EXAMINING THE ASSOCIATION BETWEEN DOMAINS OF FRAILTY AND 6-MONTH CHANGES IN HEALTH-RELATED QUALITY OF LIFE, LIVING STATUS, AND TREATMENT DECISIONAL REGRET AMONG OLDER PATIENTS REFERRED FOR CARDIAC SURGERY

by

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DEDICATIONS

I dedicate my MSc thesis to the memory of Karen Buth. A biostatistician and friend who introduced me to many of the statistical concepts and approaches used in this document.

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ABSTRACT

Background: Both age and frailty function as key preoperative risk factors for cardiac surgery. Age (chronological measurement) alone is usually a poor marker for predicting older patients' health status, most likely due to failure to reflect functional status in the measurement. Frailty status, which takes function into account, may be a better measure for older patients' health status, although multiple operational definitions of this construct exist. A small number of studies have demonstrated that frailty is a risk factor for various adverse outcomes after cardiac surgery, in older patients.

Objectives: The overall goal of this research was to determine the impact of varying degrees of frailty on the functional recovery of patients who undergo cardiac surgery. Specific objectives were as follows: (1) Determine the association between domains of frailty and change in HRQoL at baseline and 6 months post-surgery, (2) Determine the association between domains of frailty and dependent living status at 6 months post-surgery (3), determine the association between domains of frailty and treatment decisional regret at 6 months post-surgery.

Methods: A prospective cohort pre-post design was used to evaluate the exposure (frailty) and resulting outcomes (change in HRQoL; dependent living status; treatment decisional regret). Frailty was assessed preoperatively using the FACT, a frailty instrument that categorizes frailty in domains of mobility, social circumstances, daily tasks, and cognition. The primary outcome was HRQoL, measured preoperatively and at 6 months using EQ-5D-3L/EQ-VAS. Secondary outcomes were, dependent living status and treatment decisional regret, measured using the Functional Independence questionnaire, both assessed at 6 months post-surgery.

Results: Worse ADL function was positively associated with higher levels of impairment in mobility and usual function HRQoL from baseline to 6 months. As well, worse ADL function was negatively associated with greater HRQoL improvement in men as measured by index scores and across all procedure types as measured by EQ-VAS. Worse mobility function was negatively associated with higher levels of improvement in HRQoL in isolated AVR patients. Lastly, those with worse ADL function had higher odds of experiencing a dependent living status 6 months after surgery (aOR = 2.06 (1.42, 3.00)), and worse ADL (aOR = 1.89 (1.35, 2.65) and cognitive (aOR = 1.77 (1.26, 2.47) function had higher odds of regretting their decision to have surgery.

Discussion: The current study showed domain-specific frailty, particularly poor pre-operative ADL function, is negatively associated with an individual's capacity to return to optimal HRQoL post-operatively, independent living status and positively associated with experience of decisional regret. The evidence-based data has the potential to better inform patients who are at risk for loss of HRQoL and independence with cardiac surgery, allowing them to make decisions in line with values and preferences. Educating patients on the risks of frailty is an important aspect of patient-centered care and individualized prevention decision-making strategies based on patient priorities.

LIST OF ABBREVIATIONS USED

CABG	**Coronary Artery Bypass Graft**
AVR	**Aortic Valve Replacement**
HRQOL	**Health Related Quality of Life**
FACT	**Frailty Assessment in Care planning Tool**
CFS	**Clinical Frailty Scale**
FIA	**Functional Independence Assessment**
MHC	**Maritime Heart Centre**
ACS	**Acute Coronary Syndrome**
SDM	**Shared Decision Making**
ADL	**Activities of Daily Living**

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1.0 INTRODUCTION:

Life expectancy among Canadians is increasing, resulting in a growing population of older adults.[1,2] Consequently, there are older individuals developing conditions that make them candidates for invasive medical procedures. While it may be fairly stated that age is a risk factor for procedural complications, age alone is a poor discriminator of these complications among older patients who may or may not do well after complex procedures. Stated differently, chronological age (the number of years a person has been alive) and biological age (an assessment of physiological status) measure somewhat different constructs.[3] A more useful concept is the degree of frailty that an older patient has, measured as a multidimensional syndrome of loss of reserves (energy, physical ability, cognition, health) and an inability to respond to environmental stressors that result in vulnerability. [4,5] Since frail individuals are vulnerable, they also have a decreased capacity to regain or maintain homeostasis after a disrupting event.[6]

The many different definitions of frailty have led to the creation of multiple scales and indices to quantify it. Using these measures, studies have historically sought to correlate frailty to patient outcomes. A phenotype for frailty, as put forward by Fried et al., operationalized frailty within five domains: shrinking, weakness, poor endurance and energy, slowness, and low level of physical activity.[7] To qualify as frail, individuals had to have three of the five components. Using this phenotype, frailty was found to be an independent predictor of falls, disability, hospitalization, and death among American men and women, 65 years of age or older, at 3 and 7 years post-surgery. Makary et al. used the same phenotype of frailty to investigate frailty in surgical patients, 65 years of age and older. They found frailty to be an independent predictor of surgical complications, longer in-hospital stay, and discharge to a care institution.[8]

Our research group was the first to investigate frailty as a determinant of adverse cardiac surgical outcomes.[9] Using the Katz Index (a functional measure based on independence in performing six activities of basic living) combined with measures of decreased mobility (dependence on a walker) and previously documented dementia, we discovered that frail cardiac patients were at an increased risk for in-hospital mortality and discharge to institution for prolonged care (lack of independent living) as well as a shorter midterm survival rate. While up to 15% of patients referred for cardiac surgery were frail by this approach, it is considered a relatively insensitive measure as it dichotomizes frailty, and future work examining cardiac surgery outcomes would benefit from a more sensitive tool.[10]

Numerous other investigations were conducted using frailty indices, pioneered by Rockwood et al., calculated by a “deficit count” (number of symptoms, signs, diseases, disabilities or

laboratory abnormalities present in an individual divided by the total amount of deficits considered).[11] According to this operationalization, the more deficits that individuals have, the more frail they are likely to be.[12] Hastings et al. used a 44-item frailty index to investigate frailty as a risk factor of poor health-related quality of life (HRQoL) outcomes, for emergency department outpatients.[13] They found increased frailty led to an increased risk of hospitalization, nursing home admittance, and death in the 30 days following an emergency department visit. Similarly, Eeles et al. found that patients admitted to hospital for general medical services, who were deemed frail, had a shorter median survival compared to non-frail inpatients.[14]

Rockwood et al. have pioneered measurements of frailty and its impact on patients facing a variety of stressors.[15] Their development of the Clinical Frailty Scale (CFS) has several advantages as a validated measure of frailty. Specifically, it relies on clinical judgment based on patient interview covering a broad assessment of frailty, it does not require specialized testing or direct measurements avoiding the need for additional staff and equipment, and it has been validated in multiple studies. Mallery et al. have since developed a tool called the Frailty Assessment in Care Planning Tool (FACT) that measures self-reported frailty over multiple domains with multiple levels. By using a more sensitive measure, observations on the effect of frailty on outcomes can be extended to patients with lesser degrees of frailty. This measure provides increased sensitivity over multiple dimensions of frailty, and also requires less time, effort and training to administer.[16]

While previous research has demonstrated that frailty confers an increased risk of prolonged institutional care, as well as complications and mortality, the ultimate fate of surviving patients, in terms of return to home, and ultimate functional independence have yet to be established. It is critical to understand the HRQoL of frail patients at 6 months post-operatively, when there has been a sufficient chance for recovery from the invasive surgery. To date, few studies evaluate the relationship between frailty and 6-month HRQoL outcomes following surgical intervention, with a particular dearth in cardiac surgery.

To address this gap in the literature, and to improve our understanding of the contribution of frailty and age on the ultimate functional recovery of patients undergoing cardiac surgery we evaluated health related HRQoL, dependent living status and treatment decisional regret among 386 cardiac surgery patients aged 65 years or older from the QE II Health Sciences Centre in Halifax, NS and the New Brunswick Heart Centre in Saint John, NB from October 2015 and November 2019,.

2.0 BACKGROUND

2.1 Canada's aging population

Canada's population is aging. Demographic trends show that a decreasing birth rate and increased longevity will only further compound this issue.[17] From 2010 to 2063, those age 65 and over are projected to increase from slightly under 15 percent to over 25 percent of Canada's population.[18]

Trends from Statistics Canada demonstrate older adults (age 65 and over) make up the fastest-growing age group.[19] Accordingly, this demographic increased 14.1% from 2006 to 2011. In 2011, the proportion of seniors was the highest in the Atlantic provinces, Quebec, and British Columbia.[20] Nova Scotia had the highest population of seniors, 16.5%, in 2011, as well as the highest proportion of chronic conditions in the country.[21,22,23] As this shift towards an older demographic is unlikely to abate, there exists an urgency in how best to identify and evaluate HRQoL issues among this vulnerable population.

2.2 Frailty, Age and Adverse Cardiac Surgery Outcomes

Frailty is defined as a loss of physical and mental reserve which gives rise to health outcome vulnerabilities. In a recent study of hospitalized patients age≥70, 30% were found to be moderately or severely frail, and among frail surgical patients adverse outcomes are more common.[24] Makary et al. showed preoperative frailty was associated with an increased risk of postoperative complications (OR=2.54), length of stay (IRR=1.69) and discharge to an assisted living facility after previously living at home (OR=20.48).[25] Frail patients who undergo cardiac surgery were found to have an increased risk for discharge to institution for prolonged dependence on care (OR=6.3), in-hospital mortality (OR=1.8) and reduced mid-term survival (H.R. 1.5).[26] Age was also associated with increased risks of these adverse outcomes.[27,28] Currently, however, our understanding of the long term outcomes of these patients is incomplete. Given that patients with even a single measure of frailty had poor outcomes, it is important to explore the impact of degrees of frailty on patient outcomes to inform preventative efforts. Determining the impact of varying degrees of frailty on HRQoL outcomes may serve to better inform patients and clinicians involved in decision making about cardiac surgery among older adults with frailty.

2.3 Changing Face of the Cardiac Surgery Patient:

Patients referred for cardiac surgery are increasingly older, with multiple comorbidities, and are facing more challenging surgical interventions (e.g., combined valve and Coronary Artery

Bypass Graft (CABG) procedures) that carry higher morbidity and mortality rates than isolated procedures (e.g., isolated CABG). Epstein et al., utilizing a cross sectional survey demonstrated a 15% decline in the US in the rates of isolated CABG surgery.[29] At our centre, we have experienced similar changes. The Maritime Heart Center (MHC) is a single centre cardiac surgery unit located in Halifax serving the entire province of Nova Scotia and a portion of the population of Prince Edward Island. More than 1,000 major cardiac operations are performed at this center, per year. Examination of these data demonstrates a reduction in isolated CABG surgery from 80% to 61% of total cases from 1999 to 2010. During the same period, isolated valve surgery increased from 12% to 26% and combined valve/CABG cases increased from 9% to 12%. Both valve and valve plus CABG surgery are associated with higher risks of mortality and major morbidity than isolated CABG.[30]

In addition to the changing case mix, the patients referred for cardiac surgery are increasingly older. Among Halifax Infirmary patients presenting for CABG and/or valve surgery, the proportion of patients age >70 has increased from 36% to 43% in the past decade (linear trend p=0.0001). The proportion of octogenarians has increased from 7% to 12%; the proportion of frail patients has increased from 4.2% to 9.9%; the proportion of frail patients among octogenarians is over 20%; and the rate of prolonged institutional care among cardiac surgery patients has increased from 8% to 15%.[31] These findings are in agreement with other reports from the U.S.[32] These older patients are more likely to require valve surgery or combined valve/CABG procedures compared with patients age<70 (41% vs. 28%, p=0.0001). As well, older patients are more likely to present with comorbid illnesses and as urgent cases requiring hospitalization prior to surgical intervention.[33] This shift toward frail, older patients referred for complex surgeries creates a novel situation where there now exists a high degree of clinical equipoise between cardiac surgery and continued medical management.

2.4 Impact of frailty on cardiac surgical outcomes health-related quality of life, dependent living status, and treatment decisional regret

In 2014, our research group ran a pilot longitudinal study of patients undergoing cardiac surgery where frailty was determined through use of the FACT. Of 57 patients recruited from those over the age of 65 undergoing cardiac surgery, we found that fully 52% were positive for at least one category of frailty at a level of 4/7 (vulnerable). As a group these frail patients experienced higher rates of mortality, major complications, and prolonged institutional care. The FACT is a much more sensitive measure than the Katz Index (six measures of independence in activities of daily living) that was used previously. Utilizing the Katz Index along with an assessment of limited mobility and dementia, we demonstrated that 15% of patients over the age of 65 were demonstrably frail. This indicates the FACT tool is a far

more sensitive measure of frailty that is still associated with compromised outcomes in terms of mortality, morbidity, and prolonged institutional care. By evaluating frailty in this way, we are able to determine a wider variety of possible contributors to frailty, and capture more subtle degrees of frailty in vulnerable patients.

While we demonstrated that frailty confers an increased risk of discharge to institution for prolonged dependence on care, we were not able to follow patients post-discharge. It is critical to understand the longer-term outcomes of frail patients at 6 months post-operatively, when there has been a sufficient chance for recovery from the surgical insult. Moreover, the impact of surgery on the patient's HRQoL needs to be more fully explored. To this end,we measured HRQoL, using EQ-5D-3L and EQ-VAS, as well as assessed dependent living status and treatment decisional regret at 6 months post-operatively. This work has the potential to better inform patients who are at risk for loss of HRQoL and independence with cardiac surgery, allowing them to make decisions in line with their individual values and preferences. Using domains of frailty to better anticipate post-operative HRQoL outcomes could prove to better inform both potential patients and their surgical teams about the bio-psychological components that are not represented in traditional medical histories.

3.0 OBJECTIVES AND RESEARCH QUESTION

Objectives

The goal of this study was to examine the relationship between frailty among patients undergoing cardiac surgery and change in HRQoL outcomes, between baseline and 6 months post-surgery. To meet this goal, this study had three objectives:

(1) The primary objective was to determine the association between domains of frailty, as measured by the FACT, and changes in HRQoL scores from baseline to 6-month follow-up.

The secondary objectives were to: (2) Determine the association between domains of frailty and independence/dependence of living situation at 6-month follow-up; and (3) Determine the association between domains of frailty and treatment decisional regret at 6-month follow-up.

Research Questions

In this study, we proposed to answer the following research questions. Among patients aged 65 years old and older, who were referred for elective cardiac surgery in the Maritime region:

1. What is the association between varying domains of frailty as measured by the FACT and changes in HRQoL from baseline to 6-month follow-up?
2. What is the association between varying domains of frailty as measured by the FACT and dependent living status at six months?
3. What is the association between varying domains of frailty as measured by the FACT and treatment decisional regret at six months?

4.0 METHODS

4.1 Study Design

The current study used a prospective cohort pre-post design, with cross-sectional data at 6 months. Self-reported questionnaires were used to measure change in HRQoL, dependent living status, and treatment decisional regret.

4.2 Methodological approach

Enrollment and eligibility: The target population included all individuals, 65 years of age or older, set to receive a Coronary Artery Bypass Graft (CABG), Aortic Valve Replacement (AVR), or a CABG & AVR at the Halifax Infirmary or the New Brunswick Heart Centre. Exclusion criteria for this study were: emergent or urgent cases, preoperative intra-aortic balloon pumps , inotropes, cardiac shock, endocarditis, previous cardiac surgery, or a recorded ejection fraction of less than 35. Patients were asked to consent to evaluation of frailty preoperatively and measurement of HRQoL pre-operatively and at 6 months post-operatively.

Data Collection Procedures: The research team screened for patients who fit the inclusion and exclusion criteria as described above at two locations (the Halifax Infirmary and the Saint John Regional Hospital). Potential participants were approached at four locations in the hospital: inpatient wards, same-day admittance clinics, cardiovascular surgery clinics, and the cardiac catheterization clinics. Consenting patients underwent the following: Baseline Questionnaires (FACT, EQ-5D-3L, EQ-VAS) were administered to each participant and took approximately 10 minutes to complete. Follow-up questionnaires (EQ-5D-3L, EQ-VAS, and Functional Independence Assessment (FIA)) were administered to each patient at 6-months after their date of surgery and took approximately 20-25 minutes to complete. Participant information was assembled into a file and stored confidentially. Data were recorded and categorized in a secure database detailing participant information and participant scores for the appropriate questionnaires. Participant information was de-identified and recorded to assist with tracking and follow-up phone calls. This information was shared between NB and NS sites in a completely confidential manner, with study researchers performing password protection and anonymizing data before sharing.

Clinical Databases: All patients undergoing cardiac surgery at the recruiting institutions were entered into detailed observational databases that capture patient demographics, comorbidities, cardiac diagnostic data (disease severity), and procedural details. Both the MHC and Saint

John Horizon Health Network data were used to collect relevant patient data for adjusting each of the proposed models.

The study was approved by the Nova Scotia Health Authority Research Ethics Board (REB #1011856) and the Horizon Health Ethics Board (REB #2016-2205) in October 2015. The informed consent form informed patients about their rights and ensured that potential participants were completely aware their participation was voluntary, what the study entailed, that their privacy and confidentiality would be respected, and that they could withdraw from the study at any time. Written consent was obtained by each patient who agreed to participate in the study.

4.3 Measures:

Frailty (Predictor): Frailty was assessed using the Frailty Assessment in Care Planning Tool (FACT).[34] The FACT assesses four domains of frailty: mobility, socialization, usual function, and cognition, and each was measured by a seven-point scale, rated on a scale from 1 (thriving) to 7 (severely frail) (see Appendix 1-A: Participant Report on Overall Health). Cognition is further measured through memory recall and a clock drawing task.[35] The former was assessed by asking patients to remember three words (e.g. "apple", "penny", and "watch") and was coded 0: no correct recall; 1: 1 word recalled; 2: 2 or more words recalled. The second was assessed by asking patients to draw a clock with the arms of the clock pointing to "ten minutes after eleven" and was coded 0: normal clock; 1: abnormal clock.[36] (See Appendix 1-A: FACT Cognitive Assessment). A final cognitive score was obtained using the FACT Cognitive Assessment Algorithm, which prompts a series of questions[2] aligned to the seven levels of severity (coded 1-7), designed to ascertain the degree of cognitive impairment (See Appendix 1-A: FACT Cognitive Assessment Algorithm). The FACT originated from, and is linked with, the CFS, a reliable and well-validated measure of frailty.[37,38] A recent study compared the reliability of the FACT method with the CFS (which relies on clinician gestalt judgment) using the Frailty Index as the gold standard measure.[39] Compared to the CFS, the FACT correlated better with the Frailty Index (Pearson r=0.72 for the FACT versus r=0.56 for the CFS). However, unlike the Frailty Index, the FACT has the advantage of identifying the clinical drivers of frailty for each patient, which can be of value for guided decision-making.[40]

EuroQol-5 Dimension-3 Level HRQoL Descriptive System (EQ-5D-3L) and the EuroQol Visual Analogue System (EQ-VAS):

EQ-5D-3L Descriptive System

The EQ-5D-3L is a well-validated and reliable[41,42,43] generic measure of health-related quality of life consisting of two sections, the EQ-5D-3L and the EQ-VAS. It is one of the most widely used measures of health-related quality of life, with more than 180 official self-complete language versions currently available. The first section (EQ-5D-3L descriptive system) assesses an individual's HRQoL in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (See Appendix 1-B), each of which has three levels of response, recorded as: no problems (coded 1) , some problems (coded 2), or extreme problems (coded 3). EQ-5D-3L scores were evaluated in two ways: 1) by each of the five distinct domains; and 2) by combining the 5 domains into cumulative health states, which were then used to generate a single summary index score.

Generation of EQ-5D-3L health states and EQ-5D-3L single summary index scores

Each of the recorded scores (coded 1-3) generated across the five domains can be categorized as a health state. For example, a patient in health state 11111 would have no problems in any of the domains. A patient in health state 11223 would have no problems in mobility and self-care, some problems with usual activities and pain/discomfort, and extreme problems with anxiety/depression. (See Appendix 1-B for a scoring example of the EQ-5D-3L). A health state index score was calculated from individual health profiles using the Canadian value set.[44,.45,46]

EQ-VAS

The second part of the questionnaire consisted of a Visual Analogue Scale (EQ-VAS) on which the patient rates his/her perceived health, scored from 0-100 where endpoints are ‘the worst imaginable health (coded 0) and ‘the best imaginable health’ (coded 100). EQ-VAS questionnaires were administered at the same two time points as the EQ-5D-3L. Instructions to patients were included in the questionnaire.

Change in Quality of Life scores

For each of the EQ-5D-3L dimension scores, the health state index score, and the EQ-VAS scores, the variable under analysis is the change score between patient HRQoL scores at baseline and 6-month follow-up. Higher change scores for each of the EQ-5D-3L dimensions indicates greater impairment, whereas higher change scores in index and EQ-VAS scores indicate greater improvement.

Functional Independence Assessment (FIA)

The FIA is a phone-based interview consisting of 6 closed-ended questions and 6 open-ended questions to determine dependent living status (i.e. were they discharged to an institution or

still at home), functional independence, and patient's regret with the treatment decision (See Appendix 1-C). Closed-ended questions #2 and #4 were used in this study to elicit the quantifiable outcomes of dependent living status and treatment decisional regret. Question 2 asks "Which statement best describes your current living situation", with responses coded as "I live at home" (coded 0) or "I live in an institution (defined as: Nursing facility, rehabilitation centre, or home hospital)" (coded 1). Question 4 asks "Given how things have turned out, at this point in time, would you do this surgery again if you were in the same situation where you needed to have this surgery again?", with responses coded as "I live at home" (coded 0) or "I live in an institution (defined as: Nursing facility, rehabilitation centre, or home hospital)" (coded 1). The FIA was designed in response to the lack of available data surrounding ultimate functional outcomes of cardiac surgery patients following discharge from hospital. As such, little psychometric analysis has been conducted on the FIA to date.

Covariates

Covariates were selected based on previous literature indicating relevant associations with the outcomes of interest in patients referred for cardiac surgery.[47,48,49] For the purpose of this study, the following four covariates were employed: Age (dichotomized by ages 65-74 (coded 0) & 75+ (coded 1)); sex (male (coded 0) or female (coded 1)); province (Nova Scotia (coded 0); New Brunswick(coded 1)); and procedure type (isolated CABG (coded 1); Isolated Valve (coded 2) ; CABG + Valve (coded 3)).

Primary Outcome: Change in HRQoL from baseline (pre) to 6-month follow-up (post).

We hypothesized that lower self-reported FACT domain scores would experience greater improvement in HRQoL compared to those who report higher FACT domain scores. HRQoL was evaluated using the EQ-5D-3L dimension scores, the health state index score, and the EQ-VAS scores. The variable under analysis is the change score between patient HRQoL scores at baseline and 6-month follow-up.

Secondary Outcomes: Dependent living status and treatment decisional regret.

We hypothesized that lower self-reported FACT domain scores would experience greater independent living status and less treatment decisional regret compared to those who report higher FACT domain scores. Question 2 of the FIA allowed us to determine the ultimate destination of patients in terms of their living status whereas, Question 4 allowed us to begin to understand the decision-making mechanisms underlying either satisfactory or unsatisfactory patient outcomes following cardiac surgery.

Power Analysis: Based on the literature for AVR and AVR/CABG patients, we calculated that recruitment of 400 patients would provide 90% power to detect an effect size of 0.325 in EQ-5D-3L and in EQ-VAS, taking into account perioperative mortality and loss to follow-up.

4.4 Analytical approach

Descriptive data and regression assumptions for each of the objectives were assessed prior to analysis, and missing data were evaluated via multiple imputation methods (see Section 5.5: Sensitivity Analysis). 386 eligible participants were included in the study between October 2015 and November 2019. Excluded participants were due to ultimately receiving a different procedure (e.g. Percutaneous Coronary Intervention), rendering them ineligible to participate in the study. Baseline characteristics between province groups were assessed to determine if there were significant differences in preoperative demographic variables and medical characteristics between Nova Scotia and New Brunswick patient cohorts (see Table 5.1). Statistical tests appropriate to the type of variable and the distribution of data were used to evaluate significance.

Multiple linear regression, in covariate unadjusted and adjusted analyses, was used to model the relationship between level of frailty across domains of mobility, Activities of Daily Living (ADL), social and cognitive status and changes in HRQoL and self-reported general health, from baseline to 6 months, as measured by EQ-5D-3L subscores, index scores, and the EQ-VAS (objective 1). Prior to conducting the analyses the assumption of the test were evaluated and found to be tenable. Normality was assessed using normal QQ plots and histograms for outcome and predictor variables. Heteroskedasticity was assessed by inspecting scatterplots of the standardized residuals of the regression on the Y-axis and the standardized predicted values of the dependent variable on the X-axis. Tests for multicollinearity and collinearity were also performed, and assumptions for each of the HRQoL measures were found to be tenable (See Appendix 2-4). Skewness and kurtosis values were within appropriate ranges, though the EQ-5D-3L self-care sub-score showed some leptokurtic (see Appendix 2-A), yet values did not exceed 4 and thus were considered appropriate given the discrete nature of the data Follow up analyses assessed the interactions between the statistically significant predictors and statistically significant covariates in the models to test for possible effect modification by demographic characteristics.

Objective 2&3: Multiple logistic regression, in covariates adjusted and unadjusted analyses, was used to model the relationship between level of frailty across the four domains and patients' current dependent living status at the point of their 6 month phone follow up call (objective 2) as well as patients' decisional regret at the point of their 6 month phone follow

up call (Objective 3). Prior to running the analyses the assumptions of the test were evaluated and found to be tenable.

Missing Data

Listwise deletion reduced the sample size for EQ-5D-3L scores to 366 from 386 and for EQ-VAS scores to 364 from 386. For dependent living status, listwise deletion reduced the sample size to 368 from 386 and for treatment decisional regret to 359 from 386. Based on greater than 5.0% of our data missing across EQ-5D-3L, EQ-VAS, living status and decisional regret, multiple imputation (MI) was performed using IBM SPSS 25.0.[50] The Fully conditional specification (FCS) imputation method was selected, which is an iterative Markov Chain Monte Carlo (MCMC) method. The MCMC method can be used when the pattern of missing data is arbitrary.[51] We specified 20 iterations, as recommended by the literature.[52] For each iteration, and for each variable in the order specified in the variable list, the FCS method fit a univariate model using all other available variables in the model as predictors, then imputed missing values for the variable being fit. This method continues until the maximum number of iterations is reached. This results in 20 iterations of imputed datasets. The imputed datasets are each analyzed and the study results are then pooled into the final study result. For each of our analyses using MI, sensitivity analyses were performed to determine how the missing data affected the results. Analyses for the outcomes are reported for both original and multiple imputation (MI) pooled data.

All analyses were conducted using IBM SPSS version 25.0. Significance levels were set at 0.05.

5.0 RESULTS

5.1 Baseline patient characteristics

Of the 386 patients who participated in the study, 50.0% (n=193) were located in Nova Scotia and 50.0% (n=193) were located in New Brunswick. None of the preoperative characteristics of study participants were significantly associated with the patients' province of residence. The baseline preoperative characteristics are presented in Table 5.1. No statistically significant differences between the two provinces were observed between age categories ($X^2(1) = 0.19$, $p = 0.66$), gender ($X^2(1)=1.98$, $p=0.16$), and procedure type ($X^2(2)=0.25$, $p=0.69$). Given that there were no statistically significant differences between the two provinces with respect to patients' ages, sex or procedure type, we decided to collapse the data and run the following analyses using a pooled data set.

Table 5.1: Preoperative patient characteristics of age, age categories, sex, and procedure type by province, for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=386.

Clinical Characteristics	Total (n=386)	Nova Scotia (n= 193)	New Brunswick (n =193)	*p*-value
Patient age				
Median age (range), in years	72 (65-89)	72 (65-89)	73 (65-87)	0.34
Age Categories, n (%)				
65-74	268 (69.40%)	136 (69.95%)	132 (68.91%)	0.66
75≥	118 (30.60%)	57 (30.05%)	61 (31.09%)	
Sex, n (%)				0.16
Male	290 (75.10%)	151 (78.20%)	139 (72.00%)	
Female	96 (24.90%)	42 (21.80%)	54 (28.00%)	
Procedure, n (%)				0.69
Isolated CABG	235(60.90%)	121 (62.70%)	114 (59.10%)	
Isolated Valve	98 (25.40%)	48 (24.90%)	50 (25.90%)	
CABG + Valve	53 (13.70%)	24 (12.40%)	29 (15.00%)	

*** p<0.001, ** p<0.01, * p<0.05

5.2 Objective 1: Multiple Linear Regression Analyses predicting changes in quality of life from baseline to 6 month follow-up, as measured by a) EQ-5D-3L sub-score; b) Single summary Index score; c) EQ-VAS

5.2 a) EQ-5D-3L sub-score

Mobility

The unadjusted model predicting impairment change in mobility HRQoL scores from baseline to 6 months was statistically significant, indicating 6.0% of the variance for mobility can be explained by the predictor variables, $F(4,361) = 6.35$, $p<0.001$, $R^{2=}$ 0.07, adjusted $R^{2=}$ 0.06. ADL function was the sole statistically significant predicator of mobility HRQoL, $\beta = 0.16$,

sr^2=0.02, p <0.01 . After adjustment for covariates, the regression equation remained significant, F(8, 357)=3.59, p<0.001, R^2 =0.07, adjusted R^2=0.05. Results indicated that ADL function was the only statistically significant predictor of mobility HRQoL scores, as worse ADL function was positively associated with higher levels of impairment as indicated by changes in HRQoL scores from baseline to 6 months, β = 0.16, sr^2=0.02, p <0.01 (Table 5.2a). The adjusted model indicates 2% of the variance in mobility HRQoL was explained solely by ADL function.

Table 5.2a *Change in Mobility HRQoL*: Summary of Multiple Linear Regression Analysis for predicting decline in mobility quality of life subscale (EQ-5D-3L) from baseline to 6 month follow-up, by fitting FACT domains (mobility, social, ADL, and cognition) scores, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Impaired mobility from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	0.17***	3.03 (0.90)	0.04	0.06	0.003	0.17***	3.03 (0.90)	0.04	0.06	0.003
Social (FACT)[a]	0.18***	2.38 (0.94)	0.06	0.09	0.006	0.18***	2.38 (0.94)	0.06	0.10	0.006
ADL (FACT)[a]	0.23***	2.58 (1.02)	0.10	0.16**	0.02	0.23***	2.58 (1.02)	0.10	0.16**	0.02
Cognition (FACT)[a]	0.10*	1.79 (0.96)	0.01	0.01	0.0001	0.10*	1.79 (0.96)	0.01	0.01	0.0001
Age	-	-	-	-	-	0.05	-	0.03	0.02	0.0004
Sex	-	-	-	-	-	0.01	-	-0.06	-0.04	0.002
Province	-	-	-	-	-	-0.07	-	-0.08	-0.07	0.004
Procedure	-	-	-	-	-	-0.03	-	-0.04	-0.04	0.002
R^2		0.07***[b]					0.07***[c]			
Adj R^2		0.06***					0.05***			
F		*F (4,361) = 6.35****					F(8, 357) = 3.59***			

*** p<0.001, ** p<0.01, * p<0.05

[a] Worse performance or functioning

[b]Unique source of variability=0.02, shared variability=0.05, confidence limits from 0.02 to 0.12

[c]Unique source of variability=0.02 shared variability=0.05, confidence limits from 0.02 to 0.12

Self-Care

In the unadjusted model predicting change in self-care HRQoL scores from baseline to 6 months, none of the FACT scores were statistically significant predicators of self-care HRQoL, F (4,361) = 2.73, p<0.05, R2= 0.03, adjusted R2= 0.02. After adjusting for covariates, the regression model was not statistically significant, F(8, 357) = 1.88, p>0.05, R^2 =0.04, adjusted R^2=0.02. (Table 5.2b).

Table 5.2b *Change in Self-Care HRQoL*: Summary of Multiple Linear Regression Analysis for predicting decline in self-care quality of life subscale (EQ-5D-3L) between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Impaired self-care from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M(SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	0.15**	3.03 (0.90)	0.04	0.10	0.008	0.15**	3.03 (0.90)	0.05	0.10	0.008
Social(FACT)[a]	0.06	2.38 (0.94)	-0.01	-0.02	0.001	0.06	2.38 (0.94)	-0.01	-0.01	0.001
ADL(FACT)[a]	0.15**	2.58 (1.02)	0.04	0.10	0.008	0.15**	2.58 (1.02)	0.04	0.11	0.008
Cognition(FACT)[a]	0.05	1.79 (0.96)	0.01	0.01	0.001	0.05	1.79 (0.96)	0.01	0.01	0.001
Age	-	-	-	-	-	-0.02	-	-0.03	-0.04	0.002
Sex	-	-	-	-	-	0.01	-	-0.02	-0.03	0.001
Province	-	-	-	-	-	-0.01	-	0.01	0.01	0.001
Procedure	-	-	-	-	-	-0.09*	-	-0.05	-0.09	0.008
R^2			0.03*				0.04			
Adj R^2			0.02*				0.02			
F			*F* (4,361) = *2.73**				F(8, 357) = 1.88			

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

Usual Function

The unadjusted model predicting impairment change in usual function HRQoL scores from baseline to 6 months was statistically significant, indicating 9.0% of the variance for usual function can be explained by the predictor variables, F (4,361) = 10.18, p<0.001, $R^{2=}$ 0.10, adjusted $R^{2=}$ 0.09. Mobility, β = 0.15, sr^2=0.01, p <0.05, and ADL function, β = 0.21, sr^2=0.03, p <0.01, were statistically significant predicators of usual function subscores. After adjusting for covariates, mobility function (β = 0.14, sr^2=0.01, p <0.05), ADL function (β = 0.22, sr^2=0.03, p <0.01) and age category (β = -0.12, sr^2=0.01, p <0.05) statistically significantly predicted impairment in ADL. This indicated those in the older age group, with worse mobility and ADL function were positively associated with higher levels of impairment of usual function from baseline to 6 months (Table 5.2c). The adjusted model indicates 3.0% of the variance in usual function HRQoL was explained solely by ADL function.

Table 5.2c *Change in Usual Function HRQoL*: Summary of Multiple Linear Regression Analysis for predicting decline in usual function quality of life subscale (EQ-5D-3L) - between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Impaired Activities of Daily Living from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	0.26***	3.03 (0.90)	0.11	0.15*	0.02	0.26***	3.03 (0.90)	0.10	0.14*	0.01
Social (FACT)[a]	0.15**	2.38 (0.94)	0.02	0.03	0.001	0.15**	2.38 (0.94)	0.02	0.02	0.001
ADL (FACT)[a]	0.29***	2.58 (1.02)	0.14	0.21**	0.03	0.29***	2.58 (1.02)	0.14	0.22**	0.03
Cognition (FACT)[a]	0.08	1.79 (0.96)	-0.01	-0.01	0.001	0.08	1.79 (0.96)	-0.01	-0.01	0.001
Age	-	-	-	-	-	0.07	-	0.17	0.12*	0.01
Sex	-	-	-	-	-	0.15*	-	0.14	0.09	0.09
Province	-	-	-	-	-	0.01	-	-0.01	-0.01	0.01
Procedure	-	-	-	-	-	0.01	-	0.01	0.10	0.01
R^2			0.10***[b]					0.12***[c]		
Adj R^2			0.09***					0.10***		
F			*F (4,361) = 10.18****					F(8, 357) = 6.24***		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability= 0.05 shared variability= 0.05, confidence limits from 0.04 to 0.15

[c]Unique source of variability= 0.05 shared variability=0.07, confidence limits from 0.04 to 0.17

Pain and Discomfort

In the unadjusted model predicting change in pain and discomfort HRQoL scores from baseline to 6 months, the regression equation was not statistically significant ,F (4,361) = 0.33, p>0.05, $R^{2=}$ 0.01, adjusted $R^{2=}$ -0.01. After adjusting for covariates, the regression equation remained not statistically significant, F(8, 357) = 0.69, p>0.05, $R^{2=}$0.02, adjusted R^2=-0.01 (Table 5.2d).

Table 5.2d *Change in Pain and Discomfort HRQoL*: Summary of Multiple Linear Regression Analysis for predicting decline in pain and discomfort quality of life subscale (EQ-5D-3L) between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals October 2015 and November 2019, n=366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Increased Pain/Discomfort from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.01	3.03 (0.90)	-0.02	-0.02	0.004	-0.01	3.03 (0.90)	-0.03	-0.04	0.004
Social (FACT)[a]	0.04	2.38 (0.94)	0.04	0.05	0.003	0.04	2.38 (0.94)	0.04	0.06	0.003
ADL (FACT)[a]	0.02	2.58 (1.02)	0.02	0.03	0.004	0.02	2.58 (1.02)	0.01	0.02	0.004
Cognition(FACT)[a]	-0.02	1.79 (0.96)	-0.03	-0.04	0.002	-0.02	1.79 (0.96)	-0.03	-0.05	0.002
Age	-	-	-	-	-	0.03	-	0.05	0.04	0.004
Sex	-	-	-	-	-	0.08	-	0.13	0.09	0.003
Province	-	-	-	-	-	-0.06	-	-0.09	-0.07	0.004
Procedure	-	-	-	-	-	0.01	-	0.01	0.01	0.002
R^2			0.01					0.02		
Adj R^2			-0.01					-0.01		
F			*F (4,361) = 0.33*					F(8, 357) = 0.69		

*** p<0.001, ** p<0.01, * p<0.05
[a]Worse performance or functioning

Anxiety and depression

In the unadjusted model predicting change in anxiety and depression HRQoL scores from baseline to 6 months, none of the FACT scores were statistically significant predictors, F (4,361) = 2.50, $p<0.05$, $R^2= 0.03$, adjusted $R^2= 0.02$. After adjusting for covariates, the regression equation was statistically significant, F (8,357) = 2.30, $p<0.05$, $R^2= 0.05$, adjusted $R^2= 0.03$. Sex was the only significant predictor of anxiety and depression HRQoL scores from baseline to 6 months ($\beta = 0.12$, $sr^2=0.01$, $p <0.05$) (Table 5.2e).

Table 5.2e *Change in Anxiety and Depression HRQoL*: Summary of Multiple Linear Regression Analysis for predicting decline in anxiety and depression quality of life subscale (EQ-5D-3L) between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Worsened Anxiety/Depression from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	0.12*	3.03 (0.90)	0.04	0.05	0.002	0.12*	3.03 (0.90)	0.02	0.03	0.001
Social (FACT)[a]	0.10*	2.38 (0.94)	0.03	0.05	0.002	0.10*	2.38 (0.94)	0.04	0.05	0.003
ADL (FACT)[a]	0.15**	2.58 (1.02)	0.07	0.09	0.01	0.15**	2.58 (1.02)	0.07	0.08	0.008
Cognition (FACT)[a]	0.02	1.79 (0.96)	-0.03	-0.04	0.0004	0.02	1.79 (0.96)	-0.03	-0.04	0.002
Age	-	-	-	-	-	-0.02	-	-0.04	-0.03	0.001
Sex	-	-	-	-	-	0.14**	-	0.18	0.12*	0.01
Province	-	-	-	-	-	-0.05	-	-0.08	-0.06	0.004
Procedure	-	-	-	-	-	-0.08	-	-0.07	-0.08	0.006
R^2			0.03*				0.05*[b]			
Adj R^2			0.02*				0.03*			
F			*F (4,361) = 2.50**				F(8, 357) = 2.30*			

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b] Unique source of variability= 0.01 shared variability= 0.04, confidence limits from 0.01 to 0.08.

5.2 b) EQ-5D-3L single summary index score

The unadjusted model predicting improvement change in HRQoL index scores from baseline to 6-month follow-up was statistically significant, F (4,361) = 6.02, p<0.001, R^2= 0.06, adjusted R^2= 0.05. ADL function (β =-0.17, sr^2=0.02, p <0.01; β^{MI} =- 0.19, sr^{2MI}=0.02, p <0.05) was the sole statistically significant predicator of change in HRQoL index scores. After adjusting for covariates, ADL function remained as the only statistically significant predictor of HRQoL index scores (β =- 0.17, sr^2=0.02, p <0.01; β^{MI} =- 0.19, sr^{2MI}=0.02, p <0.05) (Table 5.2f). The results for the original data set and the MI pooled data were comparable (Table 5.2g). The addition of the interaction between ADL function and sex (β =-0.41, sr^2=0.01, p <0.05) contributed significantly to the change in HRQoL index scores (Table 5.2h). Sex stratified analyses indicated that the adjusted regression model predicting HRQoL index scores for men was statistically significant (F (7, 268)=3.12, p<0.01 ($R^{2=}$ 0.07, adjusted $R^{2=}$ 0.05)). ADL function (β =-0.14, sr^2=0.02, p <0.05) was a significant predicator of HRQoL index scores, indicating men with worse ADL function were negatively associated with higher levels of improvement in their HRQoL at 6 months compared to baseline (Table 5.2i). The adjusted regression equation for women was not statistically significant in predicting index scores, F (7, 82)=1.72, p>0.05, $R^{2=}$ 0.11, adjusted $R^{2=}$ 0.05. (Table 5.2j).

Table 5.2f *Change in EQ-5D-3L Index Score*: Summary of Multiple Linear Regression Analysis for predicting improvement in quality of life in single summary index score (EQ-5D-3L) between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n=366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in HRQoL Index Scores (EQ-5D-3L) from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.19***	3.03 (0.90)	-0.02	-0.08	0.005	-0.19***	3.03 (0.90)	-0.01	-0.07	0.004
Social (FACT)[a]	-0.14**	2.38 (0.94)	-0.01	-0.03	0.001	-0.14**	2.38 (0.94)	-0.01	-0.05	0.002
ADL (FACT)[a]	-0.23***	2.58 (1.02)	-0.03	-0.17**	0.02	-0.23***	2.58 (1.02)	-0.03	-0.17**	0.02
Cognition (FACT)[a]	-0.11*	1.79 (0.96)	-0.01	-0.04	0.001	-0.11*	1.79 (0.96)	-0.01	-0.03	0.001
Age	-	-	-	-	-	0.02	-	0.02	0.04	0.002
Sex	-	-	-	-	-	-0.12*	-	-0.03	-0.08	0.006
Province	-	-	-	-	-	0.08	-	0.03	0.08	0.006
Procedure	-	-	-	-	-	0.10*	-	0.03	0.09	0.01
R^2			0.06***[b]					0.09***[c]		
Adj R^2			0.05***					0.07***		
F-Statistic			*F (4,361) = 6.02****					F(8,357) = 4.14***		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.02, shared variability=0.04, confidence limits from 0.01 to 0.10

[c]Unique source of variability=0.03 shared variability=0.09, confidence limits from 0.02 to 0.14

Table 5.2g *Change in EQ-5D-3L Index Score (Multiple Imputation)*: Summary of Multiple Linear Regression Analysis with missing data multiple imputed (iterations = 20, pooled estimates) for predicting change in quality of life scores between baseline and 6 month follow-up, as measured by EQ-5D-3L index scores by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n=386.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in HRQoL Index Scores (EQ-5D-3L) from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	sr^2	**r**	**M (SD)**	**B**	**β**	sr^2
Mobility (FACT)[a]	-0.17**	3.03 (0.90)	-0.02	-0.05	0.005	-0.17**	3.03 (0.90)	-0.01	-0.04	0.004
Social (FACT)[a]	-0.12*	2.38 (0.94)	-0.01	-0.02	0.001	-0.12*	2.38 (0.94)	-0.01	0.01	0.002
ADL (FACT)[a]	-0.21***	2.58 (1.02)	-0.03	-0.19*	0.02	-0.21***	2.58 (1.02)	-0.03	-0.19*	0.02
Cognition (FACT)[a]	-0.10*	1.79 (0.96)	-0.01	-0.02	0.001	-0.10*	1.79 (0.96)	-0.01	-0.02	0.001
Age	-	-	-	-	-	0.02	-	0.02	0.06	0.002
Sex	-	-	-	-	-	-0.11*	-	-0.03	-0.09	0.006
Province	-	-	-	-	-	0.07	-	0.03	0.08	0.006
Procedure	-	-	-	-	-	0.08	-	0.02	0.08	0.01
R^2			0.05***[b]					0.07***[c]		
Adj R^2			0.04***					0.06***		
F-Statistic			*F (4,396) = 5.09****					*F (8,392) = 4.05****		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.02, shared variability=0.04, confidence limits from 0.01 to 0.09

[c]Unique source of variability=0.03 shared variability=0.09, confidence limits from 0.02 to 0.10

Table 5.2h *Change in EQ-5D-3L Index (Interaction)*: Summary of Multiple Linear Regression Analysis predicting improvement in quality of life by single summary index score (EQ-5D-3L) between baseline and 6 month follow-up, as measured by EQ-5D-3L index scores, by fitting FACT scores across domains, before and after adjustment of covariates and interaction terms for domain scores by sex and procedure for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n = 366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in HRQoL Index Scores (EQ-5D-3L) from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.19***	3.03 (0.90)	-0.02	-0.08	0.005	-0.19***	3.03 (0.90)	-0.03	-0.07	0.004
Social (FACT)[a]	-0.14**	2.38 (0.94)	-0.01	-0.03	0.001	-0.14**	2.38 (0.94)	-0.01	-0.05	0.002
ADL (FACT)[a]	-0.23***	2.58 (1.02)	-0.03	-0.17**	0.02	-0.23***	2.58 (1.02)	-0.06	-0.17*	0.02
Cognition (FACT)[a]	-0.11*	1.79 (0.96)	-0.01	-0.04	0.001	-0.11*	1.79 (0.96)	-0.04	-0.03	0.001
Age Category	-	-	-	-	-	0.02	-	0.02	0.04	0.002
Sex	-	-	-	-	-	-0.12*	-	-0.07	-0.08	0.006
Province	-	-	-	-	-	0.08	-	0.03	0.08	0.006
Procedure	-	-	-	-	-	0.10*	-	-0.09	0.09	0.001
*Mobility*Sex*	-	-	-	-	-	-0.15*	-	-0.01	-0.11	0.004
*Social*Sex*	-	-	-	-	-	-0.11*	-	-0.03	-0.14	0.003
*ADL*Sex*	-	-	-	-	-	-0.16*	-	-0.06	-0.41*	0.01
Cognition Sex*	-	-	-	-	-	-0.13	-	-0.01	-0.01	0.0001
Mobility Procedure*	-	-	-	-	-	-0.01	-	0.02	0.08	0.0004
Social Procedure*	-	-	-	-	-	-0.02	-	0.02	-0.07	0.001
ADL Procedure*	-	-	-	-	-	-0.05	-	-0.01	0.11	0.003
Cognition Procedure*	-	-	-	-	-	-0.01	-	0.02	0.08	0.006
R^2			0.06***[b]					0.12***[c]		
Adj R^2			0.05***					0.08***		
F-Statistic			*F (4,361)= 6.02****					F(*16,349*) = 2.99***		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.02, shared variability=0.04, confidence limits from 0.01 to 0.10

[c]Unique source of variability=0.03, shared variability=0.09, confidence limits from 0.02 to 0.17

Table 5.2i *Change in EQ-5D-3L Index (Sex Stratified by Men)*: Summary of Multiple Linear Regression Analysis for predicting improvement in single summary index health related quality of life score (EQ-5D-3L) in men between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n=276.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in HRQoL Index Scores (EQ-5D-3L) from baseline to 6 months for men	**r**	**M(SD)**	**B**	**β**	sr^2	**r**	**M(SD)**	**B**	**β**	sr^2
Mobility (FACT)[a]	-0.16**	2.32 (0.85)	-0.01	-0.06	0.004	-0.16**	2.32 (0.85)	-0.01	-0.06	0.003
Social (FACT)[a]	-0.17**	2.34 (0.86)	-0.03	-0.08	0.008	-0.17**	2.34 (0.86)	-0.03	-0.08	0.008
ADL (FACT)[a]	-0.20**	2.49 (0.94)	-0.03	-0.13*	0.01	-0.20**	2.49 (0.94)	-0.03	-0.14*	0.02
Cognition (FACT)[a]	-0.10	1.76 (0.94)	-0.01	-0.03	0.001	-0.10	1.76 (0.94)	-0.01	-0.03	0.001
Age Category	-	-	-	-	-	0.05	-	0.02	0.06	0.003
Province	-	-	-	-	-	0.09	-	0.03	0.08	0.005
Procedure	-	-	-	-	-	0.08	-	0.02	0.06	0.004
R^2			0.06**[b]					0.07**[c]		
Adj R^2			0.05**					0.05**		
F-Statistic			*F (4,271)=4.30***					*F (7, 268)=3.12***		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.01, shared variability=0.05, confidence limits from 0.01 to 0.11

[c]Unique source of variability=0.02, shared variability=0.05, confidence limits from 0.01 to 0.12

Table 5.2j *Change in EQ-5D-3L Index (Sex Stratified by Women)*: Summary of Multiple Linear Regression Analysis for predicting improvement in single summary index health related quality of life score (EQ-5D-3L) in women between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n=90.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in HRQoL Index Scores (EQ-5D-3L) from baseline to 6 months for women	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.19*	2.87 (1.20)	-0.02	-0.09	0.006	-0.19*	2.87 (1.20)	-0.02	-0.09	0.006
Social (FACT)[a]	-0.02	2.50 (1.15)	-0.04	-0.09	0.006	-0.02	2.50 (1.15)	-0.03	-0.09	0.006
ADL (FACT)[a]	-0.17*	3.34 (1.01)	-0.05	-0.11	0.02	-0.17*	3.34 (1.01)	-0.05	-0.11	0.01
Cognition (FACT)[a]	-0.11	1.89 (1.00)	-0.01	-0.03	0.001	-0.11	1.89 (1.00)	-0.01	-0.01	0.001
Age Category	-	-	-	-	-	-0.05	-	-0.01	-0.01	0.001
Province	-	-	-	-	-	0.08	-	0.04	0.08	0.008
Procedure	-	-	-	-	-	0.10	-	0.02	0.08	0.005
R^2			0.09*					0.07		
Adj R^2			0.07*					0.05		
F-Statistic			*F (4,85)=2.65**					*F (7,82)=1.72*		

*** p<0.001, ** p<0.01, * p<0.05
[a]Worse performance or functioning

5.2 c) EQ Visual Analogue Scale (EQ-VAS)

The unadjusted model predicting improvement change in HRQoL VAS scores from baseline to six months was statistically significant, F (4,359) = 9.92, p<0.001, R^2= 0.10, adjusted R^2= 0.09. ADL function was the only statistically significant predicator of HRQoL VAS scores, β =-0.18, sr^2=0.03, p <0.05, β^{MI} =- 0.14, sr^{2MI}=0.03, p >0.05. After adjustment for covariates, ADL function remained the sole statistically significant predictor of improvement change in HRQoL VAS scores, β =- 0.19, sr^2=0.03, p <0.01; β^{MI} =- 0.15, sr^{2MI}=0.03, p <0.01 (Table 5.2k), indicating 3.0% of the variance in improvement change in HRQoL VAS was explained solely by ADL function. The results for the original data set and the MI pooled data were comparable after adjustment (Table 5.2l).

The adjusted analysis indicated that the addition of the interaction between ADL function and procedure (β =-0.19, sr^2=0.002, p <0.05) contributed significantly to the improvement change

in HRQoL VAS scores (Table 5.2m). Procedure stratified analyses showed that the adjusted regression models predicting HRQoL VAS scores for CABG (F (8,355)=5.73, p<0.001, R^2= 0.11, adjusted R^2= 0.09), AVR (F (7, 84) = 2.65, p<0.05, R^2= 0.18, adjusted R^2= 0.11), and CABG+AVR (F (7, 41)=3.19, R^2= 0.24, adjusted R^2= 0.12) patients were statistically significant. ADL function (β =-0.19, sr^2=0.002, p <0.01) was the significant predicator of HRQoL VAS scores across all procedures (CABG: β =-0.19, sr^2=0.03, p <0.01; AVR: (β =-0.30, sr^2=0.03, p <0.05); CABG+AVR: (β =-0.44, sr^2=0.15, p <0.05), indicating worse ADL function was negatively associated with higher levels of improvement in HRQoL as measured by the VAS at 6 months compared to baseline (Table 5.2n). As well, mobility function (β =-0.26, sr^2=0.03, p <0.05) in AVR patients was a significant predictor of HRQoL VAS scores, indicating worse mobility function was negatively associated with higher levels of improvement in HRQoL as measured by the VAS at 6 months compared to baseline (Table 5.2n-p).

Table 5.2k *Change in EQ-VAS*: Summary of Multiple Linear Regression Analysis for predicting improvement in self-reported general health (EQ-VAS) between baseline and 6 months follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=364.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in VAS Scores (EQ-VAS) from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.21***	3.03 (0.91)	-2.34	-0.10	0.006	-0.21***	3.03 (0.91)	-2.49	-0.10	0.008
Social (FACT)[a]	-0.22***	2.38 (0.94)	-1.98	-0.09	0.006	-0.22***	2.38 (0.94)	-2.08	-0.10	0.006
ADL (FACT)[a]	-0.27***	2.58 (1.02)	-4.22	-0.18*	0.03	-0.27***	2.58 (1.02)	-4.45	-0.19**	0.03
Cognition (FACT)[a]	-0.17**	1.80 (0.96)	-1.39	-0.06	0.004	-0.17**	1.80 (0.96)	-1.36	-0.06	0.004
Age	-	-	-	-	-	-0.02	-	0.11	0.01	0.001
Sex	-	-	-	-	-	0.01	-	2.77	0.05	0.003
Province	-	-	-	-	-	0.02	-	0.72	0.02	0.001
Procedure	-	-	-	-	-	0.09*	-	3.27	0.11	0.01
R^2			0.10***[b]					0.11***[c]		
Adj R^2			0.09***					0.09***		
F			F(4, 359) = 9.92***					F(8, 355) = 5.73***		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.03, shared variability= 0.07, confidence limits from 0.02 to 0.14

[c]Unique source of variability=0.03 shared variability= 0.08, confidence limits from 0.03 to 0.15

Table 5.2l *Change in EQ-VAS (Multiple Imputation)*: Summary of Multiple Linear Regression Analysis with missing data multiple imputed (iterations = 20, pooled estimates) for predicting change in Visual Analog Scores between baseline and 6 month follow-up, as measured by EQ-VAS, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=386.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in VAS Scores(EQ-VAS) from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.21***	3.03 (0.91)	-2.34	-0.08	0.006	-0.21***	3.03 (0.91)	-2.53	-0.09	0.008
Social (FACT)[a]	-0.22***	2.38 (0.94)	-1.95	-0.09	0.006	-0.22***	2.38 (0.94)	-2.53	-0.08	0.006
ADL (FACT)[a]	-0.28***	2.58 (1.02)	-4.39	-0.14	0.03	-0.28***	2.58 (1.02)	-4.60	-0.15**	0.03
Cognition (FACT)[a]	-0.17**	1.80 (0.96)	-1.42	-0.07	0.004	-0.17**	1.80 (0.96)	-1.35	-0.06	0.004
Age	-	-	-	-	-	-0.03		-0.09	0.03	0.001
Sex	-	-	-	-	-	0.01		2.94	0.05	0.003
Province	-	-	-	-	-	0.02		0.61	0.02	0.001
Procedure	-	-	-	-	-	0.09*		3.31	0.10*	0.01
R^2			0.09***					0.11***[b]		
Adj R^2			0.09***					0.09***		
F			F(4, 396) = 9.89***					F(8, 392) = 5.74***		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.03, shared variability= 0.08, confidence limits from 0.02 to 0.15

Table 5.2m *Change in EQ-VAS (Interaction)*: Summary of Multiple Linear Regression Analysis for predicting improvement in self-reported general health (EQ-VAS) between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of covariates and interaction terms for domain scores by procedure for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n=366.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in HRQoL VAS Scores (EQ-VAS) from baseline to 6 months	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.21***	3.03 (0.90)	-2.34	-0.10	0.006	-0.21***	3.03 (0.90)	-2.56	-0.11	0.005
Social (FACT)[a]	-0.22***	2.38 (0.94)	-1.98	-0.09	0.006	-0.22***	2.38 (0.94)	-2.14	-0.10	0.006
ADL (FACT)[a]	-0.27***	2.58 (1.02)	-4.22	-0.18*	0.03	-0.27***	2.58 (1.02)	-3.05	-0.14	0.003
Cognition (FACT)[a]	-0.17**	1.79 (0.96)	-1.39	-0.06	0.004	-0.17**	1.79 (0.96)	-1.99	-0.08	0.008
Age Category	-	-	-	-	-	-0.02	-	0.37	0.01	0.001
Sex	-	-	-	-	-	0.01	-	2.61	0.05	0.003
Province	-	-	-	-	-	0.02	-	0.81	0.02	0.004
Procedure	-	-	-	-	-	0.09*	-	-3.27	-0.09	0.001
Mobility Procedure*	-	-	-	-	-	-0.03	-	-1.42	-0.16*	0.003
Social Procedure*	-	-	-	-	-	-0.07	-	0.75	0.08	0.001
ADL Procedure*	-	-	-	-	-	-0.11*	-	-1.65	-0.19*	0.002
Cognition Procedure*	-	-	-	-	-	-0.04	-	0.81	0.07	0.005
R^2			0.10***[b]					0.12***[c]		
Adj R^2			0.09***					0.09***		
F-Statistic			F(4, 359) = 9.92***					F(12, 351) = 4.09***		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.03, shared variability=0.07, confidence limits from 0.02 to 0.14

[c]Unique source of variability=0.05, shared variability=0.07, confidence limits from 0.04 to 0.18

Table 5.2n *Change in EQ-VAS (Procedure Stratified by CABG)*: Summary of Multiple Linear Regression Analysis for predicting improvement in self-reported general health (EQ-VAS) among CABG patients between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=223.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in VAS Scores (EQ-5D-3L) from baseline to 6 months in CABG patients	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.22***	2.56 (0.91)	-2.34	-0.09	0.006	-0.22***	2.56 (0.91)	-2.21	-0.10	0.008
Social (FACT)[a]	-0.13***	2.30 (0.83)	-1.98	-0.09	0.005	-0.13***	2.30 (0.83)	-2.07	-0.09	0.006
ADL (FACT)[a]	-0.27***	3.03 (1.01)	-4.22	-0.18*	0.03	-0.27***	3.03 (1.01)	-4.45	-0.19**	0.03
Cognition (FACT)[a]	-0.18**	1.79 (0.91)	-1.48	-0.06	0.004	-0.18**	1.79 (0.91)	-1.36	-0.06	0.003
Age Category	-	-	-	-	-	-0.02	-	0.11	0.01	0.0001
Sex	-	-	-	-	-	0.01	-	2.76	0.05	0.003
Province	-	-	-	-	-	0.02	-	0.72	0.02	0.0004
R^2			0.10***[b]					0.11***[c]		
Adj R^2			0.09***					0.09***		
F			*F (4, 359)=9.964****					*F (8,355)=5.73****		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.03, shared variability=0.07, confidence limits from 0.03 to 0.16

[c]Unique source of variability=0.03, shared variability=0.08, confidence limits from to 0.03 to 0.18

Table 5.2o *Change in EQ-VAS (Procedure Stratified by AVR)*: Summary of Multiple Linear Regression Analysis for predicting improvement in self-reported general health (EQ-VAS) among AVR patients between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=92.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in VAS Scores (EQ-5D-3L) from baseline to 6 months in AVR patients	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.35**	2.64 (0.94)	-6.81	-0.28*	0.04	-0.35***	2.64 (0.94)	-6.21	-0.26*	0.03
Social (FACT)[a]	-0.22**	2.51 (1.12)	2.34	0.08	0.006	-0.22**	2.51 (1.12)	2.50	0.09	0.008
ADL (FACT)[a]	-0.35***	3.01 (1.10)	-5.91	-0.29*	0.05	-0.35***	3.01 (1.10)	-5.91	-0.30*	0.05
Cognition (FACT)[a]	-0.05	1.78 (1.04)	2.49	0.09	0.006	-0.05	1.78 (1.04)	2.27	0.08	0.008
Age Category	-	-	-	-	-	-0.02	-	0.79	0.02	0.0004
Sex	-	-	-	-	-	-0.16	-	-3.30	-0.07	0.004
Province	-	-	-	-	-	0.09	-	2.98	0.07	0.005
R^2			0.17**[b]					0.18*[c]		
Adj R^2			0.13**					0.11*		
F			*F (4, 87)=4.59***					F(7, 84) = 2.65*		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.08, shared variability=0.09, confidence limits from 0.04 to 0.22

[c]Unique source of variability=0.08, shared variability=0.10, confidence limits from 0.05 to 0.24

Table 5.2p *Change in EQ-VAS (Procedure Stratified by CABG+AVR)*: Summary of Multiple Linear Regression Analysis for predicting improvement in self-reported general health (EQ-VAS) among CABG+AVR patients between baseline and 6 month follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospitals from October 2015 and November 2019, n=49.

	Model 1 (Unadjusted)					Model 2 (Adjusted)				
Improvement Change in VAS Scores (EQ-5D-3L) from baseline to 6 months in CABG+AVR patients	**r**	**M (SD)**	**B**	**β**	**sr^2**	**r**	**M (SD)**	**B**	**β**	**sr^2**
Mobility (FACT)[a]	-0.05	2.57 (0.76)	2.96	0.14	0.02	-0.05	2.57 (0.76)	2.73	0.08	0.01
Social (FACT)[a]	-0.15	2.45 (1.00)	-2.00	-0.11	0.01	-0.15	2.45 (1.00)	-2.30	-0.09	0.01
ADL (FACT)[a]	-0.36**	3.06 (0.90)	-6.27	-0.35*	0.09	-0.36**	3.06 (0.90)	-6.99	-0.44*	0.15
Cognition (FACT)[a]	-0.17	1.86 (1.04)	-0.87	-0.05	0.003	-0.17	1.86 (1.04)	-2.39	-0.05	0.003
Age Category	-	-	-	-	-	-0.08	-	4.80	0.08	0.008
Sex	-	-	-	-	-	0.17	-	3.21	0.08	0.008
Province	-	-	-	-	-	0.10	-	2.20	0.10	0.01
R^2			0.18*[b]					0.24*[c]		
Adj R^2			0.11*					0.12*		
F			*F (4, 44)=2.43**					*F (7, 41)=3.19**		

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

[b]Unique source of variability=0.09, shared variability=0.09, confidence limits from 0.01 to 0.34

[c]Unique source of variability=0.15, shared variability=0.09, confidence limits from 0.07 to 0.41

5.3 Objective 2: Multiple logistic regression analysis to predict change in the relationship between level of frailty across the four FACT domains and patients' current dependent living status at 6 month phone follow up call

Overall, 9.3% patients reported a dependent living status at the time of follow-up (See Appendix 5). In the unadjusted model (1), results of the multiple logistic regression assessing the relationship between level of frailty across the four domains and participant's dependent living status at 6 months indicate that ADL function was the only statistically significant predictor of dependent living status (OR = 1.95 (1.35, 2.80) $\chi^2(1) = 12.94$, p<0.001; OR^{MI} = 2.01 (1.39, 2.91) $\chi^2(1)^{MI} = 13.82$, p<0.001). After adjusting for covariates (model 2), ADL function remained the only statistically significant predictor of dependent living status (aOR = 2.06 (1.42, 3.00) $\chi^2(1)= 12.94$, p<0.001; aOR^{MI} = 2.11 (1.44, 3.09) $\chi^2(1)^{MI} = 13.53$, p<0.001), indicating those with worse ADL function had higher odds of experiencing a dependent living status 6 months after surgery (Table 5.3a). The results for the original data set and the MI pooled data were comparable (Table 5.3b).

Table 5.3a *Dependent Living Status*: Summary of Multiple Logistic Regression Analysis for predicting dependent living status (Functional Independence Assessment) at follow-up, by fitting FACT scores across domains before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n=368

	Model 1 (Unadjusted)				Model 2 (Adjusted)			
Dependent Living Status (vs independent) at 6 month follow-up	**OR (95% CI)**	**B**	**df**	**Wald χ^2**	**aOR (95% CI)**	**B**	**df**	**Wald χ^2**
Mobility (FACT)[a]	1.01 (0.70, 1.64)	0.07	1	0.09	1.05 (0.68, 1.61)	0.04	1	0.09
Social (FACT)[a]	0.91 (0.61, 1.36)	-0.09	1	0.20	0.87 (0.58, 1.30)	-0.14	1	0.20
ADL (FACT)[a]	1.95 (1.35, 2.80)***	0.67	1	12.94	2.06 (1.42, 3.00)***	0.72	1	12.94
Cognition (FACT)[a]	1.03 (0.70, 1.51)	0.03	1	0.02	1.03 (0.70, 1.51)	0.03	1	0.02
Age Category	-	-	-	-	1.18 (0.54, 2.59)	0.17	1	0.17
Sex	-	-	-	-	1.49 (0.66, 3.35)	0.36	1	0.91
Province	-	-	-	-	1.24 (0.60, 2.55)	0.21	1	0.33
Procedure Type	-	-	-	-			2	
AVR	-	-	-	-	0.88 (0.38, 2.00)	-0.13	1	0.09
CABG+AVR	-	-	-	-	0.26 (0.05-1.23)	-1.35	1	1.89

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

Table 5.3b: Summary of Multiple Logistic Regression Analysis with missing data multiple imputed (iterations = 20, pooled estimates) for predicting living status as measured by the Functional Independence Assessment at follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019.

	Model 1 (Unadjusted)				Model 2 (Adjusted)			
Dependent Living Status (vs independent) at 6 month follow-up	**OR (95% CI)**	**B**	**df**	**Wald χ^2**	**aOR (95% CI)**	**B**	**df**	**Waldχ^2**
Mobility (FACT)[a]	1.08 (0.70, 1.65)	0.07	1	0.34	1.04 (0.67, 1.59)	0.04	1	0.19
Social (FACT)[a]	0.90 (0.60, 1.34)	-0.09	1	0.41	0.86 (0.58, 1.30)	-0.15	1	0.25
ADL (FACT)[a]	2.01 (1.39, 2.91)***	0.68	1	13.82	2.11 (1.44, 3.09)***	0.75	1	13.53
Cognition (FACT)[a]	1.02 (0.70, 1.48)	0.02	1	0.02	1.03 (0.70, 1.51)	0.02	1	0.03
Age Category	-	-	-	-	1.18 (0.54, 2.59)	0.18	1	0.01
Sex	-	-	-	-	1.49 (0.66, 3.35)	0.33	1	0.40
Province	-	-	-	-	1.24 (0.60, 2.55)	0.23	1	0.08
Procedure Type	-	-	-	-			2	
AVR	-	-	-	-	0.89 (0.37, 1.91)	-0.14	1	0.10
CABG+AVR	-	-	-	-	0.28 (0.07-1.49)	-0.38	1	0.94

*** p<0.001, ** p<0.01, * p<0.05

[a]Worse performance or functioning

5.4 Objective 3: Multiple logistic regression analysis to predict change in the relationship between level of frailty across the four FACT domains and patient's treatment decisional regret at 6 month phone follow up call

Overall, 48 (13.3%) patients experienced treatment decisional regret at 6-month follow-up (See Appendix 6). In the unadjusted model (1), results of the multiple logistic regression assessing the relationship between level of frailty across the four domains and patient's treatment decisional regret at 6 months indicate that ADL (OR = 1.83 (1.32, 2.53), Wald $\chi^2(1)$= 13.38, p<0.001; OR^{MI} = 1.83 (1.32, 2.53) $\chi^2(1)^{MI}$ = 13.39, p<0.001) and Cognition (OR = 1.74 (1.25, 2.41), $\chi^2(1)$ = 10.83, p<0.01; OR^{MI} = 1.74 (1.25, 2.42) $\chi^2(1)^{MI}$ = 10.90, p<0.01) were the only statistically significant predictors of treatment decisional regret. After adjusting for covariates in Model 2, ADL (aOR = 1.89 (1.35, 2.65), $\chi^2(1)$ = 13.67, p<0.001; aOR^{MI} = 1.89 (1.34, 2.66) $\chi^2(1)^{MI}$ = 13.19, p<0.001) and cognition (aOR = 1.77 (1.26, 2.47), $\chi^2(1)$ = 11.01, p<0.01; aOR^{MI} = 1.78 (1.26, 2.50) $\chi^2(1)^{MI}$ = 11.90, p<0.01) FACT scores remained significant predictors of decisional regret, indicating those who had worse ADL and C-cognitive function had higher odds of regretting their decision to have surgery (Table 5.4a). The results for the original data set and the MI pooled data were comparable (Table 5.4b).

Table 5.4a *Treatment Decisional Regret*: Summary of Multiple Logistic Regression Analysis for predicting treatment decisional regret (Functional Independence Assessment) at follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019, n = 359.

	Model 1 (Unadjusted)				Model 2 (Adjusted)			
Treatment decisional regret(vs no regret) at 6 month follow-up	**OR (95% CI)**	**B**	**df**	**Wald χ^2**	**aOR (95% CI)**	**B**	**df**	**Wald χ^2**
Mobility (FACT)[a]	1.19 (0.78, 1.82)	0.18	1	0.68	1.16 (0.76,1.78)	0.15	1	0.49
Social (FACT)[a]	1.20 (0.82, 1.76)	0.18	1	0.86	1.11 (0.75, 1.64)	0.10	1	0.25
ADL (FACT)[a]	1.83 (1.32, 2.53) ***	0.61	1	13.38	1.89 (1.35, 2.65) ***	0.64	1	13.67
Cognition (FACT)[a]	1.74 (1.25, 2.41) **	0.55	1	10.83	1.77 (1.26, 2.47) **	0.57	1	11.01
Age Category	-	-	-	-	1.59 (0.78, 3.25)	0.46	1	1.59
Sex	-	-	-	-	1.81 (0.85, 3.84)	0.59	1	2.37
Province	-	-	-	-	1.50 (0.75, 3.02)	0.41	1	1.30
Procedure Type	-	-	-	-	-	-	2	
AVR	-	-	-	-	1.46 (0.48, 4.45)	0.38	1	0.44
CABG+AVR	-	-	-	-	1.97 (0.59, 6.57)	0.68	1	1.22

*** p<0.001, ** p<0.01, * p<0.05

[a] – Worse performance or functioning

Table 5.4b: Summary of Multiple Logistic Regression Analysis with missing data multiple imputed (iterations = 20, pooled estimates) for predicting decisional regret as measured by the Functional Independence Assessment at follow-up, by fitting FACT scores across domains, before and after adjustment of age, sex, province, and procedure type for Nova Scotia and New Brunswick Patients referred for Cardiac Surgery at the Halifax Infirmary and St John's Regional Hospital from October 2015 and November 2019.

	Model 1 (Unadjusted)				Model 2 (Adjusted)			
Dependent Living Status (vs independent) at 6 month follow-up	**OR (95% CI)**	**B**	**df**	**Wald χ^2**	**aOR (95% CI)**	**B**	**df**	**Wald χ^2**
Mobility (FACT)[a]	1.21 (0.80, 1.85)	0.19	1	0.88	1.17 (0.76, 1.79)	0.18	1	0.60
Social (FACT)[a]	1.22 (0.84, 1.77)	0.19	1	1.08	1.11 (0.75, 1.65)	0.11	1	0.25
ADL (FACT)[a]	1.83 (1.32, 2.53)***	0.61	1	13.39	1.89 (1.34, 2.66)***	0.64	1	13.19
Cognition (FACT)[a]	1.74 (1.25, 2.42)**	0.56	1	10.90	1.78 (1.26, 2.50)**	0.58	1	11.90
Age Category	-	-	-	-	1.60 (0.78, 3.23)	0.44	1	1.56
Sex	-	-	-	-	1.82 (0.86, 3.89)	0.52	1	1.94
Province	-	-	-	-	1.51 (0.75, 3.04)	0.41	1	1.09
Procedure Type	-	-	-	-			2	
AVR	-	-	-	-	1.46 (0.47, 4.46)	0.35	1	0.42
CABG+AVR	-	-	-	-	1.95 (0.57, 6.55)	0.69	1	1.27

*** p<0.001, ** p<0.01, * p<0.05

[a] – Worse performance or functioning

6.0 DISCUSSION

To our knowledge, this is the first study that has evaluated the association between frailty and 6-month changes in HRQoL, living status, and treatment decisional regret using a domain-specific measure of frailty among patients age 65 and older referred for elective cardiac surgery. Results indicate worse ADL function was positively associated with higher levels of impairment in the mobility and usual function HRQoL domains from baseline to 6 months. Older age was positively associated with higher levels of impairment in the usual function HRQoL domain from baseline to 6 months. As well, worse ADL function was negatively associated with higher levels of HRQoL improvement in men as measured by index scores and across all procedure types as measured by EQ-VAS. In AVR patients specifically, worse mobility function was negatively associated with higher levels of improvement in HRQoL as measured by the EQ-VAS. Lastly, those with worse ADL function had higher odds of experiencing a dependent living status 6 months after surgery, and those who had worse ADL and cognitive function had higher odds of regretting their decision to have surgery.

Evaluation of outcome after cardiac surgery has traditionally centered on measurement of complication and mortality rates[53], yet HRQoL measures are being increasingly used as important, broader estimates of subsequent health status. Much of the literature shows a high degree of general improvement in surgical patients HRQoL post-operatively.[54,55] While cardiac surgery has been found to generally improve HRQoL in those with significant cardiac disease, some studies indicate this is not the case for upwards of 20% of all patients.[56,57] In a study exploring HRQoL in patients one year after coronary artery bypass grafting in those ≥80 years, Blokzijl found 29% of elderly patients found their postoperative health status to be worse than preoperatively versus 10% in the younger age group.[58] Together, these findings suggest there is a subset of elderly patients who may not derive an overall benefit to HRQoL in the months after their surgical intervention.

6.1 Health-Related Quality of Life

We found patients at higher degrees of frailty, driven by ADL impairment, are at increased risk of experiencing impairment in mobility and functional HRQoL, which suggests some frail patients experience functional impairments, well after the initial surgical insult. One possible explanation for this association is the decreased baseline functional capacity of frail patients, and similarly, the reduced capacity to recover as compared to their non-frail counterparts to surgical stressors. Frailty is typically associated with dysregulations in several interdependent systems and by a variety of observable deficits, including sarcopenia,

weakness, slowness, poor balance, and lack of energy/low activity.[59] Identifying those frail patients at risk of prolonged HRQoL impairment at 6-month follow-up provides the opportunity to evaluate how they may be better prepared in anticipation for their surgical procedures. For elective patients, identification of frailty may trigger the initiation of preoperative rehabilitation or ‘‘prehab.’’ Patients recovering from a cardiac event often receive a structured rehabilitation program of physical activity, lifestyle modification advice, and psychological health interventions. The success of such programs has generated increasing interest in prehabilitation, a preemptive, preventative approach to rehabilitation therapies. Cardiac prehabilitation includes a range of preventative interventions delivered to patients awaiting cardiac surgery, including exercise regimens to improve baseline functional capacity and dietary modification to counter protein-energy malnutrition, with the aim of reducing the incidence or severity of postoperative complications. By tailoring cardiac prehab and rehab interventions to patients identified as frail could have a meaningful impact on improving HRQoL outcomes, as evaluated by the patient themselves.

While few studies have evaluated the specific associations between frailty and post-operative HRQoL among cardiac surgery patients, a systematic review of HRQoL in octogenarians undergoing cardiac surgery by Abah et al. shows overall HRQoL improvement in the majority of patients. However, between 8%–19% appear to experience a drop in HRQoL.[60,61,62] Comparisons to other studies evaluating this work is limited, as a systematic review assessing HRQoL benefits after aortic valve surgery in the elderly showed most studies are retrospective and do not compare baseline (pre-surgery) HRQoL with post-intervention HRQoL, focusing only on patients who survive the follow-up phase.[63] The current work in this thesis extends the current literature by identifying which domains of frailty are specifically at risk of functionally impaired HRQoL even after a period of recovery following cardiac surgery.

Patients in the older age category were positively associated with higher levels of impairment in the usual function HRQoL domain from baseline to 6 months. Older age is a well-documented risk factor for adverse postoperative outcomes in cardiac surgery. Older patients develop more postoperative complications, have increased hospital length of stay (LOS), and have significantly greater 30-day mortality than younger patients.[64] While some complications occur commonly in the post-operative period, many translate into need for increased intensity of support, downstream morbidity and disability. As frailty is not age dependent, nor is it necessarily a natural outcome of aging, the mechanisms associated with age-related impairment in HRQoL may be distinct from those identified in frailty, however

similar overlap likely exists in the decreased baseline functional capacity and reduced capacity to recover in older patients from the initial surgical insult.

Results of previous studies assessing the changes in HRQoL of older patients after cardiac surgery are contradictory. A study by Hendeshian et al. showed older patients undergoing CABG had a significantly lower preoperative functional level which may be retained up to 6 months after surgery. However, functional improvement after surgery was not significantly different among age groups.[65] Some studies showed improvement in quality of life and functional ability in patients older than 80, whose HRQoL after CABG surgery reached the average HRQoL characterizing the population of the same age.[66,67] Guadagnolo et al. evaluated and compared the outcomes after elective CABG in patients younger and older than 65. They found both groups of patients had similar functional benefits and that the factors associated to it were not different in various age groups.[68]

As HRQoL is increasingly being used as an additional metric to gauge success of surgical operations, it is worthwhile to identify potential methods to better retain or improve functional capacity for older adults both before and after surgery, and that patients are aware of the potential impact of surgery on function both in-hospital and after discharge. Providing educational supports for patients through the use of individualized decision aids that take age and frailty into account may serve to better align expectations with outcomes of surgery. Improved social supports identifying those older patients at risk of experiencing prolonged HRQoL issues may serve to better anticipate patient need post-operatively and prepare home supports to address the factors associated with impaired HRQoL.

This study found that worse ADL function was negatively associated with higher levels of HRQoL improvement as measured by EQ-5D-3L index change scores, however this association was only statistically significant in men. Sex differences related to the results of different diseases and efficiency of certain therapeutic procedures may be explained by the influence of biological and social factors. Given that ischemic heart disease is the leading cause of death in developed countries, it is important to address these gaps in knowledge about the discrepancies in HRQoL outcomes between men and women referred for cardiac surgery. While outcomes research in cardiac surgery shows women undergoing cardiac surgery are older, have more comorbidities and are more functionally impaired than men before surgery[69], the literature is not consistent regarding sex differences in HRQoL cardiac surgery outcomes.[70] Some studies have shown less improvement in physical functioning and activity for women than men[71,72]. In contrast, Hunt et al. did not find sex differences in HRQoL in patients 1 year after CABG surgery.[73] These conflicting results may partly be due to methodological differences. First, most studies have been retrospective in nature and few

prospective studies regarding sex differences in HRQoL exist. Second, the number of female patients included in the studies were small. Third, most of the studies have focused on isolated CABG surgery and hence there is a lack of studies including patients undergoing heart valve surgery.[74] Finally, these studies often focused on short-term recovery during the first 3 months after surgery.[75,76,77] The current study addresses some of these methodological issues by focusing on a longer-term recovery, the inclusion of valve patients, and using prospectively collected data. Though the exact reasons for this association to pertain to men alone is unclear, one possible explanation is the overall rate of women undergoing cardiac surgery in this study was approximately 20%, yielding an overall lower number of female patients compared to males.

By acknowledging the role gender has in influencing the likelihood of both experiencing HRQoL impairment and how that impairment presents following surgery, practitioners may be better situated to align patient expectation with functional capacity after discharge from hospital.

We found poor ADL function was negatively associated with higher levels of improvement in HRQoL as measured by the VAS at 6 months compared to baseline. The negative association between poor ADL function and HRQoL change in improvement is consistent across the HRQoL measures. Whereas the EQ-5D index can be regarded as a societal-based composite global HRQoL measure, the EQ-VAS is a direct HRQoL assessment from the patient's perspective. This suggests the impact of frailty on HRQoL is primarily driven by changes in ADL function and is responsive to patient-reported evaluation of their HRQoL. As with the other measures of HRQoL, frailty, as driven by poor ADL function, may have a unique effect on HRQoL for a subset of patients post-operatively, extending well beyond discharge from hospital. While the elicitation of ADL function is well documented in history and physical examinations, the addition of a domain-specific frailty assessment at the pre-operative stage may better identify those patients at risk of experiencing long-term HRQoL impairment post-operatively. These results are in agreement with previous literature. Masel et al. found that being pre-frail or frail was significantly associated with lower scores on HRQoL than being non-frail in older patients.[78] Bilotta et al. found a negative trend in HRQoL with frailty in a cross-sectional study of 239 community-dwelling outpatients referred to a geriatric medicine clinic.[79] While there exists previous literature addressing the relationship between frailty and HRQoL in surgical patients, these studies have not included a domain-specific evaluation of frailty.[80] By better understanding the relationship between those frailty domains that may more likely drive HRQoL impairment following surgery could enable practitioners to better identify those patients at risk of experiencing poor patient-reported post-operative outcomes.

Following stratification by procedure, we noted worse mobility function was negatively associated with higher levels of improvement in HRQoL as measured by the VAS at 6 months compared to baseline in isolated AVR patients. AVR is being increasingly performed in older patients and much of the literature shows good perioperative outcomes and long-term survival, yet this finding suggests a subset of AVR patient identified as frail by poor mobility function, may be particularly susceptible to HRQoL impairment following surgery. Poor mobility function pre-operatively has been shown to be an independent risk factor for postoperative complications, recovery of functioning and morbidities and mortality in major abdominal and thoracic surgery.[81] While this study did not include the severity of aortic stenosis or type of valve used in isolated AVR patients, these may be potentially relevant variables influencing HRQoL postoperatively, and may partly explain why this finding was specific to isolated AVR patients.

Previous literature among similar patient populations reinforce the current study's overall findings on frailty and HRQoL. In a prospective observational cohort study in ICUs across six hospitals in Alberta, Canada, Bagshaw et al. found frail survivors of critical illness experienced greater impairment in HRQoL and functional dependence at 6 month follow-up compared with those not frail, as measured by the CFS.[82] In an acute coronary syndrome (ACS) patient population, Lisiak et al. investigated the relationship between frailty and HRQoL during hospitalization in elderly patients with ACS, showing the presence of frailty had a negative impact on early HRQoL.[83] Taken together, these results suggest the current standard of care of cardiac patients requires greater attention to long-term follow-up functional status, especially for those patients identified as frail. Development of policy surrounding the standardization of frailty assessment and guided survivorship care plans that take post-discharge HRQoL into account would serve to better inform the care of these vulnerable patients.

6.2 Living Status

Patients with worse ADL function had higher odds (aOR = 2.06 (1.42, 3.00)) of experiencing a dependent living status 6 months after surgery. This finding indicates patients identified as frail by ADL impairment at baseline were more likely to experience greater dependency in living status after a 6-month period of recovery. This may represent ongoing physicial impairment and/or disease burden in frail patients that extends beyond the point of discharge from hospital, necessitating reliance on follow-up care in the form of assisted living facilities, nursing homes, cardiac rehab or home supports. The etiology of such impairment may arise from musculoskeletal, neurological, circulatory, or sensory conditions, all of which could lead to impairment in ADLs. While we did not identify the etiology of poor ADL function in this

study, it is nevertheless important to recognize the impact of ADL loss on the patient and how this may impact their ability to return home and function independently following surgery.[84]

Previous results from our center and other studies have shown a relationship between frailty and an increased risk of institutionalization at point of discharge, which represents functional dependence following hospitalization.[85,86,87] However, this data does not extend past the discharge event, and may not be best used as an indicator to identify ultimate functional independence for patients Further, the Canadian Cardiovascular Society Quality report includes a 365-day readmission indicator to provide a mid-term assessment of cardiac outcomes following surgery.[88] While 365-day re-admission rates can serve to ascertain whether or not a patient undergoing a particular cardiac procedure has remained free of any major adverse cardiac events, it is limited in its ability to detect what percentage of patients continue to experience symptoms or functional limitation but that does not warrant a readmission.[89] The goal of capturing living status at 6-month follow-up in the current study was, in part, an attempt to respond to these limitations of traditional quality metrics by collecting a patient-reported outcome providing additional insight as to the ultimate functional independence of older patients after surgery. The severity of functional impairments and the need for assistance with ADLs often determine whether a patient can be safely managed at home or requires follow-up care elsewhere. The culture in hospital, particularly in a perioperative pathway, focuses on discharge from hospital as the goal. While this is clearly important, rehabilitation from a major surgical insult does not end as the patient leaves hospital.[90]

Patients recovering from major surgery, especially the elderly and those with multiple comorbidities, are at greater risk of numerous surgical and medical complications in the weeks and months after surgery.[91] Portegijs et al. reported that a decline in function among older patients after 3 months of hospitalization increased the risk of entering long-term care institutions within 1 year.[92] We found the majority of patients are living independently at home at the point of their 6-month follow-up, with approximately 9% of patients in the study experiencing a dependent living status at 6-month follow-up.. In a study by Huber et al., approximately 95% of the patients at one year follow-up lived in their own homes.[93] While it is encouraging that a majority of older patients often return home following surgery, it is all the more essential to identify the risk factors associated with greater dependency after discharge, particularly for those patients identified as frail. Being able to acquire this information reliably from patient-reported data provides support for encouraging patient engagement pre-operatively in the decision making process. In turn, this would enable practitioners and care providers to tailor individualized decisional supports that clarify the

risks and benefits of a proposed treatment, particularly with regards to its impact on long-term living status.

6.3 Decisional Regret

Patients with worse ADL and Cognitive function at baseline had higher odds (ADL - OR=1.89; Cognition - OR=1.77) of regretting their decision to have surgery. Identifying which domains of frailty are associated with regret after surgery provides insight surrounding the decision-making mechanisms underlying either a satisfactory or unsatisfactory outcome following cardiac surgery, as perceived by the patient. A key consideration for older adults undergoing invasive surgery is whether they will suffer functional decline and the duration of this potential decline, as this inevitably influences the perception of whether their surgery was ultimately beneficial.[94] As we have shown worse ADL function to be negatively associated with HRQoL and independent living status, the experience of treatment decisional regret may, in part, be influenced by protracted HRQoL impairment and functional dependence after discharge from hospital.

We found an overall prevalence of decisional regret of 13.3%, indicating while most patients would go through surgery again if in the same position, there is a subset who may ultimately perceive little benefit from their surgery. If these patients were identifiable, they would likely benefit from a predictive measure of this outcome in the decision-making process leading up to a proposed treatment.

This finding is supported in the literature on the topic of decisional regret. In a study on total knee replacement surgery, Ferket et al. found that knee replacement had "minimal effects on HRQoL," and up to one-third of those who had knees replaced continued to experience chronic pain, while 1 in 5 were dissatisfied with the results.[95] In a cardiac surgery population, Abah et al. indicate that upwards of 20% appear to experience a fall in HRQoL and regret their decision to go forward with heart surgery.[96] In a systematic review by Wilson et al. evaluating regret in surgical decision-making, 57.5% of studies examined patients with a cancer diagnosis, with breast (26.0%) and prostate (28.8%) cancers being most common. Self-reported patient regret was relatively consistent with an average prevalence across studies of 14.4%.[97] Postoperative regret was associated with a history of postoperative complications (OR: 4.7) and with discordance between a patient's preferred and actual perceived decision-making role (OR: 5.3).

Multiple studies demonstrate overall improvement in HRQoL and functional status after cardiac surgery in patients over 80.[98,99] The current study's findings of ADL and cognitive FACT domain-specific associations with decisional regret may provide an indication of those

patients at greater risk of an perceived experiencing regret following cardiac surgery. Decisions to undergo cardiac surgery are complex and multifactorial, and include careful discussions between physician and patient regarding the potential benefits and risks associated with treatment options. Understanding the prevalence of and factors associated with decision regret may aid in identifying those patients who would benefit from more extensive preoperative counseling and to better optimize and frame the discussion surrounding treatment options. Shared decision-making is well established as the best practice for increasing patient satisfaction and goal-directed care.[100] In turn, how actively a patient participates in the preoperative decision making process can affect future decisional regret.[101,102] Postoperative factors such as complications, recurrence of disease, and HRQoL also may be correlated with decisional regret, but these factors have not been well studied.[103,104] Given the increased emphasis on patient centered outcomes, the topic of regret in medical and operative decision-making is increasingly valuable to address.

6.4 Study Strengths & Limitations

In this study, we have demonstrated the utility of domain-specific measures of frailty in predicting both HRQoL, living status, and treatment decisional regret. The major strength of this study is its relevance to clinical practice and patient-centered care. The additional insight towards factors that potentially influence HRQoL outcomes could be used to better align clinical practice on a daily basis through improved education of patients referred for cardiac surgery surrounding risks and benefits of a proposed treatment and the available options. Information from this study could provide general information regarding HRQoL indicators, informing patients making their surgery decision. Additionally, this project has uniquely strong collaborators in geriatrics who have shown leadership in frailty by pioneering the CFS (Dr. Rockwood) and devising the FACT for clinical use (Drs. Mallory and Moorhouse). The FACT is unique, and its specificity gives us the ability to evaluate frailty in a completely novel way. Primary data collection was advantageous in this setting, with several research staff auditing charts for accuracy and ensuring timeliness of reporting baseline and follow-up questionnaires. To the author's knowledge, it is the first study to specifically assess 6-month HRQoL outcomes among frail cardiac surgery patients. This study will act as a solid basis for future research. Future research opportunities include evaluating comorbidity load and disease burden of frail patients and its impact on HRQoL. Extending follow-up to 1,2 and 5 year outcomes of ultimate functional independence for those who have undergone cardiac surgery, as well as qualitative feedback from these patients to generate richer, patient-centred data surrounding the experience of HRQoL at these time points.. The findings from this study may promote improved patient selection that can tie-in to formalized SDM approaches were the

ultimate therapeutic choices are respectful and response to individual patient preferences, needs, and values.

There are several limitations to the study. Though the FACT tool is based on the CFS, it is a relatively recent approach to assessing frailty and as such has not yet undergone rigorous pyschometric analysis to evaluate reliability and validity across different patient populations. The FACT is also reliant on self-reported data to guide decision-making around frailty status. More comprehensive measures of frailty (e.g. CGA), although more time-consuming and thus costly to administer, may be more appropriate for measuring preoperative frailty. Ideally, in addition to the measures used, frailty assessment would include an assessment of specific health comorbidities, nutrition, depression, social supports, etc. Previous research in identifying domain-specific deficiencies suggests problems in cognitive capacity may be under-reported when relying solely on patient-reported data.[105] As such, social desirability bias may have arisen through the use of self-reported data, however the use of standard cognitive assessments in the FACT via word recall and clock drawing tasks were used in an effort to identify these potential cognitive issues.

We were also limited in our follow-up period in which our outcomes were measured. It is inevitable that HRQoL worsens immediately following surgery and hopefully improves as the patient recovers. We decided a 6-month follow-up period would allow sufficient time for patients to heal from the initial surgical insult and be in a position to best comment on their HRQoL at the follow-up phone call. As well, the 6-month follow-up period allowed enough time to lapse to show change, but not so much time that new health issues may confound the score.[106] This time period has been previously chosen as an appropriate follow-up window by our colleagues at the Division of Geriatric Medicine at Dalhousie University.[107] However, including additional follow-up times may have yielded different results, yet our data only provide a single post-operative time point to capture outcomes. While there is evidence of general improvement over the first postoperative year[108], a number of studies detailing HRQoL at multiple time points found no significant interval change.[109,110]

We did not differentiate those patients with prolonged intensive care necessitated by complications, which may have influenced patient-reported outcomes post-operatively. Most studies on uncomplicated heart valve surgery have established that HRQoL improves with surgery and approximates that of the general population.[111,112,113] However, studies on the HRQoL of cardiac patients with prolonged intensive care necessitated by complications have indicated this group of patients experiences greater impairment of HRQoL than those with uncomplicated postoperative periods.[114,115,116]

Finally, our study did not have available at the time, the living status of each patient prior to hospitilization for the index procedure. It is arguable that a patient who comes to a hospital from an institution and is discharged back to the same institution is not the same as a patient who lives at home initially and is discharged to an institution after their hospital course. Therefore, future work will need to distinguish those patients discharged to an institution after a surgical procedure based on their place of origin, or the level of care they were receiving before their operation.[117]

7.0 IMPLICATIONS

Two essential reasons to offer cardiac surgery as a treatment path are to improve HRQoL and prognosis. While much of the literature is focused on the development and continual refinement of preoperative risk calculators to help surgeons estimate an individual's chance of mortality and other major adverse cardiac events as a complication of planned cardiac surgery, there is little to guide the likelihood of an improved HRQoL following surgery. Surgical interventions that work well for healthier individuals may not provide the same level of benefit to more vulnerable patients. For these reasons, there is a need to identify and measure frailty as part of the routine care of older adults, especially for those facing decisions about invasive medical or surgical treatments. Despite this, many health assessments fail to generate a comprehensive understanding of frailty due to insufficient attention to the interacting domains of frailty. The Frailty Assessment for Care Planning Tool (FACT) screens the essential domains that contribute to frailty based on cognition, mobility, social engagement and function. The FACT provides a clinically feasible application of a validated tool to identify frailty in patient populations that are considering invasive medical or surgical procedures.[118] While the reasons for poor patient-reported post-operative HRQoL among elective surgical patients are likely multiplicitous and interacting (e.g. comorbid health conditions[119], poor social supports & social isolation[120], nutrition[121]), the current study indicates that the inclusion of a domain-specific frailty assessment at the pre-operative stage of patients referred for cardiac surgery may better identify those individuals at risk of experiencing prolonged HRQoL impairment. As we showed across HRQoL measures in our study, pre-operative ADL function is an important domain to consider when evaluating a patient's capacity to return to optimal HRQoL post-operatively. Including FACT scores into prediction algorithms of perioperative risk could serve to better identify those patients who may benefit most from formalized shared decision making (SDM) programs to better inform them of associated risks of surgery, alongside care plans that include directed prehabilitation and rehabilitation programs for preventing protracted disability in older patients. Taken together, these pursuits would enable clinicians to help patients better understand the potential consequences of surgery following discharge, improving the quality of patients' informed consent and ultimately providing optimal care that is responsive and respectful of a patients individual goals and values.[122] The current study identifies several areas to consider in striving towards the broader goal of aligning care with an individual's frailty status. By understanding the mechanisms associated with frailty status and patient-reported outcomes like HRQoL, we are better positioned to provide accurate and meaningful information to patients beyond traditional measures associated with surgical success.

8.0 CONCLUSIONS

The need for clear communication about treatment options, risks and benefits, in terms of patient-reported outcome is of great importance. Similarly, the elicitation of patient preference is urgently needed among this population. Given the increase in the referral of frail, older patients for cardiac surgery who are vulnerable to loss of life and independence, the need for identifying the risk factors associated with prolonged HRQoL impairment, dependent living status and decisional regret is compelling. Implementing SDM with the use of decision aids and conversation supports, calibrated to patient frailty, would be very effective at delivering care that is better aligned with patients' goals and preferences. Sharing with patients how their cognitive and functional status may be affected after surgery and considerations such as long-term HRQoL will allow them to make an informed choice that is in line with their individual goals and values.[123]

Lastly, it is an ethical imperative to improve education in frail patients as they represent both a growing and high-risk group of cardiac patients. The addition of a frailty element in the cardiac surgery consultation process could prove to better inform both potential patients and their surgical teams about the bio-psychological components that are not represented in traditional medical histories. These outcomes will inform future iterations of our work in patient education and decision aids, and better inform future patients about the issues and outcomes that they care most deeply about.

APPENDICES

Appendix 1-A: FACT Questionnaire

Addressograph/Sticker

Participant Report on Overall Health

Instructions: To be completed by **the participant**. (1) First, answer the two yes/no questions on the top row. (2) Then, in each column, check THE BOX that **BEST** describes your **USUAL** abilities at home.

	ARE YOU **WALKING** AT YOUR USUAL LEVEL TODAY? ☐ yes ☐ no			ARE YOU YOUR USUAL SELF TODAY IN TERMS OF MEMORY? ☐ yes ☐ no
	Usual Mobility (getting round)	**Social**	**Daily Tasks**	**Memory**
1	O Fit, exercise regularly (e.g. swimming, exercise class)	O I'm in charge of organizing social events	O I still work at a job or do a high level hobby (e.g. building model airplanes)	O Impress others with memory and thinking
2 & 3	O Active/exercise occasionally	O Socialize weekly and have someone to count on if needed	O I can do all the things I used to do without any help, but finds it harder	O I am worried about my memory, but my family (caregiver) is not concerned
4	O Starting to slow down and often tired during the day	O Socialize less than weekly OR might not have someone to count on if needed	O I am not dependent on others but my symptoms often limit activities	CONCERNS: (choose any that apply)
5	O Walking slower and regularly need a cane or walker	O Socialize rarely	O I need help with some everyday activities that I could previously do alone such as housework, or banking, or taking medications correctly	O Trouble remembering details of current news and/or recent events
6	O I need the help of another person when using stairs, walking on uneven ground or getting in/out of the bath OR O I have fallen **more than** once in the past 6 months (not on ice)	O Mostly house-bound	O I need help with all activities outside the home (e.g. banking, shopping) and reminders for some activities in the home such as choosing appropriate/ fresh clothes for the day or reminders to bathe	O Often repeat stories or questions
7	O I always need someone's help or supervision when walking OR O I need help using a wheelchair	O House-bound and isolated: OR O Caregiver stress/or no available caregiver to meet care needs	O I need the help of another for bathing, toileting or dressing	O Often forget the names of close family members such as adult children
8	O I am unable to get out of bed and need help from others to move from bed to chair	O Unable to participate in any social exchange, even when visited	O I depend on others for all aspects of daily life	O Trouble remembering almost everything

Name of Participant_____ **Signature (participant)**_____ **Relationship with collateral**_____

path clinic

FACT Cognitive Assessment

Explanation for testing: "*Part of my role is to look at your overall health, so I'm going to ask you some questions which may not seem to be related to the reason that you're here today*"

1. Ask the patient to, "Repeat the following 3 words and remember them for later:

   APPLE PENNY WATCH

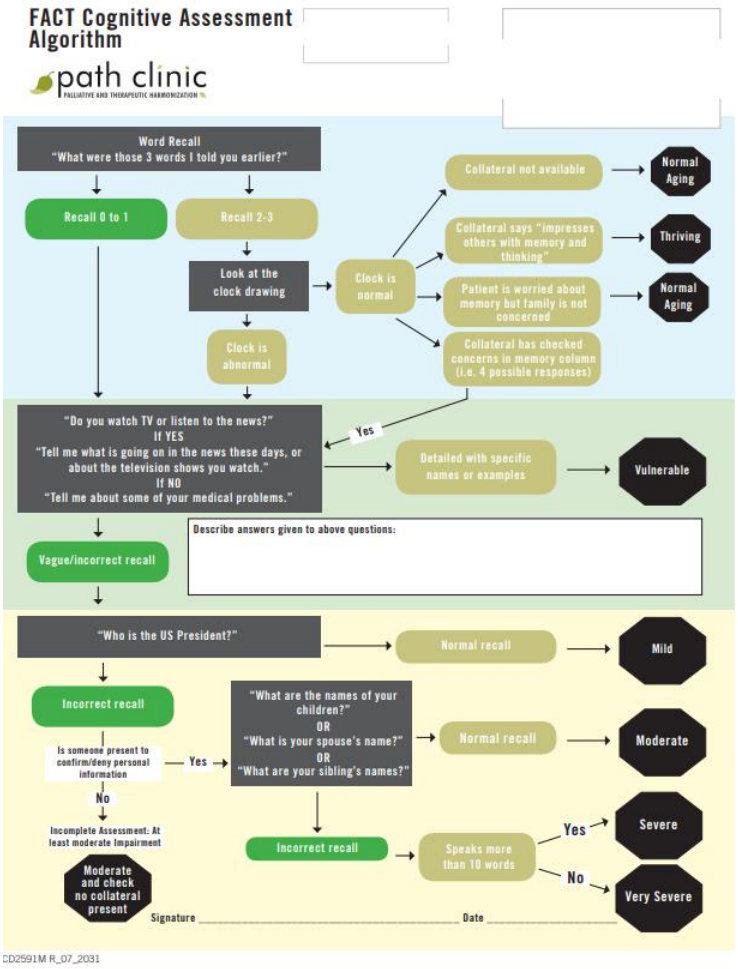
2. Have the patient "Draw a clock" on a separate piece of blank paper (provided) "and place the hands of the clock at ten minutes after eleven."

3. Ask the patient "What were those words I asked you to remember?" and record their answer in the space below:

   Answers must be exact (e.g. "clock" is not acceptable).

   _____ _____ _____

4. Determine a cognitive score by following the Cognitive Flow Sheet



Frailty Assessment for Care-planning Tool (FACT)

FINAL SCORING SHEET

path clinic
PALLIATIVE AND THERAPEUTIC HARMONIZATION

	Mobility is at baseline? ○ YES ○ NO			Cognition is at baseline? ○ YES ○ NO
	Baseline Mobility	**Social**	**Function**	**Cognition**
1. Thriving	○ Fit, exercises regularly (among fittest for age)	○ In charge of organizing social events	○ Still working at job or high level hobby	○ **Thriving**: impresses others with memory and thinking
2+3. Normal Aging	○ Active/exercises occasionally	○ Socializes weekly & would have a caregiver if needed	○ Subjective impairment (i.e. Does everything on own but finds things more difficult)	○ **Normal aging**: patient worried about memory but family (caregiver) is not ○ **Normal aging**: patient worried, collateral not available
4. Vulnerable	○ Starting to slow down and often tired during the day	○ Socializes less than weekly OR might not have a caregiver if needed	○ Not dependent on others but symptoms often limit activities	○ **Vulnerable**: minor deficits on testing **(cognitive impairment, not dementia)**
5. Mild	○ Walking slower and regularly uses (or should use) a cane or walker	○ Socializes rarely	○ Needs help with some instrumental activities of daily living (IADLS) (e.g. housework, banking or medications)	○ **Mild stage dementia:** Vague/incorrect recall of current events, can recall name of US president
6. Moderate	○ Needs help of another person when using stairs, walking on uneven ground, or getting in/out of bath OR Has fallen more than once in the past 6 months, excluding slip on ice	○ Mostly house-bound	○ Needs assistance or dependent for IADLS and cueing with basic activities of daily living (BADLS) (e.g. help choosing what to wear or requires reminders to bathe)	○ **Moderate stage dementia:** Incorrect recall of US President, can recall name of children/spouse ○ No collateral present
7. Severe	○ Always needs someone's help or supervision when walking OR Unable to propel self in manual wheelchair	○ House-bound and isolated OR caregiver stress/or no available caregiver to meet care needs	○ Needs hands on help with BADLS (bathing, toileting, dressing)	○ **Severe stage dementia:** Unable to name children, spouse or siblings
8. Very Severe	○ Bed bound, unable to participate in transfers	○ Unable to participate in any social exchange, even when visited	○ Dependent for all aspects of daily life	○ **Very severe stage dementia:** Limited language skills with few words verbalized

Appendix 1-B: EQ-5D-3L And EQ-VAS

By placing a check-mark in one box in each group below, please indicate which statements best describe your own state of health today.

Mobility
- I have no problems in walking about ❑
- I have some problems in walking about ❑
- I am confined to bed ❑

Self-Care
- I have no problems with self-care ❑
- I have some problems washing or dressing myself ❑
- I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*
- I have no problems with performing my usual activities ❑
- I have some problems with performing my usual activities ❑
- I am unable to perform my usual activities ❑

Pain/Discomfort
- I have no pain or discomfort ❑
- I have moderate pain or discomfort ❑
- I have extreme pain or discomfort ❑

Anxiety/Depression
- I am not anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am extremely anxious or depressed ❑

This example shows how a health state is described using the EQ-5D-3L descriptive system:

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY
- I have no problems in walking about ☑
- I have some problems in walking about ☐
- I am confined to bed ☐

SELF-CARE
- I have no problems with self-care ☑
- I have some problems washing or dressing myself ☐
- I am unable to wash or dress myself ☐

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)
- I have no problems with performing my usual activities ☐
- I have some problems with performing my usual activities ☑
- I am unable to perform my usual activities ☐

PAIN/DISCOMFORT
- I have no pain or discomfort ☐
- I have moderate pain or discomfort ☐
- I have extreme pain or discomfort ☑

ANXIETY/DEPRESSION
- I am not anxious or depressed ☐
- I am moderately anxious or depressed ☑
- I am extremely anxious or depressed ☐

Levels of perceived problems are coded as follows:

☑ ☐ ☐ Level 1 is coded as a '1'

☐ ☑ ☐ Level 2 is coded as a '2'

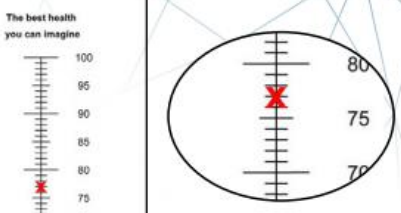
☐ ☐ ☑ Level 3 is coded as a '3'

This example identifies the state 11232.

This example from the EQ-5D-3L Paper Self-Complete shows how the EQ VAS is scored.

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine. 0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = **77**



For example, the response above should be coded as 77

Appendix 1-C: Functional Independence Assessment Phone Follow-up

6 Month Phone Follow-Up

Functional Independence

1. After you were discharged from the hospital you had surgery in:

- ☐ I was discharged and returned home for good.
- ☐ I was discharged but had to be readmitted to an institution

1b. If discharged home, did you require rehospitalization at any point after your surgery?

- ☐ Yes
- ☐ No

2. Which statement best describes your current living situation?

- ☐ I live at home by myself.
- ☐ I live in an institution (nursing home, rehab, home hospital)

2b. With whom do you live, and what level of care does the person you live with provide?

3. How satisfied are you with your current quality of life (including independence)?

- ☐ Extremely satisfied
- ☐ Somewhat satisfied
- ☐ Neutral
- ☐ Somewhat unsatisfied
- ☐ Extremely unsatisfied

3b. What factors lead to your feeling satisfied/unsatisfied with your current quality of life?

3c. What, if anything, is better, what, if anything, is worse?

---

4. Given how things have turned out, at this point in time, would you do this surgery again if you were in the same situation where you needed to have this surgery again?

- ☐ Yes
- ☐ No

4b. Why or why not?

5. Did you have adequate information to make the decision about surgery?

- ☐ Yes
- ☐ No

5b. What was the information that helped you make your decision? What information did you lack?

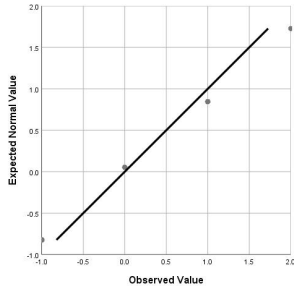
6. What advice would you give to another patient facing the same surgery decision?

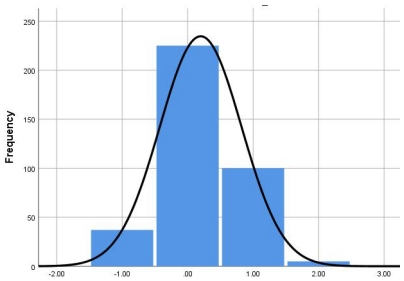
Appendix 2-A: Normal QQ Plots, Histograms, Frequency tables for outcome and predictor variables

Outcome Variables

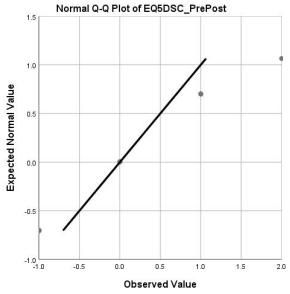
A) EQ-5D-3L Subscores

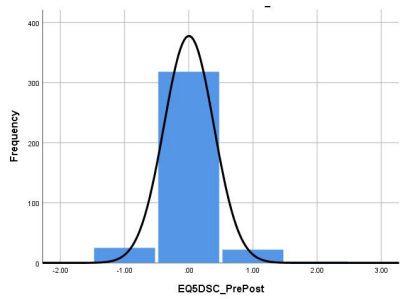
EQ-5D-3L Mobility Change Scores



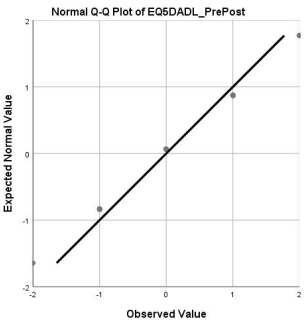


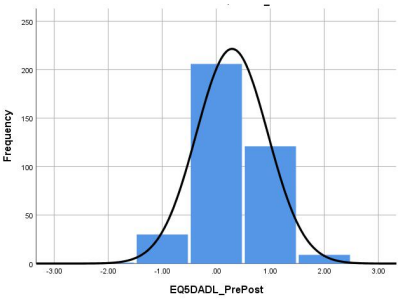
EQ-5D-3L Self-Care Change Scores



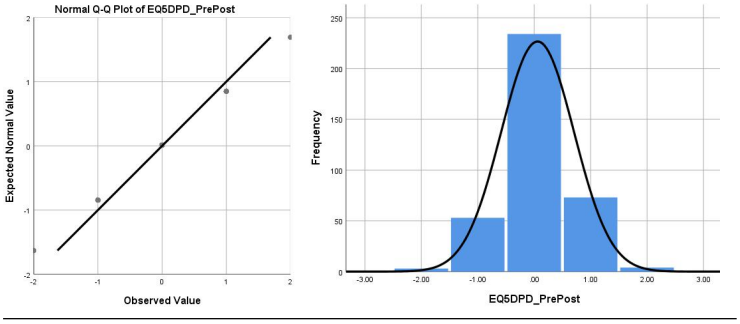


EQ-5D-3L Usual Function (ADL) Change Scores

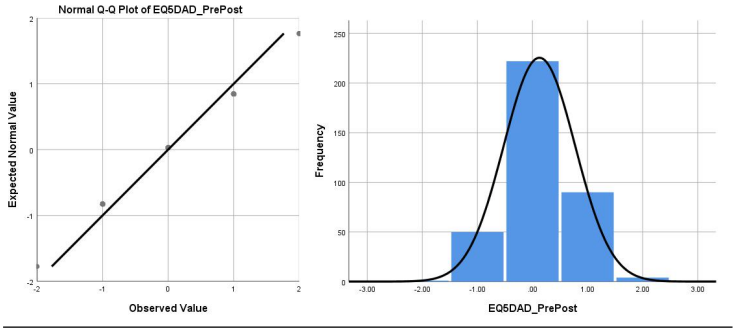




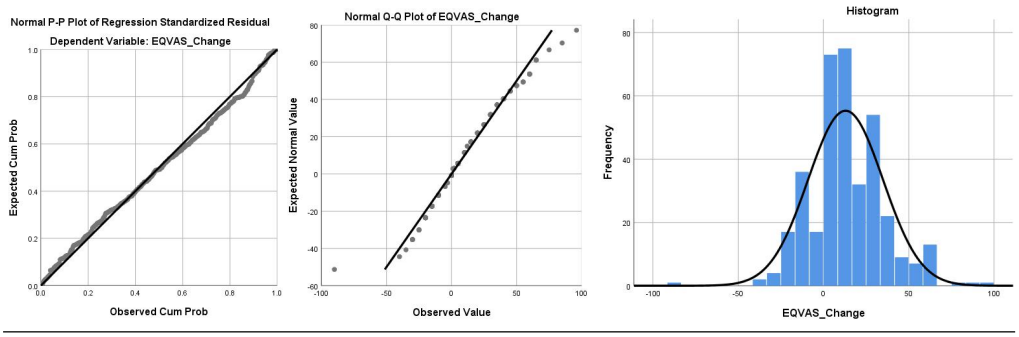
EQ-5D-3L Pain/Discomfort Change Scores



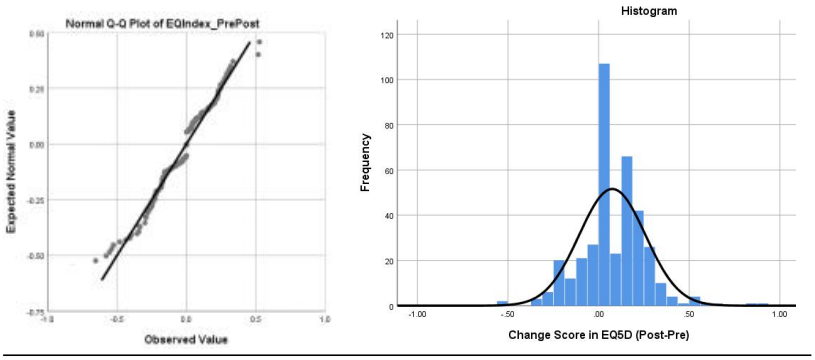
EQ-5D-3L Anxiety/Depression Change Scores



B) EQ-5D-3L VAS Change Scores

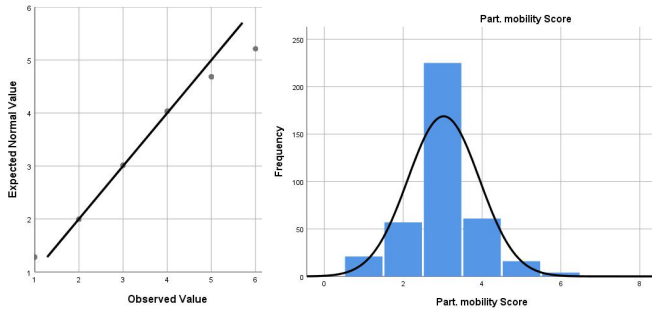


C) EQ-5D-3L Index Change Scores

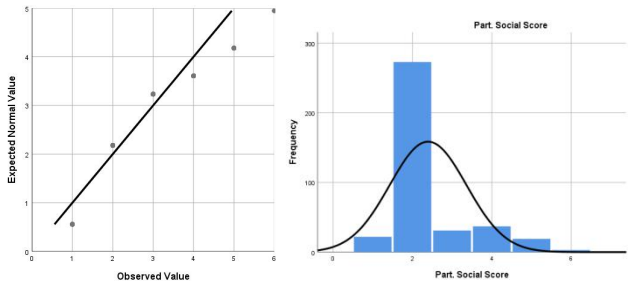


Predictor Variables

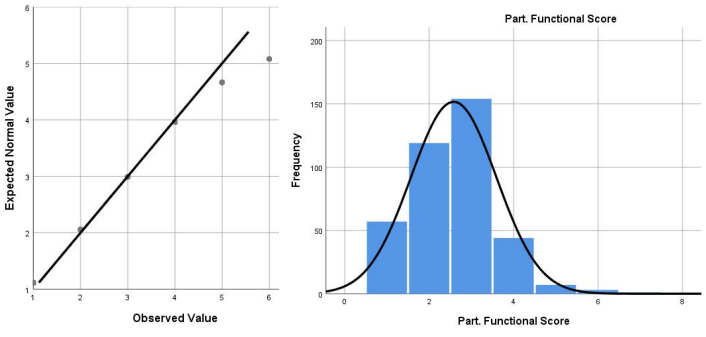
Participant FACT-Mobility Score



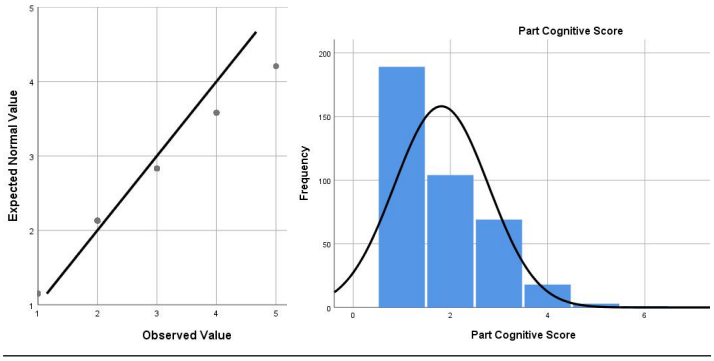
Participant FACT - Social Score



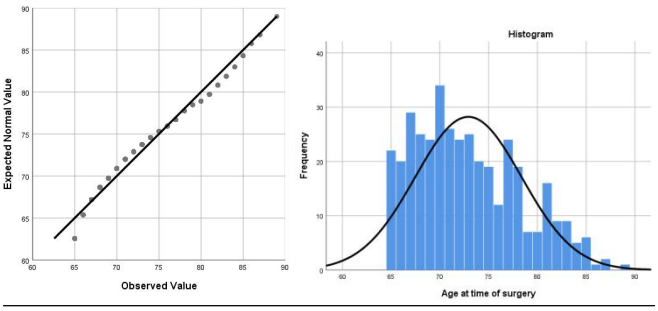
Participant FACT- ADL Score



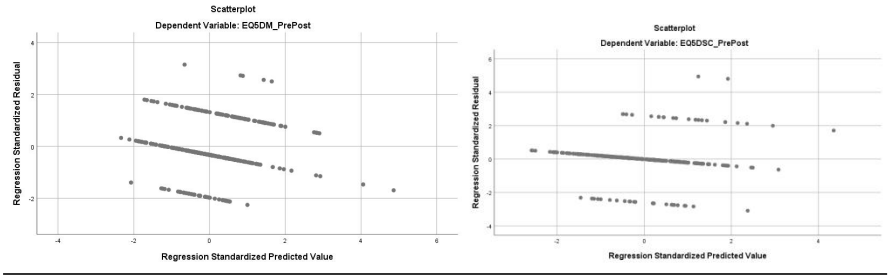
Participant FACT- Cognitive Score

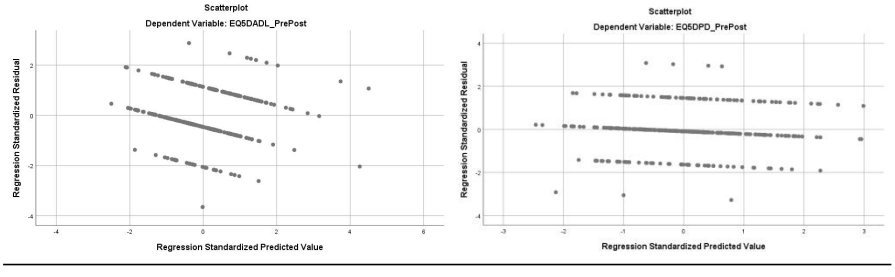


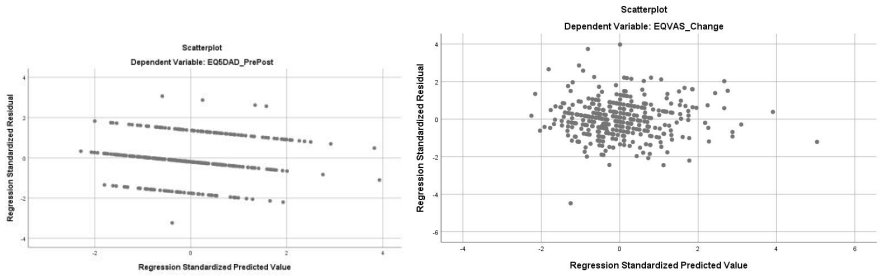
Age at Time of Surgery



Appendix 2-B: Heteroskedasticity Evaulation of predicted vs standardized residuals of each of the EQ5D3L subscores





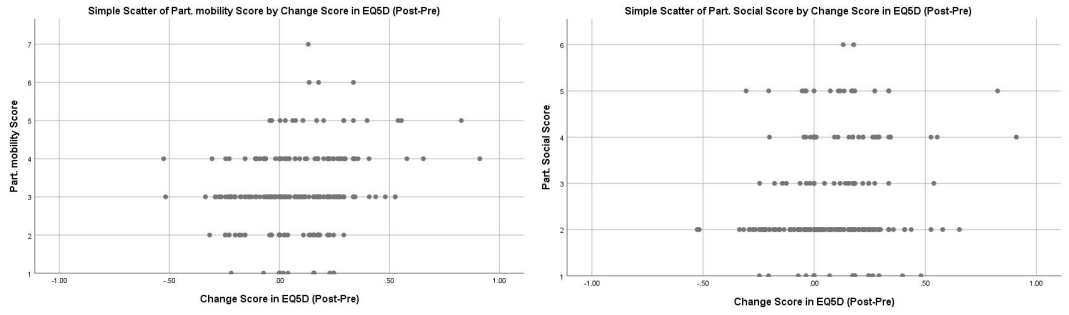


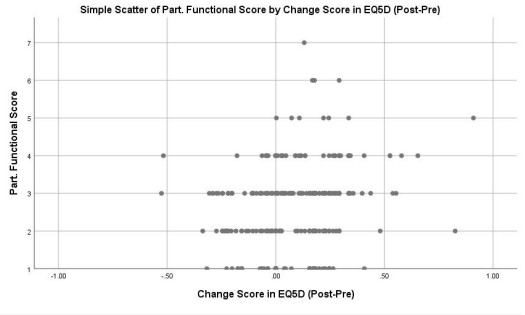
Appendix 2-C: VIF values for EQ5D3L Subscores

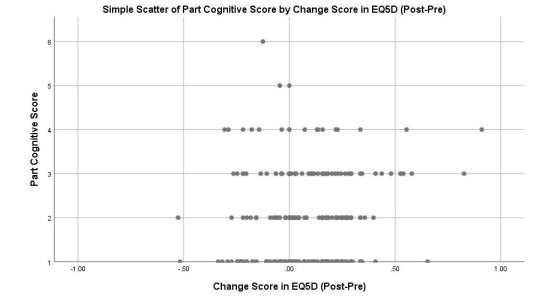
Model		Collinearity Statistics	
		Tolerance	VIF
1	(Constant)		
	Part. mobility Score	.718	1.394
	Part. Social Score	.764	1.309
	Part. Functional Score	.685	1.459
	Part Cognitive Score	.855	1.170
	Age Category	.969	1.032
	Sex as Num	.948	1.055
	Prov Check	.987	1.013
	ProcType as Num	.985	1.015

Model		Collinearity Statistics	
		Tolerance	VIF
1	(Constant)		
	Part. mobility Score	.718	1.394
	Part. Social Score	.764	1.309
	Part. Functional Score	.685	1.459
	Part Cognitive Score	.855	1.170
	Age Category	.969	1.032
	Sex as Num	.948	1.055
	Prov Check	.987	1.013
	ProcType as Num	.985	1.015

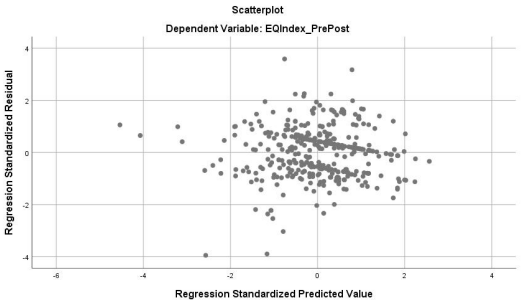
Appendix 3-A: *Change in EQ-5D3L Index Score and linear relationship to the frailty domain predictors*







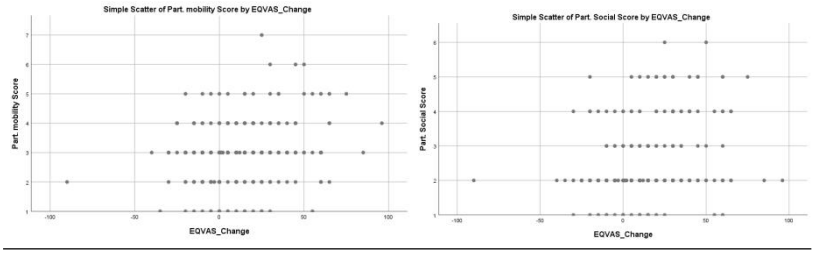
Appendix 3-B: Heteroskedasticy Evaluation

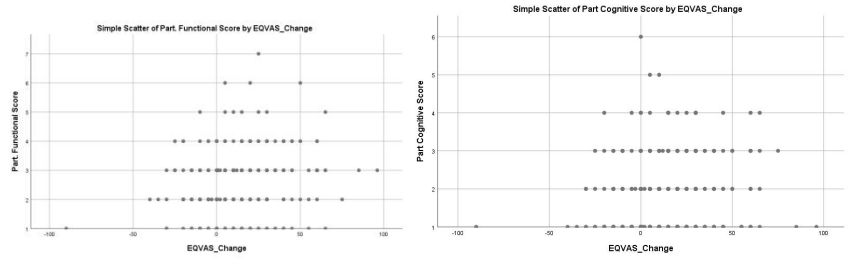


Appendix 3-C: Multicollinearity Evaluation

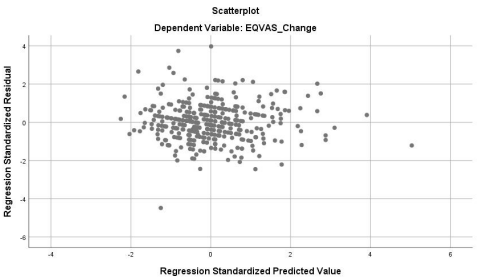
Model		Collinearity Statistics	
		Tolerance	VIF
1	(Constant)		
	Part. mobility Score	.718	1.394
	Part. Social Score	.764	1.309
	Part. Functional Score	.685	1.459
	Part Cognitive Score	.855	1.170
	Age Category	.969	1.032
	Sex as Num	.948	1.055
	Prov Check	.987	1.013
	ProcType as Num	.985	1.015

Appendix 4-A: Change in EQ-5D3L VAS Scores and Linear relationship to the frailty domain predictors





Appendix 4-B: Heteroskedasticy Evaluation



Appendix 4-C: Multicollinearity Evaluation

Model		Collinearity Statistics	
		Tolerance	VIF
1	(Constant)		
	Part. mobility Score	.717	1.394
	Part. Social Score	.758	1.319
	Part. Functional Score	.684	1.463
	Part Cognitive Score	.852	1.174
	Age Category	.986	1.014
	Sex as Num	.967	1.034
	Prov Check	.983	1.017
	ProcType as Num	.948	1.055

Appendix 5: Frequency Distribution of Living Status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	I live at home	334	86.5	90.3	90.3
	I live in an institution	36	9.3	9.7	100.0
	Total	370	95.9	100.0	
Missing	-9	16	4.1		
Total		386	100.0		

Appendix 6: Frequency Distribution of Decisional Regret

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	313	81.1	86.7	86.7
	No	48	12.4	13.3	100.0
	Total	361	93.5	100.0	
Missing	-9	25	6.5		
Total		386	100.0		

Appendix 7: Missing Values Analysis

	Missing	
	Count	Percent
FACT_PMob	1	.3
FACT_PSoc	1	.3
FACT_PFunc	1	.3
FACT_PCog	2	.5
EQ5DM_PrePost	19	4.9
EQ5DSC_PrePost	19	4.9
EQ5DADL_PrePost	19	4.9
EQ5DPD_PrePost	19	4.9
EQ5DAD_PrePost	19	4.9
EQVAS_PrePost	21	5.4
EQIndex_PrePost	19	4.9
FI1A	19	4.9
FI4	25	6.5
PVTest	0	.0
AgeCategory	0	.0
Proctype_num	0	.0
sex_num	0	.0

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