a deposit box.

4.3.4. Participants' potential distress

The extent of disturbance or discomfort caused by participation was expected to be minimal. Firstly, the content of the questionnaires mainly referred to symptoms and daily concerns related to heart disease, topics patients commonly discussed with health professionals when undergoing revascularisation. Secondly, the content of the interview schedule referred mainly to their perception of well being, symptoms (experienced before/now) and concerns related to everyday life.

Additionally, patients were made aware that they could ask for a break at any time, had the right not to answer particular questions if they did not want to and withdraw at any time without having to give a reason for doing so.

Also, due to my experience as a counselor and trainee health psychologist, I conducted the interviews (both structured and semi-structured) as sensitively as possible. During the debriefing, I checked how participants were feeling, how their experience of being interviewed was and I advised them to discuss any concerns raised from our discussion with their doctors. Patients were under the care of the hospital and retained access to medical care. Also, an information leaflet with daily care centers that provide psychological support services (free of charge) was given to patients in case they wanted to further discuss any emotional issues with an expert. Moreover, the local supervisor, a qualified health psychologist was at their disposal in case they needed psychological support. However, this never occurred.

Given their medical status, specific actions were taken to ensure the safety and comfort of patients who visited the researcher's office for interviews (study 2, Part 2). A private, air-conditioned, fire and sound-proofed room with toilet services was available for conducting the interviews. In this way, patients' security and privacy was ensured. The office was located near to bus and rail stations so easy access was ensured. Parking services were offered too, providing convenient access. During their visit, beverages and cookies were offered to patients in an effort to make them feel as comfortable as possible.

4.3.5. The researcher's safety and potential distress

Specific consideration was given to the researcher's safety, especially when she visited patients' homes as part of data collection in Study 2, Part 2. Hospitals are protected environments with safeguards in place if any unusual or hazardous situation occurs. Patients' home environments, however, were of unknown safety. Therefore an effort was made to emphasise the benefits of patients coming to the researcher's office. Although most interviews did take place in the researcher's office, in two cases participants insisted for the interviews to take place at their home. The researcher visited their homes, accompanied by her spouse who was aware of the procedure; he remained in a separate room, with closed doors, throughout the course of the interview and did not interfere in the process in any way. Both patients had ensured there would be no distractions from other family members during the interview; they were very polite, friendly and tried to make the researcher feel comfortable.

Considerations regarding any distress on part of the researcher were dealt with by discussing with supervisors any concerns, frustrations or distress as often as was needed or asked for. This did not happen often but there were times that the researcher became frustrated, for instance, when it was discovered that many participants had been "lost" at the yearly follow up. Supervisors guidance and support towards the researcher was provided and vital throughout the PhD.

4.4.Summary of method

This chapter provided details about the rationale for the methods used in order to achieve the thesis aim, namely to explore Greek individuals' perspectives of their HRQoL after CR. Based on the data selected from a sample of 487 individuals, two studies were conducted and will be presented in the following chapters.

After the validation of the four versions of the CROQ-Gr (Study 1) which is presented in the next chapter (chapter 5), a mandatory step since the study would be conducted with Greek patients, a mixed methods longitudinal study (actually a 3-part study) with a sequential explanatory research design (presented in Chapters 6,7 and 8) will help to address the study's research questions. Part 1 (quantitative component), with data collection at three different time points and a rigorous statistical analysis (multilevel modelling) will allow to detect HRQoL changes as well as its pattern over a one-year period following CR with the use of the CROQ-Gr and exploring potential predictors. Part 2 (qualitative component) with data collected on a subset of 10 patients analysed using the Interpretative Phenomenological (IPA) approach may refine and provide a deeper understanding by exploring participants' point of view and experience and capturing their meaning-making process. Part 3, the integration of the findings for each component (quantitative and qualitative) at the interpretation stage, following an explanatory synthesis, thematically organized to present key aspects, will allow to address thesis research questions.

Chapter Five

Translation, adaptation and validation of the Coronary Revascularization Outcome Questionnaire (CROQ) into Greek

5.1.Introduction

As stated in the previous chapters, in order to conduct the longitudinal mixed methods study with Greek patients the first step was to translate the Coronary Revascularization Outcome Questionnaire (CROQ) into Greek and validate its Greek version (CROQ- Gr); Part of this chapter is already published (Takousi et al., 2016). The CROQ is a patient-based scientific instrument, specifically designed for measuring HRQoL and health outcomes of patients undergoing coronary revascularization. This scientifically robust tool allows rigorous assessment of Health Related Quality of Life (HRQoL) and other health outcomes in clinical trials, responding to the need for specificity and sensitivity. The main objective of this chapter is to present and discuss the multi-step process followed for the adaptation and psychometric validation of the Greek version; CROQ-Gr. This chapter begins with reviewing the guidelines regarding a measure's cultural adaptation and continues with presenting the CROQ English version.

5.1.1. Cultural adaptation and validation of patient-based instruments

An instrument which has already been developed, validated and thus widely used in one culture, is not necessarily valid and reliable in every language and culture. Therefore, a simple literal translation on the part of the researcher(s) is inadequate to achieve the goal of validation; a multi-step process is required. However, there is no consensus approach for the cultural adaption of an instrument (Acquadro, Conway, Hareendran, & Aaronson, 2008; Maneesriwongul & Dixon, 2004; Marquis et al., 2005; Wang, Lee, & Fetzer, 2006). The literature identifies at least 17 methods for an instrument's translation, cultural adaption and validation (Acquadro, Conway, Hareendran, & Aaronson, 2008). Among them, the most broadly discussed and followed guidelines are those of the American Association of Orthopedic Surgeons (Beaton, Bombardier, Guillemin, & Ferraz, 2000; Guillemin, 1995; Guillemin, Bombardier, & Beaton, 1993), the World Health Organization (WHO (Ginieri-Coccossis et al., 2001; Nedjat, Montazeri, Holakouie, Mohammad, & Majdzadeh, 2008; Saxena et al., 2005; Skevington, 2002; WHO, 2010)), the International Quality of Life Assessment (IQOLA (Bullinger et al., 1998; Gandek & Ware, 1998; Gandek et al., 1998; Leung et al., 2010; Li, et al., 2003; Montazeri, Goshtasebi, Vahdaninia, & Gandek, 2005; Montazeri, Vahdaninia, Mousavi, & Omidvari, 2009; SAC & Lohr, 2002; Wagner et al., 1998)), the Scientific Advisory Committee of the Medical Outcomes Trust (SAC (Lohr, 2002)), and finally, the Universalist Approach of Herdman and colleagues (Herdman, Fox-Rushby, & Badia, 1997, 1998; Reichenheim & Moraes, 2007).

Nevertheless, the majority of guidelines for the translation and validation of a measure agree upon a multi-stage procedure focusing on equivalence between the two versions (the original and the adapted one). It involves at least two forward translators, one or two back translators, a synthesis of findings, a review by an expert panel, pre-testing and a formal testing of the instrument's reliability and validity (Acquadro et al., 2008). Briefly, the guidelines adopted in the present study are similar to the three-stage process suggested by IQOLA research team (Bullinger et al., 1998; Gandek et al., 1998; Ware & Gandek, 1998; Ware et al., 1995). The decision for following these particular guidelines was made due to the fact that these guidelines were followed for the translation and validation of the SF-36 which is the most widely adapted instrument of HRQoL globally.

Stage 1 involves forward and backward translations and pilot testing (Bullinger, et al., 1998; Gandek et al., 1998; Streiner & Norman, 2008).

Stage 2 focuses on testing the scaling assumptions; five core assumptions should be explored: 1) equal item variance 2) missing data, 3) equality of item – scale correlations, 4) item discriminant validity and 5) reliability (DeVellis, 2003; Streiner & Norman, 2008; Ware & Gandek, 1998).

Stage 3 focuses on validation, which refers to the degree to which a measure captures the concepts for which it was designed and ensures the uniqueness of the items' contribution to the scale. Typically, three types of validity are assessed: content, construct and criterion (McDowell, 2006; Streiner & Norman, 2008; Ware & Gandek, 1998). All types assess the degree of confidence that can be placed in inferences drawn from scores (Streiner & Norman, 2008).

The relevant literature also highlights that an important aspect of a good instrument is its "sensitivity to change" and "responsiveness". These terms are often used interchangeably. In general terms, they refer to an instrument's ability to capture changes over time. However, there is a conceptual difference between these two notions (Corzillius, Fortin, & Stucki, 1999; Liang, 2000). Responsiveness refers to a measure's capacity to capture clinically meaningful changes that are important to patients or to physicians. Sensitivity to change refers to a measurement's capacity to detect statistically significant change regardless of whether the change is meaningful to the decision-maker. This distinction is of importance because statistically significant change (difference) in state over time may not be synonymous with clinically important change and vice versa (Kazis, Anderson, & Meenan, 1989; Pardasaney et al., 2012). A discussion of these guidelines can be found in Appendix 5.1

In short, an instrument's translation and testing its reliability and validity is a rather demanding procedure. The aim of this study is to detect the acceptability, reliability, and validity of the CROQ's Greek versions. The following research questions will be addressed:

1. Does the Coronary Revascularization Outcome Questionnaire Greek version (CROQ-Gr) seem straightforward and relevant to Greek patients?
2. Is there evidence to support the reliability of the CROQ-Gr?
3. Is there evidence to support the validity (both internal and external) of the CROQ-Gr?
4. Is there evidence to support that the CROQ-Gr is sensitive to change?

5.2.Methods

5.2.1. Participants

An opportunity sample was recruited between March 2010 and September 2012 and followed for one year. Patients recruited were either candidates for coronary revascularization (PCI or CABG) or had undergone a revascularization during the study period. Details about recruitment can be found in chapter 4.

5.2.2. Material

Two instruments were used in this study: the CROQ and the Greek version of SF-36v2. Both of them were introduced in Chapter 4.

Briefly, the CROQ consists of four versions; one pre-PCI, one post-PCI, one pre-CABG and one post-CABG. The two pre-operative versions are identical for the two procedures and capture four domains containing 32 core evaluative items (*symptoms, physical functioning, psychosocial functioning* and *cognitive functioning*) and one descriptive item that is not taken into account when computing scale scores. The two post-operative versions consist of 44 (PCI) and 49 (CABG) core evaluative items and three items that are not taken account of when computing scale scores. The two additional domains in the post-operative versions are *adverse effects* and *satisfaction with outcome* (Table 5.1). Total scores are reported on a 0-100 scale. Higher scores indicate higher HRQoL level.

Table 5.1 CROQ- subdomains and number of items per scale

Subdomain	Number of items	
Common items in pre & post - versions	***PCI[†]***	***CABG[‡]***
Symptoms *(e.g. chest pain due to angina)*	7	7
Physical functioning *(e.g. limited in moderate activities, such as making the bed?)*	8	8
Psychosocial functioning *(e.g. family being overprotective toward you?)*	14	14
Cognitive functioning *(e.g. have difficulty reasoning and solving problems)*	3	3
Not classified *(e.g. During the past 4 weeks, have you had chest pain, chest tightness or angina at rest? On exertion? Both?)*	1	1
Additional items in post - version		
Satisfaction *(e.g. how satisfied are you with the Results of your heart operation)*	6	6
Adverse effects *(e.g. sensitivity around the groin wound)*	6	11
Not classified *(e.g. Since your heart operation, have you been re-admitted to hospital)*	2	2
Total	47	52

[†] PCI= Percutaneous Coronary Interventions
[‡] CABG= Coronary Artery Bypass Graft Surgery

The SF-36v2™ consists of 36 questions focusing on eight areas: physical functioning (PF-10 items), role limitations due to physical health problems (RP- 4 items), bodily pain (BP- 2 items), general health perceptions (GH-5 items), vitality (VT-4 items) tapping energy levels and fatigue, social functioning (SF-2 items), role limitations due to emotional problems (RE-3 items) and mental health (MH-5 items). Also it includes one item measuring health transition (Ware, 2008). The average score of PF, GH, RP, BP create the Physical Component Summary (PCS) while VT, SF, RE, MH create the Mental Component Summary (MCS). Higher scores indicate higher HRQoL level. Total scores are reported on a 0-100 scale. Higher scores indicate higher HRQoL level.

5.2.3. Procedure

A three stage procedure (described earlier) was followed in order to established the CROQ Greek version: 1) translation, 2) testing assumptions, 3) validation

5.2.3.1. *Stage I: translation*

Concerning the translation stage a series of forward and backward translations of the questionnaire were conducted. The CROQ was translated into Greek by two translators with English language qualifications, but having Greek as a mother tongue. In the forward translation into the Greek language, the translators were asked to focus on conceptual rather than on literal equivalence by considering the definition of the original term/wording and trying to translate it in the most appropriate way. Then, an expert panel was formed by the principal investigator, a BPS chartered psychologist (with English language qualifications) and an operational cardiologist who revised the preliminary CROQ-Greek version. Afterwards, a preliminary draft of the CROQ - post CABG Greek version was piloted at two different hospitals through an approximately 45-minute face-to-face semi-structured interview in a hospital setting with patients who had undergone revascularization 2-5 months earlier and were having a follow-up appointment.

Participants were given the information sheet, which introduced the researcher and explained the purpose of the study emphasizing that the goal was to test the questionnaire's suitability (Willis, 2005). After giving their written consent, and being reminded that they could withdraw at any time, an interview took place with 15 patients (male 80%, n=12) with mean age M=65.73 years (SD=9.10), in order to evaluate the questionnaire format, the clarity of the instructions and items, appropriateness of wording, the content validity, and feasibility (regarding the burden on the respondent).

Firstly, attention was given to the layout and appearance of the questionnaire because this can affect response rates (Jackson, & Furnham, 2000). For example, the colour of the questionnaire may influence response rates (Brennan, & Charbonneau, 2005). Therefore, an instrument identical to the original one was created (in terms of size, instructions, order, grouping of items, response categories), but in three different layouts: one printed on white paper with black letters and grey shading where appropriate (identical to the original one), a second one printed on a light purple paper with black letters and grey shading, and a third, printed on white paper with black letters but with coloured shading and box borders which grouped items. All three were presented to the participants in order to choose the most "attractive" one. Secondly, the clarity, relevance, and appropriateness of wording of the instructions for each subscale (domain), the items and their rating was investigated through verbal probing, a cognitive interviewing technique (Willis, 2005).

Transcription was carried out using the Jeffersonian system (Atkinson & Heritage, 1984; Braun & Clarke, 2006; Jefferson 2004). This system refers to a standardized way (a coding scheme) of guiding verbatim transcription facilitating the conversion of oral language into written. Finally, the open question that the instrument contains was asked, "*Is there anything else* *you would like to tell us about your heart condition or heart operation that is not covered in this questionnaire?"* Additionally, a brief demographic questionnaire and a short medical record were piloted as supplementary materials (concerning format, appropriateness of wording and clarity). For each participant's answer the researcher completed a structured answer sheet as the literature recommends in order to make changes where items appeared difficult or misleading. After minor modifications by the expert panel based on the interviews' qualitative analysis, the final translation back to English was conducted by two different individuals (a bilingual individual born in Greece backtranslated the PCI versions and a bilingual individual born in the USA backtranslated the CABG versions). Then it was sent to the developer in order to get her consent to proceed with the instrument's psychometric evaluation.

5.2.3.2. *Stage II & III: testing of scaling assumptions and validation*

A total of 472 participants were given the information sheet, which introduced the researcher and explained the purpose of the study. After agreeing to participate in the survey, participants signed the consent form, being reminded that they could withdraw at any time without the need for an explanation. After that, participants proceeded with the tasks, depending on the procedure they were to undergo. The pre- PCI or CABG version was administered to the patients on a face-to-face basis. The majority of patients completed the questionnaire by themselves except for a few participants that asked the researcher to help them due to sight problems. All administrations lasted approximately 15-30 minutes and were carried out by the same researcher using a standard procedure and standardised instructions. After the completion of the questionnaire, a brief medical record and some basic demographic data were obtained. Moreover, in order to ensure a high follow-up response rate where the data would be obtained by telephone, the researcher followed Streiner and Norman's (2008) suggestions regarding questionnaire administration. Based on these guidelines, participants who completed the questionnaire prior to their surgical procedure were asked to indicate contact hours that suited them.

A few more points should be mentioned concerning the procedure of this phase. Firstly, the SF-36v2 (Ware & Gandek, 1998) was administered to every 2nd patient. Moreover, in order to avoid order bias, in half the administrations the SF-36v2 was presented first and in the other half the CROQ was presented first.

Secondly, due to the fact that percutaneous coronary interventions (PCI) are administered mostly ad hoc during angiography, patient recruitment was made prior to the coronary angiography without the researcher being aware which patients would have heart surgery. Late in the afternoon of the same day, the head of the coronary interventional office let the researcher know the name of patients who underwent coronary revascularization. The questionnaires completed by patients who did not undergo heart surgery were destroyed on the same day.

The first follow-up was carried out three months later by telephoning the number given by the patients through a "call display" phone number where individuals may be aware of who is calling them, based on suggestions concerning phone surveys (Streiner & Norman, 2008). The 3-month post revascularization follow-up interval was selected based on the suggestions of CROQ authors who maintain that a three-month period is generally considered as an average recovery period for the procedure and only a minority of patients will still be experiencing adverse effects from the particular procedure (Schroter & Lamping, 2004). An update on medical record information was also obtained. Last but not least, the first 20 patients (excluding those administered both the CROQ (Schroter & Lamping, 2004) and SF-36v2 (Ware, & Gandek, 1998)) of each procedure (PCI or CABQ) were recalled two weeks after the 3-months procedure in order to collect data for checking test-retest reliability.

5.2.4. Statistical analysis

To evaluate the acceptability, reliability and validity of the CROQ-Gr, a range of analyses were conducted (Field, 2005; Ware et al., 1995). Tests and criteria are summarized in Table 5.2.

5.2.4.1. Acceptability

Descriptive analysis was carried out in order to estimate instrument acceptability (missing data and response frequencies - ceiling and floor effects) and equal item variance. Missing data was dealt with in line the CROQ developer's guidance (Schroter, 2001) which is based on the algorithm recommended for scoring the SF-36v2 (Ware, 2007). If at least 50% of items in a scale were completed, a person-specific estimate (mean of the non-missing items) was substituted for the missing items. A missing scale score would be assigned if over 50% of the items in a scale were missing, as a result the case would be excluded from the analysis; however no such case was identified. What is important to mention is that the criterion of acceptability regarding ceiling/floor scores might be broken due to the fact that CR aims to increase patients' condition; ceiling scores might be present.

5.2.4.2. Reliability

Scale reliability analysis was carried out with the use of Cronbach's α for internal consistency and intraclass correlation coefficients (ICC) for test-retest reliability.

Table 5.2 Psychometric tests and criteria for the validation of the CROQ-Gr (PCI and CABG scales)

Psychometric property	Criteria for acceptability
Acceptability	Missing data for scales <10% Low ceiling/floor values before revascularization (Streiner & Norman, 2008)
Reliability	
Internal consistency	Cronbach's α for scales >*.70* Item-total correlations >.30 Items discriminant validity = low to moderate zero correlations.
Test-retest reliability	ICC>.70 (Streiner & Norman, 2008; Field, 2005)
Validity	
Content validity	Patients' and experts opinion as well as literature review that items are representative of impact of PCI/CABG
Construct validity(within scale)	Cronbach's α for scales >*.70* Principal axis factor analysis (factor loadings$\geq$ .35) Small intercorrelations between scales score
Construct validity (external criteria)	moderate to strong correlations for similar constructs measured by each instrument r =.10 defined as *small* r =.30 defined as *moderate* r =.50 defined as *large* (Field, 2005)
Sensitivity to change	Paired-t test; statistically significant change set at $p<.05$ (Field,2005)
Responsiveness	Effect size (ES) calculated in accordance to Cohen's *d (post CR mean- prior CR mean divided by standard deviation of mean of prior CR* d =.20 defined as *small* d =.50 defined as *moderate* d =.80 defined as *large* (Schroter and Lamping, 2004; Field, 2005)

5.2.4.3. Validity

In order to assess construct validity (within scale), beyond the Cronbach's *α,* principal axis factoring extraction (PFA) with varimax rotation and coefficient suppression at 0.35 was carried out to identify the factor structure. Zero-order correlation coefficients were calculated to check equality of item-scale correlations and item discriminant validity.

In order to measure construct validity (against external criteria), correlation coefficients (Spearman's *rho*) were calculated for assessing external discriminant and convergent validity between the CROQ and SF-36v2 scale scores. The scoring of the SF-36v2 was carried out with the use of the Health Outcomes Scoring Software 3.0 (Ware, 2007).

5.2.4.4. Sensitivity to change and responsiveness

Sensitivity to change was calculated with the use of paired t-tests. Significance level was set at $p<0.05$

Responsiveness was detected through calculation of ES with the use of Cohen's *d* index. Statistical analyses were conducted with the use of SPSS 20 (IBM, 2011).

5.3. Results

A total of 487 coronary patients were recruited between March 2010 and September 2012. Among them 15 patients participated only in the translation phase, whereas 472 patients participated in the psychometric phase. Patients' mean age was *M* = 60.4 years (*SD* = 10.9) ranging from 32 to 89 and 76.1% (n = 371) were males. Table 5.3 displays the participant demographic and medical features per coronary revascularization procedure.

Table 5.3 Demographic and medical characteristics of the study participants per CR type

	N(%)/Mean(SD) (n=472)	N(%)/Mean(SD) PCI* (n=307)	N(%)/Mean(SD) CABG** (n=165)	t/χ^2	*p* Value
Age (yr)	60.43(10.89)	59.68(11.44)	61.83(9.65)	-2.16	0.031
Sex (female %)	113(23.9)	72(23.5)	41(24.8)	0.12	0.736
Place of residence (%)				29,94	0.001
Athens	365(77.3)	261(85.0)	104(63.0)		
Other big city	31(6.6)	12(11.1)	19(11.5)		
Rural areas	76(16.1)	34(3.9)	42(25.5)		
Marital status(%)				1.82	0.213
Unmarried/living alone	87(18.4)	62(20.2)	25(15.2)		
Married	385(81.6)	245(79.8)	140(84.8)		
Educational status(%)				1.46	0.283
6 years or less	122(25.8)	82(26.7)	40(24.2)		
7-12 years (high school	226(47.9)	150(48.9)	76(46.1)		
12^+ years	124(26.3)	74(24.1)	50(29.3)		
Occupational status				5.58	0.129
Unemployed	69(14.6)	47(15.3)	22(13.3)		
Public/Private servant	123(26.1)	89(29.0)	34(20.6)		
Freelance	97(20.6)	56(18.2)	41(24.8)		
Pensioner	183(38.8)	115(37.5)	68(41.2)		
Risk factors (%)					
CHD family history	235(49.8)	154(50.3)	81(49.1)	0.07	0.847
Hypertension	175(37.1)	114(37.6)	61(37.0)	0.04	0.505
Cholesterol	153(32.4)	92(30.4)	62(37.2)	2.26	0.148
Diabetes	133(28.2)	76(25.1)	57(34.8)	4.89	0.032
Smoking	238(50.4)	161(53.0)	77(46.7)	1.70	0.209
BMI***(kg/m^2)	28.62(4.45)	28.44(4.9)	28.93(4.70)	1.13	0.260
Methods of CR		307(65.0)	165(35.0)	42.7	<0.001
PCI				15.5	<0.001
Metal Stent		117(38.1)			
Drug eluting Stent		187(60.9)			
CABG				41.8	<0.001
Off Pump			41(24.8)		
On Pump			123(75.5)		

* PCI= Percutaneous Coronary Interventions **Coronary Artery Bypass Grafting

***__BMI Categories:__ Underweight = <18.5, Normal weight = 18.5–24.9, Overweight = 25–29.9, Obesity = BMI of 30 or greater

5.3.1. Stage I: translation and cultural adaptation

The translations of the two individuals with an English language qualification were almost identical. Two minor changes were made by the panel. The first one referred to the 2nd question "During the past 4 weeks how many times have you taken nitros (nitroglycerin tablets or spray) for chest pain, chest tightness or angina?" where the word *spray* was deleted as Greek cardiologists usually do not prescribe spray. The second change was made for the physical functioning domain. In this domain, it was agreed to adopt the wording of the items of the Greek version of the SF-36 (Papa, et al., 2006). It seemed a good solution partly because Dr Schroter (the author of the CROQ) had borrowed the items for this domain from the English version of the SF-36 and, partly, because some items appeared not to be relevant to the situation in Greece. For instance, it would not be appropriate to ask participants "…has your heart condition limited you in your usual daily activity in moderate activities such as *bowling and playing golf*", since the majority of Greeks do not play golf and rarely bowl.

The preliminary questionnaire was completed by fifteen post CABG patients, with a mean age *M* = 65.73 years (*S.D.* = 9.10), the majority (80%, n=12) were males. This is an indication of the fact that more males than females undergo coronary artery bypass graft surgery. Concerning the questionnaire appearance, 87% of participants preferred the white-colored shading appearance and none chose the purple one. Regarding the CROQ's clarity and appropriateness of wording 10 participants answered positively for all 52 items, 5 considered two instructions: "During the past 4 weeks how many times have you taken nitros for chest pain, chest tightness or angina?" and "During the past 4 weeks how much trouble has your heart condition caused?" as not clear enough. Furthermore, 5 participants suggested that two items were "not clear enough and/or inappropriate": "moderate activities (e.g. playing racquetball on the beach)" and "climbing several flights of stairs" from the physical functioning domain.

All participants confirmed the clarity of the response scale. Concerning comprehension, analysis of the examined items showed that the majority of patients could give accurate synonyms indicating appropriate comprehension. Two items were misunderstood or misinterpreted by a few individuals. Misunderstanding appeared for the "nitros" item/question in the symptoms domain and "overprotection" in the psychosocial domain. Nitros were interpreted as ordinary pills for heart or hypertension by 7 patients. Overprotection was interpreted as a special care/interest from family members or friends by 8 participants.

All these findings lead the scientific panel at its 2nd meeting to make some minor modifications to the questionnaire for which Dr Schroter gave her consent.

5.3.2. Stage II to III: scaling assumption for PCI version

Out of the 307 PCI patients, 76.5% (n=235) were males. At recruitment, participants' mean age was *M*=59.68 years (*SD*=11.44) with a range of 32-89 years.

5.3.2.1. ***Acceptability***

Concerning equal item variance, the *SD* of items in each scale was quite similar (Appendix 5.1). Moreover, all PCI versions had good acceptability with little missing data per subscale (Table 5.4). With the exception of the *physical functioning* scale the total number of instances with missing data was quite small.

Table 5.4 Acceptability and Reliability of the CROQ-Gr PCI (pre and post versions)

		Acceptability		Reliability	
CROQ scale	Score (range 0-100) mean (SD)	Missing data (range)	Floor / ceiling effects	Internal consistency (Cronbach's α)	Test-retest (ICC)
CROQ-PCI _pre(n=244)					
Symptoms (7 items)	63.62(18.73)	2.3%(0.4-6.0)	0%/1.7%	.71	--
Physical functioning (8 items)	56.29(28.24)	8.3%(0.8-19.0)	2.9%/20.2%	.92	--
Psychosocial functioning (14 items)	67.34(15.96)	1.1%(0.4-2.0)	2.5%/19.9%	.91	--
Cognitive functioning (3 items)	82.98(18.45)	0.5%(0.4-0.8)	0.5%/50.4%	.88	--
CROQ-PCI _post (n=244)					
Symptoms (7 items)	90.34(11.41)	0%(0-0.2%)	0%/35.3%	.75	.80
Physical functioning (8 items)	89.08(14.96)	5.4%(0-18%)	1.3%/48.2%	.83	.87
Psychosocial functioning (14 items)	84.51(12.13)	1.9%(0-3.6%)	0%/6.3%	.84	.86
Cognitive functioning (3 items)	89.73(15.11)	1.1%(0-2.4%)	0.4%/51.8%	.86	.96
Adverse effects (6 items)	97.50(5.88)	0.6%(0.4-1.2%)	0%/77.3%	.81	.89
Satisfaction (6 items)	85.99(3.85)	1.6%(0.4-5.1%)	2.8%/27.5%	.77	.94

The two items that demonstrated moderate to high levels of missing data were "*climbing two or more flights of stairs*" and "*walking a kilometre*". This was partially expected as Greek individuals culturally prefer to use elevators and cars in daily life. Moreover, all subscales demonstrated low to moderate floor/ceiling effects with an exception of *cognitive functioning* and *adverse effects*.

5.3.2.2. Reliability

Regarding reliability, in both pre and post PCI versions, subscales exceeded the criterion of ≥0.70 for both internal consistency (Cronbach's *alpha*) and temporal stability (test-retest, ICC; Table 5.3; Streiner & Norman, 2008). As for item-scale correlation (items are more strongly correlated with their own scale than with other scales) the criterion of correlation >0.30 was reached for both versions (Appendix 5.2). However, for the post procedure version a few *symptom* items demonstrated a low correlation with their subscale (r=0.17).

5.3.2.3. Validity

5.3.2.3.1. Content validity

Content validity was evaluated during the development of the CROQ-Gr versions and in the preliminary and pilot studies. A review of the literature regarding patients' quality of life and other health issues after coronary revascularization as summarised above, expert opinion and advice as well as the face-to-face interviews provided support for the content validity of CROQ-Greek versions. In particularly, a literature overview was conducted on issues regarding coronary heart disease and its treatment in relation to the biopsychosocial model (BPS; Engel, 1980). Parts of that review are presented in chapter 1 and 2. Patients' opinions regarding content validity were elicited through face to face interviews as presented in section 5.3.1. During those interviews individuals were asked to comment on each item regarding its relevance, clarity and simplicity. Furthermore, experts opinion and advice about the CROQ's content validity was taken into account based on four criteria; relevance, clarity, simplicity, and ambiguity as suggested by Yaghmaie (2003) during two panel meetings. Specifically, the first panel meeting took place at Thriasio hospital prior to the patient interviews. It consisted of four individuals: an operational cardiologist, a surgeon, a health psychologist and the researcher. The second panel meeting took place at Metropolitan hospital and consisted of six people; the same four persons as above plus a second operational cardiologist and another surgeon. As stated in section 5.3.1 during the first panel meeting relevance and clarity was discussed resulting in two changes: The first occurred in the 2nd question ("During the past 4 weeks how many times have you taken nitros (nitroglycerin tablets or spray) for chest pain, chest tightness or angina?" where the word *spray* was deleted as Greek cardiologists usually do not prescribe spray), while the he second was in relation to the physical functioning domain ("…has your heart condition limited you in your usual daily activity in moderate activities such as *bowling and playing golf*"; since the majority of Greeks do not play golf and rarely bowl, this was replaced by *playing racquetball on the beach*).

The second panel meeting took place after analyzing the patient interviews. During this meeting each item was assessed based on the four criteria as stated above (Yaghmaie, 2003) with the following process: The researcher read clearly and loudly the question or the item and then asked panel members "do you believe that this item is a) very relevant? b) very clear? c) very simple? d) meaning is clear (i.e. in terms of ambiguity)?. If each member answered "yes" to each question then the next item was presented. In cases where one or more members of the panel replied "no" or raised any concerns, a brainstorming of suggestions took place with the best possible alternatives. When a mutually agreed change was established, the researcher made a note and proceeded to the next question/item. Special attention was given to items that appeared as not very clear from the patient interviews even if they were very clear to panel. In these cases the researcher highlighted that the particular item was not very clear to patients and asked the panel to propose a common accepted alternative. It is important to state that the researcher had the role of meeting coordinator and kept notes; she was not involved in any decision making.

Specifically, the following alterations were made as a result of the second panel meeting:

A) *Symptoms* domain

1) In the 2nd question, the word "nitros" was replaced by the word "sublingual" as suggested by some individuals and the cardiologist agreed.
2) In the 4th question the word "suffering" was added in brackets as a clarification.

B) *Physical functioning* domain

1) In the 1st item the phrase "playing racquetball on the beach" was deleted as irrelevant
2) In the 3rd item referring to "climbing several flights of stairs" the clarification "two or more" was added in brackets.

C) *Psychosocial functioning* domain

1) In the 1st item after the phrase "overprotective toward you" the clarification "overdoing" was added in brackets.

Last but not least, both the demographic questionnaire and medical record questions were confirmed by all participants as clear.

*5.3.2.3.2. **Construct validity (within scale)***

In addition to the high levels of internal consistency and intraclass correlation coefficients described above, additional support for the construct validity of the CROQ-Gr can be demonstrated from the findings of the factor analysis. A four factor solution following principal axis factoring (loadings ≥0.35) with Varimax rotation was selected a priori for the common items in the pre- and post-CR versions, as per the procedure described for the development of the CROQ. For all versions, the Kaiser-Meyer-Olkin test verified sampling adequacy (KMO >.78) and Bartlett's test confirmed sphericity ($p<.001$). Four factors had Eigen values that were greater than 1 and items loaded on their expected factor (Table 5.5). However, the four factor model of rotated squared loadings explained between 41.7% to 50.3% of the variance, depending on the version, implying a moderate explanatory power. Results were almost identical to the original English version.

Following the original development of the CROQ, a separate PFA should be carried out in order to assess the construct validity of the two additional subdomains of the post-PCI version. Following developer instructions a second PFA was conducted (Table 5.6 shows the item loadings). Once again however, this only explained a relatively low percentage of variability. The two factor model explained 42.1% of the variance. Concerning the reliability of these two subdomains, a good level of internal consistency and test-retest reliability had been found (as demonstrated earlier in Table 5.3).

Table 5.5 PFA* for CROQ-Gr PCI score items (pre and post versions)

	Factors for pre-PCI					Factors for post-PCI			
	1	2	3	4		1	2	3	4
Chest pain			.68				.37	.49	
Discomfort			.66					.58	
Shortness of breath			.45					.56	
Angina radiates			.54					.42	
Palpitations			.43					.48	
Sublingual per day			.19					.44	
Troubles	.51		.41					.50	
Moderate activities	.59						.49	.35	
Lifting	.70						.45		
Climbing two or more flights	.79						.67		
Climbing one flight	.80						.61		
Bending	.74						.67		
Walking a km	.83						.68	.31	
Walking 100 m	.85						.57		
Bathing	.61						.58		

Table 5.5 PFA* for CROQ-Gr PCI score items (pre and post versions)

	Factors for pre-PCI					Factors for post-PCI			
	1	2	3	4		1	2	3	4
Overprotective environment		.50				.42			
Burden on others		.38	.39			.35			
Restriction of social activities		.60				.47			
Go far from home		.55				.50			
Worried about heart condition		.61				.65			
Worried about overdoing		.38				.54			
Worried about sudden attack		.52				.70			
Frightened by pain		.73				.65			
Uncertain about future		.69				.64			
Depressed		.61				.30			
Frustrated / impatient		.55				.48			
Enjoyment of life		.62				.69			
Positive outlook of health		.50				.64			
Plan ahead	.36	.48				.31			
Reasoning and solving problems				.83					.75
Forget				.93					.80
Concentration				.80					.78

*PFA=Extraction Method: Principal Axis Factoring. Rotation Method: Varimax with Kaiser

Table 5.6 PFA for CROQ-Gr PCI post version additional items

	Factor	
	1	2
Post pain in groin wound	.50	
Post tenderness	.55	
Post numbness or tingling	.62	
Post bruising	.78	
Post catheter point	.57	
Post concern for bruises	.80	
Post satisfaction about results	.39	.41
Post satisfaction about operation info		.78
Post satisfaction about recovering info		.82
Post heart condition after operation		.50
Post recovery		.48
Post results from heart operation		.54

5.3.2.3.3. Construct validity (against external criteria)

Construct validity against external criteria was examined through the correlations between the CROQ-Gr and the SF-36v2 subscales (Table 5.7). Correlations between the CROQ-PCI and the SF-36v2 physical component summary score (PCS) at baseline were stronger for the *Symptoms* and *Physical Functioning* subscales than for the *Psychosocial Functioning* subscale. Conversely, correlations between the CROQ and the SF-36v2 mental component summary score (MCS) at baseline were stronger for the *Psychosocial Functioning* subscale than for the *Symptoms* and *Physical Functioning* subscales. The CROQ's *cognitive function* domain was not expected to be correlated with any summary score as it is not measured by the SF-36v2.

Table 5.7 Spearman rho correlation between CROQ-Gr PCI and SF-36v2

CROQ –PCI scales	**SF-36v2**									
	PF	**RP**	**BP**	**GH**	**V**	**SF**	**RE**	**MH**	**PCS**	**MCS**
Baseline (N=50)										
Symptoms	.64**	.40**	.49**	.50**	.187	.09	.16	-.06	**.64****	.04
Physical functioning	.86**	.27	.48**	.42**	.41**	.31*	.26	.08	**.72****	.31*
Psychosocial functioning	.27	.07	.40**	.44**	.70**	.49**	.37**	.64**	.36*	**.71****
Cognitive functioning	.16	.15	.17	.02	.17	.14	.08	.11	.18	.15
Adverse effects	---	---	---	---	---	---	---	---		
Satisfaction	---	---	---	---	---	---	---	---		
3 months after heart surgery (N=45)										
Symptoms	.44**	.39**	.15	.26	.23	.11	-.04	.15	**.42****	.17
Physical functioning	.80**	.36*	.26	.43**	.10	.47**	.08	.01	**.67****	.22
Psychosocial functioning	.24	.25	.16	.42**	.59**	.52**	.45**	.76**	.37*	**.77****
Cognitive functioning	-.16	-.28	-.12	.01	-.21	-.11	-.27	-.27	-.06	.30
Adverse effects (chest)	-.00	.33*	.11	.16	.06	.08	-.06	-.06	.22	.06
Adverse effects (leg/arm)	.17	.06	-.06	-.2	-.06	.05	-.09	-.08	-.01	-.01
Satisfaction	.44**	.39**	.15	.26	.23	.11	-.04	.14	**.42****	.17

*Correlations between scales that purport to measure similar aspects of health related quality of life. Weak correlation ($r \leq 0.40$); moderate correlation ($0.40 < r < 0.70$); strong correlation ($r \geq 70$). -MCS, mental component summary score; PCS, physical component summary score; PCS & MCS are summaries of SF-36v2; PF=Physical Functioning, RP=Role Physical, BP=Bodily Pain, GH=General Health, V=Vitality, SF=Social Functioning, RE=Role Emotional, MH= Mental Health

5.3.2.4. Sensitivity to change

A series of paired t-tests demonstrate the statistically significant difference between pre (T1) and post (T2) coronary intervention. As Table 5.8 demonstrates CR has a large size effect on PCI-CROQ scores.

Table 5.8 Descriptive statistics and sensitivity to change as indicated by CROQ-Gr PCI between baseline and 3 months post treatment

CROQ PCI subscales (n=195)	T1	T2	*t* 0-3mths	*d*
Symptoms	63.66(18.28)	90.29(12.17)	18.39**	**1.46**
Physical functioning	54.84(26.96)	88.39(15.43)	17.05**	**1.24**
Psychosocial functioning	62.33(16.62)	83.33(12.62)	16.45**	**1.26**
Cognitive functioning	83.79(17.62)	91.08(15.09)	4.63*	**0.41**

*p<0.05, **p≤0.01

5.3.3. Stage II to III : scaling assumption for CABG version

Out of 165 CABG patients 75.15% (*n*=124) were males. Participants' mean age was *M*=61.83 years (*SD*=9.65) with a range of 44-82 years.

5.3.3.1. Acceptability

Concerning equal item variance, the *SD* of items in each scale is quite similar. Moreover, both CABG versions had good acceptability with little missing data per subscale (Table 5.8). With exception of the *physical functioning* scale the total number of instances with missing data was quite small. The two items that demonstrated moderate to high levels of missing data are "*climbing two or more flights of stairs*" and "*walking a kilometre*", as in the PCI versions.

Furthermore, all subscales in the pre-revascularization version demonstrated low to moderate floor/ceiling effects with the exception of *cognitive functioning* where the ceiling index is quite high (Table 5.9). In contrast, the post-revascularization version had elevated percentages suggesting ceiling effects for *symptoms*, *physical functioning* and *adverse effects* (leg/arm).

Table 5.9. Acceptability and Reliability of CROQ-Gr CABG (pre & post versions)

		Acceptability		Reliability	
CROQ scale	Score (range 0-100) mean (SD)	Missing data (range)	Floor / ceiling effects	Internal consistency (Cronbach's α)	Test-retest (ICC)
CROQ-CABG _pre (n=161)					
Symptoms (7 items)	59.27 (16.84)	1.5%(0-4%)	0%/0%	.80	--
Physical functioning (8 items)	41.36 (21.33)	7.8%(0-18%)	0.7%/0%	.85	--
Psychosocial functioning (14 items)	71.41 (16.98)	3.5%(0-8.7%)	0%/0%	.93	--
Cognitive functioning (3 items)	80.33 (14.97)	0%(0-0.6%)	0%/15.8%	.83	--
CROQ-CABG _post (n=144)					
Symptoms (7 items)	93.84 (7.95)	0%(0-0.7%)	0%/39.8%	.83	.82
Physical functioning (8 items)	89.08 (14.54)	6.4%(0-24%)	1.3%/47%	.87	.97
Psychosocial functioning (14 items)	84.95 (13.32)	1.9%(0-5.8%)	0%/6.3%	.93	.95
Cognitive functioning (3 items)	83.95 (17.13)	1.3%(0-2.6%)	0 %/7 %	.92	.98
Adverse effects (11 items)	84.19(12.74)	0.4%(0-2.6%)	0%/19.2%	.84	.87
Adverse effect chest (5 items)	76.67 (18.68)	0.4%(0-2.6%)	0%/10.7%	.86	
Adverse effect leg/arm (6 items)	90.35 (13.71)	0.2%(0-2.2%)	0%/40%	.87	
Satisfaction (11 items)	72.99 (22.23)	1.8%90-7.9%)	0%/5.5%	.85	.94

5.3.3.2. Reliability

Regarding reliability, in both the pre and post CABG versions, subscales exceeded the criterion of ≥0.70 for both internal consistency (Cronbanch's *alpha*) and temporal stability (test-retest, ICC; Table 5.9; Streiner & Norman, 2008). As for the item-scale correlation (items are more strongly correlated with their own scale than with other scales) the criterion of correlation >0.30 was reached for both versions (Appendix 5.2).

5.3.3.3. Validity

5.3.3.3.1. Content validity

Content validity was assessed during the development of the CROQ-Gr versions and in the preliminary and pilot studies. A review of the literature regarding patients' quality of life and other health issues after coronary revascularization as summarised above, expert opinion and advice as well as the face-to-face interviews provided support for the content validity of the CROQ-Greek versions. The process followed was the same as for the PCI version, as described in section 5.3.2.3.1

5.3.3.3.2. Construct validity (within scale)

In addition to the high levels of internal consistency and intraclass correlation coefficients described above, additional support for the construct validity of the CROQ-Gr can be demonstrated from the findings of the factor analysis. A four factor solution following principal axis factoring (loadings ≥0.35) with Varimax rotation was selected a priori for the common items in the pre- and post-CR versions, as per the procedure described for the development of the CROQ. For all versions, the Kaiser-Meyer-Olkin test verified sampling adequacy (KMO >.80) and Bartlett's test confirmed sphericity (p<.001). Four factors had Eigen values greater than 1 and items loaded on their expected factor (Table 5.10). However, the four factor model of rotated squared loadings explained only 50.3%-51.6% of the variance, depending on

Table 5.10 PFA for CROQ-Gr CABG core items (pre and post versions)									
	Factors pre- CABG					Factors post- CABG			
	1	2	3	4		1	2	3	4
Factor 1: Symptoms									
Chest pain			.51					.64	
Discomfort			.48					.74	
Shortness of breath			.63					.53	
Angina radiates			.64					.51	
Palpitations			.47					.43	
Sublingual per day			.63	.51				.37	
Troubles			.54				.36	.65	
Factor 2: Physical functioning									
Moderate activities		.46					.69		
Lifting		.52					.56	.38	
Climbing two or more flights		.58					.80		
Climbing one flight		.66	.40				.77		
Bending		.66				.40	.50		
Walking a km		.79					.77		
Walking 100 m		.54					.59		
Bathing		.54				.35	.60		
Factor 3: Psychosocial functioning									
Overprotective environment	.63					.49			
Burden on others	.62					.47			
Restriction of social activities	.72					.63			
Go far from home	.78					.61			
Worried about heart condition	.40					.63			
Worried about overdoing	.66					.52			
Worried about sudden attack	.68					.66		.37	
Frightened by pain	.59					.82			
Uncertain about future	.71			.39		.76			
Depressed	.70			.44		.78			
Frustrated / impatient	.79					.79			
Enjoyment of life	.65			.46		.72			
Positive outlook of health	.55			.35		.71			
Plan ahead	.67					.74			
Factor 4: Cognitive functioning									
Reasoning and solving problems				.56					.86
Forget				.68					.84
Concentration				.80					.92

the version, implying a moderate explanation. For the post-CABG version, very low correlations were found for two items hypothesized to belong to the *symptom* scale; the “sublingual intake frequency” and “troubles”. However, these two items did not strongly correlate with other items belonging to a different conceptual domain. These two items were retained for clinical reasons. With the exception of those two items, results were almost identical to the original English version.

As for the two additional scales of the post-CABG version, the Kaiser-Meyer-Olkin test verified sampling adequacy (KMO >.72) and Bartlett’s test confirmed sphericity (*p*<.001). However, the factor analysis did not confirm the original construct (Table 5.11).

Table 5.11 PFA* for CROQ-Gr CABG- post version additional items							
Two factors analysis	Factors			Three factors analysis	Factors		
	1	2			1	2	3
Factor 1: adverse effects in chest				**Factor 1: adverse effects in chest**			
Pain in the chest wound	.76			Pain in the chest wound	.41		**.74**
Infection in the chest wound	.75			Infection in the chest wound	.53		**.75**
Tenderness around chest wound	.67			Tenderness around chest wound			**.69**
Numbness or tingling around chest wound	.69			Numbness or tingling around chest wound			**.84**
Bruising on chest	.59			Bruising on chest			**.72**
				Factor 2: adverse effects in leg & arms			
Pain in leg or arm wound		.78		Pain in leg or arm wound		**.72**	.54
Any other pain in leg or arm		.59		Any other pain in leg or arm		**.65**	
Infection in leg or arm		.69		Infection in leg or arm		**.76**	
Numbness in leg or arm		.87		Numbness in leg or arm		**.82**	.37
Bruising in leg or arm		.76		Bruising in leg or arm		**.73**	
Swollen feet or ankles		.66		Swollen feet or ankles		**.64**	
Factor2: satisfaction				**Factor 3: satisfaction**			
Satisfaction about results	.91			Satisfaction about results	**.84**		.40
Satisfaction about operation info	.87			Satisfaction about operation info	**.76**		.46
Satisfaction about recovering info	.76			Satisfaction about recovering info	**.70**		.36
Heart condition after operation	.59			Heart condition after operation	**.65**		
Recovery	.41			Recovery	**.49**		
Results from heart operation	.61			Results from heart operation	**.67**		
*Extraction Method: Principal Axis Factoring. Rotation Method: Varimax with Kaiser Normalization.							

A clear distinction between different *adverse effects* items was found. Therefore, a three factor model was carried out. In this factor analysis (Table 5.11), item loadings exceeded the criterion of ≥0.35. The majority of items were scaling successes. However, a probable scaling failure was found for an item of the *adverse effects* domain, the "infections to chest wound-10b" item, which strongly correlated with *satisfaction* items. The three factor model accounted for 63.7% of the variance. This index suggests a moderate to high explanation.

5.3.3.3.3. ***Construct validity (against external criteria)***

Construct validity against external criteria was examined through the correlations between the CROQ and the SF-36v2 subscales (Table 5.12). Correlations between the CROQ-CABG and the SF-36v2 physical component summary score (PCS) at baseline were stronger for the *symptoms* and *physical functioning* subscales than for the *psychosocial functioning* subscale. Conversely, correlations between the CROQ and the SF-36v2 mental component summary score (MCS) at baseline were stronger for the *psychosocial functioning* subscale than for the *symptoms* and *physical functioning* subscales. CROQ's *cognitive functioning* domain was not expected to be correlated with any summary score, as it is not measured by the SF-36v2.

Table 5.12 Spearman rho correlation between CROQ-Gr CABG and SF-36v2

CROQ –CABG scales	SF-36v2									
	PF	RP	BP	GH	V	SF	RE	MH	PCS	MCS
Baseline (N=52)										
Symptoms	**.29***	**.56****	**.30***	.16	.22	.28*	.30*	.20	**.40****	.29*
Physical functioning	**.71****	**.58****	**.80****	**.60****	.21	-.01	.19	.12	**.91****	.15
Psychosocial functioning	-.03	.05	.12	.06	**-.10**	**.72****	**.77****	**.81****	.05	**.81****
Cognitive functioning	.23	.24	.22	-.07	**.39****	**.40****	**.39****	**.42****	.23	**.54****
Adverse effects	---									
Satisfaction	---									
3 months after heart surgery (N=50)										
Symptoms	**.01**	**-.13**	**.17**	**.42****	-.06	-.15	-.22	.02	**.10**	-.14
Physical functioning	**.49****	**.20**	**.35***	**.44****	.40**	.21	.33*	.28*	**.49****	.37**
Psychosocial functioning	.35*	.38**	.11	.03	**.31***	**.34***	**.60****	**.38****	.33*	**.54****
Cognitive functioning	.16	.20	.24	.03	**-.03**	**-.10**	**-.06**	**-.23**	.28*	**-.10**
Adverse effects (chest)	-.01	.05	.11	-.07	.09	.14	.07	-.14	.04	.04
Adverse effects (leg/arm)	-.19	.17	-.08	-.12	-.02	-.07	-.14	-.36*	-.03	-.17
Satisfaction	.17	.14	.13	-.01	.16	.12	.09	.15	.17	.12

$^{*}p<0.05$ $^{**}p\leq 0.01$

-Correlations between scales that purport to measure similar aspects of health related quality of life. Weak correlation ($r \leq 0.40$); moderate correlation ($0.40 < r < 0.70$); strong correlation ($r \geq 70$).

-MCS, mental component summary score; PCS, physical component summary score; PCS & MCS are summaries of SF-36v2; PF=Physical Functioning, RP=Role Physical, BP=Bodily Pain, GH=General Health, V=Vitality, SF=Social Functioning, RE=Role Emotional, MH= Mental Health

5.3.3.4. Sensitivity to change

A series of paired t-test demonstrate the statistically significant difference between pre and post coronary intervention. As Table 5.13 shows CABG-CROQ post scores significantly differ from those pre revascularization. Also CABG-CROQ scores demonstrate that CR has a large positive effect on patients' *symptoms*, *physical functioning*, *psychosocial functioning* and a low effect on *cognitive functioning*.

Table 5.13 Descriptive statistics and sensitivity to change as indicated by CROQ-Gr CABG between baseline and 3 months post treatment

CROQ PCI subscales (n=119)	T1	T2	*t* 0-3mths	*d*
Symptoms	60.36 (15.27)	94.29(6.83)	22.26**	2.16
Physical functioning	41.39(19.61)	89.81(14.21)	24.62**	2.47
Psychosocial functioning	71.46(16.13)	84.53(13.62)	6.29**	0.81
Cognitive functioning	81.40(13.88)	84.42(17.34)	1.65	0.22

**p≤0.01

5.4. Discussion

The aim of this study was to develop a Greek version of the CROQ (for both PCI and CABG procedures) and test it against rigorous scientific criteria in order to fill the gap in the literature. Both versions were examined at two time points: prior to coronary revascularization, and 3 months after revascularization.

5.4.1. Findings

Results showed that the adapted Greek version of the CROQ is a practical and scientifically sound patient-based instrument able to measure health related quality of life and other health issues before and after coronary revascularization. Generally, results are promising, revealing that the CROQ-Gr is acceptable to patients and satisfies the majority of the rigorous psychometric criteria set regarding reliability, validity and responsiveness. Findings are in accordance with results reported by the CROQ developers (Schroter & Lamping, 2004) as well as with its other language adaptations; Italian (Pintor et al., 2002), Farsi (Shahali et al., 2008) and Japanese (Seki et al., 2010).

However, a few issues should be highlighted in order to draw a clear conclusion regarding the instrument's characteristics. These issues are related to cultural issues as well as to specific psychometric aspects (acceptability, construct and concurrent validity and responsiveness) that may influence results.

5.4.1.1. *Cultural issues*

Overall, Greek people are willing to participate in a research study. Actually, occasionally patients perceived their inclusion in the study as a specific interest in their experience, and were very enthusiastic and detailed in their answers, especially during the follow-up where questionnaire administration was carried out over the phone.

Moreover, when interpreting findings, cultural issues (Marquis et al., 2005) should be considered due to the fact they could influence the total scores obtained for each subscale, which in turn could influence conclusions about research questions.

First of all, observing the scores obtained through the CROQ-Gr and by the English (original) version (Schroter & Lamping, 2004), scores obtained through the Greek PCI version were rather higher. This may be an indication of cultural discrepancy that has been reported before (Li, Wang, & Shen, 2003). Perhaps Greek patients do perceive their HRQoL to be rather "good" despite health issues. The literature indicates that patients in different cultures tend to selectively express symptoms as well as physical and/or psychological functioning in culturally acceptable ways. This is based on how people perceive, sense and articulate their physical and mental problems. For instance, regarding their culture, individuals might suppress upsetting thoughts while others might adopt a more active way of expressing and facing problems, rather than ignoring them (U.S. Department of Health and Human Services, 2001).

Secondly, Greek people tend to systematically avoid physical activities. This claim can be supported by various studies suggesting that Greeks tend to be an inactive population. Research findings reveal that the vast majority of Greeks demonstrate low physical activity and tend to avoid exercising, walking or running, preferring a sedentary lifestyle, driving and using the elevator, especially those living in urban areas (Athyros et al., 2005; Milias et al., 2006; Pitsavos, et al., 2006; Pitsavos, Panagiotakos, Lentzas, & Stefanadis, 2005). Between 2002 and 2005, a shift has been noted; many individuals, in an effort to maintain a healthy body, increase fitness or control their weight, have developed a more active lifestyle. This shift could be explained by the plethora of public educational interventions that support a "therapeutic" role of physical activity which took place in Greece right after its entry into the EU. However, this observation was mostly related to younger females (Athyros et al., 2005; Pitsavos et al., 2005) and higher income individuals (Tzormpatzakis & Sleap, 2007).

Thirdly, concerning the *psychological functioning* scale, a few more issues should be considered, especially in items related to the impact of the heart condition on family and friends and the extent to which it has interfered with individuals' social activities. The Greek population is more collectivist (Audickas, Davis, & Szczepańska, 2006), has tight family relationships and bonds and is more socially oriented than countries such as the UK. When a family member becomes ill, s/he becomes the family's focus of attention and care. Thus the majority of respondents, especially male, responded automatically that they are "a lot" overprotected by family because the concept of overprotection seems to be the standard for family care. For instance, with this particular item, many participants added to their answer that the whole family showed intense care and concern about their heart condition, which is actually different from overprotection.

5.4.1.2. *Psychometric aspects needing special attention*

5.4.1.2.1. *Acceptability and Scoring*

Generally, the CROQ-Gr is an instrument that is easily completed and accepted by patients. However, regarding acceptability, a great number of missing values were observed for *physical functioning* in all versions, in all intervals. The most commonly missing items were related to "Climbing two or more flights of stairs", "and "Walking 1 km". This observation could be related to the complexity of the questions and/or cultural issues as discussed elsewhere.

In terms of the complexity of the questions, an issue emerging from both the qualitative and quantitative parts of the study is whether the "walking" questions referred to walking on a flat surface or uphill. When the particular inquiry was made, the researcher suggested a flat surface. Nevertheless, fundamental problems may be present due to this uncertainty. When participants respond to these questions without clarification, having in mind one or the other situation, they may answer differently, creating inconsistency, or do not answer the question at all due to confusion and producing missing data. It essential to point out that when participants had the opportunity to ask, they stated limitations when walking uphill but not on a flat surface. These concepts suggest the need to reduce confusion. Upon resolving this problem instrument acceptability, content validity and sensitivity to change could become even stronger.

Concerning the scoring, the CROQ scoring is time consuming, especially for missing data, compared with other instruments (e.g. SF-36v2). The development of software would resolve this difficulty. For instance, using the software for the SF-36v2 scoring and total score calculation is very easy; calculations and transformation are automatically done in a few minutes. Moreover, with the use of software, human errors in both data entry and scoring are minimized as data are inserted in the data sheet through completing an electronic form (Saris-Baglama, et al., 2009).

5.4.1.2.2. ***Construct validity***

Regarding construct validity, results should be interpreted keeping in mind that the four factor model at all time-points explained only a moderate variability in scores in both the PCI and CABG versions. In both the PCI and CABG versions, the most "problematic" item for both pre and post operation version was in the *symptoms* scale, "*sublingual intake frequency*". One could suggest its exclusion (Zhang et al., 2013). However, it was retained for clinical reasons. Moreover, a few other "problematic" items with a probable scaling failure in the CABG version are related to "troubles faced due to the health condition" in the symptoms scale and "bending" in the *physical functioning* scale.

The researcher made a great effort to recruit as many CABG patients as possible. However the mission became more and more difficult as fewer and fewer coronary surgical procedures are carried out in the allied hospitals. This phenomenon might be partly explained by the financial crisis existing in Greece leading to cut in the public health system. In many cases hospitals do not have the resources or the necessary personnel to proceed with such operations (Efthimiadou, 2012). In some others EOPYY (the national health insurance agency) cannot afford the cost (Efthimiadou, 2012). Another reason for the reduction in the number of bypasses might be related to the technological and scientific advances in the field of heart surgery. A great number of coronary bypasses are made through Minimally Invasive Direct Coronary Artery Bypass (MIDCAB; discussed elsewhere). Evidence based findings suggest that MIDCAB surgery is preferred when a bypass for one or two coronary arteries is required as it results in less pain after surgery, a shorter hospital stay, a faster recovery, an earlier return to work and fewer complications while conventional CABG is indicated for bypassing three or more arteries (Eagle et al., 1999). Therefore, coronary patients may decide to undergo MDDCAB instead of traditional CABG.

Finally, another interesting finding was related to *adverse effects*. In the Greek CABG version a clear division was revealed between problems related to chest wounds and problems related to leg/arm wounds. However, for reasons of consistency with other CROQ adaptations it is kept as one.

5.4.1.2.3. Construct validity based on external criteria

Regarding validity based on external criteria, the present study showed that the PCS score of the SF -36 correlates with the CROQ scales *symptoms* and *physical functioning*, and that the MCS score of the SF-36v2 correlates with the CROQ's *psychological functioning* scale. However, item-total correlations did not show strong correlations (e.g. for *symptoms*); an issue that was present also in the Japanese version (Seki et al., 2010). This raises various concerns and highlights the need for further testing. However, this problem might be present due to two crucial reasons. The first one is the small sample size (< 50). The second explanation may lie in the fact that these two tools do not measure exactly the same constructs. For instance, the CROQ *symptoms* or *physical functioning* scale is unlikely to correlate with the SF-36v2 Bodily Pain subscale as coronary revascularized individuals, especially those who undergo a PCI treatment, may experience angina or dyspnea over a one-year period, but they do not experience bodily pain. It is not unexpected that the biggest correlation between the two measures exists for the *physical functioning* scale which contains many similar items. Nevertheless both measures aim to demonstrate quality of life, but the CROQ is a condition-specific measure while the SF-36v2 is a generic measure. Thus, they emphasise different issues.

5.4.2. Strengths and Limitations

Concerning the study's limitations, a few methodological issues should be highlighted. These issues are mostly related to the mode of administration, the sample size and the establishment of validity.

5.4.2.1. *Administration mode*

The present study used a different mode of administration compared to the original one. Instead of mailed or self administration, it used self-administration prior to revascularization and telephone administration in post-revascularization follow-up. The high response rate at both time points suggests that the particular mode is rather acceptable to the Greek population. As experts maintain (Bowling, 2005) a trained and friendly interviewer (although financially more costly relative to mail) is able to obtain a greater response rate, observe various issues to inform questionnaire improvement and rephrase a question when it is not comprehended as long as s/he uses the same vocabulary in all cases of rephrasing the same item. Of course, it should be pointed out that responses could be affected by interviewer biases, respondent social desirability biases (Bowling, 2005) or interviewer characteristics (e.g. age and sex (Moun, 1998)).

5.4.2.2. *Sample and analysis issues*

First of all, the results of the present study should be interpreted with caution and cannot be generalized (Streiner & Norman, 2008). The sample is not large and not random (<300 participants per measurement and the vast majority of them Attica residents). In some analyses for some versions the sample size was rather low. This may affect the results. Furthermore, another systematic error that may be present is selection biases. Selection biases refer to different characteristics of those who are selected and those who are not (Streiner & Norman, 2008; Sutton & French, 2004). For instance, severely ill individuals were excluded. Moreover, some individuals may have been more willing to participate as their doctor had informed them about the research during their last contact, so they had more time to consider their participation. Also, some patients were approached on the basis of clinician recommendations who believed that they might like to participate. The latter issue, in addition to the good level of response rate may raise concerns regarding social desirability bias (i.e. the tendency of participants to answer in a way that they can be viewed favourably by others; Miller, 2012). This in turn, may have influenced the validity of the results (Streiner & Norman, 2008). Furthermore, regarding content validity, although the researcher made an effort for the CROQ-Gr to be assessed by both patients and the expert panels, it might have been better to have kept a more detailed record in order to be able to measure and present judge agreement in a quantitative way too. The lack of such data may raise some concerns about the accurate assesssmnet of the content validity (Yaghamie, 2003; Waltz & Bausell, 1983) of the CROQ- Gr version.

Concerning its strengths, it should be mentioned that the study has involved rigorous scientific criteria for the psychometric evaluation of the CROQ-Gr version highlighting few weaknesses which can influence questionnaire construct validity. Additionally, this study demonstrates that the CROQ-Gr can be administered in a different way referring to interviewer administration as well as mailed or self administration that were used in previous international studies. Finally, the present study has recruited patients with different ages, sexes and marital, occupational and educational status. This implies that this disease-specific instrument, although not adjusted for demographic variables, is feasible and sensitive to detect improvement (if any) of HRQoL across a wide demographic. Finally, sensitivity analysis showed that the CROQ-Gr is somewhat more sensitive in detecting certain kinds of problems tailored to patients undergoing coronary revascularization compared to a generic measure of HRQoL. Thus, the use of the CROQ-Gr could allow researchers and clinicians to draw a more precise conclusion in relation to overall quality of life of this particular population.

5.4.3. Implications/recommendations

The findings of the present study have a number of important implications. From a theoretical point of view this study supports Schroter and Lambing's (2004) findings that suggest that the HRQoL concept in CR can be measured through four different aspects (*symptoms*, *physical*, *psychosocial* and *cognitive functioning*). However, it should be borne in mind that the PFA of the CROQ-Gr was carried out on the same items as in the original CROQ and different factors may have emerged with the inclusion of different items. In other words, there may be other factors that are potentially important (e.g. emotional growth) that may have influenced the outcome but for which there are no relevant items in the CROQ. The measurement of these aspects could allow a clearer understanding of the effect of coronary revascularization and help to determine the impact of other factors (e.g. individual characteristics such as age and sex or co-morbidities such as diabetes) on outcomes following interventions, thereby enhancing clinical interpretability. For instance, the literature suggests that males benefit more compared to females in terms of general HRQoL after PCI (Blankenship et al., 2013). However, since no other disease/treatment-specific instrument incorporates *symptoms, physical, psychosocial and cognitive functioning* and detects post-treatment adverse effects, this conclusion might not be warranted. Thus, future research should include the CROQ in order to be more confident in conclusions that would enhance best practice.

Regarding suggestions for further research, the development of a shorter version could be very helpful for reducing respondent burden and increasing data quality (Bowling, 2005), especially when research aims to explore many related issues (e.g. personality, mood) and thus may use many instruments. The adaptation of the CROQ-Gr to be relevant to other CR procedures such as MIDCAB or robotic CR would be in line with recent medical developments and thus would allow investigation of their impact on patients' well-being. Also, the investigation of alternative modes of administration is needed in order to increase the utility of CROQ. The development and testing of different forms of administrations such as online or via smartphone might also be useful. An electronic online form may increase participation, especially in post-revascularization follow-ups of patients with physical or time restrictions, as an online form can be completed from any location and at any time as long as the patient has access to the internet. The expansion into smartphone administrations could help doctors get an instant picture of their patients' HRQoL in everyday practice, avoiding time-consuming calculations, or else help researchers to get instant snapshots of each subdomain of HRQoL.

Concerning practice, health professionals may use the CROQ for a number of reasons: a) for gaining a better understanding of the patient's experience which in turn will facilitate doctor-patient communication and promote the collaboration of doctor and patient in treatment decisions; b) for drawing a clear conclusion about a patient's condition and disease burden; c) for measuring disease severity and to make decisions about whether a patient should be referred to an interventional/surgery cardiologist for revascularization treatment; and d) for assessing effectiveness of rehabilitation.

5.5.Conclusion

As the Greek version of the CROQ (GROQ-Gr) is a practical and a scientifically rigorous instrument, its use in clinical trials could allow forming a clear and detailed picture about patients' HRQoL and health outcomes after coronary revascularization. Therefore, it can be used in the data collection for exploring the quantitative research questions investigated in study 2.

Furthermore, in health settings, it could be used as a single tool by cardiologists in order to capture and record their patients' health outcomes following their operation. Finally, researchers with an interest in patients' HRQoL undergoing coronary revascularization should be encouraged to make use of the CROQ either solely or in combination with generic measures for more appropriate monitoring.

Chapter Six

Study 2, Part One, The influence of Coronary Revascularization on Patients' Health Related Quality of Life over a one year period

6.1.Introduction

The systematic review with the meta-analysis (chapter 3) has revealed that people who have undergone CR experience greater improvement in their Quality of Life than those treated with medication. Taking health as a whole, it could be commented that CR would seem to maximise improvement in health. However, the heterogeneity in the findings and methods used by various studies did not allow the investigation of factors that positively or negative influence the outcome (e.g. demographic or clinical characteristics). One factor that contributed to the heterogeneity was the type of HRQoL instrument used. Most studies used a generic measure. However, as argued earlier, the use of a disease-specific instrument may provide more insightful results and, thus, allow drawing a more accurate conclusion. Therefore, one of the main goals of this study is to provide a longitudinal examination of the level of change of patients' HRQoL after CR with the use of a disease-specific instrument, and discuss the results in relation to previous evidence.

Furthermore, the duration of follow-up varies dramatically among studies. A great number of studies draw conclusions with a short or middle term follow-up (1-11 months). This however may affect conclusions about the level of change of patients' HRQoL after CR. Studies with a longer follow-up (e.g. 12 months or greater) demonstrate a lower level of improvement after CR than those with a shorter one. This suggests that in order to be able to draw a more appropriate conclusion, at least a 12-month follow-up should be obtained. Moreover, due to the differences between short- and long-term follow-up) in the change in patients' HRQoL after CR, a longitudinal study with data collection prior to treatment (missing for most of the studies) and more than 1 month follow-up could help predict the pattern of improvement over one year. Therefore, another goal of this study is to detect not only the extent of change at 3 months (a cut point for short-term measurement suggested by many researchers, e.g. Schroter et al., 2004), and at 12 months (long-term), but also to identify the pattern of change over 1 year period.

Also, few published studies make comparisons regarding the extent of change of HRQoL (overall and its dimensions) between different types of CR; the majority of them focus either on the CABG or PCI procedure. This in turn, along with the great heterogeneity in design among them, does not allow health care professionals to draw confident conclusions about the beneficial or harmful aspects of each treatment, which is a crucial aspect for both doctors and patients (e.g. for making treatment suggestions, adequately inform patients about the pros and cons of treatment and allowing them to make informed decisions). Thus another aim is to investigate whether there are differences in levels of change in patients' HRQoL (overall and its dimensions) between the two types of CR.

Moreover, many studies only present the range of the sample's demographic and clinical features; that is, they do not present any analysis or adequate data to determine whether these factors may influence the outcomes. Therefore, another goal is to investigate the effect of a variety of demographic and clinical features on the outcomes.

To this end, the present study has incorporated a number of features discussed above to improve the research design, and addresses the following research questions:

1) What is the trajectory of change in HRQoL over a one-year period post CR?
2) Does the type of CR influence the level of change?
3) What are the predictors of change in HRQoL over a one-year period?
4) What is the trajectory of change in HRQoL specific aspects (symptoms, physical, psychosocial, cognitive function) and what are the predictors of change in each subdomain?

6.2.Methods

6.2.1. Design

A longitudinal design was employed for the aims of the present study. Data collection was carried out from March 2010 to September 2013 with data collected from each participant at three different time points; immediately prior to CR (PCI or CABG) and then 3 and 12 months post treatment.

6.2.2. Participants

In total, 472 (307 PCI and 165 CABG) coronary patients were recruited. In particular, 405 participants were recruited prior to CR (baseline, T1) while 321 completed the 3 month follow-up (T2, response rate 79.26%) and 291 completed the 12 month follow-up (T3, response rate 71.85 %). Additionally, 67 participants who had had their CR 3 months prior to recruitment were included (T2) and, out of these individuals, 38 completed the 12 month follow-up (T3 response rate for this subsample 56.72%). Thus, T1 includes 405 individuals, T2 includes 388 individuals and T3 includes 329 individuals. Figure 6.1 illustrates sample size per type of CR and measurement time point.

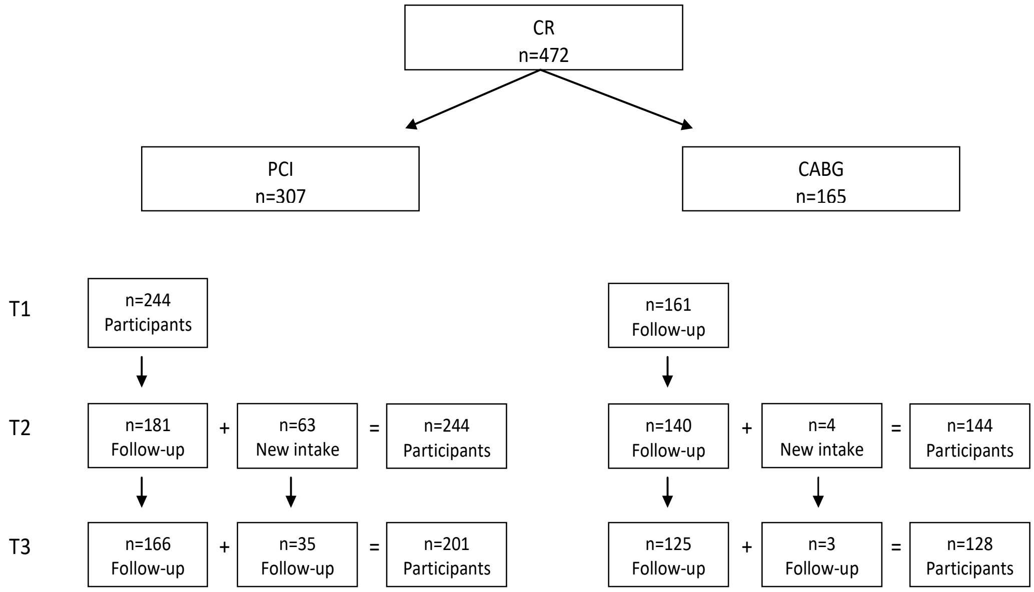

Figure 6.1 Flow diagram showing research participants per CR type and measurement time point. T1= prior to treatment, T2= 3 months after treatment, T3= 12 months after treatment

The demographic and clinical characteristics of participants per type of CR have been presented in chapter 5, Table 5.3. Briefly, the sample represents a normal proportion of smokers while there is higher proportion of diabetes and overweight individuals compared to the general population (WHOQOL group, 2008). Furthermore, the demographic clinical and behavioural features only significantly differ between individuals treated with CABG and PCI with respect to average age and diabetes condition. The mean age of individuals treated with CABG was a little bit higher compared to patients treated with PCI while a higher proportion of individuals with diabetes underwent PCI.

6.2.3. Materials

For the present study as presented in the Methods chapter (Chapter 4) three questionnaires were used: the Greek version of the Coronary Revascularization Outcome Questionnaire (CROQ (Schroter & Lamping, 2004)), a questionnaire capturing demographic characteristics and a questionnaire capturing individuals' clinical and behavioural features.

As demonstrated in chapter 5 of the present thesis, the CROQ-Gr is a valid and reliable disease-specific questionnaire that evaluates HRQoL and health outcomes before and after the two common operational heart procedures; Percutaneous Coronary Interventions (PCI) and Coronary Artery Bypass Graft Surgery (CABG).

6.2.4. Procedure

After obtaining ethical approval to carry out the research by the University of Hertfordshire relevant institutional ethics committee, formerly the School of Psychology Ethics Committee with Devolved Accountability (ECDA; Appendix 4.7) potential participants were approached. Initially, a general call for participants was made in hospital settings (after obtaining ethical approval from the scientific committee of participating hospitals). This announcement included an introduction to the researcher, the aim of the study and the request for volunteers. It was highlighted that the decision regarding participation in the study would not affect their medical care. Patients willing to participate were escorted to a private room provided by each hospital. There, the researcher both orally and in writing (Appendix 4.9.1) informed potential participants about the details and aim of the study, what was expected from them and the duration of their participation. Participants agreeing to participate signed the consent form (Appendix 4.10.1), being reminded that they could withdraw at any time without the need for providing an explanation and that this would not affect their medical care in any way. After that, the appropriate booklet was administered to participants. A 6-page booklet was administered to the vast majority of participants enrolled prior to treatment which consisted of the CROQ PCI or CABG pre-revascularization version, demographic and clinical and behavioural (e.g. smoking) information. A subset of participants were recruited 3 months post treatment. These patients were met prior to their follow-up meeting with their doctors. The procedure followed was identical to the one described above.

The follow-up was made 3 months and 12 months after treatment through telephone calls. An 8-page booklet was administered at both times consisting of the CROQ PCI or CABG post-revascularization version, and questions regarding medical and behavioural information to update patient information. Sessions lasted approximately 15-30 minutes, depending on the booklet being administered and were carried out by the same researcher using a standard procedure and standardised instructions. All booklets were stored in a locked cupboard in the researcher's office, except from approximately 120 booklets completed by patients who did not subsequently undergo PCI; these booklets were destroyed the same evening after a meeting with doctors which clarified that these patients had not undergone the procedure. At the last follow-up, participants were debriefed and thanked for their participation.

For further information about the procedure followed please see the Method section in Chapter 4 where a detailed description of the recruitment and data collection process is presented.

6.2.5. Statistical analysis

Analysis was conducted with the use of mixed models and in particular, conditional growth models, a type of multilevel modeling (MLM) for longitudinal or repeated measures, in order to detect the effect of the type of CR treatment on health related quality of life (HRQoL) as measured with the coronary revascularization outcome questionnaire (CROQ-Gr), for the different time points, controlling for several demographic and clinical variables. Mixed models were selected because they permit detecting changes over a period of time (repeated measures) both within and between individuals without being affected by missing data in a longitudinal study due to loss of follow-up or dropouts; unequal data per participant over time can be treated by flexible specification of the time variable and produce aggregate-level as well as individual-level growth curves (Kwok et al., 2008; Ntoumanis, 2014). Also by treating "time" as a continuous variable instead of a discrete one can increase statistical power for the detection of growth effects (Kwok et al., 2008).

A series of models were initially tested as suggested by Chen and Peace (2011) and Singer, & Willett (2003) in order to determine the best model. All models have been computed with maximum likelihood estimation (ML) and AR(1) (first-order autoregressive structure) where it is assumed that the data are continuous and the relationship between changes in variances is systemic) following guidelines reported in the literature (Curran, Obeidat, & Losardo, 2010; Kwok et al., 2008; Singer & Willett, 2003). Also, for comparative reasons, in order to detect the best fitting model, Schwarz's Bayesian Information Criterion (BIC) was used (Schwarz, 1978). The BIC was selected as the most appropriate compared to -2LL (negative log likelihood criterion) as it takes into consideration both the statistical goodness of fit and the number of parameters to estimate the degree of fit. When fitting models, it is possible to increase the likelihood by adding parameters, resulting in an overfitting. BIC resolves this problem by introducing a penalty term for the number of parameters in the model (Nishii, 1984), so conclusions based on the BIC index about the model fit are more likely to be accurate. The smaller BIC value the better the fit.

The initial steps followed (prior to the analysis) was to calculate the participants' Body Mass Index (BMI; weight/height^2), restructure the data (discrete time points to become continuous; Field, 2013) and then change the coding of the time variable due to unequal time spacing (from 1-3 to 0-4 where 0 represents baseline data (Time0), 1 represents 3-month follow-up (Time1) and 4 represents the 12-month follow-up (Time2)). To test the quadratic (nonlinear) trend over the measurement time points, the time variable was defined by squaring the linear term (i.e. time^2=0 (baseline), time^2=1 (3-month), time^2=16 (12-month)).

Concerning the statistical analysis, the first step was to determine the best fit for the time trend; time (level 1 variable) as a predictor was nested with individuals (level 2 variable) and with the response variable CROQ Total scores. Thus, a series of mixed models were computed. In particular, six models were compared: (1) Model A represents ordinal linear least square regression with Time as a predictor, (2) Model B = Time as a predictor with random intercept, (3) Model C = Time and Time^2 as predictors with random intercept, (4) Model D = Time and Time^2 as predictors with random intercept and linear term, (5) Model E = Time and Time^2 as predictors with random intercept and quadratic term, (6) Model F = Time and Time^2 as predictors with random intercept, linear and quadratic terms. In all models the response variable was CROQ Total scores.

The second step was to detect the CR type of treatment effects. Thus the best model regarding Time trend was further investigated by adding the effect of CR type (PCI, CABG;

level 3 variable). Again in order to detect the best model 3 different models were computed and compared: (1) Model 1= Time, Time^2 and CR type of treatment as predictors with random intercept, linear and quadratic terms (i.e. no interaction between Time and CR type of treatment or Time^2 and CR type of treatment), (2) Model 2= Time, Time^2, CR type of treatment and Time x CR type of treatment interaction as predictors with random intercept, linear and quadratic terms (i.e. an interaction term only between Time and CR type of treatment), (3) Model 3= Time, Time^2 Type of treatment, Time x CR type of treatment interaction, and Time^2 x CR type of treatment interaction as predictors with random intercept, linear and quadratic terms (i.e. an interaction term between Time and CR type of treatment and between Time^2 x CR type of treatment). In all models the response variable was CROQ Total scores.

The third step was to investigate further the best model of step two by adding potential predictors, meaning all individual level covariates (time-invariant (e.g. demographic and medical characteristics) and time-varying (i.e. smoking and BMI representing individuals' behavioural characteristics that were updated in all three time points) with random intercept, linear and time terms. Included in the model were also all the two way interaction terms between those potential predictors with time and CR type of treatment.

Next, the same analysis was repeated for each CROQ subdomain (symptoms, physical, psychosocial, cognitive functioning) as the response variable. For adverse effects and satisfaction, as these were measured only at two time points, 3 months and 12 months post treatment, two new variables were created indicating the difference in each case. Then multiple linear regression models were developed with the response variables *adverse effects difference* and *satisfaction difference* respectively in order to examine the fixed effects of all individual level covariates (time-invariant and time-varying potential predictors). The level of significance was set at 0.05. Analyses were performed using SPSS 20.00 (IBM, 2011) and the R package nlme (Baayen, 2008; Baayen, Davidson, Bates, 2008; Pinheiro, & Bates 2000; Pinheiro et al., 2016). The popularity of R has increased substantially in recent years especially for its graphic capability and utility for nonlinear mixed models analyses (Muenchen, 2016; Revelle, 2016). Concerning reporting in relation to the best fitting model, for fixed effects beta values (B; the mean values of the coefficient) and standards errors (SE) are reported, while for random effects standard deviations (SD) are reported showing the level of variability. For the final growth models in addition to B and SE, t statistics, *p* values, and CI (95% confidence interval; lower-upper) values are reported.

6.3.Results

Regarding behavioural changes, smoking status was reduced by 74.79% (178 individuals quit smoking) 3 months post treatment. McNemar's test indicated that there was a significant difference in the percentage of participants who stopped smoking between CABG patients and PCI ($p<0.001$). A greater percentage of CABG (98%) patients compared to PCI patients (63%) quit smoking 3 months after treatment. However, at 12 months, a 17.5% (n=31) relapse in smoking cessation was observed one year post treatment. In fact, 27 individuals treated with PCI and 4 people treated with CABG started to smoke again between the 3rd and 11th month post treatment. Moreover, a minor increase in BMI was observed between baseline and 12 months post treatment ($M_{\text{difference}}=0.56$, $SD=3.36$) with no essential difference between groups (approximately 100 grams). This observation suggests that participants were overweight prior to treatment (Table 5.3) and one year post treatment instead of losing weight they had gained a few grams.

Moreover, in the open ended questions in the CROQ where participants were asked "*is there anything else you would like to tell us about your heart condition or heart operation that is not covered*" 27.8% (n=131) of participants made a comment. The comments were related to concerns about various stressful issues and their effect on their heart condition. In fact, of those answering this question, 62.6% (n=82) mentioned financial issues and fear of unemployment, 22.1% (n=29) mentioned family issues (e.g. problems in their relationship with a member of the nuclear family), and 15.3% (n=20) mentioned other health problems. Table 6.3 displays the type and frequency of issues (based on keywords) extracted from participants' response to the CROQ open-ended question mentioned.

Table 6.3. Participants' responses to the CROQ open-ended question (n=131)

Life stressors	Subtype	N (%)
Financial stress	Unemployment	13 (9.9)
	Low salary	15(11.5)
	Reduction in pension	19(14.5)
	Salary not paid on several occasions	31(23.6)
	Medical expenses	4 (3.1)
Family issues	Bad communication with offspring	6 (4.6)
	Bad communication with partner	11(8.4)
	Recent divorce	3 (2.2)
	Bad communication with parents	1 (0.8)
	Health problem of a family member	5 (3.8)
	Death of a member of the nuclear family	3 (2.3)
Health related issues	Diabetes	8 (6.1)
	Frozen shoulder	1 (0.8)
	Cholesterol	2 (1.5)
	Smoking	5 (3.8)
	Increased weight	4 (3.1)

6.3.1. CROQ Total scores over a one-year period

The descriptive analysis of the *CROQ Total* scores indicated an increase over a one-year period. Table 6.3.1 displays participants' mean scores on *CROQ Total* over a one-year period in overall and by the CR type of treatment for all individuals characteristics measured; the mean scores of all groups after CR treatment have increased.

Table 6.3.1 Descriptive statistics for CROQ Total scores per CR type over a one-year period (n=472)

CROQ Total			Type of CR					
			PCI			CABG		
			index			index		
			T1	T2	T3	T1	T2	T3
Overall		*Mean*	67.56	88.42	86.62	63.09	88.18	88.93
		SD	13.54	9.38	9.34	12.13	7.67	6.47
Age group Mean age (60.43)	<60.43	*Mean*	68.32	89.63	86.42	66.86	89.45	90.14
		SD	14.31	8.60	9.80	8.19	7.44	5.17
	>60.43	*Mean*	66.63	87.23	86.84	59.56	86.74	87.63
		SD	12.55	9.98	8.82	14.07	7.73	7.46
Sex	male	*Mean*	68.50	89.47	86.77	64.76	89.88	90.64
		SD	13.48	7.35	9.37	12.01	6.90	5.18
	female	*Mean*	64.52	85.44	86.17	57.60	82.81	83.14
		SD	13.41	13.23	9.33	10.98	7.57	7.12
Marital status	unmarried/live alone	*Mean*	67.74	87.47	87.52	58.10	86.94	81.62
		SD	15.82	11.06	13.27	14.83	9.49	10.23
	married	*Mean*	67.51	88.64	86.44	63.94	88.37	89.75
		SD	12.91	8.97	8.38	11.46	7.37	5.38
Educational status	six years or less	*Mean*	66.89	84.84	85.49	62.75	85.41	86.64
		SD	12.68	10.89	11.36	15.47	8.01	4.51
	7-12 years	*Mean*	68.81	90.09	87.19	62.90	88.11	89.89
		SD	12.56	7.05	8.00	10.08	7.45	7.49
	12^{+} years	*Mean*	65.91	89.62	86.87	63.42	90.24	88.93
		SD	16.05	10.43	9.13	12.20	7.28	5.17
Occupational status	unemployed	*Mean*	61.71	91.06	87.60	60.60	84.81	81.17
		SD	13.05	8.46	9.43	9.67	7.72	7.75
	public/private servant	*Mean*	69.31	88.77	85.95	69.95	92.72	92.99
		SD	14.05	9.45	11.15	6.37	7.48	4.41

Table 6.3.1 Descriptive statistics for CROQ Total scores per CR type over a one-year period (n=472)

CROQ Total			Type of CR					
			PCI			CABG		
			index			index		
			T1	T2	T3	T1	T2	T3
	free-lancer	*Mean*	71.39	91.17	87.68	61.47	90.07	89.99
		SD	12.23	6.35	7.08	13.65	5.40	3.97
	pensioner	*Mean*	67.06	85.94	86.11	61.26	85.36	88.66
		SD	13.22	10.19	8.76	12.94	7.59	6.18
Family history CHD	no	*Mean*	66.18	87.68	87.03	63.26	87.42	88.69
		SD	12.43	9.83	7.85	12.28	8.11	5.15
	yes	*Mean*	68.89	89.16	86.21	62.92	88.95	89.12
		SD	14.46	8.93	10.66	12.05	7.17	7.42
Hypertension	no	*Mean*	66.68	88.22	85.96	61.42	88.84	90.91
		SD	12.96	9.48	10.05	13.19	6.91	5.52
	yes	*Mean*	68.94	88.77	87.71	65.57	86.80	85.69
		SD	14.45	9.24	7.96	9.65	8.91	6.70
Cholesterol	no	*Mean*	66.91	89.45	86.81	63.26	89.05	88.34
		SD	13.65	8.48	9.62	12.23	8.01	5.92
	yes	*Mean*	68.94	86.11	86.22	62.53	86.29	90.27
		SD	13.15	10.85	8.80	11.98	6.67	7.66
Diabetes	no	*Mean*	67.94	88.56	86.75	63.08	89.29	90.82
		SD	13.53	9.24	9.91	11.84	7.42	5.56
	yes	*Mean*	66.02	88.05	86.23	62.84	85.79	85.72
		SD	13.47	9.81	7.58	12.68	7.75	6.75
Smoking	no	*Mean*	66.12	89.00	89.06	61.33	88.66	89.69
		SD	12.05	9.18	7.83	13.62	7.50	5.37
	yes	*Mean*	68.60	88.22	83.49	65.18	68.21	81.29
		SD	14.48	7.00	10.12	9.77		7.16
BMI	normal weight (18.5-24.9)	*Mean*	66.27	87.11	85.93	62.48	90.83	90.60
		SD	13.24	7.95	7.66	12.95	7.70	5.85
	overweight (25.0-29.9)	*Mean*	67.64	89.04	86.25	60.90	88.96	88.34
		SD	13.60	9.80	8.69	13.75	7.63	4.43
	obese (<29.9)	*Mean*	68.41	88.47	86.93	65.24	86.08	88.45
		SD	14.08	10.27	10.74	10.13	7.40	4.43
T1= prior to treatment, T2 = 3 months after treatment, T3= 12 months after treatment								

6.3.1.1. *Changes in CROQ Total scores : Time and type of CR treatment effects*

As described in the analysis section, the first step was to detect the best fitting model for the time trend. Table 6.3.2 shows the values of the six models compared, demonstrating based on the BIC index that the 6th model (model f, Time and Time^2 as predictors with random intercept, linear and quadratic terms) was the best mixed model for describing the time trend of the *CROQ Total* scores.

Table 6.3.2 Parameter estimates and model fit statistics for first and second order polynomials of CROQ Total score growth over a one-year period

	Model a	Model b	Model c	Model d	Model e	Model f
Fixed effects	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)
Intercept	73.53(0.53)**	73.53(0.53)**	65.76(0.52)**	65.73(0.56)**	65.74(0.54)**	65.75(0.65)**
Time	4.27(0.24)**	4.27(0.24)**	28.28(0.82)**	28.37(0.80)**	28.35(0.81)**	28.19(0.89)**
Time^2	NA	NA	-5.71(0.19)**	-5.73(0.18)**	-5.73(0.19)**	-5.69(0.19)**
Random effects	SD	SD	SD	SD	SD	SD
Residuals	13.14	13.12	8.80	8.43	8.57	5.46
Intercept	NA	0.001	5.74	7.71	6.89	11.96
Time	NA	NA	NA	1.16	NA	15.42
Time^2	NA	NA	NA	NA	0.20	3.14
Model fit						
BIC	9070.01	9084.07	8510.48	8493.06	8506.50	8385.14

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous
Time= Linear, Time^2= Quadratic
Model a= Ordinal linear least square regression with Time as a predictor
Model b= Time as a predictor with random intercept
Model c= Time and Time^2 as predictors with random intercept
Model d = Time and Time^2 as predictors with random intercept and linear term
Model e= Time and Time^2 as predictors with random intercept and quadratic term
Model f= Time and Time^2 as predictors with random intercept, linear and quadratic terms
In all models response variable *CROQ Total* scores
$^{**}p<0.001$

The analysis demonstrated that the mean initial status (baseline) of the *CROQ Total* scores was 65.75 (β = 65.75, *SE* = 0.65, t=100.89, $p < 0.01$). Time had a significant positive linear effect on *CROQ Total* scores (β = 28.19, *SE* = 0.89, t= 31.69, $p < 0.01$), as well as a significant negative quadratic effect (β = -5.69, *SE* = 0.19, t= -30.13, $p < 0.01$). The acceleration (calculated based on Singer, & Willett, 2003) was 16.81 points [i.e. 28.19/ (2 (-5.69))]. According to these results, the *CROQ Total* scores increased at the beginning, but this trend slowed down later on. Compared to the linear change trajectory (28.19), the rate of quadratic growth (-5.69) was small, thus a positive change on *CROQ Total* following CR can be assumed.

In order to detect the effect of the CR type on *CROQ Total* scores, the best model of the time trajectory was further investigated by adding the type of treatment (PCI/CABG) variable. The model with the smallest BIC value was the second (Time, Time^2, CR type of treatment as predictors and the interaction term Time x CR type of treatment with random intercept, linear and quadratic terms) as Table 6.3.3 suggests.

Table 6.3.3 Parameter estimates and model fit statistics for first and second order polynomials and treatment interactions of CROQ Total score growth over a one-year period

	Model 1	Model 2	Model 3
Fixed effects	B (SE)	B (SE)	B (SE)
Intercept	65.90(0.71)**	67.87(0.73)**	67.53(0.82)**
Time	28.18(0.89)**	27.63(0.89)**	26.41(1.13)**
Time^2	-5.68(0.19)**	-5.67(0.18)*	-5.41(0.24)**
Type of treatment†	-0.40(0.74)	-2.85(0.92)**	-4.50(1.31)**
Time x Type of treatment	NA	1.22(0.27)**	-4.36(1.81)
Time^2 x Type of treatment	NA	NA	-0.67(0.39)
Random effects	SD	SD	SD
Residual	5.46	5.37	5.37
Intercept	11.93	11.83	11.80
Time	15.40	15.44	15.39
Time^2	3.14	3.17	3.15
Model fit			
BIC	8391.90	8379.16	8383.12

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion

Random covariate = AR1 heterogeneous, Time= Linear, $Time^2$= Quadratic, †Type of treatment = CABG

Model 1=Time, $Time^2$ and CR type of treatment as predictors with random intercept, linear and quadratic term
Model 2=Time, $Time^2$, CR type of treatment as predictors and Time x CR type of treatment interaction term with random intercept, linear and quadratic terms
Model 3=Time, $Time^2$, CR type of treatment as predictors, Time x CR type of treatment interaction term, and $Time^2$ x CR type of treatment interaction term with random intercept, linear and quadratic terms
In all models response variable *CROQ Total* scores
$^{**}p<0.001$, $^{*}p<0.05$

The results demonstrated that the average initial status (baseline) of *CROQ Total* scores for CABG patients was lower compared to PCI patients while a greater increase in CROQ Total scores for CABG patients was revealed in the rate of change in linear trends. The marginal means of CR type as a predictor for *CROQ Total* scores can be estimated by employing the following formulas:

CROQ Total marginal means for 0 months (baseline) = β_0, 3 months = $\beta_0 + \beta_1$ x Time1 + β_2 x $Time1^2$ and 12 months = $\beta_0 + \beta_1$ x Time2+ β_2 x $Time2^2$, where

Time1 = 1 and Time2 = 4,

CR type of treatment: PCI = 0 and CABG = 1,

β_0 = 67.87 (baseline mean score of CROQ Total) - 2.85 x type of treatment,

β_1 = 27.63 (linear mean change of CROQ Total) + 1.22 x type of treatment,

β_2 = -5.67 (quadratic mean change of CROQ Total).

Thus, for PCI the marginal mean prior to treatment is 67.87 and at 3 months it is 89.83 [(67.87 + (27.63 x 1) + (-5.67 x 1^2)], resulting in a mean change of 21.96 points from the baseline mean score (89.83-67.87). For CABG the marginal mean prior to treatment is 65.02 and at 3 months it is 88.20 [(67.87-2.85) + (27.63+1.22) x 1-5.67 x 1^2], resulting in a mean change of 23.18 points from the baseline mean score (88.20-65.02).

Concerning the marginal mean for PCI at 12 months, this is 87.67 [(67.87 + (27.63 x 4) + (-5.67 x 4^2)], resulting in a mean change of 19.80 points from the baseline mean score (86.67-66.87), while the marginal mean for CABG at 12 months is 89.70 [(67.87-2.85)+((27.63+1.22) x 4)) + (-5.67 x 4^2)], resulting in a mean change of 24.68 points from the baseline mean score (88.70-64.02), as Figure 6.2 illustrates.

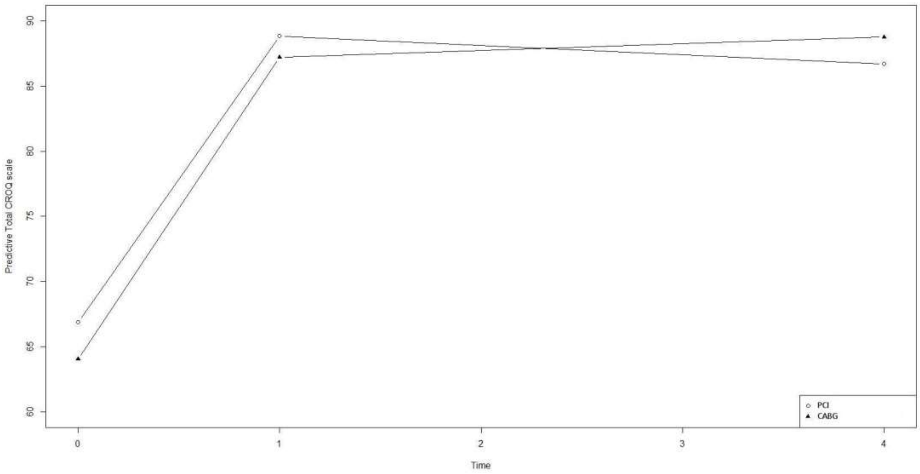

Figure 6.2 Marginal means of CROQ Total scores per CR type of treatment. Time0= baseline scores, Time1= 3 month mean scores, Time4=12 month mean scores.

The variability of CROQ Total scores within individuals per CR type at the 3 measurement time-point can be seen in Figure 6.3.

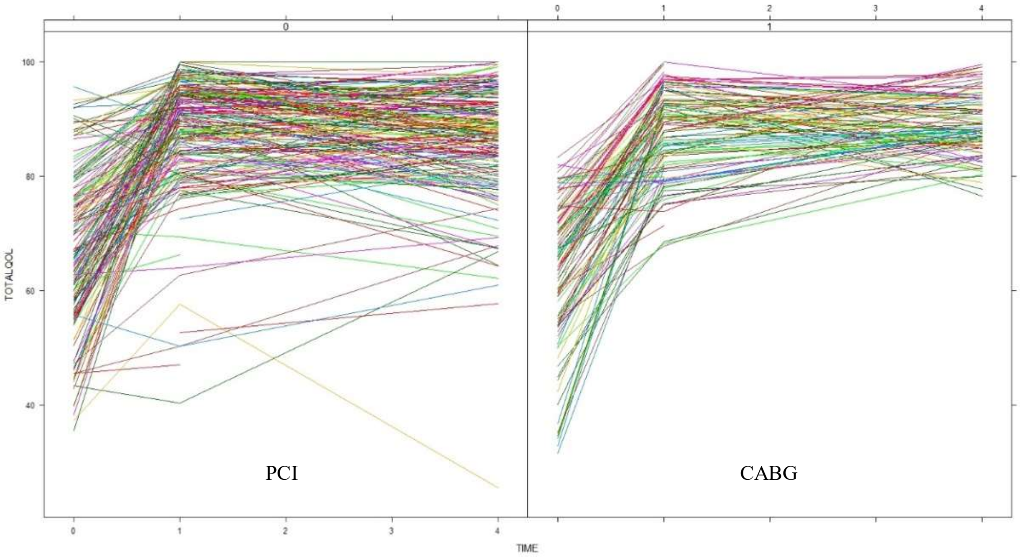

Figure 6.3 CROQ Total scores as a function of time for all patients by type of CR treatment. Time0= baseline scores, Time1= 3 month scores, Time4=12 month scores.

Hence overall, it can be assumed that over one year period, on the *CROQ Total*, patients treated with CABG experienced a greater mean change compared to patients treated with PCI. However, CR type did not remain a significant predictor of the *CROQ Total* change after adjusting for all time invariant and time-varying predictors as the following section reveals.

6.3.1.2. *Predictors of CROQ Total score change over a one-year period*

In the final conditional growth model, the effects of all individual level covariates as well as well as the two time-varying predictors (i.e. smoking and BMI) were investigated. Included in the model were also all the two-way interaction terms of those potential predictors with time and CR type of treatment. The following Table 6.3.4 summarizes the fixed and random effects of the model.

Table 6.3.4 Growth model for changes in CROQ Total scores over a one-year period

Fixed effects	B(SE)	df	t	*p*	95% Confidence Interval	
					Lower Bound	**Upper Bound**
Intercept	52.94(6.12)	530	8.65	0.00	41.22	64.66
Time	31.75(2.25)	530	14.09	0.00	27.44	36.07
Time^2	-5.79(0.22)	530	-26.00	0.00	-6.21	-5.36
Type of treatment (CABG)	5.43(9.45)	428	0.57	0.57	-12.67	23.54
Place of residence (Rural Area)	-2.15(1.75)	428	-1.23	0.22	-5.50	1.20
Age	0.06(0.07)	428	0.79	0.43	-0.08	0.20
Sex (Female)	-3.98(1.22)	428	-3.26	**0.00**	-6.32	-1.64
Marital status (Married)	-0.25(1.30)	428	-0.19	0.85	-2.73	2.23
Educational status†						
7-12 years	3.11(1.32)	428	2.36	**0.02**	0.59	5.64
12$^+$ years	1.26(1.53)	428	0.83	0.41	-1.66	4.19
Occupational status‡						
Public/private servant	0.37(1.59)	428	0.23	0.82	-2.68	3.42
Free lancer	3.90 (1.78)	428	2.18	**0.03**	0.48	7.32
Pensioner	-2.10(1.76)	428	-1.19	0.23	-5.48	1.28
CHD Family history (yes)	1.68(1.01)	428	1.66	0.10	-0.26	3.61
Hypertension (yes)	1.37(1.04)	428	1.32	0.19	-0.63	3.37
Cholesterol (yes)	-2.98(1.10)	428	-2.71	**0.01**	-5.09	-0.88
Diabetes (yes)	-0.21(1.20)	428	-0.17	0.86	-2.51	2.10
BMI	0.31(0.11)	530	2.75	**0.01**	0.09	0.53
Smoking (yes)	1.25(1.05)	530	1.19	0.23	-0.76	3.26
Time x Type of treatment	0.50(0.43)	530	1.18	0.24	-0.32	1.32
Time x Place of residence	0.69(0.48)	530	1.45	0.15	-0.22	1.60
Time x Age	0.00(0.02)	530	0.00	1.00	-0.04	0.04
Time x Sex	1.00(0.35)	530	2.84	**0.00**	0.33	1.67
Time x Marital status	-0.24(0.41)	530	-0.59	0.55	-1.03	0.54
Time x Educational status†						
7-12 years	0.03(0.40)	530	0.07	0.95	-0.73	0.79
12$^+$ years	0.39(0.45)	530	0.86	0.39	-0.48	1.25
Timex Occupational status‡						
Public/private servant	-0.51(0.49)	530	-1.05	0.29	-1.45	0.42
Free lancer	-0.88(0.52)	530	-1.67	0.10	-1.88	0.13
Pensioner	0.32(0.53)	530	0.59	0.55	-0.70	1.34
Time x CHD Family history	-0.38(0.30)	530	-1.27	0.20	-0.95	0.19
Time x Hypertension	-0.04(0.30)	530	-0.15	0.88	-0.62	0.53
Time x Cholesterol	0.57(0.32)	530	1.75	0.08	-0.05	1.19

Table 6.3.4 Growth model for changes in CROQ Total scores over a one-year period

Fixed effects	B(SE)	df	t	*p*	95% Confidence Interval	
					Lower Bound	Upper Bound
Time x Diabetes	-0.29(0.35)	530	-0.83	0.41	-0.96	0.38
Time x BMI	-0.10(0.04)	530	-2.58	**0.01**	-0.17	-0.03
Time x Smoking	-1.58(0.36)	530	-4.40	**0.00**	-2.27	-0.89
Type of treatment x Place of residence	0.60(2.21)	428	0.27	0.79	-3.64	4.84
Type of treatment x AGE	-0.03(0.13)	428	-0.26	0.79	-0.28	0.21
Type of treatment x Sex	-3.81(2.09)	428	-1.83	0.07	-7.81	0.19
Type of treatment x Marital status	4.41(2.36)	428	1.87	0.06	-0.11	8.94
Type of treatment x Educational status†						
7-12 years	-0.99(2.35)	428	-0.42	0.68	-5.50	3.53
12$^+$ years	1.25(2.71)	428	0.46	0.65	-3.96	6.45
Type of treatment x Occupational status‡						
Public/private servant	1.96(2.92)	428	0.67	0.50	-3.63	7.55
Free lancer	-5.09(2.99)	428	-1.70	0.09	-10.82	0.65
Pensioner	-2.06(3.16)	428	-0.65	0.51	-8.11	3.99
Type of treatment x CHD Family history	-0.73(1.57)	428	-0.47	0.64	-3.73	2.27
Type of treatment x Hypertension	-0.21(1.75)	428	-0.12	0.90	-3.57	3.15
Type of treatment x Cholesterol	0.72(1.70)	428	0.43	0.67	-2.54	3.99
Type of treatment x Diabetes	-1.05(1.75)	428	-0.60	0.55	-4.40	2.29
Type of treatment x BMI	-0.22(0.16)	530	-1.35	0.18	-0.54	0.09
Type of treatment x Smoking	-1.46(1.89)	530	-0.77	0.44	-5.07	2.16
Random effects	***SD***					
Residuals	4.44					
Intercept	11.74					
Time	15.84					
Time^2	3.25					
Model fit						
BIC	7662.15					

†Educational status compared to six years or less

‡Occupational status compared to unemployed

The above results demonstrate that after adjusting for potential predictors, the *CROQ Total* score initially increased with time and then decreased (β=31.75, *SE*=2.25, p<0.01 and β=-5.79, *SE*=0.22, p<0.01 respectively), though remaining much higher than baseline scores. The CR type of treatment did not remain a significant predictor of *CROQ Total* scores either for the baseline scores, or for the mean change over the one year period ($p>0.05$).

Concerning the effect of Time, taking into account also the significant interaction terms, due to the presence of the quadratic effect, interpretation should be based on specific time points. For example, if Time1 denotes the value of Time at a specific time and BMI the body mass index of the patient, then if time increases by one unit, the *CROQ Total* score will increase on average by (31.75-0.10 x BMI) -5.79 (2 x Time1 +1) units for male patients that do not smoke, by (32.75-0.10 x BMI) -5.79 (2 x Time1 +1) units for female patients that do not smoke (where 32.75= time + female effect), by (30.17-0.10 x BMI) -5.79 (2 x Time1 +1) units for male patients that smoke (where 30.17= time – smoking effect) and by (31.17-0.10 x BMI) -5.79 (2 x Time1 +1) for female patients that smoke (where 31.71= time + female – smoking effect), if the other variables are kept constant.

Females on average showed a lower score of *CROQ Total* by 3.98 units at the baseline compared to males. This reduction, however, decreased by one unit every time that Time increased by one unit, leading to a slightly greater mean change of 0.02 units for females compared to males with the same features one year after CR. Specifically, female sex at Time0 = - 3.98, at Time1 =-2.98 (3.98-1; where 1 represents the value of the interaction term sex x time) and at Time2= 0.02 [(3.98-(1x4)); where 4 represents the value of Time2]. Taking into account that the positive change is tiny, an equal mean change between males and females after CR can be assumed.

Also, a crossover interaction was revealed between smoking and Time. At the baseline smoking was not associated with differences in *CROQ Total* score (it had a positive non-significant effect on CROQ Total), but one year post CR smokers showed on average a significant lower *CROQ Total* score by 5.07 units compared to non-smokers with the same features one year after CR, specifically smokers at Time0 = 1.25, at Time1 =-0.33 (1.25-1.58; where 1.58 represents the value of the interaction term smoking x time) and at Time2= -5.07 [(1.25-(1.58x4)); where 4 represents the value of Time2].

Regarding the remaining individual and time-varying covariates it should be noted that education, profession, cholesterol and BMI were statistically significant predictors of *CROQ Total* score at baseline when keeping the other variables constant; Patients with 7-12 years of education showed a higher score on average by 3.11 units compared to individuals with up to 6 years of education. Patients with increased cholesterol levels showed a lower score on average by 2.98 units and patients working as free-lancers showed a higher score on average by 3.90 units compared to those without a job, of when keep the rest of the variables fixed. The lack of significant time x educational or occupational status interactions imply that those differences do not significantly change after treatment. Finally, when BMI increases by 1 unit individuals demonstrated a higher *CROQ Total* score at baseline on average of 0.31 units; this increase, however, becomes lower by 0.10 units every time that time increases by 1 unit (b=-0.10, SE=0.04, p<0.001).

To sum up, based on the marginal means of the effect of Time, even after adjusting for treatment type (see Section 6.3.1.1), CHD patients following CR showed an increase, on average, in *CROQ Total* one year post CR. Furthermore (again see Section 6.3.1.1), individuals treated with PCI demonstrated a small decrease in the mean change between 3 and 12 months, while individuals treated with CABG demonstrated a small increase in the mean change between 3 and 12 months.

After adjusting for potential predictors, results revealed that the *CROQ Total* score initially significantly increased with time and then significantly decreased, remaining however much higher to baseline scores. The type of treatment was not a significant predictor for *CROQ Total* anymore. Moreover, the effect of Time depended on sex, BMI and smoking; on average it seemed to be larger for females that did not smoke and had a low BMI. Moreover, as time increases, females show on average a significantly higher *CROQ Total* score compared to males and smokers show on average a significantly lower *CROQ Total* score compared to non-smokers. Individuals with 7- 12 years of education compared to individuals with up to 6 years, patients without increased cholesterol levels compared to those with increased cholesterol levels and free-lancers compared to the those without a job showed a larger *CROQ Total score* following CR.

6.3.2 The Symptoms subdomain

The descriptive analysis of the CROQ's *symptoms* scores indicated an increase over a one-year period. Table 6.3.5 displays participants' mean scores for the *symptoms* subdomain over a one-year period overall and by CR type of treatment for all individual characteristics measured; the mean scores after CR treatment increased for all groups.

Table 6.3.5 Descriptive statistics for Symptoms scores per CR type over a one-year period (n=472)

Symptoms			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
Overall		*Mean*	63.62	90.35	87.17	59.27	93.85	97.85
		SD	18.77	11.41	12.67	16.77	7.85	5.18
Age group *Mean* age (60.43)	<60.43	*Mean*	67.23	91.75	85.30	61.83	94.83	98.01
		SD	17.82	9.41	13.83	13.35	6.74	4.68
	>60.43	*Mean*	59.24	88.96	89.32	56.87	92.78	97.68
		SD	19.05	12.98	10.85	19.22	8.82	5.71
Sex	male	*Mean*	65.40	91.21	87.13	61.36	94.66	98.74
		SD	17.91	10.54	13.18	16.73	7.39	3.59
	female	*Mean*	57.86	87.90	87.28	52.39	91.18	94.84
		SD	20.46	13.39	11.17	15.16	8.80	8.01
Marital status	unmarried/live alone	*Mean*	65.96	89.30	88.67	51.23	90.09	89.88
		SD	16.26	14.11	12.83	14.05	13.79	10.86
	married	*Mean*	63.00	90.59	86.87	60.63	94.44	98.75
		SD	19.38	10.73	12.65	16.86	6.32	3.08
Educational status	six years or less	*Mean*	60.34	88.04	87.29	63.55	91.99	99.26
		SD	19.41	13.73	12.27	20.88	11.06	2.10
	7-12 years	*Mean*	66.28	91.66	86.97	59.39	93.32	97.93
		SD	16.41	10.09	12.08	14.32	6.93	4.41
	12^{+} years	*Mean*	61.92	90.93	87.39	55.49	96.34	96.54
		SD	21.77	10.09	14.47	16.18	5.21	7.63
Occupational status	unemployed	*Mean*	62.71	92.38	88.10	55.88	94.25	92.86
		SD	18.96	10.19	11.64	12.22	6.14	9.19
	public/private servant	*Mean*	65.97	90.90	85.44	65.17	94.70	98.71
		SD	18.59	10.23	14.08	13.18	5.45	2.70
	free-lancer	*Mean*	68.09	93.94	86.67	53.94	96.89	98.97
		SD	18.37	8.41	13.27	16.16	4.86	2.18
	pensioner	*Mean*	59.92	87.61	88.42	60.54	91.23	98.40
		SD	18.58	13.14	11.63	18.92	10.01	5.03
Family history CHD	no	*Mean*	63.49	90.13	89.31	60.13	93.21	97.64
		SD	17.61	12.25	9.81	17.51	9.61	5.10
	yes	*Mean*	63.75	90.64	85.07	58.38	94.52	98.02
		SD	19.90	10.58	14.75	16.03	5.39	5.28
Hypertension	no	*Mean*	61.45	90.41	86.62	57.40	93.13	98.07
		SD	18.19	11.46	12.89	17.98	7.38	4.48
	yes	*Mean*	67.44	90.23	88.07	62.01	95.09	97.62
		SD	19.10	11.39	12.33	14.21	8.62	6.19

Table 6.3.5 Descriptive statistics for Symptoms scores per CR type over a one-year period (n=472)								
Symptoms			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
Cholesterol	no	*Mean*	63.10	91.15	87.26	60.53	96.43	98.06
		SD	18.62	11.03	12.82	15.95	6.03	4.68
	yes	*Mean*	64.72	88.54	86.98	56.64	88.89	97.48
		SD	18.98	12.11	12.45	18.00	8.62	6.31
Diabetes	no	*Mean*	63.91	90.20	86.95	58.79	93.83	97.95
		SD	18.05	10.45	13.18	16.43	6.52	4.53
	yes	*Mean*	62.40	90.75	87.78	59.81	93.82	97.81
		SD	20.74	13.78	11.21	17.45	10.03	6.17
Smoking	no	*Mean*	61.21	90.92	90.35	58.73	94.71	98.32
		SD	17.30	10.62	10.50	18.17	6.20	4.60
	yes	*Mean*	65.36	90.32	83.22	59.91	82.14	91.96
		SD	19.64	10.35	13.68	15.06	14.13	9.39
BMI	normal weight (18.5-24.9)	*Mean*	63.90	88.42	85.85	56.19	93.65	99.64
		SD	20.06	11.11	11.79	15.72	5.55	1.13
	overweight (25.0-29.9)	*Mean*	61.26	90.72	88.12	56.54	96.33	99.60
		SD	18.23	11.46	13.40	17.77	4.79	1.68
	obese (<29.9)	*Mean*	66.59	90.99	86.35	62.86	91.47	97.62
		SD	18.04	12.00	12.64	16.08	8.80	1.84

T1= prior to treatment, T2 = 3 months after treatment, T3= 12 months after treatment

6.3.2.1 Changes in the Symptoms subdomain: Time and Type of CR treatment effects

As described in the analysis section, the first step was to detect the best fitting model for the time trend. Table 6.3.6 shows the values for the six models compared. According to the BIC index the 6th model (model f, Time and Time^2 as predictors with random intercept, linear and quadratic terms) was the best mixed model for describing the trend for *symptoms* scores.

Table 6.3.6 Parameter estimates and model fit statistics for first and second order polynomials of Symptoms score growth over a one-year period

	Model a	Model b	Model c	Model d	Model e	Model f
Fixed effects	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)
Intercept	72.09(0.70)**	72.08(0.70)**	61.85(0.69)**	61.76(0.75)**	61.80(0.72)**	61.79(0.90)**
Time	5.78(0.31)**	5.78(0.31)**	37.27(1.19)**	37.37(1.11)**	37.33(1.15)**	37.33(1.22)**
Time^2	NA	NA	-7.50(0.25)**	-7.51(0.25)**	-7.50(0.27)**	-7.50(0.25)**
Random effects	SD	SD	SD	SD	SD	SD
Residuals	17.39	17.38	12.93	11.79	12.39	8.29
Intercept	NA	0.01	5.14	9.82	7.62	16.10
Time	NA	NA	NA	2.56	NA	19.81
Time^2	NA	NA	NA	NA	0.37	3.94
Model fit						
BIC	9706.33	9720.40	9207.77	9178.20	9203.46	9076.60

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous
Time= Linear, Time^2= Quadratic
Model a= Ordinal linear least square regression with Time as a predictor
Model b= Time as a predictor with random intercept
Model c= Time and Time^2 as predictors with random intercept
Model d = Time and Time^2 as predictors with random intercept and linear term
Model e= Time and Time^2 as predictors with random intercept and quadratic term
Model f= Time and Time^2 as predictors with random intercept, linear and quadratic terms
In all models response variable *symptoms* scores
$^{**}p<0.001$

The analysis demonstrated that the mean initial status (baseline) of the *symptoms* scores was 61.79 (β = 61.79, *SE* = 0.90, t=68.69, $p < 0.01$). Time had a significant positive linear effect on the *symptoms* scores (β = 37.33, *SE* = 1.22, t= 30.58, $p < 0.01$), as well as a significant negative quadratic effect (β = -7.50, *SE* = 0.25, t= -28.93, $p < 0.01$). The acceleration (calculated according to Singer, & Willett, 2003) was 22.33 points [i.e. 37.33/ (2 (-7.50))]. These results suggest that the, s*ymptoms* scores increased at the beginning, but this trend slowed down later on. Overall, a positive effect on the *symptoms* subdomain following CR can be assumed.

To examine the effect of the CR type on the *symptoms* scores, the best model of time trajectory was further investigated by adding the CR type of treatment (PCI/CABG) variable. Based on the BIC index, the best model describing *symptoms* trends was the second (Time,

Time^2, CR type of treatment as predictors and the interaction term Time x CR type of treatment with random intercept, linear and quadratic terms) as Table 6.3.7 suggests.

Table 6.3.7 Parameter estimates and model fit statistics for first and second order polynomials and treatment interactions of Symptoms score growth over a one-year period

	Model 1	Model 2	Model 3
Fixed effects	B (SE)	B (SE)	B (SE)
Intercept	59.53(0.97)**	62.13(1.01)**	63.58(1.14)**
Time	37.47(1.22)**	36.22(1.22)**	33.75(1.54)**
Time^2	-7.53(0.25)**	-7.49(0.26)**	-6.96(0.33)**
Type of treatment†	4.88(0.82)**	-0.75(1.18)	-4.39(1.83)*
Time x Type of treatment	NA	2.84(0.43)**	9.16(2.46)**
Time^2 x Type of treatment	NA	NA	-1.38(0.53)*
Random effects	SD	SD	SD
Residual	8.48	8.27	8.25
Intercept	16.51	16.07	15.95
Time	20.18	19.65	19.46
Time^2	4.03	3.98	3.94
Model fit			
BIC	9052.89	9019.73	9020.01

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous, Time= Linear, Time^2= Quadratic, †Type of treatment = CABG

Model 1=Time, Time^2 and CR type of treatment as predictors with random intercept, linear and quadratic term
Model 2=Time, Time^2, CR type of treatment as predictors and Time x CR type of treatment interaction term with random intercept, linear and quadratic terms
Model 3=Time, Time^2, CR type of treatment as predictors, Time x CR type of treatment interaction term, and Time^2 x CR type of treatment interaction term with random intercept, linear and quadratic terms
In all models response variable *symptoms* scores
$^{**}p<0.001$, $^{*}p<0.05$

Results showed that CABG patients scored slightly lower compared to PCI patients in terms of mean initial status (baseline) for the *symptoms* subdomain but the rate of change in linear trends was greater for CABG patients. The marginal means for the CR type as a predictor for the *symptoms* subdomain can be estimated by employing the following formulas:

Symptoms marginal means at 0 months (baseline) = β_0, 3 months = $\beta_0 + \beta_1 \times \text{Time1} + \beta_2 \times \text{Time1}^2$ and 12 months = $\beta_0 + \beta_1 \times \text{Time2} + \beta_2 \times \text{Time2}^2$, where

Time1 = 1 and Time2 = 4,

CR type of treatment: PCI = 0 and CABG = 1,

$\beta_0 = 62.13 - 0.75$ x type of treatment,

$\beta_1 = 36.22 + 2.84$ x type of treatment,

$\beta_2 = -7.49$

For PCI the marginal mean prior to treatment was 62.13 and at 3 months was 90.86, resulting in a mean change of 28.73 points from the baseline mean score. For CABG the marginal mean prior to treatment was 61.38 and at 3 months was 92.95, resulting in a mean change of 31.57 points from the baseline mean score.

Concerning the marginal mean for PCI at 12 months this was 87.17, resulting in a mean change of 25.04 points from the baseline mean score, while the marginal mean for CABG at 12 months was 97.78, resulting in a mean change of 36.40 points from the baseline mean score, as Figure 6.4 illustrates.

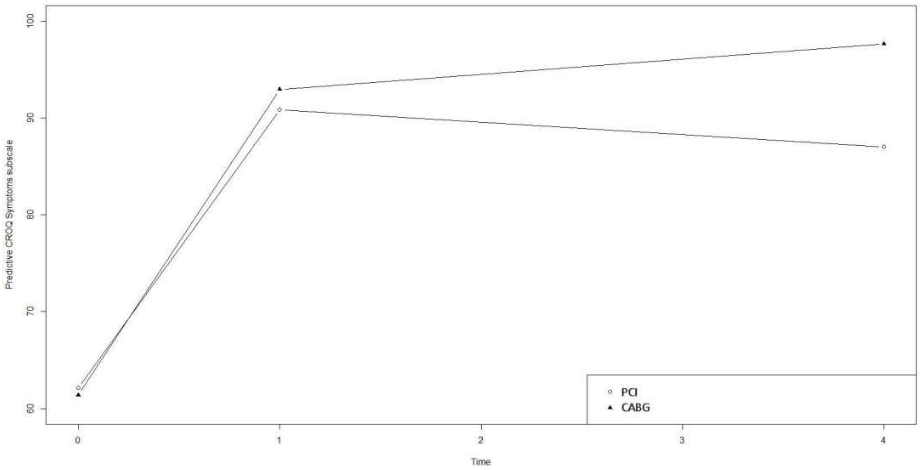

Figure 6.4 Marginal means of the Symptoms subdomain scores per CR type of treatment. Time0= baseline scores, Time1= 3 month mean scores, Time4=12 month mean scores.

Hence overall, it can be assumed that over one year period, in the *symptoms* subdomain, patients treated with CABG experienced a greater mean change compared to patients treated with PCI.

The variability of *Symptoms* subdomain scores within individuals per CR type at the 3 month measurement time points can be seen in Figure 6.5.

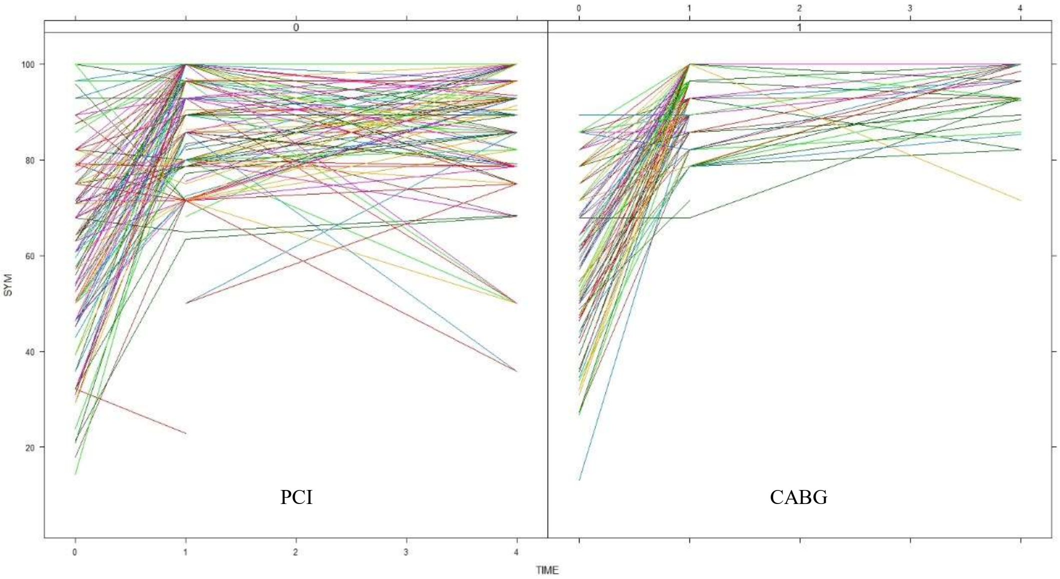

Figure 6.5 Symptoms subdomain scores as a function of Time for all patients by type of CR treatment. Time0= baseline scores, Time1= 3 month scores, Time4=12 month scores.

6.3.2.2.Predictors of Symptoms subdomain change over a one-year period

In the final conditional growth model, the effects of all individual level covariates as well as well as the two time-varying predictors (i.e. smoking and BMI) were investigated. Included in the model were also all the two-way interaction terms of these potential predictors with Time and CR type of treatment. The following Table 6.3.8 summarizes the fixed and random effects of the model.

Table 6.3.8 Growth model for changes in Symptoms scores over a one-year period

Fixed effects	Est (SE)	df	t	*p*	95% Confidence Interval	
					Lower Bound	Upper Bound
Intercept	64.07(8.07)	530	7.94	0.00	48.61	79.52
Time	36.91(3.67)	530	10.06	**0.00**	28.98	43.93
Time^2	-7.64(0.30)	530	-25.11	**0.00**	-8.22	-7.06
Type of treatment (CABG)	-1.08(11.25)	428	-0.10	0.92	-22.63	20.47
Place of residence (Rural Area)	-1.54(2.20)	428	-0.70	0.48	-5.76	2.67
Age	-0.16(0.10)	428	-1.66	0.1	-0.34	0.02
Sex (Female)	-4.22(1.56)	428	-2.70	**0.01**	-7.21	-1.23
Marital status (Married)	-0.86(1.68)	428	-0.51	0.61	-4.09	2.37
Educational status†						
7-12 years	0.81(1.69)	428	0.48	0.63	-2.43	4.05
12$^+$ years	-2.42(1.96)	428	-1.24	0.22	-6.18	1.33
Occupational status‡						
Public/private servant	-0.93(2.06)	428	-0.45	0.65	-4.88	3.01
Free lancer	2.25(2.30)	428	0.98	0.33	-2.15	6.65
Pensioner	-2.65(2.27)	428	-1.17	0.24	-6.99	1.70
CHD Family history (yes)	-0.63(1.29)	428	-0.49	0.62	-3.09	1.83
Hypertension (yes)	2.25(1.33)	428	1.69	0.09	-0.3	4.81
Cholesterol (yes)	-2.12(1.41)	428	-1.51	0.13	-4.82	0.58
Diabetes (yes)	1.86(1.53)	428	1.21	0.22	-1.07	4.79
BMI	0.32(0.15)	530	2.07	**0.04**	0.02	0.61
Smoking (yes)	2.19(1.45)	530	1.51	0.13	-0.58	4.97
Time x Type of treatment	2.13(0.72)	530	2.94	**0.00**	0.74	3.52
Time x Place of residence	0.24(0.81)	530	0.29	0.77	-1.31	1.78
Time x Age	0.08(0.04)	530	1.96	0.06	0.00	0.15
Time x Sex	1.14(0.61)	530	1.86	0.06	-0.03	2.31
Time x Marital status	-0.19(0.71)	530	-0.27	0.78	-1.55	1.17
Time x Educational status†						
7-12 years	0.66(0.69)	530	0.96	0.34	-0.65	1.98
12$^+$ years	1.53(0.78)	530	1.96	0.06	0.04	3.03
Timex Occupational status‡						
Public/private servant	-0.40(0.85)	530	-0.47	0.64	-2.02	1.23
Free lancer	-0.71(0.91)	530	-0.78	0.44	-2.45	1.04

Table 6.3.8 Growth model for changes in Symptoms scores over a one-year period

Fixed effects	**Est (SE)**	**df**	**t**	***p***	**95% Confidence Interval**	
					Lower Bound	**Upper Bound**
Pensioner	0.06(0.92)	530	0.07	0.95	-1.71	1.84
Time x CHD Family history	-0.27(0.51)	530	-0.53	0.60	-1.25	0.71
Time x Hypertension	-0.54(0.52)	530	-1.04	0.30	-1.54	0.46
Time x Cholesterol	0.23(0.56)	530	0.41	0.68	-0.84	1.29
Time x Diabetes	-0.41(0.60)	530	-0.68	0.50	-1.55	0.74
Time x BMI	-0.14(0.06)	530	-2.21	**0.03**	-0.26	-0.02
Time x Smoking	-2.06(0.59)	530	-3.48	**0.00**	-3.19	-0.93
Type of treatment x Place of residence	0.59(2.54)	428	0.23	0.81	-4.27	5.46
Type of treatment x AGE	0.04(0.15)	428	0.27	0.79	-0.25	0.33
Type of treatment x Sex	-1.94(2.41)	428	-0.8	0.42	-6.55	2.68
Type of treatment x Marital status	3.57(2.81)	428	1.27	0.20	-1.81	8.96
Type of treatment x Educational status†						
7-12 years	-0.74(2.75)	428	-0.27	0.79	-6.02	4.53
12^{+} years	1.23(3.17)	428	0.39	0.70	-4.85	7.30
Type of treatment x Occupational status‡						
Public/private servant	-0.90(3.39)	428	-0.26	0.79	-7.39	5.59
Free lancer	-3.49(3.48)	428	-1.00	0.32	-10.15	3.18
Pensioner	0.09(3.65)	428	0.02	0.98	-6.91	7.09
Type of treatment x CHD Family history	1.11(1.80)	428	0.62	0.54	-2.34	4.56
Type of treatment x Hypertension	2.23(2.04)	428	1.09	0.28	-1.68	6.15
Type of treatment x Cholesterol	-4.40(1.96)	428	-2.24	**0.02**	-8.16	-0.64
Type of treatment x Diabetes	-0.59(1.99)	428	-0.3	0.77	-4.4	3.23
Type of treatment x BMI	-0.08(0.21)	530	-0.4	0.69	-0.48	0.31
Type of treatment x Smoking	-3.73(2.60)	530	-1.44	0.15	-8.7	1.24
Random effects	***SD***					
Residuals	7.28					
Intercept	15.47					
Time	20.42					
Time^2	4.20					
Model fit						
BIC	8253.57					

†Educational status compared to six years or less ‡Occupational status compared to unemployed

The above results demonstrate that after adjusting for potential predictors, the *symptoms* mean score initially increased with time and then decreased (β=36.91, *SE*=3.67, p<0.01 and β=-7.64, *SE*=0.30, p<0.01 respectively), although remaining much higher than the baseline scores.

Concerning the effect of Time, taking into account also the significant interaction terms, due to the presence of the quadratic effect, interpretation should be based on specific time points. For example, if Time1 denotes the value of Time at a specific time and BMI the body mass index of the patient, then if Time increases by one unit, the *symptoms* score will increase on average by (36.91-0.14 x BMI) -7.64 (2 x Time1 +1) units for PCI patients that do not smoke, by (39.04-0.14 x BMI) -7.64 (2 x Time1 +1) units for CABG patients that do not smoke (where 39.04=time + time x type of treatment), by (34.85-0.14 x BMI) -7.64 (2 x Time1 +1) units for PCI patients that do smoke (where 34.85= time – time x smoking) and by (36.98-0.10 x BMI) -7.64 (2 x Time1 +1) for CABG patients that do smoke (where 36.98= time = time x type of treatment - time x smoking), if the other variables are kept constant.

The CR type of treatment was not associated with differences in *symptoms* score at baseline; it had a negative non-significant effect (p>0.05). A crossover interaction effect between Time and CR type of treatment on *symptoms* score (p<0.01) was revealed, suggesting that as time increased, patients treated with CABG showed a significantly higher symptoms score on average. Specifically, for individuals with the same characteristics one year after CR, patients treated with CABG demonstrated a greater mean change of 7.47 units compared to patients treated with PCI; CABG treatment at Time0 = - 1.08, at Time1 = 1.05 (1.08-2.13; where 2.13 represents the value of the interaction term CABG x Time) and at Time2= 7.47 [(1.08-(2.13x4)); where 4 represents the value of Time2].

Females scored lower on the *symptoms* subdomain by 4.22 units (*p*=0.01) at baseline compared to males when keeping the other variables constant. This reduction, however, tended to decrease as time increased at an almost significant level (*p*=0.06), resulting in a slight greater mean change of 0.34 units for females compared to males with the same features. Specifically, female sex at Time0 = - 4.22, at Time1 =-3.08 (4.22-1.14; where 1 represents the value of the interaction term sex x time) and at Time2= 0.34 [(4.22-(1.14x4)); where 4 represents the value of Time2].

Also, a crossover interaction was revealed between smoking and Time. At baseline smoking was not associated with differences in *symptoms* score (it had a positive non-significant effect on *symptoms, p*>0.05) keeping the other variables constant, but one year post CR smokers showed on average a significant lower *symptoms* score (indicating more symptoms) by 6.05 units compared to non-smokers with the same features. Specifically smokers at Time0 = 2.19, at Time1 =-0.13 (2.19-2.06; where 2.06 represents the value of the interaction term smoking x time) and at Time2= -6.05 [(2.19-(2.06x4)); where 4 represents the value of Time2].

BMI was revealed as an independent significant predictor of the *symptoms* score at baseline. When BMI increases by one unit individuals demonstrated a better *symptoms* scores at baseline on average by 0.32 units, when keeping the other variables constant; this increase, however, decreases by 0.10 units every time that time increases by one unit (*p*=0.04).

Briefly, the results suggest that CHD patients following CR experienced significantly fewer heart-related *symptoms* one year after CR (section 6.3.2.1); After adjusting for potential predictors the *symptoms* score initially increased with time and then decreased, although remaining much higher compared to baseline scores. Moreover, the effect of time depended on the CR type of treatment, BMI and smoking; on average, it seemed to be larger for individuals treated with CABG, who did not smoke and had a low BMI. Finally, as time increased patients treated with CABG compared to those treated with PCI and females compared to males on average showed a better *symptoms* score, while smokers compared to non-smokers on average showed a significantly worse *symptoms* score.

6.3.3 The Physical functioning subdomain

The descriptive analysis of the *Physical functioning* scores indicated an increase over a one-year period. Table 6.3.9 displays participants' mean scores in the *physical functioning* subdomain over a one-year period overall and by CR type of treatment for all individual characteristics measured; the mean scores after CR treatment increased for all groups.

Table 6.3.9 Descriptive statistics for Physical functioning scores per CR type over a one year period (n=472)

			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
Overall		*Mean*	56.29	89.08	85.40	41.35	89.09	92.29
		SD	28.30	14.97	17.16	21.15	14.54	10.93
Age group *Mean* age (60.43)	<60.43	*Mean*	57.22	91.07	85.65	48.05	90.05	94.04
		SD	29.22	13.23	16.26	21.66	13.89	10.39
	>60.43	*Mean*	55.15	87.12	85.11	35.06	88.04	90.36
		SD	27.22	16.31	18.23	18.71	15.26	11.27
Sex	male	*Mean*	57.91	91.19	86.29	44.01	91.61	93.55
		SD	27.98	12.84	17.35	21.57	12.51	10.75
	female	*Mean*	51.04	83.08	82.84	32.60	80.88	88.33
		SD	28.93	18.66	16.49	17.25	17.61	10.73
Marital status	unmarried/live alone	*Mean*	57.28	86.61	88.47	35.87	89.80	85.42
		SD	30.85	18.14	16.04	25.23	10.67	16.71
	married	*Mean*	56.02	89.64	84.79	42.28	88.99	93.02

Table 6.3.9 Descriptive statistics for Physical functioning scores per CR type over a one year period (n=472)

			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
		SD	27.65	14.14	17.36	20.34	15.07	9.95
Educational status	six years or less	*Mean*	54.81	83.13	84.80	37.66	87.13	90.63
		SD	27.14	18.30	19.46	24.01	16.13	13.42
	7-12 years	*Mean*	58.55	92.00	85.24	42.57	88.13	92.19
		SD	27.39	11.13	16.25	21.24	14.79	9.86
	12^{+} years	*Mean*	53.87	90.99	86.46	41.94	92.19	95.16
		SD	31.25	14.89	16.18	18.11	12.48	8.02
Occupational status	unemployed	*Mean*	46.87	91.77	85.98	40.46	83.33	87.50
		SD	26.24	12.22	17.56	20.24	19.05	12.30
	public/private servant	*Mean*	60.74	90.22	83.10	57.17	94.15	96.50
		SD	29.98	14.20	17.88	21.55	12.49	7.01
	free-lancer	*Mean*	62.46	93.01	89.33	39.79	93.11	94.08
		SD	26.77	10.86	10.85	17.22	9.27	10.77
	pensioner	*Mean*	54.20	85.53	84.94	34.33	85.42	90.20
		SD	27.62	17.24	18.95	19.49	15.55	11.47
Family history CHD	no	*Mean*	50.83	88.89	86.55	44.21	89.27	93.01
		SD	25.27	15.73	17.19	21.74	13.11	8.46
	yes	*Mean*	61.57	89.28	84.38	38.38	88.91	91.63
		SD	30.12	14.30	17.20	20.24	15.99	12.80
Hypertension	no	*Mean*	54.73	88.27	84.10	42.79	89.58	94.47
		SD	26.90	15.48	18.24	22.12	13.36	6.90
	yes	*Mean*	59.16	90.51	87.57	38.85	88.24	88.89
		SD	30.59	13.99	15.06	19.57	16.71	14.95
Cholesterol	no	*Mean*	56.51	89.13	85.20	43.20	91.45	93.00
		SD	28.62	15.45	17.14	22.25	13.21	10.39
	yes	*Mean*	55.69	88.97	85.81	37.83	84.57	91.25
		SD	27.54	13.89	17.32	18.86	16.14	11.82
Diabetes	no	*Mean*	56.44	89.43	85.03	40.32	89.28	92.41
		SD	28.43	14.24	17.51	20.34	15.05	11.79
	yes	*Mean*	55.78	88.13	86.45	43.08	88.78	92.47
		SD	27.99	16.87	16.27	22.79	13.80	9.10
Smoking	no	*Mean*	54.95	90.56	91.60	39.10	89.74	92.87
		SD	26.22	14.04	14.52	20.25	14.21	10.67

Table 6.3.9 Descriptive statistics for Physical functioning scores per CR type over a one year period (n=472)

			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
	yes	*Mean*	57.25	86.18	76.72	44.01	37.50	86.25
		SD	29.75	14.76	16.87	22.01	13.15	12.02
BMI	normal weight (18.5-24.9)	*Mean*	51.99	87.73	85.46	46.88	85.42	98.75
		SD	29.57	14.94	19.44	26.54	16.61	3.95
	overweight (25.0-29.9)	*Mean*	57.62	89.67	83.97	38.19	92.36	91.78
		SD	29.28	15.68	16.52	21.50	13.11	8.60
	obese (<29.9)	*Mean*	57.62	88.57	86.22	41.32	86.1	89.38
		SD	27.41	14.72	17.17	17.13	15.64	11.80

6.3.3.1.Changes in Physical functioning: Time and Type of CR treatment effects

As described in the analysis section, the first step was to detect the best fitting model for the time trend. Table 6.3.10 shows the values for the six models compared. Based on the BIC index the 6th model (model f, Time and Time^2 as predictors with random intercept, linear and quadratic terms) was the best mixed model for describing the time trend of the *physical functioning* scores.

Table 6.3.10 Parameter estimates and model fit statistics for first and second order polynomials of Physical functioning score growth over a one-year period

	Model a	Model b	Model c	Model d	Model e	Model f
Fixed effects	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)
Intercept	63.67(0.98)**	63.67(0.98)**	50.39(0.99)**	50.35(1.10)**	50.36(1.05)**	50.38(1.32)**
Time	7.44(0.43)**	7.44(0.44)**	48.57(1.69)**	48.88(1.56)**	48.81(1.61)**	48.45(1.76)**
Time^2	NA	NA	-9.79(0.39)**	-9.86(0.36)**	-9.76(0.37)**	-9.76(0.37)**
Random effects	SD	SD	SD	SD	SD	SD
Residuals	24.21	24.18	18.18	16.45	17.16	10.83
Intercept	NA	0.01	8.46	15.28	12.50	24.38
Time	NA	NA	NA	3.58	NA	29.88
Time^2	NA	NA	NA	NA	0.58	5.91

Table 6.3.10 Parameter estimates and model fit statistics for first and second order polynomials of Physical functioning score growth over a one-year period

Model fit	Model a	Model b	Model c	Model d	Model e	Model f
BIC	10455.66	10469.62	10024.43	9977.63	10008.16	9838.82

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous
Time= Linear, Time^2= Quadratic
Model a= Ordinal linear least square regression with Time as a predictor
Model b= Time as a predictor with random intercept
Model c= Time and Time^2 as predictors with random intercept
Model d = Time and Time^2 as predictors with random intercept and linear term
Model e= Time and Time^2 as predictors with random intercept and quadratic term
Model f= Time and Time^2 as predictors with random intercept, linear and quadratic terms
In all models response variable *physical functioning* scores
$^{**}p<0.001$

The analysis demonstrated that the mean initial status (baseline) for the *physical functioning* scores was 50.38 (β = 50.38, *SE* = 1.32, t=38.05, $p < 0.01$). Time had a significant positive linear effect (β = 48.45, *SE* = 1.76, t= 27.39, $p < 0.01$), as well as a significant negative quadratic effect (β = -9.76, *SE* = 0.37, t= -26.38, $p < 0.01$). The acceleration was 28.93 points [i.e. 48.45/ (2 (-9.76))] (Singer, & Willett, 2003). According to the results, *physical functioning* scores increased at the beginning, but this trend slowed down later on. Overall, a positive change on *physical functioning* scores following CR can be assumed.

To investigate the effect of CR type on *physical functioning* scores, the best model of the time trajectory was further investigated by adding the CR type of treatment (PCI/CABG) variable. The best model describing the trend of the *physical functioning* scores, having the lowest BIC value, was the third (Time, Time^2, CR type of treatment as predictors, and Time x CR type of treatment and Time^2 x CR type of treatment interaction terms with random intercept, linear and quadratic terms) as Table 6.3.11 suggests.

Table 6.3.11 Parameter estimates and model fit statistics for first and second order polynomials and treatment interactions of Physical functioning score growth over a one-year period

	Model 1	Model 2	Model 3
Fixed effects	B (SE)	B (SE)	B (SE)
Intercept	50.46(1.41)**	52.97(1.43)**	56.31(1.63)**
Time	48.44(1.76)**	46.99(1.76)**	41.35(2.20)**
Time^2	-9.76(0.37)**	-9.72(0.37)**	-8.52(0.46)**
Type of treatment†	-0.19(1.25)	-6.67(1.67)**	-15.08(2.61)**
Time x Type of treatment	NA	3.37(0.56)**	17.84(3.51)**
Time^2 x Type of treatment	NA	NA	-3.11(0.74)**
Random effects	SD	SD	SD
Residual	10.83	10.77	10.71
Intercept	24.36	23.64	23.32
Time	29.85	29.29	28.65
Time^2	5.90	5.89	5.75
Model fit			
BIC	9845.83	9820.05	9809.91

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous, Time= Linear, Time^2= Quadratic, †Type of treatment = CABG

Model 1=Time, Time^2 and CR type of treatment as predictors with random intercept, linear and quadratic term
Model 2=Time, Time^2, CR type of treatment as predictors and Time x CR type of treatment interaction term with random intercept, linear and quadratic terms
Model 3=Time, Time^2, CR type of treatment as predictors, Time x CR type of treatment interaction term, and Time^2 x CR type of treatment interaction term with random intercept, linear and quadratic terms
In all models response variable *physical functioning* scores
$^{**}p<0.001$, $^{*}p<0.05$

Results demonstrated that the mean initial status (baseline) of the *physical functioning* scores for CABG patients was lower compared to PCI patients, a greater increase, however, was revealed for CABG patients in the rate of change in both linear and quadratic trends. The marginal means for CR type as predictor can be estimated by employing the following formulas: *Physical functioning* marginal means at 0 months (baseline) = β_0, 3 months = $\beta_0 + \beta_1$ x Time1 + β_2 x Time1^2 and 12 months = $\beta_0 + \beta_1$ x Time2+ β_2 x Time2^2, where

Time1 = 1 and Time2 = 4,

CR type of treatment: PCI = 0 and CABG = 1,

β_0 = 56.32-15.09 x type of treatment,

$\beta_1 = 41.36 + 17.84$ x type of treatment,

$\beta_2 = -8.52+3.11$ x type of treatment.

For PCI the marginal mean prior to treatment was 56.32 and at 3 months it was 89.16, resulting in a mean change of 32.84 points from the baseline mean score. For CABG the marginal mean prior to treatment was 41.23 and at 3 months it was 88.80, resulting in a mean change of 47.57 points from the baseline mean score.

Concerning the marginal mean for PCI, at 12 months this was 85.44, resulting in a mean change of 29.12 points from the baseline mean score, while the marginal mean for CABG at 12 months was 91.95, resulting in a mean change of 50.72 points from the baseline mean score, as Figure 6.6 illustrates. Hence overall, it can be assumed that over a one year period, in the *physical functioning* subdomain patients treated with CABG experienced a greater mean change compared to patients treated with PCI.

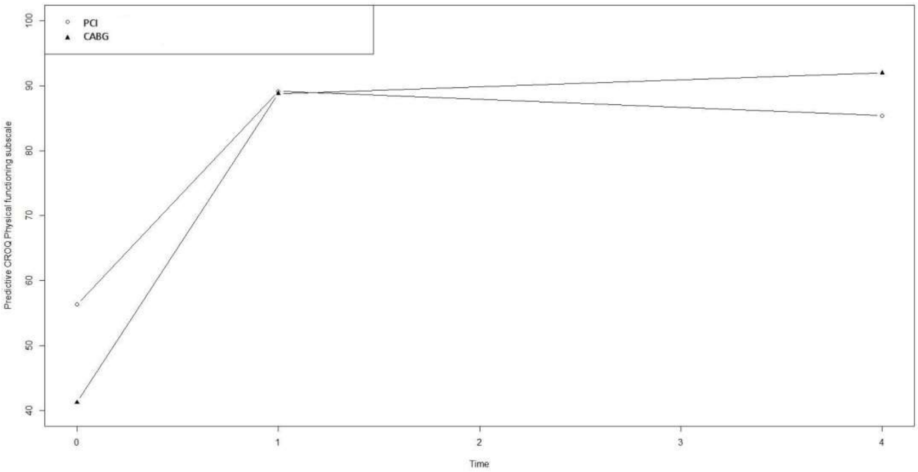

Figure 6.6 Marginal means of the Physical functioning subdomain scores per CR type of treatment. Time0= baseline scores, Time1= 3 month mean scores, Time4=12 month mean scores.

The variability of the *physical* functioning scores within individuals per CR type at the 3-month measurement time po can be seen in Figure 6.7.

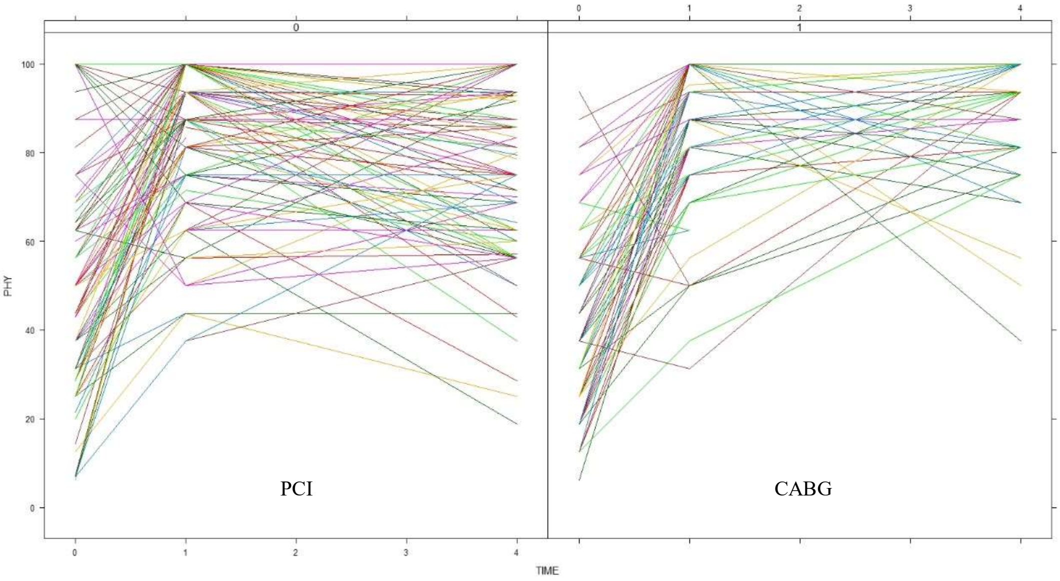

Figure 6.7 Physical functioning subdomain scores as a function of Time for all patients by type of CR treatment. Time0= baseline scores, Time1= 3 month scores, Time4=12 month scores.

6.3.3.2.Predictors of Physical functioning change over a one-year period

In the final conditional growth model, the effects of all individual level covariates as well as the two time-varying predictors (i.e. smoking and BMI) were investigated. Included in the model were also all the two-way interaction terms for these potential predictors with time and CR type of treatment. The following Table 6.3.12 summarizes the fixed and random effects of the model.

Table 6.3.12 Growth model for changes in Physical functioning scores over a one-year period						
					95% Confidence Interval	
Fixed effects	**Est (SE)**	**df**	**t**	***p***	**Lower Bound**	**Upper Bound**
Intercept	26.25(11.46)	529	2.29	0.02	4.31	48.20
Time	48.17(4.81)	529	10.02	**0.00**	38.97	57.67
$Time^2$	-8.52(0.52)	529	-16.53	**0.00**	-9.51	-7.53
Type of treatment (CABG)	-7.03(17.08)	428	-0.41	0.68	-39.73	25.67
Place of residence (Rural Area)	-2.63(3.17)	428	-0.83	0.41	-8.70	3.43
Age	0.22 (0.14)	428	1.61	0.11	-0.04	0.47
Sex (Female)	-8.49 (2.23)	428	-3.81	**0.00**	-12.75	-4.22
Marital status (Married)	0.41 (2.39)	428	0.17	0.86	-4.18	4.99
Educational status†						
7-12 years	6.20 (2.41)	428	2.57	**0.01**	1.58	10.82
12^+ years	3.47 (2.79)	428	1.24	0.21	-1.88	8.82
Occupational status‡						
Public/private servant	2.10 (2.92)	428	0.72	0.47	-3.49	7.70
Free lancer	5.21 (3.27)	428	1.59	0.11	-1.05	11.48
Pensioner	-5.07 (3.23)	428	-1.57	0.12	-11.25	1.12
CHD Family history (yes)	2.90 (1.84)	428	1.58	0.12	-0.62	6.42
Hypertension (yes)	2.66 (1.90)	428	1.40	0.16	-0.98	6.30
Cholesterol (yes)	-2.35 (2.01)	428	-1.17	0.24	-6.20	1.49
Diabetes (yes)	-1.56 (2.19)	428	-0.71	0.48	-5.75	2.63
BMI	0.50 (0.22)	529	2.30	**0.02**	0.08	0.91
Smoking (yes)	-0.08 (2.06)	529	-0.04	0.97	-4.03	3.86
Time x Type of treatment	17.48 (4.46)	529	3.92	**0.00**	8.94	26.01
Time 2 x Type of treatment	-3.36 (0.94)	529	-3.58	**0.00**	-5.16	-1.56
Time x Place of residence	0.49 (0.99)	529	0.49	0.62	-1.41	2.39
Time x Age	-0.02 (0.05)	529	-0.52	0.61	-0.12	0.07
Time x Sex	1.57 (0.74)	529	2.11	**0.04**	0.15	2.99
Time x Marital status	-1.51 (0.86)	529	-1.75	0.08	-3.16	0.14
Time x Educational status†						
7-12 years	0.50 (0.95)	529	0.53	0.60	-1.32	2.32
12^+ years	-0.78 (1.03)	529	-0.75	0.45	-2.74	1.19
Timex Occupational status‡						
Public/private servant	-0.78 (1.03)	529	-0.75	0.45	-2.74	1.19
Free lancer	0.07 (1.11)	529	0.06	0.95	-2.05	2.19

Table 6.3.12 Growth model for changes in Physical functioning scores over a one-year period

Fixed effects	Est (SE)	df	t	*p*	95% Confidence Interval	
					Lower Bound	Upper Bound
Pensioner	0.75 (1.12)	529	0.67	0.50	-1.40	2.91
Time x CHD Family history	-0.19 (0.62)	529	-0.31	0.76	-1.39	1.00
Time x Hypertension	-0.11 (0.64)	529	-0.17	0.86	-1.32	1.11
Time x Cholesterol	0.82 (0.68)	529	1.20	0.23	-0.48	2.11
Time x Diabetes	0.60 (0.73)	529	0.83	0.41	-0.79	2.00
Time x BMI	-0.12 (0.08)	529	-1.46	0.15	-0.27	0.04
Time x Smoking	-3.34 (0.74)	529	-4.49	**0.00**	-4.77	-1.92
Type of treatment x Place of residence	3.30 (3.80)	428	0.87	0.39	-3.98	10.58
Type of treatment x AGE	0.28 (0.22)	428	1.25	0.21	-0.15	0.71
Type of treatment x Sex	-6.74 (3.60)	428	-1.87	0.06	-13.64	0.16
Type of treatment x Marital status	4.39 (4.19)	428	1.05	0.29	-3.63	12.41
Type of treatment x Educational status†						
7-12 years	-4.87 (4.11)	428	-1.18	0.24	-12.75	3.01
12^{+} years	0.45 (4.73)	428	0.10	0.92	-8.61	9.52
Type of treatment x Occupational status‡						
Public/private servant	3.13 (5.07)	428	0.62	0.54	-6.58	12.85
Free lancer	-6.40 (5.21)	428	-1.23	0.22	-16.38	3.58
Pensioner	-6.03 (5.48)	428	-1.10	0.27	-16.52	4.47
Type of treatment x CHD Family history	-6.12 (2.70)	428	-2.27	**0.02**	-11.30	-0.95
Type of treatment x Hypertension	-4.04 (3.06)	428	-1.32	0.19	-9.90	1.82
Type of treatment x Cholesterol	-1.10 (2.94)	428	-0.37	0.71	-6.73	4.53
Type of treatment x Diabetes	4.23 (2.99)	428	1.42	0.16	-1.50	9.97
Type of treatment x BMI	-0.69 (0.30)	529	-2.32	**0.02**	-1.26	-0.12
Type of treatment x Smoking	0.97 (4.29)	529	0.23	0.82	-7.23	9.18
Random effects	***SD***					
Residuals	9.18					
Intercept	22.72					
Time	30.71					
Time^2	6.20					
Model fit						
BIC	8947.48					

†Educational status compared to six years or less ‡Occupational status compared to unemployed

The above results demonstrate that after adjusting for potential predictors, the *physical functioning* score initially increased with time and then decreased (β=48.17, *SE*=4.81, *p*<0.01 and β=-8.52, *SE*=0.52, *p*<0.01 respectively), although remaining much higher than baseline scores.

Concerning the effect of Time, taking into account also the significant interaction terms, due to the presence of the quadratic effect, the interpretation should be based on specific time points. For example, if Time1 denotes the value of Time at a specific time, then if time increases by one unit *physical functioning* will increase on average by 48.17-8.52 (2 x Time1 +1) units for PCI male patients that do not smoke, by 65.65-11.88 (2 x Time1 +1) units for CABG male patients that do not smoke (65.55= time + time x type of treatment interaction) and 11.88= time^2 + time^2 x type of treatment interaction, by 49.74-8.52 (2 x Time1 +1) units for PCI female patients that do not smoke (where 49.74=time + time x sex interaction), by 67.22-11.88 (2 xTime1 +1) units for CABG female patients that do not smoke (where 67.22= time + time x type of treatment interaction + time x sex interaction) , by 44.83-8.52 (2·x Time1 +1) units for PCI male patients that smoke (where 44.83= time - time x smoking interaction), by 46.40-8.52 (2 x Time1 +1) units for PCI female patients that smoke (where 46.40= time + time x sex interaction - time x smoking interaction), by 62.31-11.88 (2 x Time1 +1) units for CABG male patients that smoke (where 62.31= time + time x time of treatment interaction - time x smoking interaction) and by 63.88-11.88 (2 x Time1 +1) units for CABG female patients that smoke (where 63.88= time + time x type of treatment interaction + time x sex interaction - time x smoking interaction), if the other variables are kept constant.

The CR type of treatment was not associated with differences in *physical functioning* score at baseline; it had a negative non-significant effect ($p>0.05$). The crossover interaction between Time and CR type of treatment revealed on the *physical functioning* score ($p<0.01$) suggests that as the time increases, patients treated with CABG on average show a significantly higher *physical functioning* score. Specifically, for individuals with same the characteristics one year after CR, patients treated with CABG demonstrated a greater mean change of 9.13 units compared to patients treated with PCI; CABG treatment at Time0 = - 7.03, at Time1 = 7.09 [((-7.03+17.48-3.36); where 17.48 represents the value of the interaction term CABG x Time and 3.36 represents the value of the interaction term CABG x Time^2] and at Time2= 9.13[(-7.03+(17.48x4)- (-3.36x16); where 4 represents the value of Time2 and 16 represents the value of Time2^2].

Females scored lower on the *physical functioning* subdomain by 8.49 units ($p=0.01$) at baseline compared to males keeping the other variables constant. This reduction, however, tended to decrease as time increased at an almost significant level ($p=0.06$), resulting in a lower mean change of 2.21 units for females compared to males with the same features. Specifically, female sex at Time0 = - 8.49, at Time1 =-6.92 ((-8.49+1.57); where 1 represents the value of the interaction term sex x time) and at Time2= -2.21. [(-8.49+(1.57x4)); where 4 represents the value of Time2].

Also, a crossover interaction was revealed between smoking and Time. At baseline smoking was not associated with differences in *physical functioning* score (it had a negative non-significant effect on *physical functioning,* $p>0.05$) keeping the other variables constant. One year post CR, however, smokers showed on average a significantly lower score on *physical functioning* by 13.44 units compared to non-smokers with the same features. Specifically smokers at Time0 = -8.08, at Time1 =-3.42 ((-0.08+(-3.34)) where 3.34 represents the value of the interaction term smoking x time) and at Time2= -13.44 [(-0.08+(-3.34x4)); where 4 represents the value of Time2].

Furthermore, individuals treated with CABG with a CHD family history will have a lower score on *physical functioning* by 6.12 units if the remaining variables are kept constant. When BMI increases by one unit a PCI patient will have a higher score of *physical functioning* on average by 0.50 but a CABG patient will show a lower score of *physical functioning* on average by 0.19 units, keeping the other variables constant. Patients with 7-12 years of education scored higher on *physical functioning* at baseline by 6.2 units on average, and this difference seems to not change significantly after CR, due to a lack of a significant interaction between these two variables.

Briefly, the results suggest that CHD patients following CR experience a significant increase in *physical functioning* subdomain scores one year post CR (section 6.3.3.1). After adjusting for potential predictors, the *physical functioning* score initially increased with time and then decreased, remaining much higher compared to baseline scores however. Moreover, the effect of time on *physical functioning* depended on CR type, sex and smoking status; on average it seemed to be larger for females treated with CABG who did not smoke. As the time increased, patients treated with CABG on average showed a significantly greater *physical functioning* score compared to those treated with PCI. Females compared to males demonstrated a significantly worse *physical functioning* score which tended to become smaller. Smokers compared to non-smokers showed on average a significantly worse *physical functioning*. Also patients treated with CABG with a CHD family history compared to patients treated with CABG without CHD family history on average scored lower on *physical functioning* following CR. Individuals with 7-12 years of education compared to those with up to 6 years of education on average scored lower on *physical functioning* following CR.

6.3.4 The psychosocial functioning subdomain

The descriptive analysis of the CROQ *psychosocial functioning* scores indicated an increase over a one-year period. Table 6.3.13 displays participants' mean *psychosocial functioning* scores over a one-year period overall and by CR type of treatment for all individual characteristics measured; the mean scores after CR treatment increased for all groups.

Table 6.3.13 Descriptive statistics for Psychosocial functioning scores per CR type over a one-year period (n=472)

Psychosocial functioning			Type of CR					
			PCI			CABG		
			Prior to treatment	3-month post treatment	12-month post treatment	Prior to treatment	3-month post treatment	12-month post treatment
Overall		*Mean*	67.34	84.51	84.03	71.42	84.97	87.23
		SD	15.97	12.13	13.35	16.79	13.32	10.23
Age group *Mean* age (60.43)	<60.43	*Mean*	66.91	82.82	81.23	71.15	82.52	87.88
		SD	17.59	11.11	13.96	13.86	15.46	10.01
	>60.43	*Mean*	67.85	86.18	87.28	71.67	87.74	86.50
		SD	13.80	12.88	11.88	19.23	9.76	10.50
Sex	male	*Mean*	67.62	84.98	83.92	72.69	86.87	90.20
		SD	16.31	10.22	13.23	16.50	12.09	8.26
	female	*Mean*	66.41	83.20	84.36	67.23	78.99	77.92
		SD	14.89	16.41	13.83	17.29	15.30	10.33
Marital status	unmarried/ live alone	*Mean*	68.61	85.52	84.52	65.61	87.41	78.42
		SD	18.16	12.99	14.44	18.61	12.03	11.05
	married	*Mean*	67.00	84.29	83.93	72.40	84.59	88.17
		SD	15.36	11.94	13.17	16.34	13.51	9.73

Table 6.3.13 Descriptive statistics for Psychosocial functioning scores per CR type over a one-year period (n=472)

Psychosocial functioning			Type of CR					
			PCI			CABG		
			Prior to treatment	3-month post treatment	12-month post treatment	Prior to treatment	3-month post treatment	12-month post treatment
Educational status	six years or less	*Mean*	65.84	84.78	84.63	71.84	88.31	85.57
		SD	13.68	14.33	13.55	20.47	10.90	8.62
	7-12 years	*Mean*	70.64	84.46	85.30	69.91	85.58	89.00
		SD	16.21	10.27	13.03	15.06	11.26	10.24
	12^{+} years	*Mean*	62.56	84.21	80.72	73.29	81.25	84.68
		SD	16.56	12.98	13.48	16.26	17.33	11.03
Occupational status	unemployed	*Mean*	61.92	88.24	84.86	64.66	80.56	73.74
		SD	16.50	10.90	12.32	16.01	7.17	7.16
	public/private servant	*Mean*	65.58	82.03	81.15	71.38	91.07	90.07
		SD	18.04	10.82	15.24	12.67	10.90	7.05
	free-lancer	*Mean*	72.21	82.48	82.07	69.73	81.44	91.31
		SD	14.21	10.38	11.93	19.06	17.76	9.68
	pensioner	*Mean*	68.89	85.61	87.10	74.48	85.42	87.30
		SD	13.95	13.68	12.39	17.01	11.27	8.98
Family history CHD	no	*Mean*	67.27	84.40	84.59	68.87	83.25	86.32
		SD	16.56	12.52	13.09	17.11	15.88	9.76
	yes	*Mean*	67.40	84.67	83.49	74.06	86.71	88.05
		SD	15.43	11.81	13.71	16.14	9.89	10.65
Hypertension	no	*Mean*	66.48	83.18	82.68	67.67	86.47	89.31
		SD	16.01	12.76	14.11	17.62	10.64	10.38
	yes	*Mean*	68.47	86.87	86.28	77.32	81.85	83.37
		SD	16.12	10.58	11.73	13.55	17.08	8.86
Cholesterol	no	*Mean*	66.07	85.61	84.07	68.79	85.32	86.49
		SD	16.42	11.41	13.14	16.80	14.27	10.44
	yes	*Mean*	70.04	82.04	83.95	75.99	84.01	88.48
		SD	14.75	13.36	13.87	15.97	11.27	9.75
Diabetes	no	*Mean*	68.52	83.89	83.28	73.23	84.31	88.47
		SD	15.99	12.26	14.09	15.78	14.50	9.17
	yes	*Mean*	62.93	86.22	86.12	67.89	86.06	84.74
		SD	15.60	11.65	10.87	18.21	10.58	11.62
Smoking	no	*Mean*	65.08	85.57	86.34	70.89	84.60	88.12
		SD	14.98	11.83	12.36	19.05	13.51	9.52
	yes	*Mean*	68.97	82.70	81.30	72.04	73.21	81.43
		SD	16.50	9.73	13.65	13.77	12.11	7.53

Table 6.3.13 Descriptive statistics for Psychosocial functioning scores per CR type over a one-year period (n=472)

Psychosocial functioning			Type of CR					
			PCI			CABG		
			Prior to treatment	3-month post treatment	12-month post treatment	Prior to treatment	3-month post treatment	12-month post treatment
BMI	normal weight (18.5-24.9)	*Mean*	66.63	85.03	80.99	67.61	89.09	87.32
		SD	15.83	9.43	11.20	15.43	8.79	10.22
	overweight (25.0-29.9)	*Mean*	68.06	84.05	84.30	71.59	87.62	87.88
		SD	15.84	14.20	13.25	18.23	11.12	9.68
	obese (<29.9)	*Mean*	66.82	85.09	84.81	73.11	77.94	87.14
		SD	16.81	11.75	14.37	16.23	15.94	10.57

T1= prior to treatment, T2 = 3 months after treatment, T3= 12 months after treatment

6.3.4.1 Changes in Psychosocial functioning: Time and type of CR treatment effects

As described in the analysis section, the first step was to detect the best fitting model for the time trend. Table 6.3.14 shows the values for the six models compared. Based on the BIC index the 6th model (model f, Time and Time^2 as predictors with random intercept, linear and quadratic terms) was the best mixed model for describing the time trend of the *psychosocial functioning* scores.

Table 6.3.14 Parameter estimates and model fit statistics for first and second order polynomials of Psychosocial functioning scores growth over a one-year period

	Model a	Model b	Model c	Model d	Model e	Model f
Fixed effects	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)
Intercept	74.22(0.61)**	74.32(0.62)**	69.04(0.69)**	69.04(0.69)**	69.04(0.69)**	69.02(0.81)**
Time	3.29(0.27)**	3.28(0.25)**	19.69(1.13)**	19.69(1.13)**	19.69(1.13)**	19.45(1.25)**
Time^2	NA	NA	-3.89(0.26)**	-3.89(0.26)**	-3.89(0.26)**	-3.83(0.27)**
Random effects	SD	SD	SD	SD	SD	SD
Residuals	14.99	13.85	12.11	12.10	12.10	7.66
Intercept	NA	5.68	6.94	6.94	6.95	14.47
Time	NA	NA	NA	0.01	NA	20.83

Table 6.3.14 Parameter estimates and model fit statistics for first and second order polynomials of Psychosocial functioning scores growth over a one-year period

	Model a	Model b	Model c	Model d	Model e	Model f
$Time^2$	NA	NA	NA	NA	0.01	4.32
Model fit						
BIC	9369.47	9365.06	9178.87	9192.94	9192.94	9096.21

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous
Time= Linear, $Time^2$= Quadratic
Model a= Ordinal linear least square regression with Time as a predictor
Model b= Time as a predictor with random intercept
Model c= Time and $Time^2$ as predictors with random intercept
Model d = Time and $Time^2$ as predictors with random intercept and linear term
Model e= Time and $Time^2$ as predictors with random intercept and quadratic term
Model f= Time and $Time^2$ as predictors with random intercept, linear and quadratic terms
In all models response variable *psychosocial functioning* scores
$^{**}p<0.001$

The analysis demonstrated that the mean initial status (baseline) for the *psychosocial functioning* scores was 69.02 (β = 69.02, *SE* = 0.81, *t*=84.88, *p* < 0.01). Time had a significant positive linear effect (β = 19.45, *SE* = 1.25, *t*= 15.57, *p* < 0.01 as well as a significant negative quadratic effect (β = -3.83, *SE* = 0.27, *t*= -14.22, *p* < 0.01). The acceleration (Singer, & Willett, 2003) was 11.79 points (i.e. 19.45/ (2 (-3.83)) = 16.81). According to the results, the *psychosocial functioning* scores increased at the beginning, but this trend slowed down later on. Overall, a positive change on *psychosocial functioning* scores following CR can be assumed.

To investigate the effect of CR type on *psychosocial functioning* scores, the best model of the time trajectory was further investigated by adding the CR type of treatment (PCI/CABG) variable. The best model describing the data trends, having the lowest BIC value, was the first (Time, $Time^2$, CR type of treatment as predictors with random intercept, linear and quadratic terms) as Table 6.3.15 illustrates.

Table 6.3.15 Parameter estimates and model fit statistics for first and second order polynomials and treatment interactions of Psychosocial functioning scores growth over a one-year period

	Model 1	Model 2	Model 3
Fixed effects	B (SE)	B (SE)	B (SE)
Intercept	68.22(0.89)**	68.55(0.93)**	67.51(1.04)**
Time	19.31(1.25)**	19.27(1.26)**	21.44(1.58)**
Time^2	-3.84(0.27)**	-3.84(0.27)**	-4.31(0.34)**
Type of treatment†	2.08(0.99)*	1.24(1.16)	3.88(1.65)**
Time x Type of treatment	NA	0.53(0.37)	-5.13(2.56)*
Time^2 x Type of treatment	NA	NA	1.23(0.55)*
Random effects	SD	SD	SD
Residual	7.65	7.60	7.58
Intercept	14.37	14.43	14.37
Time	20.91	21.01	20.81
Time^2	4.33	4.34	4.30
Model fit			
BIC	9098.97	9103.99	9106.03

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous, Time= Linear, Time^2= Quadratic, †Type of treatment = CABG

Model 1=Time, Time^2 and CR type of treatment as predictors with random intercept, linear and quadratic term
Model 2=Time, Time^2, CR type of treatment as predictors and Time x CR type of treatment interaction term with random intercept, linear and quadratic terms
Model 3=Time, Time^2, CR type of treatment as predictors, Time x CR type of treatment interaction term, and Time^2 x CR type of treatment interaction term with random intercept, linear and quadratic terms
In all models response variable *psychosocial functioning* scores
$^{**}p<0.001$, $^{*}p<0.05$

Results demonstrated that the mean initial status (baseline) for the *psychosocial functioning* scores for CABG patients were higher compared to PCI patients. However, no significant time x treatment interaction was revealed for *psychosocial functioning.* The marginal means of CR type as predictor can be estimated by employing the following formulas:

Psychosocial functioning marginal means at 0 months (baseline) = β_0, 3 months = $\beta_0 + \beta_1$ x Time1 + β_2 x Time1^2 and 12 months = $\beta_0 + \beta_1$ x Time2+ β_2 x Time2^2, where

Time1 = 1 and Time2 = 4,

CR type of treatment: PCI = 0 and CABG = 1,

$\beta_0 = 68.22 + 2.08$ x type of treatment,

$\beta_1 = 19.51$ x type of treatment,

$\beta_2 = -3.84$

For PCI the marginal mean prior to treatment was 68.22 and at 3 months it was 83.89, resulting in a mean change of 15.67 points from the baseline mean score. For CABG the marginal mean prior to treatment was 70.3 and at 3 months it was 86.90, resulting in a mean change of 15.67 points from the baseline mean score.

Concerning the marginal mean for PCI at 12 months this was 84.82, resulting in a mean change of 16.60 points from the baseline mean score, while the marginal mean for CABG at 12 months was 86.90, resulting in a mean change of 16.60 points from the baseline mean score, as Figure 6.8 illustrates. Hence overall, it can be assumed that over a one year period, in the *psychosocial functioning* subdomain, patients treated with PCI or CABG experienced a similar change as Figure 6.8 illustrates.

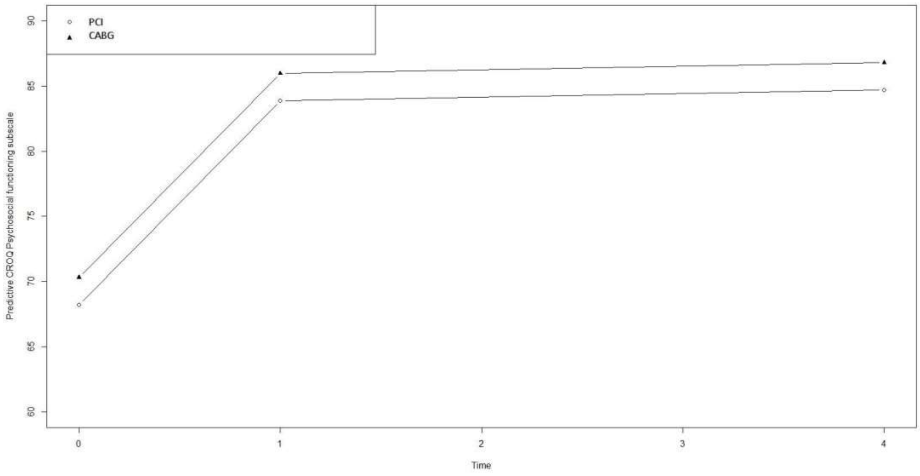

Figure 6.8 Marginal means of the Psychosocial functioning subdomain scores per CR type of treatment. Time0= baseline scores, Time1= 3 month mean scores, Time4=12 months mean scores.

The variability of the *psychosocial functioning* scores within individuals per CR type at the 3-month measurement time point can be seen in Figure 6.9.

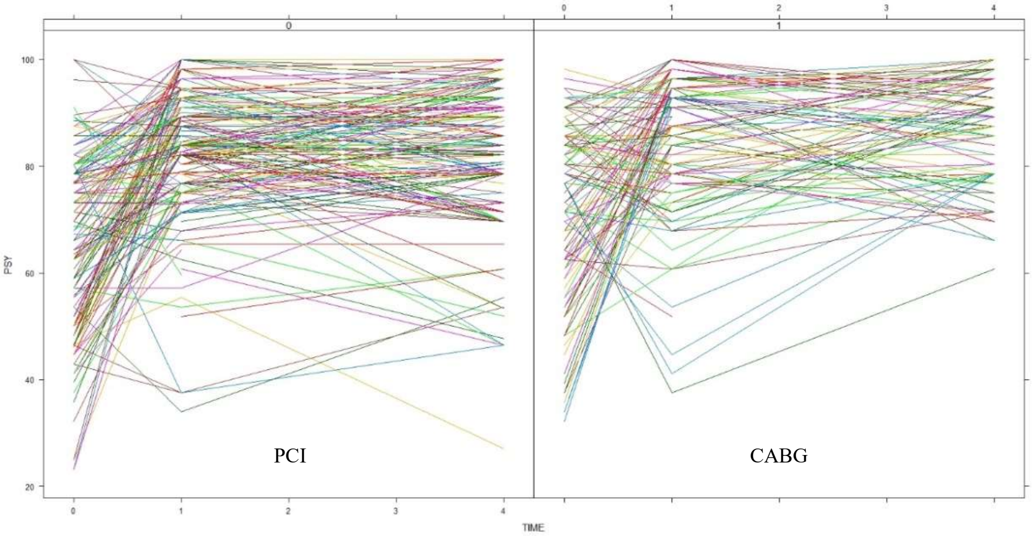

Figure 6.9 Psychosocial functioning subdomain scores as a function of Time for all patients by type of CR treatment. Time0= baseline scores, Time1= 3 month scores, Time4=12 month scores.

6.3.4.2 Predictors of Psychosocial functioning change over a one-year period

In the final conditional growth model, the effects of all individual level covariates as well as the two time-varying predictors (i.e. smoking and BMI) were investigated. Included in the model were also all the two-way interaction terms for these potential predictors with time and CR type of treatment. The following Table 6.3.16 summarizes the fixed and random effects of the model.

Table 6.3.16 Growth model for changes in Psychosocial functioning scores over a a one-year period

Fixed effects	**Est (SE)**	**df**	**t**	***p***	**95% Confidence Interval**	
					Lower Bound	**Upper Bound**
Intercept	46.72 (8.39)	531	5.57	0.00	30.64	62.80
Time	20.69(3.27)	531	6.32	**0.00**	14.41	26.96
$Time^2$	-4.11 (0.31)	531	-13.20	**0.00**	-4.71	-3.52
Type of treatment (CABG)	3.09 (12.94)	428	0.24	0.81	-21.72	27.89
Place of residence (Rural Area)	0.65 (2.36)	428	0.27	0.78	-3.88	5.18
Age	0.23 (0.10)	428	2.36	**0.02**	0.04	0.43
Sex (Female)	-2.14 (1.66)	428	-1.29	0.20	-5.33	1.04
Marital status (Married)	-3.07 (1.75)	428	-1.75	0.08	-6.43	0.29
Educational status†						
7-12 years	2.88 (1.79)	428	1.61	0.11	-0.55	6.31
12^+ years	-0.31 (2.06)	428	-0.15	0.88	-4.27	3.65
Occupational status‡						
Public/private servant	-1.51 (2.15)	428	-0.70	0.48	-5.63	2.61
Free lancer	1.56 (2.42)	428	0.64	0.52	-3.08	6.19
Pensioner	-0.91 (2.38)	428	-0.38	0.70	-5.48	3.65
CHD Family history (yes)	1.40 (1.37)	428	1.02	0.31	-1.23	4.03
Hypertension (yes)	4.50 (1.42)	428	3.18	**0.00**	1.78	7.22
Cholesterol (yes)	-2.35 (1.50)	428	-1.57	0.12	-5.21	0.52
Diabetes (yes)	-1.71 (1.64)	428	-1.04	0.30	-4.85	1.44
BMI	0.27 (0.16)	531	1.72	0.09	-0.03	0.57
Smoking (yes)	1.20 (1.44)	531	0.84	0.40	-1.55	3.95
Time x Place of residence	0.89 (0.67)	531	1.32	0.19	-0.40	2.17
Time x Age	0.03 (0.03)	531	0.82	0.41	-0.04	0.09
Time x Sex	0.42 (0.52)	531	0.80	0.42	-0.58	1.42
Time x Marital status	0.86 (0.61)	531	1.43	0.15	-0.30	2.03
Time x Educational status†						
7-12 years	0.91 (0.59)	531	1.55	0.12	-0.21	2.03
12^+ years	0.59 (0.67)	531	0.88	0.38	-0.69	1.86
Timex Occupational status‡						
Public/private servant	-0.39 (0.72)	531	-0.54	0.59	-1.77	0.99
Free lancer	-0.33 (0.78)	531	-0.42	0.67	-1.81	1.16
Pensioner	0.06 (0.79)	531	0.08	0.94	-1.44	1.57
Time x CHD Family history	-0.56 (0.44)	531	-1.26	0.21	-1.40	0.29

Table 6.3.16 Growth model for changes in Psychosocial functioning scores over a a one-year period

Fixed effects	**Est (SE)**	**df**	**t**	***p***	**95% Confidence Interval**	
					Lower Bound	**Upper Bound**
Time x Hypertension	-0.39 (0.45)	531	-0.88	0.38	-1.25	0.47
Time x Cholesterol	-0.58 (0.48)	531	-1.22	0.22	-1.50	0.33
Time x Diabetes	0.04 (0.51)	531	0.08	0.94	-0.94	1.02
Time x BMI	-0.08 (0.06)	531	-1.34	0.18	-0.18	0.03
Time x Smoking	-0.86 (0.50)	531	-1.71	0.09	-1.82	0.10
Type of treatment x Place of residence	-6.61 (3.02)	428	-2.19	**0.03**	-12.39	-0.82
Type of treatment x AGE	-0.02 (0.17)	428	-0.13	0.90	-0.35	0.31
Type of treatment x Sex	-5.58 (2.83)	428	-1.97	0.06	-11.00	-0.15
Type of treatment x Marital status	4.14 (3.18)	428	1.30	0.19	-1.95	10.23
Type of treatment x Educational status†						
7-12 years	-0.20 (3.18)	428	-0.06	0.95	-6.31	5.91
12^+ years	1.81 (3.67)	428	0.49	0.62	-5.22	8.84
Type of treatment x Occupational status‡						
Public/private servant	7.63 (3.96)	428	1.93	0.06	0.05	15.22
Free lancer	-1.35 (4.07)	428	-0.33	0.74	-9.14	6.44
Pensioner	1.48 (4.28)	428	0.34	0.73	-6.73	9.68
Type of treatment x CHD Family history	2.31 (2.13)	428	1.09	0.28	-1.77	6.40
Type of treatment x Hypertension	-2.79 (2.37)	428	-1.18	0.24	-7.34	1.76
Type of treatment x Cholesterol	3.67 (2.32)	428	1.58	0.11	-0.77	8.12
Type of treatment x Diabetes	0.37 (2.38)	428	0.15	0.88	-4.20	4.94
Type of treatment x BMI	-0.20 (0.23)	531	-0.89	0.37	-0.65	0.24
Type of treatment x Smoking	2.27 (2.48)	531	0.92	0.30	-2.48	7.02
Random effects	***SD***					
Residuals	6.80					
Intercept	14.37					
Time	21.43					
Time^2	4.47					
Model fit						
BIC	8341.18					

†Educational status compared to six years or less ‡Occupational status compared to unemployed

The above results demonstrate that after adjusting for potential predictors, the *psychosocial functioning* scores initially increased with time and then decreased (β=20.69, *SE*=3.27, $p<0.01$ and β=-4.11, *SE*=0.31, $p<0.01$ respectively), although remaining much higher than baseline scores. The type of treatment is not a significant predictor for *psychosocial functioning* ($p>0.05$).

Concerning the effect of Time, taking into account also the significant interaction terms, due to the presence of the quadratic effect, the interpretation should be based on specific time points. For example if TIME1 denotes the value of Time at a specific time then if time increases by one unit *psychosocial functioning* will be increased by 20.69-4.11(2 x Time1 +1) units, keeping all remaining covariates constant. Moreover, for each additional year older that participants were at baseline, there was a 0.23 increase in their psychosocial functioning over the 12 months; the lack of a time x age interaction demonstrates that this relationship did not change significantly after CR treatment. Interestingly, patients with hypertension scored on average higher on *psychosocial functioning* by 4.5 units; the lack of a time x hypertension interaction demonstrates that this relationship did not change significantly after CR treatment. Finally, the significant interaction effect between CR type of treatment and place of residence highlights that CABG individuals living in rural areas showed a lower score by 6.61 units, keeping the other variables constant. This finding suggests that CABG patients living in Attica demonstrated a higher score on average by 3.09 units on *psychosocial functioning* compared to patients living in Attica treated with PCI, keeping the other variables constant. On the other hand, CABG patients living in rural areas had a lower score on average in this subdomain by 3.52 (i.e. type of treatment-type of treatment x place of residence) units compared to PCI patients living in rural areas.

Briefly, the results suggest that CHD patients following CR experience a significant increase in *psychosocial functioning* one year post CR (section 6.3.4.1). After adjusting for potential predictors the *psychosocial functioning* score initially increased with time and then decreased, remaining however much higher compared to baseline scores. The type of treatment was not a significant predictor of *psychosocial functioning.* In this subdomain only age and hypertension were revealed as individual predictors of the outcome. As the age of the patient increased the psychosocial functioning scores increased too. Also patients with hypertension had a greater level of *psychosocial functioning* prior to CR and this difference remained after CR. Finally, CABG individuals living in rural areas demonstrated a lower level in *psychosocial functioning*.

6.3.5 The Cognitive functioning subdomain

The descriptive analysis of the *cognitive functioning* scores as shown in Table 6.3.17 indicated that participants' mean scores on *cognitive functioning* over a one-year period varied. Patients treated with CABG seemed to experience a decline in this subdomain.

Table 6.3.17 Descriptive statistics for Cognitive functioning scores per CR type over a one-year period (n=472)

Cognitive functioning			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
Overall		*Mean*	82.98	89.74	89.87	80.34	83.95	78.55
		SD	18.45	15.12	15.07	14.98	17.31	14.86
Age group *Mean* age (60.43)	<60.43	*Mean*	81.93	92.86	93.52	86.41	90.70	80.82
		SD	17.80	13.76	12.63	12.21	12.70	13.36
	>60.43	*Mean*	84.26	86.67	85.65	74.63	76.52	76.05
		SD	19.21	15.80	16.56	15.16	18.70	16.10
Sex	male	*Mean*	83.05	90.50	89.76	80.98	85.11	80.14
		SD	19.04	13.70	15.96	14.49	16.74	14.47

Table 6.3.17 Descriptive statistics for Cognitive functioning scores per CR type over a one-year period (n=472)

Cognitive functioning			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
	female	*Mean*	82.76	87.58	90.19	78.20	80.20	73.56
		SD	16.57	18.51	12.31	16.53	18.82	15.21
Marital status	unmarried/live alone	*Mean*	79.10	88.44	88.43	79.71	78.25	72.78
		SD	19.54	12.08	19.72	17.23	20.35	19.58
	married	*Mean*	84.02	90.03	90.15	80.44	84.81	79.17
		SD	18.06	15.73	14.02	14.63	16.73	14.24
Educational status	six years or less	*Mean*	86.56	83.42	85.22	77.95	70.98	71.11
		SD	17.99	17.55	19.64	13.78	18.12	13.28
	7-12 years	*Mean*	79.77	92.24	91.23	79.73	85.90	80.49
		SD	18.36	12.25	13.71	12.16	15.87	16.74
	12+ years	*Mean*	85.29	92.36	92.92	82.96	91.17	79.35
		SD	18.48	15.32	8.74	19.36	13.02	8.67
Occupational status	unemployed	*Mean*	75.35	91.87	91.48	81.40	81.11	70.59
		SD	21.11	13.95	10.64	13.26	12.37	17.33
	public/private servant	*Mean*	84.95	91.92	94.11	86.08	90.97	86.67
		SD	16.51	15.32	14.48	10.30	12.36	11.39
	free-lancer	*Mean*	82.81	95.24	92.63	82.44	89.40	75.61
		SD	16.42	8.87	10.83	20.64	12.02	12.33
	pensioner	*Mean*	85.23	85.00	83.99	75.69	77.31	79.55
		SD	18.81	16.31	17.62	11.87	21.19	15.64
Family history CHD	no	*Mean*	83.14	87.31	87.69	79.84	82.88	78.31
		SD	18.08	16.14	14.73	15.02	20.53	13.48
	yes	*Mean*	82.83	92.03	91.91	80.85	85.07	78.77
		SD	18.88	13.75	15.22	15.02	13.21	16.11
Hypertension	no	*Mean*	84.08	91.03	90.44	77.82	86.52	81.54
		SD	18.99	13.04	15.27	16.04	14.07	13.80
	yes	*Mean*	80.71	87.46	88.92	84.11	79.08	72.89
		SD	17.55	18.06	14.77	12.09	21.46	15.00
Cholesterol	no	*Mean*	81.95	91.89	90.73	80.52	83.30	75.82
		SD	18.97	11.83	14.82	13.71	17.77	13.72
	yes	*Mean*	85.29	84.87	88.14	79.64	85.03	83.67
		SD	17.26	19.95	15.53	17.08	16.64	15.69
Diabetes	no	*Mean*	82.86	90.70	91.76	80.00	90.04	84.22
		SD	18.19	14.46	14.53	16.52	12.79	12.41
	yes	*Mean*	82.99	87.11	84.57	80.60	71.97	67.88
		SD	19.71	16.61	15.42	11.67	18.90	12.88

Table 6.3.17 Descriptive statistics for Cognitive functioning scores per CR type over a one-year period (n=472)

Cognitive functioning			Type of CR					
			PCI			CABG		
			T1	T2	T3	T1	T2	T3
Smoking	no	*Mean*	83.24	88.96	87.93	76.59	84.96	79.50
		SD	19.13	15.25	15.49	16.00	17.15	14.00
	yes	*Mean*	82.80	93.67	92.71	84.75	80.00	72.00
		SD	18.01	11.48	14.08	12.40	13.22	21.81
BMI	normal weight (18.5-24.9)	*Mean*	82.56	87.27	91.43	79.26	95.19	76.67
		SD	14.95	13.01	10.30	12.32	9.65	18.66
	overweight (25.0-29.9)	*Mean*	83.62	91.72	88.62	77.28	79.54	73.68
		SD	18.85	15.37	14.61	17.06	17.27	10.99
	obese (<29.9)	*Mean*	82.62	89.24	90.34	83.68	87.35	84.00
		SD	20.01	16.73	17.22	14.04	17.12	11.42

T1= prior to treatment, T2 = 3 months after treatment, T3= 12 months after treatment

6.3.5.1 Changes in Cognitive functioning: Time and type of CR treatment effects

As described in the analysis section, the first step was to detect the best fitting model for the time trend. Table 6.3.18 shows the values for the six models compared. Based on the BIC index the 3rd model (model c, Time and Time^2 as predictors with random intercept) was the best mixed model for describing the time trajectory of the *cognitive functioning* scores.

Table 6.3.18 Parameter estimates and model fit statistics for first and second order polynomials of Cognitive functioning score growth over a one-year period

	Model a	Model b	Model c	Model d	Model e	Model f
Fixed effects	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)
Intercept	84.10(0.67)**	83.98(0.70)**	81.82(0.81)**	81.82(0.81)**	81.82(0.81)**	81.88(0.85)**
Time	0.59(0.30)*	0.63(0.26)*	7.26(1.31)**	7.26(1.31)**	7.26(1.31)**	7.25(1.40)**
Time^2	NA	NA	-1.57(0.31)**	-1.57(0.31)**	-1.57(0.31)**	-1.58(0.31)**
Random effects	SD	SD	SD	SD	SD	SD
Residuals	16.62	14.37	14.12	14.12	13.91	10.58
Intercept	NA	8.40	8.54	8.54	8.54	13.54

Table 6.3.18 Parameter estimates and model fit statistics for first and second order polynomials of Cognitive functioning score growth over a one-year period

	Model a	Model b	Model c	Model d	Model e	Model f
Time	NA	NA	NA	0.01	NA	20.17
Time^2	NA	NA	NA	NA	1.57	4.25
Model fit						
BIC	9603.79	9567.85	9549.01	9563.06	9563.06	9553.01

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous
Time= Linear, Time^2= Quadratic
Model a= Ordinal linear least square regression with Time as a predictor
Model b= Time as a predictor with random intercept
Model c= Time and Time^2 as predictors with random intercept
Model d = Time and Time^2 as predictors with random intercept and linear term
Model e= Time and Time^2 as predictors with random intercept and quadratic term
Model f= Time and Time^2 as predictors with random intercept, linear and quadratic terms
In all models response variable *cognitive functioning* scores
$^{**}p$<0.001

The analysis demonstrated that the mean initial status (baseline) for the *cognitive functioning* scores was 81.82 (β = 81.88, *SE* = 0.81, t=100.28, p < 0.01). Time had a significant positive linear effect (β = 7.26, *SE* = 1.31, t= 5.50, p < 0.01) as well as a significant negative quadratic effect (β = -1.57, *SE* = 0.31, t= -5.13, p < 0.01). The acceleration (Singer, & Willett, 2003) was 4.12 points [(i.e. 7.26/ (2 (-1.57))]. According to the results, the *cognitive functioning* scores increased at the beginning, but this trend slowed down later on. Overall, a positive small change on *cognitive functioning* scores following CR can be assumed.

To investigate the effect of the CR type on *cognitive functioning* scores, the best model of the time trajectory was further investigated by adding the CR type of treatment (PCI/CABG) variable. Based on the BIC lowest value, the model describing better the *cognitive functioning* trends was the second (Time, Time^2, CR type of treatment as predictors and the interaction term Time x CR type of treatment with random intercept) as Table 6.3.19 shows.

Table 6.3.19 Parameter estimates and model fit statistics for first and second order polynomials and treatment interactions of Cognitive functioning scores growth over a one-year period

	Model 1	Model 2	Model 3
Fixed effects	B (SE)	B (SE)	B (SE)
Intercept	84.16(0.92)**	82.83(0.96)**	82.61(1.02)**
Time	7.11(1.32)**	8.11(1.32)**	8.76(1.66)**
Time^2	-1.54(0.31)**	-1.57(0.31)**	-1.73(0.38)**
Type of treatment†	-6.20(1.17)**	-2.90(1.41)**	-2.36(1.64)
Time x Type of treatment	NA	-2.24(0.53)**	-3.95(2.67)
Time^2 x Type of treatment	NA	NA	0.41(0.62)
Random effects	SD	SD	SD
Residual	14.15	13.94	13.93
Intercept	7.92	8.14	8.15
Time	NA	NA	NA
Time^2	NA	NA	NA
Model fit			
BIC	9529.09	9518.35	9524.95

NA= not applicable; ML= maximum likelihood; BIC= Schwarz's Bayesian Criterion
Random covariate = AR1 heterogeneous, Time= Linear, Time^2= Quadratic, †Type of treatment = CABG

Model 1=Time, Time^2 and CR type of treatment as predictors with random intercept, linear and quadratic term
Model 2=Time, Time^2, CR type of treatment as predictors and Time x CR type of treatment interaction term with random intercept, linear and quadratic terms
Model 3=Time, Time^2, CR type of treatment as predictors, Time x CR type of treatment interaction term, and Time^2 x CR type of treatment interaction term with random intercept, linear and quadratic terms
In all models response variable *cognitive functioning* scores
$^{**}p<0.001$, $^{*}p<0.05$

Results showed that CABG patients scored lower compared to PCI patients at the mean initial status (baseline) of the *cognitive functioning* subdomain and had a lower increase in linear trends. In quadratic trends, however, patients treated with CABG demonstrated a great decline. The marginal means of CR type as a predictor for *cognitive functioning* subdomain can be estimated by employing the following formulas:

Cognitive functioning marginal means at 0 months (baseline) = β_0, 3 months = $\beta_0 + \beta_1$ x Time1 + β_2 x Time1^2 and 12 months = $\beta_0 + \beta_1$ x Time2+ β_2 x Time2^2, where

Time1 = 1 and Time2 = 4,

CR type of treatment: PCI = 0 and CABG = 1,

$\beta_0 = 82.83 - 2.90$ x type of treatment,

$\beta_1 = 8.11 - 2.24$ x type of treatment

$\beta_2 = -1.57$

For PCI the marginal mean prior to treatment was 82.83 and at 3 months it was 89.37, resulting in a mean change of 6.54 points from the baseline mean score. For CABG the marginal mean prior to treatment was 79.93 and at 3 months it was 84.23, resulting in a mean change of 4.30 points from the baseline mean score.

Concerning the marginal mean for PCI at 12 months this was 90.15, resulting in a mean change of 7.32 points from the baseline mean score, while the marginal mean for CABG at 12 months was 78.29, resulting in a mean change of -1.64 points from the baseline mean score, as Figure 6.10 illustrates. Overall, it can be assumed that patients treated with CABG experience a decline in cognitive functioning one year after CR, while patients treated with PCI experience an increase in this subdomain as illustrated by Figure 6.10.

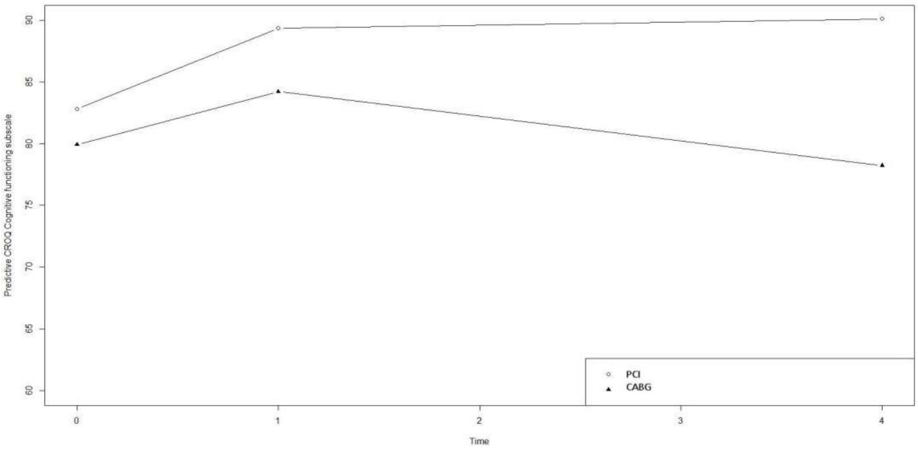

Figure 6.10 Marginal means of the Cognitive functioning subdomain scores per CR type of treatment. Time0= baseline scores, Time1= 3 month mean scores, Time4=12 months mean scores.

The variability of the *cognitive functioning* scores within individuals per CR type at the 3 month measurement time point can be seen in Figure 6.11.

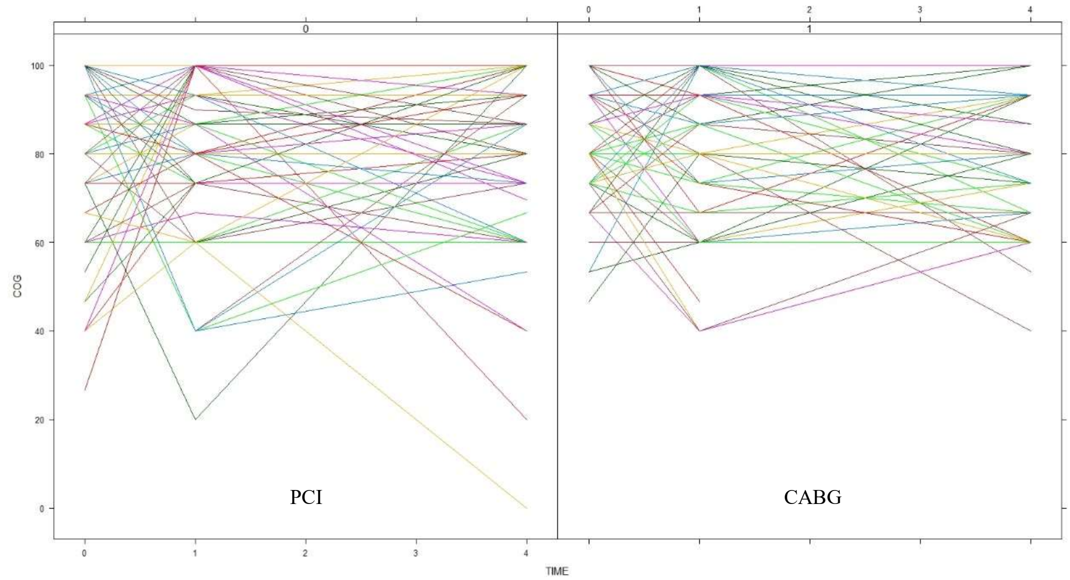

Figure 6.11 Cognitive functioning subdomain scores as a function of Time for all patients by type of CR treatment. Time0= baseline scores, Time1= 3 months scores, Time4=12 months scores.

6.3.5.2 Predictors of Cognitive functioning change over a one-year period

In the final conditional growth model, the effects of all individual level covariates as well as well as the two time-varying predictors (i.e. smoking and BMI) were investigated. Included in the model were also all the two-way interaction terms for these potential predictors with time and CR type of treatment. The following table 6.3.20 summarizes the fixed and random effects of the model.

Table 6.3.20 Growth model for changes in Cognitive functioning scores over a one year period

Fixed effects	Est (SE)	df	t	*p*	95% Confidence Interval	
					Lower Bound	Upper Bound
Intercept	81.88(10.32)	530	7.93	0.00	62.11	101.65
Time	11.97(4.49)	530	2.67	**0.01**	3.38	20.56
Time^2	-1.79(0.35)	530	-5.12	**0.00**	-2.46	-1.12
Type of treatment (CABG)	3.08(15.54)	428	0.20	0.84	-26.70	32.85
Place of residence (Rural Area)	-3.89(2.81)	428	-1.39	0.17	-9.27	1.49
Age	-0.11(0.12)	428	-0.87	0.38	-0.34	0.13
Sex (Female)	0.94(2.06)	428	0.46	0.65	-3.00	4.88
Marital status (Married)	3.69(2.14)	428	1.72	0.09	-0.42	7.80
Educational status†						
7-12 years	-2.08(2.21)	428	-0.94	0.35	-6.32	2.16
12$^+$ years	1.27(2.54)	428	0.50	0.62	-3.59	6.13
Occupational status‡						
Public/private servant	5.95(2.67)	428	2.23	**0.03**	0.84	11.07
Free lancer	7.82(2.98)	428	2.62	**0.01**	2.11	13.53
Pensioner	5.29(2.93)	428	1.80	0.07	-0.33	10.90
CHD Family history (yes)	1.33(1.68)	428	0.79	0.43	-1.88	4.54
Hypertension (yes)	-4.44(1.74)	428	-2.55	**0.01**	-7.78	-1.10
Cholesterol (yes)	-1.08(1.84)	428	-0.59	0.56	-4.60	2.44
Diabetes (yes)	1.26(2.01)	428	0.63	0.53	-2.59	5.12
BMI	0.04(0.19)	530	0.20	0.85	-0.33	0.40
Smoking (yes)	-0.00(1.72)	530	0.00	1.00	-3.30	3.29
Time x Type of treatment	-2.09(0.92)	530	-2.26	**0.02**	-3.86	-0.32
Time x Place of residence	1.31(1.00)	530	1.31	0.19	-0.60	3.22
Time x Age	-0.04(0.05)	530	-0.85	0.39	-0.14	0.05
Time x Sex	0.06(0.77)	530	0.08	0.94	-1.41	1.54
Time x Marital status	-0.47(0.89)	530	-0.52	0.60	-2.17	1.24
Time x Educational status†						
7-12 years	1.41(0.86)	530	1.63	0.10	-0.24	3.06
12$^+$ years	0.64(0.98)	530	0.65	0.52	-1.24	2.51
Timex Occupational status‡						
Public/private servant	-1.53(1.06)	530	-1.43	0.15	-3.57	0.51
Free lancer	-2.50(1.14)	530	-1.93	0.06	-4.69	-0.31
Pensioner	-1.50(1.16)	530	-1.29	0.20	-3.72	0.73

Table 6.3.20 Growth model for changes in Cognitive functioning scores over a one year period

Fixed effects	**Est (SE)**	**df**	**t**	***p***	**95% Confidence Interval**	
					Lower Bound	**Upper Bound**
Time x CHD Family history	0.18(0.64)	530	0.27	0.78	-1.05	1.41
Time x Hypertension	0.64(0.66)	530	0.98	0.33	-0.61	1.90
Time x Cholesterol	0.31(0.70)	530	0.45	0.65	-1.02	1.65
Time x Diabetes	-2.05(0.75)	530	-2.72	**0.01**	-3.49	-0.61
Time x BMI	0.01(0.08)	530	0.16	0.87	-0.14	0.17
Time x Smoking	0.20(0.73)	530	0.28	0.78	-1.20	1.60
Type of treatment x Place of residence	5.76(3.50)	428	1.64	0.10	-0.95	12.48
Type of treatment x AGE	-0.27(0.20)	428	-1.33	0.18	-0.66	0.12
Type of treatment x Sex	-1.58(3.29)	428	-0.48	0.63	-7.89	4.73
Type of treatment x Marital status	-0.27(3.69)	428	-0.07	0.94	-7.35	6.81
Type of treatment x Educational status†						
7-12 years	4.10(3.70)	428	1.11	0.27	-2.99	11.20
12^{+} years	0.98(4.30)	428	0.23	0.82	-7.25	9.21
Type of treatment x Occupational status‡						
Public/private servant	-2.42(4.71)	428	-0.51	0.61	-11.44	6.60
Free lancer	-8.45(4.82)	428	-1.75	0.08	-17.69	0.78
Pensioner	-5.74(5.02)	428	-1.14	0.25	-15.35	3.88
Type of treatment x CHD Family history	1.84(2.50)	428	0.74	0.46	-2.95	6.63
Type of treatment x Hypertension	8.29(2.75)	428	3.02	**0.00**	3.03	13.57
Type of treatment x Cholesterol	1.20(2.73)	428	0.44	0.66	-4.04	6.44
Type of treatment x Diabetes	-4.81(2.81)	428	-1.71	0.09	-10.20	0.57
Type of treatment x BMI	0.31(0.27)	530	1.12	0.26	-0.22	0.83
Type of treatment x Smoking	2.78(2.73)	530	1.02	0.31	-2.46	8.02
Random effects	***SD***					
Residuals	13.77					
Intercept	5.94					
Time	NA					
Time^2	NA					
Model fit						
BIC	8668.79					

†Educational status compared to six years or less ‡ Occupational status compared to unemployed

The above results demonstrate that after adjusting potential predictors, the *cognitive functioning* score initially increased with time and then decreased (β= 11.97, *SE*=4.49, p<0.05 and β= -1.79, *SE*=0.35, p<0.01, respectively).

Concerning the effect of Time, taking into account also the significant interaction terms, due to the presence of the quadratic effect, the interpretation should be based on specific time points. For example, if Time1 denotes the value of Time at a specific time then if time increases by one unit *cognitive functioning* will increase by 11.97-1.79(2 x Time1 +1) units for the PCI patients without diabetes, by 9.88-1.79(2 x Time1 +1) units for the CABG patients without diabetes (where 9.88= time - time x treatment interaction), by 9.92-1.79(2 x Time1 +1) units for the PCI patients with diabetes (where 9.92= time- time x diabetes interaction) and by 7.83-1.79(2·x Time1 +1) units for the CABG patients with diabetes (where 7.83=time - time x type of treatment interaction - time x diabetes interaction).

The CR type of treatment was not associated with differences in *cognitive functioning* scores at baseline; it had a positive non-significant effect (p>0.05). A crossover interaction effect between Time and CR type of treatment was revealed on the *cognitive functioning* score (p<0.01) suggesting that as time increased, patients treated with CABG on average showed a significantly lower value on the *cognitive functioning*. Specifically, for individuals with otherwise the same characteristics one year after CR, patients treated with CABG demonstrated on average a significant lower *cognitive functioning* score by 5.28 units compared to patients treated with PCI; CABG treatment at Time0 = 3.08, at Time1 = 0.99 (3.08-2.09; where 2.09 represents the value of the interaction term Time x Type of treatment) and at Time2= -5.28 [(3.08-(2.09x4)); where 4 represents the value of Time2].

Also, a crossover interaction was revealed between diabetes and Time. At baseline diabetes was not associated with differences in the *cognitive functioning* score (it had a positive non-significant effect on the *cognitive functioning score, p*>0.05) keeping the rest of the variables fixed. However, as time increased, patients with diabetes showed on average a significant lower value on the *cognitive functioning* score. Specifically, individuals with diabetes on average showed a lower score on *cognitive functioning* by 6.94 units compared to patients without diabetes with similar features one year post CR; individuals with diabetes at Time0 = 1.26, at Time1 =-0.79 (1.26-2.05; where 2.05 represents the value of the interaction term time x diabetes) and at Time2= -6.94 [(1.26-(2.05x4)); where 4 represents the value of Time2].

Also, PCI patients with hypertension on average showed a lower score on *cognitive functioning* by 4.44 units compared to PCI patients with no hypertension, while CABG patients with hypertension scored higher, on average by 3.85 units (i.e. type of treatment – type of treatment x hypertension) compared to CABG patients with no hypertension prior to CR keeping the other variables constant.

Finally, patients working in the public/private sector on average scored higher on *cognitive functioning* by 5.95 units compared to those without a job and patients working as free-lancers on average scored higher by 7.82 units compared to the those without a job prior to CR keeping the other variables constant. The lack of significant interaction between time and occupational status suggests that the above differences remained the same post CR, in this subdomain.

Briefly, results suggest that CHD patients following CR experienced a significant increase in *cognitive functioning* one year post treatment (section 6.3.5.1), but this increase was not experienced by all patients. After adjusting for potential predictors, the *cognitive functioning* score initially increased with time and then decreased, remaining however, much higher compared to baseline scores. Moreover, the effect of time depended on CR type of treatment and diabetes. The time effect was greater for patients treated with PCI without diabetes. Moreover, as time increased, PCI patients on average showed a significantly higher *cognitive functioning* score compared to CABG patients. Individuals with diabetes on average showed a significantly lower *cognitive functioning* score compared to patients without diabetes. Also, CABG patients with hypertension on average showed a significantly greater *cognitive functioning* score compared to CABG patient without hypertension. Individuals working in the public or private sector or free-lancers compared to those without a job on average showed a greater *cognitive functioning* score following CR.

6.3.6 Adverse effects

The descriptive analysis of *adverse effects* scores indicated fewer adverse effects between 3 and 12 months after CR (Table 6.3.2.1); the mean scores for all groups increased, revealing a reduction in adverse effects experienced.

Table 6.3.21 Descriptive statistics for Adverse effects scores per CR type

Adverse effects			Type of CR			
			PCI		CABG	
			T2	T3	T2	T3
Overall		*Mean*	97.46	99.37	84.46	97.31
		SD	5.92	3.69	12.54	4.39
Age group *Mean* age (60.43)	<60.43	*Mean*	97.84	99.55	86.69	97.69
		SD	5.28	2.35	10.75	4.07
	>60.43	*Mean*	97.08	99.17	81.92	96.88
		SD	6.50	4.81	13.96	4.72
Sex	male	*Mean*	97.89	99.23	87.73	97.87
		SD	5.26	4.16	10.56	4.17
	female	*Mean*	96.22	99.76	73.55	95.53
		SD	7.43	1.72	12.60	4.64

Table 6.3.21 Descriptive statistics for Adverse effects scores per CR type

Adverse effects			Type of CR			
			PCI		CABG	
			T2	T3	T2	T3
Marital status	unmarried/live alone	*Mean*	97.07	100.00	83.25	95.27
		SD	6.26	0.00	19.89	5.85
	married	*Mean*	97.54	99.24	84.64	97.52
		SD	5.86	4.03	11.11	4.18
Educational status	six years or less	*Mean*	96.93	98.82	79.55	95.45
		SD	6.52	5.95	14.27	5.73
	7-12 years	*Mean*	97.39	99.40	84.48	97.86
		SD	5.84	2.62	12.43	3.55
	12+ years	*Mean*	98.20	100.00	88.18	97.43
		SD	5.36	0.00	10.13	4.69
Occupational status	unemployed	*Mean*	98.48	99.65	75.88	95.86
		SD	3.93	2.08	11.95	4.12
	public/private servant	*Mean*	97.92	99.79	87.98	98.36
		SD	5.70	1.61	11.40	4.47
	free-lancer	*Mean*	97.52	99.67	88.23	98.62
		SD	4.70	2.03	8.32	3.15
	pensioner	*Mean*	96.68	98.71	82.60	96.13
		SD	7.09	5.70	14.23	4.96
Family history CHD	no	*Mean*	97.15	99.05	84.00	97.00
		SD	6.53	4.89	12.73	4.61
	yes	*Mean*	97.74	99.68	84.95	97.59
		SD	5.30	1.91	12.42	4.19
Hypertension	no	*Mean*	96.76	99.09	84.48	97.84
		SD	6.63	4.53	13.82	4.01
	yes	*Mean*	98.70	99.84	84.28	96.31
		SD	4.14	1.42	9.93	4.90
Cholesterol	no	*Mean*	97.60	99.48	83.95	97.45
		SD	5.79	2.45	13.78	4.48
	yes	*Mean*	97.13	99.14	85.35	96.93
		SD	6.24	5.41	9.78	4.26
Diabetes	no	*Mean*	97.27	99.42	88.18	97.90
		SD	6.07	3.85	11.12	3.85
	yes	*Mean*	97.98	99.23	77.04	96.18
		SD	5.51	3.25	12.08	5.11
Smoking	no	*Mean*	97.57	99.40	85.22	97.47
		SD	5.60	4.26	11.32	4.34

Table 6.3.21 Descriptive statistics for Adverse effects scores per CR type

Adverse effects			Type of CR			
			PCI		CABG	
			T2	T3	T2	T3
	yes	*Mean*	98.19	99.32	93.18	95.00
		SD	4.56	2.78		5.18
BMI	normal weight (18.5-24.9)	*Mean*	96.65	100.00	92.55	96.82
		SD	6.42	0.00	10.48	5.38
	overweight (25.0-29.9)	*Mean*	97.17	98.94	84.94	98.09
		SD	6.52	5.40	11.32	4.30
	obese (<29.9)	*Mean*	98.39	99.43	80.03	96.59
		SD	4.74	2.63	13.94	2.88

T2= 3 months after treatment, T3= 12 months after treatment

The variability of *adverse effects* scores within individuals per CR type at the 2 measurement time points can be seen in Figure 6.12.

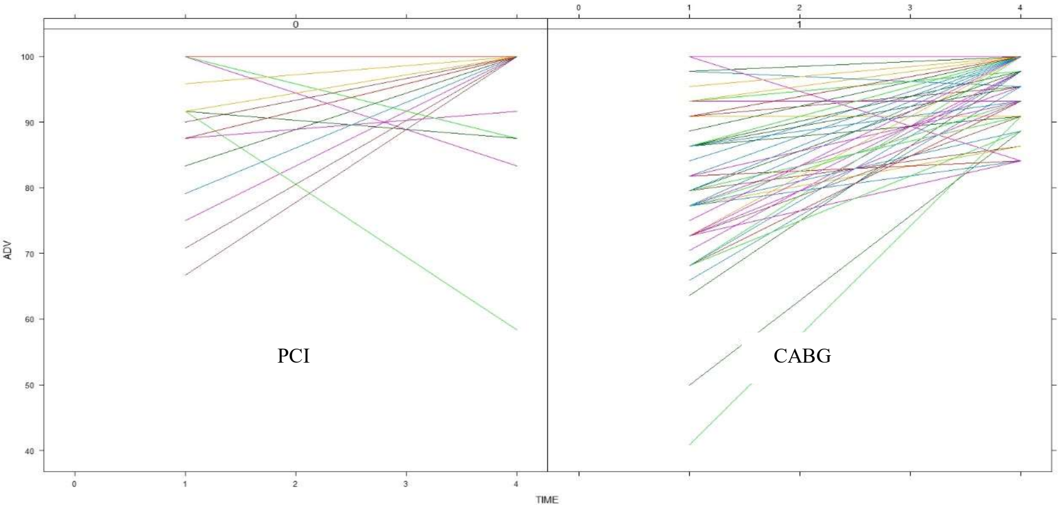

Figure 6.12 Adverse effects subdomain scores as a function of time for all patients by type of CR treatment. Time1= 3 month scores, Time4=12 month scores.

6.3.6.1 Predictors of adverse effects

In order to investigate predictors of *adverse effects*, as described in the analysis section, a new variable was created calculating the difference between the 3 and 12 month scores. The following Table 6.3.22 summarizes the results of the linear regression model for the *adverse effects difference* between 3 and 12 months after CR.

Table 6.3.22 Regression model for mean difference in adverse effects between 3 and 12 months

Fixed effects	**Est (SE)**	**t**	***p***	**95% Confidence Interval**	
				Lower Bound	**Upper Bound**
Intercept	4.63(5.45)	0.85	0.40	-6.1	15.35
Type of treatment (CABG)	6.88(11.62)	0.59	0.55	-15.99	29.75
Place of residence (Rural Area)	3.34(2.32)	1.44	0.15	-1.22	7.92
Age	-0.08(0.08)	-0.97	0.33	-0.25	0.08
Sex (Female)	-2.14(1.37)	-1.56	0.12	-4.83	0.56
Marital status (Married)	0.01(1.56)	0.01	0.99	-3.07	3.09
Educational status†					
7-12 years	-0.76(1.53)	-0.50	0.62	-3.76	2.24
12^{+} years	-1.10(1.72)	-0.64	0.52	-4.49	2.29
Occupational status‡					
Public/private servant	-1.24(1.79)	-0.69	0.49	-4.76	2.28
Free lancer	-1.84(2.02)	-0.91	0.36	-5.82	2.13
Pensioner	-1.42(2.07)	-0.69	0.49	-5.49	2.65
CHD Family history (yes)	-0.20(1.21)	-0.17	0.87	-2.60	2.19
Hypertension (yes)	1.42(1.20)	1.19	0.24	-0.94	3.78
Cholesterol (yes)	-0.59(1.29)	-0.46	0.65	-3.13	1.95
Diabetes (yes)	1.81(1.38)	1.31	0.19	-0.91	4.52
Type of treatment x Place of residence	-2.51(2.97)	-0.85	0.40	-8.36	3.33
Type of treatment x AGE	-0.15(0.18)	-0.83	0.41	-0.51	0.21
Type of treatment x Sex	-4.89(2.69)	-1.82	0.07	-10.2	0.41
Type of treatment x Marital status	-8.46(3.73)	-2.27	**0.02**	-15.79	-1.12
Type of treatment x Educational status†					

Table 6.3.22 Regression model for mean difference in adverse effects between 3 and 12 months

Fixed effects	Est (SE)	t	*p*	95% Confidence Interval	
				Lower Bound	Upper Bound
7-12 years	1.79(3.55)	0.50	0.61	-5.19	8.77
12^{+} years	0.52(3.85)	0.13	0.89	-7.06	8.10
Type of treatment x Occupational status‡					
Public/private servant	1.07(3.73)	0.29	0.77	-6.28	8.42
Free lancer	2.90(3.75)	0.77	0.44	-4.49	10.29
Pensioner	3.80(4.07)	0.93	0.35	-4.22	11.82
Type of treatment x CHD Family history	0.71(1.98)	0.36	0.72	-3.19	4.61
Type of treatment x Hypertension	0.35(2.45)	0.14	0.89	-4.46	5.17
Type of treatment x Cholesterol	-0.13(2.25)	-0.06	0.95	-4.56	4.30
Type of treatment x Diabetes	-9.85(2.20)	-4.47	0.00	-14.18	-5.51

The multiple linear regression analysis demonstrated two significant interactions: a) type of treatment x marital status and b) type of treatment x diabetes. Married patients treated with CABG showed a larger decrease in adverse effects score by 8.46 units compared to patients treated with CABG who lived alone keeping the remaining variables constant. Furthermore patients with diabetes treated with CABG showed a larger decrease in the adverse effects score by 9.85 units compared to CABG patients without diabetes when keeping the remaining variables constant. Briefly, married individuals and people with diabetes treated with CABG demonstrated a larger decrease in adverse effects.

6.3.7 Satisfaction

The descriptive analysis of *satisfaction* scores indicated an increase between 3 and 12 months after CR (Table 6.3.23); the mean scores for all groups increased. However, patients treated with PCI demonstrated a greater level of satisfaction shortly after treatment compared to patients treated with CABG.

Table 6.3.23 Descriptive statistics for Satisfaction scores per CR type

Satisfaction			Type of CR			
			PCI		CABG	
			T2	T3	T2	T3
Overall		*Mean*	85.99	86.44	72.45	86.60
		SD	14.58	16.18	22.74	12.61
Age group *Mean* age (60.43)	<60.43	*Mean*	82.48	82.49	76.33	89.15
		SD	15.07	17.02	21.81	12.68
	>60.43	*Mean*	89.44	91.01	67.80	83.87
		SD	13.27	13.89	23.16	12.05
Sex	male	*Mean*	87.59	87.19	78.59	88.77
		SD	13.42	13.85	18.33	10.07
	female	*Mean*	81.42	84.30	53.84	79.95
		SD	16.77	21.53	24.93	16.86
Marital status	unmarried/live alone	*Mean*	84.57	84.38	71.76	81.60
		SD	14.33	20.92	30.13	17.43
	married	*Mean*	86.31	86.85	72.57	87.15
		SD	14.66	15.10	21.38	11.95
Educational status	six years or less	*Mean*	87.98	90.42	67.42	84.66
		SD	14.36	16.16	23.01	8.84
	7-12 years	*Mean*	85.68	85.38	69.94	84.60
		SD	14.19	15.55	22.87	13.48
	12 years +	*Mean*	84.03	83.60	81.90	92.82
		SD	15.69	16.83	20.18	11.60
Occupational status	unemployed	*Mean*	83.54	84.11	59.31	70.02
		SD	14.58	21.56	26.94	17.62
	public/private servant	*Mean*	85.92	84.49	88.51	88.44
		SD	14.71	14.85	13.62	9.12
	free-lancer	*Mean*	80.23	84.65	81.70	95.06
		SD	13.51	13.09	7.11	6.88

Table 6.3.23 Descriptive statistics for Satisfaction scores per CR type

Satisfaction			Type of CR				
			PCI			CABG	
			T2	T3		T2	T3
	pensioner	*Mean*	89.46	90.23		64.94	85.04
		SD	14.16	15.21		24.44	8.58
Family history CHD	no	*Mean*	86.71	87.11		69.15	87.55
		SD	13.97	15.26		24.85	11.09
	yes	*Mean*	85.26	85.70		76.29	85.77
		SD	15.23	17.13		19.54	13.84
Hypertension	no	*Mean*	85.44	86.14		70.27	85.90
		SD	14.55	16.60		24.49	13.75
	yes	*Mean*	86.94	86.94		75.72	87.56
		SD	14.68	15.55		19.63	10.26
Cholesterol	no	*Mean*	86.51	85.82		77.71	86.66
		SD	13.57	17.08		18.99	13.91
	yes	*Mean*	84.80	87.69		61.67	86.15
		SD	16.69	14.21		26.12	9.55
Diabetes	no	*Mean*	85.93	85.77		77.95	89.47
		SD	13.70	16.37		23.26	9.81
	yes	*Mean*	86.13	88.33		61.59	81.28
		SD	16.89	15.62		17.69	15.15
Smoking	no	*Mean*	87.57	90.37		73.61	88.39
		SD	13.40	13.26		21.76	11.26
	yes	*Mean*	82.18	81.29		84.72	68.33
		SD	15.59	18.24		17.23	9.23
BMI	normal weight (18.5-24.9)	*Mean*	86.66	86.00		75.93	82.08
		SD	10.70	15.55		25.15	15.80
	overweight (25.0-29.9)	*Mean*	84.53	85.75		76.82	86.48
		SD	16.37	15.89		17.09	10.95
	obese (<29.9)	*Mean*	87.43	86.63		64.97	88.73
		SD	15.32	17.22		24.99	9.83

T2 = 3 months after treatment, T3= 12 months after treatment

The variability of *satisfaction* scores within individuals per CR type at the 2 measurement time points can be seen in Figure 6.13.

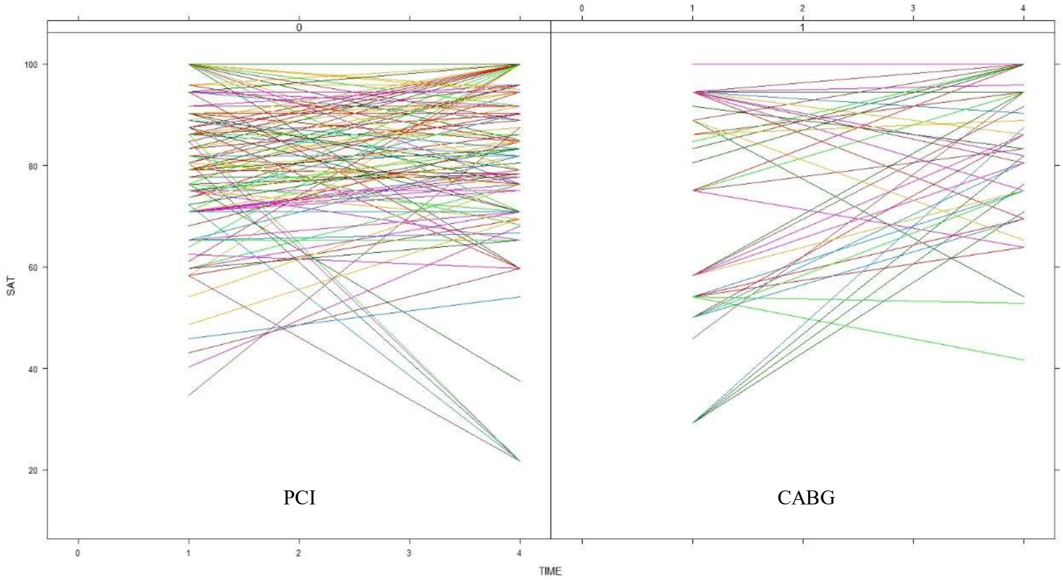

Figure 6.13 Satisfaction subdomain scores as a function of time for all patients by type of CR treatment. Time1= 3 month scores, Time4=12 month scores.

6.3.7.1 Predictors of Satisfaction

To investigate potential predictors of *satisfaction scores*, as described in the analysis section, a new variable was created calculating the difference between the 3 and 12 month scores. The following Table 6.3.24 summarizes the results of the linear regression model for the *satisfaction difference* between 3 and 12 months after CR.

Table 6.3.24 Regression model for mean difference in satisfaction between 3 and 12 months

Fixed effects	Est (SE)	t	*p*	95% Confidence Interval	
				Lower Bound	Upper Bound
Intercept	-0.05(11.00)	0.00	1.00	-21.71	21.62
Type of treatment (CABG)	-35.43(28.73)	-1.23	0.22	-92.01	21.16

Table 6.3.24 Regression model for mean difference in satisfaction between 3 and 12 months

Fixed effects	**Est (SE)**	**t**	***p***	**95% Confidence Interval**	
				Lower Bound	**Upper Bound**
Place of residence (Rural Area)	3.48(4.68)	0.74	0.46	-5.73	12.69
Age	0.00(0.17)	0.00	1.00	-0.34	0.34
Sex (Female)	-0.92(2.75)	-0.33	0.74	-6.33	4.49
Marital status (Married)	-2.67(3.16)	-0.84	0.40	-8.89	3.56
Educational status†					
7-12 years	3.07(3.07)	1.00	0.32	-2.97	9.11
12^{+} years	2.48(3.47)	0.71	0.48	-4.36	9.31
Occupational status‡					
Public/private servant	1.69(3.61)	0.47	0.64	-5.42	8.79
Free lancer	-2.21(4.08)	-0.54	0.59	-10.25	5.82
Pensioner	1.25(4.16)	0.30	0.76	-6.95	9.45
CHD Family history (yes)	-1.92(2.44)	-0.79	0.43	-6.93	2.89
Hypertension (yes)	1.82(2.41)	0.76	0.45	-2.92	6.57
Cholesterol (yes)	-1.58(2.59)	-0.61	0.54	-6.69	3.53
Diabetes (yes)	0.76(2.78)	0.27	0.79	-4.71	6.22
Type of treatment x Place of residence	-12.23(6.25)	-1.96	0.06	-24.53	0.07
Type of treatment x AGE	1.00(0.46)	2.19	**0.03**	0.10	1.90
Type of treatment x Sex	-10.97(6.00)	-1.83	0.07	-22.79	0.85
Type of treatment x Marital status	-11.70(7.76)	-1.51	0.13	-26.99	3.58
Type of treatment x Educational status†					
7-12 years	-2.06(7.77)	-0.27	0.79	-17.36	13.23
12^{+} years	2.22(9.33)	0.24	0.81	-16.16	20.60
Type of treatment x Occupational status‡					
Public/private servant	-2.16(8.66)	-0.25	0.80	-19.23	14.90
Free lancer	-14.09(8.18)	-1.72	0.09	-30.20	2.02
Pensioner	-24.75(8.81)	-2.81	**0.01**	-42.09	-7.40
Type of treatment x CHD Family history	11.63(4.41)	2.63	**0.01**	2.94	20.32
Type of treatment x Hypertension	-5.16(6.11)	-0.85	0.40	-17.20	6.87
Type of treatment x Cholesterol	-14.56(5.21)	-2.79	**0.01**	-24.82	-4.30
Type of treatment x Diabetes	-13.95(4.91)	-2.84	**0.00**	-23.61	-4.29

†Educational status compared to six years or less ‡Occupational status compared to unemployed

The multiple linear regression analysis demonstrated five significant interactions: a) type of treatment x age; when the age of a CABG patient increased by 1 year, the *satisfaction* score after 12 months on average increased by one unit compared to the satisfaction score after 3 months, b) type of treatment x occupational status; retired patients treated with CABG showed a larger decrease in satisfaction score between 3 and 12 months by 24.75 units compared to the CABG patients without a job, c) type of treatment x cholesterol; CABG patients with high cholesterol levels demonstrated a larger decrease in satisfaction score between 3 and 12 months on average by 14.56 units compared to patients without high cholesterol levels treated with CABG, d) type of treatment x diabetes; CABG patients with diabetes showed a larger decrease in satisfaction score between 3 and 12 months by 13.95 units compared to individuals without diabetes treated with CABG, and e) type of treatment x CHD family history; patients with a previous CHD history treated with CABG showed a larger increase in satisfaction score between 3 and 12 months by 11.63 units compared to individuals without CHD family history treated with CABG, when keeping the remaining variables constant. Briefly, as time increased, a larger increase in satisfaction level showed by retired patients, patients with high cholesterol levels or diabetes treated with CABG.

6.4 Discussion

6.4.3 Findings

The present study aimed to detect the extent to which CR affects the HRQoL level of CHD patients over a one-year period, what might be the pattern of change, whether the type of CR treatment influences the outcome as well as to investigate the predictive value of various individual characteristics (demographic, medical and behavioural) on the change in HRQoL over a one-year period.

Results demonstrated that the *overall HRQoL* level increases dramatically after treatment. One year post treatment, for most individuals the gain remains large but somewhat lower than the one experienced three months post treatment. Concerning the effect of type of CR treatment on the overall HRQoL over one year, patients treated with CABG experienced a greater mean change compared to patients treated with PCI, but this difference did not remain significant after controlling for individual characteristics. In fact, the final growth model showed that the benefit experienced by patients with either treatment did not significantly differ. However it should be noted that the effect of CR type on subdomains is mixed. Thus the effect of type of CR treatment remains a challenging issue.

Moreover, results revealed that the effect of Time depends mainly on sex, BMI and smoking. Females and individuals who do not smoke and have close to normal BMI seem to experience the greatest improvement. These findings are in line with the literature (e.g. Blankenship, et al., 2013; Soo Hoo, Gallagher, & Elliott, 2014) and the meta-analysis (Chapter 3) suggesting that these factors (e.g. smoking; Blankenship, et al., 2013; Rumsfeld et al., 2004; Taira et al., 2000) have a stronger influence on the outcome than type of treatment. Also the findings of the present study support research evidence highlighting that females do not benefit less from CR compared to males and that the differences observed in studies comparing solely post-CR scores may be due to the poorer preoperative HRQoL (e.g. Lansky et al., 2005; Hartman et al., 2014). An explanation of such variability in research findings may be related to the statistical analysis used (e.g. lack of investigation of interaction effects) or reflect differences in CHD adjustment and level of “positive growth” following CR or being a CHD survivor. As the literature suggests, individuals after experiencing a traumatic event such as heart surgery or surviving a heart attack, often experience post-traumatic growth (e.g. greater appreciation of life, motivation to change leading to personal growth; Bluvstein, Moravchick, Sheps, Schreiber, & Bloch, 2013; Waight, Strodl, Sheridan, & Tesar, 2015) which influences their perspective and evaluation of HRQoL. This phenomenon tends to be experienced more strongly females (Leung et al., 2012).

Also the results support recent studies suggesting that smokers demonstrate poorer HRQoL outcome compared to non-smokers following CR (e.g. Jang et al., 2015) but are contrary to studies suggesting that BMI is not related to HRQoL outcome (e.g. Jarvinen et al., 2007).

Concerning the *symptoms* subdomain, results showed that individuals experience a positive change after coronary revascularization. However, the largest effect of CR on this domain was experienced during the first three months. At 12 months, it still remained much greater than the baseline level, but lower than at three months post treatment. Moreover, the results revealed that the effect of time depends on CR type of treatment, BMI and smoking; it seems to be larger for individuals who are treated with CABG, do not smoke and have low BMI. For the 12 month follow up, fewer *symptoms* were reported by patients treated with CABG compared to ones treated with PCI, by females compared to males and by non-smokers compared to smokers. It may be that the relapse in smoking cessation between 3 and 12 months, which is much greater among PCI patients, reflects the reporting of more symptoms at 12 months post-CR by individuals treated with PCI. In any case, the literature highlights that smokers experience increased CHD symptoms post operation compared to quitters (e.g. Rumsfeld et al., 2004).

Regarding *physical functioning*, similar to the symptoms subdomain, results showed that individuals experience a positive change after coronary revascularization. However, the largest effect of CR on this domain was during the first three months. At 12 months it still remained much greater than at baseline level, but lower than at 3 months. Moreover, the effect of time on *physical functioning* interacts with CR type, sex and smoking status. Females, those treated with CABG and non-smokers seem to benefit most. Existing research evidence (e.g. Martin et al., 2012; Peric et al., 2010) found that female sex and smoking are independent predictors of lower *physical functioning* after CABG compared to males and to non-smokers, although no interaction effects were reported.

In relation to the *psychosocial functioning* results suggest that CHD patients following CR experience a significant increase in this subdomain. Similar to other HRQoL subdomains the largest effect of CR on this domain was during the first three months. At 12 months it remained much greater than at baseline, but reduced after 3 months. In this subdomain only age and hypertension predicted the outcome. Patients with hypertension had a greater level of *psychosocial functioning* prior to CR and this difference remained after CR. Also, older patients reported greater increases in their psychosocial functioning. Existing research evidence (Kurfirst et al., 2004) suggests either that age is not a valid predictor of HRQoL following CR, or that younger patients benefit more after heart surgery especially in cognitive components of HRQoL (e.g. Hokkanen, Järvinen, Huhtala, & Tarkka, 2014). The findings of the present study contradict both these claims. An explanation might be the instrument used. As discussed elsewhere, data the present study used the CROQ which is a disease/treatment specific instrument and thus more sensitive when capturing change. Finally, CABG individuals living in rural areas demonstrated less improvement in *psychosocial functioning* compared to individuals treated with PCI living in rural areas or individuals treated with CABG and living in urban areas. This observation may be explained by the fact that CABG is a more "severe" heart operation compared to PCI, as involving a general anesthesia, sternotomy, removal of a vein usually from a leg or arm, and involving a longer hospital stay and recovery in general, as well as greater level of complications (e.g. wound infections, atrial fibrillation (Halonen et al., 2007; Salehi-Omran et al., 2007; Toumpoulis, Anagnostopoulos, Derose, & Swistel, 2005), implying the need for good healthcare (well-equipped hospital and qualified surgeon at very least). In Greece, rural areas have only small hospitals (known as hospital health care centres; Kontodimopoulos, Nanos, & Niakas, 2006), lacking the necessary equipment and doctors for such surgeries. Demanding surgeries are carried out in big cities (Siskou, Kaitelidou, Papakonstantinou, & Liaropoulos, 2008). Thus rural dwellers need to temporarily move to a big city, such as Athens and often seek private health care due to an understaffed public health care system (Siskou, Kaitelidou, Papakonstantinou, & Liaropoulos, 2008). Taking into consideration moving, operation expenses and follow up visit to doctors which in and of themselves are factors associated with high level of distress, those individuals may lose their sense of control and balance in their life, factors eliciting further distress (Helman, 2007).

Regarding *cognitive functioning,* results showed that many CHD patients following CR experience a significant increase in this subdomain. This observation though was not similar for all individuals undergoing CR; the effect of time seems to depend on CR type of treatment and diabetes. Patients treated with PCI without diabetes experienced higher cognitive functioning compared to PCI individuals with diabetes or CABG patients (with or without diabetes). Independently, one year after CR, individuals treated with CABG seemed to experience a decline in *cognitive functioning* while individuals treated with PCI seemed to experience an improvement. These findings are aligned with some previous research evidence (e.g. Phillips-Bute et al., 2006; McKhann et al., 2009) but contradict other evidence suggesting no difference in cognitive functioning between patients treated with different revascularization treatments (e.g.

Kennedy et al., 2013; Währborg et al., 2004) especially when co-morbidities are controlled for (Cormack et, 2012; Sun et al., 2012). Moreover, the results are in line with previous research findings suggesting worse cognitive functioning for individuals with diabetes after CABG (e.g. Krannich et al., 2012). Finally, having hypertension seems to be an independent predictor of lower increase in *cognitive functioning* compared to individuals without hypertension after CR. Research evidence demonstrates similar results (Selnes & McKhann, 2005).

Concerning *adverse effects* and *satisfaction*, patients treated with PCI seem very satisfied and show low levels of adverse effects at 3 months post treatment compared to patients treated with CABG. These findings are in line with the literature (e.g. Salehi-Omran et al., 2007; Sellier, 2007). However, the results showed that at 12 months individuals who underwent CABG demonstrated a greater improvement reaching the same level as those treated with PCI. This observation seems to be in line with the greater increase of CABG patients in *physical functioning* between 3 and 12 months; as individuals experience a reduction in adverse effects their *physical functioning* increases more strongly. Significant predictors of the mean difference were marital status and diabetes; married patients and patients with diabetes treated with CABG showed a greater improvement in adverse effects. In terms of satisfaction, significant predictors of the mean difference were retired patients treated with CABG, patients with high cholesterol levels or diabetes treated with CABG; these patients suggested a greater increase in satisfaction with treatment. The findings are in line with the limited literature in these areas (i.e. adverse effects and satisfaction with coronary revascularization treatment; Shroter, 2001).

6.4.4 Strengths and limitations

The current study has several strengths. First of all it adds to the existing knowledge about individuals' different experience and changes in HRQoL over one year after treatment. It is one of the few longitudinal studies that makes use a CR-specific HRQoL instrument with a 12 month follow-up. Moreover, it follows recommendations (Pragodpol & Ryan, 2013) for detecting factors that predict the trajectory of HRQoL in cardiac patients since the concept of HRQoL may change over time, but the majority of predictors are usually constant (fixed); the study tested a number of demographic, medical and behavioural characteristics demonstrating significant predictors regarding HRQoL level at different time points over a one-year period. Furthermore, the present study demonstrates the changes in total HRQoL level after coronary revascularization as well as the effect of each CR type both on total HRQoL and its subdomains providing the required data for calculation of effect sizes. These are important issues because as the meta-analysis revealed, the literature has a dearth of studies that examine HRQoL in both procedures simultaneously and there is lack of studies that provide adequate data (e.g. Mean scores and *SD*) per HRQoL subdomain. All these issues covered increase study quality which, based on the criteria used in the meta-analysis, can be rated with a 7.5 which puts it up near the top of the studies reviewed.

On the other hand, there are a few limitations that should be mentioned. First the sample size was not large (especially for CABG treatment with fewer than 200 participants) and not random. This limits generalizability. Moreover, the majority of individuals were residents of Athens with a higher proportion of overweight participants compared to the general population. Another limitation is the lack of a detailed medical profile for each patient. Various factors related to patients' medical characteristics (e.g. severity of angina) were not controlled for and thus the results may be misleading. Research evidence demonstrates that individuals with multi-vessel CHD have fewer symptoms and greater HRQoL post CABG compared to those treated with PCI (Abdallah et al., 2013). Therefore the results should be interpreted with caution.

Furthermore, many patients treated with CABG were recruited from a private hospital in contrast to PCI who were recruited from public ones. This might imply differences in financial status, another variable that was not measured, and possibly differences in stress e.g. about costs, as the majority of patients treated in private hospitals have private health insurance. Empirical research shows that people on a low income tend to have poor HRQoL and increased psychological distress (Ackerman, Graves, Wicks, Bennell, & Osborne, 2005). Also a number of individuals who underwent CABG reported having at least one session with a health professional, usually a health or clinical psychologist prior to hospital discharge. This may have created differences in individuals' perceptions which in turn may have influenced their scoring. As the literature highlights, even a single structured supporting session may influence individuals' perception of HRQoL (Phillips et al., 2004).

Furthermore, there are a number of researchers (e.g. Walters, 2009) who suggest that longitudinal studies should use both disease specific and generic HRQoL instruments for more accurate results, especially when the research sample may have multiple morbidities. Moreover, a challenge that remains to be addressed is whether a disease specific HRQoL measure is more sensitive to a generic one in the long-term. As HRQoL is a dynamic concept that changes over time and individual shifts are present, a generic instrument could capture essential aspects not addressed via the disease-specific one (e.g. psychological distress not immediately related to the health condition).

Finally, issues such as response shift (Schwartz et al., 2007) or adjustment processes (e.g. Taylor, 1983; discussed in Chapter 2) that may influence individuals' evaluation of their HRQoL over time were not investigated. Thus the increase in HRQoL level following CR treatment or the lack of CR type effect in some subdomains (i.e. psychosocial functioning) observed might be challenged in terms of whether it reflects a "true" estimation of CR effect or interferes with changes of individuals' internal standards, values and the conceptualization of quality of life.

6.4.5 Implications for theory, research and practice

The present study is a vivid illustration of the dynamic process of HRQoL. As results have shown, individuals' subjective evaluation of HRQoL changes between three and twelve months after CR treatment.

Findings highlight the importance of examining HRQoL level across multiple time points (at least 3) to capture HRQoL changes over time as well as detect factors that might influence the outcome. The use of multilevel modelling provides an opportunity to examine both the effect of time over several measurement points and develop growth models examining various predictors without restrictions such as the assumption of homogeneity of regression slopes, and excluding cases due to missing data (i.e. excluding participants that have not participated in all measured timepoints). Measurement of HRQoL over multiple timepoints would help health professionals construct a less ambiguous picture of change trends and related factors and, in turn, would allow them to target interventions at a time point that would benefit patients most. Moreover, further research should be carried out investigating whether the type of diabetes is related to the outcome. The limited research that has been carried out in this area in relation to CR outcome suggests that the issue with cognitive deficits observed following CABG may be related only to insulin-dependent individuals (Kadoi, Saito, Fujita, & Goto, 2005; Kubal, Srinivasan, Grayson, Fabri, & Chalmers, 2005). Furthermore, for researchers aiming to investigate the influence of treatment on the pattern of HRQoL over several time points, it might be beneficial to explore some additional factors that may interfere with subjective evaluations over time. For instance, measuring response shift (Ahmed, Mayo, Wood-Dauphinee, Hanley, & Cohen, 2004) or exploring adjustment (Foxwell, Morley, & Frizelle, 2013) that may influence individuals' evaluations of their HRQoL over time (Hamidou, Dabakuyo, & Bonnetain, 2011) and may allow to draw more robust conclusions concerning the estimated effect of treatment over time.

Health providers should take into consideration that smoking and BMI are two negative predictors of HRQoL outcome after CR and that it would be helpful to facilitate their patients' behaviour modification. Also, cardiologists should consider diabetes mellitus when deciding on the type of CR treatment; although there is a tendency to suggest CABG treatment more often to individuals with diabetes compared to PCI (NICE team guidelines, 2012), individuals with diabetes tend to demonstrate a decline in cognitive functioning after CABG. However, women experience a similar increase in HRQoL after CR as men, especially when BMI and smoking are controlled for. Thus sex should not be considered when making decisions about CR treatment, at least in relation to HRQoL.

Finally, policies regarding equal access to health services in rural areas should be implemented, especially for patients needing cardiac surgery; improving health care in rural areas may contribute positively to psychosocial well-being particularly in CABG patients.

6.5 Conclusion

Individuals treated with CR experience an increase in their HRQoL level after treatment. One year post treatment, the gain remains large for most individuals but it is somewhat lower than the one experienced three months post treatment. Moreover, individuals treated with CABG tend to experience a larger increase compared to PCI patients in the subdomains of symptoms and physical functioning but a decline in the subdomain of cognitive functioning. This contradiction may account for there being no significant difference in the effect of type of treatment on overall HRQoL. Smoking and BMI were the most prominent negative predictors of low mean change in most HRQoL subdomains. Patients with diabetes when treated with CABG experience a cognitive decline.

The results of the present study regarding the positive effect of CR on individuals' HRQoL based on their subjective evaluation might be challenged without a greater insight into individuals' understanding and making meaning process. If taking into consideration that CHD is a chronic disease, an adjustment process to CHD may interfere with the positive effect on measured HRQoL. Thus a further in-depth exploration of the patient experience would be helpful to draw more robust conclusions. The next qualitative study (the second component of the mixed methods study) aims to capture individuals' understanding of their disease and CR treatment and its influence on their perspective of HRQoL as well as adjustment related issues. In order to do so an Interpretative Phenomenologcal approach (IPA; Smith et al., 2009) was selected which guides researchers to focus more on the patients' meaning-making process. Also this approach would allow the researcher to explore concerns about lifestyle modifications, especially in relation to smoking, which was identified as a negative predictor of improvement in HRQoL level following CR.

Chapter Seven

Study 2, Part Two. Individuals making sense of HRQoL one year after CR: An Interpretative Phenomenological Analysis

7.1 Introduction

The quantitative part of the present mixed methods study (Chapter 6) shows an overall improvement in Health Related Quality of Life (HRQoL) following coronary revascularization (CR). The quantitative results showed various factors as being influential to the pattern of overall HRQoL change and its subdomain over a one-year period following CR; among the most influential factors were CR type, smoking status, BMI and diabetes mellitus. Concerning female sex, an individual feature mostly suggested in the literature as a predictor of lower improvement following PCI or CABG, especially in the physical functioning domain (Martin et al., 2012; Yeng, Gallagher, & Elliott, 2016), the results showed that females experienced greater improvement following CR when do not smoke and are not overweight. As previously discussed, these findings are important and build upon previous research. However, they do not provide the scientific community with a deeper understanding of how coronary heart disease (CHD) patients make sense of HRQoL, how they view themselves and their life after CR. Such understanding could provide a complimentary insight. Thus the present qualitative component of the mixed methods study aims to capture individuals' understanding of their disease and CR treatment and its influence on their perspective of HRQoL exploring adjustment related issues. Also, it puts a special emphasis on exploring concerns about life style modifications, especially in relation to smoking which was identified as a predictor of a lower increase in HRQoL following CR. Specifically the qualitative part intends to: 1) explore further the relevance and meanings of the main domains of quality of life, as defined in the coronary revascularization outcome questionnaire (CROQ); 2) contribute qualitative insights into quality of life after CR, including both patients who have undergone coronary artery bypass graft surgery (CABG) and those who have been treated with percutaneous coronary intervention (PCI); 3) examine the way individuals adopt behaviour change and consider the implications of this for practice. This chapter begins with an overview of the literature on qualitative research related to HRQoL after CR, then presents the methods and procedure followed in the course of data collection and data analysis. The main part of this chapter provides an extensive presentation and discussion of the qualitative findings.

7.1.1 Overview of qualitative literature; patients experience of quality of life after CR

The literature on the quality of life of patients after CR is largely dominated by quantitative studies that assess the impact of the therapeutic intervention on patients' everyday life through measurements of pre-defined items. Starting from the recognition that, quality of life is a multi-dimensional and fluid concept, there has been an increasing number of qualitative studies in the last two decades that aim to capture the meaning and variability of lived experience beyond the researchers' pre-defined constructs. This section will review the literature on qualitative studies of patients' experience of quality of life after CR in order to move towards defining the conceptual context and aims of the current study.

The vast majority of qualitative studies have focused on patients who have undergone CABG, exploring patients' lived experience after CABG or patients' perception of factors that influence lifestyle changes after CABG (e.g. Abbasi, Mohammadi, Nasrabadi, Fuh, & Sadeghi, 2014; Angus, 2001; Goldsmith, Lindholm, & Bute, 2006; Leegaard, Nåden, & Fagermoen, 2008; Leegaard, Rustøen, & Fagermoen, 2010; Tolmie, Lindsay, & Belcher, 2006; Tung, Hunter, & Wei, 2008). Only few studies have explored PCI patients' experience and factors that may influence their behaviour change (Astin, Closs, McLenachan, Hunter, & Priestley, 2009; Peterson et al., 2010).

An interesting synthesis (Leegaard & Fagermoen, 2008) of 19 qualitative studies published between 1991-2006 that had used either thematic analysis or grounded theory, aimed to explore patients' experience after CABG and highlighted several important themes. In short, this review applied thematic analysis and demonstrated that many individuals experience fears (e.g. of the unknown future, being a burden), losses (reduced independence, mandatory life changes), as well as the paradox of feeling alone while being supported by others. Furthermore, a very recent article (Abbasi, Mohammadi, Nasrabadi, Fuh, & Sadeghi, 2014), to date the only study on the topic using IPA, focused on understanding the lived experience of 11 patients at least six months post CABG. The study findings revealed that patients perceive their experience as a "re-birth", especially in terms of bodily sensation and function.

Qualitative research on PCI (Astin, Closs, McLenachan, Hunter, & Priestley, 2008; Astin, et al., 2009; Peterson, et al., 2010) highlights that PCI patients, similar to CABG patients, experience a fear of the unknown future. Many patients perceive PCI as a turning point to make life changes (re-prioritizing). They make changes in their stance towards life (e.g. quit work, spend more time with the family, and enjoy simple everyday things). Some others, however, do not experience PCI in the same way. The absence of bodily evidence (e.g. lack of a scar) and the feeling of being healthy (lack of symptoms) result in perceiving the health condition to be of minor importance. This perception, accompanied by the lack of adequate and correct information provided by the medical services, reduces their effort to make lifestyle changes (e.g. in terms of diet, physical activity) in both the short- and long-term.

With respect to all previous published studies, although they reveal important findings and provide cumulative knowledge in the area of cardiac health, there are a few issues that need to be addressed. The findings do not build a complete picture of the phenomenon under investigation. With very few exceptions (these exceptions concern studies with patients after CABG (e.g. Abassi et al., 2014; Tomie et al., 2006), the aim of most qualitative studies has been the exploration of individuals' lived experience shortly after CR, exploring some aspects of QoL (e.g. Lindsay, Smith, Hanlon, & Wheatley, 2000; Peterson et al., 2010). However, as QoL is a fluid multi-dimensional notion, a qualitative study using in-depth individual interviews exploring people's lived experience after a longer follow-up post treatment could provide greater insights. Interviewing patients at a greater temporal distance to the experience of treatment can inform us further of the process that individuals follow in order to make sense of their life, potential shifts over time in their points of view regarding the meaning of living a good life, their persistent concerns and their interpretation, as well as the strategies that they adopt in order to practise (or not) everyday lifestyle modifications.

Furthermore, in most studies, the methods used for data analysis focus on demonstrating either the most important themes in participants' accounts by using thematic analysis, or categories revealing similarities and differences by using grounded theory. These methods imply limited interpretation of the phenomenon through participants' viewpoints as, especially in the latter case, the aim is to develop theories to generate concepts which may provide an explanation of individual ways to resolve their main concerns focusing mainly on social processes. Thus they lose important idiographic elements as well as individual processes that may be of primary concern, particularly when this knowledge can form the foundation for tailored interventions aiming to foster an individual's sense of a good life. Also, they do not provide a deeper understanding of the process that individuals follow in order to adopt and justify various modifications in their lifestyle. For instance, Peterson et al. (2010) highlight that patients unsuccessfully treated with PCI quit smoking but they do not provide the reader with any insight into why successfully treated patients are less willing to quit smoking. Tomie et al. (2006) demonstrate that individuals acknowledge that stress has a negative impact on their health and try to avoid it as a coping strategy. Yet, the authors do not explain the process that individuals undergo in order to gain such an understanding and how an individual sense of self as well as behaviour is influenced as a result of this understanding. As Smith (2010) underlines, illness experience might be better understood within an IPA framework. He considers this approach more insightful as it focuses on exploring the unique human experience as it is perceived and interpreted by individuals themselves. In turn, this can facilitate more effective interventions aiming to promote living a good life.

To this end, this study, by using IPA aims to gain a deeper understanding of patients' subjective meanings of what constitutes a good life in the context of their experience of heart disease and CR treatment that might be helpful in designing more effective programmes for rehabilitation, secondary prevention and promotion of long lasting behavioural/life-style changes. In order to achieve the study's aim the following research questions will be addressed:

1) How does having been diagnosed with CHD and undergone CR influence CHD patients' perspectives regarding QoL?

2) How do CHD individuals experience life changes after CR and what might be the adjustment process that follows?
3) What concerns do CHD individuals have about life style modifications, in particular smoking cessation?

7.2 Methods

7.2.1 Participants

In total, 13 people were contacted from two lists compiled in the course of the quantitative studies; the first included individuals treated with PCI and the second individuals treated with CABG, who had participated in all three quantitative assessment points and were smokers or ex-smokers. One participant never replied, one declined to participate and one was excluded after she cancelled the interview appointment three times. Thus, a purposive sample of 10 individuals participated in this study (5 from each CR procedure), 6 males and 4 females. Their ages ranged between 42-70 years. All of them were Greek, in terms of ethnicity, and the majority were high school or university graduates. Table 7.1 displays the participants characteristics. As the developer of IPA argues, a very small number of interviews between four and ten (even, a single case study) could be enough for developing a deep understanding of an experience (Smith et al., 2009). For a greater discussion about sample sizes in qualitative studies please see appendix 7.1

Table 7.1 Participant Profile

Name[*]	Age	Sex	Marital status	Time after CR in months	Type of CR	Smoking status
Joanna	46	Female	Married	13	CABG	Smoker
Nathan	70	Male	Married	12	CABG	Ex-smoker[**]
Giannis	63	Male	Married	12	CABG	Ex-smoker
Nasos	63	Male	Married	13	CABG	Ex-smoker
Dina	65	Female	Married	14	CABG	Ex-smoker
Illianna	42	Female	Married	11	PCI	Ex-smoker
Petros	54	Male	Married	12	PCI	Smoker
Charis	50	Male	Married	12	PCI	Smoker
Maria	47	Female	Married	13	PCI	Smoker
Gerassimos	64	Male	Divorced	15	PCI	Smoker
*pseudonyms ** prior to CR						

7.2.2 Data collection

In-depth semi-structured interviews were carried out for data collection. According to the recommendation of IPA experts (Smith, Flowers, & Larkin, 2009; Smith & Osborn, 2003), this type of interview can provide rich data for analysis as it is guided by a flexible interview schedule. This also allows researchers to investigate other important issues related to the subject under investigation mentioned by each participant. The particular interview schedule consists of ten open-ended questions (Appendix 4.6). The development of the questions was based on two aspects of quality of life (*physical* and *psychosocial well-being*) examined in the quantitative component of the study and highlighted in the relevant literature. In addition, it included questions on changes in attitude, behaviour and lifestyle, as well as other questions that allowed participants to discuss issues related to quality of life that had not been directly asked about or covered. Also, prompting questions were used to allow better exploration and understanding of issues revealed during discussion. The interview schedule was reviewed and approved by the supervisors and tested for relevance and clarity in a mock interview.

Participants could choose the place where the interview would take place; either the researcher's office (8) or their own homes (2). The interviews lasted between 45 and 150 minutes. All interviews were audio-recorded and then transcribed verbatim by the researcher based on Silverman's (2000) guidelines. At the transcription stage all information that could identify participants was removed. Ethical approval was granted for the study by the University of Hertfordshire Ethics Committee (Appendix 4.7.1), and all participants gave their oral and written consent (a detailed discussion about ethical considerations is presented in Chapter 4: Methods).

7.2.3 Analysis

The methodological approach adopted in the design of the qualitative interviews and analysis of the interview data was in accordance with Interpretative Phenomenological Analysis guidelines, for which a small number of participants is adequate since emphasis is on understanding subjective experience rather than identifying similarities and differences between individuals. Interpretative Phenomenological Analysis (IPA; Smith, 2009) was chosen as the most appropriate approach for the analysis of interviews in the present study among other qualitative analyses for reasons discussed in Chapter 4. First of all, IPA best suits the research aims as it was developed to explore individuals' understanding and sense making of various phenomena as expressed in their own words. Secondly, it is interpretative with a double hermeneutic heuristic. In other words, the researcher makes an effort to understand and make sense of individuals' points of view and their understanding of the particular experience. Thirdly, IPA is idiographic in nature. It treats each case as a case study and afterwards explores convergence and divergence across themes from the analysis of different interviews (Larkin, Watts, & Clifton, 2006; Smith et al., 2009). Finally, it is useful in the field of health psychology research as it is able to give "voice" to the individual experience of disease/illness as well as reveal the individual meanings attributed to it. This insight has been shown to be very useful in improving best clinical practice (Curry, Nembhard, & Bradley, 2009), and shaping health care policy (Cassidy, Reynolds, Naylor, & De Souza, 2011).

The exact steps followed for IPA are described in the Method chapter.

7.2.4 Strategies to ensure quality

The assessment criteria for the quality of qualitative research differ dramatically from those for quantitative research. According to Smith et al. (2009), the developer of the IPA approach, Yardley's (2000) guidelines are most appropriate. Those guidelines place emphasis on four main principles: a) sensitivity to context, b) commitment and rigour, c) transparency and coherence, and d) impact and importance.

Sensitivity to context refers to four different aspects of sensitivity that should be demonstrated by the researcher: presentation of the theoretical and empirical background of the literature related to the research; being sensitive to participants' points of view and their socio-cultural stance; being sensitive to ethical issues; being sensitive in the data analysis. In the present study, sensitivity to the context has been established partly in the introductory chapters (Chapter 1 & 2) and partly in the introduction to this chapter. Sensitivity to participants has been established by asking them open-ended questions as well as by using prompting questions to encourage them to speak about essential aspects of their experience. Moreover, interviews conducted in the researcher's office were made in a calm and safe environment with minimal decor. All interviews were conducted at a mutually agreed time between the researcher and participant. Furthermore, the researcher's genuine interest in individuals' points of view and non-critical attitude (i.e. unconditional positive regard; Rogers, 1962) also ensured sensitivity towards participants and reduced social desirability biases (Silverman, 2013). Active listening, mirroring and summarizing techniques were used to help the researcher gain confirmation from the participants of their understanding of their utterances. Sensitivity to ethical issues was established by ensuring participants' anonymity (using pseudonyms) and by respecting their rights. Sensitivity in data analysis was established by supporting the analysis and interpretation with participant quotes and trying to be as open-minded as possible to avoid my own biases, based on existing knowledge.

Commitment and rigour refers to the demonstration of the researcher's systematic engagement with the topic, competence and skill in the method followed, thorough data collection and in-depth data analysis. Participants' openness was also encouraged by the fact that, due to the longitudinal nature of the research for this thesis, an previous relationship had been established between participants and the researcher. Also, an interview debriefing schedule was presented at the end of the discussion allowing participants to comment on the interview procedure and make recommendations for improvement (Appendix 4.12). Researcher engagement with the topic and related skills were obtained by attending seminars on IPA, practicing a mock interview prior to data collection and having constant supervision by an expert in IPA during data collection as well as during data analysis.

Transparency and coherence refers to a clear and coherent description of the process followed and how the methodological principles underlying IPA have been accomplished during both data collection and analysis. Moreover, it refers to the relevance between interpretation and supporting quotes from the interviews as well as to the researcher's reflexivity about her own influence on data analysis and interpretation. Concerning my influence on data analysis and interpretation, first of all I acknowledge that, due to lack of prior experience with IPA research, some aspects of the participants' experience may have not received the attention that participants would like. Moreover, as a Greek middle-aged individual with a congenital heart disease, interpretation of individuals' accounts may have been influenced by my own projections and experience of the impact of the disease on quality of life. Also, due to my training in two psychological disciplines, health and counseling, my professional background may have prejudiced the way the data have been interpreted trying to find a deeper meaning in simple, straightforward issues. In an effort to avoid possible misconceptions, transparency and coherence in this study have been established in part by the detailed description of the steps followed and their relevance to IPA as described in the Method chapter. In the course of the analysis, an experienced researcher in IPA was involved in reviewing the data and considering individual interpretations. This involved, firstly, discussions of coding of themes and sub-themes with reference to the transcript in the course of analysis of the first interview and, secondly, comparisons and clarifications of the themes derived from all interviews to confirm the consistency and validity of analysis. The thesis supervisors also revised the interview schedule (as stated in previous paragraphs), monitored the analysis process and reviewed the data and the table of themes constructed from all interviews. In that way, leading questions and interpretation bias (Silverman, 2013) were reduced.

Finally, impact and importance refers to the importance of a research study regarding novelty and usefulness. The present qualitative study can be argued to provide readers with a unique knowledge in the field of coronary disease about how individuals who have undergone CR (both CABG and PCI) make sense of their quality of life one year after treatment, using IPA. Efforts have been made to understand the constructive nature of individuals' experience, the meaning that they give to this experience and how this affects their perception of quality of life. This understanding in turn can inform professional understanding of individuals' needs and thus what is required for effective interventions aiming to improve individuals' sense of quality of life.

7.3 Findings

Four superordinate themes were extracted from the ten semi-structured interviews by making use of Interpretative Phenomenological Analysis (IPA). These four superordinate themes are:

Modes of patienthood: "Your psychology is everything"
The self in the body: "I am a new person now"
Self and others: "So what if they see it differently…relax…you cannot control everything"
Towards living a good life: "Pull the sheet that blurs your mind"

In this section, the superordinate themes, ,themes and subthemes (Table 7.2; Appendix 7.2 with text examples) will be shaped by the narrative of findings and will be supported by quotes, verbatim extracts, from the interviews.

The reader should note that some minor changes in verbatim extracts have been made in order to improve readability as these quotes represent conceptual translations from Greek. Moreover, dotted lines within brackets (...) indicate that some material is not presented, while words in square brackets [ ] represent added material in order to give a more explicit sense of what interviewees were referring to. The names of participants presented in the narratives are pseudonyms to ensure anonymity.

Table 7.2 Master table of themes

Superordinate themes	Themes	Subthemes
Modes of Patienthood	Experiencing disease &its treatment: "*it's scary… many thoughts come to your mind*"	Confrontation with the diagnosis & treatment
		Clinical interactions
		Receiving medical treatment
		Feeling helpless
	Living a post-CR life: "*I have quality of life, but there are other things that you can't amend*"	Defying patienthood
		Other concerns gaining primacy
		Differences of stage of life
	Searching for understanding: *"I had a lot to time to think about it… why …why all this happened"*	Perception of disease causality
		Self-responsibility
The self in the body	Sensing the altered body: "*I feel different now…but sometimes troubles me what tomorrow will bring"*	The body becomes visible
		Fear of the unknown future
	Experiencing a new me: *"It's not that you do not stress yourself out but the intensity is different"*	Developing psychological self
		My body-my self
Self and others	You are alone: "*and I was left alone, all alone*"	Being alone hurts
		Feeling disappointed
	In need of support: "*I felt as if they wanted to help*"	Receiving practical support
		What you really need
	Changes in relating with others: "*You should see things differently*"	Thinking in a different way
		Behaving in a different way
Towards living a good life	Positive growth: "*If I didn't go through this I wouldn't realize… life is too short*"	Increased appreciation of life
		Personal growth
		Strengthening relationships
	Strategies to regaining control: *"I felt so good that I* was alive ... *there are so many things that I would like to do*	Setting boundaries
		Minimizing the impact of the disease
		Avoiding emotional expression
		Using humor
		Making comparisons with others
	Challenges in living a new life style: *"I want to change but…"*	Getting expert's support
		Persuading the self
		Quitting smoking

7.3.1 "Your psychology is everything": Modes of patienthood

This superordinate theme demonstrates how interviewees have experienced their patienthood (condition of being/becoming a patient, moving into another social category from being a healthy person to being an ill person; Aujoulat, Marcolongo, Bonadiman, & Deccache, 2008; Helman, 2007). This includes reflections on how they experienced diagnosis and treatment, a year before the interview, and how their life and perceptions have evolved during the last 12 months post CR.

7.3.1.1 *Experiencing disease and its treatment: "It's scary … many thoughts come to your mind"*

Reflecting on their illness experience, most participants explained that the diagnosis of coronary heart disease and their clinical experience of the treatment they received played a key role in how they identified as cardiac patients. Their narratives primarily refer to feelings and emotional shifts that they experienced; feeling disturbed at being treated as a medical case, being annoyed at aspects of care as a hospital patient and feeling scared in confronting the possible outcome of treatment.

For some, the absence of sufficient information on the therapeutic procedure increase feelings of discomfort or lack of control and this may enhance fear of death. Petros describes how he felt in his initial encounters with the doctor and his diagnosis, emphasizing how the limited information provided by his doctor raised feelings of fear of the "unknown" procedure of treatment.

> *"You get a fright… that's exactly how you feel [because] no one tells you anything… and that's the worst because you imagine*

> *different things. The doctor simply told me "don't be scared, it's nothing, it has become a routine operation now". [But] you don't know, does this thing hurt? [and] that they whisper… oh that scares you… the doctor and his assistant speaking in whispers… that whispering sound killed me… at some point I felt that I might not get out [of hospital] ever again. I mean I believed it… [and then] many thoughts come to mind. You [imagine] your kids passing in front of you, you think of your father, your mother… "(Petros)*

For many participants negative feelings related to the process of surgical treatment are reduced as a sense of control is gradually regained, highlighting the important role of the sense of control in emotional adjustment. For instance, Petros (among many others) describes how the anxiety he experienced during the therapeutic intervention was replaced by tears of happiness when he realized that it was over and he was alive and able to re-experience simple every day things implying a re-appreciation of life. Also, from his perspective, being prepared in the sense of having received some information beforehand would have given at least some comfort.

> *"when they brought me out, they took me [to a room] next to the window, and I saw the street and the cars passing by, and my eyes got wet. I mean I couldn't believe it [that I was alive]. Your psychology is everything. When someone goes into the surgery room you have to tell him some things… that he has to keep calm and he'll be able to see his loved ones again in a few hours" (Petros)*

Although all participants described their experience regarding the CR procedure as "nothing", many expressed intense post-treatment suffering, mostly emotional, as a result of poor interactions with medical staff.

Some interviewees describe their impressions of the indifferent or rude behaviour of the medical staff during their stay in hospital. Even though participants did not always directly describe it in their narratives, this may be related to feeling disempowered and being in need of the best care that one can get. As the quotes below show, Illianna experienced various negative emotions such as anger and indignation during her short stay in the hospital as a result of the inappropriate attitude of nurses.

> *"The girl who just finished her studies and who's doing her practical training, does she have the right to speak rudely to you, to make fun of or ignore the patient's calls?" (Illianna)*

Some others suggest that being in need of medical care during hospitalization could be stressful as they have to cope with novel and unfamiliar situations. Individuals may experience lack of privacy and distressing feelings resulting from sharing other patients' experiences, as in the case of Charis.

> *"The intensive care is a bit tiring... you can't find peace and quiet... it would be better if not so many people were together in the intensive [care unit]. Old ones, young ones, all together (...) We happened to have this case of a man who had a heart attack and almost died... and that almost brought everyone else down..." (Charis)*

Although for these participants distressing feelings are related to the hospital context and their worry about medical care, when individuals have to cope with medical uncertainty about appropriate treatment of side effects, such feelings are intensified. Joanna, for instance, who underwent CABG and had a long hospital stay due to several side effects, explains how she felt when doctors did not know how to treat her. She emphasises how overuse of drugs produced various side effects and made her feel insecure and desperate: "*I had become a guinea pig*", she emphatically described.

> *I was drinking a handful of pills and swallowed them all together (...) they were doing experiments… All those things that happened to me were not because of the heart but pharmaceutical [side-effects] in reality (...) [and they kept saying] "we don't know what else to do to you". When they tell you that it makes you feel insecure (...) and I was saying what do I do now, do they want me to kill myself?" (Joanna)*

Feeling frustrated and humiliated may also be triggered by a prolonged stay in hospital or repeated treatment for side effects. As Joanna further highlights, doctors' attitudes towards her as if she had nearly died, a delay in getting physical support from hospital staff as well as the limited facilities for personal hygiene, raised her feelings of shame and loss of dignity.

> *Because ok, it's not so nice looking at someone with terror… looking at him as if saying "I wonder how can you be alive", [nor] calling for the nurse and have her say "coming now… coming now" and you want to go to the bathroom since that morning and end up going in the afternoon… that brings you to a point that you're embarrassed of what you have… it's the absolute humiliation (...) and this thing in the hospitals, that they provide almost nothing, that you can't wash yourself, that's like uncivilized life on mountains. It deprives you of your dignity. It tears you down from the beginning"(Joanna)*

7.3.1.2 Living a post-CR life:“I have quality of life, but there are other things that you can’t amend”

Participants’ accounts demonstrate that the treatment outcome is linked with the maintenance (or not) of a stage of patienthood. Those who experienced various side effects due to surgery (CABG treatment) or hospitalization as in the cases of Joanna, Nasos and Dina describe the previous year of their life as a life of continuing suffering “*full of pain and hardship*” and identify themselves as patients due to post-treatment complications. As Dina and Nasos explained

> *“I don’t have angina anymore, in that way I feel all right… The pain chest due to surgery disappeared three-four months after the surgery, but, my leg… it hurts (...). It started from the area of the wound from which they [doctors] took the graft. It never fully recovered. Now, a year after surgery and it still numbs, sometimes so badly that hurts … Many times I cannot walk without my walking stick (Dina).*

> *“My whole troubles are because of the bacterial infection I caught in the hospital. If I didn’t have that, I would have been fine (…) The [chest] inflammation was so bad that anti-inflammatory drugs did nothing, and the infection spread. I was going to the doctor, he recommended hospitalization (…) part of the treatment was to cut a piece in order to clean the wound (…) a few weeks later the same was repeated… don’t say much, this process was repeated eight times. During those episodes I’ve experienced terrible pain”(Nasos)*

For many participants, the scary experience of treatment or diagnosis soon became less important, described “*like a bad nightmare*”. Many individuals who had no side effects, focus on an interpretation of their condition based on heart symptoms and any concerns are related to the maintaining the treatment’s positive outcome as in the case of Giannis, Charis, Petros, Nathan, Gerassimos and Grigoris. For instance, participants who "feel all right" may not identify as a cardiac patient defying the chronic aspect of the disease. As Grigoris said:

> *"To be honest I don't feel any symptoms, and after treatment (...) I don't view myself as having a health problem, the surgery "fixed" that problem." (Grigoris)*

Many participants who seem to defy patienthood tend to place a focus on other issues, on other coexisting problems and perceive them as more influential on their life. For some participants other coexisting problems are related to health problems, especially that of diabetes (Nathan and Petros), while for some others coexisting problems refer to financial and family problems. For instance, Petros's account demonstrates how he perceives that, since his heart problem was diagnosed and treated, he is done with it, while it is diabetes that has affected his everyday functioning.

> *The sugar [diabetes] is troubling me more than the heart. I mean I measure my blood sugar two or three times a day... I've never really bothered about the heart (...) Sugar is a more devious disease it's not something you can fix, you say will it affect my kidneys? My feet? (Petros)*

Others including Gerassimos, Giannis, Charis, and Maria perceive critical life events to have primacy over cardiac patienthood. Although these individuals acknowledge that health is an essential factor for living a good life, they emphasise ongoing life issues that already existed in their life previous to CR. Thus, they interpret the disease and its clinical management as an interruption of pre-existing concerns, to which they turned their attention again after treatment. For example, within Charis's account, the major theme was financial problems. His unemployment status has made him feel inadequate to take care of his family's needs which are more important than personal health.

> *"It's not that it doesn't play a role [your health] but your finances come first in any case. When you have obligations and you can't cover them, your life sucks. It doesn't matter if you have some health problem or not (...) think of me, I came from my village when I was 17 and I've always worked, I've stayed at home [unemployed] for over a year now?" (Charis)*

In Maria's account the major theme was the loss of her husband and the responsibilities that were automatically transferred to her. The absence of "his support", having to raise two children alone and being in charge of the family business, leaves her limited time for attending to her personal health.

> *"My priority is taking care of my children and since my husband died I have to be both a father and a mother (...) I took over the family business too. I run all day long and since I don't have any obvious problem ... I don't have time for such things [medical examinations]"(Maria)*

Moreover, a number of interviewees suggest that the stage of life has influenced how they understand and view their lives approximately one year post diagnosis and CR. The heart disease may be seen as just another problem expected with older age, or else its impact on their vitality and functioning which have already diminished with age may not be so great. For instance, Dina, similar to Nathan and Giannis, said:

> *"I'm not some youngster anymore (...) not that I think of me as old (...) any way you look at it I'm not as robust as I was when I was young (...) we grow up and health problems are expected… some sugar [diabetes], some [high] blood pressure" (Dina)*

7.3.1.3 Searching for understanding:"I had a lot to time to think about it… why …why all this happened"

All participants described efforts to understand why that "problem" (the disease and its treatment) appeared. Many interviewees borrow meanings from the medical discourse on the development of heart disease emphasise heredity and stress. For instance, similar to other participants, Joanna said

> *"Out of the 50 doctors I have been to, statistically everyone asked me if I have stress, everyone. The first thing they asked was if you have inherited it and second if you have stress, thus it plays a very big role."(Joanna)*

This in turn, initiates a self-reflection process about disease manifestation in an effort to gain a better understanding of what aspects of self may have contributed to disease development. Female interviewees mostly explained that the stress experienced is related to internal factors, putting emphasis on their tendency for "perfectionism". As Illianna, by adopting the prevailing medical discourse, explains, her efforts to have everything under control as soon as possible and as well as possible might have caused the disease.

> *“It was stress [that caused my heart problem]. As they told me at the hospital, I am a perfectionist. I am a person who wants to have everything under control, I am a bit demanding, impatient and I want to do what can be done, or what I judge has to be done now, to do it immediately now! Whatever I turn my hand to, I want it to be perfect or at least as good as possible. That’s the reason why I didn’t want a woman coming to help me with the housework. Once or twice that I tried, I ended up doing the housework again on my own, that [housework] I had paid a Romanian woman to do (...) My perfectionism caused all this.” (Illianna)*

Joanna, in addition to perfectionism, emphasises her tendency to suppress her own emotions. She perceives that her difficulty to express how she felt increased the levels of stress.

> *It’s the stress… because I was a perfectionist, and my introversion. I will get furious and I don’t express it ... I keep it inside and tell myself it doesn’t matter, it will pass ... of course this is not the right way to deal with it” (Joanna)*

On the other hand, many male participants explained their stress as a cause of the disease, but attributed it to external factors. Most of the time increased stress, before as well as after diagnosis, concerned uncontrollable issues related to financial restrictions that damaged their self-perception and lead them to experience discrepancies from the masculine role of the provider. For instance, Charis describes how essential it is to earn money in order to provide for his family and how the absence of work makes him experience stressful feelings of inferiority as he has had to carry out household chores and activities traditionally connected with the female role.

> *It's the stress… [struggling] to earn money and support your family... Can you imagine me now (...) While I should be taking care of my children now, I'm playing the happy housewife instead" (Charis)*

Similarly for Giannis, although he acknowledges that stress is damaging to health, he perceives it as inevitable sometimes. His job problems increase his stress as he feels that he is not able to offer his family simple things and regrets his spending behaviour

> *"Stress is a bad thing… but when you have financial problems, or your business is going worse and worse, what can you do, can you not stress out? And as time passes you stress our even more… do you know what it's like to not be able to take your wife and kid for a day out, get them an ice-cream, when in the past I would spend a bulk of money on foolish things?" (Giannis)*

Depending on people's attributions about the sources of their stress, concerns about responsibility and self-blame may arise. For instance, although Nathan is troubled with his difficulty to provide financial assistance to his children, he considers this is due to external factors and thus feels less responsible and stressed about it. As he said:

> *"I feel sad… I'm stressing out, I would like to help to my children more ... but what can I do, fight God?" (Nathan)*

Others, such as Gerassimos, exert severe self-criticism and blames himself for both overwhelming levels of stress and unhealthy behaviours that affect his body.

> *"The blame is all mine. It's my fault, my wrong behavior brought us to this point... I was smoking, drinking, working exhaustively.... And here are the results." (Gerassimos)*

The above quotes demonstrate that self-reflection is part of an explanatory process whereby people come to consider what caused their heart disease and whether their behavioural patterns contributed to it.

Overall, this superordinate theme encapsulates people's experiences of becoming a medical case and how they faced up to having to undergo an urgent medical procedure. For some, uncertain treatment of CR side effects and long periods of hospitalization made them feel helpless in the face of a life-threatening disease. For others, whose negative experience was restricted to interactions with medical staff, becoming cardiac patients was less scary and frustrating. In effect, participants connected their perceptions about their life one year post diagnosis and CR to the presence or absence of adverse effects as well as other life concerns. Whether and how they identify themselves as patients or attempt to defy patienthood affects their response to everyday life adjustments that is variously explained as making compromises and living a balanced life. Participants trying to gain a sense of understanding about the reasons for CHD development, borrow meanings from the related medical discourse and emphasise stressful aspects of self and their own unhealthy behaviours and responsibility.

People's causal attribution of the disease as well as the fear of the re-occurrence of a cardiac event, emerge as an attention to the embodied self and constant efforts to change aspects of their individual and relational self in an effort to find ways of mastering. In effect, many participants experience a positive adjustment as the following superordinate themes describe.

7.3.2 “I am a different person now”: The self in the body

This superordinate theme captures how interviewees experience themselves one year post diagnosis and treatment focusing on the individual body-self. Overall, this includes reflections and considerations such as that they experience a different sensation of their body after treatment, that the treatment was a turning point, a trigger for rethinking their self and stance to life, and how these have in turn made them experience a different sense of self.

7.3.2.1 Sensing the altered body:“I feel different now… but it sometimes worries me what tomorrow will bring”

Participants, reflecting on their body sensation after CR, explain how they perceive their body and how this sensation makes them feel. Within all interview accounts, there are descriptions explaining that the body becomes more “visible” after treatment and for some it is at this point that they pay attention to their bodies for the first time. As in the case of Gerassimos:

> *“I didn’t pay any attention to my body. I didn’t take care of it. I took it as self-evident that I was young and strong. (...) I think I was a different person coming out of the hospital. Maybe it was the first time I really looked at myself.”(Gerassimos)*

Many interviewees (including Gerassimos, Illiana, Petros, Charis, Maria, Nathan and Giannis) have experienced a bodily restoration. For instance, Giannis’ account demonstrates how he has visualized his heart before and after treatment, emphasising how the revascularizated heart gives life to the whole body and makes him feel revitalized.

> *“I imagine my heart, as if it was into the mire, sort of crumbled and black, and now I see it glowing. And thereafter your whole being glows… let’s not forget that the heart is like the carburetor of the motorbike… now I have a new carburetor and the speedometer is starting off from zero… even though I’m an old BMW, I can beat new cars”(Giannis)*

Others experience a detachment from their body as a result of CR. Three of the interviewees who were treated with CABG (Dina, Joanna, Nasos) experienced a body-self discrepancy. They compared their body at present to their body before CR and perceive it as less efficient, inadequate, placing restrictions on their freedom. For instance, Dina’s account points out how her body does not help her be fully functional in everyday tasks and how this makes her feel as half a woman.

> *“My body does not help me anymore (...) I have become half a person” (Dina)*

Nasos’ account is in line with Dina’s describing a general loss in bodily function.

> *“We get minus in everything (...) Before, it was fine, I was going wherever I wanted, did whatever I wanted, hard work, now… now this is out of the question. There is no strength… even though I say I will do this I will do that, then I can’t come up to that.” (Nasos)*

Joanna explains how she feels that her body has lost part of its femininity and vitality, saying that it “*doesn’t rock as it used to do*”. Her account highlights how she feels about her body, emphasizing that she is free from heart symptoms but she faces problems with her legs, sometimes experiencing herself as paralyzed.

> *“My feet hurt, I can’t go up and down the stairs as I used to do before (...) I don’t get tired, I don’t get short of breath, I mean, as a heart it may have its problems but I know what bothers me today is my feet, I can’t take good steps. There are times I feel as if I’m paralysed.” (Joanna)*

Among those participants’ sensing their body as renewed, feelings of insecurity and fear are experienced as a result of considering an unknown future; some individuals are afraid that the positive health outcomes may be temporary. Many participants explain that, to some extent, they have thoughts and worries about “*what tomorrow will bring*” and the consequences of this change on their lives. For example, Illianna, Giannis, and Maria describe how, even though they feel well at present, they still have concerns about how their bodies may turn in the future and what the consequences of bodily reactions or a potential death might be.

> *“My body is fine. The examinations prove it, but if I tell you the bare truth... I’m afraid that my heart might stop, or that its condition may get worse and I get to lose all I have and all the things I want to do in the future. That is, having a child, travelling to distant destinations (...) but I don’t know how long my body will last.”(Illianna)*

> *"I feel fine, but it's the heart, I am afraid I may not be here to see my child grow up." (Giannis)*

> *"I feel strong like a bull... but still sometimes I'm afraid I may die and what will happen to my children?" (Maria)*

As the above quotes demonstrate many participants experienced a kind of bodily revitalization following treatment, but the fear of the unknown future seems to have an adaptive value as it empowers individuals to make positive changes to aspects of the individual self as the following themes describe.

7.3.2.2 Experiencing a new me: "It's not that you do not stress yourself out but the intensity is different"

As evident in participants' accounts, changes in body sensations and the self-reflection process may create shifts in the psychological self and sense of the body-self.

Many participants experienced a change in aspects of the self. Their accounts emphasise changes in the psychological self. For example, Petros describes how he became more easy-going when he understood that life is too short to pay attention to trivial details and damage yourself.

> *"In the beginning I was getting angry with them [family] for the slightest little thing. Now I don't steam up... life is too short to bother with trivial things and ruin your calmness."(Petros)*

Joanna describes how her detachment from everyday activities made her realize that things can be done "*well*" without her interference.

> *"I am more relaxed, more distanced… you think you do things perfectly and that's the only way things work… I have now seen a lot of things can be done properly, and function well without me interfering at all." (Joanna)*

Maria also experiences this change as she describes herself as tougher.

> *"I'm not as mushy as I used to be… I have become tougher and I don't easily forgive mistakes… and [I am] more bitter and sarcastic." (Maria)*

A few participants explain how the experience of CR and self-reflection have impacted their body-self sensation; the realization of what really matters make them consider their bodily strength and limit unnecessary bodily activities. For instance, Petros illustrates how irascible and ready to get into fights he was prior to treatment and how calm he has become after realizing his exaggerated response to others' behaviour.

> *"Look, I don't get into arguments now, I see things differently, I keep much calmer. Before, I was short-tempered over little things. I took everything personally."(Petros)*

Giannis recounts how the new self avoids getting stressed

> *“In the past, I would flip out for no reason. I would easily lose my temper. Now, I don’t steam up, I don’t get into arguments at all (...) And with my colleagues too, I don’t quarrel whereas I did before (...) Before… we could even end up coming to blows.” (Giannis)*

Another issue voiced by a few participants who are emphasizing the importance of not stressing yourself, concerns the diminished bodily strength in relation to maintaining an active sexual life. Also, Giannis describes:

> *“Having sex with your wife is important… it’s not that you neglect her if you don’t do it, but how can I say... you feel good too.”(Giannis)*

Charis also places particular emphasis on his sexual self, perceiving it as an integral aspect of the self. The vitality of this subject is demonstrated within his accounts by describing how he experienced feelings of overwhelming discomfort as a result of his wife’s restraint, and how he coped with it by discussing this subject with his doctors.

> *"During the first months the situation was intolerable… my wife wouldn't let me touch her for fear something might happen to me. In a doctor's appointment, I asked him what I can and what I cannot do… I don't say we do the acrobatics but… we're still young, our blood is warm."(Charis)*

Joanna's accounts also show how essential a sexual life is for one's identity, by highlighting the vital importance of sexual satisfaction and equating it to a survival need similar to food. As Joanna said:

> *"Sex is of vital importance! Just like food, so it was with sex too…I don't have a physical problem, but then again the sensation, the pleasure is not the same (...) I'm ruined in that respect."(Joanna)*

Joanna does not communicate this to her doctor in the face of serious health problems, as she considers *"this was the least important in the midst of all those problems I had"* and, in contrast to Charis, she feels that the problem remains unresolved. Using a past tense in her description implies that she has accepted the loss of a vital aspect of herself, while this adjustment has been facilitated by focusing on staying alive.

Overall, it is the experiential and meaning-making process that refers to how participants perceive and reflect on their body-self that comes to the core in this superordinate theme. Participants begin to have a different relationship to their bodies after CR which, for some, is positive while it has a negative meaning for others. Experiencing bodily changes and fear of the unknown mobilizes them to develop new aspects of self. While some behavioural changes are welcomed and more easily adopted, other aspects of the self, especially those concerning sexuality, may be viewed as more vital and yet more difficult to deal with in the face of life threatening issues, as in Joanna's accounts.

7.3.3 "So what if they see it differently ... relax ... you cannot control everything": Self and others

This superordinate theme illustrates individuals' feelings and attitudes concerning the relational aspects of the self. In particular, the issues of interest and reference here have included how individuals feel about the way they have been treated by others during the last year, what kind of support, if any, they have received and how a comparative consideration of their own behaviour towards others prior to the disease has made them start relating with others in a different way.

7.3.3.1 You are alone "and I was left alone, all alone"

Another key aspect of the individuals' experience concerns how they view the self in relation to the way they have been treated by others. Many of the participants report having experienced feelings of loneliness and some of them were hurt by the responses and attitudes of their family members. For instance, Joanna describes how she felt alone in the hospital and explains how the attitude of people close to her, especially their behaviour towards her children, had disappointed her.

> *"I was very much hurt by the fact that I was alone. Do you know how it feels like when your own people don't stand by you? Those you considered your own? Very much [hurt]... and all this has to*

> *do with my children. Because ... er ... I was expecting they would support my children. Do you know what it is like when your kid calls you at the hospital and tells you "ask aunt not to bring those foods again because, they bring us, for five days now, five days of lentil soup." I mean is this possible? You shouldn't give so much worth to others around you, and invest emotionally, because that hurts you." (Joanna)*

Joanna, among others, realized that she was alone while being in hospital and explains that her feeling of being disappointed arose mostly from the fact that people whom she counted on did not meet her needs and expectations. Some others become hurt by their friends. Charis's account demonstrates how annoyed and disappointed he felt because of the absence of his "supposed friends", in his own words, emphasising their lack of attention to his wife's financial needs.

> *"Do you know what bothered me most? That they didn't care to ask if my wife needed anything. If we have the money... I hadn't got the retirement compensation and most people around me knew."(Charis)*

In contrast, some other interviewees had felt satisfied and supported by others as their friends have met their expectations. As Petros says:

> *"They are good friends. They came to see me, they asked my wife if we needed anything ... and then ... how can I say, they stood by us. I believe they would go into fire for me. It's not that my brothers are bad people but see...I'm closer to these few friends." (Petros)*

The above quotations demonstrate that many interviewees felt alone, in the course of hospitalization and recovery as well as in their life as CHD survivours. The intensity of loneliness initiated a re-evaluation of their relationships, highlighting the need for closer bonds and emotional support.

7.3.3.2 In need of support: “I felt as if they wanted to help”

Many participants, although they received some kind of support, may also have felt alone in that the support experienced may not have been consistent over time or in line with their needs. For instance, Maria describes how supported she felt by getting practical aid and how those feelings disappeared and she felt alone when this support diminished over time.

> *“I felt as if they wanted to help, each in their own way, and even more on financial matters of the company. But you know after a while everyone goes back to their problems and they forget you.” (Maria)*

Joanna placed particular emphasis on the kind of support that she received from a friend who took her on car trips or went out for coffee with her.

> *“It was Olga only… only she was strong, a good friend… she took me on car trips, took me out for coffee… She really helped me a lot.”(Joanna)*

Joanna implied that going out with her friend helped her temporarily escape from being a patient and her health or life concerns and, thus, made her feel emotionally supported. The emphasis that she put on her words demonstrates that she perceived the emotional support as more important and valuable than the practical one.

Also, within Gerassimos' accounts, he highlights that the only support that he experienced from his family was financial assistance for payments to the doctor, private nurse and hospital stay. In his terms, the lack of emotional support reflected his own previous behaviour towards them; he perceived their attitude as a paying back for his own emphasis on material support.

> *"They paid for the doctor, the hospital, the private duty nurse... How can I complain that they didn't support me enough? They gave back to me what I was giving them all those years… money."* *(Gerassimos)*

Gerassimos brings to light another aspect regarding the absence of the required emotional support by maintaining that one cannot expect to get without giving. Self-reflection about his relationship with others allowed him to realize that the practical support that he used to offer to his family is less precious than the emotional one. In such ways many participants, like Gerassimos, report that feelings of being alone have forced them to reflect on various aspects of the relational self.

7.3.3.3 Changes in relating with others “You should see things differently”

Interviewees’ reflections about their relational self may have affected how they have related to others. For many their re-evaluation had a determining impact on the manifestations of the relational self.

Some become detached from their extended family. For instance, Joanna explains how the realization that “*I was left alone*” throughout the difficult phases of hospitalization and post-treatment experience, have mobilized her to alter her behaviour and become more detached from members of her family of origin.

> *“And I say wait a minute, why do I have to invest emotionally, to suppress my emotions and the others… have him saying I was squandering my money, and that I was insensitive, hey there, why not behave accordingly too, why do I have to swallow it, at the end of the day it’s my money I’m wasting not his. I should at least behave the way that makes me feel good. Isn’t that so? Why do I have to feel oppressed? I was suppressing what I wanted to say, my whole life, to avoid provoking others, and so what? This has changed (...) I responded to their behaviour and I changed.”(Joanna)*

The experience of the disease has also led her to become less protective towards her children, recognizing that things can be done without her contribution.

> *“Why do I have to do everything? When there is someone else who can do it, why do you have to do everything on your own? You think that only you can do things perfectly and that’s the only way they work well. Kids can do things on their own and detach from me.” (Joanna)*

In contrast, for Gerassimos, his experience and self re-evaluation resulted in becoming more attached to his nuclear family members. His accounts show that he perceives a new relational self and he tries to enhance emotional bonds through various activities.

> *"I now do more constructive things... I will cook, even though not often, and I will invite [the family] over for dinner all together, and [we will] play some games. I will ask my sons to come over to watch football together... and give my partner a hug while watching a movie together" (Gerassimos)*

Others have become detached from their social network. For example, Charis explains how he became detached from his ex-colleagues as a result of the disappointment he had experienced due to their lack of support, highlighting that real friendship is tested in hard times. As Charis said:

> *"The truth is, most of them, I pushed them away...A friend in need is a friend indeed. In joy and parties, everyone is a friend." (Charis)*

Yet others become more balanced in their interactions, as in the case of Maria. Her account highlights the positive impact of the re-evaluation of her relational self. Maria describes how she perceives herself as more clever and explains how strong she feels at present as a result of this change.

> *"You can't fool me anymore. And I can tell you this, I think with all this I've grown stronger" (Maria)*

Overall, this superordinate theme demonstrates how the CHD and CR experience makes many people realize that they are alone and how this realization generates feelings of disappointment and the need for re-evaluation of multiple aspects of the self in relation to others. All participants referred to practical support. However, even those who received it suggested that this was not enough as they emphasized that they felt alone during disease management and recovery. Thus, even though the need for emotional support is implied, it is not directly described in most participants' narratives. This, in turn, mobilizes a self-talk in which participants consider their self before and after their disease experience as well as engage in a dialogue with multiple aspects of their relational self. The outcome of this kind of re-thinking concerns changes in the way they relate to others. Individuals who recognize that they used to be detached from significant others attempt to establish closer relationships, as in the case of Gerassimos, whereas others have suggested the need to distance oneself when being disappointed by friends, as in the case of Charis, or by family, as in the case of Joanna.

7.3.4 "Pull the sheet that blurs your mind": Towards living a good life

This superordinate theme captures individuals' new stance towards life as CHD survivors highlighting a positive growth and bringing to light coping strategies as well as perceived needs, and practices. Specifically, individual accounts vividly describe what kinds of positive growth they have experienced in effect to their disease-related experiences; what strategies individuals have developed and/or adopted for regaining control of their life and regain self-esteem; what challenges they have had to address in order to live in accordance with a healthy lifestyle.

7.3.4.1 Positive growth: " If I didn't go through this I wouldn't realize… life is too short"

All participants' narratives demonstrate evidence that through survival a positive growth emerged. The strong feelings of being alive elicited an increased appreciation of life, a willingness for personal growth and an effort to establish meaningful relationships.

In many participants' accounts it was highlighted that after being diagnosed with CHD and surviving the coronary revascularization they started to gradually appreciate living, enjoying small everyday things, "*beauties of life*", which they rarely enjoyed before diagnosis. For instance, Nathan and Petros said:

> *"I feel all right, but you never know what tomorrow could bring. Why lose precious time by focusing on pointless issues? ... I prefer to make enjoyable things ... things I couldn't do before ... sitting in my balcony early in morning hearing the song of birds." (Nathan)*

> *"Nothing is as in the past. I enjoy everything I do (...) even having my breakfast. Few months ago I was always in rush ... I swallowed my food ... I had never paid attention to the nice smell of fried eggs and fresh butter." (Petros)*

Many narratives show that participants perceive their CHD diseases experience as "*a life lesson*", enabling them to gain some personal strength. Some, as in the case of Maria, Giannis, Nathan, and Illianna, experienced emotional growth by becoming "*tougher*", "*stronger*", "s*elf-controlled*", "*less stressed*". Some interviewees explained further that this emotional growth initaly developed in an effort to prevent disease progression also helps them with dealing more efficiently with difficult situations. As Illianna describes, being able to manage her stress levels resulted in more efficient coping with demanding situations in her workplace

> *"Prior to it [diagnosis], I couldn't cope very efficiently with difficult situations (...) especially, with parents of kids with special needs. It needs a lot of calm and patience to persuade them to seek expert help. After the diagnosis where I have to calm down for my own sake, I've realized that I could deal better with those parents." (Illianna)*

Many participants highlighted that surviving CHD and CR was perceived as a "*second chance*" in life giving rise also to a willingness for self-development, a need to learn new things and acquire new skills. For some this willingness was motivated by the need for personal progress as in the case of Nathan.

> *"For many years I was static, after recovering from CABG I've decided to go change that. As I said earlier I love gardening... recently I enrolled in a local free of charge gardening seminar." (Nathan)*

However, for others as in the case of Gerassimos, their willingness was motivated by the new way of relating with significant others. As Gerassimos explained

> *"I try to be closer to my loved ones (...) I cook for them at least once a week, (....) I went to a cookery school… I am not yet a very good cook but as they say [family members] I am on the right path (...) it is valuable to me to dine all together where we can relax and share our news…" (Gerassimos)*

Gerassimos' account highlights the acquisition of a new skill, that of cook, but also reveals his effort to build a strong meaningful relationship with his family members after his understanding of their superficial relationship triggered by how he felt in hospital and shortly after discharge. He alludes to the fact that cooking is the route for showing them that he cares and the gathering and sharing on the occasion of cooked lunch or dinner helps in developing and establishing emotional bonds.

7.3.4.2 Strategies to regain control: "I felt so good that I was alive…there are so many things that I would like to do"

Considering a good life in the course of the year following CR, participants' accounts are different in two ways. Those who have positively adjusted and use active coping strategies (e.g. setting boundaries, and suppressing self-expression) and those who, under the influence of persisting health problems, consider their post-CR life trajectory as an ongoing project adopting strategies that may minimize the impact of the disease and treatment in their lives in an effort to regain control. In both cases the use of self-enhancement strategies was vivid in many participants' narratives.

Many of those adopting more active coping explained the importance of putting limits on "*self exaggeration*" or other exaggerated demands. For instance, Dina describes how for her this meant withdrawal from responding to her husband's constant demands.

> *"I just don't get myself to do whatever he asks for… Dina bring my slippers, Dina bring me a glass of water… if he wants water he can go and get it himself." (Dina)*

Charis, among others, explains that he has adopted restricted expression as a strategy to control others' insistence on identifying him as a patient. For instance, Charis describes how he has become more introverted as a way to cope with his family overprotective attitude. As he said:

> *"There are many times I catch them [nuclear family member] talking secretly to each other (...) I tell them, why don't you guys tell me too, and they answer "you don't worry, we'll take care of things on our own"...with that kind of behavior on their part [excluding me], they make me not tell them, even when I do have something, I'm thinking that since they treat me like that when I feel well, imagine what they will do if I tell them I'm in pain or something's bothering me." (Charis)*

Some participants may use humour to minimize the impact of the disease on the body-self; it was often not mentioned directly in participants' narratives but both coping strategies seem to facilitate control over negative feelings. For example, Joanna tries to adjust to her sense of loss of her sexual self after CR treatment by using humour. As she said laughing,*"Greece has lost a sexy woman"*.

Others avoid reference to their body sensation in an effort to suppress negative feelings, which facilitates acceptance of their current condition and adjustment maintenance. As Dina said, *"I can't go on discussing the symptoms over and over again"*.

Some may give a temporal dimension to their condition in order to gain a sense of control over their life. As Nasos said,*"things will get better over time"*. Yet, others deny their patienthood by downplaying both the severity of their heart disease as well as its chronic nature and describing it as something that was present in the past and now has gone. As Nathan said *"It was nothing, it's gone now"*.

For some others strategies to regain control over their life involve the rebuilding of their challenged self-esteem. These individuals explained how comparisons with other people of their age may help them to feel better, allowing them to rebuild their self-esteem and challenge the sense of the body experienced after CR. For example, Nasos similar to Dina and Petros compared himself with other individuals of his social group assessing his own situation positively and in effect, feeling enhanced. As he said:

> *"look every Sunday when I go to the church I see many people of my age and while they have not undergone a bypass they use a stick to move... and I tell to myself ... you see Nasos you are much better than they are" (Nasos)*

Although participants developed various coping strategies to regain control over their life as presented in the previous paragraphs, highlighting once more the adaptive value of control, various challenges still remain to be addressed as the following theme suggests.

7.3.4.3 Challenges in living a new life style: “I want to change but…”

Participants explain the difficulty of making and maintaining the necessary changes in their everyday lifestyle. Common challenges mentioned relate to making the required changes when they do not have expert support, persuading themselves to make changes and quitting smoking in particular.

Many interviewees explain how helpful it may be to get expert support in managing various necessary changes. For instance, Illianna describes how useful it would be to get in writing all the relevant information and guidance from doctors and hospitals. As to this, she emphasized her own experience of difficulty and suffering in the effort to quit smoking without help, which instead could have been facilitated by the hospital’s smoking cessation clinic.

> *“it would be useful if they gave you their [medical] directives in written form as well as the different referrals[to medical examinations] you potentially need. Similarly, since there are different departments in the hospitals, they should make sure you get all the information and advice you need in order to do the changes you should, not only after surgery but in general. For example, I got into so much trouble in quitting smoking whereas later on I found out that I could have got some help from within [the hospital].”(Illianna)*

Illianna’s account suggests that individuals’ adjustment to new lifestyles might be facilitated if the existing health system was better organized. The lack of patient-centered approaches in health care and poor organization of health services in those terms may lead to unnecessary suffering for the patient and lack of adherence to doctors’ advice. In effect, participants’ accounts indirectly express concerns about unsuccessful secondary prevention and fear of future recurrence.

Other participants explain that the greater challenge they have experienced is the lack of motivation to adopt or maintain the lifestyle changes recommended by doctors. For instance, Charis describes how he feels bored at following doctors' advice in relation to walking on a regular basis, and how his daughter and family push him to go walking at the weekends.

> *"Just as the doctor had told me, I have to go walking, but I'm bored going on weekdays, except when my daughter or my wife drags me along for a walkabout."(Charis)*

Charis's account suggests that walking is boring, implying that it may be important but he does not enjoy it. This attitude can be explained by his unwillingness to identify himself as a patient and thus to acknowledge walking as an important self-care practice which may promote his health. At the same time he highlights the importance of social support in following doctors' advice. Similarly, Giannis explains the importance of social support for maintaining a change but also considers will power as an essential aspect for accomplishing a necessary change. As he said:

> *"Sometimes those around you are of great help. Look, let's say, I have stopped walking as I used to. But if my wife came along to keep me company maybe I wouldn't quit... Of course the most important thing is your will. If you have sheer will, everything is possible."(Giannis)*

Also Giannis explains how his will power may be influenced by the perceived necessity of a change. His accounts describe how he mostly followed doctors' advice, highlighting the crucial role of self-evaluation of the damaging impact of a habit on health.

> *"[my doctor said] I have to be attentive to my diet, go walking, give up smoking and drinking… I've done that! Not 100% but about 70% of it. I quit smoking! I quit it cold turkey. I quit drinking cold turkey. Those things that I can't give up, I don't find them so very bad for me that's why I don't give up."(Giannis)*

The above quotes imply that individuals' motivation for life adjustment and decision towards a behaviour change may be increased if their awareness of the beneficial effect of that change is enhanced.

Other participants perceive it as very challenging to quit addictive behaviour; smoking is the key example in this case. Quitting smoking as one of the main behavioural changes expected from CR patients is related to a sense of gaining control and minimizing its negative impact on health. On the other hand, the value of quitting smoking is debated in participants' narratives (e.g. Maria, Joanna, Gerassimos) as they suggest that smoking, even a couple of cigarettes only, is important for keeping emotional control in certain situations, as for example, when you have to deal with stress.

> *"My little [son] Kostas had an epileptic episode. I said that if I managed to survive seeing this… because I can bear anything but not when it comes to my children. I mean I had numb arms and by*

> *the time I felt worried... I couldn't feel my feet and felt like fainting. So I thought since I could hold on through this, I told*
>
> *myself that I do have a strong heart after all. But there it was, as soon as this was over, I lit a cigarette."(Joanna)*

Also, smoking a cigarette may be seen as extremely helpful towards achieving other kinds of behaviour change. Maria as a few other participants (e.g. Petros, Joanna) connects smoking to controlling eating.

> *"I remember when I had quit I wanted to put something in my mouth all the time… while the cigarette covers for that" (Maria)*

For those participants who were smokers, smoking is related to notions of pleasure and freedom versus living a life of restrictions. Even if they acknowledge that it is an unhealthy habit, they perceive it as a way to get some pleasure in life after CR. As Petros among others (Maria, Charis, Gerassimos, Joanna) pointed out:

> *"I know it's bad for me [my health], but we've given up far too many things now to quit smoking too."(Petros)*

Overall, this superordinate theme demonstrates how being a CHD survivours may elicit a positive growth and how individuals make an effort to to live a good life. Some aspects of positive growth that many participants experienced were related to a greater appreciation of life, personal growth and need to develop meaningful relationships. Furthermore, some individuals set boundaries against social conventions and exaggerated expectations of the self and others use mechanisms such as humor, suppression of emotion and denial to accept the impact of the disease in their life as coping strategies to regain control over their lives. People's sense of control may be compromised by the absence of expert support as some individuals may experience difficulty achieving and maintaining necessary lifestyle modifications. In turn, although not directly expressed, this may increase feelings of low self-efficacy. Some people reduce the inner conflict of unaccomplished changes in lifestyle by defying patienthood, as in the case of Charis, by minimizing their significance due to a lack of awareness, as in the case of Giannis, or by consciously choosing to maintain pleasure in life, as in the case of Petros.

7.4 Discussion

Employing an IPA framework, this part of the study aimed to explore subjective meanings of HRQoL among 10 individuals one year after CR in order to gain a deeper understanding of how surviving CHD has influenced individuals' sense of self and their life, the process by which individuals make sense of their experience, and what concerns they may have about life style modifications.

7.4.1 Findings

Four superordinate themes have been revealed: *Modes of patienthood, The self in the body, Self and others, Towards living a good life.* Overall, these themes reflect individuals' lived experience concerning CR and the year that follows as CHD survivors as well as the meaning making process of their experience that has elicited shifts in ways the view themselves, social relationships and life.

Regarding the influence of CHD on individuals' perspectives regarding QoL, participants' accounts showed that after undergoing CR many CHD patients experienced changes in their embodied self as well as in the way they view life. Many individuals after CR experienced feelings of happiness and gratefulness at being alive. They reported strong emotions accompanied by a different bodily sensation, shifts in their perspectives regarding QoL leading to a greater appreciation of bodily autonomy, a willingness for personal growth, an effort to re-build or strengthen their relationships with their loved ones and a re-appraisal of life.

These findings are consistent both with various theoretical frameworks and research evidence. Participants' narratives reflected how people with CHD make sense of themselves and their QoL in line with the biopsychosocial model (focusing on physical, psychological and social aspects as described by Engel (1980) and suggested by the WHO (1948)) and the fundamental aspects of self that shape identity (i.e. the individual self which reflects one's unique characteristics, the relational self which reflects dyadic bonds that are shared with close others (family, friends) and the collective self which reflects similarities and identification with social groups (Sedikides, Gaertner, & O'Mara, 2011)).

Furthermore, participants' quotes provided evidence that the concept of quality of life is a continuously changeable notion over the life-span which is influenced by people's experiences.

Their perspectives regarding QoL can shift as their points of view and standards change as Response Shift theory suggests (Sprangers & Schwartz, 1999). Briefly, this theory states with regard to the QoL concept that the phenomenon of the "meaning" of an individual's self-assessment can alter with time as a result of a change in the individual's internal standards, a change in the components that comprise QoL, and redefinition of QoL (Schwartz et al., 2007; Sprangers & Schwartz, 1999; Schwartz & Sprangers, 1999; Visser et al., 2013).

Moreover, participants' narratives provide support for Tedeschi & Calhoun's (1996) post traumatic growth model (PTG) which suggests that after experiencing a traumatic event or life crisis, individuals experience positive changes and emotional growth as a response to it. It is not the traumatic event itself, but rather the experience that motivates individuals to "re-build" their lives (Tedeschi & Calhoun, 2004). PTG's most evident manifestations are related to increased life appreciation, increased sense of personal strength, changing priorities, more meaningful interpersonal relationships, and a richer spiritual life (Tedeschi & Calhoun, 2004). Research evidence indicates that PTG is related to better HRQoL in various chronic diseases (Arpawong, Richeimer, Weinstein, Elghamrawy, & Milam, 2013; Kahana, Feeny, Youngstrom, & Drotar, 2006; Minkin, 2014). The findings of a recent qualitative study (Waight, Strodl, Sheridan, & Tesar, 2015) exploring post-traumatic growth in post-surgical coronary artery bypass graft (CABG) patients revealed that patients experienced two types of growth following CABG; 'greater appreciation of life' (living in the moment instead of focusing on what the future may bring) and 'new possibilities' as they view surgery as the route that helped them to improve their physical functioning.

These issues suggest that reaching conclusions about the true effect of CR based on individuals' subjective perceptions regarding their QoL might be biased if such issues are not taken into consideration.

Regarding individuals' experience about life changes and adjustment, participants suggested that they experienced patienthood from the moment they were diagnosed with heart disease but one year later they have returned to their everyday life. Many people perceive the state of being a patient as ending shortly after treatment and hospital discharge. Participants reflecting on their experience perceive treatment as a simple process, but many of them highlight medical care as a traumatic, distressing experience raising feelings of fear, frustration, loss of dignity and helplessness. This they consider to be a result of poor doctor-patient communication in terms of the limited amount of information given and inappropriate treatment by the medical/nursing staff. These findings are in line with the literature. A recent systematic review of 46 studies (both quantitative and qualitative (Parker et al., 2007) show that patients feel less stressed when health professionals show empathy, encourage questions and provide clarifying information aligned to their needs. However, it should be noted that, among those studies reviewed, there was a study carried out in Greece (Iconomou, Viha, Koutras, Vagenakis, & Kalofonos, 2002), in which authors the claimed that the need for information was not related to emotional distress. Research evidence from other chronic diseases (e.g. cancer) also highlights the beneficial impact of offering information to patients as it engenders a sense of control that can in turn help to reduce distress and increase self-efficacy (Chan, Webster, & Bennett, 2009). Moreover, previous research shows that staff behaviour and the hospital environment have an important impact on patients' dignity; the lack of privacy in hospitals, staff being curt and authoritarian can threaten patients' dignity (Baillie, 2009).

Shortly after hospital discharge, identifying as a patient or not is strongly related to the side effects experienced post treatment (as highlighted by CABG patients). Individuals with no symptoms feel healthy and defy patienthood and other pre-existing stressful issues (health or social) become the focus of the individual's attention. Similarly, the literature (Astin, Closs, McLenachan, Hunter, & Priestley, 2009; Peterson, et al., 2010) indicates that individuals experiencing CR as a simple process, with absence of bodily evidence (e.g. surgery scar) and lack of symptoms, perceive this particular disease as acute instead of chronic.

To recap, many individuals think of their CR experience as rather frightening, not merely due to the process but due to interactions with medical staff. A year after hospital discharge they recall it as a past nightmare which allowed them to have "fixed" the problems and return to their everyday life.

After giving an overview of their experience in relation to their CHD diagnosis and CR, and perceiving disease as controlled due to CR with no serious consequences in their everyday life, individuals tried to gain a sense of understanding its cause. Adopting the medical discourse related to the causality of heart disease, in particular stress and unhealthy habits (e.g. smoking, unhealthy diet), all participants reflected on their attitude and behaviour prior to diagnosis in an effort to evaluate their own responsibility. This understanding helped them to develop various strategies in order to gain a sense of mastery over their life. Research evidence (Lin, Wang, Tung, & Furze, 2012), similar to this study's findings, shows that many cardiac patients hold inaccurate beliefs about heart disease, while others may hold accurate illness beliefs but intentionally minimize the problem in order to reduce distress level and gain a sense of control. All these are in line with Leventhal's (1992) Self Regulation Model (SRM) and cognitive adaptation theory (CAT; Taylor, 1983). Both theories, SRT (Leventhal, Meyer, & Nerenz, 1980; Meyer, Leventhal, & Gutmann, 1985) and CAT (Taylor, 1983) agree upon the assumption that understanding disease and causality allows individuals to develop coping strategies (either approaching or denying the problem) in order to re-gain control (a sense of mastery; Taylor, 1983) or re-build/re-establish their state of normality (Meyer, Leventhal, & Gutmann, 1985) that was disrupted through the disease-related experiences.

After reflecting on their responsibility for causing the disease, participants' focus of attention becomes their bodily sensation. Individuals suggest that in the absence of side-effects, they experience a bodily revitalization. Previous research findings similarly reveal that individuals experience a bodily "reincarnation" after CR (Abbasi, et al., 2014; Astin, Closs, McLenachan, Hunter, & Priestley, 2008) and a sense of improved quality of life (Tolmie, Lindsay, & Belcher, 2006). However, there are individuals, especially after CABG, who experience a negative impact due to the treatment's side-effects and make efforts to adjust to a continual changing embodied self, highlighting the restrictions that persisting problems pose on motivation As bodily self is a core aspect of the individual self, for those people adjustment may be more difficult, requiring more time to be achieved. In either case, the experience of a fear, the fear of re-occurrence or disease progression and the impact that it may have on their embodied self and their overall life emerges in participants' narratives.

The positive feeling of being alive on the one hand and the negative feeling of fear of re-occurrence or disease progression on the other, combined with self-responsibility for disease development, motivates individuals to work on aspects of the self, both the psychological and relational self. Individuals tend to demonstrate a dramatic shift, a unique shift based on self-responsibility attributions; they become calmer, less perfectionist, emotionally tougher. These findings are consistent with those of Peterson et al. (2010) and Abassi et al. (2014) who suggested that many patients treated either with PCI or CABG perceive the treatment as a turning point provoking changes in their self-perception and behaviour.

Many participants discussing changes in aspects of the embodied self described another aspect, just as important but less often discussed in the literature, that of the sexual self. Individuals discussing the changes they experienced in that aspect of self suggested that it may be unwelcome as other changes and that they face difficulties in adjusting to these changes and ask for expert help as individuals. Especially females tend to be more reluctant to discuss sexual issues with their doctors, believing that others (e.g. doctors, partners) may perceive their sexual life as a secondary issue with minor importance when dealing with a life-threatening disease. Recent research shows that very few females receive counselling or discussion about sexual concerns and most of the time this is only at their request (Abramsohn et al., 2013). Research further supports these claims indicating that both doctors (Doherty, Byrne, Murphy, & McGee, 2011; Nicolai et al., 2013) and nurses (Goossens et al., 2011; Jaarsma et al., 2010) in cardiology practice rarely address sexual issues with the patients either due to lack of time and training to discuss sexual issues (Nicolai et al., 2013) or lack of adequate knowledge and a fear of provoking embarrassment in patients (Goossens et al., 2011). In light of these findings, when QoL is explored, sexuality should be included as it is an essential aspect of the self.

Participants also experienced shifts in the relational self. As in the present study, qualitative research findings show that heart disease patients often experience feelings of loneliness despite the existence of supportive relationships (Leegaard et al., 2008). Feeling distanced from significant others initiates a self-talk with multiple aspects of their relational self in an effort to gain understanding of the reasons for such experience. Individuals who recognize that they used to be detached from significant others attempt to establish closer relationships, whereas others experience a need to distance themselves from people who have disappointed them. According to the interpersonal social-cognitive theory (Andersen & Chen, 2002), the repertoire of relational selves is shaped by the interaction with significant others and this has an impact on self-definition and behaviour. As research evidence demonstrates, the maintenance of strong relational bonds with significant others is fundamental for people's well-being (Baumeister & Leary, 1995).

In terms of changes in everyday life, individuals with CHD may develop various strategies, including denial in order to minimize the impact of disease and internal conflict, and comparison with others in order to re-gain or increase their self–esteem.

To reiterate, the meaning making process of CHD survivors as suggested by participants embraces representations of disease and its impact on current and future life. Many individuals acknowledging their responsibility in disease development make conscious efforts for mastering disease progression and gaining a sense of control over themselves and their life. In effect, they work towards changing those aspects perceived as maladaptive.

This process seems to be aligned with Leventhal and colleagues' (1980) Self-Regulation Model (SRM) which provides a framework for understanding how individual symptoms and emotions experienced during a health threat or diagnosis can influence illness perception (illness beliefs) and guide subsequent coping behaviour, as discussed elsewhere (Chapter 2).

Regarding the concerns that CHD individuals have about life style modifications, challenges are attributed to both external and internal factors. People may experience low self-efficacy when expert support is limited. As research demonstrates, self-efficacy is a key component in CHD self-management (Katch & Mead, 2010). Other concepts related to low adherence to doctors' advice seem to be patienthood denial, lack of awareness of the significance of a change, lack of support from significant others, or efforts to maintain certain kinds of pleasure in their lives. These findings are in line with research evidence in the field of heart diseases. Based on a recent review (Murray, Fenton, Honey, Bara, Hill, & House, 2013), social support, education and knowledge, as well as beliefs and emotions were the main issues related to making lifestyle changes and maintaining a healthy lifestyle.

Concerning smoking cessation, one of the most challenging lifestyle modifications among CHD patients, three themes emerged from the participants' accounts; a lack of accurate knowledge regarding smoking and CHD, a lack of support (by experts or family members) and a conscious refusal to quit smoking as a way to cope with anxiety and stress as well as a way to maintain pleasure in everyday life. In the latter case, as participants who continue to smoke one year post CR suggested, they felt that the damage (the consequence) of smoking cessation would be greater than continuing to smoke. Some participants' quotes suggested that the value of emotional well-being might be of greater importance than physical well-being and health, while some other narratives implied that smoking may have a positive effect by helping them to control and reduce high stress which can cause problems with their heart. Research evidence, coming mostly from patients with cancer who continue to smoke, supports these findings (Duffy, Louzon, & Gritz, 2012).

In light of these findings, these aspects may be helpful if included in interventions aiming to increase CHD self-management and in particular, smoking cessation.

7.4.2 Significance of the study and limitations

The present study provides the fields of heart disease and health psychology with a deeper understanding of how individuals who underwent CR make sense of their experience and life one year after treatment. This study seems to be the first study in this area using IPA to capture the points of view of individuals who have undergone both CR types (CABG and PCI). In other words, it could be claimed that it is the first study that explores and captures the complex process that individuals undergo in order to make sense of their lives one year after CR, enlightening the multi-dimensional nature of quality of life as well as the interaction of multiple selves that may lead individuals to interpret their lives differently over time. Moreover, the findings of the present study in relation to the positive growth experienced by CHD survivors provide further insight and support for the Post-traumatic growth model (PTG- Tedeschi & Calhoun, 1996) in the field of heart disease.

Some of the themes revealed in the present study are adding novel insights (e.g. interaction of multiple selves, belief that CHD is curable) to existing knowledge in the heart disease literature while some others (e.g. minimization of disease impact) support previous research in the field. However, the uniqueness relies on peoples' interpretations and explanations of the process they undergo in order to make sense of their life one year after treatment. Thus, it can be argued that one major contribution of this study in the field of heart disease is that, by employing IPA, it has been revealed that many individuals after CR, especially those who received PCI treatment, perceive their disease as an acute condition which occurred and was treated in the past, bearing no more concern to the present. Although CHD is a life-threatening condition, many participants perceive it as less damaging compared to other medical conditions (e.g. diabetes) and less important to other life issues (e.g. financial). They come to pay less attention to it as long as it does not affect their independence and dignity. As a result, they gradually deny its presence in order to return to a state of “normality”. However, as they adopt the medical discourse of CHD causality, they develop various cognitive and problem-focused coping strategies in order to prevent having to reface such a challenging condition. These coping strategies are developed after undergoing a re-evaluation of their multiple selves and can lead individuals to modify all aspects of the self that are linked with their attribution of disease causality. These strategies, whether maladaptive or not, lead in most cases to an inner growth resulting in positive psychological changes, meaningful relationships and appreciation of life.

Another essential finding is that individuals perceive the self as being a multidimensional interrelated self; when one aspect is affected, all aspects are influenced. Sexual self is an integral part of the self and thus its well-being is a critical aspect of one’s life.

Finally, an essential finding of the present study is that individuals give priority to the psychological self compared to the bodily self, especially when it comes to behaviour modifications. For instance, although they acknowledge that smoking is harmful for their bodily health they do not quit this unhealthy habit if they perceive it as a way to improve emotional status. Thus, the present study also illuminates further the area of patients’ adherence/non-adherence to doctors’ advice by revealing a deeper understanding of the motives, the challenges as well as the cognitive processes that individuals undergo in order to decide, make and maintain lifestyle changes. This understanding may be particularly helpful to health care practice as it can guide multidisciplinary teams both in primary and secondary health settings to develop tailored interventions to increase patients’ adherence to lifestyle modifications.

However, a few notable limitations are present in the current study. It could be claimed that as individuals underwent different types of CR, the sample violates the rule of homogeneity. The decision to treat the participants as one group serves the purpose of avoiding a pre-defined differentiation of experiences of quality of life in terms of CR procedure. Furthermore, data collection, analysis, as well as interpretation of the accounts might be influenced by the fact that this study is the researcher's first attempt at employing IPA. In other words, although the research followed specific guidelines to safeguard the study's quality as described earlier, the researcher's lack of experience may have influenced aspects of data collection and data analysis. For a researcher with some work experience that focuses on evidence-based practice it is extremely hard to distance themselves from the pre-existing theoretical perspective as well as ignore the existing literature on the topic. It was for this reason that an external researcher was involved in reviewing and commenting on the analysis process, in an attempt to control individual weakness and possible misconceptions. Moreover, the lack of triangulation on data collection could be another limitation of the present study; only semi-structured face-to-face interviews were employed for data collection. Thus, the reader could argue that findings may be biased due to the limited richness of the data. Smith (2003), however, suggests that the use of focus groups should be carefully considered within the IPA framework because the group discussion may fend off the idiographic aspect of IPA. Thus, it might reduce one of the basic notions of IPA, the in-depth exploration of individuals' experience.

7.4.3 Implications for theory, practice and research

The findings of the present study are in agreement with the biopsychosocial framework of quality of life. However, based on participants' accounts, quality of life is not a stable concept; it should be perceived as a continually changeable notion that is influenced by individuals' stage of life, identity processes, experiences and context. Also, in the field of quality of life, theoretical perspectives should incorporate sexuality as a key aspect both in terms of functioning and satisfaction (physical and psychological dimensions). Furthermore, findings provide support for adjustment theories (SRM, Cameron, & Leventhal, 2003; CAT, Taylor, 1983) as well as PTG as conceptualized by Tedeschi & Calhoun (1996).

Regarding clinical practice within hospitals, the communication skills of medical staff should be reviewed and improved. The findings of the current study highlight the importance of this in order to minimize individual distress and feelings of loss of dignity.

Special attention should be given to establishing multidisciplinary teams in cardiac health care settings. The role of a health psychologist, sex therapist and dietician could boost best practice and quality of patients' care. Health professionals should also place particular emphasis on exploring individuals' process of adjustment and help them to accept the chronic nature of their disease as well as enhance their motivation to adopt a healthier lifestyle.

In short, tailored motivational interventions based on the findings of the present study should include psychoeducation (Janssen, De Gucht, van Exel, & Maes, 2013), focus on enlarging self-efficacy (Katch & Mead, 2010) and motivational interviewing (Rollnick, Miller, & Butler, 2008), targeting minimally physical exercise (e.g. walking) and smoking cessation. Interventions aiming to increase patients' social support can also be beneficial as support seems to have a reinforcing power on individuals' maintenance of a lifestyle change.

Concerning research, the present study highlights that quality of life cannot be captured solely by standardized self-report measures as each individual may experience the same phenomenon in a different way; the qualitative research paradigm should be espoused too. Also, researchers should pay attention to the disease adaptation process and the positive growth that individuals may experience when exploring changes in HRQoL after treatment, as these concepts seem to affect the outcome. Lack of such considerations may lead to biased results. Furthermore, as the present study's findings show, in the absence of side-effects individuals focus on other pre-existing problems. Consequently, exploring lived experience and quality of life over time, other stressful events should be investigated as well since they seem to have an influential effect on individuals' understanding and perceptions about their overall quality of life. Future research may include attention to retrospective accounts of how people define and experienced a good life before CR as well as after CR, as this study has focused on the latter only.

Researchers also should pay attention to the stage of life that individuals are at. Older adults may experience good adjustment not due to the beneficial effect of CR upon their life but due to their view that heart disease or side-effects of treatment are only problems to be expected with older age (Hendry & McVittie, 2004). Nevertheless, further qualitative research focusing on exploring individuals' coping strategies and challenges that they may face one year post CR treatment is needed in order to gain a greater insight into this topic, which in turn will allow the development of more advanced tailored interventions.

7.5 Conclusion

The present study aimed to explore how individuals make sense of a good life in relation to their health disease condition, one year after CR. Findings demonstrate that many individuals one year post treatment suggest that they do live a good live. This is considered in terms of continuation, where they perceive that the disease experience has not substantially affected their life, or is seen as an achievement, as long as they have managed to regain a sense of balance and purpose in life post treatment. Overall, individuals describe their experience as a life lesson.

Participants perceiving their disease as controllable or curable due to CR treatment, and fearing reoccurrence, try to gain a sense of understanding of disease causality. Individuals, in adopting the medical discourse regarding causes of CHD development and progression, place particular emphasis on stress and start a critical re-assessment of multiple aspects of self in accordance with Engel's biopsychosocial model. In order to controltheir disease and gain a sense of mastery they make a constant effort to change aspects of their self resulting in shifts in their attitude, behaviour and understanding of the essence of living a good life, eliciting a positive growth in terms of increased life appreciation, personal growth and development of meaningful relationships.

Furthermore, participants face various challenges in living a healthier lifestyle and attribute this to both external and internal factors. Smoking cessation is difficult as smoking seems to be viewed as a way to control other related factors (e.g. weight) as well as a way of maintaining some sense of emotional well-being.

Having gained a greater insight into individuals' understanding, meaning-making process and concerns regarding lifestyle modifications, the next step is the interpretation, the integration of the findings of the quantitative and qualitative components in order to address the research questions of the mixed methods study.

Chapter Eight

General discussion

8.1 Introduction

This thesis aimed to investigate CHD patients' perspectives of the influence of coronary revascularisation (CR) on their health related quality of life (HRQoL) as defined by the World Health Organization (WHOQoL team, 1993), since health issues like CHD can be more efficiently addressed if viewed in a holistic, biospychosocial approach (Blankenship, et al., 2013; Engel, 1980). CR is one of the main treatments of CHD consisting of two types: percutaneous coronary intervention (PCI) and coronary bypass graft surgery (CABG)). In order to achieve this aim a series of study were conducted.

Initially an in-depth examination of the relevant research evidence has been carried out by conducting a systematic review with meta-analytic techniques of the influence of CR on patients' HRQoL. The findings of the review based on 34 studies demonstrated that patients experience a moderate improvement in their HRQoL level after CR treated with either type (PCI or CABG). The length of a study (on average, studies with longer follow-up demonstrated lower effect sizes), the measurement used (studies using disease-specific instruments demonstrated higher effect sizes) and its quality (on average, as quality increases, effect size decreases) seem to be the main factors influencing outcomes. The limited research, however, on the one hand and the lack of adequate data on the other, did not allow for a full understanding and identification other potential predictors of the outcome.

Taking into consideration the findings of the systematic review, the extremely limited research in this field in Greece (where the incidence of CHD has been constantly increasing over the last decades, and where CR treatment is mostly applied) as well as the author's advocacy of the mixed methods stance (where the advantages of quantitative and qualitative research methods can be combined to draw a clearer picture; Creswell, 2014), two studies were carried out: (1) The translation, adaptation and validation of the Coronary Revascularization Outcome Questionnaire (CROQ; a disease/treatment specific instrument) into Greek, and (2) The longitudinal mixed methods study. The latter was the main research study following a sequential explanatory design and refers to a 3-part study; two research parts (a quantitative component focusing on patients' subjective ratings of and a qualitative component focusing on patients' lived experience of HRQoL), and an interpretation part (the integration of the findings for the different research components) which aimed to address the main research questions of this thesis:

1) How do Greek individuals with CHD conceptualize HRQoL?
2) How do aspects of the disease experience after CR and meaning-making processes inform individuals' perspectives on their HRQoL?

In this final Discussion chapter, the key findings of each of these studies are firstly summarized. Then, an explanatory synthesis of the main study's research component findings, thematically organized to address key aspects of the main research questions, is presented. Following the in-depth understanding of CHD patients' perspectives on their HRQoL one year after CR, an extensive discussion on the implications of the findings is presented, providing recommendations for theory, future research and clinical applications.

8.2 Summary of the findings

8.2.1 The validity and reliability of the CROQ - Gr

The validity and reliability study of the Greek version of the Coronary Revascularization Outcome Questionnaire (CROQ (Schroter & Lamping, 2004)) showed that the CROQ-Gr is acceptable to patients and satisfies the majority of the rigorous scientific criteria set in terms of reliability, validity and sensitivity to change.

In particular, the acceptability of the measure was rather good, with a high response rate which was greater than 0.70 and a low level of missing data which was lower than 10% for almost all subscales; with the exception of the *Physical functioning* subscale where the missing data ranged between 0 and 24%. The CROQ-Gr also demonstrated a good level of reliability; with an internal consistency greater than 0.70 and intraclass correlation coefficients (ICC) greater than 0.80 for all subscales. Regarding validity, the content validity was detected to be very good, firstly through face-to-face interviews of fifteen patients, and secondly, through expert opinion expressed during two panel meetings. Construct validity within scale was satisfactory. The four factor model of rotated squared loadings explained between 41.7% and 50.3% of the variance, depending on the version. The construct validity against external criteria (compared to the SF-36v2 subscales) was shown to be adequate. The *Symptoms* and *Physical functioning* subscales of the CROQ-Gr correlated more strongly with the *Physical Component Summary* of the SF-36v2 than with the *Mental Component Summary*. Conversely, the *Psychological Functioning* subscale of the CROQ-Gr correlated more strongly with the *Mental*

Component Summary of the SF-36v2 than with the *Physical Component Summary*. Finally, the CROQ-Gr was demonstrated to be sensitivity to change (post-CR scores significantly differed from those pre CR).

8.2.2 The mixed methods study

8.2.2.1 Quantitative results

The longitudinal quantitative component aimed to detect changes in patients' HRQoL (both overall and in subdomains) following CR over a 12-month period based on individuals' subjective evaluation as captured by the CROQ-Gr, exploring as well various clinical, behavioural and demographic predictors.

Results demonstrated that the majority of people with CHD report an increase in their HRQoL following CR. The trajectory of change, however, is not constant; initially it increases with time, and then decreases, though remaining at a higher level compared to prior to CR . Regarding the influence of CR treatment type on patients' HRQoL level a year after CR, the mixed findings do not allow a clear conclusion. Main predictors of the mean change were related to sex, BMI and smoking; females with low BMI that did not smoke tended to demonstrate a larger increase in HRQoL after CR.

Regarding the subdomains, the pattern of change was similar to the one reflected in overall HRQoL. Concerning the influence of CR treatment type, an interaction between Time and CR treatment type in three HRQoL subdomains was found. Specifically, in the *Symptoms* and *Physical functioning* subdomains as time increased, individuals treated with CABG seemed to experience a greater mean change compared to individuals treated with PCI even after controlling for individuals' biological, medical and behavioural characteristics. On the other hand, in the *Cognitive functioning* subdomain individuals treated with CABG seemed to experience a negative mean change compared to individuals treated with PCI who seemed to experience a positive mean change, even after controlling for individuals' biological, medical and behavioural characteristics. The main predictors of mean change in the *Symptoms* subdomain seemed to be CR treatment type, BMI and smoking; individuals treated with CABG with a low BMI who did not smoke tended to demonstrate a greater increase after CR in this subdomain.

Main predictors of the mean change in *Physical functioning* seem to be CR treatment type, sex and smoking status; female non-smoking individuals treated with CABG tended to show the greatest increase in this subdomain after CR. The main individual characteristic predictors of the *Psychosocial functioning* outcome were age and hypertension; increasing age and no hypertension predicted greater level of functioning in this subdomain after CR. Main predictors of the mean change *Cognitive functioning* were CR treatment type and diabetes; patients treated with PCI without diabetes tended to demonstrate a greater increase in this subdomain after CR. At this point it is essential to highlight that individuals treated with CABG with diabetes tended to demonstrate a negative mean change (a decline in cognitive functioning level compared to prior to CR). Regarding adverse effects, the results suggested that patients treated with CABG three months post treatment experienced more side effects but at 12 months the condition of most participants had improved. In terms of *Satisfaction*, patients treated with CABG especially retired individuals and individuals with co-morbidities (e.g., diabetes, high cholesterol) tended to show low level of satisfaction with the treatment. In contrast individuals with a family history of CHD tended to indicate a greater level of satisfaction with CABG treatment.

8.2.2.2 Qualitative findings

The qualitative data and analysis using an Interpretative Phenomenological (IPA) approach aimed to refine and provide a deeper understanding of the perspectives of individuals with CHD, by exploring participants' point of view and experience, placing particular emphasis on understanding and explaining issues revealed in the quantitative results (e.g. smoking-related issues). In terms of individuals' lived experience, participants, reflecting on their experience one year after treatment, perceived CR as a simple process and their negative experience was mostly related to medical care. Many participants with no symptoms or adverse effects tended to misperceive CHD, viewing their health condition as an acute disease treated with CR. Trying, however, to understand disease causality they tended to adopt a medical discourse especially in relation to stress, as a factor that can be controlled by themselves and reflected on their own responsibility for causing the disease. Feeling grateful for being alive, sensing a different body, a "revitalized body" as many participants suggested, but also having a fear of re-occurrence or disease progression, motivated individuals to work towards aspects of self in an effort to regain control over their life, which had been disturbed by the CHD diagnosis. In effect, dramatic changes in their views of self and life were observed highlighting a positive growth; a greater appreciation of life, personal growth and an effort to build more meaningful relationships. Challenges that participants faced in making lifestyle changes were attributed to both external and internal factors. Concerning smoking, there emerged a lack of accurate knowledge regarding the link between smoking and CHD, a lack of support (by experts or family members) and conscious denial as a way to cope with every day anxiety and stress on the one hand, and obtaining pleasure in everyday life from smoking on the other.

8.3 Integration and interpretation of findings (Part Three)

8.3.1 How do Greek individuals with CHD conceptualize HRQoL?

Findings provide support for the notion that HRQoL is a multi-dimensional concept; participants' reports suggested that they espouse a view of HRQoL consistent with the biopsychosocial model (Engel, 1980; WHO, 1948). In fact, individuals make sense of their HRQoL by evaluating their symptoms, physical, psychological and social well-being, which are perceived not as discrete concepts but as being interconnected. Changes in one aspect provoke changes in another and vice versa. In other words, this critical re-assessment of different aspects of their selves resulted in a shift in their attitude, behaviour and understanding of the essence of living a good life.

Moreover, as participants highlighted, sexuality is an important aspect of their life. Thus, in the field of the HRQoL related to coronary disease, sexuality should be incorporated as a key aspect both in terms of functioning and satisfaction (physical and psychological dimensions).

Also, based on participants' perspectives and the shifts indicated, QoL, with or without a health related aspect, is not a stable concept; it should be perceived as a continuously changeable notion that is influenced by individuals' experiences, context and stage of life. These findings are in agreement with the suggestions by many scholars (e.g. Beeken, Eiser, & Dalleys, 2011) that HRQoL is a dynamic concept and it may change over time as human beings adjust to their life conditions and alter their internal standards, expectations, needs and values.

A final important issue is that individuals, especially those who attempt to move beyond the identification as patients, no longer suffer symptoms and perceive CHD as a distant experience of no grave importance to their current life. They reduce emphasis on the health condition in their attempts to make meaning of quality of life at 12 months; in other words they focus on the broader concept of QoL rather on the narrower notion of HRQoL. This points out that they do not necessarily conflate HRQoL and QoL, suggested in the literature, but redirect attention to other broader issues.

8.3.2 How do aspects of the disease experience after CR and meaning-making processes inform individuals' perspectives on their HRQoL?

8.3.2.1 Individuals' experiences of CR treatment and satisfaction

Some individuals through their subjective evaluations especially those treated with CABG demonstrated a low level of satisfaction with treatment and medical care compared to patients treated with PCI. Individuals' accounts support these findings by expressing that CR might be a simple process, but, being in need of and receiving medical care can be a very traumatic experience. Feelings of fear, frustration, loss of dignity and helplessness can arise due to distant and/or insensitive treatment by the medical/nursing staff (e.g. limited or absent information, lack of empathy). For patients treated with PCI, whose hospital stay is only a few hours or a day and interaction with hospital staff is limited, negative feelings and dissatisfaction are of short duration. For CABG patients whose treatment is more complicated and who need more hospital care the negative feelings might be long lasting, influencing their experience and level of satisfaction negatively. These findings are consistent with earlier research showing that limited information, poor communication (Shiloh et al., 2014) and authoritarian or cruel behaviour on the part of medical staff can elicit unpleasant feelings and challenge patients' emotional well-being as well as levels of satisfaction with medical care (Baillie, 2009; Lekidou, Trivellas & Ipsilandis, 2007; Parker et al., 2007; Thorne et al., 2013).

On the other hand, as the quantitative results indicated, patients with a family history of CHD especially those treated with CABG indicated increased satisfaction with treatment. This may reflect a reduced attention to communication aspects as they may view CABG as a more appropriate treatment due to their CHD history, which is a risk factor for disease progression and likelihood of a heart attack as mentioned in their narratives; an issue that due to lack of further research evidence needs greater exploration.

8.3.2.2 Individuals' views of their overall HRQoL one year after CR

Most individuals' subjective evaluations suggested a better overall HRQoL 12 months after CR compared to that prior to treatment. This claim is supported by both the quantitative and qualitative studies reported in this thesis, providing further support for existing research evidence (e.g. Blankenship et al., 2013).

The qualitative findings suggested that this change, however, is not solely connected with the CR treatment, but also with the cognitive process that people underwent as a result of their experience (both disease and treatment). Their experience triggered a shift in the way they view themselves and life. In effect, they experience changes in aspects of self and the meaning of living a good life, leading to positive growth. Based on individuals' accounts they experienced an increased appreciation of life and every day simple things, a sense of personal strength, and a willingness to build more meaningful interpersonal relationships.

These points are in line with other research findings demonstrating that many patients view CR treatment as a turning point in their lives (Höfer, Doering, Rumpold, Oldridge, & Benzer, 2006; Peterson, et al., 2010) because it triggers many changes in individuals' understanding of living a good life and personal strength (Abbasi et al., 2014; Tolmie et al., 2006; Waight, Strodl, Sheridan, & Tesar, 2015). In terms of theory, all these positive changes are in line with the Post–Traumatic Growth model (PTG) which suggests that, after facing a life threatening event, people tend to experience positive changes (Tedeschi & Calhoun, 1996). The positive growth concept may also provide some explanation of female non-smokers' overall greater increase in their perceptions of HRQoL. A recent meta-analysis (Vishnevsky, Cann, Calhoun, Tedeschi, & Demakis, 2010) showed that females after a crisis (e.g. surviving CHD) tend to experience greater positive growth compared to males. Taking into consideration the suggestions in the literature that PTG is positively related to individuals' HRQoL, this implies a potential adaptive value (Barskova & Oesterreich, 2009). However, the finding of this thesis regarding the predictive value of female sex on HRQoL level of change should be considered with caution until further research clarifies the degree to which sex influences the effect of PTG on HRQoL following CR.

Nevertheless, as the quantitative results showed, also supported by the meta-analysis, the increased functionality following CR tended to decline slightly over the one-year period, although it still remained greater than the baseline level. One possible explanation might be the lack of adherence to doctors' recommendations regarding lifestyle changes, especially regarding physical activity and smoking cessation, which can reduce the effectiveness of treatment (Levesque, Li, & Pahal, 2012). The quantitative analysis showed that few patients quit smoking or, if they do, few maintain smoking cessation, especially when treated with PCI. Results also revealed smoking as a negative predictor of the HRQoL outcome, an issue which is well documented in literature (e.g. Jang et al., 2015). The qualitative findings supported the quantitative results indicating that a number of patients failed to adhere to doctors' suggestions about lifestyle modifications after treatment. The accounts of many individuals highlighted their unwillingness to quit smoking (an issue that will be discussed in greater depth later) or increase their physical activity (e.g. walking). Empirical research demonstrates that individuals without symptoms may perceive their disease as less severe and are less likely to adhere to doctors' advice resulting in a reduction in health (DiMatteo, 2004); issues that will be further elaborated on in the following sections.

8.3.2.2.1 CHD symptoms and physical wellbeing

Individuals' evaluations of their symptoms and physical wellbeing indicated that their CHD related symptoms were improved as well as their physical functioning. This improvement was greater for patients treated with CABG. Many participants' accounts supported the quantitative results and provided further explanation of this finding. As individuals explained, being a CHD survivor elicited a special attention to their body, resulting in a different relationship to it. For many this increased bodily awareness was positive as they experienced a revitalized body while for some others it was negative, mostly due to treatment side effects; as side effects decreased over time their physical functioning increased. Similarly, the literature shows that people experience a bodily rebirth after CR (Abbasi et al., 2014; Astin et al., 2008). However, it should be noted that the accounts of some older participants suggested that individuals may experience a deterioration of their body which might be related to the treatment, but is viewed as a "consequence" that is expected with older age. Thus particular attention should be given to older adults and the influence of the CR on their physical functioning. These findings are in line with previous research evidence (e.g. Hendry & McVittie, 2004; Kleinspehn-Ammerlahn, Kotter-Grühn, & Smith, 2008).

8.3.2.2.2 Psychosocial wellbeing

Participants' evaluations of their psychosocial wellbeing indicated that their psychosocial functioning increased following CR. Many accounts supported these findings, highlighting the interconnection with physical well-being; as participants experienced a bodily revitalization their psychosocial wellbeing increased too. Again participants' narratives suggested that their experience triggered a shift in their prerception of psychological and social aspects of the self. Specifically, individuals modified themselves by becoming more easygoing and consciously avoiding health damaging, pointless, or stressful situations (e.g. easily getting into arguments). Consequently, they modified their relational self by becoming more attached or detached from significant others. As the interpersonal social-cognitive theory (Andersen & Chen, 2002) suggests, the repertoire of relational selves is shaped by the interaction with significant others which, in turn, has an impact on self-definition and behaviour. The path that individuals chose to follow depended mostly on their evaluation of the support offered toward others prior to diagnosis and the way that the others have behaved towards them when they were in need. In line with other research findings (Leegaard & Fagermoen, 2008) many participants mentioned that they felt alone even in the presence of practical support, implying indirectly the lack of emotional support. Most of them, however, may minimize the importance of this need (as they did not state it directly) because of another important need, fundamental to humans, that of maintaining relational bonds (Baumeister & Leary, 1995).

8.3.2.2.3 Sexual wellbeing

A complementary issue that emerged from the qualitative findings was related to individuals' sexual wellbeing. Many participants' accounts suggested that this aspect of self is a vital part of the overall HRQoL for both males and females; an issue rarely explored or measured. Female participants, however, seemed to be more reluctant to discuss issues of sexuality with their doctors. The literature reveals that a healthy sex life is an essential factor in someone's overall quality of life (Steinke & Patterson-Midgley, 1998). Many individuals after a Myocardiac Infarction may experience concerns about sex (e.g. fears related both to sexual functioning and satisfaction (Mosack & Steinke, 2009)) but often are embarrassed to discuss them with their doctors. Furthermore, recent research findings show that very few patients (Mosack et al., 2009), especially females, receive counseling or discuss sexual concerns with medical staff and this is usually a result of their own preference (Abramsohn et al., 2013). Empirical evidence further supports these claims indicating that both doctors (Doherty et al., 2011; Nicolai et al., 2013) and nurses (Goossens et al., 2011; Jaarsma et al., 2010) in cardiology practice rarely address sexual issues with patients. This is either due to lack of time and training in discussing sexual issues (Nicolai et al., 2013) or lack of adequate knowledge and a fear of provoking embarrassment in patients (Goossens et al., 2011).

8.3.2.3 Individuals' understanding of CHD; adjustment and lifestyle modifications

8.3.2.3.1 <u>CHD</u>

Shortly after discharge, many individuals who don't have symptoms or adverse effects deny patienthood and misinterpret their CHD. Participants' accounts suggested that they viewed CR as a permanent treatment of CHD. Thus it could be claimed that they held various inaccurate beliefs regarding their heart condition; as being acute and cured. The findings support research previous evidence suggesting that CHD individuals after CR in the absence of any bodily evidence (e.g. a surgery scar) and lack of symptoms perceive the heart disease as an acute treatable disease denying its chronic nature (Peterson et al., 2010; Astin et al., 2009).

These views on the hand may indicate inaccurate knowledge regarding CHD that should be dealt with tailored interventions aiming to increasing accurate knowledge of CHD. On the other hand, this denial may be an avoidance coping strategy in an effort to minimize disease severity and its impact on the individual's life. In effect this strategy helps patients regain control over their life and reach a sense of equilibrium, as many researchers espousing the Self-Regulation theory would suggest (Cameron & Leventhal, 2003; Leventhal, Leventhal, & Contrada, 1998). This claim, however, needs further exploration as this study did not directly measure individuals' illness representations.

Research evidence (Lin, Wang, Tung, & Furze, 2012) shows that there are many cardiac patients who hold misconceptions (inaccurate beliefs) while some other may hold accurate illness beliefs but intentionally minimize the problem in order to reduce distress level (Platt, Green, Jayasinghe, & Morrissey, 2014).

8.3.2.3.2 *Surviving CHD*

The majority of patients, in either case (misinterpretation of CHD or a strategy to regain a sense of control), have concerns regarding a re-occurrence of their disease or disease progression. As an overall prevention strategy, they understate the reasons for why the disease may have developed in the first place and then they work towards aspects of self and develop various coping strategies to prevent re-occurrence. Specifically, many participants influenced by the medical discourse on the causes of heart disease, especially that of stress and overwhelming anxiety, were critical of their past attitudes and behaviours.

They mainly identified aspects of the self that had caused stress and anxiety and made a constant effort to change demonstrating a remarkable shift in those aspects as mentioned in the previous sections. Some essential everyday coping strategies that were captured in individuals' accounts, relevant to people's adjustment process to regain a sense of control over their lives, were setting boundaries, repressing negative thoughts and emotions, minimising disease influence and comparing their functioning to others with a similar profile (e.g. in terms of age).

These findings support research evidence in the CHD field regarding positive adjustment (Abbasi et al., 2014; Helgeson, 2003; Helgeson, 1999, Helgeson & Fritz, 1999; Peterson et al., 2010; Schröder, Schwarzer, & Konertz, 1998; Tolmie et al., 2006.) as well as Taylor's (1983) cognitive adaptation theory (CAT). As this theory suggests, the adjustment process involves searching for meaning (e.g. what caused the disease? why did this happen to me?), making efforts to regain mastery over the situation (e.g. what I can do to prevent recurrence?) and efforts to restore self-esteem through self-enhancement (i.e. comparison with others of the same status). This research evidence raises concerns regarding the "pure" influence of CR on the life of individuals with CHD without acknowledging the influence of adjustment and positive growth (as mentioned elsewhere).

8.3.2.3.3 *Lifestyle modifications; an emphasis on smoking*

Challenges that participants face in lifestyle modifications are attributed to both external and internal factors. People may experience low self-efficacy when the support of experts is limited. As research demonstrates, self-efficacy is a key component in CVD self-management (Katch & Mead, 2010). Other concepts related to low adherence to doctors' advice seem to be patienthood denial, lack of awareness of the significance of a change, lack of support from significant others, or efforts to maintain certain kinds of pleasure in life. These findings are in line with research evidence in the field of heart disease. Based on a recent review (Murray, Fenton, Honey, Bara, Hill, & House, 2013), social support, education and knowledge, as well as beliefs and emotions were the main issues related to making lifestyle modifications and maintaining a healthy lifestyle.

Regarding smoking the quantitative results indicated that smoking is a valid predictor of lower HRQoL change after CR. However, a great number of individuals did not make any effort to stop smoking and many individuals that tried to quit shortly after treatment, twelve months later experienced a relapse, especially those treated with PCI. Empirical evidence further supports these findings (Tolmie et al., 2006). In fact, individuals after CABG tend to quit smoking permanently while PCI patients are less willing to make or maintain this behaviour modification (Hammal, Ezekowitz, Norris, Wild, & Finegan, 2014). The qualitative findings suggested that smoking cessation is one of the most challenging lifestyle modifications among CHD patients due to lack of accurate knowledge regarding the relationship between smoking and CHD, and lack of support (by experts or family member) as well as due to a conscious decision not to quit their smoking habit not only as a way to cope with anxiety and stress but also as a way to maintain a kind of pleasure in everyday life. In the latter case, as participants who continued to smoke one year post CR suggested, they felt that smoking cessation would be more damaging compared to maintaining their habit. Some participants' quotes alluded that emotional wellbeing might be of greater importance than physical wellbeing and health, while others' narratives implied that smoking may have a positive effect by helping them to control and reduce high stress which can cause problems to their heart muscle. Research evidence in the CHD field (e.g. Kärner, Tingström, Abrandt-Dahlgren, & Bergdahl, 2005) and other chronic diseases (e.g.

cancer; Duffy, Louzon, & Gritz, 2012) support these findings. In light of this evidence, these aspects may be helpful if included in interventions aiming to increase CHD self-management and in particular, smoking cessation.

8.4 Novelty and clinical importance

This thesis contributes new insights of clinical and research importance to the field of cardiac health and health psychology in a number of ways. First of all it provides an updated systematic review with a meta-analysis. This is the first meta-analysis in the field investigating the impact of CR on individuals' HRQoL as well as comparing the impact of different CR treatments (CABG and PCI).

Furthermore, it fills a gap in the Greek literature by validating a robust and scientifically valid and reliable instrument to detect HRQoL and health outcomes after coronary revascularization. Currently the CROQ-Gr is the only disease-specific instrument in the field.

Moreover, the main study, the longitudinal mixed methods study, enables researchers to build a more complete picture about and an in-depth understanding of the HRQoL of individuals with CHD who are treated with CR as well as helps gain a greater understanding of predictors and issues related to the outcome.

Firstly, the quality of evidence is enhanced by combining the strengths of quantitative and qualitative research methods and at the same time, minimizing the weakness of each (Curry et al., 2009) and by using robust methods for data collection (e.g. use of a valid and reliable disease/treatment specific instrument, with data collected at multiple time points) and data analysis (e.g. multilevel modelling and interpretative phenomenological analysis). Secondly, the final integration and interpretation of findings helped not only to portray more holistically patients' perspectives of their HRQoL following CR, but also gain complementary insight by a) revealing factors rarely investigated (e.g. sexual issues) or issues rarely explored (e.g. positive growth) in the CHD field, b) providing possible explanations and highlighting various issues detected in the quantitative component (e.g. the true effect of CR on individuals' perspectives of their HRQoL), c) capturing the complex process that individuals undergo in order to make sense of their life, d) demonstrating some of the process of decision-making about everyday life style modification (e.g. smoking), and e) portraying some needs that should be addressed either by further research or tailored interventions.

Overall, the present thesis informs the fields of heart disease and health psychology by building upon the existing literature and offering a deeper understanding of how individuals who undergo CR assess and make sense of their lives one year after treatment. It is the first study in this area capturing individuals' points of view following both CR types (CABG and PCI) one year post treatment with mixed methods. The findings can help health professionals to promote the best therapeutic regimen in daily practice and facilitate transition, rehabilitation, as well as secondary prevention.

8.5 Limitations

Even though the researcher made efforts to enhance quality, a number of limitations should be considered.

Regarding design, in the present thesis a sequential explanatory mixed methods design was employed. However, taking into consideration the variation of individuals' HRQoL at baseline, the incorporation of a qualitative study at baseline could be useful to better understand illness representations as findings already suggest that perceptions of illness affect how individuals identify as patients and consider their quality of life. Also, the use of focus groups in the CROQ translation phase could provide some sense of consensus on the topics, which could supplement individual input and would be less time-consuming.

Concerning the participants, the sample is not very large (<300 participants per type of CR) and not random. The majority of individuals were residents of Athens. This may have affected the results as people living in rural areas may have demonstrated different HRQoL levels at baseline or 12 months post treatment, affecting the overall effect size and thus conclusions. A recent review (Smith et al., 2008) of many developed countries all over the world has shown that rurality in and of itself is not directly related to rural-urban disparities, but may be a sign of individuals' greater levels of unhealthy behaviours, a lower tendency to look after their health (especially due to lack of confidence) or access to health services. Also, although efforts were made to reduce biases, due the nature of the study social desirability bias might be present (Streiner & Norman, 2008).

None of the patients participated in a rehabilitation programme, so this variable cannot have affected the findings. However, many patients treated with CABG in contrast to PCI had at least one session with a health professional, usually a health or clinical psychologist, prior to hospital discharge. This may have created differences in individuals' meaning-making of their experience, adjustment and lifestyle modification. Thus, this might have caused variation in individuals' evaluation of HRQoL one year post treatment. Even a 60 minute well-structured psychoeducational session may positively influence QoL (Phillips et al., 2004).

Also, for the qualitative study it could be claimed that as individuals underwent different types of CR, the sample violates the rule of homogeneity. The decision to treat the participants as one group served the purpose of avoiding a pre-defined differentiation of experiences of quality of life in terms of CR procedure. Furthermore, the lack of triangulation (using more than one method, e.g. focus group) during data collection could be mentioned as another limitation of the present study; only in depth semi-structured face-to-face interviews were employed for data collection. However, this claim can be challenged since triangulation in data collection might violate the idiographic aspect of IPA, which primarily aims to explore an individual's experience (Smith et al., 2009).

Regarding measurement issues, a full clinical record of how many arteries had been revascularized was not obtained. This information was requested from patients. However, as there were instances where patients didn't know, this information was not included in the analysis. The literature suggests that individuals with multi-vessel coronary heart disease have fewer symptoms and greater HRQoL post CABG compared to those treated with PCI (Abdallah et al., 2013). Furthermore, the clinical record questionnaire used in this study cannot be viewed as rigorous and might be challenged in terms of its accuracy as it makes use of a single dichotomous item for capturing relevant information. Single and/or dichotomous items, as the literature suggests are not the best way to capture such information (Gregory & Radovinsky, 2012; Streiner & Norman, 2008). Moreover, time since diagnosis was not captured. Although such information might not be always known (e.g. for individuals undergoing PCI), a record would be helpful in order to investigate its predictive value. Finally, response shift (Schwartz et al., 2007) was not measured. An effort to capture changes in the way that CHD individuals evaluate their HRQoL would be beneficial; as the study's findings revealed various factors related to adjustment and positive growth may influence their interpretation and would allow to build a clearer picture of the contribution of CR to CHD individuals' perspectives regarding their HRQoL.

The literature highlights that important factors may be ignored and can influence the true effect size of a treatment (Ring, Hofer, Heuston, Harris, & O'Boyle, 2005). In order to address such issues, a number of scholars suggest that quantitative researchers should make use of both disease-specific and generic measures (e.g. Walters, 2009) for more accurate results especially when the research sample may have multiple morbidities. Thus, it might be beneficial, in addition to the CROQ-Gr, to use a generic measure such the WHOQOL-BREF **(**Ginieri-Coccossis, Triantafillou, Tomaras, Soldatos, Mavreas, & Christodoulou, 2011) which captures the broader (global) QoL as it measures environmental, spiritual, independence and sexual aspects of QoL beyond the physical and psychosocial ones. After all, as the findings of the mixed methods study suggest many individuals one year after CR tend to focus more on their QoL rather on their HRQoL.

Finally, regarding the qualitative analysis, as this was the first attempt by the researcher to employ IPA (Smith et al., 2009), her lack of prior experience may have affected the findings. However, the researcher's commitment to IPA guidelines on the one hand and the constant supervision and the involvement of an external researcher in reviewing the analysis process on the other, minimized the researcher's weakness and possible misinterpretations.

8.6 Implications

8.6.1 For theory

The thesis findings support the notion that HRQoL can be defined by the biopsychosocial approach as described by Engel (1980) and the World Health Organization (WHOQOL group, 1993). Individuals make sense of their quality of life by evaluating their physical, psychological and social wellbeing all of which are interrelated. Furthermore, HRQoL cannot be perceived as a static concept but rather as fluid. People tend to change their point of view in an effort to adjust to their life conditions and alter their internal standards, values, and needs as well as expectations. Finally, HRQoL in the field of CR should include sexuality. In fact, as the WHO group (2006) suggests, sexuality is a core aspect of human life and is interconnected with physical, psychological, mental and social well-being. Thus, sexuality should not be viewed as a distinct concept but rather as an aspect of quality of life (Steinke et al., 2013) and so it should to be included in research of both HRQoL and QoL.

Furthermore, the findings of this thesis provide some support that HRQoL is related to Leventhal's Self-Regulation Model (SRM (Leventhal, et al., 1980)); although illness perceptions are not directly measured, the qualitative findings support such claims. Briefly, the model suggests that when a threatening event is present (in this case the presence of CHD) individuals' "status quo" becomes unbalanced and, therefore, they are internally motivated to undergo a problem-focused procedure in order to regain a sense of balance. The first stage is to make sense of a problem (interpretation of threat's representation; "illness beliefs"), the second one is to find ways to deal with it (coping) and the final is to assess the effectiveness of coping. As has been captured in the qualitative study, one aspect of making sense of their lives is the evaluation of the disease. This evaluation includes its causality, its time line (acute vs chronic), the severity of consequences, its curability and their control over it. Based on this evaluation patients maintain or deny their patient identity as well as develop strategies to prevent disease re-occurrence and to gain a sense of equilibrium. This process is aligned to the self-regulatory theory. Research evidence, in the field of CR suggests that positive illness perceptions are significantly correlated to and predict better QoL (Foxwell, Morley, & Frizelle, 2013).

Moreover the findings of this thesis support the concepts of perceived benefits and post-traumatic growth (PTG) following heart disease and revascularisation. These concepts refer to individuals' experience of positive changes in response to challenging traumatic events or life crises. PTG is an ongoing rather than a static process influenced by life span wisdom (Tedeschi & Calhoun, 1996). It is not the traumatic event itself, but rather the experience that motivates individuals to "re-build" their lives (Tedeschi & Calhoun, 2004). PTG's most evident manifestations are related to increased life appreciation, increased sense of personal strength, changing priorities, more meaningful interpersonal relationships, and a richer spiritual life (Tedeschi & Calhoun, 2004). Although perceived benefits and PTG are understudied in heart disease, the limited literature, mostly with patients after a heart attack (Affleck, Tennen, Croog, & Levine, 1987; Garnefski, Kraaij, Schroevers, & Somsen, 2008; Hassani, Afrasiabifar, Khoshknab, & Yaqhmaei, 2009; Petrie, Buick, Weinman, & Booth, 1999; Bluvstein, Moravchick, Sheps, Schreiber, & Bloch, 2013; Leung et al., 2010; Sheikh, 2004), reveals that individuals experience positive changes after the challenging event. Waight et al. (2015), exploring PTG in fifteen post-CABG patients found that individuals experience cognitive growth following CABG. Patients' accounts revealed a greater appreciation of life (i.e. living the moment without worrying about the future) and recognition of new possibilities for adopting a healthier lifestyle. Research findings (Barskova & Oesterreich, 2009) of studies on people with chronic disease including heart disease demonstrate a positive association between HRQoL and PTG. The limited research in the field of cardiac patients treated with coronary revascularization shows evidence about the relationship between PTG and HRQoL. For instance, Leung et al.

(2010, 2012) found that individuals who experience PTG have a greater psychological functioning, and females experience a greater PTG compared to men. Also Ai et al.'s (2013) findings demonstrated that CABG survivors with an increased spirituality (an aspect of PTG) had better HRQoL.

8.6.2 For practice

Regarding practice, this study provides novel findings, it also adds weight to the field of cardiac health.

Regarding clinical practice within hospitals, the communication skills of medical staff should be enhanced. The findings of the thesis suggest that being in medical care might be very frustrating. Participants complain about inappropriate confrontation by staff (doctors and nurses) as well as limited interaction which results in feelings of helplessness and loss of dignity. A more patient-centered approach would be helpful to overcome such issues. According to research (Frankel, 1995; Ha & Longnecker, 2010), the most essential skills to promote hospital staff-patient communication are active listening, empathy and support. Active listening to individuals' concerns and needs for information to increase control, satisfaction, self-efficacy; Appropriate genuine interest and cognitive understanding to enhance trust and commitment to treatment; Attending to concerns over shame and humiliation to minimize loss of dignity.

Regarding practice after discharge, rehabilitation teams should keep in mind that individuals try to adjust by re-evaluating the self. This process can be extremely difficult raising a variety of negative feelings. As patients give primacy to the psychological self, they develop various coping strategies to minimize the impact of the disease. This in turn may result in denying patienthood and conscious avoidance of changes in behaviour, especially those they may perceive as a threat to their emotional well-being. Therefore, health professionals should place particular emphasis on exploring individual adjustment processes based on the SRM (Cameron, & Leventhal, 2003) and CAT (Taylor, 1983).

Furthermore, emphasis should be given to interventions based on the SRM (particularly in relation to adherence) and to test the extent that they are effective. According to participants, illness beliefs may shape their attitudes and behaviours. Thus, interventions based on this model are likely to be effective. In fact, a recent study (Duncan et al., 2014) aiming to improve middle aged males' physical activity and healthy eating demonstrated that simple smartphone interventions based on SRM (e.g. messages addressing inaccurate beliefs) are effective to achieve their goals.

Also, the findings regarding CHD individuals' positive growth might be useful to health professionals in promoting PTG (Tedeschi & Calhoun, 1996) in order to reduce distress and promote well-being in individuals with a cardiac disease.

Moreover, social support, especially the emotional aspect seems to have a reinforcing power on individuals maintaining a change, as suggested by participants' accounts. Thus specific interventions targeting family members should include coaching on emotional support and then examine their effectiveness.

Findings also demonstrate the need to establish a multidisciplinary team in cardiac health care settings. The role of a health psychologist, sex therapist and dietician will boost best practice and quality of patients care. As many participants stated "psychology is the a and z" (the be-all and end-all), health psychologists trained in health communication and qualified in behaviour change could help to reduce both pre-operative and post-operative negative feelings. This is especially the case for sexual activity which, as stated by participants, is an important aspect of life and is often influenced by the fear that sexual activity may damage the heart and provoke recurrent events. According to a literature review by Steinke (2015) of 20 published studies between 2000 and 2011 sexual intercourse is poorly associated with myocardial infarction (MI) or arrhythmia, and sexual counselling can assist patients to maintain (or regain if lost) their quality of sexual life.

Additionally, health professionals supporting smoking cessation in cardiac patients should include cognitive and behavioural techniques that decrease anxiety and stress. Based on the findings of the present study, individuals after CR continue or restart smoking to control anxiety and maintain a kind of pleasure in their life. Also, interventions for smoking cessation in CR populations should include a long-term follow-up as many individuals relapse after the first 3 months of cessation. As researchers suggest, cigarette smoking should be perceived as a chronic relapsing behaviour, and cessation may need a long-term approach (Rennard, & Daughton, 2014).

8.6.3 For research

Concerning research, the present study highlights that quality of life cannot be captured solely by quantitative measures as each individual may experience the same phenomenon in a different way; the qualitative research paradigm should be adopted too. Thus, in the field of HRQoL research mixed methods studies should be conducted to maximize insight.

The CROQ-Gr was rigorously validated and should be used in the field of coronary revascularization. However, the development of a shorter version could be very helpful for reducing respondent burden and increasing data quality (Bowling, 2005), especially when research aims to explore many related issues (e.g. personality, mood) and thus may use many instruments. As has been observed in the present study, participants, although willing to give their opinion and participate, did not like to devote a lot of time to it. For instance, when they had to complete more than one questionnaire (e.g. for concurrent criterion related validity), a large number of individuals left the second instrument incomplete. Even with phone contact, when contact exceeded twenty minutes their reluctance and tension was obvious by giving sharp and monotonous replies (e.g. “not at all, not at all, not at all”). Furthermore, adapting the CROQ-Gr to be relevant to other CR procedures such as MIDCAB or robotic CR would allow investigation of the impact of these treatments on patients’ well-being in line with recent medical developments. Also, an investigation of alternative modes of administration is needed in order to increase the utility of the CROQ. The development and testing of different forms of administrations such as online or via a smartphone might be useful. An online form could increase participation, especially in post-revascularization follow-ups, of patients with physical or time restrictions, as an online form can be completed from any location and at any time as long as the patient has access to the internet. The expansion into smartphone administrations could help doctors get an instant picture of their patients’ HRQoL in everyday practice, avoiding time-consuming calculations, or else help researchers to get instant snapshots of each subdomain of HRQoL.

Moreover, more high quality longitudinal studies including patients form both CR types with large samples using disease-specific instruments are needed in order to draw confident conclusion about predictors of HRQoL following CR. As suggested by experts (Downs & Black, 1998; CASP, 2013; Noyez et al., 2011), researchers should design and conduct their study meeting a variety of criteria such as address a clearly focused issue; use valid and reliable measures; consider confounding factors; make efforts to minimize bias; take into account losses of patients to follow-up; use appropriate statistical tests to assess the main outcomes; and obtain a long enough follow up (at least 12 months in CR).

Furthermore, longitudinal studies should use both disease-specific HRQoL instruments and generic instruments. As individuals tend to deny patienthood in the long term and consider QoL that is not “health related”, a generic instrument could capture broader aspects of QoL.

Also, in order for longitudinal studies to allow a clear conclusion about predictors of short and long term HRQoL after treatment, more potential moderators should be examined. For instance, medical (e.g. angina severity, number of vessels revascularized, type of diabetes), behavioural (e.g. adherence to medication, diabetes management, obesity, alcohol use) and psychological (e.g. personality, illness representations, mood, stress) factors could be assessed to identify their predictive value.

Moreover, as the present study’s findings show, in the absence of side effects individuals focus on other pre-existing problems. Consequently, other stressful events should be investigated since they also seem to have an influence on individuals’ understanding and perceptions about their quality of life. Future research may include attention to retrospective accounts of how people define and experienced a good life before CR as well as after CR as this study focused on the latter only. This would provide a greater insight into changes in subjective experience.

Researchers should pay attention to the individual’s stage of life. Although quantitative research evidence about changes in HRQoL following CR suggest no effect of age (Barolia et al., 2012; Gjeilo et al., 2012; Merkouris et al., 2009; Li et al., 2012), the qualitative study’s findings demonstrate that age may play an important role in individuals’ perception about their quality of life. They may experience living a good life not due to the beneficial effect of CR upon their life but due to their view that heart disease or side effects of treatment are life problems and are to be expected with older age (Hendry & McVittie, 2004).

Yet, as the qualitative study findings revealed HRQoL might be tied up with illness representation. Future research might usefully include a questionnaire measuring individuals' illness beliefs and their change over a one-year period to detect changes in HRQoL.

Another related topic that would be useful to be investigated is the relation between SRM (Cameron & Leventhal, 2003), PTG (Tedeschi & Calhoun, 1996) and HRQoL in patients after coronary revascularization as present thesis findings imply some connection, though not directly measured or explored. To date, there is a dearth of literature on this topic. Among the very few researchers that investigated such a connection were Leung, and colleagues (2010). Their findings suggested that PTG was related to increased psychosocial functioning and lower physical functioning. Also PTG was greater for CHD individuals' holding positive illness perceptions and a sense of control over it. Thus further research on this area would be helpful to build a better understanding.

Further qualitative research should be carried out focusing on exploring individuals' coping strategies, challenges in post-CR life (especially in terms of adopting a healthy lifestyle) as well as PTG as these aspects are poorly explored in CR. These efforts might be very rewarding as they can guide health professionals in designing and implementing tailored interventions that would prolong the beneficial effect of CR on individuals' quality of life.

Finally, an interesting issue to be investigated would be how well prepared health professionals working in smoking cessation are to cope with smokers with heart disease that deny patienthood, or those who believe that continuing to smoke is better than being stressed.

8.7 Final conclusion

The current thesis aimed to explore Greek CHD patients' perspectives of their HRQoL following CR (Coronary Artery Bypass Grafting (CABG) or Percutaneous Coronary Interventions (PCI)), as well as detect and explain individual disparities. In order to achieve these aims a series of studies were conducted. The main study of the thesis was a longitudinal mixed methods study, following a sequential explanatory design. The synthesis of findings highlighted the benefits of using a mixed methods longitudinal design in exploring HRQoL. Both quantitative and qualitative findings support the notion that HRQoL is a multidimensional, continuingly changeable concept providing support for the World Health Organization's definition. Also, they support the assumption that CR has a positive influence on individuals' HRQoL. The effect of CR type needs further investigation as mixed findings were revealed in the present thesis. The pure effect of CR on individuals' HRQoL seems difficult to investigate without taking into consideration individuals' adjustment processes and positive growth triggered by the CR.

The Self Regulation Model (SRM) might be considered a useful theoretical framework for developing theory-based interventions aiming to alter patients' false beliefs since individuals' making-meaning process seems to be aligned with it. Finally, the complementary insights concerning smoking (a factor associated with poorer mean change in HRQoL level over a one year period) may help health care providers to develop smoking cessation interventions tailored to cardiac patients.

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Appendices

1.1 Personality type and CHD

In terms of personality, a lot of discussion has taken place for types A and D as potential risk factors for coronary heart disease. Type A personality (TAP) is characterized by an excessive drive, time urgency, and hostility. Empirical data have provided mixed evidence for the association between type A and CHD. For instance, Schwalbe (1990) reviewing five studies concluded that there is a relationship between TAP and the development of CHD, although two out of the five studies did not demonstrate any such evidence. Kawachi et al., (1998) found that TAP can predict CHD incidence if the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) is used. On the other hand, a systematic review (Myrtek, 2001) of 25 studies has suggested that type A personality cannot significantly predict CHD development. This shift in research evidence about the relation between TAP and CHD could be partly explained by early researchers' desire to demonstrate evidence in favour of their theory and employing less stringent methods. In addition there are explanations suggesting that the cardiologists Friedman and Rosenman developed the Type A Behaviour Pattern (TABP) back in the 50's in order to minimize research findings about the relation between tobacco use and the development of CHD (Petticrew, Lee, & McKee, 2012); in other words suggesting an attempt to direct attention to a cause of CHD other than smoking. This claim (Petticrew et al., 2012) is supported by evidence that all related research and supportive findings of the relationship between TAP and CHD were produced by studies (e.g. The Western Collaborative Group Study, 1974) conducted by the two fathers of the theory or fellows funded by the "Philip Morris" tobacco industry.

1.2 CHD treatment

1.2.1 Medical therapy (MED)

One approach of treatment for CHD is the pharmacological therapy (the term “medical” refers to medication and it is adopted in order to be consisted with literature on CHD). Medical therapy for angina pectoris includes five categories of drugs: beta-blockers, calcium blockers, nitrates, aspirin and other antiplatelet drugs, and antilipid drugs. Most of these drugs act by dilating the coronary arteries and as a result improve the supply of blood and oxygen to the heart muscle, which in turn reduces the blood pressure and heart workload. Sublingual glyceryltrinitrate (GTN) is the standard treatment for immediate symptom control. GTN is used during an angina attack or prior to a task which might induce an attack. It is taken under the tongue as a tablet, where it is quickly absorbed to provide fast symptom relief. Medical therapy (MED) for angina can be used successfully to treat some patients for many years. In fact, many studies maintain that for stable angina in a low risk cardiac population modern medical therapy could be equally effective as coronary revascularisation (Deedwania, Carbajal, & Bobba, 2007; Prasad, Rihal, & Holmes, 2008).

Furthermore, there is some evidence, even though not consistent throughout the literature, that even after coronary revascularization, medication may be necessary for reducing the atherosclerotic process and prevent death (Filion, Pilote, Rahme, & Eisenberg, 2007; Jaber, et al., 2005) or myocardial infarction (Jaber, et al., 2005).

1.2.2 Coronary Revascularization

1.2.2.1 PTCA/PCI

Percutaneous transluminal coronary angioplasty (PTCA) was introduced in 1977 by Dr Gruntzig and his colleagues as an invasive (nonsurgical) method of coronary revascularization (Holmes & Williams, 2008). It is used in order to open the blocked artery. It involves cardiac catheterization (the insertion of a fine tube into a vein in the groin or sometimes in the arm, then through the coronary artery and across the blocked section). A balloon placed at the end of the catheter is inflated to widen the vessel disrupting the material blocking it (usually asa result of atherosclerosis). Then, the balloon is deflated and removed, resulting in an enlarged artery through which blood can flow to the heart muscle. PTCA is carried out under local anaesthesia and patients are mobile the following day. Usually this process requires a brief hospital stay not exceeding 36 hours. The main short-term adverse effects from catheterization are symptoms such as pain, tenderness and bruising at the wound area. Long-term negative outcomes consist mostly of restenosis (artery re-blockage due to atherosclerosis) causing approximately 30% of patients having to undergo the procedure again (Bittl, 1996).

Within less than a decade (Holmes & Williams, 2008) a new method was developed in response to this problem: implanting intracoronary stents (bare metal stent, BMS) during PTCA. Stents are tiny metal tubes that are delivered by a catheter at the narrowed area in order to keep the artery open, thus preventing the collapse of the vessel and reducing the likelihood of restenosis or regrowth of atherosclerosis. In fact, results from clinical trials showed that coronary stenting significantly reduces restenosis (e.g. from 35% of incidences of restenosis after PTCA balloon treatment to 19% after angioplasty with stent (Mercado, et al., 2001)) and improves clinical outcomes by minimizing the major adverse cardiac events and repeated revascularization (Agostoni et al., 2006).

Although coronary restenosis after the insertion of a stent is reduced dramatically, the problem still exists (Butany, Carmichael, Leong, & Collins, 2005). The primary cause for the stenosis of a stented artery could be attributed to the neointima (Hoffmann et al., 2001). The neointima refers to a new thin tissue that can be formed on the stent. Stent design, surface material, and vessel damage related to the procedure have been implicated as predictors of neointima proliferation (Hoffmann, et al., 2001; Kastrati et al., 2000). To overcome this problem, intracoronary brachytherapy was developed (Sheppard, Eisenberg, Donath, & Meerkin, 2003).

Manufacturers have tried to create Drug-Eluting Stents (DES) to cope with neointima. Nowadays, many drug-eluting stents are either in use ordeveloped. Current research findings indicate that drug eluting stents decrease the rate of restenosis from 31.7% to 10.5% with bare metal stents (Roiron, Sanchez, Bouzamondo, Lechat, & Montalescot, 2006). DES seem to be extremely beneficial at least in the short term. Research evidence highlights that without being more harmful than BMS (James et al., 2009; Morice et al., 2002), DES can be very useful in addressing neointima, especially for patients with a higher likelihood for restenosis (e.g. patients with diabetes (Kumbhani, Bavry, Kamdar, Helton, & Bhatt, 2008)) or with relatively small vessels (Douglas & King, 2007) and those of older age (Douglas et al., 2009). Dibra et al. (2007) suggest that DES is a more effective type of treatment for those patients with incidents of bare-metal in-stent stenosis.

All these changes and improvements have had an influence on the naming of treatment procedures as well. Rather than PTCA, the non-surgical procedures (no matter whether it is a balloon angioplasty or stent implantation, bare metal stent or drug eluting stent) are now referred to by the broader term Percutaneous Coronary Intervention (PCI). Therefore, this latter term has been adopted in the current thesis and will be used from now on to refer to all types of non-surgical revascularisation procedures.

In summary, many novel methods have been introduced in the domain of non-surgical coronary artery treatment. Each one has its own advantages and disadvantages. However, all procedures have some possible consequences such as myocardial infarction.

1.2.2.2 CABG

The first Coronary Artery Bypass Grafting (CABG) was performed by Goetz, Rohman and their colleagues in 1960 (Mueller, Rosengart, & Isom, 1997). For many years, CABG was the established surgical method for the treatment of CHD (reducing angina and mortality rates). However, after the introduction of PCI, CABG was performed only for severe CHD. The mainstream CABG involves an opening in the chest bone (sternoctomy), which gives the cardiac surgeon adequate access to the heart. During this process, it was (and sometimes still is) necessary to stop the heart beating and the flow of blood through the heart and lungs. A heart/lung bypass machine artificially takes over the heart's job of pumping and the lungs' job of breathing; this procedure is known as on pump CABG or as cardiopulmonary bypass surgery (CPB). Arteries or veins (usually from the patient's leg or arm) are used as a graft which is attached to the aorta, the main blood vessel of the heart, and to the coronary artery to bypass the blockage.

Due to the nature of the CABG procedure, full recovery can take a long time. The majority of patients are discharged about five days after the operation (Peterson, et al., 2002). Patients are usually advised to stay at home for one month after surgery, a recovery period allowing their wounds to heal. Around 3 months after CABG, most patients are expected to minimally have returned to their pre-surgery level of functioning. However, patients have reported recovery problems after the specific surgical procedure that may be present for a long time after discharge. For instance, many patients report pain, haematoma and infection in their leg from where the veins were removed to be used as grafts, although this has been reduced with the use of a new less invasive method for vein harvesting (Athanasiou, et al., 2003; Khan, et al., 2010; Markar, Kutty, Edmonds, Sadat, & Nair, 2010). Moreover, a great number of patients, especially those with diabetes or who are obese, show deep chest wound infections (Olsen, et al., 2002). Deep sternal infection can result in a longer hospital stay or increased mortality rates (Fowler et al., 2005; Steingrimsson, Gottfredsson, Kristinsson, & Gudbjartsson, 2008; Toumpoulis, Anagnostopoulos, Derose, & Swistel, 2005) as well as psychological distress (Taillefer, et al., 2006). This last outcome could be explained, firstly, by the fact that people with post-surgery chest pain experience greater levels of anxiety and depression (Taillefer, et al., 2006). Secondly, this relates to the fact that some infections, such as media stenitis, can cause chest pain, shortness of breath and dysphoria (Park, & Vallires, 2005), symptoms identical to angina that had patients undergo CABG in the first place. Patients may misinterpret the sternal discomfort due to inflammation as the pre-CABG angina pain and become distressed, fearing a failed operation.

In short, research demonstrates several adverse postoperative outcomes following CABG. These include: mortality, myocardial infarction (Kendel, 2009), chest wall pain (Lahtinen, Kokki, & Hynynen, 2006) fluid retention and peripheral oedema, leg wound pain and inflammation, heart block, pulmonary oedemas and acute lung injury, deep vein thrombosis, pulmonary embolism (Kendel, 2009), sternal wound infections (Salehi-Omran et al., 2007), atrial fibrillation (Halonen, et al., 2007; Mathew, et al., 2004; Prasongsukarn, et al., 2005), and more rarely neuro-ophthalmological complications (Shaw, et al., 1987; Thurtell, Besser, & Halmagyi, 2008), and gastrointestinal complications (GIC) (Andersson, Nilsson, Brandt, Hoglund, & Andersson, 2005; Yoshida et al., 2005; Zhang, et al., 2009).

Another negative outcome after CABG mentioned by many experts concerns neurocognitive impairment; yet, this remains controversial. Cognitive impairment after CABG has been mentioned as a common adverse event (Funder, Steinmetz, & Rasmussen, 2009; Liu et al., 2009; Newman et al., 2001), especially longitudinally (at 5 years (Stygall et al., 2003)). A systematic review conducted by van Dijk and his colleagues (2000) showed that 22.5% of patients who underwent cardiopulmonary bypass experienced cognitive declines. According to the particular review, cognitive impairment includes short-term subtle cognitive deficits, such as problems with short-term memory, concentration, attention, new learning, thinking clearly, processing information, and making decisions as well as major neurological complications, like stroke. However, there are a number of studies showing that there is some cognitive decline but it does not differ significantly between patients who underwent surgical revascularization and non-surgical patients, both at 3 year (Selnes, et al., 2007) and 6 year follow-up (Selnes, et al., 2008). An explanation for these conflicting results might be the difference in methodology adopted in each study (e.g. lack of control group or preoperative measurement such as dementia) and the age of the sample. For instance, in studies that have recruited an older age group and followed up for several years cognitive decline might be present due to the normal aging process and progression of cerebrovascular disease and not due to CABG (Selnes, 2008).

In response to such negative clinical outcomes produced by on pump CABG, a new process has been developed where CABG is performed directly on the beating heart without the use of a cardiopulmonary bypass, via a median sternotomy. Nowadays, this procedure is known as off pump CABG or OPCAB and it is globally used in approximately 1/3 of patients (Stavridis, 2006). However, the literature is inconsistent concerning the superiority of the off-pump vs on-pump cardiac surgery. A number of meta-analyses and reviews suggest that this new procedure in cardiac surgery has reduced the number of hospital days and incidence of atrial fibrillation (Bainbridge, Martin, & Cheng, 2005; Moller, Penninga, Wetterslev, Steinbruchel, & Gluud, 2008; Sedrakyan, Wu, Parashar, Bass, & Treasure, 2006) but has not lessened the postoperative rates of stroke or myocardial infarction or mortality compared with on-pump CABG (Angelini et al., 2009; Bainbridge, et al., 2005; Chu et al., 2009; Feng, Shi, Zhao, & Xu, 2009). Others maintain that the main benefit of off-pump CABG is a reduced incidence of stroke in high risk patients (Abu-Omar, & Taggart, 2009). Some meta-analyses and recent studies maintain that retrospective analyses support the notion that off pump CABG improves mortality and lessens the incidence of adverse events (Halkos & Puskas, 2009; Serrano et al., 2010; X. Sun et al., 2009)**.** Yet other researchers conclude that there is no difference between the two procedures concerning health outcomes or mortality in either low or high risk patients (Angelini, et al., 2009) in annual follow-ups (Shroyer, et al., 2009). However, there is one issue on which the majority of recent studies seem to agree. Patients treated either with on or off pump CABG do not differ significantly in long-term neurocognitive impairment (e.g. one to 5 years after surgery (Marasco, Sharwood, & Abramson, 2008; Shroyer, et al., 2009; Stroobant, van Nooten, De Bacquer, Van Belleghem, & Vingerhoets, 2008)).

Advances in cardiac surgery have resulted in the development of a novel surgical method for performing CABG using smaller incisions which do not require the use of cardiopulmonary bypass or median sternotomy, known as minimally invasive coronary artery bypass grafting (MIDCAB). In such procedures, the surgeon operates directly on the beating heart through a small (6-8 cm) incision in the chest (Benetti, et al., 2010; McGinn, et al., 2009) although the incision might be slightly larger for certain patients (e.g. in obese patients). Research evidence suggests that this new surgical technique is effective in increasing survival rates and in minimising major adverse cardiac and cerebral events both in the short-term and long-term (Holzhey, et al., 2007). It involves significantly fewer wound infections but there is no major difference in postoperative hospital stay (Markar, et al., 2010).

Advances are ongoing and yet another new procedure has been introduced known as totally endoscopic robotic cardiac surgery (TECAB). Although research is quite limited on this, there is evidence that patients treated with this process with either off-pump or on-pump approaches show a significant reduction in major adverse cardiac events (MACE) 6 months after surgery. Findings suggest that the incidence of major adverse cardiac events is quite low, up to 5% (de Canniere, et al., 2007), and restenosis is present in a few patients only at three-month follow-up (Folliguet, et al., 2010).

In summary, a lot of advances have been made in the domain of surgical treatment of coronary artery disease. Each of these has advantages and disadvantages. New techniques, such as TECAB, seem promising for greater effectiveness with less adverse effects but further research needs to be carried out in order to be able to draw clear conclusions.

2.1 Instruments widely used to measure HRQoL in the Coronary Revascularization field

There are a plethora of self-administered measurements that are widely used in the field of HRQoL research (Bowling, 2005). In the following paragraphs, generic and specific HRQoL measures related to CR will be introduced in order to present the most frequently used measures as well as their approach to the concept, by highlighting their constitutive domains.

Generic measures

SF-36 & RAND-36

The SF-36v2^{TM} Health Survey is the most widely used questionnaire for measuring QoL. The SF-36 is a valid and reliable scale (Ware, 2000; Ware, Keller, Gandek, Brazier, & Sullivan, 1995; Ware & Sherbourne, 1992) translated successfully into many languages (e.g. Chinese (Li, Wang, & Shen, 2003); French (Leplege, Ecosse, Verdier, & Perneger, 1998) ; Italian (Apolone, & Mosconi, 1998); Japanese (Fukuhara, Bito, Green, Hsiao, & Kurokawa, 1998); Dutch (Aaronson, et al., 1998); Greek (Anagnostopoulos, Niakas, & Pappa, 2005; Pappa, Kontodimopoulos, & Niakas, 2005)). It consists of 36 items in eight subscales: physical functioning (PF-10 items), role limitations due to physical health problems (RP-4 items), bodily pain (BP-2 items), general health perceptions (GH-5 items), vitality (VT-4 items) tapping energy levels and fatigue, social functioning (SF-2 items), role limitations due to emotional problems (RE-3 items) and mental health (MH-5 items). It also includes one item measuring health transition (Ware, 2008). These subscales are measured on a 3-6 point Likert scale and then transformed to a 0-100 score. Higher scores indicate better status (e.g. in body pain items, the higher the score, the lower the pain). Moreover, it can be combined into two component summary scales; the physical component summary (PCS) that includes PF, GH, RP, BP subscales and the mental component summary (MCS) that includes VT, SF, RE, MH subscales.

In many research papers these two summaries are provided, in relation to norms established in a US population (Ware, 2008). Moreover, there are two shorter versions, the SF-20 and SF-12.

The RAND-36 is an exact replication of the content of the SF-36 (Ware & Sherbourne, 1992). Both were adapted from longer instruments completed by patients participating in the Medical Outcomes Study (MOS) (Hays, Sherbourne, & Mazel, 1993). However, the RAND uses a different scoring algorithm compared to the SF-36. The scores for PCS and MCS for the SF-36 (or its shorter versions) are based on principal component analysis and orthorgonal rotation assuming that the two summary scores are uncorrelated. For the RAND-36 (and its shorter versions), however, these two summary scores are based on non-orthogonal rotation implying correlation between physical and mental health components (Hays, Prince-Embury, & Chen, 1998). Research evidence suggests that this difference may affect the outcome. For instance, Lee, Browne and Villanueva (2008), in their study with 5,641 individuals, demonstrated that the results (PCS and MCS scores) measured by the SF-12 suggest that participants experienced lower dysfunction in both aspects compared to RAND-12 scores that revealed moderate to severe dysfunction.

WHOQOL and WHOQOL-BREF

The World Health Organization Quality of Life (WHOQOL) is a quality of life assessment developed by the WHOQOL Group based on the World Health Organization (WHOQOL group, 1993) definition of QoL. The WHOQOL has two versions: 1) one version consists of 100 items (WHOQOL-100; WHOQOL group, 1994) which produces scores relating to specific features of QoL (e.g. positive feelings, social support, financial resources), scores relating to broader domains (e.g. physical, psychological, social relationships) and a score relating to the overall

QoL and general health; 2) another shorter version consists of 26 items (WHOQOL group, 1998) that produces scores related only to broader domains. Both of them have been translated into more than 20 languages (e.g. Lithuanian, Chinese, Italian, Russian, Polish, Czech, Greek) and research evidence demonstrates that both are valid and reliable. Both WHOQOL versions are used in clinical practice, clinical trials, health research evaluation and policy making.

The WHOQOL-BREF is more often used as an alternative to the WHOQOL-100 in evaluating improvement in quality of life following major therapeutic interventions for physical, psychological, and environmental domains. As stated earlier, it consists of 26 questions containing two global items on overall self-rated QOL and general health, and 24 items that are categorized into four domains, each aiming to assess respectively, physical capacity (7 items), psychological wellbeing (6-items), social relationships (3-items) and the environment (8 items). The four domains are scored on a 5-point Likert scale. Domains are scored in a positive direction. To calculate the final score per domain a two-step transformation of raw data is employed. The first one converts scores to a range between 4-20 and the second one converts domain scores to a 0-100 scale.

EQ-5D

The EQ-5D (EuroQol Group, 1990) is a valid and reliable five item scale evaluating mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The EQ-5D has been translated into many languages (e.g. Greek (Kontodimopoulos et al., 2008); Taiwanese (Chang et al., 2007); Portuguese (Ferreira, Ferreira, Pereira, & Oppe, 2014); Arabic (Aburuz, Bulatova, Twalbeh, & Gazawi, 2009)). Each item has three levels (no problems, some problems, extreme problems). A health score index is then calculated between 0 and 1, where 0 indicates death and

1 represents perfect health. In many cases, item scores are converted to a summary score in order to compare with the US norms.

NHP

The Nottingham Health Profile (Hunt, McEwen, & McKenna, 1985; S. M. Hunt, et al., 1981) is another valid and reliable instrument (Wiklund, 1990) translated into many languages other than English (e.g. Spanish, (Alonso, Anto, & Moreno, 1990); French, (Bucquet, Condon, & Ritchie, 1990); Greek, (Vidalis & Syngelakis, 2000); Japanese, (Nishimura et al., 2004); Danish, (Thorsen, McKenna, & Gottschalck, 1993)).

It includes 45-items measuring subjective health status and consists of two parts. Part 1 consists of 38 items over six domains: physical ability (PA-8 items), pain (P-8 items), sleep (S-5 items), energy level (EL-3 items), social isolation (SI-5 items) and emotional reactions (ER-9 items). Part 2 consists of 7 items capturing seven aspects of daily life (paid employment, jobs around the house, social life, personal relationships, sex life, hobbies and interests, and holidays). However, in the majority of QoL studies only the first part is administered. Scores range between 0 (best possible health) to 100 (worst possible health).

Disease-specific measures

MacNew

The MacNew Heart Disease Health-Related Quality of Life instrument assesses HRQoL in patients with coronary [ischaemic] heart disease (Hofer, et al., 2004; Lim, Valenti, & Knapp, 1993). The MacNew is valid and reliable in many languages (e.g. Chinese (Yu, Thompson, Yu,

& Oldridge, 2008); Dutch (De Gucht, Van Elderen, van der Kamp, & Oldridge, 2004); UK English (Dempster, Donnelly, & O'Loughlin, 2004); Farsi/Iran (Asadi-Lari, Javadi, Melville, Oldridge, & Gray, 2003); German (Hofer, et al., 2004); Turkish (Daskapan et al., 2008) and Russian (Geulayov et al., 2013). The MacNew has been translated into Greek as well but its psychometric properties have not been fully tested (Merkouris, et al., 2009).

The MacNew is a 27-item instrument focusing on three domains: emotional function (11 items), social function (10 items) and physical limitation (6 items). These domains are measured on a 7-point Likert scale where 1 indicates poor functioning and 7 high functioning.

SAQ

The Seattle Angina Questionnaire (SAQ (Spertus, et al., 1995)) is an instrument developed to measure the HRQoL of patients with CHD. The SAQ is a 19-item questionnaire consisting of 5 domains: physical limitations (9 items), angina stability (1 item), angina frequency (2 items), treatment satisfaction (4 items) and quality of life (3 items). Domains are scored on a 5 or 6-point Likert scale, where 1 indicates poor functioning and 5 or 6 high functioning and then transformed to a 0 - 100 scale score. The SAQ has been translated into and validated in many languages (e.g. Japanese (Seki, et al., 2010); UK English (Garratt, Hutchinson, & Russell, 2001); Norwegian (Pettersen, Reikvam, & Stavem, 2005). However, while there is a plethora of SAQ translations, its psychometric properties have not been examined in line with scientific guidelines and criteria. As Zhang et al. (2013) have highlighted, researchers should not use simple translations without cultural adaptation because results may be misleading. For instance, the SAQ Chinese version has been used since 1996, but the validity and reliability of the translated version have never been appraised in published research. A recent mixed methods study (Zhang, et al., 2013) on 1,787 patients demonstrated that the existing version is unsuitable to Chinese patients. For instance, the results of the quantitative part of the study demonstrated that internal consistency for the QoL domain was lower than the acceptable criterion (Cronbach's α ≥0.70), the exploratory factor analysis indicated a four- instead of a five-factor model, while occasionally items in one subscale were strongly correlated to items in another subscale (e.g. "*difficulty of taking pills*" was highly related to the QoL subdomain). Furthermore, the findings of the qualitative part of the study showed that many participants did not fully understand many questions resulting in less accurate responses and/or a lot of missing data. Similarly, there is a Greek version that is widely used but there is no published paper demonstrating its validity and reliability in Greek patients.

Coronary revascularization specific measure

CROQ

The coronary revascularisation outcome questionnaire (CROQ (Schroter & Lamping, 2004)) was developed to evaluate HRQoL and health outcomes before and after the two common revascularisation procedures, that is PCI and CABG, capturing also aspects of recovery. Research evidence demonstrates that the original English version (Schroter, 2001; Schroter & Lamping, 2004, 2006) as well as its adaptations (e.g. the Italian (Colangelo, Dilaghi, Bobbio, Gensini, & Pinna Pintor, 2006; Pintor, 2002); the Persian (Shahali, 2008); and the Japanese version (Seki, et al., 2010)) have rigorous psychometric properties.

The CROQ consists of four versions; one pre-PTCA, one post-PTCA, one pre-CABG and one post-CABG. The two pre-operation versions (pre-PTCA and pre-CABG) are identical for the two procedures and capture four domains containing 32 core evaluative items and one descriptive item, although the latter is not taken into account for the calculation of scale scores. More specifically, the four domains refer to: symptoms (7 items), physical functioning (8 items), psychosocial functioning (14 items), and cognitive functioning (3 items). The two post-operation versions contain the same 33 items as the pre-PTCA/CABG versions as well as two more domains calculated from 12 (post-PTCA version) or 17 (post-CABG version) core evaluative items. In addition, they include two items that are not taken into account when calculating scale scores; for example, "*Since your heart operation, have you been readmitted to hospital for an overnight stay for any reason to do with your heart condition or heart operation?*". The two additional domains are *adverse effects* (6 items for the post-PTCA version and 11 for the post-CABG version) and *satisfaction with outcome* (6 items for both versions). The CROQ subscales are measured on 3 to 6-point Likert scales and then transformed to 0-100 score. Furthermore, at the end of all versions there is an open-ended question: "*Is there anything else you would like to tell us about your heart condition or heart operation that is not covered in this questionnaire? If so please write bellow*".

3.1 List of studies excluded from the systematic review with meta-analysis

Table 3.1 List of studies excluded from the systematic review with meta-analysis

N	Citation	Reason for Exclusion
1	Baldassarre,2002	Data Only for MCS & PCS
2	Barry, 2006	Insufficient data
3	Brotons ,2001	Old data(1996-1997) &MSC+PCS
4	Covinsky, 2008	Old data (1993-1998)
5	El Baz, 2009	Data Only MCS & PCS
6	Grady,2011	Data Only for MCS & PCS
7	Haddock,2003	Data Only for MCS & PCS
8	Halpin, 2008	Insufficient data
9	Herlitz, 2005 ;2001;2003;2000	Old data(1988-1991)
10	Ho, 2005	Old data(1992-1996)
11	Karlsson, 2000	Old data(1990-1994)
12	Kattainen,2005;2006	QoL instrument used-15D
13	Kendel, 2011	Not all subdomains reported
14	Khoueiry,2011	Not all subdomains reported
15	Krzych,2009	Not all subdomains reported
16	Loponen, 2007;2008	QoL instrument used-15D
17	Loponen,2009	QoL instrument used-15D
18	Martin, 2008	Not pure CR- Insufficient data for CABG
19	Melo, 2000	Old data-Portuguese
20	Panagopoulou, 2006	Not all subdomains reported
21	Pedersen, 2011	Insufficient data-post
22	Permanyer, 2001	Insufficient data
23	Phillips Bute, 2003	Old data (1992-2002)+ins data
24	Phillips Bute, 2006	Insufficient data
25	Simchen, 2001	Old data(1994)
26	Spertus,2004	Not all subdomains reported
27	Thornton, 2005	Not all subdomains reported
28	van Domburg, 2010	Insufficient data
29	Spertus,2004	Not all subdomains reported
30	Tully,2008	Insufficient data –only median
31	Favaro,2007	Insufficient data-graphs with means
32	Rumsfeld, 2003	Old data(1992-1996)
33	Parry,2012	Not all subdomains reported
34	Zwoliński,2013	Old data(1990-1999/1993)
35	Nedeljković,2011	Not all subdomains reported
36	Ghanta ,2011	Old data (1994-1999)
37	Sen , 2012	Insufficient data

3.2 Quality scoring for the studies

Table 1 Studies’ quality scoring

Study	Criteria										Total/10
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	
	Is the hypothesis/aim/ objective of the study ?	Are patients characteristics clearly described ?	Were the main outcome measures used accurate (valid and reliable)? For valid but not disease specific =0.5	Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Have the characteristics of patients lost to follow-up been described?	Were losses of patients to follow-up taken into account?	Is the procedure described ?	Were the statistical tests used to assess the main outcomes appropriate?	Are the main findings of the study clearly described?	Loss data greater to lower to 20% ?	
Azzopardi (2009)	1.00	1	0.5	0	0	0	1	0.5	1	1	**6**
Barolia (2012)	1.00	0.5	0.5	0	0	0	0.5	1	1	1	**5.5**
Benzer (2003)	1.00	0	1	0	1	0	1	1	1	0	**6**
Cohen (2011)	0.50	1	0.5	1	0	0.5	1	1	1	0	**6.5**
Colak (2008)	1.00	1	0.5	0	1	0	0	1	1	0	**5.5**
Damgaard (2011)	1.00	1	0.5	0	1	0	1	1	1	0	**6.5**
de Quadros (2011)	0.50	1	0.5	0	0	0	0.5	0.5	0.5		**3.5**
Denvir (2006)	1.00	1	0.5	0	1	0	1	1	1		**6.5**
Gjeilo (2008)	1.00	0	0.5	0	1	0	0.5	0.5	1	1	**5.5**

Hofer (2006;2005)	1.00	0.5	1	0	1	0	0.5	1	1	0	**6**
Houlind (2012)	1.00	1	0.5	0	1	0	0.5	0.5	1	0	**5.5**
Hunt (2000)	1.00	1	0.5	0	0	0	0.5	0.5	1	1	**5.5**
Jensen (2006)	1.00	1	0.5	1	0.5	0	1	0.5	1	0	**6.5**
Kiebzak (2002)	1.00	0	0.5	0	0	0	1	1	1	0	**4.5**
Krannich (2007)	1.00	1	0.5	0	0	0	0.5	0.5	0.5	0	**4**
Krecki (2010)	1.00	1	0.5	0	0.5	0	0.5	0.5	1	0	**5**
Li (2010)	1.00	1	0.5	0.5	1	0	0.5	1	1	1	**7.5**
Lie (2009)	1.00	1	0.5	0	1	0	1	0.5	1	1	**7**
Lukkarinen (2006)	1.00	0	0.5	0	1	0	0.5	1	1	0	**5**
Martin (2012)	1.00	1	0.5	0	1	0	0	0.5	1	0	**5**
Mathisen (2005)	1.00	1	0.5	0.5	0	0	0.5	0.5	1	0	**5**
Melberg (2010)	1.00	1	0.5	0	0	0	1	1	1		**5.5**
Merkouris (2009)	1.00	1	1	0	0	0	0.5	0.5	1	0	**5**
Peric (2010; 2006)	1.00	1	0.5	0	0	0	0.5	0.5	0.5	0	**4**
Pfaffenberger (2010)	1.00	1	0.5	0	0.5	0	0.5	0.5	1	1	**6**
Pirraglia (2003)	1.00	1	0.5	0.5	0	0	0.5	0.5	0.5	0	**4.5**
Puskas (2004)	1.00	1	0.5	0	0	0	0.5	1	1	0	**5**
Rothenhäusler (2010)	1.00	1	0.5	0.5	1	0	1	1	1	0	**7**
Škodová (2011)	1.00	1	0.5	1	1	0	1	1	1	0	**7.5**
Viswanathan (2011)	1.00	1	0.5	0	0	0	1	0.5	1		**5**
Weilu (2011)	1.00	1	0.5	0	0	0	1	0.5	1	1	**6**
Weintraub (2008)	1.00	0	0.5	0	0	0	1	1	1	0	**4.5**
Wong (2007)	1.00	1	0.5	0	0	0	1	0.5	1	0	**5**
Zang (2003)	0.50	0.5	0.5	1	0.5	0	0.5	0.5	1	1	**6**

4.1 Differences in demographic and medical characteristics between individuals who participated in all measurement points and those who did not

Table 4.1 Differences in demographic and medical characteristics between individuals who participated in all measurement points and those who did not

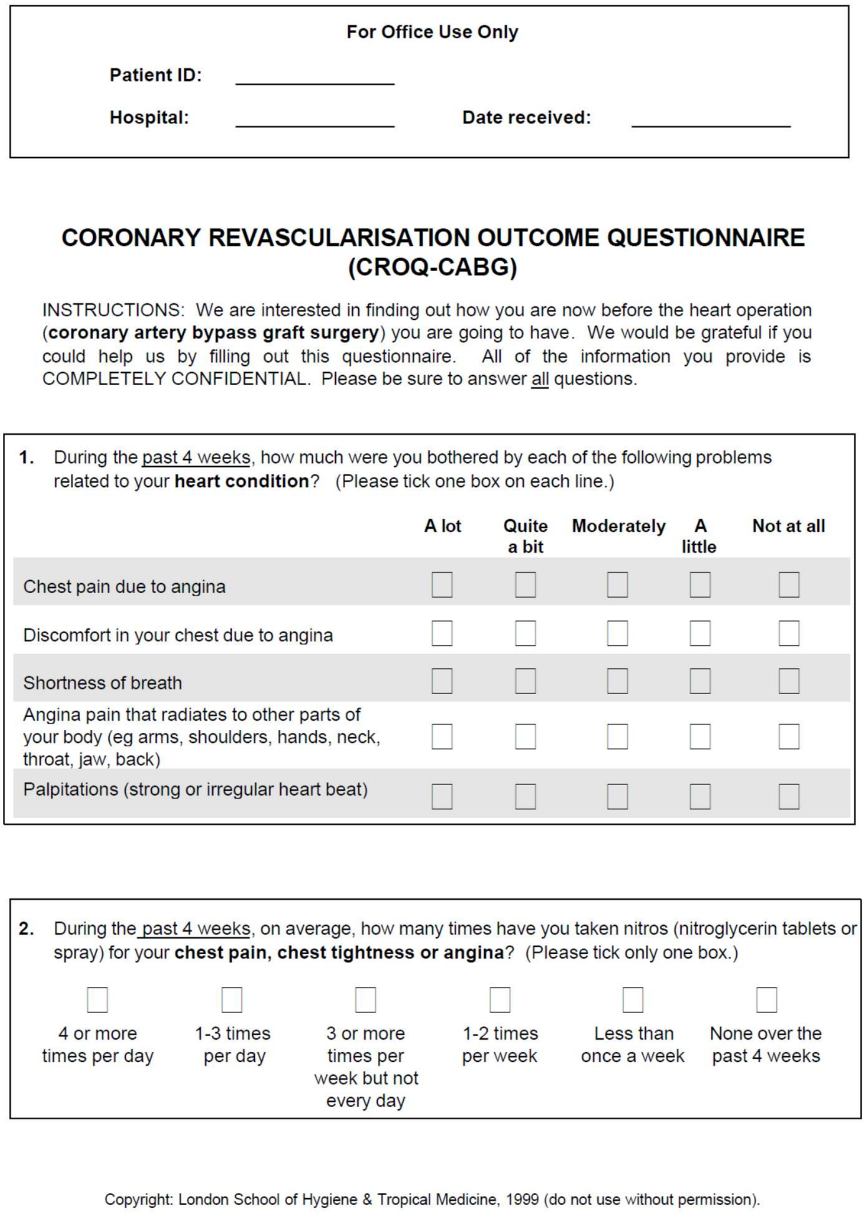
	N(%)/Mean(SD) (n=472)	**N(%)/Mean(SD) 3 points (n=291)**	**N(%)/Mean(SD) 1 or 2 points (n=181)**	***p* Value**
Age (yr)	60.43(10.89)	59.90(10.81)	61.72(11.01)	0.097
Sex (female %)	113(23.9%)	80(26%)	26(18.8%)	0.059
Place of residence (%)				0.202
Athens	365(77.3%)	256(76.6%)	109(79.9%)	
Other big city	31(6.6%)	27(8.1%)	4(2.9%)	
Rural areas	76(16.1%)	51(15.3%)	25(18.1%)	
Marital status(%)				<0.001
Married	385(81.6)	287(85.9)	98(71%)	
Unmarried/living alone	87(18.4)	47(14.1)	40(29%)	
Educational status(%)				0.673
6 years or less	122(26%)	85(25.5%)	37(27%)	
7-12 years (high school)	226(48.31%)	166(49.8%)	60(43.8%)	
12^+ years	122(26%)	82(24.6%)	40(29.2%)	
Occupational status				0.014
Unemployed	69(14.6)	56(16.8)	13(9.4)	
Public/Private servant	123(26.1)	86(25.7)	37(26.8)	
Freelance	97(20.6)	76(22.8)	21(15.2)	
Pensioner	183(38.8)	116(34.7)	67(48.6)	
Risk factors (%)				
CHD family history	235(49.9%)	170(51.1%)	65(47.1%)	0.479
Hypertension	175(37.5)	123(36.9%)	52(38.8%)	0.751
Cholesterol	153(32.8%)	112(33.6%)	41(30.6)	0.586
Diabetes	133(28.5%)	99(29.7%)	34(25.4%)	0.367
Smoking	238(50.7%)	175(52.7%)	63(46.0%)	0.189
BMI (kg/m^2)**	28.62(4.45)	28.81(4.45)	28.08(4.43)	0.121
Method of CR				0.011
PCI	307(65%)	205(61.4%)	102(73.9%)	
CABG	165(35%)	129(38.6%)	36(26.1%)	

*Participants: lost at some point (due to drop out or death) and those recruited for 1st time 3 months post treatment

****BMI Categories:** Underweight = <18.5, Normal weight = 18.5–24.9, Overweight = 25–29.9, Obesity = BMI of 30 or greater

4.2CROQ versions

4.2.1 CROQ before Coronary revasculariazation (PCI and CABG versions are identical, therefore only the CABG version is presented)



For Office Use Only

Patient ID: ________________

Hospital: ________________ **Date received:** ________________

CORONARY REVASCULARISATION OUTCOME QUESTIONNAIRE (CROQ-CABG)

INSTRUCTIONS: We are interested in finding out how you are now before the heart operation (**coronary artery bypass graft surgery**) you are going to have. We would be grateful if you could help us by filling out this questionnaire. All of the information you provide is COMPLETELY CONFIDENTIAL. Please be sure to answer all questions.

1. During the past 4 weeks, how much were you bothered by each of the following problems related to your **heart condition**? (Please tick one box on each line.)

	A lot	**Quite a bit**	**Moderately**	**A little**	**Not at all**
Chest pain due to angina	☐	☐	☐	☐	☐
Discomfort in your chest due to angina	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐
Angina pain that radiates to other parts of your body (eg arms, shoulders, hands, neck, throat, jaw, back)	☐	☐	☐	☐	☐
Palpitations (strong or irregular heart beat)	☐	☐	☐	☐	☐

2. During the past 4 weeks, on average, how many times have you taken nitros (nitroglycerin tablets or spray) for your **chest pain, chest tightness or angina**? (Please tick only one box.)

☐	☐	☐	☐	☐	☐
4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks

3. During the past 4 weeks, have you had **chest pain, chest tightness or angina:**
(Please tick only one box.)

☐ At rest?
☐ On exertion?
☐ At rest and on exertion?
☐ Not at all?

4. During the past 4 weeks, how much trouble has your **heart condition** caused you?
(Please tick only one box.)

☐ A lot
☐ Quite a bit
☐ Some
☐ A little
☐ None

5. The following questions ask about activities which you might do during a typical day. During the past 4 weeks, has your **heart condition** limited you in your usual daily activities? Please indicate whether your heart condition limits you a lot, limits you a little, or does not limit you at all in the activities listed below. (Please tick one box on each line.)

ACTIVITIES	**Yes, Limited A Lot**	**Yes, Limited A Little**	**No, Not Limited At All**
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
Lifting or carrying groceries	☐	☐	☐
Climbing **several** flights of stairs	☐	☐	☐
Climbing **one** flight of stairs	☐	☐	☐
Bending, kneeling or stooping	☐	☐	☐
Walking **half a mile**	☐	☐	☐
Walking **one hundred yards**	☐	☐	☐
Bathing or dressing yourself	☐	☐	☐

6. The next questions ask about the impact of your **heart condition** on your family and friends and the extent to which it has interfered with your social activities. During the past 4 weeks, how often have you experienced the following as a result of your **heart condition**:
(Please tick one box on each line.)

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
Family or friends being overprotective toward you?	☐	☐	☐	☐	☐
Feeling like you are a burden on others?	☐	☐	☐	☐	☐
Feeling restricted in your social activities (like visiting with friends, relatives, etc)?	☐	☐	☐	☐	☐
Feeling worried about going too far from home?	☐	☐	☐	☐	☐

7. The next questions ask about your feelings about your **heart condition**. During the past 4 weeks, how often have you felt: (Please tick one box on each line.)

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
Worried about your heart condition?	☐	☐	☐	☐	☐
Worried about doing too much or over-doing it?	☐	☐	☐	☐	☐
Worried that you might have a heart attack or die suddenly?	☐	☐	☐	☐	☐
Frightened by the pain or discomfort of your heart condition?	☐	☐	☐	☐	☐
Uncertain about the future?	☐	☐	☐	☐	☐
Depressed?	☐	☐	☐	☐	☐
Frustrated or impatient?	☐	☐	☐	☐	☐
That your heart condition interfered with your enjoyment of life?	☐	☐	☐	☐	☐
That it was difficult to keep a positive outlook about your health?	☐	☐	☐	☐	☐
That it was difficult to plan ahead (eg vacations, social events, etc.)?	☐	☐	☐	☐	☐

8. The next questions ask about problems related to your **heart condition**. During the past 4 weeks, how much of the time did you: (Please tick one box on each line.)

	All of the time	**Most of the time**	**A good bit of the time**	**Some of the time**	**A little of the time**	**None of the time**
Have difficulty reasoning and solving problems, for example making plans, making decisions, learning new things?	☐	☐	☐	☐	☐	☐
Forget, for example things that happened recently, where you put things or appointments?	☐	☐	☐	☐	☐	☐
Have difficulty doing activities involving concentration and thinking?	☐	☐	☐	☐	☐	☐

9. Is there anything else you would like to tell us about your **heart condition** or **heart operation** that is not covered in this questionnaire? If so, please write below.

____

____

____

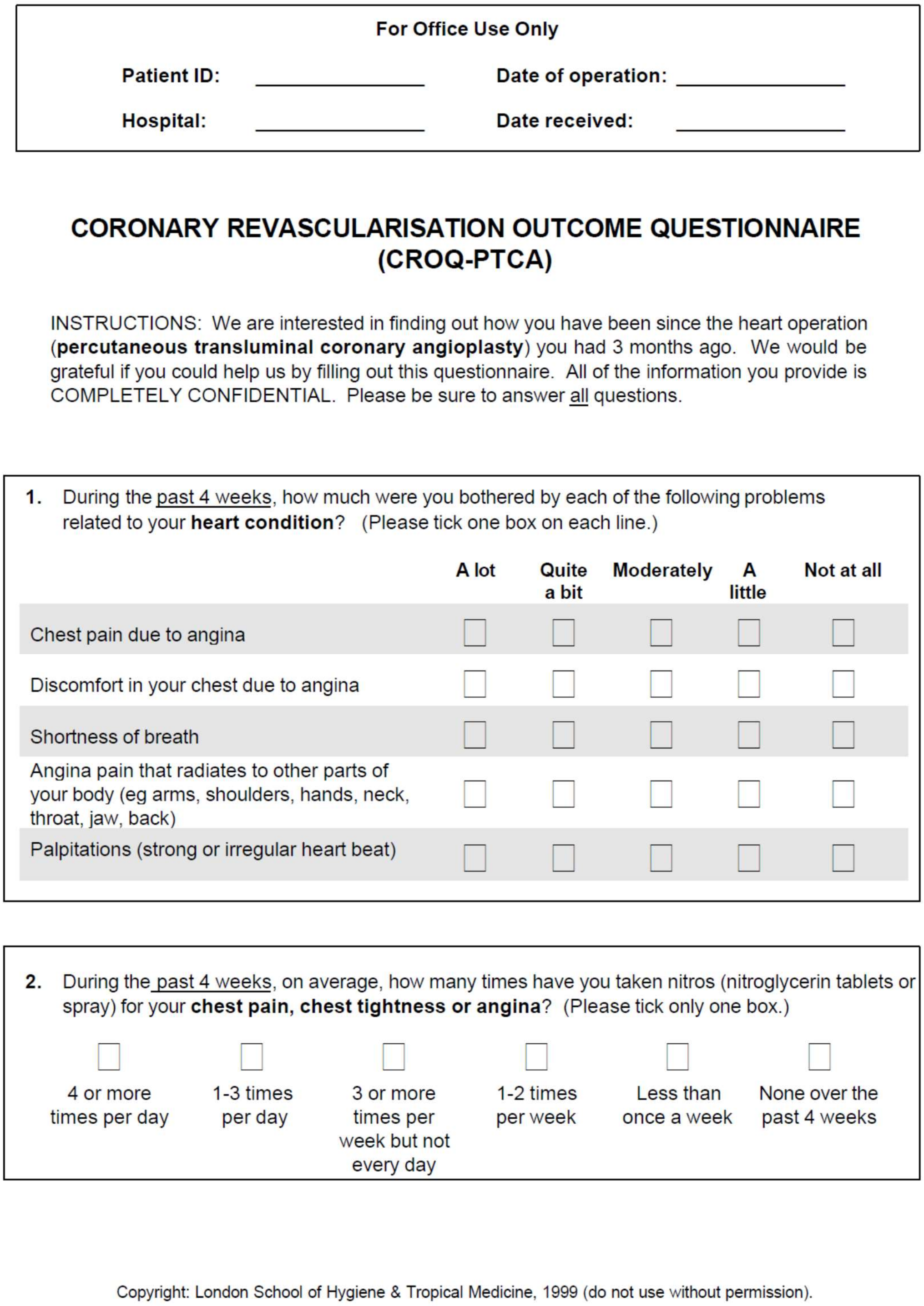
____

____

Please check that you have answered all the questions on each page.

THANK YOU FOR YOUR HELP

4.2.2 CROQ -PCI post treatment



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Patient ID: ________________ **Date of operation:** ________________

Hospital: ________________ **Date received:** ________________

CORONARY REVASCULARISATION OUTCOME QUESTIONNAIRE (CROQ-PTCA)

INSTRUCTIONS: We are interested in finding out how you have been since the heart operation (**percutaneous transluminal coronary angioplasty**) you had 3 months ago. We would be grateful if you could help us by filling out this questionnaire. All of the information you provide is COMPLETELY CONFIDENTIAL. Please be sure to answer all questions.

1. During the past 4 weeks, how much were you bothered by each of the following problems related to your **heart condition**? (Please tick one box on each line.)

	A lot	**Quite a bit**	**Moderately**	**A little**	**Not at all**
Chest pain due to angina	☐	☐	☐	☐	☐
Discomfort in your chest due to angina	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐
Angina pain that radiates to other parts of your body (eg arms, shoulders, hands, neck, throat, jaw, back)	☐	☐	☐	☐	☐
Palpitations (strong or irregular heart beat)	☐	☐	☐	☐	☐

2. During the past 4 weeks, on average, how many times have you taken nitros (nitroglycerin tablets or spray) for your **chest pain, chest tightness or angina**? (Please tick only one box.)

☐	☐	☐	☐	☐	☐
4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks

3. During the past 4 weeks, have you had **chest pain, chest tightness or angina:**
(Please tick only one box.)

☐ At rest? ☐ On exertion? ☐ At rest and on exertion? ☐ Not at all?

4. During the past 4 weeks, how much trouble has your **heart condition** caused you?
(Please tick only one box.)

☐ A lot ☐ Quite a bit ☐ Some ☐ A little ☐ None

5. The following questions ask about activities which you might do during a typical day. During the past 4 weeks, has your **heart condition** limited you in your usual daily activities? Please indicate whether your heart condition limits you a lot, limits you a little, or does not limit you at all in the activities listed below. (Please tick one box on each line.)

ACTIVITIES	**Yes, Limited A Lot**	**Yes, Limited A Little**	**No, Not Limited At All**
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
Lifting or carrying groceries	☐	☐	☐
Climbing **several** flights of stairs	☐	☐	☐
Climbing **one** flight of stairs	☐	☐	☐
Bending, kneeling or stooping	☐	☐	☐
Walking **half a mile**	☐	☐	☐
Walking **one hundred yards**	☐	☐	☐
Bathing or dressing yourself	☐	☐	☐

6. The next questions ask about the impact of your **heart condition** on your family and friends and the extent to which it has interfered with your social activities. During the past 4 weeks, how often have you experienced the following as a result of your **heart condition**:
(Please tick one box on each line.)

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
Family or friends being overprotective toward you?	☐	☐	☐	☐	☐
Feeling like you are a burden on others?	☐	☐	☐	☐	☐
Feeling restricted in your social activities (like visiting with friends, relatives, etc)?	☐	☐	☐	☐	☐
Feeling worried about going too far from home?	☐	☐	☐	☐	☐

7. The next questions ask about your feelings about your **heart condition**. During the past 4 weeks, how often have you felt: (Please tick one box on each line.)

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
Worried about your heart condition?	☐	☐	☐	☐	☐
Worried about doing too much or over-doing it?	☐	☐	☐	☐	☐
Worried that you might have a heart attack or die suddenly?	☐	☐	☐	☐	☐
Worried that your symptoms might return?	☐	☐	☐	☐	☐
Frightened by the pain or discomfort of your heart condition?	☐	☐	☐	☐	☐
Uncertain about the future?	☐	☐	☐	☐	☐
Depressed?	☐	☐	☐	☐	☐
Frustrated or impatient?	☐	☐	☐	☐	☐
That your heart condition interfered with your enjoyment of life?	☐	☐	☐	☐	☐
That it was difficult to keep a positive outlook about your health?	☐	☐	☐	☐	☐
That it was difficult to plan ahead (eg vacations, social events, etc.)?	☐	☐	☐	☐	☐

8. The next questions ask about problems related to your **heart condition**. During the past 4 weeks, how much of the time did you: (Please tick one box on each line.)

	All of the time	**Most of the time**	**A good bit of the time**	**Some of the time**	**A little of the time**	**None of the time**
Have difficulty reasoning and solving problems, for example making plans, making decisions, learning new things?	☐	☐	☐	☐	☐	☐
Forget, for example things that happened recently, where you put things or appointments?	☐	☐	☐	☐	☐	☐
Have difficulty doing activities involving concentration and thinking?	☐	☐	☐	☐	☐	☐

9. Since your heart operation, have you been re-admitted to hospital for an overnight stay for any reason to do with your **heart condition or heart operation**? Please give as many details as you can below.

☐ No

☐ Yes

Date of Admission	Name of hospital	Reason for hospital stay	Number of days

10. The next questions ask about problems you might have had **since your heart operation**. During the past 4 weeks, how much were you bothered by the following problems? If you did not have the problem, tick the last box "Not at all". (Please tick one box on each line.)

	A lot	**Quite a bit**	**Moderately**	**A little**	**Not at all**
Pain in your groin wound	☐	☐	☐	☐	☐
Tenderness around your groin wound	☐	☐	☐	☐	☐
Numbness or tingling in your groin area	☐	☐	☐	☐	☐
Bruising around your groin wound or thigh	☐	☐	☐	☐	☐
Problems in your groin where the catheter was inserted	☐	☐	☐	☐	☐
Concern over the appearance of your bruises	☐	☐	☐	☐	☐

11. The next question asks about how satisfied you are with your **heart operation**. How satisfied are you with the: (Please tick one box on each line.)

	Very dissatisfied	**Somewhat dissatisfied**	**Somewhat satisfied**	**Very satisfied**
Results of your heart operation?	☐	☐	☐	☐
Information you were given about your heart operation?	☐	☐	☐	☐
Information you were given about how you might feel while recovering from your heart operation?	☐	☐	☐	☐

12. Overall, how would you describe your **heart condition** now compared to before you had your heart operation? (Please tick one box.)

☐ Much worse ☐ A little worse ☐ About the same ☐ A little better ☐ Much better

13. Has your recovery from your **heart operation** so far been: (Please tick one box.)

☐ Slower than you expected? ☐ About what you expected? ☐ Faster than you expected? ☐ Did not know how long it would take?

14. Are the results from your **heart operation**: (Please tick one box.)

☐ Worse than you expected? ☐ About what you expected? ☐ Better than you expected?

15. Is there anything else you would like to tell us about your **heart condition** or **heart operation** that is not covered in this questionnaire? If so, please write below.

____

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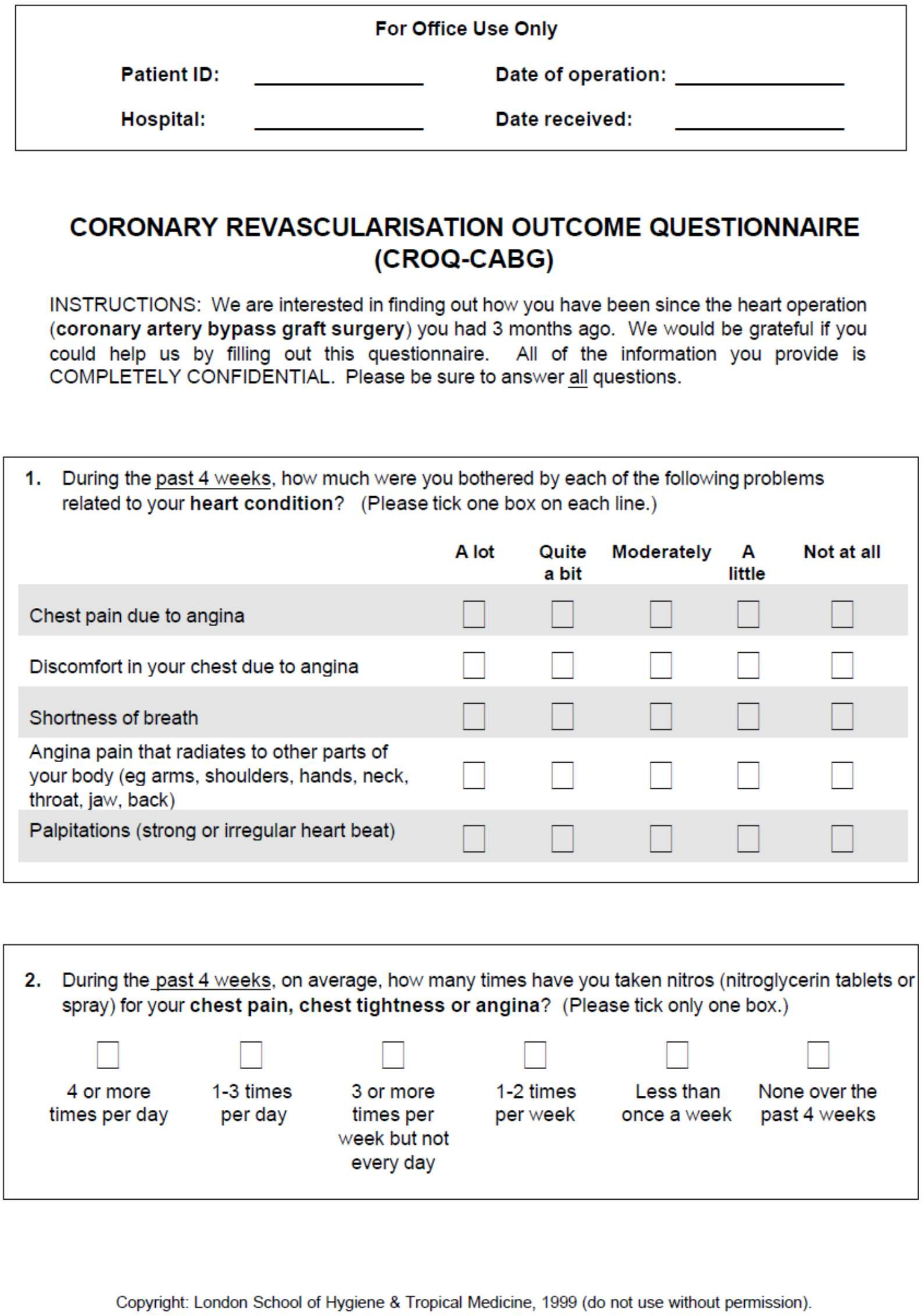
Please check that you have answered all the questions on each page.

THANK YOU FOR YOUR HELP

4.2.3 CROQ -CABG post treatment



For Office Use Only

Patient ID: _______________ **Date of operation:** _______________

Hospital: _______________ **Date received:** _______________

CORONARY REVASCULARISATION OUTCOME QUESTIONNAIRE (CROQ-CABG)

INSTRUCTIONS: We are interested in finding out how you have been since the heart operation (**coronary artery bypass graft surgery**) you had 3 months ago. We would be grateful if you could help us by filling out this questionnaire. All of the information you provide is COMPLETELY CONFIDENTIAL. Please be sure to answer all questions.

1. During the past 4 weeks, how much were you bothered by each of the following problems related to your **heart condition**? (Please tick one box on each line.)

	A lot	**Quite a bit**	**Moderately**	**A little**	**Not at all**
Chest pain due to angina	☐	☐	☐	☐	☐
Discomfort in your chest due to angina	☐	☐	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	☐
Angina pain that radiates to other parts of your body (eg arms, shoulders, hands, neck, throat, jaw, back)	☐	☐	☐	☐	☐
Palpitations (strong or irregular heart beat)	☐	☐	☐	☐	☐

2. During the past 4 weeks, on average, how many times have you taken nitros (nitroglycerin tablets or spray) for your **chest pain, chest tightness or angina**? (Please tick only one box.)

☐	☐	☐	☐	☐	☐
4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks

3. During the <u>past 4 weeks</u>, have you had **chest pain, chest tightness or angina:**
(Please tick only one box.)

☐ At rest?
☐ On exertion?
☐ At rest and on exertion?
☐ Not at all?

4. During the <u>past 4 weeks</u>, how much trouble has your **heart condition** caused you?
(Please tick only one box.)

☐ A lot
☐ Quite a bit
☐ Some
☐ A little
☐ None

5. The following questions ask about activities which you might do during a typical day. During the <u>past 4 weeks</u>, has your **heart condition** limited you in your usual daily activities? Please indicate whether your heart condition limits you a lot, limits you a little, or does not limit you at all in the activities listed below. (Please tick one box on each line.)

<u>ACTIVITIES</u>	**Yes, Limited A Lot**	**Yes, Limited A Little**	**No, Not Limited At All**
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
Lifting or carrying groceries	☐	☐	☐
Climbing **several** flights of stairs	☐	☐	☐
Climbing **one** flight of stairs	☐	☐	☐
Bending, kneeling or stooping	☐	☐	☐
Walking **half a mile**	☐	☐	☐
Walking **one hundred yards**	☐	☐	☐
Bathing or dressing yourself	☐	☐	☐

6. The next questions ask about the impact of your **heart condition** on your family and friends and the extent to which it has interfered with your social activities. During the past 4 weeks, how often have you experienced the following as a result of your **heart condition**:
(Please tick one box on each line.)

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
Family or friends being overprotective toward you?	☐	☐	☐	☐	☐
Feeling like you are a burden on others?	☐	☐	☐	☐	☐
Feeling restricted in your social activities (like visiting with friends, relatives, etc)?	☐	☐	☐	☐	☐
Feeling worried about going too far from home?	☐	☐	☐	☐	☐

7. The next questions ask about your feelings about your **heart condition**. During the past 4 weeks, how often have you felt: (Please tick one box on each line.)

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
Worried about your heart condition?	☐	☐	☐	☐	☐
Worried about doing too much or over-doing it?	☐	☐	☐	☐	☐
Worried that you might have a heart attack or die suddenly?	☐	☐	☐	☐	☐
Worried that your symptoms might return?	☐	☐	☐	☐	☐
Frightened by the pain or discomfort of your heart condition?	☐	☐	☐	☐	☐
Uncertain about the future?	☐	☐	☐	☐	☐
Depressed?	☐	☐	☐	☐	☐
Frustrated or impatient?	☐	☐	☐	☐	☐
That your heart condition interfered with your enjoyment of life?	☐	☐	☐	☐	☐
That it was difficult to keep a positive outlook about your health?	☐	☐	☐	☐	☐
That it was difficult to plan ahead (eg vacations, social events, etc.)?	☐	☐	☐	☐	☐

8. The next questions ask about problems related to your **heart condition**. During the past 4 weeks, how much of the time did you: (Please tick one box on each line.)

	All of the time	**Most of the time**	**A good bit of the time**	**Some of the time**	**A little of the time**	**None of the time**
Have difficulty reasoning and solving problems, for example making plans, making decisions, learning new things?	☐	☐	☐	☐	☐	☐
Forget, for example things that happened recently, where you put things or appointments?	☐	☐	☐	☐	☐	☐
Have difficulty doing activities involving concentration and thinking?	☐	☐	☐	☐	☐	☐

9. Since your heart operation, have you been re-admitted to hospital for an overnight stay for any reason to do with your **heart condition or heart operation**? Please give as many details as you can below.

☐ No
☐ Yes

Date of Admission	Name of hospital	Reason for hospital stay	Number of days

10. The next questions ask about problems you might have had **since your heart operation**. During the past 4 weeks, how much were you bothered by the following problems? If you did not have the problem, tick the last box "Not at all". (Please tick one box on each line.)

	A lot	**Quite a bit**	**Moderately**	**A little**	**Not at all**
Pain in your **chest wound**	☐	☐	☐	☐	☐
Infection in your **chest wound**	☐	☐	☐	☐	☐
Tenderness around your **chest wound**	☐	☐	☐	☐	☐
Numbness or tingling around your **chest wound**	☐	☐	☐	☐	☐
Bruising on your **chest**	☐	☐	☐	☐	☐
Pain in your **leg or arm wound**	☐	☐	☐	☐	☐
Any other pain in your **leg or arm** due to your operation	☐	☐	☐	☐	☐
Infection in your **leg or arm wound**	☐	☐	☐	☐	☐
Numbness or tingling in your **leg or arm** due to your operation	☐	☐	☐	☐	☐
Bruising on your **leg or arm** where a vein was removed	☐	☐	☐	☐	☐
Swollen feet or ankles	☐	☐	☐	☐	☐

11. The next question asks about how satisfied you are with your **heart operation**. How satisfied are you with the: (Please tick one box on each line.)

	Very dissatisfied	**Somewhat dissatisfied**	**Somewhat satisfied**	**Very satisfied**
Results of your heart operation?	☐	☐	☐	☐
Information you were given about your heart operation?	☐	☐	☐	☐
Information you were given about how you might feel while recovering from your heart operation?	☐	☐	☐	☐

12. Overall, how would you describe your **heart condition** now compared to before you had your heart operation? (Please tick one box.)

☐ Much worse

☐ A little worse

☐ About the same

☐ A little better

☐ Much better

13. Has your recovery from your **heart operation** so far been: (Please tick one box.)

☐ Slower than you expected?

☐ About what you expected?

☐ Faster than you expected?

☐ Did not know how long it would take?

14. Are the results from your **heart operation**: (Please tick one box.)

☐ Worse than you expected?

☐ About what you expected?

☐ Better than you expected?

15. Is there anything else you would like to tell us about your **heart condition** or **heart operation** that is not covered in this questionnaire? If so, please write below.

____

____

____

____

____

Please check that you have answered all the questions on each page.

THANK YOU FOR YOUR HELP

4.3 SF-36

SF-36v2® HEALTH SURVEY (FOUR-WEEK RECALL)

SCRIPT FOR INTERVIEW ADMINISTRATION

These first questions are about your health now and your current daily activities.

Please try to answer every question as accurately as you can.

1. **In general, would you say your health is...** *[READ RESPONSE CHOICES]*

(Circle one number)

Excellent	1
Very good	2
Good	3
Fair	4
or Poor	5

2. **Compared to one year ago, how would you rate your health in general now? Would you say it is...** *[READ RESPONSE CHOICES]*

(Circle one number)

Much better now than one year ago	1
Somewhat better now than one year ago	2
About the same as one year ago	3
Somewhat worse now than one year ago	4
or Much worse now than one year ago	5

Now I'm going to read a list of activities that you might do during a typical day.
As I read each item, please tell me if your health now limits you a lot, limits you a little, or does not limit you at all in these activities.

3a. **First, vigorous activities, such as running, lifting heavy objects, participating in strenuous sports. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

(SF-36v2® Standard Interview Script, United States (English))

3b. **. . . moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3c. **. . . lifting or carrying groceries. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3d . **. . . climbing several flights of stairs. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3e. **. . . climbing one flight of stairs. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3f . **. . . bending, kneeling, or stooping. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3g. **. . . walking more than a mile. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3h . **. . . walking several hundred yards. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3i . **. . . walking one hundred yards. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot	1
Yes, limited a little	2
No, not limited at all	3

3j. **. . . bathing or dressing yourself. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot 1
Yes, limited a little 2
No, not limited at all 3

The following four questions ask you about your physical health and your daily activities.

4a. **During the past four weeks, how much of the time have you had to cut down on the amount of time you spent on work or other daily activities as a result of your physical health?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
or None of the time 5

4b. **During the past four weeks, how much of the time have you accomplished less than you would like as a result of your physical health?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
or None of the time 5

4c. **During the past four weeks, how much of the time were you limited in the kind of work or other regular daily activities you do as a result of your physical health?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

4d. **During the past four weeks, how much of the time have you had difficulty performing work or other regular daily activities as a result of your physical health, for example, it took extra effort?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

The following three questions ask about your emotions and your daily activities.

5a. **During the past four weeks, how much of the time have you had to cut down the amount of time you spent on work or regular daily activities as a result of any emotional problems, such as feeling depressed or anxious?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

5b. **During the past four weeks, how much of the time have you accomplished less than you would like as a result of any emotional problems, such as feeling depressed or anxious?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

5c. **During the past four weeks, how much of the time did you do work or other regular daily activities less carefully than usual as a result of any emotional problems, such as feeling depressed or anxious?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

6. **During the past four weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? Has it interfered . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
or Extremely	5

7. **During the past four weeks, how much did pain interfere with your normal work, including both work outside the home and housework? Did it interfere . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Not at all	1
A little bit	2
Moderately	3
Quite a bit	4
or Extremely	5

8. **How much bodily pain have you had during the past four weeks? Have you had . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

None	1
Very mild	2
Mild	3
Moderate	4
Severe	5
or Very severe	6

The next questions are about how you feel and how things have been with you during the past four weeks.

As I read each statement, please give me the one answer that comes closest to the way you have been feeling; is it all of the time, most of the time, some of the time, a little of the time, or none of the time?

9a. **How much of the time during the past four weeks . . . did you feel full of life?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9b. **How much of the time during the past four weeks . . . have you been very nervous?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9c. **How much of the time during the past four weeks . . . have you felt so down in the dumps that nothing could cheer you up?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9d. **How much of the time during the past four weeks . . . have you felt calm and peaceful?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9e. **How much of the time during the past four weeks . . . did you have a lot of energy?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9f. **How much of the time during the past four weeks . . . have you felt downhearted and depressed?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9g. **How much of the time during the past four weeks . . . did you feel worn out?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9h. **How much of the time during the past four weeks . . . have you been happy?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

9i. **How much of the time during the past four weeks . . . did you feel tired?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

10. **During the past four weeks, how much of the time has your physical health or emotional problems interfered with your social activities like visiting with friends or relatives? Has it interfered . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time	1
Most of the time	2
Some of the time	3
A little of the time	4
or None of the time	5

These next questions are about your health and health-related matters.

Now, I'm going to read a list of statements. After each one, please tell me if it is definitely true, mostly true, mostly false, or definitely false. If you don't know, just tell me.

11a. **I seem to get sick a little easier than other people. Would you say that's . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Definitely true	1
Mostly true	2
Don't know	3
Mostly false	4
or Definitely false	5

11b. **I am as healthy as anybody I know. Would you say that's . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Definitely true	1
Mostly true	2
Don't know	3
Mostly false	4
or Definitely false	5

11c. **I expect my health to get worse. Would you say that's . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Definitely true	1
Mostly true	2
Don't know	3
Mostly false	4
or Definitely false	5

11d. **My health is excellent. Would you say that's . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Definitely true	1
Mostly true	2
Don't know	3
Mostly false	4
or Definitely false	5

4.4 Demographic Information

Demographics

Date of birth:……………………………………

Place of residence: ………………………………..

Please tick with √ each condition that represents you best:

Sex : Male ☐ Female ☐

Family Status :

- ☐ Single
- ☐ Married
- ☐ Divorced
- ☐ Other ……………………………

Educational Status :

- ☐ Primary School (1- 6 Years)
- ☐ Secondary School (7- 12 Years)
- ☐ University(15+ Years)
- ☐ Other ……………………………

Occupational Status :

- ☐ Unemployed
- ☐ Public Servant/ Private Sector
- ☐ Free Lancer
- ☐ Pensioner
- ☐ Other

4.5 Medical Information

Medical Record *

Do you have a family history of CHD?
☐ Yes
☐ No

Please tick with ✓ if you have or take medication for
☐ Hypertension
☐ Cholesterol
☐ Diabetes

Please state your weight ……… and height …………

Are you a smoker? Please tick with ✓ the condition that represents you
☐ Yes
☐ No
☐ Former

Do you know the number of arteries that have been revascularized? If yes please indicate the number ……………….

Do you know the kind of revascularization that your doctor have carried out?
☐ Angioplasty
☐ Metal stent
☐ Drug eluting stent
☐ On-Pump
☐ Off-Pump

*In case of follow up only 2 questions were asked
1 **Please state your weight ………**
2 **Are you a smoker? Please tick with ✓ the condition that represents you**

4.6 Interview Schedule

Interview schedule

Opening questions

1. A) How would you describe your life during the last year?

B) What do you think caused coronary disease?

C) How would you describe yourself now?

<u>*Prompts*</u> :

-appearance
-character
-sociality
-activities

HRQoL in general

2. What does “quality of life” mean to you?

<u>*Prompts*</u>

-what makes a good life in general?
-to you, in particular?
-in relation to health?

HRQoL, symptoms and physical functioning area

3. How do you feel your body after CR

<u>*Prompts*</u>:

have you observed any changes (before and after intervention/surgery)?
-experience of symptoms (presence/absence/recurrence in the last year)
-performance of everyday life activities (ability/ease/difficulty)-can you describe any particular activity that makes you tired?

HRQoL psychosocial functioning area

4. How do you experience your social life after CR?

<u>*Prompts*</u>:

-have your family and friends changed their behaviour towards you (before CR/now)?
-have you changed the way you relate to your family and friends (before CR/now)?
-have you made any changes in your social activities (before CR/now)?

5. How do you feel about your heart condition?

<u>*Prompts*</u>:

-what feelings do you have about your heart?
-can you describe specific thoughts, images?

Changes in attitude towards self and life

6. Have you observed any changes regarding the way you perceive life after CR?

Prompts:

-how do you perceive yourself in relation to your heart condition?

-have you noted any changes in the way you enjoy life (define and experience life enjoyment)?

-what might be the reasons that lead to this/these change(s)?

7. Have there been any life events (apart from CR) that have affected the way you perceive yourself and your life?

Changes in lifestyle/behavioural changes

8. Can you describe any changes in aspects of your lifestyle and habits that you made/had to make/intended to make after CR? (for each change mentioned with particular emphasis on smoking)

Prompts:

-why? what was the trigger(s)/ the source of information?

9. How did you feel about changing (then and now)/having to change these aspects?

Prompts:

-what factors contributed (facilitated/impeded) to obtaining or/and maintaining these changes

Ending

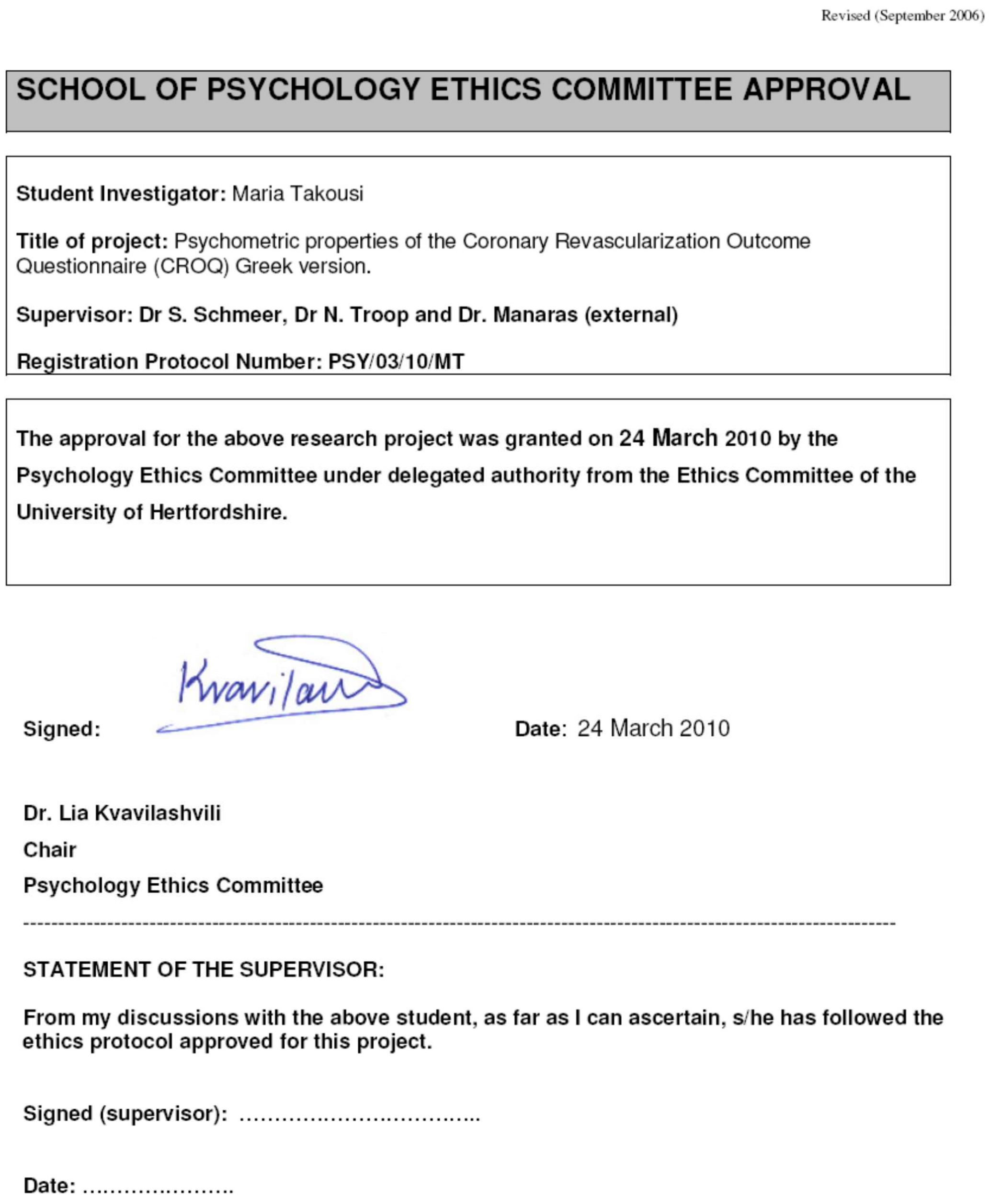
10. what would you say to an individual who now faces CR ?
11. is there anything else that you would like to add in relation to your experience of CR?

General Prompts during the interview

- What comes to your mind?
- Could you say more about this?
- Could you give me an example of this?
- You mean that .....(repeating the respondent’s phrase to ask for clarification or prompt further exploration)

4.7 University of Hertfordshire (UH) Ethics Committee Approval

4.7.1 Study 1 & 2 UH Ethics Committee Approval



Revised (September 2006)

SCHOOL OF PSYCHOLOGY ETHICS COMMITTEE APPROVAL

Student Investigator: Maria Takousi

Title of project: Psychometric properties of the Coronary Revascularization Outcome Questionnaire (CROQ) Greek version.

Supervisor: Dr S. Schmeer, Dr N. Troop and Dr. Manaras (external)

Registration Protocol Number: PSY/03/10/MT

The approval for the above research project was granted on 24 March 2010 by the Psychology Ethics Committee under delegated authority from the Ethics Committee of the University of Hertfordshire.

Signed: **Date:** 24 March 2010

Dr. Lia Kvavilashvili
Chair
Psychology Ethics Committee

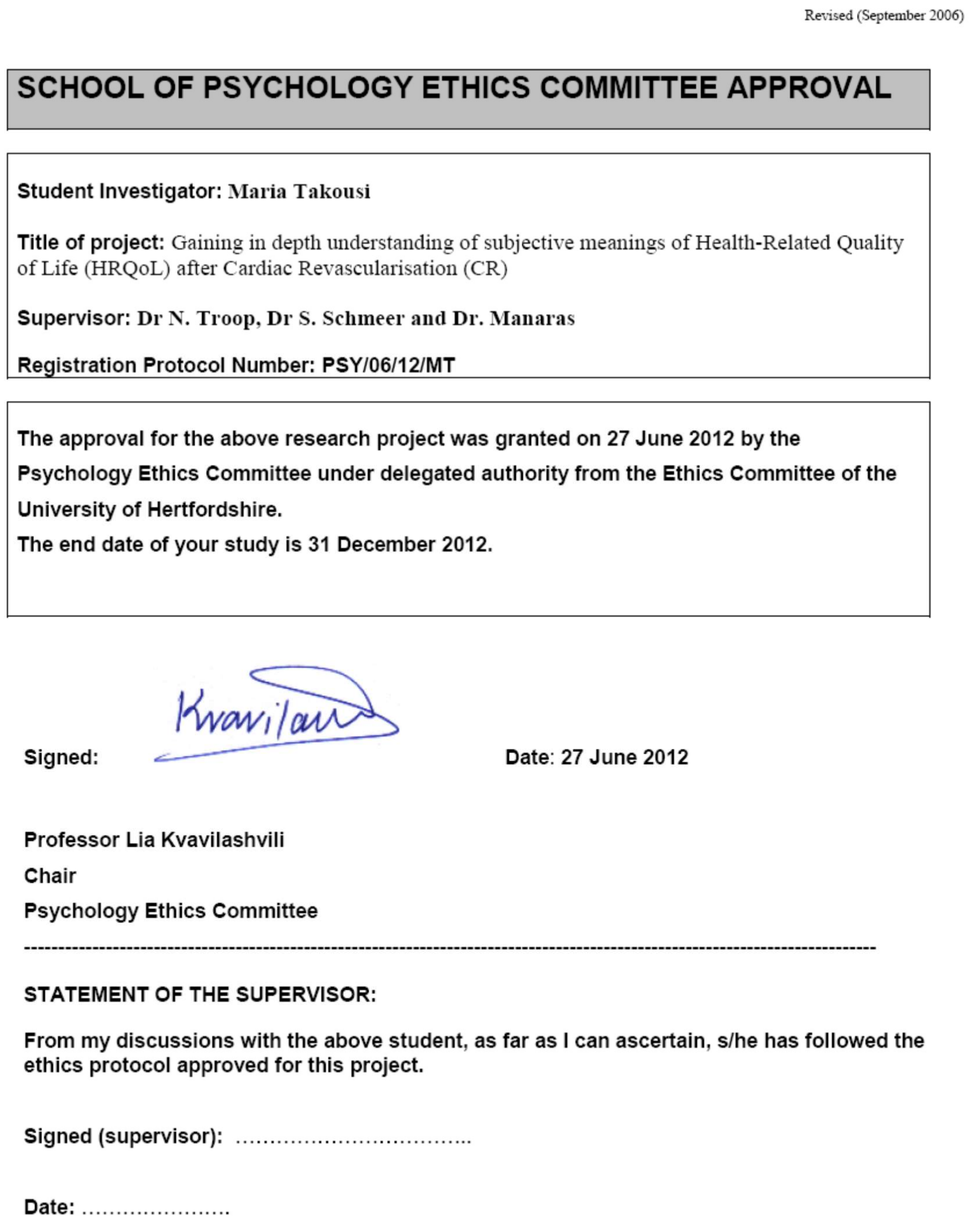
STATEMENT OF THE SUPERVISOR:

From my discussions with the above student, as far as I can ascertain, s/he has followed the ethics protocol approved for this project.

Signed (supervisor): ……………………………..

Date: ………………….

4.7.2 Study 3 UH Ethics Committee Approval



Revised (September 2006)

SCHOOL OF PSYCHOLOGY ETHICS COMMITTEE APPROVAL

Student Investigator: **Maria Takousi**

Title of project: Gaining in depth understanding of subjective meanings of Health-Related Quality of Life (HRQoL) after Cardiac Revascularisation (CR)

Supervisor: **Dr N. Troop, Dr S. Schmeer and Dr. Manaras**

Registration Protocol Number: PSY/06/12/MT

The approval for the above research project was granted on 27 June 2012 by the Psychology Ethics Committee under delegated authority from the Ethics Committee of the University of Hertfordshire.
The end date of your study is 31 December 2012.

Signed: **Date: 27 June 2012**

Professor Lia Kvavilashvili
Chair
Psychology Ethics Committee

STATEMENT OF THE SUPERVISOR:

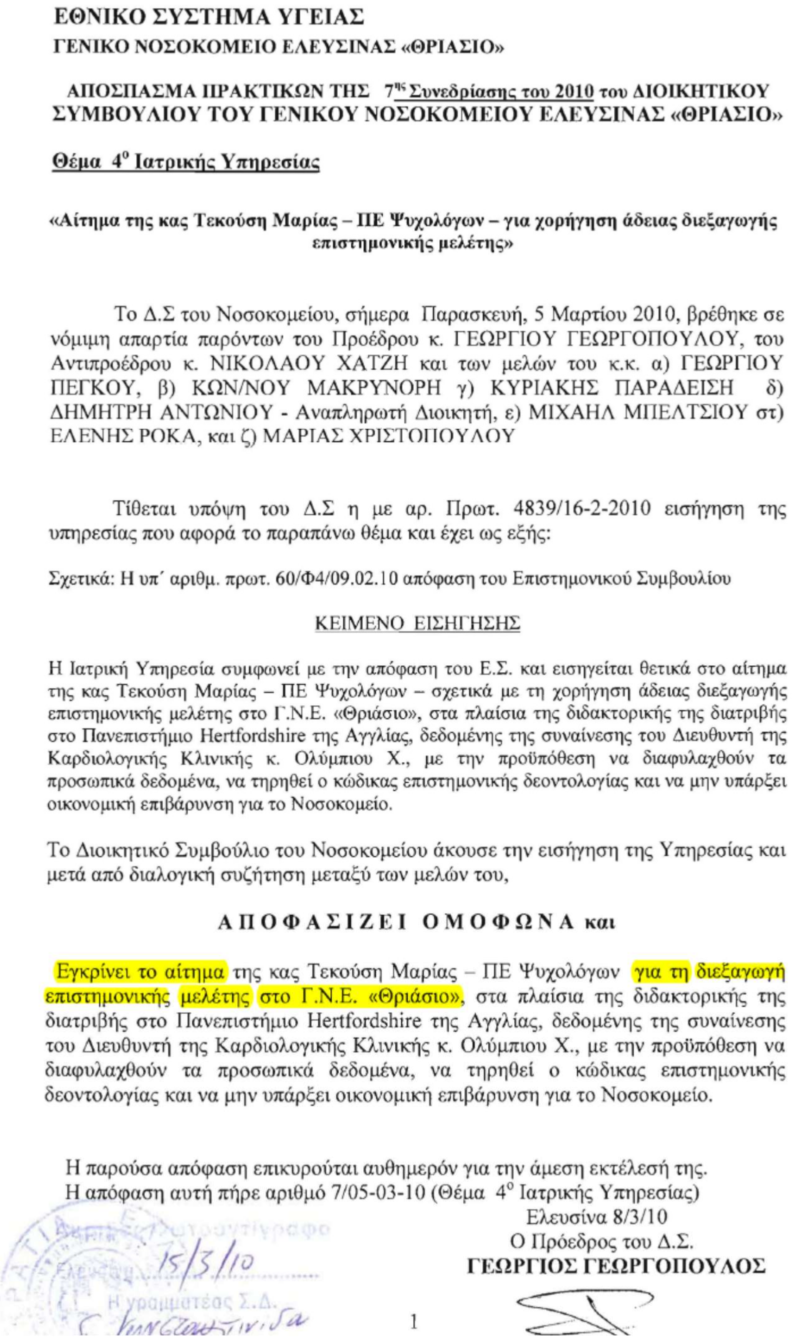
From my discussions with the above student, as far as I can ascertain, s/he has followed the ethics protocol approved for this project.

Signed (supervisor): ……………………………..

Date: ………………….

4.8 Scientific Committee Approval from Participating Hospitals

4.8.1 Thriassio Hospital Scientific Committee Approval



ΕΘΝΙΚΟ ΣΥΣΤΗΜΑ ΥΓΕΙΑΣ
ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΕΛΕΥΣΙΝΑΣ «ΘΡΙΑΣΙΟ»

ΑΠΟΣΠΑΣΜΑ ΠΡΑΚΤΙΚΩΝ ΤΗΣ 7ης Συνεδρίασης του 2010 του ΔΙΟΙΚΗΤΙΚΟΥ ΣΥΜΒΟΥΛΙΟΥ ΤΟΥ ΓΕΝΙΚΟΥ ΝΟΣΟΚΟΜΕΙΟΥ ΕΛΕΥΣΙΝΑΣ «ΘΡΙΑΣΙΟ»

Θέμα 4° Ιατρικής Υπηρεσίας

«Αίτημα της κας Τεκούση Μαρίας – ΠΕ Ψυχολόγων – για χορήγηση άδειας διεξαγωγής επιστημονικής μελέτης»

Το Δ.Σ του Νοσοκομείου, σήμερα Παρασκευή, 5 Μαρτίου 2010, βρέθηκε σε νόμιμη απαρτία παρόντων του Προέδρου κ. ΓΕΩΡΓΙΟΥ ΓΕΩΡΓΟΠΟΥΛΟΥ, του Αντιπροέδρου κ. ΝΙΚΟΛΑΟΥ ΧΑΤΖΗ και των μελών του κ.κ. α) ΓΕΩΡΓΙΟΥ ΠΕΓΚΟΥ, β) ΚΩΝ/ΝΟΥ ΜΑΚΡΥΝΟΡΗ γ) ΚΥΡΙΑΚΗΣ ΠΑΡΑΔΕΙΣΗ δ) ΔΗΜΗΤΡΗ ΑΝΤΩΝΙΟΥ - Αναπληρωτή Διοικητή, ε) ΜΙΧΑΗΛ ΜΠΕΛΤΣΙΟΥ στ) ΕΛΕΝΗΣ ΡΟΚΑ, και ζ) ΜΑΡΙΑΣ ΧΡΙΣΤΟΠΟΥΛΟΥ

Τίθεται υπόψη του Δ.Σ η με αρ. Πρωτ. 4839/16-2-2010 εισήγηση της υπηρεσίας που αφορά το παραπάνω θέμα και έχει ως εξής:

Σχετικά: Η υπ΄ αριθμ. πρωτ. 60/Φ4/09.02.10 απόφαση του Επιστημονικού Συμβουλίου

ΚΕΙΜΕΝΟ ΕΙΣΗΓΗΣΗΣ

Η Ιατρική Υπηρεσία συμφωνεί με την απόφαση του Ε.Σ. και εισηγείται θετικά στο αίτημα της κας Τεκούση Μαρίας – ΠΕ Ψυχολόγων – σχετικά με τη χορήγηση άδειας διεξαγωγής επιστημονικής μελέτης στο Γ.Ν.Ε. «Θριάσιο», στα πλαίσια της διδακτορικής της διατριβής στο Πανεπιστήμιο Hertfordshire της Αγγλίας, δεδομένης της συναίνεσης του Διευθυντή της Καρδιολογικής Κλινικής κ. Ολύμπιου Χ., με την προϋπόθεση να διαφυλαχθούν τα προσωπικά δεδομένα, να τηρηθεί ο κώδικας επιστημονικής δεοντολογίας και να μην υπάρξει οικονομική επιβάρυνση για το Νοσοκομείο.

Το Διοικητικό Συμβούλιο του Νοσοκομείου άκουσε την εισήγηση της Υπηρεσίας και μετά από διαλογική συζήτηση μεταξύ των μελών του,

ΑΠΟΦΑΣΙΖΕΙ ΟΜΟΦΩΝΑ και

Εγκρίνει το αίτημα της κας Τεκούση Μαρίας – ΠΕ Ψυχολόγων για τη διεξαγωγή επιστημονικής μελέτης στο Γ.Ν.Ε. «Θριάσιο», στα πλαίσια της διδακτορικής της διατριβής στο Πανεπιστήμιο Hertfordshire της Αγγλίας, δεδομένης της συναίνεσης του Διευθυντή της Καρδιολογικής Κλινικής κ. Ολύμπιου Χ., με την προϋπόθεση να διαφυλαχθούν τα προσωπικά δεδομένα, να τηρηθεί ο κώδικας επιστημονικής δεοντολογίας και να μην υπάρξει οικονομική επιβάρυνση για το Νοσοκομείο.

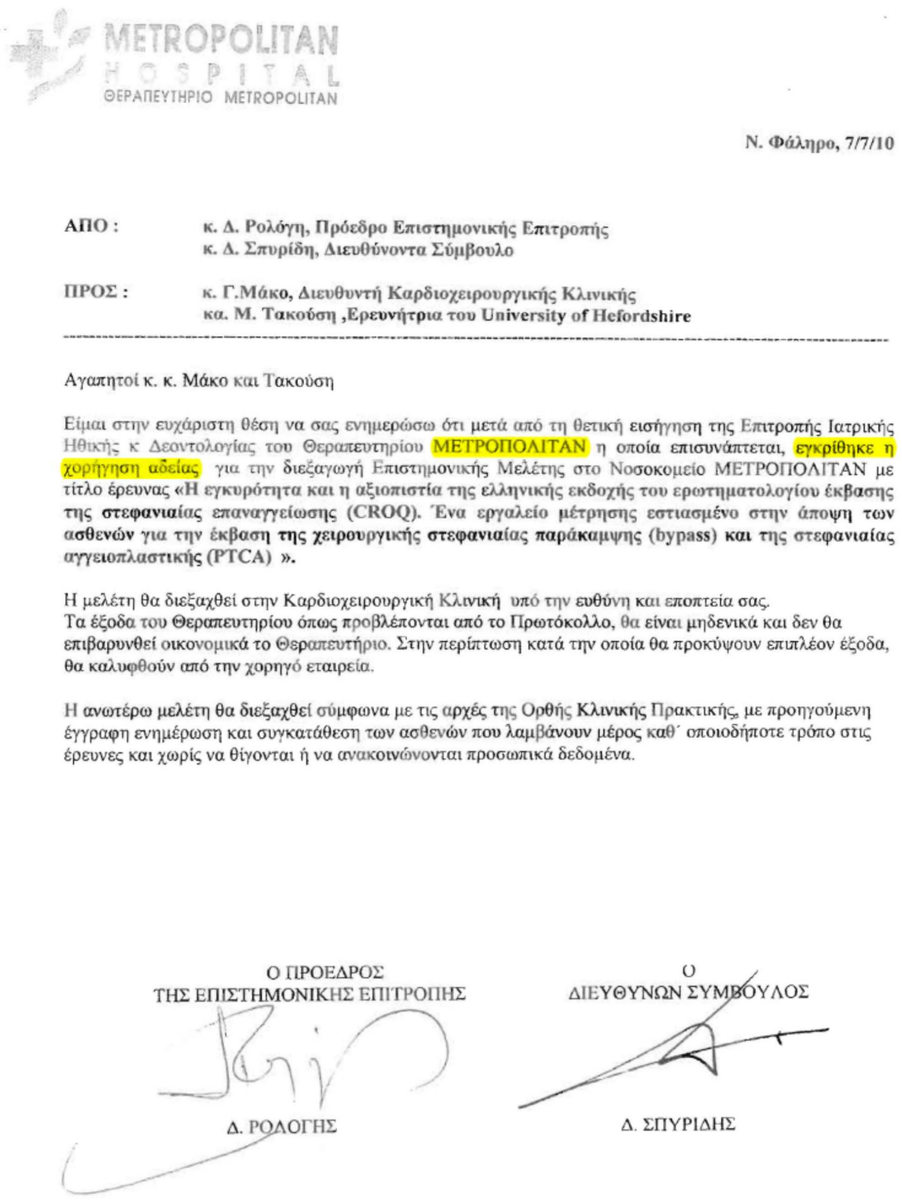
Η παρούσα απόφαση επικυρούται αυθημερόν για την άμεση εκτέλεσή της.
Η απόφαση αυτή πήρε αριθμό 7/05-03-10 (Θέμα 4° Ιατρικής Υπηρεσίας)

Ελευσίνα 8/3/10
Ο Πρόεδρος του Δ.Σ.
ΓΕΩΡΓΙΟΣ ΓΕΩΡΓΟΠΟΥΛΟΣ

Ακριβές Φωτοαντίγραφο
Ελευσίνα 15/3/10
Η γραμματέας Σ.Δ.
Κωνσταντινίδα

1

4.8.2 Metropolitan Hospital Scientific Committee Approval



METROPOLITAN
HOSPITAL
ΘΕΡΑΠΕΥΤΗΡΙΟ METROPOLITAN

Ν. Φάληρο, 7/7/10

ΑΠΟ : **κ. Δ. Ρολόγη, Πρόεδρο Επιστημονικής Επιτροπής**
κ. Δ. Σπυρίδη, Διευθύνοντα Σύμβουλο

ΠΡΟΣ : **κ. Γ.Μάκο, Διευθυντή Καρδιοχειρουργικής Κλινικής**
κα. Μ. Τακούση ,Ερευνήτρια του University of Hefordshire

Αγαπητοί κ. κ. Μάκο και Τακούση

Είμαι στην ευχάριστη θέση να σας ενημερώσω ότι μετά από τη θετική εισήγηση της Επιτροπής Ιατρικής Ηθικής κ Δεοντολογίας του Θεραπευτηρίου ΜΕΤΡΟΠΟΛΙΤΑΝ η οποία επισυνάπτεται, εγκρίθηκε η χορήγηση αδείας για την διεξαγωγή Επιστημονικής Μελέτης στο Νοσοκομείο ΜΕΤΡΟΠΟΛΙΤΑΝ με τίτλο έρευνας **«Η εγκυρότητα και η αξιοπιστία της ελληνικής εκδοχής του ερωτηματολογίου έκβασης της στεφανιαίας επαναγγείωσης (CROQ). Ένα εργαλείο μέτρησης εστιασμένο στην άποψη των ασθενών για την έκβαση της χειρουργικής στεφανιαίας παράκαμψης (bypass) και της στεφανιαίας αγγειοπλαστικής (PTCA) ».**

Η μελέτη θα διεξαχθεί στην Καρδιοχειρουργική Κλινική υπό την ευθύνη και εποπτεία σας.
Τα έξοδα του Θεραπευτηρίου όπως προβλέπονται από το Πρωτόκολλο, θα είναι μηδενικά και δεν θα επιβαρυνθεί οικονομικά το Θεραπευτήριο. Στην περίπτωση κατά την οποία θα προκύψουν επιπλέον έξοδα, θα καλυφθούν από την χορηγό εταιρεία.

Η ανωτέρω μελέτη θα διεξαχθεί σύμφωνα με τις αρχές της Ορθής Κλινικής Πρακτικής, με προηγούμενη έγγραφη ενημέρωση και συγκατάθεση των ασθενών που λαμβάνουν μέρος καθ΄ οποιοδήποτε τρόπο στις έρευνες και χωρίς να θίγονται ή να ανακοινώνονται προσωπικά δεδομένα.

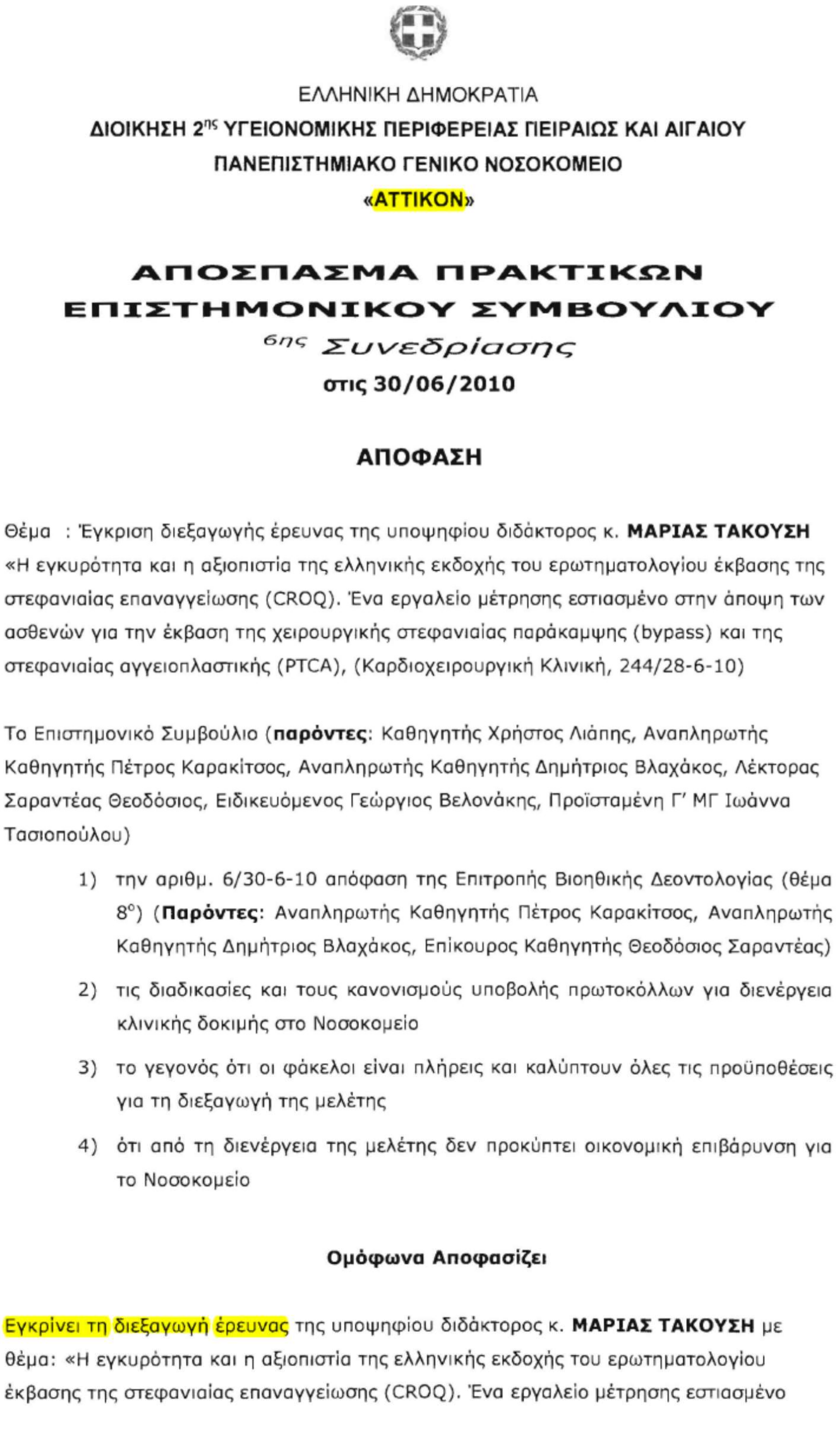
Ο ΠΡΟΕΔΡΟΣ
ΤΗΣ ΕΠΙΣΤΗΜΟΝΙΚΗΣ ΕΠΙΤΡΟΠΗΣ

Δ. ΡΟΛΟΓΗΣ

Ο
ΔΙΕΥΘΥΝΩΝ ΣΥΜΒΟΥΛΟΣ

Δ. ΣΠΥΡΙΔΗΣ

4.8.3 Attikon Hospital Scientific Committee Approval



ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
ΔΙΟΙΚΗΣΗ $2^{ης}$ ΥΓΕΙΟΝΟΜΙΚΗΣ ΠΕΡΙΦΕΡΕΙΑΣ ΠΕΙΡΑΙΩΣ ΚΑΙ ΑΙΓΑΙΟΥ
ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ
«ΑΤΤΙΚΟΝ»

ΑΠΟΣΠΑΣΜΑ ΠΡΑΚΤΙΚΩΝ ΕΠΙΣΤΗΜΟΝΙΚΟΥ ΣΥΜΒΟΥΛΙΟΥ

$6^{ης}$ Συνεδρίασης

στις 30/06/2010

ΑΠΟΦΑΣΗ

Θέμα : Έγκριση διεξαγωγής έρευνας της υποψηφίου διδάκτορος κ. **ΜΑΡΙΑΣ ΤΑΚΟΥΣΗ** «Η εγκυρότητα και η αξιοπιστία της ελληνικής εκδοχής του ερωτηματολογίου έκβασης της στεφανιαίας επαναγγείωσης (CROQ). Ένα εργαλείο μέτρησης εστιασμένο στην άποψη των ασθενών για την έκβαση της χειρουργικής στεφανιαίας παράκαμψης (bypass) και της στεφανιαίας αγγειοπλαστικής (PTCA), (Καρδιοχειρουργική Κλινική, 244/28-6-10)

Το Επιστημονικό Συμβούλιο (**παρόντες**: Καθηγητής Χρήστος Λιάπης, Αναπληρωτής Καθηγητής Πέτρος Καρακίτσος, Αναπληρωτής Καθηγητής Δημήτριος Βλαχάκος, Λέκτορας Σαραντέας Θεοδόσιος, Ειδικευόμενος Γεώργιος Βελονάκης, Προϊσταμένη Γ' ΜΓ Ιωάννα Τασιοπούλου)

1) την αριθμ. 6/30-6-10 απόφαση της Επιτροπής Βιοηθικής Δεοντολογίας (θέμα $8^{ο}$) (**Παρόντες**: Αναπληρωτής Καθηγητής Πέτρος Καρακίτσος, Αναπληρωτής Καθηγητής Δημήτριος Βλαχάκος, Επίκουρος Καθηγητής Θεοδόσιος Σαραντέας)
2) τις διαδικασίες και τους κανονισμούς υποβολής πρωτοκόλλων για διενέργεια κλινικής δοκιμής στο Νοσοκομείο
3) το γεγονός ότι οι φάκελοι είναι πλήρεις και καλύπτουν όλες τις προϋποθέσεις για τη διεξαγωγή της μελέτης
4) ότι από τη διενέργεια της μελέτης δεν προκύπτει οικονομική επιβάρυνση για το Νοσοκομείο

Ομόφωνα Αποφασίζει

Εγκρίνει τη διεξαγωγή έρευνας της υποψηφίου διδάκτορος κ. **ΜΑΡΙΑΣ ΤΑΚΟΥΣΗ** με θέμα: «Η εγκυρότητα και η αξιοπιστία της ελληνικής εκδοχής του ερωτηματολογίου έκβασης της στεφανιαίας επαναγγείωσης (CROQ). Ένα εργαλείο μέτρησης εστιασμένο στην άποψη των ασθενών για την έκβαση της χειρουργικής στεφανιαίας παράκαμψης (bypass) και της στεφανιαίας αγγειοπλαστικής (PTCA), (Καρδιοχειρουργική Κλινική, 244/28-6-10)

Υπεύθυνος: Μαρία Τακούση

Διευθυντής: Αναπλ. Καθ. Χρ. Ρόκκας

Παραπέμπει το θέμα στις αρμόδιες Υπηρεσίες για περαιτέρω ενέργειες

Ο Πρόεδρος του Επιστημονικού Συμβουλίου

Καθηγητής Χρήστος Δ. Λιάπης

Καθηγητής Χρήστος Δ. Λιάπης
Πρόεδρος Επιστημονικού Συμβουλίου
Π.Γ.Ν. "ΑΤΤΙΚΟΝ"

Ακριβές αντίγραφο
εκ του πρωτοτύπου
Χαϊδάρι 30-7-10

Ο ΠΡΟΪΣΤΑΜΕΝΟΣ
ΓΡΑΜΜΑΤΕΙΑΣ

ΡΙΤΑΣ ΑΧΙΛΛΕΑΣ

4.9 Participant information Sheet

4.9.1 Participant information Sheet (for study 1 & 2)

PARTICIPANT INFORMATION SHEET

I am a Greek PhD candidate in the field of health psychology from the University of Hertfordshire conducting a study on quality of life for people with your medical condition.

If you agree to take part you will be asked to complete a questionnaire about your heart condition, your physical symptoms and functioning in everyday life in the last 4 weeks. Generally, this takes approximately 15 minutes.

If you agree we will also contact you 2 to 3 months and twelve months (6 months in case of the 2nd stage) after today in order to measure your improvement. This will be done by telephone (at a number provided by yourself, at a time that suits you) for approximately 15 minutes. The phone call after 12 months will be the final one.

Any data you do provide today will remain both **confidential and anonymous** and will be used only for the purposes outlined here.

We are also asking for your permission to record some information (e.g. weight, previous medical history etc) from your medical record which will remain **confidential and anonymous** as well and your permission to keep this information in our files for three years after the completion of study (February, 2012).

You may use the contact number below should any queries or concerns arise in the future regarding the particular study. **If you have any concerns about your medical condition please contact your doctor.**

You will have an opportunity to ask questions now and at the end of the session.

Please note that any information you may supply today will only be used for the purposes outlined here, and you may withdraw your assistance at any time if you wish and without explanation. Moreover, keep in mind that the study is being carried out independently of the hospital and your decision with regard to your participation will not affect your health care.

Thank you for your participation

Name of Researcher: Maria Takousi
Contact Tel. no: 6937392080

The study is supervised by Dr Stefanie Schmeer, Dr Nick Troop and Dr Irene Manaras. For further details, requests or complaints you can contact Dr S. Schmeer (s.schmeer@herts.ac.uk) at the University of Hertfordshire, UK or Dr. I. Manaras at IST College, Greece. Call number: 2104822222 (office hours: 12-6)

The study has been approved by the University of Hertfordshire Ethics Committee; Protocol number PSY/03/10/MT

4.9.2 Participant information Sheet (for study 3)

Pre-interviewing Briefing Sheet

Title of project: Gaining in depth understanding of subjective meanings of HRQoL after CR

Thank you for agreeing to participate in the present study. As you already know I am a Greek PhD candidate in the field of health psychology from the University of Hertfordshire conducting a study on quality of life for people with your medical condition. Currently, I am interested in find out your perception about life changes and HRQoL after Coronary Revascularization.

Therefore, I will ask you some questions about your experiences and perception and I will record your responses as we discussed. The recording will allow me to capture any single word of your sayings. I will ask you specific questions already scheduled for the purpose of research, but I may ask you also some questions related to your sayings e.g. to find out more about your experience.

Any data you do provide today will remain both **confidential and anonymous** and will be used only for the purposes outlined here.

The interview is expected to be between 1-$1^{1/4}$ hours long. If you do not wish to reply to a question, please feel free to make it clear and we proceed to the next question. If you would like to stop the interview at any time, it is your right to do so without any explanations.

Do you have any questions you would like to ask me before beginning?

Please note that any information you may supply today will only be used for the purposes outlined here, and you may withdraw your assistance at any time if you wish and without explanation. Moreover, keep in mind that the study is being carried out independently of the hospital and your decision with regard to your participation will not affect your health care.

Thank you for your participation.

Name of Researcher: Maria Takousi

Contact Tel. no: 6937392080

Note: This study has been approved by School of Psychology Ethics Committee at the University of Hertfordshire (United Kingdom). Registration Protocol Number: **PSY/06/12/MT**. Furthermore, the study is supervised by Dr Nick Troop, Dr Stefanie Schmeer and Dr Irene Manaras. For further details, requests or complaints you can contact Dr N. Troop (n.a.troop@herts.ac.uk) or Dr S. Schmeer (s.schmeer@herts.ac.uk) at the University of Hertfordshire, UK or Dr. I. Manaras (imanaras@ist.eud.gr) at IST College, Greece. Call number: 2104822222 (office hours: 12-6)

4.10 Consent Form

4.10.1 Consent Form (for study 1 & 2)

CONSENT FORM

I …………………………………………………………………..(please write your name) give my full consent to take part in the research investigation carried out by Maria Takousi with the full understanding that I may withdraw at any time without giving any reason.

If I withdraw from the study, the data that I have submitted will also be withdrawn at my request. I have received an information sheet explaining what the study entails and what will be expected from me.

I understand that the information that I will submit will be confidential, and used only for this study. I have read and understood the above information.

Please tick one box on each line
I agree ☐ /do not agree ☐ to participate in the study.

I grant ☐ /do not grant ☐ access to my medical records.

Signed: ____

Date of birth: ___________________________________

Date: ____

Telephone number: ______________________________

Preferred contact hours: _____________________________

Researcher: Maria Takousi _________________________

Please keep in mind that any concerns about your medical condition should be discussed with your doctor.

The study has been approved by the University of Hertfordshire Ethics Committee; Protocol number PSY/03/10/MT

4.10.2 Consent Form (for study 3)

Consent form

Title of project: Gaining in depth understanding of subjective meanings of HRQoL after CR

Name of researcher: *Maria Takousi, PhD candidate in Psychology.*

To be completed by participant (Please initial each box):

1. I confirm that I have read and understand the information sheet for the present study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I realize that I am able to leave the study at any time without reason.	
3. I consent record my interview	
4. I understand that relevant sections of the data collected by this study would be looked at by authorised persons from the University of Hertfordshire. Anonymised sections of the data collected may also be looked at by representatives from academic and professional assessment bodies in order to assess the quality of this doctoral research project and possibly a peer research group to check for data themes. All will have a duty of confidentiality to you as a research participant	
5. I agree to take part in the above study.	
6. I agree that anonymised quotes from my interview may be used in any publications	
7. I understand that any concerns about my medical condition should be discussed with my doctor.	

Participant Name: **Signature:**

Date:

The study has been approved by the University of Hertfordshire Ethics Committee; Protocol number PSY/06/12/MT

4.11 Debriefing

4.11.1 debriefing (for study 1 & 2)

***DEBRIEFING** (baseline and 3months)*

The information you have provided will be used for creating a scientific questionnaire that will evaluate individuals' health outcomes and health-related quality of life after coronary angioplasty/ bypass. Also, the information you have provided will be used in detecting the impact of Coronary Revascularization in patients' HRQoL.

The particular instrument measures important aspects of a patient's health condition such as symptoms, physical functioning etc. and you have helped us in measuring them more precisely.

Please keep in mind that any concerns about your medical condition should be discussed with your doctor.

Do you have any further questions regarding the study?

***Thank you for your help**.*

You may contact me in the future on: 6937392080 Maria Takousi

The study is supervised by Dr Stefanie Schmeer, Dr Nick Troop and Dr Irene Manaras. For further details, requests or complaints you can contact Dr S. Schmeer (***s.schmeer@herts.ac.uk)*** at the University of Hertfordshire, UK or Dr. I. Manaras at IST College, Greece. Call number: 2104822222 (office hours: 12-6)

The study has been approved by the University of Hertfordshire Ethics Committee; Protocol number **PSY/03/10/MT**

DEBRIEFING *(12 months)*

The information you have provided will be used for creating a scientific questionnaire that will evaluate individuals' health outcomes and health related quality of life after coronary angioplasty/ bypass. Also, the information you have provided will be used in detecting the impact of Coronary Revascularization in patients' HRQoL.

The particular instrument measures important aspects of a patient's health condition such as symptoms, physical functioning etc. and you have helped us in measuring them more precisely and finding out how well the questionnaire measures these things after one year.

Please mind that any concerns about your medical condition should be discussed with your doctor.

Do you have any further questions regarding the study?

That's it! Thank you for everything.

You may contact me in the future on: 6937392080 Maria Takousi

The study is supervised by Dr Stefanie Schmeer, Dr Nick Troop and Dr Irene Manaras. For further details, requests or complaints you can contact Dr S. Schmeer (***s.schmeer@herts.ac.uk)*** at the University of Hertfordshire, UK or Dr. I. Manaras at IST College, Greece. Call number: 2104822222 (office hours: 12-6)

The study has been approved by the University of Hertfordshire Ethics Committee; Protocol number **PSY/03/10/MT**

4.11.2 Debrifing (for study 3)

Debriefing Sheet

The information you have provided will be used for investigating health outcomes and health related quality of life after coronary angioplasty/ bypass among individuals. More precisely, the questionnaire phase (quantitative research) is developed to measure and assess the impact of CR in relation to the dimensions (symptoms, physical, psychosocial and cognitive functioning) of HRQoL in short and long term. The interview phase (qualitative research) is developed to explore how individuals make sense of HRQoL and which individuals concerns regarding life changes are related to HRQoL.

Please mind that any concerns about your medical condition should be discussed with your doctor.

Do you have any further questions regarding the study?

Thank you for your participation.

Name of Researcher: Maria Takousi

Contact Tel. no: 6937392080

Note: This study has been approved by School of Psychology Ethics Committee at the University of Hertfordshire (United Kingdom). Registration Protocol Number: < **PSY/06/12/MT**>. Furthermore, the study is supervised by Dr Nick Troop, Dr Stefanie Schmeer and Dr Irene Manaras. For further details, requests or complaints you can contact Dr N. Troop (n.a.troop@herts.ac.uk) or Dr S. Schmeer (s.schmeer@herts.ac.uk) at the University of Hertfordshire, UK or Dr. I. Manaras (imanaras@ist.eud.gr) at IST College, Greece. Call number: 2104822222 (office hours: 12-6)

4.12 Participant comments on interview

Interview Schedule De-Briefing.

Participant name ....

Date...

I. State the purpose of study

- To explore individual's understanding of HRQoL after CR
- To investigate individual's perception of change to life style due to CR
- To ensure personal experience is heard.

II. Detect participant's experience about the interview

How did you find the interview? It was any part hard for you?

....

....

....

In your opinion, could anything be done differently? Would you like anything differently?

....

....

....

Could you make some recommendations in order to help me improve the interview?

……

……

……

III. Discover any unresolved themes raised from the interview

Do you have any questions which you feel still need answering?

……

……

……

Are there any concerns raised due to the interview?

……

……

……………………………………………………………………………………

IV. Future concerns and contact with researcher.

If you have any concerns or further queries about this research please do not hesitate to contact the researcher or the project supervisor.

The researcher and supervisor will be available for contact up to 12 months after participation.

Do you wish to be contacted to check themes? Yes ☐ No☐

4.13 Leaflet for psychosocial support services

INFORMATION LEAFLET

ON SUPPORT AVAILABLE IF YOU FEEL DEPRESSED

Everyone may feel depressed or anxious. These emotions are natural reactions to disappointment or apprehension. However, if you think your mood has been low for some time and is affecting your ability to cope with day-to-day life, you should contact your GP or counselling services and/or seek help and advice from professional organisations. Some of these organisations are listed below:

Hellenic Counselling Association
George 9, Plateia Kanigos, Athens
Tel: 211 4055774, http://www.hac.com.gr/

Association of Greek Psychologists
Leof. Basilisis Amalias 42, Athens
Tel: 210 6913500, http://www.seps.gr/

Thriassio Hospital- Psychiatric Department
Patriahou Grigoriou e 4, Aspropyrgos Attikis
Tel:210 5571855

Telephone center for psychosocial support (free of charge)
Tel: 197 & 210

4.14 Table of themes for the 1st interview

Mater theme 1: Experiencing the disease and its impact				
Themes	**Subthemes**	**Key words**	**Page**	**Text**
Becoming a patient	Clinical interactions	Mistrust of doctors	44	*Youngsters who were in their practical training… they were looking at me in terror… and with a sorrowful look .and I told them don't look at me like that… patients should not be looked at in this way,because it frustrates you, as if they wanted to burst into tears*
		Mistrust of the Greek health care system	4	*I had no confidence tothe Greek medical system*
		Frustration with the hospitals' cleaning services	32 32	*In the hospitals, that they provide almost nothing, that you can't wash yourself* *That brings you to a point that you're embarrassed of what you have… it's the absolute humiliation*
	Confronting medical uncertainty	Feeling like a guinea pig	1	*I had become a guinea pig. I was drinking a handful of pills and swallowed them all together*
		Doctors experiments with drugs	3	*They were doing experiments… all those things that happened to me were not because of the heart but pharmaceutical [side-effects] in reality*
		Over-consuming drugs	8-9	*Now drink magnesium and them potassium ... Whatever… a plethora of pills.*
		Medical uncertainty makes you feel insecure And despaired	33 35	*"We don't know what else to do to you", when they tell you that it makes you feel insecure* *And I was thinking… what they wanted me to do, did they want me to kill myself?*
		Ineffective treatment Expecting divine(God's) help	7	*And I was saying, since doctors cannot help me, something higher will help me*
	Feeling helpless	Feeling scared in the hospital	23	*Why do they run like loons ... don't they know that this terrifies the patient?*
		Feelling helpless/ loss of dignity/humiliation	32	*you callfor the nurse and have her say "coming now… coming now" and you want to go to the bathroom since that morning and end up going in the afternoon… it's the absolute humiliation*
		Feeling angry when treated as nearly dead	44	*Looking at him as if saying "I wonder how can you be alive"*
Living a post - surgery life	Experiencing multiple health problems	Disturbed bodily functionality Fearing diabetes Diabetes is a sneaky disease	2	*When I got the mi my whole body became desynchronized ..* *What I am afraid most is* *It is a sneaky disease.*

		It can destroy your organs and cause more damage to the heart		*It can destroy your kidneys, eyesight. The heart even more. You can get gangrene and have your handsmutilated.*
		Diabetes is a more frightening problem	3	*This is because I fear it more than the heart. And I face trouble to control it.*
	Living in grief (grief, loss of freedom desires and choices)	Body functions limit desires - (self pity- new dysfunctional body blocks life choices) Loss of freedom	18 20 19	*I'm not like before when I could do what I liked in life* *I cannot get on a plane and go anywhere I want.* *You do not have freedom*
		Grief about limited choices and suppressed desires	20	*From now on I cannot have a new boyfriend, not that I want to but if I did….*
		Grief about loss of body independence	33	*My body is falling apart … My poor body*
		Grief for self- irreversible life path	30	*It never came back on track*
	Feeling overprotected	Husband acting as lifeguard	24	*He hadn't slept for days…. He stood over me all night longlike the grim reaper*
	Everydaylife adjustments	Bland life/ losing pleasure	33	*[you can] never eat sweets, no bread, almost no pasta, some rice only… whereas… whereas I was living on sweets … you can't eat salt…. having to eat a burger without salt is tragic*
		Bland life/limitated-foods diet	33	*There are a million of foods that automatically go out. The cheese and stuff etc….*

Mater theme 2: The self in the body				
Themes	**Subthemes**	**Key words**	**Page**	**Text**
Experiencing the altered body	Body distortion	Loss of parts /body is falling apart	8	*Each time that I had a bath, I was observing my skin falling to pieces.*
	Fear of unknown future	Fear of the unknown when you have a sick body	12	*I am afraid … the future*
Acceptance of the weak body	Acceptance	Acceptance of body weakness and behaviour modification in terms of mobility (changes in bodily function)	20 25 27	*I don't have the same physical strength* *The body doesn't "rock" as it used to* *I can do everything, but move more slowly*
Self-reflection	Perceptions of disease causality	Causes of the health problem Heredity & stress & perfectionist and introvert	9 10	*Heredity, my father suffers from CHD* *it's the stress… because I was a perfectionist, and my introversion* *I will get furious and I don't express it…*
	Disease as a trigger	The old blind me (body and mind interaction)	16	*If I didn't go through this I wouldn't realize*
		Self criticism	14	*I believed that I was smarter than them but now I realize that I was the stupid one*
Experiencing a new me	Psychological self	Less anxious	42	*It's not that you do not stress yourself out but the intensity is different*
		Detached/depressed	9	*I am more detached from everything now*
		Less controlling/ less perfectionist /more easy going	9 43	*Why should I pay attention to all these?* *You think that only you can do things perfectly and that's the only way they work well. But I've seen that a lot of things can be done properly and work well without me interfering*
	Sexual self	Loss of sexuality	31 31	*I don't have a physical problem, but then again the sensation, the pleasure is not the same* *I'm ruined in that respect*
		Anger about the loss of sexuality	30	*Sex is of vital importance! Just like food, so it was with sex too…now… I lost it and that pissed me off*

Mater theme 3: Self and others				
Themes	**Subthemes**	**Key words**	**Page**	**Text**
You are alone	Being alone hurts	Being alone hurts (realizations)	16	*I was very much hurt by the fact that I was alone.*
		Feel abandoned	15	*I was left alone, completely alone*
	Disappointed	Disappointed with the extended family's attitude Feeling hurt from others' lack of compassion	23 12	*What hurts me most is the attitude of the members of my extended family* *It is hard to realise that your family believes you are dying*
Support	Practical and emotional support	Increased practical support from friends Practical support from the nuclear family Limited practical support from family	17 35 16 24 24 16 17	*Irrelevant people have helped me* *He offered me 50.000 euros* *Olga only …she was strong, a good friend… she took me on car trips, took me out for coffee… she really helped me a lot* *My children also helped me a lot.* *Do you know how it feels like when your own people don't stand by you?* *I was expecting they would support my children.* *When I returned home after the surgery nobody offered to help me… I had to cook for my children…*
Aspects of gender identity	Being a social person	The polite	9	*I was very social and friendly with everyone*
	Being a women	The feminine	34	*In the past I was very good looking and attractive*
	Being a daughter	Over-offering	28	*I had assumed all of my father's responsibilities… a Joanna of all trades*
	Being a mother	The patient	18	*I did a lot of patience to grow up my children*
Changes in relating with others	Behaving in a different way	Changes in feelings and behaviour	16	*I changed towards those who hurt me*
	Giving back what you get	Mirroring their behaviour	10 16 17	*You become insensitive* *Their behaviour forced me to change* *She was strong, a good friend… why should I alter my behaviour towards her?*
	Promoting independence	Be more independent as a mother	10	*You know… I would like to become more independent … I don't want to be with them all the time*

		Allowing children to be more independent	42	*They can do things by themselves*

Mater theme 4: Strategies for living a good life				
Themes	**Subthemes**	**Key words**	**Page**	**Text**
Regaining control	Setting boundaries	Share responsibilities	10	*Why should everything be done by me? Kostas can tidy up his room*
	Avoiding emotional expression	Not sharing feelings - disclosure makes problems difficult to control fear (facilitates suppression)	44 44	*I think that if I share my feelings, the problem will become worse* *It's been so much time now, even with Olga I don't discuss it any more*
	Minimizing the impact of the disease	Minimize the impact of the disease (minimize dysfunction to accept a new self)	33	*I have been destroyed a little bit*
		Change is superficial - new attitude not new personality	9 11 14	*Personality doesn't change* *Personality doesn't change the attitude towards others becomes different,* *My way of thinking and behaving changed*
	Humor	Humor- use of humor to reduce anxiety and insecurity	31 44	*Greece has lost a sexy woman* *I was joking with the doctors*
	Becoming doctor of the self	Focus on the self to find solution and gain self-control	8	*I've started to observe the impact on my body… when a drug caused side effects I stopped taking it*
		Be cautious, mistrust helps to control medical insecurity	44	*Youngsters who were in their practical training*
	Smoking to achieve emotional control	Smoking for emotional control (to reduce anxiety and stress that harms you heart)	39	*I couldn't feel my feet and felt like fainting. So I thought since I could hold on through this, I told myself that I do have a strong heart after all. But there it was, as soon as this was over, I lit a cigarette*
Finding meaning of good life	Achieving autonomy	What makes sense in life –dignity & autonomy /independence (first for me then for kids) Dependence makes you vulnerable (you don't have control)	38 10 38	*To be independent* *When you are not independent your dignity vanishes* *Quality of life is to be independent*
	Prioritizing the self	Rely on yourself to survive	10	*You have to learn to survive on your own*
		No need to be over-offering	42	*You shouldn't exhaust yourself because you don't help yourself that way*
		Protect yourself & your kids	34	*You learn to protect yourself and your kids*

5.1 Guidelines for translating and validating measures

The following paragraphs discuss the three stage process (Ware, et al., 1995) for translating and validating measures

5.1.1 Stage I: translation

This step involves forward and backward translations and pilot testing. A minimum of two individuals should independently translate the source instrument into the target language. The translators should be fluent in the target language (preferably native speakers) as well as having a good knowledge of the source language and they should focus on the conceptual instead of the literal equivalence. In other words, they should translate the meaning rather than the literal words, avoiding any medical terms and trying to create a version that is easy to read and understand (e.g. avoiding long, complicated sentences). After that, the two translators and the main researcher agree upon a preliminary forward translation and give this to a bilingual scientific panel. The scientific panel should resolve any possible discrepancies between the forward and the original version of the questions and thus, create a revised forward version. Afterwards, the back translation should be made by two different individuals whose mother tongue is ideally the original language as well as having a good understanding of the target language. Any possible inconsistency should be resolved by the scientific panel. Additionally, a small pre-pilot (preliminary) study with the target group (e.g. patients) should be run to assess acceptability, feasibility and understanding of the translated version and obtaining a basic level of content and face validity.

5.1.2 Stage II: test of scaling assumptions

The second stage focuses on testing the scaling assumptions. Five core assumptions should be explored: 1) equal item variance 2) missing data, 3) equality of item – scale correlations, 4) item discriminant validity and 5) reliability

5.1.2.1 __Equal item variance__

Equal item variance means that items measuring the same concept (e.g. physical functioning) should have approximately equal variance in order to contribute equally to the total scale score. To demonstrate equal item variance, descriptive statistics should be run illustrating the mean and the S.D. ranges for all items within each scale. In order to satisfy this assumption the items within each scale should demonstrate similar Standard Deviations of Likert Scores (S.D.S) compared to other items in the scale.

5.1.2.2 __Missing data__

In addition, descriptive statistics should demonstrate the amount of missing data. The proportion of missing data plays an important role in the degree of confidence that can be placed in a scale's measurement. For instance, a large amount of missing data from a particular item could indicate problems in wording or understanding. A low level of missing data can indicate a good level of instrument comprehension and acceptability on the part of respondents (Streiner & Norman, 2008).

5.1.2.3 ***Equality of item-scale correlations***

Equality of item-scale correlation refers to the assumption that the items include approximately the same amount of information about the construct being measured. In other words, the correlations between items within the same scale should be generally similar. The strength of correlation should be >0.40. However, other experts in the field of psychometrics suggest that a value for item-scale correlation >0.20 is acceptable (Streiner & Norman, 2008).

5.1.2.4 ***Item discriminant validity***

Item discriminant validity refers to the assumption that items of unrelated concepts should have a minimal correlation between them. In order to find support for item discriminant validity, the relationship between an item and its hypothesized scale should be significantly higher than the correlations between that item and all other scales. The standard criteria to assess item discriminant validity is based on standard errors. Two standard errors or more (≥2) indicates scaling success, meaning that the item-scale correlation is significantly higher for the hypothesized scale than for the competing scale. One (1) standard error indicates probable scaling success, meaning that the item-scale correlation is higher for the hypothesized scale than for the competing scale, but not significantly. Minus one (-1) standard error indicates probable scaling failure, meaning that the item-scale correlation is lower for the hypothesized scale than for the competing scale, but not significantly. Minus two standard errors (≥-2) indicates scaling failure, meaning that the item-scale correlation is significantly lower for the hypothesized scale than for the competing scale (Ware, 2004; Ware & Gandek, 1998). In recent years, computer programmes (e.g. Quality Metric Health Outcomes Scoring^{TM} Software 3.0) have been used to test scaling assumptions (Saris-Baglama et al., 2009). However, nowadays, many researchers use either inter-rater correlations (Danansuriya, Rajapaksa, & Varni, 2011) or zero-order correlations (Chorpita et al., 2010; Miller, Vachon, & Lynam, 2009; Schoofs, Hermans, & Raes, 2010) for establishing item discriminant validity. They accomplish this goal by demonstrating that items hypothesized to belong to one scale do not strongly correlate with items of another "irrelevant" scale (Streiner & Norman, 2008).

5.1.2.5 ***Reliability of instrument***

Reliability refers to the degree to which an instrument is free from measurement error. The reliability of an instrument can be assessed by using two basic methods: *internal consistency* and *test-retest reliability*.

Internal consistency

Internal consistency, as the term implies, demonstrates the degree to which items of a scale measure the same construct (i.e. scale homogeneity) and can be assessed with the use of the Cronbach's α (Cronbach, 1951) coefficient for items with three or more response choices (DeVellis, 2003; Field, 2005; Hays & Revicki, 2005; Marks, 2004; Streiner & Norman, 2008). The Cronbach's α coefficient ranges from 0 to 1. The higher the value, the greater the consistency. For establishing internal consistency in a scale the α coefficient should ideally be greater than 0.70 for group comparisons (Anastasi & Urbina, 1997; Streiner & Norman, 2008).

Test-retest reliability

Test-retest reliability, as the term suggests, reveals measurement stability. Test-retest reliability is measured by assessing the consistency between scores obtained by the same person on two different occasions (Anastasi & Urbina, 1997; Netemeyer, Bearden, & Sharma, 2003). Generally, test-retest reliability is evaluated by the Pearson Intra-class Correlation Coefficients (ICC) which represents the correlation between results for the two different time points. To establish test-retest reliability results should reach at least the criterion of 0.70 (Hays & Revicki, 2005; Streiner, & Norman, 2008; Ware & Gandek, 1998).

5.1.3 Stage III: Validation

Validity refers to the degree to which a measure captures the concepts for which it was designed and the appropriateness of the items contributing to the scale. Typically, three types of validity are assessed: content, construct and criterion (DeVellis, 2003; McDowell, 2006; Ware & Gandek, 1998). All types measure the degree of confidence concerning the inferences drawn from scores (Streiner & Norman, 2008).

5.1.3.1 Content validity

Content validity is the extent to which the content of a scale is representative and relevant to the conceptual domain(s) it is aiming to measure (Haynes, Richard, & Kubany, 1995; Hays & Revicki, 2005; Stewart, Hays, & Ware, 1998; Streiner, & Norman, 2008; Sutton, & French, 2004;). In the International Quality of Life Assessment (IQOLA) project, content validity was achieved through focus group studies, formal cognitive tests and empirical studies in many countries (Ware, 2004; Ware et al., 1995). Usually, content validity is achieved by carrying out a literature review and by interviewing representatives of target groups and specialists in the target field in order to obtain both patients' and experts' point of view (Burns, 2010; Creswell & Clark, 2007). With such an approach both "content relevance" (the degree to which the content is relevant to participants) and "content coverage" (the degree to which all aspects of the subject area are covered) can be obtained (Streiner & Norman, 2008). Content relevance is often assessed with an additional approach known as *Judgment stage* (Lynn, 1986; Waltz & Bausell, 1983; Wynd, Schmidt, & Schaefer, 2003), which involves firstly a quantitative analysis and then a qualitative one (Haynes, Richard, & Kubany, 1995). In this approach, at least 5 experts (judges) are recruited to rate each item, after a detailed description of each of the domains by the researcher, on a four point scale where 1 indicates totally irrelevant content and 4 reflects extremely relevant content (Streiner & Norman, 2008). In addition, they are asked to propose alternatives for each item that scores between 1 and 3. Then with the use of the Cohen's Kappa coefficient the researcher calculates inter-rater agreement. Cohen's Kappa should be above 0.70 (Wynd, Schmidt, & Schaefer, 2003). The qualitative analysis focuses on the analysis of items with less than 0.70 of agreement which are then discussed with the five judges in order to make the appropriate changes. Often a very similar process is also adopted in the first stage (translation stage) for evaluating the conceptual equivalence between the source and the target instrument (Ware, 2004). Moreover, content validity can also be improved by comparing patient responses to items with open ended questions such as " *is there anything else you would like to tell us...*" (Schroter, 2001).

5.1.3.2 Construct validity

Construct validity refers to the degree to which an instrument correlates with variables in a way consistent with the theoretical framework (Stewart, Hays & Ware, 1998). In order to establish construct validity various analyses should be conducted; within-scale (internal) and in comparison to external criteria (external).

Construct validity : internal

In order to demonstrate within-scale construct validity, the structure of the scale should be identified (Gandek & Ware, 1998; Hays & Revicki, 2005).

Factor analysis is usually performed to determine the structure of a scale. It can be carried out to verify that items are correctly grouped together, that items in the same scale measure the same construct, that items in different scales measure different constructs, and finally, to identify items that contribute little to their intended scale. Items that measure a particular construct, such as physiological functioning, should load highly on the same factor and not on others measuring dissimilar constructs, such as cognitive functioning.

When factors of a model are set a priori, Confirmatory Factor Analysis is usually applied (Stevens, 1996) using the AMOS, LISREL or R programme. However, when cultural adaptation is the aim of the study, exploratory analysis can be carried out using SPSS to run Principal Axis Factoring extraction with a fixed number of factors (Newsom, 2005).

The first step for this process is to produce a correlation matrix among the variables under investigation in order to confirm that there are positive correlations among items under the same factor. Frequently, the step of generating a Scree plot is excluded since the number of factors for extraction is set a priori. Afterwards, data quality is investigated both by the Kaiser-Meyer-Olkin index which tests sampling adequacy (≥0.70), and by Bartlett's Test of Sphericity which reveals whether the existing correlations among variables allow factor analysis ($p<0.05$). Then, the type of extraction is chosen (Principal Components Analysis (PCA) or Principal Axis Factoring (PAF). In research aiming at the cultural adaptation of a measure, PAF with a varimax rotation is commonly selected (Burges, Fernandez, Autonell, Melloni, & Bulbena, 2007; Dianat, Ghanbari, & AsghariJafarabadi, 2014; Ferrer et al., 2006; Karteroliotis, 2008; Khodadady & Ghahari, 2011). An explanation might be that a PCA may provide poor estimates of loadings when sample is small (Snook & Gorsuch, 1989). Minimum acceptable factor loading values are between 0.30 and 0.40, depending on sample size (Field, 2005). Items may load on more than one factor (crossloading) and it is not always clear which factor they belong to. If the value of the difference between the crossloading items is greater than 0.20, the item is generally assumed to load on the factor for which it had the highest loading; if the difference is less than 0.20, the item should be 'flagged' as being related to more than one factor (Field, 2005).

Construct validity : external

To ascertain the construct validity of a scale with external criteria usually two fundamental aspects should be established: convergent and discriminant validity.

Convergent validity refers to the extent to which different ways of measuring the same construct intercorrelate providing similar results. Conversely, *discriminant validity* refers to the degree to which a measure does not correlate greatly with measures that do not theoretically measure the same construct (Hays, & Revicki, 2005). For example, the physical functioning scale of two different instruments should be highly correlated (homotrait-heteromethod). In contrast, a cognitive functioning scale should not correlate with a physical functioning scale (heterotrait-heteromethod or homomethod). Usually, these two subtypes of validity are evaluated simultaneously by using the multitrait-multimethod approach (Campbell & Fiske, 1959; Gandek & Ware, 1998; Hays & Revicki, 2005).

5.1.3.3 Criterion validity

Criterion validity consists of two basic subtypes; concurrent and predictive validity.

Concurrent validity, the most common type in psychometrics, represents the extent to which the results of an instrument correlates with the another measure (usually the most widely used in a particular research field) or other proven scientific tool that measures the same concept (Ratanawongsa et al., 2008). For instance, a gold standard to measure a self reported blood pressure instrument against might be a blood pressure monitor. As experts suggest true 'gold standard' HRQoL instruments are not available, thus criterion validity is very rarely established (Hays & Revicki, 2005). Efforts to establish criterion validity are often made by using the SF-36 (Seki et al., 2010).

Predictive validity refers to the prognostic ability that a measure has regarding another concept that is theoretically related (Hays & Revicki, 2005). For instance, it could be theorized that a measure of HRQoL should be able to predict how fast patients will return to work after coronary revascularization.

5.1.4 Sensitivity to change

In the literature, the terms "responsiveness" and "sensitivity to change" are often used interchangeably. In general terms, they refer to an instrument's ability to capture changes over time. However, there is a conceptual difference between these two notions (Corzillius, Fortin, &

Stucki, 1999; Liang, 2000). Responsiveness refers to a measure's capacity to capture clinically meaningful changes that are important to patients or to physicians. Sensitivity to change refers to a measurement's capacity to detect any change in state regardless whether the change is relevant or meaningful to the decision-maker. This distinction is of importance because a statistically significant change (difference) in state over time may not be synonymous with a clinically important change and vice versa (Kazis, Anderson, & Meenan, 1989; Pardasaney et al., 2012).

Sensitivity to change is used to detect mean changes between two intervals by using paired *t*-tests (Anastasi & Urbina, 1997). *Responsiveness* as stated above, aims to capture clinically meaningful change. Various ways for determining clinically meaningful change have been suggested in the literature (Revicki, Hays, Cella, & Sloan, 2008). However, no clear consensus exists regarding the best way to determine it (Crosby, Kolotkin, & Williams, 2003; Revicki, Hays, Cella, & Sloan, 2008). A great number of researchers (Crosby, Kolotkin, & Williams, 2003; Eisen, Ranganathan, Seal, & Spiro, 2007; Revicki, Hays, Cella, & Sloan, 2008) focus on determining responsiveness through distribution-based estimates (e.g. effect size (ES; Cohen, 1988), standardized response mean (SRM; Guyatt, Bombardier, & Tugwell, 1986), and standard error of measurement (SEM; Wyrwich, Tierney, & Wolinsky, 1999)). Cohen (1988) suggested that effect size represents a standardized measure of individual (or group) change over time and "can be viewed as indicative of clinically meaningful change" (p. 274, Eisen, Ranganathan, Seal, & Spiro, 2007). ES can be measured by Cohen's *d*, which is calculated by dividing the difference between pre-test and post-test scores by the standard deviation (SD) at pre-test (Cohen, 1988; Kinnear & Gray, 2008; Revicki, Hays, Cella, & Sloan, 2008). Using Cohen effect sizes of 0.20 are defined as small, 0.50 as moderate and 0.80 or greater as large (Cohen, 1988; Crosby, Kolotkin, & Williams, 2003; Liang, Fossel, & Larson, 1990). The basic limitations for determining responsiveness through ES are a) that SD and therefore effect size can be strongly influenced by sample size and b) ES does not account for the variation in change (Crosby, Kolotkin, & Williams, 2003; Revicki, Hays, Cella, & Sloan, 2008).

5.2 Descriptive statistics for CROQ versions to assess item equal variance

5.2.1 Descriptive Statistics for PCI items per version

Table 1. Descriptive statistics for CROQ-Gr PCI items of baseline version

Subdomain	N	Min	Max	Mean	Std. Dev
PCI pre version					
Symptoms					
chest pain	244	1	5	3.11	1.26
discomfort	244	1	5	3.16	1.30
shortness of breath	244	1	5	3.02	1.26
angina radiates	244	1	5	3.77	1.35
palpitations	244	1	5	4.04	1.22
times per day	244	1	5	4.34	1.25
troubles	244	1	5	3.41	.94
Physical functioning					
moderate activites	244	1	3	2.43	.63
lifting	244	1	3	2.50	.65
climbing two or more flights of stairs	244	1	3	1.69	.78
climbing one flight of stairs	244	1	3	1.82	.77
bending	244	1	3	2.13	.77
walking a kl	244	1	3	1.84	.82
walking 100 m	244	1	3	2.16	.75
bathing	244	1	3	2.38	.60
Psychosocial functioning	244				
overprotective environ	244	1	5	3.46	1.13
burden on others	244	2	5	4.02	.88
restriction of social activities	244	1	5	3.85	.98
go far from home	244	2	5	3.96	.89
worried about heart cond	244	1	5	3.17	.99
worried about overdoing	244	1	5	3.12	1.01
worried about sudden attack	244	1	5	3.47	.89
frightened by pain	244	1	5	3.66	.85
uncertain about future	244	1	5	3.55	.98
depressed	244	1	5	3.65	1.06
frustrated / impatient	244	1	5	3.24	1.05
enjoyment of life	244	1	5	3.51	1.07
positive outlook of health	244	2	5	3.49	1.13
plan ahead	244	2	5	4.01	1.06
Cognitive functioning					
reasoning and solving problems	244	1	6	5.08	1.05
forget	244	1	6	5.17	1.07
concentration	244	1	6	5.14	1.08

Table 2. Descriptive statistics for CROQ-Gr PCI items of post 3 months version

	N	Min	Max	Mean	Std. Dev
Subdomain					
Symptoms					
post chest pain	254	4	5	4.87	.33
post discomfort	254	3	5	4.79	.46
post shortness of breath	254	3	5	4.76	.45
post angina radiates	254	4	5	4.93	.25
post palpitations	254	1	5	4.81	.46
post intake frequency	254	3	5	4.94	.28
post troubles	254	2	5	4.72	.55
Physical functioning					
post moderate activities	254	1	3	2.88	.36
post lifting	254	1	3	2.78	.44
post climbing two or more flights	254	1	3	2.46	.63
post climbing one flight of stairs	254	1	3	2.76	.47
post bending	254	1	3	2.85	.44
post walking a km	254	1	3	2.74	.49
post walking 100 m	254	1	3	2.86	.37
post bathing	254	2	3	2.89	.30
Psychosocial functioning					
post overprotective environ	254	1	5	3.95	1.06
post burden on others	254	2	5	4.55	.70
post restriction of social activities	254	2	5	4.44	.85
post go far from home	254	2	5	4.67	.67
post worried about heart cond	254	1	5	4.13	.84
post worried about overdoing	254	1	5	4.54	.80
post worried about sudden attack	254	1	5	4.37	.80
post frightened by pain	254	1	5	4.70	.69
post uncertain about future	254	1	5	4.40	.82
post depressed	254	1	5	4.36	.91
post frustrated / impatient	254	1	5	4.20	.89
post enjoyment of life	254	1	5	4.10	.94
post positive outlook of health	254	1	5	4.28	.85
post plan ahead	254	1	5	4.56	.74
Cognitive functioning					
post reasoning and solving problems	254	2	6	5.60	.76
post forget	254	1	6	5.56	.78
post concentration	254	1	6	5.64	.77
Adverse effects					
post pain in groin wound	254	3	5	4.92	.29
post tenderness	254	3	5	4.89	.34
post numbness or tingling	254	4	5	4.94	.23

Table 2. Descriptive statistics for CROQ-Gr PCI items of post 3 months version (continued)

	N	Min	Max	Mean	Std. Dev
post bruising	254	3	5	4.85	.41
post catheter point	254	4	5	4.94	.24
post concern for bruises	254	3	5	4.84	.43
Satisfaction					
post satisfaction about results	254	2	4	3.73	.50
post satisfaction about operation info	254	1	4	3.45	.66
post satisfaction about recovering info	254	1	4	3.53	.72
post heart condition after operation	254	2	4	3.72	.38
post recovery	254	1	4	3.60	.67
post results from heart operation	254	1	4	3.41	.80

5.2.2 Descriptive Statistics for CABG items per version

Table 1. Descriptive statistics for CROQ-Gr CABG items of baseline version

	N	Min	Max	Mean	S D
Symptoms					
chest pain	146	2	5	3.05	.79
discomfort	146	1	5	3.13	1.09
shortness of breath	146	1	5	2.99	1.02
angina radiates	146	1	5	3.63	.99
palpitations	146	1	5	3.73	1.09
sublingual times per day	146	2	5	4.13	1.09
troubles	146	1	5	2.92	.85
Physical functioning					
moderate activities	146	1	3	1.98	.49
lifting	146	1	3	1.96	.58
climbing two or more flight of stairs	146	1	3	1.64	.57
climbing one flight of stairs	146	1	3	1.63	.68
bending	146	1	3	1.83	.66
walking a km	146	1	3	1.64	.67
walking 100 m	146	1	3	1.84	.58
bathing	146	1	3	2.11	.58
Psychosocial functioning					
overprotective environment	146	2	5	3.68	.79
burden on others	146	2	5	4.11	.85
restriction of social activities	146	2	5	4.08	.85
go far from home	146	2	5	4.16	.84
worried about heart condition	146	2	5	3.42	.87
worried about overdoing	146	2	5	3.71	1.03
worried about sudden attack	146	2	5	3.84	.88
frightened by pain	146	2	5	3.79	.93
uncertain about future	146	1	5	3.66	1.01
depressed	146	1	5	3.73	1.07
frustrated / impatient	146	2	5	3.55	1.13
enjoyment of life	146	2	5	3.92	1.01
positive outlook of health	146	2	5	3.97	.95
plan ahead	146	2	5	4.27	.91

Table 1. Descriptive statistics for CROQ-Gr CABG items of baseline version					
	N	Min	Max	Mean	S D
Cognitive functioning					
reasoning and solving problems	146	2	6	5.12	.76
forget	146	2	6	4.95	.94
concentration	146	3	6	5.01	.90

Table 2. Descriptive statistics for CROQ-Gr CABG items of post 3 months version

Subdomain	N	Min	Max	Mean	S D
Symptoms					
post chest pain	133	3	5	4.66	.53
post discomfort	133	3	5	4.72	.51
post shortness of breath	133	3	5	4.58	.51
post angina radiates	133	3	5	4.85	.37
post palpitations	133	3	5	4.93	.28
post sublingual intake freq.	133	3	5	4.94	.28
post troubles	133	3	5	4.55	.57
Physical functioning					
post moderate activities	132	2	3	2.94	.24
post lifting	132	2	3	2.86	.34
post climbing two or more flights	132	1	3	2.60	.52
post climbing one flight of stairs	132	1	3	2.62	.51
post bending	132	2	3	2.84	.36
post walking a km	132	1	3	2.67	.48
post walking 100 m	132	2	3	2.77	.42
post bathing	132	2	3	2.88	.32
Psychosocial functioning					
post overprotective environment	132	2	5	3.73	.76
post burden on others	132	3	5	4.52	.57
post restriction of social activities	132	3	5	4.51	.67
post go far from home	132	3	5	4.48	.68
post worried about heart cond	132	2	5	4.01	.79
post worried about overdoing	132	3	5	4.64	.58
post worried about sudden attack	132	3	5	4.48	.75
post frightened by pain	132	2	5	4.36	.86
post uncertain about future	132	2	5	4.54	.77
post depressed	131	2	5	4.69	.66
post frustrated / impatient	132	2	5	4.27	.89
post enjoyment of life	132	2	5	4.26	.87

Table 2. Descriptive statistics for CROQ-Gr CABG items of post 3 months version (continued)

	N	Min	Max	Mean	S D
post positive outlook of health	132	2	5	4.61	.67
post plan ahead	129	2	5	4.73	.58
Cognitive functioning					
post reasoning and solving problems	132	3	6	5.18	.91
post forget	132	3	6	5.10	.98
post concentration	132	3	6	5.31	.87
Adverse effects					
croq.post.10a_cabg	132	2	5	4.01	.93
croq.post.10b_cabg	131	2	5	4.42	.90
croq.post.10c_cabg	132	1	5	3.55	1.06
croq.post.10d_cabg	132	2	5	3.97	.87
croq.post.10e_cabg	132	2	5	4.38	.81
croq.post.10f_cabg	132	1	5	4.53	.83
croq.post.10g_cabg	131	2	5	4.84	.50
croq.post.10h_cabg	132	1	5	4.82	.62
croq.post.10i_cabg	132	1	5	4.39	.93
croq.post.10j_cabg	131	2	5	4.61	.63
croq.post.10k_cabg	132	1	5	4.34	.85
Satisfaction					
satisfaction about results	127	1	4	3.40	.78
satisfaction about operation info	123	1	4	3.28	.88
satisfaction about recovering info	117	1	4	3.19	.99
post heart condition after operation	130	3	4	3.80	.33
post recovery	129	1	4	2.62	1.15
post results from heart operation	127	1	4	2.85	1.06

5.3 Zero-order item intercorrelations

5.3.1 Zero-order item intercorrelations for PCI versions

Table 1. Zero-order item intercorrelations for CROQ-Gr PCI pre revascularization (minimum-maximum)

Scale	Sym	Ph	Psy	Cogn
Sym	0.12-0.75	0.04-0.41	0.04-0.21	0.02-0.11
Ph		0.16-0.60	0.05-0.37	0.03-0.20
Psy			0.56-0.77	0.01-0.25
Cogn				0.85-0.91

Table 2. Zero-order item intercorrelations for CROQ-Gr PCI post revascularization (minimum-maximum)

Scale	Sym	Ph	Psy	Cogn.	Satisfaction	Adverse effects
Sym	0.15-0.46	0.13-0.36	0.03-0.36	0.01-0.32	0.02-0.29	0.01-0.26
Ph		0.57-0.79	0.06-0.45	0.09-0.25	0.09-0.24	0.01-0.30
Psy			0.38-0.72	0.06-0.29	0.07-0.36	0.07-0.32
Cogn				0.72-0.79	0.04-0.13	0.01-0.23
Satisfaction					0.56-0.82	0.11-0.38
Adverse effects						0.62-0.85

5.3.2 Zero-order items' intercorrelations for CABG versions

Table 1. Zero-order item intercorrelations for CROQ-Gr CABG pre revascularization (minimum-maximum)				
Scale	**Sym**	**Ph**	**Psy**	**Cogn**
Sym (7 items)	**0.20-0.59**	0.03-0.40	0.02-0.40	0.02-0.40
Ph 8 items	-	**0.33-0.69**	0.07-0.35	0.07-0.25
Psy 14 items	-	-	**0.21-0.75**	0.03-0.24
Cogn. 3 items	-	-	-	**0.57-0.66**

Table 2. Zero-order item intercorrelations for CROQ-Gr CABG post revascularization (minimum-maximum)							
Scale	**1**	**2**	**3**	**4**	**5**	**6**	**7**
1. Sym (7 items)	**0.12-0.60**	0.03-0.46	0.02-0.33	0.05-0.23	0.11-0.62	0.02-0.60	0.01-0.38
2. Ph (8 items)		**0.26-0.84**	0.01-0.37	0.01-0.26	0.03-0.36	0.01-0.23	0.01-0.34
3. Psy (14 items)			**0.21-0.73**	0.01-0.21	0.04-0.35	0.04-0.49	0.04-0.47
4. Cogn. (3 items)				**0.74-0.90**	0.02-0.42	0.06-0.47	0.16-0.52
5. Satisfaction (6 items)					**0.29-0.88**	0.13-0.59	0.05-0.40
6. Adverse effects (chest- 5items)						**0.44-0.73**	0.08-0.52
7. Adverse effects (leg/arm- 6items)							**0.45-0.81**

7.1 Sample sizes for qualitative studies

There are no specific set rules for determining the right sample size in qualitative studies (Baker, Edwards, & Doidge, 2012; Patton, 1990; Strauss, & Corbin, 2015; WHO, 2004). A number of scholars (e.g. Patton, 1990) suggest that qualitative sample size may be determined in relation to the time allotted, resources available and the study's aims which guide the kind of qualitative analysis.

However, it is generally accepted that the sample size for qualitative studies, although much smaller compared to quantitative studies, should be large enough to capture most possible perspectives. To accomplishing such a goal, saturation should be reached; saturation is present when adding more participants to the study does not result in gaining additional perspectives or information (Glaser, & Strauss, 1967). O'Reilly and Parker (2013), however argued that the concept of saturation in qualitative research and in particular in grounded theory "does not refer to the point at which no new ideas emerge, but rather means that categories are fully accounted for, the variability between them are explained and the relationships between them are tested and validated and thus a theory can emerge (p. 3). Nevertheless, various suggestions exist concerning sample size. For instance:

Morse (1994) suggests for an ethnographic approach, approximately 30 - 50 participants, for grounded theory 30 - 50 interviews, and for phenomenological studies at least 6.

Creswell (2014) suggests for a thematic or grounded theory a sample size of 20 – 30 while for phenomenological studies he recommends 5 to 25.

Smith and Osborn (2003) suggest for an interpretative phenomenological analysis (IPA) 5-10 participants. They argue that although the basic logic is to have a sample of approximately 15-20 individuals, for IPA the danger of such large sample is that the researchers will be overwhelmed by the vast amount of data generated and they will not be able to produce a sufficiently penetrating analysis. This actually is the reason that the majority of IPA studies published have very small number of participants (five or six).

7.2 Master table of themes

1. Modes of Patienthood: “*Your psychology is everything*”	
0.1. Experiencing the disease & its treatment: “*it’s scary… many thoughts come to your mind*”	
Confrontation with the diagnosis & treatment	*“You get a fright… that’s exactly how you feel…“The doctor simply told me “don’t be scared, it’s nothing, it has become a routine operation now” [but] you don’t know, does this thing hurt?”*
Clinical interactions	*“Youngsters who were in their practical training”*
Receiving medical treatment	*“The intensive care is a bit tiring… you can’t find peace and quiet*
Feeling helpless	*“looking at someone with terror… looking at him as if saying “I wonder how can you be alive”*
0.2. Living a post-CR life: “*I have quality of life, but there are other things that you can’t amend*”	
Defying patienthood	*“I don’t suppose it has affected my life… I don’t consider it a health problem ”*
Other concerns gaining primacy	*“The sugar[diabetes] is troubling me more than the heart”*
Differences of stage of life	*“the operation hasn’t influenced my self-perception. The age maybe...”*
0.3. Search for understanding: “I had a lot of time to think about it… why…why all this happened	
Perception of disease causality	*“It’s the stress… because I was a perfectionist, and my introversion”*
Self responsibility	*“The blame is all mine. It’s my fault, my wrong behavior brought us to this point…”*
2. The self in the body: “*I am different person now*”	
2.1. Sensing the altered body: “*I feel different now… but sometimes it troubles me what tomorrow will bring*”	
The body becomes visible	*“doesn’t say as used to do ”*
Fear of the unknown	*“but it’s the heart, I am afraid I may not …”*
2.2. Experiencing a new me: *“It's not that you do not stress yourself out but the intensity is different”*	
Developing psychological self	*“I am more relaxed... more distanced”*
My body-my self	*“I don’t say we do the acrobatics but… we’re still young, our blood is warm ”*
3. Self and others: “*So what if they see it differently ... relax ... you cannot control everything*”	
3.1. You are alone: “*and I was left alone, all alone*”	
Being alone hurts	*“I was very much hurt by the fact that I was alone”*
Feeling disappointed	*“Do you know what bothered me most? That they didn’t care to ask if my wife needed anything”*
3.2. In need of support: “*I felt as if they wanted to help*”	
Receiving practical support	*“more on financial matters”*
What you really need	*“she took me on car trips, took me out for coffee… She really helped me a lot”*
3.3. Changes in relating with others: “*You should see things differently*”	
Thinking in a different way	“*Why do I have to do everything?*”
Behaving in a different way	“*The truth is, most of them (ex friends), I pushed them away”*
4. Towards living a good life: “*Pull the sheet that blurs your mind*”	
4.1. Positive Growth : If I didn’t go through this I wouldn’t realize… life is too short	
Increased appretiation of life	“*Now I enjoy everything I do*”
Personal growth	“*I am stronger now*”
Strengthening relationships	*“I share quality time with my loved ones”*
4.2. Strategies to regaining control: *“I felt so good that I* was alive *…there are so many things that I would like to do”*	

Setting boundaries	“*I just don’t get myself to do whatever he asks for* ”
Minimizing the impact of the disease	“*It was nothing , it’s gone now* ”
Avoiding emotional expression	“*I can’t go on discussing the symptoms over and over again* ”
Using humor	*“Greece has lost a sexy woman*
Making comparisons with others	*“I am better compared to him”*
4.3. Challenges in living a new life style: *“I want to change but…”*	
Getting expert’s support	“*it would be useful if they gave you [medical] directives* ”
Persuading the self	“*Just as the doctor had told me, I have to go walking, but I’m bored*
Quitting smoking	“*we’ve given up far too many things now to quit smoking too* ”