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# Investigating Associations Between Anxiety Sensitivity and Patient Outcomes in a Cardiac Rehabilitation Program: A One Health Approach

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# Abstract

Cardiac Rehabilitation (CR) is an exercise-based program, aimed at improving ones' cardiovascular health. A substantial majority of patients referred to CR do not enroll, complete, or achieve clinical targets in the program due to patient-level factors. The objective of this thesis was to investigate relationships between anxiety sensitivity (AnxS) and patient outcomes in CR. Self-reported questionnaires were completed across two time points, with patient information being abstracted from medical records. Stakeholders associated with reducing the burden of AnxS in CR were also identified using snow-ball sampling. Findings suggest that resting diastolic blood pressure is associated with the interrelationships between AnxS, anxiety, and depression. A larger sample size is needed to establish concrete relationships between AnxS and patient outcomes in CR. This evidence may support the need to target AnxS for treatment. Stakeholders with high power and influence may also be beneficial in implementing changes to CR guidelines, if necessary.



Keywords: Cardiovascular Disease, Cardiac Rehabilitation, Exercise, Mental Health, Anxiety Sensitivity, Anxiety, Depression, One Health

## Summary for Lay Audience

Cardiac Rehabilitation (CR) is an effective exercise-based program with the goal of improving the cardiovascular health of its patients. Across Ontario, most patients who are referred to CR do not fully participate, complete, or achieved guideline recommended targets of the program. Research has shown that depression and anxiety play a role with these observations. Anxiety sensitivity (AnxS) is a personality trait of interest that we believe may impact ones' ability to obtain the full benefits of CR. Individuals with high AnxS feel unsafe or threatened when they experience anxiety related symptoms (i.e., increased heart rate). We explored whether individuals with high AnxS would engage in less physical activity, less exercise, and not achieve guideline recommended targets. We administered 5 self-reported questionnaires at two different times, separated by 6 weeks. We also collected clinical information from each patient's medical record. We observed that individuals with high AnxS, high symptoms of anxiety, and high symptoms of depression were more likely to report an at-risk diastolic blood pressure. Establishing relationships between AnxS and patient outcomes in CR may be important as research suggests that AnxS may be easier to treat compared to other psychological factors. This study must be done with more participants to make more accurate conclusions of our findings. We also identified stakeholders of high influence and power who could potentially help reduce the burden of AnxS in CR. If after further exploration AnxS shows evidence of impacting patient outcomes in CR, these stakeholders could help treat AnxS in CR. This can be done by conducting research-based initiatives leading to the modification of existing CR guidelines.

# Dedication

I dedicate this thesis to both my parents, Chizoma and Ifeanyi Osuji, who have supported me and provided unconditional love. I also dedicate this thesis to my sister, Amaka Osuji, for her unconditional support and continuously showing faith throughout my academic journey.

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## List of Abbreviations:

(Abbreviations are in alphabetical order)

| | |
|---|---|
| 6MWT | 6-Minute Walk Test |
| AF | Atrial Fibrillation |
| AFSS | Atrial Fibrillation Severity Scale |
| AnxS | Anxiety Sensitivity |
| ASI | Anxiety Sensitivity Index |
| ASI-3 | Anxiety Sensitivity Index-3 |
| ASI-R | Anxiety Sensitivity Index-Revised |
| ASP | Anxiety Sensitivity Profile |
| BMI | Body Mass Index |
| BP | Blood Pressure |
| CABG | Coronary Artery Bypass Grafting |
| CACPR | Canadian Association of Cardiovascular Prevention and Rehabilitation |
| CAD | Coronary Artery Disease |
| CBT | Combined Cognitive Behavioural Therapy |
| CCN | Cardiac Care Network |
| CCS | Canadian Cardiovascular Society |
| CHF | Congestive Heart Failure |
| CMHA | Canadian Mental Health Association |
| CPRP | Cardiovascular Prevention and Rehabilitation Program |
| CR | Cardiac Rehabilitation |
| CRNO | Cardiac Rehabilitation Network of Ontario |
| CRSP | Cardiac Rehabilitation and Secondary Prevention |
| CVD | Cardiovascular Diseases |
| DASI | Duke Activity Status Index |
| DBS | Decisional Balanced Scale |
| GAD | Generalized Anxiety Disorder |
| GODIN | Godin Leisure-Time Questionnaire |
| HbA1c | Hemoglobin A1c |
| HDL-c | High Density Lipoprotein (Cholesterol) |

| | |
|---|---|
| HPAPQ | Healthy Physical Activity Participation Questionnaire |
| HSREB | Health Sciences Research Ethics Board |
| ICD | Implantable Cardioverter Defibrillator |
| IPAQ | International Physical Activity Questionnaire |
| LDL-c | Low Density Lipoprotein (Cholesterol) |
| MDD | Major Depressive Disorder |
| MDQ | Mediterranean Diet Questionnaire |
| MET | Metabolic Equivalent of Task |
| MI | Myocardial Infarction |
| MVP | Mitral Valve Prolapse |
| NSS | Not Statistically Significant |
| NYHA | New York Heart Association |
| OHIP | Ontario Health Insurance Plan |
| OPA | Ontario Psychological Association |
| OSN | Ontario Stroke Network |
| PDD | Persistent Depressive Disorder |
| PHQ-4 | Patient Health Questionnaire-4 |
| PHR | Patient Health Record |
| PTSD | Posttraumatic Stress Disorder |
| RCT | Randomized Controlled Trial |
| SAD | Social Anxiety Disorder |
| SARS | Severe Acute Respiratory Syndrome |
| SCAD | Spontaneous Coronary Artery Dissection |
| UHN | University Health Network |
| WHO | World Health Organization |

# Chapter 1

## 1.0. Introduction

Cardiovascular diseases (CVD) are a class of disorders associated with the heart and the vasculature, including coronary artery disease (CAD), ischemic stroke, heart failure, arrhythmia, and heart valve disease.[1] While mortality rates from CVD have trended downward in the last 30 years [2], the prevalence of people living with CVD has increased, thus subsequently increasing the associated burden on society.[3] Cardiac rehabilitation (CR) was first established in the 1970s and is supported with strong evidence of reducing mortality and morbidity related to CVD in a cost-effective manner.[4,5]

## 1.1. Cardiovascular Rehabilitation and Secondary Prevention

Contemporary CR programming encompasses cardiovascular rehabilitation and secondary prevention, including optimization of pharmacotherapy; for the purposes of this thesis, we will be using the acronym "CR" to denote "cardiovascular rehabilitation and secondary prevention". CR programs are delivered by certified clinicians. The Canadian Guidelines for Cardiac Rehabilitation and Cardiovascular Disease Prevention describe CR programs encompassing the following: 1. Systematic patient referral processes; 2. Patient assessments; 3. Health behaviour interventions and risk factor modifications; 4. Adaptations for program models to improve accessibility, especially for under-served populations; 5. Development of self-management techniques based around individualized assessment, problem-solving, goal setting and follow up; 6. Exercise training; 7. Leisure-time activities; 8. Outcomes assessment and performance measurement; and 9. Continuous quality improvement programs.[6,7] In Ontario, CR is considered the standard of care

for patients who suffer from or whom have experienced a cardiac-related event.[8] For these patients, CR plays a critical role in the reduction and control of CVD risk factors.[6] The scientific literature almost universally supports the effectiveness of CR programs based on well-established evidence of reduced morbidity and mortality, healthcare utilization, and increased quality of life.[9] Based on current clinical guidelines, referral to CR is considered standard of care and part of necessary comprehensive care for individuals after the diagnoses of cardiovascular disease (CVD) or a cardiovascular event.[10,11]

A substantial number of studies have reported on the efficacy of exercise-based CR programs to improve quality of life, to reduce the risk of reinfarction, and to reduce the risk of cardiac and all-cause mortality (the latter by 20-50%).[4] Not surprisingly, CR also results in improved exercise capacity,[12] which will be discussed in more detail later in this chapter. Additionally, cardiovascular disease risk factors such as cholesterol, blood pressure, insulin sensitivity, and excess body weight are also improved by CR.[4] In addition to individual-level benefits, the cost-effectiveness of the program provides promising population-level benefit, including but not limited to a reduction in all hospital admissions.[13]

Unfortunately, despite the overwhelming evidence to support the cost-effective benefit of CR, referral, enrollment, participation, and completion of CR in Canada remain discouragingly low due to both system and patient-level barriers. In Canada approximately one-third of eligible patients participate in CR.[7] Within Ontario, only 22% of eligible patients enroll into CR.[7]

## 1.2. System-level Barriers to Optimizing Patient Outcomes in Cardiac Rehabilitation

Although patient-level barriers to CR are the focus of this thesis, understanding system-level barriers to participation and completion of CR provides general insight on population-level

burdens related to CR. Studies have reported insufficient program capacity for eligible patients regionally and nationally across Canada. A 2011 analysis of CR capacity in Ontario concluded that program availability was only 34%, meaning that 35,000 patients annually were unable to access care because of system-level limits on service availability.[14] As of 2018, 182 programs were active nationally, 72 programs in Ontario, 17 in Quebec, 93 found across the remaining provinces, and no CR programs currently exist within the three territories.[15] The discrepancy in program availability across Canada is reported to be potentially due to differences in provincial reimbursement policies.[16] For example, CR services provided in Ontario are to the discretion of hospital budgets[17] in comparison to Quebec where patients are expected to cover CR expenses through their individualized insurance coverages.[16] Tran *et al.* has also reported inadequate geographic distribution of available programs. A substantial majority of these programs were situated in either an urban or suburban regions, thus disproportionally reflecting the need of CR across urban and rural populations.[15] Additionally, a substantial majority of programs did not have another CR program within a 20-kilometer radius.[15] This large distance may result in an inconvenience for those who do not live near a CR program to participate and complete CR.[15] Referral and enrollment to CR for eligible patients have also been reported to be substantially low, being 34%[18] and 20%[19], respectively.

## 1.3. Patient-level Barriers to Optimizing Patient Outcomes in Cardiac Rehabilitation

In addition to these system-level barriers, there are important patient factors that contribute to sub-optimal patient outcomes in CR. Patient outcomes are defined as CR enrollment, participation, completion, and achievement of clinical targets. Sociodemographic and socioenvironmental characteristics are examples of individual level-factors that are associated with these outcomes.[7,20]

For example, due to inadequate government funding, a proportion of CR patients are expected to pay the remaining of what is not covered by the Ontario Health Insurance Plan (OHIP), with low income patients being largely affected.[14] As a consequence, patients residing in low-income status neighborhoods are significantly less likely to complete CR compared to those with high-income.[21] There is also evidence that women are less likely to be referred[22], enrolled[23], and complete CR compared to men.[24,25]

In addition to these patient-level factors, there has been an increased awareness of the influence of patient mental health factors on patient outcomes in CR. Current research has explored the role of depression with regards to sex, age, cardiovascular diagnosis, and CR referral/entry, and patient outcomes in a CR program.[26,27] Anxiety has also been a mental health factor of interest with its relationship between CR clinical outcomes. These relationships have been the focus of research to date and will be discussed in more detail within this chapter. More recently, anxiety sensitivity (AnxS), defined as a learned cognitive trait that predisposes people to fearful interpretations of inner processes and events[28], has been investigated for its relationships to both depression and anxiety and for its potential role in influencing patient outcomes in CR.

## 1.4. Depression and Anxiety as Barriers to Participation in Cardiac Rehabilitation

Much of the literature supports both depression and anxiety as barriers to optimal patient outcomes in CR. Understanding relationships between depression, anxiety, and CR will demonstrate the need to investigate a similar, yet conceptually different construct, AnxS.

### 1.4.1. Depression in Patients Participating in Cardiac Rehabilitation

Depression, a range of mood disorders, is both a medical and mental health illness that negatively impacts the way affected individuals think, feel, and act on a day-to-day basis.[29] "Depression" is an umbrella term used to characterize conditions ranging from self-reported depressive symptoms and depressive episodes, to clinical diagnoses such as Major Depressive Disorder (MDD) or Persistent Depressive Disorder (PDD), among many others, that can and do affect people differently at different times.

There is an enormous literature on the association between CVD and depression. Studies report that about 40% of patients who have suffered a major cardiac-related event have also been diagnosed with MDD.[30] Multiple studies have reported that depression can both worsen the prognosis for multiple CVDs and can also increase the risk of myocardial infarction (MI), and stroke.[31–34] A recent 2021 review reported that individuals surviving an acute MI have significantly lower levels of depression compared to individuals not surviving. Hopelessness, a dimension of depression, has been reported to predict all-cause mortality in patients with coronary heart failure (CHF). Consistent with these findings, studies have reported depression to be a reliable predictor for CVD.[35,36] On the reverse side, there is also evidence that CVD may also cause depression.[37] Given the strong association between depression and CVD, it is expected that depression impacts patient outcomes in CR. Depressed CR patients are significantly less likely to complete CR.[26] In addition, gender differences are seen as women report higher levels of depressive symptoms compared to men at baseline of CR.[38] As a response to this issue, evidence-based guidelines for CR have been restructured, recommending that patients be routinely screened for depression due to its high prevalence among those with CVD.[39]

### 1.4.2. Anxiety in Patients Participating in Cardiac Rehabilitation

Anxiety disorders are a group of mental health disorders characterized by frequent, intense, excessive fear and worry, and are responses that are substantially different in intensity and frequency to "normal" stress responses to common, everyday events.[40] Like depression, anxiety is an umbrella term used to characterize a spectrum of conditions ranging from self-reported symptoms of anxiety to clinical diagnoses such as Generalized Anxiety Disorder (GAD) and Social Anxiety Disorder (SAD), among many others. Compared to depression there has been less investigation of associations between anxiety and CVD. Nonetheless, anxiety has also been reported to be significantly associated with CVD risk factors such as hypertension, specific types of CVD such as CAD, heart failure, and an overall increased risk of CVD mortality.[41–44] For example, 20-30% of patients who have experienced acute coronary syndrome have reported elevated levels of anxiety.[45,46] Individuals exhibiting higher baseline symptoms of anxiety have demonstrated a lower likelihood of completing CR, particularly at the early stages of the program.[39] Similar to depression, women report higher levels of anxiety compared to men at baseline of CR.[38] Evidence-based guidelines for CR have also been modified to routinely screen for anxiety also due to its high prevalence among those with CVD.[39]

## 1.5. Anxiety Sensitivity

This section will aim to define AnxS, discuss distinctions from and relationship to depression and anxiety, and explore what is currently known about the relationship between AnxS and CVD, exercise, and CR.

### 1.5.1. Defining Anxiety Sensitivity

AnxS is defined as a learned cognitive trait that predisposes people to fearful interpretations of inner processes and events[28] and is conceptually distinct from anxiety.[47] Whereas anxiety is defined as the anticipation of future threat[48], AnxS is defined as interpretating physiological responses elicited by anxiety as threatening.[28] For example, an individual with high AnxS who experiences an elevated heart rate after an exercise session, is much more likely than someone with low AnxS to respond to the elevated heart rate with excessive fear that they are experiencing a heart attack. In the context of the current investigation, AnxS is important to understand because of demonstrated and potential associations with other mental health factors, cardiovascular health outcomes, and exercise, which have been extensively investigated in CR. AnxS has also been evidenced to be targeted for treatment with interventions like cognitive restructuring, psychoeducation, interoceptive exposure, and other cognitive behavioural therapy (CBT) styled approaches.[49] However, the role and potential influence of AnxS has been understudied in CR.

### 1.5.2. Measuring Anxiety Sensitivity

The measurement of AnxS has evolved over the past two decades, as the construct itself has become more precise and the understanding of its component factors has improved. The Anxiety Sensitivity Index (ASI original) was developed in 1986. The original ASI consisted of 16 items, each item being scored from 1 to 4, with total scores ranging from 0 to 64. Later investigation provided evidence that AnxS could be divided into 3 factors: fear of (1) physical symptoms; (2) publicly observable anxiety symptoms; and (3) cognitive dyscontrol.[50,51]

In 1998, the Anxiety Sensitivity Index-Revised (ASI-R), consisting of an extensive 36 items, was developed to prove that AnxS could be divided into multiple factors. Taylor and Cox (1998) added a fourth dimension within the AnxS construct: (1) fear of respiratory symptoms;

(2) fear of publicly observable anxiety reactions; (3) fear of cardiovascular symptoms; and (4) fear of cognitive dysfunction.[51] The validity of the ASI-R was later demonstrated in several studies, one of which was by Deacon *et al.* (2003), where they used two non-clinical samples to investigate their hypothesis of AnxS having a structure comprised of four dimensions. Although this study provided evidence that the ASI-R was more valid and reliable compared to the original ASI, several items on the ASI-R reported both the fear of a sensation and the belief that sensations result in danger, making the definition of AnxS unclear.[52]

Taylor and Cox (1998) also developed the Anxiety Sensitivity Profile (ASP) which added two extra dimensions to the ASI-R: fear of (5) gastrointestinal symptoms; and (6) fear of dissociative and neurological symptoms.[51,52] This was an attempt to assess additional domains that the ASI-R could examine but was not used as much compared to the other AnxS indexes due to its length of 60 items. Taylor *et al.* (2007) then developed the Anxiety Sensitivity Index-3 (ASI-3), which is a more stable and multidimensional tool used to assess AnxS in both clinical and non-clinical samples and has also demonstrated greater validity and reliability in comparison to the previously designed measures.[52,53] With a total of 18 items, each item of the ASI-3 is also scored from 1-4, with the total score ranging from 0 to 72.[54]

### 1.5.3. Relationships between Anxiety Sensitivity, Depression, and Anxiety

The literature has established AnxS as a distinct construct that can be independently targeted for treatment.[28] AnxS is also known to be related to anxiety and mood disorders. AnxS is predictive of developing a wide range of anxiety related disorders[55,56], as individuals with high AnxS are more likely to develop an anxiety related disorder compared to those with low AnxS.[52,56–58] Studies examining the association between AnxS and depression have generally reported an association,

though more modest than the association between AnxS and anxiety disorders. Olatunji and Wolitzky-Taylor (2009) meta-analysis investigated differences in AnxS between individuals with anxiety disorders, depressive disorders, and healthy individuals. Results suggested that participants in the anxiety group reported higher AnxS scores compared to those in the mood disorder group. Naragon-Gainey (2010) conducted a similar meta-analysis to investigate the relationship between AnxS, depressive disorders, and anxiety disorders. Results supported strong relationships between AnxS with each of depression, generalized anxiety disorder (GAD), and posttraumatic stress disorder (PTSD). Additionally, AnxS was more closely associated to distress disorders, such as depression, GAD and PTSD, compared to fear disorders, such as panic, agoraphobia, social anxiety disorder, and specific phobias.[56] While depression, anxiety, and AnxS are similar, they are distinct from each other, each are measured separately, and each are addressed differently in a clinical setting. Therefore, there is a need to better understand the role of AnxS and its relationship to depression, anxiety, and cardiovascular disease symptomology, along with CR adherence and completion in patients enrolled in CR programs.

## 1.6. Anxiety Sensitivity and its Potential Impact in Cardiac Rehabilitation

### 1.6.1. Anxiety Sensitivity and Cardiovascular Disease Risk Factors Targeted During Cardiac Rehabilitation

A variety of studies have explored the association between AnxS and the traditional CVD risk factors, indicators of pre-clinical CVD, and CVD symptoms. For example, Farris and Abrantes (2017) demonstrated that smokers with CVD report significantly higher AnxS compared to smokers without any cardiovascular health implication.[59] The importance of this is key as smoking cessation is an important clinical outcome in CR.

Hypertension has been historically noted as a risk factor for CVD, with literature starting to report its association with AnxS. Studies suggest that individuals with mild to moderate hypertension reported significantly higher AnxS compared to those with normal BP.[60,61] Those with mild to moderate hypertension did not report significantly more anxiety compared to individuals with normal BP[60], providing further evidence of a conceptual difference between AnxS and anxiety. One study suggests that non-compliance to hypertensive medication may be attributable to misinterpretation of normal medication side effects.[62] Alcántara *et al.* (2014) reported that nearly double the patients with high AnxS were non-adherent to their BP medication compared to those with low AnxS. They concluded that patients with high AnxS were more likely to misinterpret their bodily sensations as threatening when they took their BP medication, which made them more likely to avoid taking it as prescribed.

In addition to hypertension, AnxS has been evidenced to be associated with other risk factors for CVD. Seldenrijk *et al.* (2013) suggests that individuals with significantly higher AnxS demonstrated a significantly increased likelihood of the presence of carotid plaque and increased arterial stiffness, even in healthy patients. Interestingly, depression and anxiety partially mediated the association between AnxS and increased stiffness.[63] Investigation of anxiety and/or depression potentially mediating associations between AnxS and patient outcomes assessed in CR is currently understudied and merits further investigation.

In addition to CVD risk factors, studies have reported associations between AnxS and higher levels of self-reported symptoms in patients with CVD. Ong *et al.* (2006) reported that individuals with high AnxS reported significantly greater atrial fibrillation (AF) symptom severity. Additionally, Chiaie et al. (1996) reported that AnxS was significantly higher in patients with mitral valve prolapse compared to healthy individuals.[64]

There is emerging evidence that AnxS is associated with CVD risk factors. More research is needed to explore whether AnxS can serve as an independent risk factor for incident CVD and whether mitigating AnxS in patients with CVD might improve patient outcomes in CR.

### 1.6.2. Anxiety Sensitivity and Exercise, a Critical Component of Cardiac Rehabilitation

Exercise is a key and central component of CR, therefore, understanding what is known about AnxS and exercise is important. This section will discuss the associations between AnxS and exercise and discuss the impact exercise has on AnxS.

#### 1.6.2.1. Associations Between Anxiety Sensitivity and Exercise

The literature suggests AnxS to be significantly associated with both physical activity and exercise. Studies report that individuals with high AnxS engage in significantly less physical activity than individuals with low AnxS.[65] More specific to aerobic exercise, Hearon and Harrison (2020) hypothesized that AnxS would be associated with greater sedentary time. Contrary to their hypothesis, AnxS was not a significant predictor for sedentary time, but higher AnxS was associated with less aerobic exercise.[66] Moshier *et al.* (2013) also reported that individuals with low AnxS engage in significantly more vigorous exercise compared to individuals with high AnxS.[67] Interestingly, the association was not significant when gender/sex was added to the model; the effect of sex on this association will be discussed later in this section. Studies also suggest that AnxS is significantly predictive of exercise behaviour, indicating that individuals with high AnxS at baseline are significantly less likely to improve their exercise behaviour after one week.[68] AnxS was also able to predict change in cardiorespiratory fitness measured as peak metabolic equivalents

(MET; 1 MET = 3.5 ml $O^2$ / kg body wt / min) achieved on an exercise stress test.[68] A review by Horenstein, Potter, and Heimburg also addressed this association they investigated AnxS as a possible risk factor for chronic medical conditions. They speculate that avoidance of exercise by individuals with high AnxS may be due to fear of physiological sensations (e.g., increased heart rate) accompanying physiological arousal caused by exercise.[69]

With clear evidence of AnxS being associated with exercise, a few studies evaluated the impact of gender in this relationship. McWilliams and Asmundson reported significant associations between exercise and AnxS among men but not women, suggesting that only men with high AnxS reported less physical activity.[70] DeWolfe *et al.* (2020) conducted a study to specifically investigate the gender differences in physical activity, and to determine whether this relationship was mediated by AnxS. Their findings suggest that women engaged in significantly less physical activity compared to men and AnxS partly mediated the relationship between gender and physical activity.[71]

As stated previously, research suggests that body weight may play a moderating role in the AnxS and exercise interaction. Hearon *et al.* (2014) reported that AnxS, body mass index (BMI), and their interaction, were predictors for duration engaged in physical activity. Obese individuals with high AnxS engaged in less physical activity compared to obese individuals with low AnxS.[72] Smits *et al.* (2010) reported findings consistent with Hearon *et al.* (2014), where an interaction was found between AnxS, exercise and BMI. Additionally, they reported that fear of exercise was significantly greater in individuals with high BMI and high AnxS.[73]

### 1.6.2.2. The Impact of Exercise on Anxiety Sensitivity

Despite the sub-optimal exercise outcomes in individuals with high AnxS, individuals able to participate in exercise have demonstrated significant reductions in AnxS. Many studies assessing the impact of exercise on AnxS were done using sample sizes of young adults, hence, the implications of these studies in relation to CR are uncertain. As previous studies mentioned have reported associations between AnxS and tolerance of exercise, studies have reported that individuals engaging in a single session of aerobic exercise we able to reduce their AnxS significantly more than those who do did not engage in exercise at all.[74–76] Broman-Fulks *et al.* (2004) investigated the effects of high vs. low intensity aerobic exercise-induced physiological arousal on AnxS. Significant reductions in AnxS were observed in the high intensity exercise group, with reduction maintained after a 1-week follow-up.[77] In comparison, the low intensity exercise group did not demonstrate a significant reduction in AnxS up until 1-week follow-up. Consistent with Broman-Fulks hypotheses, a reduction in AnxS after engaging in just low intensity exercise is promising, supporting the impact of exercise on clinically relevant psychological factors.

There is also evidence that gender may moderate the impact that exercise has on AnxS, as men have shown a significantly larger reduction in AnxS during exercise treatment compared to women.[78] Interestingly, Medina *et al.* also observed no significant difference between genders. They speculate the physiological response to exercise could be responsible for the mid-treatment difference found between sexes. Sabourin *et al.* (2011) investigated barriers to exercise in women with high AnxS. Results suggested that compared to individuals with low AnxS, individuals with high AnxS perceived more barriers and benefits to exercise.[79] Notably, they also demonstrated that individuals who perceived more barriers than benefits to exercise reported significantly lower

fitness scores compared to individuals who perceived more benefits to barriers.[79] This may elicit clinical complications for treating anxiety-related disorders among high AnxS individuals who perceive more barriers than benefits to exercise.

Zvolensky *et al.* observed that individuals who engaged in exercise did not only significantly reduce their AnxS, but also demonstrated abstinence from smoking compared to individuals who did not exercise.[80] As previously mentioned, the importance of this finding is key as smoking cessation is a patient outcome assessed in CR. Additional studies comment on relationships between AnxS, smoking, and exercise, but that analysis is beyond the scope of this thesis.

Studies have also evaluated the effectiveness of CBT combined with exercise. Sabourin *et al.* (2016) reported reductions of AnxS in individuals who engaged in a combined CBT and exercise treatment compared to individuals who were educated on the importance of exercise, nutrition, and sleep[81], although this study was done exclusively with women. Consistent with findings reported by Sabourin, Smits *et al*. (2008) reported that AnxS was reduced significantly post-treatment and at follow-up evaluations of a combined CBT and exercise treatment. Additionally, AnxS mediated the relationship between both depression and anxiety with exercise with mediation being stronger among individuals with high AnxS.[82] As previously mentioned, depression and anxiety are routinely assessed in CR, so this finding may provide clinical implications.

Reported reductions in AnxS using exercise, CBT, or both is promising as it supports the feasibility and effectiveness of potentially targeting AnxS.

### 1.6.3. Anxiety Sensitivity and Cardiac Rehabilitation

To date, only two studies have investigated AnxS in CR. Farris *et al.* (2018) explored the association between AnxS and fear related to negative consequences of exercise in CR participants. On average, patients reported a moderate level of AnxS, yet of those patients, nearly one-third of them reported high AnxS.[83] Further analysis deemed AnxS to be associated with fear of exercise, with patients being more likely to drop out of either centre-based or home-based programs. In a more recent study by Kraemer *et al.*, analysis was done to examine the effects of each dimension of AnxS (physical, cognitive, and social) on exercise tolerance. Opposed to the previous study, this investigation focused on patients enrolled in a cardiopulmonary rehabilitation program. Consistent with previous studies, it was reported that increased levels the physical dimension of AnxS were associated with low exercise tolerance.[84] Kraemer *et al.* speculate that individuals with cardiopulmonary conditions reporting high AnxS may experience distress when exertion-related symptoms (i.e. elevated heart rate) are stimulated in patients, subsequently resulting in exercise avoidance. Given the limited literature on the direct role of AnxS in CR, this area of research merits further investigation.

## 1.7. Summarizing and Synthesizing Existing Literature: What is known and Knowledge Gaps about the Role of Anxiety Sensitivity in Cardiac Rehabilitation

To date there has been very little investigation of AnxS in relation to CR patient outcomes. Current evidence demonstrates that AnxS is significantly related to anxiety, yet more moderately related to depression. As depression and anxiety are important influencers of deleterious CR outcomes, understanding the concurrent relationships among AnxS, depression, and anxiety within CR may have important clinical implications. Key existing literature that evaluates AnxS and its

associations with a variety of patient outcomes has also been highlighted. Though limited, a few studies have indicated that increased AnxS is associated with hypertension, heart disease, and other CVD risk factors. Further investigation is needed to understand what the relationship is between AnxS and changes of these variables in individuals participating in CR. Importantly, studies with exercise have reported that individuals with high AnxS engage in less physical activity compared to individuals with low to moderate AnxS. More promising results, however, have indicated that even participating in just one 30-minute session of exercise may significantly reduce AnxS. It is important to understand the relationship between AnxS and exercise as it and physical activity are fundamental components of CR. Psychological treatment has also been reported to decrease AnxS both independently and in combination with exercise, which indicates a potential target for treatment. By investigating the relationships between AnxS and these factors within the scope of CR, possible mitigation interventions can be designed to increase CR participation and achieve appropriate risk factor targets in CR. As stated earlier in this chapter, much of the current literature focuses on a much younger population. This thesis will study a CR population by collecting and analyzing data from patients enrolled in a CR program in London, Ontario.

# Chapter 2

## 2.0. Rationale

It has been firmly established that CR is both efficacious and cost-effective, yet participation in and completion of CR remain alarmingly low across Ontario. Anxiety, and especially depression, are important barriers to patient completion of CR. In addition to depression and anxiety, understanding the importance of AnxS and how it may mediate or moderate the impact of depression and anxiety on CR outcomes is advancing.

The novelty of this thesis is in prospectively investigating whether AnxS influences patient outcomes in CR, as targeting AnxS for treatment may provide clinical therapeutic benefit. Evidence demonstrates that while anxiety and depression are associated with worse CR outcomes, AnxS is associated with each of these, and compared to them, may be a modifiable psychological factor to target for treatment.[28] Therefore, the overall research problem of this thesis is to investigate whether AnxS is associated with patient outcomes in cardiac rehabilitation.

## 2.1. General Hypothesis

We hypothesized that individuals with high anxiety sensitivity enrolled in cardiac rehabilitation will have sub-optimal clinical outcomes from their participation in a cardiac rehabilitation program.

## 2.2. Using a One Health Approach to Address the Research Question

### 2.2.1. What is One Health and What is a One Health Approach

The term One Health was first used following the occurrence of the severe acute respiratory syndrome (SARS) virus and avian influenza H5N1, when the link between animal and human health started to become recognized as threatening.[85] According to the Centers for Disease Control and Prevention (CDC), One Health is defined as a "collaborative, multisectoral, and transdisciplinary approach — working at the local, regional, national, and global levels — with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment."[86] The CDC adds that "One Health is an approach that recognizes that the health of people is closely connected to the health of animals and our shared environment. One Health is not new, but it has become more important in recent years. This is because many factors have changed interactions between people, animals, plants, and our environment." Stakeholder involvement is a fundamental way to facilitate collaboration both within and across multiple sectors at the local, regional, national, and global levels. Khan *et al.* (2018) evaluated the functioning of collaboration of stakeholders within and between One Health networks in Africa, Asia, and Europe. Their results suggest the need and importance of increasing collaborations across sectors and paying more attention to the environmental health aspect of the approach.[87] The Public Health Agency of Canada (PHAC) has also highlighted disease surveillance, response, and prevention as key features that make up One Health.[88]

Historically, zoonotic disease, vector-borne disease (i.e. rift valley fever)[89], and additional communicable disease complications have benefitted from using a One Health approach to resolve health issues. However, there is growing recognition of the need to extend this approach to chronic diseases.[86]

### 2.2.2. The Application of the One Health Approach to Address the Research Question

Addressing the research question using the One Health approach was done by: 1. Applying the PHAC version of the health problem in CR, addressing human, animal, and environmental aspects of One Health; and 2. Engagement of multisectoral stakeholders along the continuum of prevention, detection, and treatment to develop and implement realistic solutions that optimize the health and well-being of participants enrolled in CR.

Human health is one of the core pillars within the One Health framework that may have clinical implications in CR. As previously mentioned in Chapter 1, the prevalence of people living with CVD has increased, subsequently increasing the associated burden on society.[3] To evaluate the influence of this pillar, relationships between AnxS and CVD risk factors in CR were investigated.

To address the environmental pillar of One Health, the influence of social environmental factors on AnxS was investigated. Amid the COVID-19 pandemic, individuals across the globe have been faced with prolonged social isolation due to extensive social distancing measures.[90,91] Arguably, older individuals have been impacted the most by set social distancing guidelines, with many self-reporting loneliness.[90,91] In a cross-sectional study exploring adverse outcomes associated with loneliness, high self-reported loneliness was associated with greater depression and anxiety.[92,93] Loneliness was also associated with increased CVD[93], implying an interaction between the social environmental and human health pillar. Social environmental factors, such as marital status, and its impact on AnxS were investigated. Though exploring the influence of COVID-19 in CR was beyond the scope of this thesis, it played a huge part of the context within this thesis.

Although animal health was not directly investigated in this thesis, translational animal models have also played a significant role when investigating CVD and its associated adverse outcomes. Research with small animals such as mice and rabbits have been advantageous and are continuously used to advance our knowledge on the progression and mechanisms associated with CVD.[94] CVD translational research has supported the importance of and clear need to mitigate adverse cardiac outcomes experienced by individuals through CR. This is yet another example of the interconnection between the human and animal health pillars in the One Health approach.

Collaboration among transdisciplinary stakeholders play a critical role in preventing, detecting, and mitigating adverse health outcomes.[85,86] There is currently a gap in knowledge dissemination and implementation strategies when clinically relevant publications are produced.[95] Bridging this gap through stakeholders is a key component of the One Health approach. In this thesis, identified stakeholders who can contribute to reducing the burden associated with AnxS, depression, and anxiety may have clinical implications in CR. The use of stakeholders has proven to be effective when mitigating adverse outcomes associated with infectious diseases.[85]

To fully investigate the clinical implications of AnxS in CR and to formulate possible mitigation strategies, a One Health approach was employed in this thesis.

## 2.3. Aims and Hypotheses (Revised)

**Specific Aim 1:** To investigate the associations between anxiety sensitivity and sociodemographic, socio-environmental, and clinical characteristics at initial assessment of CR enrollment.

**Hypothesis 1a**: Females will have higher levels of anxiety sensitivity compared to males.

**Hypothesis 1b:** Individuals with partners will have lower levels of anxiety sensitivity compared to individuals without partners.

**Hypothesis 1c**: Individuals with higher levels of anxiety sensitivity will have less favourable clinical characteristics.

**Specific Aim 2:** To investigate interrelationships between anxiety sensitivity, symptoms of anxiety, and symptoms of depression, and how these are associated with CVD risk factor characteristics at initial assessment of CR enrollment.

**Hypothesis 2**: Individuals with higher levels of anxiety sensitivity combined with higher symptoms of anxiety and/or depression will have less favourable CVD risk factor characteristics.

**Specific Aim 3:** To determine if anxiety sensitivity at initial assessment predicts change in physical activity, exercise capacity, and diet at 6-week follow-up.

**Hypothesis 3:** Individuals with higher levels of anxiety sensitivity will have smaller improvements in physical activity, exercise capacity, and diet after 6-week follow-up.

**Specific Aim 4**: To identify key stakeholders within different disciplines who have the power, influence, and potential to assist in investigating, preventing, and mitigating the burden associated with anxiety sensitivity in CR.

# Chapter 3

## 3.0. Materials and Methods

In this chapter, Section 3.1 through Section 3.7 will explain the methods used to address aims 1-3, while section 3.8 through to the end of the chapter will intend to address aim 4.

## 3.1. Study Design

This study used an observational, prospective, longitudinal cohort design for patients referred to and participating in the Cardiac Rehabilitation and Secondary Prevention Program at St. Joseph's Health Care London. The sample consisted of consecutively consenting patients. Approval was obtained by the Health Sciences Research Ethics Board (HSREB) at Western University and the Lawson Health Research Institute in London, Ontario. Copies of both approval letters can be seen in **Appendix A** of this thesis. In response to the Provincial state-of-emergency and Guidance from Provincial (CorHealth Ontario)[96] and National (Canadian Cardiovascular Society) [97] bodies, the St. Joseph's CR program shifted to virtual delivery of CR programing in the spring of 2020 which continued throughout the summer of 2020 (**see Appendix B for detailed flow diagram**).

## 3.2. CR Program for Patients in this Study

Due to the COVID-19 pandemic, CR programming was completed on a virtual basis. This was the mode of delivery for all patients going through CR in this study. Virtual CR programming comprised of multi-disciplinary interventions to optimize patients' physical activity, exercise, nutrition, anxiety, depression, and pharmacotherapy risk profiles.[12] As restrictions eased in the fall of 2020, virtual programming continued, with some cardiopulmonary exercise test (CPET) assessments resuming as necessary for appropriate clinical care. CPET assessments included

evaluation of resting and peak measures of heart rate and blood pressure (systolic and diastolic), as well as metabolic assessments such as VO2 peak.

## 3.3. Study Outcomes

There is one primary outcome for the revised study, as follows:

1. Primary:
    a. Changes, and/or improvement in clinical characteristics for patients enrolled in the cardiac rehabilitation and secondary prevention program.
    b. Achievement of clinical/therapeutic outcomes for patients enrolled in the cardiac rehabilitation and secondary prevention program. Note, because most patients in this study have only completed initial assessment, achievement of these targets cannot be evaluated at this time.

Definition of Primary Outcomes

Per evidence-based clinical care guidelines and standards defined for CR in Canada[98], there are 7 therapeutic outcomes defined for patients. A description of these therapeutic goals and a brief overview of how we will be quantifying and measuring these goals in this study is included below[1]:

(1) Physical activity: Cumulative minutes – By the time of discharge, patients would be expected to achieve a total of 150 minutes of physical activity each week.[98] Minutes of physical activity will be measured via the Godin Leisure-Time Questionnaire (GODIN), a validated self-reported questionnaire that consists of 4 questions.[99] The first 3 questions are scored based on frequency of vigorous, moderate, or mild engagement of physical activity

[1] A complete copy of each self-reported tool is included in Appendix C of this document.

for at least 15 minutes in the past week, multiplied by 9, 6, and 3, respectively and then totally.[100] Scores were than categorized into active (24 points or more), moderately active (14 to 23 points), or sedentary (less than 14 points).[100] Godin and Sheppard reported strong reliability of this assessment tool by assessing leisure-time physical activity across different populations, different countries, and different seasons.[100] The tool has also been successfully validated to be correlated with percentile VO2 max and percentile body mass, which are two determinants of physical fitness, with p-values of <0.001 and <0.01, respectively.

(2) Exercise: Exercise capacity – the therapeutic goal is to achieve a 0.5 MET increase from baseline to discharge.[98] A MET is defined as a unit expressing rate of oxygen consumption while performing a specific activity. This was approximated using the Duke Activity Status Index (DASI), which is a reliable and validated self-reported questionnaire consisting of 12 questions.[101] The total DASI score ranged from 0 to 58.2 points.[102] Raw DASI scores were then converted to METs to estimate peak rate of oxygen intake. Hlatky reported a significant spearman correlation (0.80) between DASI scores and peak oxygen intake, supporting its validity in estimating METs.[101] Scores were than categorized into poor (1-4 METs), moderate (4-7 METs), good (7-10 METs), or excellent (over 10 METs) level of METs achieved.[103]

(3) Diet – the therapeutic goal for all patients who enter CR is to be offered clinical support and education on making dietary changes consistent with the Mediterranean Diet.[98] In this study, dietary status was assessed using the Mediterranean Diet Questionnaire (MDQ), which is a reliable, validated self-reported questionnaire consisting of 14 questions.[104–106] Each question was given a score of either 0 or 1, with total score ranging from 0 to 14.

Scores were then categorized into low (score of 5 or less), moderate (score between 6 to 9), or high (score of 10 or more) levels of adherence to the Mediterranean diet.[104]

(4) Blood pressure – the specific therapeutic target for blood pressure is tailored to each patient based on a complex algorithm as established by the Hypertension Canada Guidelines.[98,107] The general target for each patient is 140/90 mmHg. The resting diastolic and systolic blood pressures were categorized as within target (<90mmHg/<140mmHg) or at risk (>90mmHg/>140mmHg). All measurements were abstracted from the patient's health record.[107]

(5) Blood lipids – the therapeutic goal was a low density lipoprotein (LDL-c) reduction of 50% or a level of <2 mmol/L.[98] Non-high-density lipoproteins (non-HDL-c) were assessed in this study and categorized as within target (<2.6mmol/L) or at risk (>2.6mmol/L). All measurements were abstracted from the patient's health record.[108]

(6) Glucometabolic control – this was determined by the level of hemoglobin A1c (HbA1c) as recommended by the Canadian Diabetes Association guidelines[98,109], HbA1c was categorized as meeting target (<7.0%) or at risk (>7.0%).[110] All HbA1c measurements were abstracted from the patient's health record.

## 3.4. Study Predictor Variables (Independent Variables)

Key objectives for this study were to better understand AnxS, how it may impact outcomes from CR, and how it may interrelate with anxiety and depression to impact outcomes from CR. For this study, these key constructs (independent variables) were measured as follows:

(1) Anxiety Sensitivity: This was measured using ASI-3, which is a reliable and validated questionnaire, compared to earlier versions of the tool, comprised of 18 questions (see

**Section 1.5.2.**).[52,53] An internal consistency test reported the reliability of each of the 3 subscales within the questionnaire with Cronbach consistency scores above 0.70. Factorial validity was confirmed across six replication samples in both clinical and non-clinical populations.[53] Each question was scored from 1 to 4, with total scores ranging from 0-72. Scores were categorized into high (greater than 22 points), moderate-to-high (17-22 points), or low (less than 17 points) levels of AnxS.[111]

(2) Symptoms of Anxiety: This was measured using the Patient Health Questionnaire-4 (PHQ-4), which is a reliable, validated questionnaire which has been routinely used as part of standard of care in CR.[112] Further, the PHQ-4 has been reported to be sensitive for detecting change in health status across a 3-month timespan.[113] The PHQ-4 is comprised of 4 questions, 2 of those questions specifically address anxiety. Each of the questions were scored from 0-3, resulting in a total possible score of 6. A clinical cut off score of 3 was used to identify an individual exhibiting high levels of anxiety.[114]

(3) Symptoms of Depression: This was measured using the Patient Health Questionnaire-4 (PHQ-4), with the remaining 2 questions specifically addressing depression.[112] Scoring and clinical cut off scores for symptoms of depression are identical to symptoms of anxiety on the PHQ-4 as mentioned above.

### 3.4.1. Covariates

Additional variables (covariates), including information regarding age, patient demographics, and clinical characteristics, were necessary to understand key relationships between the predictor variables (AnxS, anxiety, and depression) and study outcomes (defined above) to address the research question using the One Health approach. All necessary sociodemographic (biological

sex), socio-environmental (marital status), and clinical characteristics (adherence to Mediterranean diet, resting blood pressures, blood lipid, and blood glucose) were abstracted from the patient's medical record, maintained by the CR Program at St. Joseph's Health Care London.

## 3.5. Participant Enrollment and Consent

A complete overview of the patient referral, study screening, consenting process, and the data collection process is included in the study flow diagram (**See Figure 1 of Appendix B**).

Patients are referred to the CR Program at St. Joseph's Health Care London, by a physician (family practitioner, cardiologist, or another specialist). Upon receipt of this referral, the clinical team at the CR Program at St. Joseph's Health Care London mails each referred patient a comprehensive information packet including information about their CR intake appointment, as well as a general research pamphlet (UWO REB approved) informing them that they may be contacted for interest in taking part in research activities within the CR Program at St. Joseph's Health Care London; this pamphlet allows for the research staff to directly contact patients if the patients do not opt-out from being contacted (refer to Figure 1 in **Appendix B** for the opt-out process). Patients indicating that they did not want to learn more about the study or that they were not interested in participating, were not contacted further. Patients not indicating any of the previously mentioned were then screened by the research team for eligibility in the study. Patients were eligible to join if it was their first time enrolling in a CR program. Patients were considered ineligible if they were unable to complete the verbal informed consent unaided and/or enrolled in the Atrial Fibrillation Navigator study, the latter being because they were or could have been enrolled in related research.

Patients not indicating that they were not interested in participating were then contacted by the research team to: (1) determine method of sending the letter of information to the patient, and

(2) schedule a follow-up appointment at a time of their convenience, to review the letter of information and complete verbal informed consent. Patients were then sent a copy of the documented consent via mail or email per patient preference. (See Figure 1 in **Appendix B**). Once consent was received, the patient was then successfully enrolled into the study.

## 3.6. Study Procedures

For this study, procedures included completion of self-reported questionnaires by participants and abstraction of data from the electronic medical record for CR Program at St. Joseph's Health Care London. As described in detail below, participants were asked to complete these questionnaires at initial assessment and at 6-week follow-up points during their 6-month participation in the CR program. This data was collected between February to July of 2021. Information relating to study outcomes and covariates were abstracted from the electronic medical record. Information on medication was not collected or included in this study due to the lack of variation between participants, making such data not as informative. A summary of the data collection procedures is included in **Table 1** below.

Table 1: Data Collection Assessment Instruments

| Data Category | | Data Source | Data Collection Period |
|---|---|---|---|
| Primary Outcomes | Physical Activity | GODIN | Initial assessment and 6-week follow-up |
| | Exercise Capacity | DASI | |
| | Diet | MDQ | |
| | Blood Pressure (Resting systolic and diastolic) | PHR | Intake of CR |
| | Blood Glucose Control (HbA1c) | | |
| | Blood Lipid Control (non-HDL-c) | | |
| Predictor Variables | Anxiety Sensitivity | ASI-3 | Initial assessment and 6-week follow-up |
| | Depression | PHQ-4 | |
| | Anxiety | | |
| Covariates | Age, Patient Sociodemographic, Socioenvironmental, and Clinical Characteristics | PHR | Intake of CR |

*Abbreviations: GODIN, Godin leisure-time Questionnaire; DASI, Duke Activity Status Index; MDQ, Mediterranean Diet Questionnaire; PHR, Patient Health Record; ASI-3, Anxiety Sensitivity Index-3, PHQ-4, Patient Health Questionnaire-4*

Questionnaire Administration

Following consent, arrangements were made with each consenting participant regarding the collection of the self-reported questionnaires. As part of the previously mentioned informed consent process, participants were given options in which they preferred to complete the questionnaires. The available options were as follows:

a. **Phone call** – The student researcher will call the participant and go through all questions on each questionnaire via REDCap. REDCap is a hospital approved web-based data management system that lets participants directly answer questions. REDCap stores information following the hospital security guidelines and policies.
b. **Videocall** – The student researcher will videocall the participant via WebEx, a hospital approved application, and complete each questionnaire. Data from each questionnaire will be documented and stored in REDCap.
c. **Mail** – The student researcher will send a prepaid postage envelope with all questionnaires enclosed. The participant will be responsible for sending back the envelope with all questionnaires completed. Once the questionnaires are returned, the student researcher will replicate the responses into REDCap.
d. **Online via REDCap** – The student researcher will email the participant a link to REDCap for them to complete the questionnaires independently online.

Participants were also given an optional reminder one week prior to their next set of questionnaires – options for reminders included either a phone call, email, or mail out. Participants enrolled in the study who had not completed questionnaires on their scheduled date were sent up to two reminder requests over the course of the subsequent three weeks. If they did not complete those questionnaires, they were not contacted until the next scheduled time point for data collection.

## 3.7. Data Management

As previously mentioned, all data completed by participants in this study were confidentially added into REDCap by either a member of the research team or directly by the participant

themselves. REDCap was also setup to include a scoring algorithm for each of the self-reported questionnaires – data abstracted from REDCap included answers to each question and each participant's respective score for each questionnaire.

## 3.8. Data Analysis

All statistical analyses were performed using SPSS software.[115] Descriptive analytic approaches such as mean, standard deviation, and proportions were used to characterize sociodemographic, socio-environmental, and clinical characteristics of participants. A test of normality was conducted for each of the study outcomes using the Shapiro-Wilk Test. Dependent on the outcome of normality, study outcomes were reported with either means and standard deviations, or median and $25^{th}/75^{th}$ percentiles. Due to non-normal results of reported GODIN, DASI, and blood pressure data using the Shapiro-Wilk test, we exclusively relied on the Chi-Square, a univariate statistical test, to investigate the relationship between AnxS and the study outcome variables for the following reasons:

a. Appropriate test to use for non-normality of the tested variables
b. Addresses the challenges of outliers in the small sample size in the study
c. Results are easily interpretable using this test

Although adherence to Mediterranean diet scores, blood lipid, and blood glucose data were reported as normal, to be consistent with how we evaluated non-normal data, the Chi-Square Test was used. The use of other statistical tests (i.e., t-tests and regression) will be revisited when a larger sample size is obtained.

## 3.9. Identifying Key Stakeholders

An element of an approach used by the RECARE project[116] was used in this thesis to systematically identify a diverse range of stakeholders to investigate, prevent, and mitigate the burden associated with the mental health factors in CR. The first step was to establish identification criteria between the student researcher and members of research committee. This allowed for a common objective to be set about the purpose of each stakeholder and their potential engagement in their project.[116] Identification criteria established for this was to incorporate multidisciplinary stakeholders, as characterized by the One Health definition[85,86], across the following four sectors: 1. academia; 2. advocacy groups; 3. government and 4. non for-profit organizations. Stakeholders from all sectors were affected by or affected the burden associated with AnxS in CR. This was determined by assessing the official websites of these stakeholders for this information. In addition, all stakeholders had relation to one or more of the 3 pillars of One Health (human, animal, and environmental health). The second step of the approach was to provide key identification characteristics of the stakeholders such as their location, level of function (local, regional, national), and level of interest (field of activity, form of role, and their sector).[116] Next, an extension of existing stakeholder networks were created using "snowball sampling".[116] For the purposes of this thesis, members of the research committee served as the first identified stakeholders. The snowball sample framework was applied twice by using a Google search engine to collect relevant information relating to the research team and identifying affiliated stakeholders through the official websites of each stakeholder. The primary focus of the search was to identify positions and organizations of the stakeholders rather than naming them. The stakeholders were then categorized by sector, location, regional jurisdiction, field of activity/role, and rank of influence. Rank of influence was estimated using a score between 1 (high), 2 (moderate), or 3

(low) determined by the current position held by the stakeholder, their ability to lead research in CR, and their ability to implement system-level changes to established guidelines and/or access to health care services. A rank of 1 represented a high level of power/influence, a rank of 2 represented a moderate level of power/influence, and a rank of 3 represented a low level of power/influence. The final phase of this approach was to determine possible mitigation strategies using the stakeholders with the highest power/influence. Accordingly, identified stakeholders with a rank of influence equal to 1 were then grouped with a reporting of their potential impact of reducing the burden associated with AnxS in CR.

# Chapter 4

## 4.0. Results

A total of 186 patients who enrolled in CR were forwarded to the research team to screen for eligibility. Of the 186 patients, 7 patients were not eligible to join the study, 68 participants consented to participate in the study, 59 of consented participants completed baseline questionnaires for this study, and 31 completed 6-week follow-up questionnaires. A more detailed breakdown can be seen below in **Figure 1**.

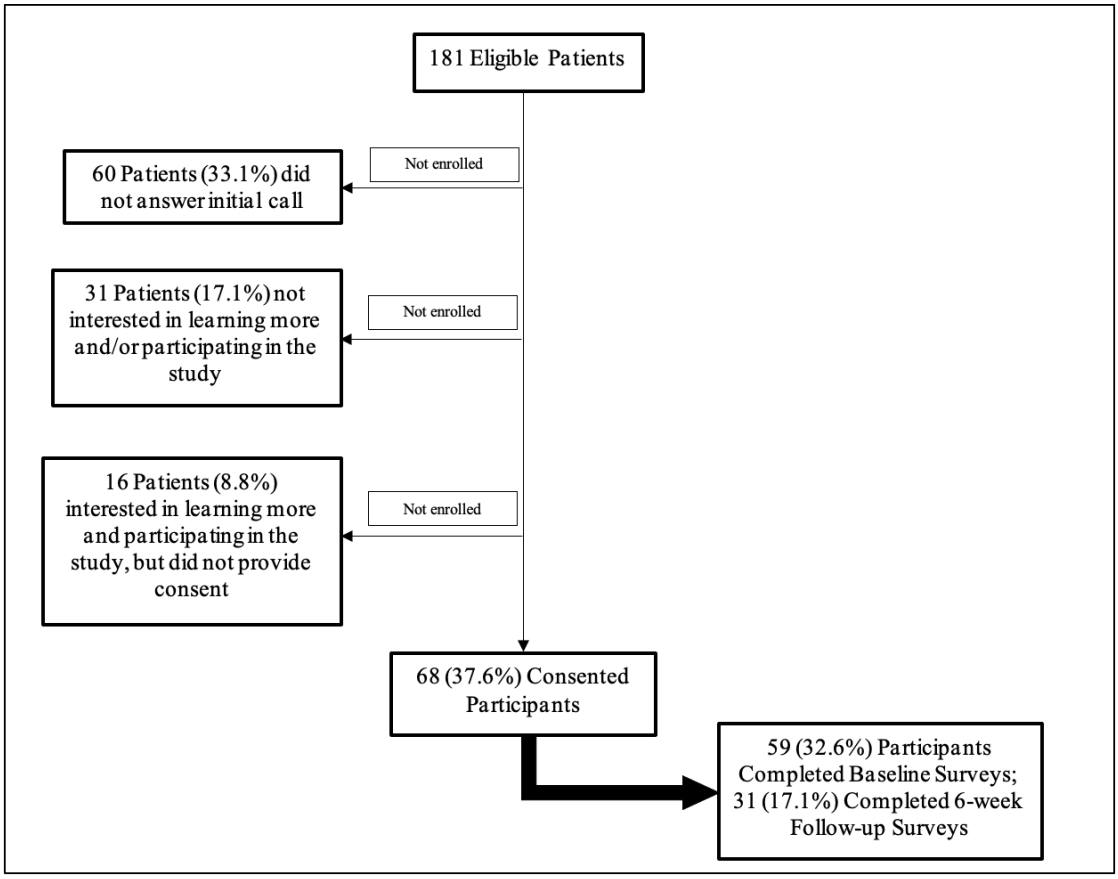


Figure 1: Cardiac Rehabilitation Participant Enrollment, Consent, and Baseline Completion of Questionnaires

Sociodemographic, socio-environmental, and clinical characteristics of participants who completed baseline questionnaires were reported as presented in **Table 2**. Most participants were male and under the age of 65. Sociodemographic and socio-environmental characteristics demonstrated that most participants lived in an urban area (76.2%), were married or in common-law (64.4%), and were either retired or worked full-time (76.3%). Clinical characteristics demonstrated that the top 3 reasons for referral were individuals with coronary angioplasty (27.1%), coronary artery bypass grafting (16.9%), and (repaired) valvular heart disease (11.9%). It is important to note that some participants may have been referred for more than 1 event. Most participants reported a BMI (derived from reported weight and height) in the overweight (33.3%) or obese range (31.7%), with a majority not reporting any history of diabetes (71.2%). Most participants reported a history of hypertension (54.2%), dyslipidemia (62.7%), and CVD (62.7%). Additionally, a vast majority of patients reported no history of a sedentary lifestyle (93.2%).

Table 2: Sociodemographic and Socio-environmental, and Clinical Characteristics of Study Participants

| | |
|---|---|
| *N* | 59 |
| *Male (%) ** | 78.0 |
| *Age, median/mean (SD), y* | 64.2/63.6 (12.8) |
| *Age group, %, y* | |
| <50 | 16.9 |
| 50-65 | 37.3 |
| >65 | 45.8 |
| **Sociodemographic/Socioenvironmental Characteristics** | |
| *Classification of Residing Area* | |
| Urban | 76.2 |
| Rural | 22.0 |
| Missing | 1.8 |
| *Marital Status, %* | |
| Married/Common Law | 64.4 |
| Not Married | 28.8 |
| Missing | 6.8 |
| *Occupational Status, %* | |
| Retired | 45.8 |

| | |
|---|---|
| Full-time | 30.5 |
| Part-time | 3.4 |
| Long-term disability | 6.8 |
| Missing | 13.5 |
| **Clinical Characteristics** | |
| *Reason for Referral, %* | |
| CHF | 5.08 |
| CABG | 16.9 |
| Valvular Heart Disease | 11.9 |
| Coronary Angioplasty | 27.1 |
| Cardiac Arrest | 3.4 |
| MI | 13.5 |
| Unstable Angina Pectoris | 1.7 |
| Stable Coronary Artery Disease/Angina | 1.7 |
| ICD | 1.7 |
| AF | 5.1 |
| SCAD | 1.7 |
| Other | 3.4 |
| Missing | 6.82 |
| *Month of Intake, %* | |
| January | 3.4 |
| February | 33.9 |
| March | 45.8 |
| April | 15.2 |
| Missing | 1.7 |
| *NYHA Score, %* | |
| 1 = No symptoms | 64.4 |
| 2= Mild symptoms | 8.5 |
| 3= marked limitation of activity due to symptoms | 1.7 |
| Missing | 25.4 |
| *CCS Score, %* [96] | |
| 0= Asymptomatic | 69.5 |
| 1= Presence of angina during strenuous, rapid, or prolonged ordinary activity | 5.1 |
| Missing | 25.4 |
| *Mean BMI, kg/m$^2$* * | 29.8 |
| *BMI category, %* | |
| <18.5 (underweight) | 0 |
| 18.5 to 24.9 (normal) | 15.0 |
| 25 to 29.9 (overweight) | 33.3 |
| 30 and over (obese) | 31.7 |
| Missing | 20.0 |
| *History of Hypertension, %* | |
| Yes | 54.2 |
| No | 44.1 |
| Missing | 1.7 |

| | |
|---|---|
| *History of Diabetes Mellitus, %* | |
| Yes | 27.1 |
| No | 71.2 |
| Missing | 1.7 |
| *History of Dyslipidemia, %* | |
| Yes | 62.7 |
| No | 35.6 |
| Missing | 1.7 |
| *Family History of CVD, %* | |
| Yes | 62.7 |
| No | 35.6 |
| Missing | 1.7 |
| *Smoking Status, %* | |
| Former smoker | 42.4 |
| Current smoker | 13.6 |
| Non-smoker | 40.7 |
| Missing | 3.3 |
| *History of Sedentary Lifestyle, %* | |
| Yes | 5.1 |
| No | 93.2 |
| Missing | 1.7 |

***Missing Data*

*Abbreviations for Table 2 above: AF, atrial fibrillation; BMI, body mass index; CCS, Canadian Cardiovascular Society; CABG, coronary artery bypass grafting; CHF, congestive heart failure; CVD, cardiovascular disease; ICD, implantable cardioverter defibrillator; MI, myocardial infarction; NYHA, New York Heart Association; SCAD, spontaneous coronary artery dissection*

Study outcomes were tested for normality, with reported means, medians, and levels of variance. Using a Shapiro-Wilk test, (error) distributions of physical activity, exercise capacity, resting diastolic blood pressure, and resting systolic blood pressure deviated significantly from normality ($p<0.05$). In contrast, scores of adherences to the Mediterranean diet, non-HDL-c, and HbA1c did not deviate significantly from normality ($p>0.05$). A detailed description of findings can be found below in **Table 3**.

Table 3: Descriptive Statistics for Study Outcome Variables

| **Study Outcome** | **Continuous Variable** Median ($25^{th}$/$75^{th}$ percentile) or Mean (SD) | **Categorical Variable** Category (%) | **Normality** (Shapiro-Wilk test statistic, p-value) |
|---|---|---|---|
| Physical Activity: Godin Leisure-time Activity * | 40.5 mins (25.0/59.2) | Active (24 pts+): 67.8<br><br>Moderately Active (14-23 pts): 10.2<br><br>Sedentary (<14pts): 10.2<br><br>Missing: 11.8 | Not normal (0.740, <0.001) |
| Exercise Capacity: Duke Activity Status Index * | 7.2 METs (5.7/9.0) | Excellent (10+ METs): 0<br><br>Good (7-10 METs): 52.5<br><br>Moderate (4-7 METs): 37.3<br><br>Poor (1-4 METs): 3.4<br><br>Missing: 6.8 | Not normal (0.956, 0.043) |
| Diet: Mediterranean Diet Questionnaire * | 7.7 pts (2.5) | High Adherence (10+pts): 25.0<br><br>Moderate Adherence (6-9pts): 50.0<br><br>Low Adherence (5 or less pts): 18.3<br><br>Missing: 6.7 | Normal (0.970, 0.179) |
| Resting Diastolic Blood Pressure: Patient Health Record * | 75.0mmHg (69.0/80.0) | At Target (<90mmHg): 78.0<br><br>At Risk (>90mmHg): 1.7<br><br>Missing: 20.3 | Not normal (0.896, <0.001) |

| Study Outcome | **Continuous Variable** Median ($25^{th}$/$75^{th}$ percentile) or Mean (SD) | **Categorical Variable** Category (%) | **Normality** (Shapiro-Wilk test statistic, p-value) |
|---|---|---|---|
| Resting Systolic Blood Pressure: Patient Health Record * | 126.0mmHg (114.0/140.0) | At Target (<140mmHg): 61.0<br><br>At Risk (>140mmHg): 18.6<br><br>Missing: 20.4 | Not normal (0.948, 0.035) |
| Non-HDL-c: Patient Health Record * | 3.0mmol/L (1.3) | At Target (<2.6mmol/L): 39.0<br><br>At Risk (>2.6mmol/L): 50.8<br><br>Missing: 10.2 | Normal (0.964, 0.113) |
| HbA1c: Patient Health Record * | 6.0% (0.9) | At Target (<7.0%): 72.9<br><br>At Risk (>7.0%): 15.3<br><br>Missing: 11.8 | Normal (0.949, 0.191) |

**Missing Data*
*Abbreviations for Table 3 above; HbA1c, hemoglobin; HDL-c, high density lipoprotein cholesterol*

Study predictor variables were tested for normality, with reported means, medians, and levels of variance. Using the Shapiro-Wilk test, study predictor variables were tested for normality. Results suggest that AnxS, symptoms of depression, and symptoms of anxiety did not meet the criteria to be normally distributed ($p<0.001$). Reports suggest that 35% of participants have moderately high to high AnxS while most participants did not have symptoms of depression (76.3%) and anxiety (81.4%). A detailed description of findings can be found below in **Table 4**.

Table 4: Descriptive Statistics for Study Predictor Variables

| **Study Predictor Variable** | **Continuous Variable** Median ($25^{th}$/$75^{th}$ percentile) or Mean (SD) | **Categorical Variable** Category (%) | **Normality** (Shapiro-Wilk test statistic, p-value) |
|---|---|---|---|
| Anxiety Sensitivity: ASI-3 * | 12.0 (7.8, 19.0) | High [‡] (22+pts): 20.0<br><br>Moderately High [‡] (17-22pts): 15.0<br><br>Low [‡] (<22pts): 55.0<br><br>Missing: 10.0 | Not normal (0.886, <0.001) |
| Symptoms of Depression: PHQ-4 * | 1.0 (0, 2.0) | High (3-6 pts) [†]: 22.0<br>Low (0-2) 76.3<br>Missing: 1.7 | Not normal (0.793, <0.001) |
| Symptoms of Anxiety: PHQ-4 * | 1.0 (0, 2.0) | High (3-6 pts) [†]: 16.9<br>Low (0-2): 81.4<br>Missing: 1.7 | Not normal (0.791, <0.001) |

**Missing Data*
*[‡]Cut-points for ASI-3 were established by Allan et al. 2014* [111]
*[†]Scores 3 or greater are recognized in clinical settings as a positive screen for symptoms of anxiety and depression*
*Abbreviations for Table 4 above: Anxiety sensitivity; ASI-3, Anxiety Sensitivity Index-3; PHQ-4, Patient Health Questionnaire-4*

## 4.1. Results: Associations between Anxiety Sensitivity, Sociodemographic, Socio-environmental, and Clinical Characteristics

In this section, the results of analyses addressing specific aim 1 are presented.

**Specific Aim 1:** investigate the associations between anxiety sensitivity and sociodemographic, socio-environmental, and clinical characteristics at initial assessment.

**Hypothesis 1a**: Females will have higher levels of anxiety sensitivity compared to males.

**Hypothesis 1b:** Individuals with partners will have lower levels of anxiety sensitivity compared to individuals without partners.

**Hypothesis 1c**: Individuals with higher levels of anxiety sensitivity will have less favourable clinical characteristics.

Univariate associations between AnxS, sociodemographic, socio-environmental, and clinical characteristics were assessed using a Chi-Square test with results presented in **Table 5**. Results indicated that AnxS was not significantly associated with sex, marital status, physical activity, exercise capacity, adherence to the Mediterranean diet, resting diastolic blood pressure, resting systolic blood pressure, non-HDL-c, and HbA1c at initial assessment ($p>0.05$). The association between adherence to the Mediterranean diet and AnxS was the only study outcome to approach statistical significance ($p=0.074$). This suggests that there may be a trend of individuals with high AnxS reporting low adherence to the Mediterranean diet.

Table 5: Associations between Anxiety Sensitivity, Sociodemographic, Socio-environmental, and Clinical Characteristics at Initial Assessment

| **Dependent Variable** | **ASI Category:** Low (<17 pts) (n, % within ASI category) | **ASI Category:** Moderately High (17-22 pts) (n, % within ASI category) | **ASI Category:** High (>22 pts) (n, % within ASI category) | **Significance** (Pearson Chi-Square test statistic, p-value) |
|---|---|---|---|---|
| **Sociodemographic Characteristic** | | | | |
| Sex * | Male: 27, 81.8<br><br>Female: 5, 15.2 | Male: 7, 77.8<br><br>Female: 2, 22.2 | Male: 10, 83.3<br><br>Female: 2, 16.7 | NSS (0.869, 0.929) |
| **Socioenvironmental Characteristic** | | | | |
| Marital Status * | Married: 21, 70.0<br><br>Not Married: 9, 30.0 | Married: 7, 77.8<br><br>Not Married: 2, 22.2 | Married: 8, 72.7<br><br>Not Married: 3, 27.3 | NSS (0.211, 0.900) |
| **Clinical Characteristics** | | | | |
| Physical Activity * | Active (24+ pts): 22, 78.6<br><br>Moderately Active (14-23 pts): 3, 10.7<br><br>Sedentary | Active (24+ pts): 7, 100<br><br>Moderately Active (14-23 pts): 0,0<br><br>Sedentary | Active (24+ pts): 7, 58.3<br><br>Moderately Active (14-23 pts): 3, 25.0<br><br>Sedentary | NSS (4.585, 0.333) |

| **Dependent Variable** | **ASI Category:** Low (<17 pts) (n, % within ASI category) | **ASI Category:** Moderately High (17-22 pts) (n, % within ASI category) | **ASI Category:** High (>22 pts) (n, % within ASI category) | **Significance** (Pearson Chi-Square test statistic, p-value) |
|---|---|---|---|---|
| | (<14 pts): 3, 10.7 | (<14 pts): 0,0 | (<14 pts): 2, 16.7 | |
| Exercise Capacity * | Excellent (10+ METs): 0,0<br><br>Good (7-10 METs): 17, 56.7<br><br>Moderate (4-7 METs): 13, 43.3<br><br>Poor (1-4 METs): 0,0 | Excellent (10+ METs): 0,0<br><br>Good (7-10 METs): 6, 75.0<br><br>Moderate (4-7 METs): 1, 12.5<br><br>Poor (1-4 METs): 1, 12.5 | Excellent (10+ METs): 0,0<br><br>Good (7-10 METs): 5, 41.7<br><br>Moderate (4-7 METs): 6, 50.0<br><br>Poor (1-4 METs): 1, 8.3 | NSS (6.062, 0.195) |
| Mediterranean Diet Adherence * | High (10+ pts): 10, 31.3<br><br>Moderate (6-9 pts): 18, 56.3<br><br>Low (5 or less pts): 4, 12.5 | High (10+ pts): 1, 11.1<br><br>Moderate (6-9 pts): 6, 66.7<br><br>Low (5 or less pts): 2, 22.2 | High (10+ pts): 3, 30.0<br><br>Moderate (6-9 pts): 2, 20.0<br><br>Low (5 or less pts): 5, 50.0 | NSS (8.528, 0.074) |
| Resting Diastolic Blood Pressure * | Within Target (<90mmHg): 26, 96.3<br><br>At Risk (>90mmHg): 1, 3.7 | Within Target (<90mmHg): 6, 100.0<br><br>At Risk (>90mmHg): 0,0 | Within Target (<90mmHg): 11, 100.0<br><br>At Risk (>90mmHg): 0,0 | NSS (0.644, 0.725) |
| Resting Systolic Blood Pressure * | Within Target (<140mmHg): 18, 66.7<br><br>At Risk (>140mmHg): 9, 33.3 | Within Target (<140mmHg): 6, 100.0<br><br>At Risk (>140mmHg): 0,0 | Within Target (<140mmHg): 9, 81.8<br><br>At Risk (>140mmHg): 2, 18.2 | NSS (3.273, 0.195) |
| Non-HDL-c * | Within Target (<2.6mmol/L): 11, 39.3<br><br>At Risk (>2.6mmol/L): 17, 60.7 | Within Target (<2.6mmol/L): 4, 50.0<br><br>At Risk (>2.6mmol/L): 4, 50.0 | Within Target (<2.6mmol/L): 5, 41.7<br><br>At Risk (>2.6mmol/L): 7, 58.3 | NSS (0.294, 0.863) |
| HbA1c * | Within Target (<7.0%): 24, 82.8 | Within Target (<7.0%): 7, 87.5 | Within Target (<7.0%): 9, 81.8 | NSS |

| Dependent Variable | ASI Category: Low (<17 pts) (n, % within ASI category) | ASI Category: Moderately High (17-22 pts) (n, % within ASI category) | ASI Category: High (>22 pts) (n, % within ASI category) | Significance (Pearson Chi-Square test statistic, p-value) |
|---|---|---|---|---|
| | At Risk (>7.0%): 5, 17.2 | At Risk (>7.0%): 1, 12.5 | At Risk (>7.0%): 2, 18.2 | (0.125, 0.939) |

**Missing Data*
*Abbreviations for Table 5 above: MET, Metabolic Equivalent; HbA1c, Blood Glucose; Non-HDL-c, non-high density lipoprotein cholesterol; NSS, not statistically significant (p>0.05)*

## 4.2. Results: Interrelationships between Anxiety Sensitivity, Anxiety, Depression, and Clinical Characteristics

In this section, the results of analyses addressing specific aim 2 are presented.

**Specific Aim 2:** To investigate interrelationships among anxiety sensitivity, symptoms of anxiety, and symptoms of depression, and how these are associated with clinical characteristics at initial assessment.

**Hypothesis 2**: Individuals with higher levels of anxiety sensitivity combined with higher symptoms of anxiety and/or depression will have less favourable clinical characteristics.

Univariate associations between anxiety and depression, as measured using the PHQ-4, were assessed using a Chi-Square test. The associations reported in **Table 6** support that there is a statistically significant association between the anxiety and depression subscales within the PHQ-4 ($p<0.05$).

Table 6: Associations between Symptoms of Depression and Symptoms of Anxiety

| | | **Anxiety Category *** | | | **Significance** (Pearson Chi-Square test statistic, P-value) |
|---|---|---|---|---|---|
| **Depression Category *** | | **Low** (0-2 pts) | **High** (3-6 pts) † | **Total** | Significant (9.816, 0.002) |
| **Low** (0-2 pts) | Count | 41 | 4 | 45 | |
| | Within Depression Category (%) | 91.1 | 8.9 | 100.0 | |
| | Within Anxiety Category (%) | 85.4 | 40.0 | 77.6 | |
| **High** (3-6 pts) † | Count | 7 | 6 | 13 | |
| | Within Depression Category (%) | 53.8 | 46.2 | 100 | |
| | Within Anxiety Category (%) | 14.6 | 60.0 | 22.4 | |
| **Total** | Count | 48 | 10 | 58 | |
| | Within Depression Category (%) | 82.8 | 17.2 | 100 | |
| | Within Anxiety Category (%) | 100 | 100 | 100 | |

**Missing Data*
*†Scores 3 or greater are recognized in clinical settings as a positive screen for symptoms of anxiety and depression*

Univariate associations between AnxS and symptoms of anxiety were assessed using a Chi-Square test. The associations presented in **Table 7**, support that there is a statistically significant association between AnxS and symptoms of anxiety ($p<0.05$).

Table 7: Associations between Anxiety Sensitivity and Symptoms of Anxiety

| | | **Anxiety Sensitivity Category *** | | | | **Significance** (Pearson Chi-Square, P-value) |
|---|---|---|---|---|---|---|
| **Anxiety Category *** | | **Low** (<17 pts) | **Moderate to High** (17-22 pts) | **High** (>22 pts) | **Total** | Significant (8.676, 0.013) |
| **Low** (0-2 pts) | Count | 30 | 8 | 7 | 45 | |
| | Within Anxiety Category (%) | 66.7 | 17.8 | 15.6 | 100.0 | |
| | Within AnxS Category (%) | 93.8 | 88.9 | 58.3 | 84.9 | |
| **High** (3-6 pts) † | Count | 2 | 1 | 5 | 8 | |
| | Within Anxiety Category (%) | 25.0 | 12.5 | 62.5 | 100.0 | |
| | Within AnxS Category (%) | 6.3 | 11.1 | 41.7 | 15.1 | |
| **Total** | Count | 32 | 9 | 12 | 53 | |
| | Within Anxiety Category (%) | 60.4 | 17.0 | 22.6 | | |
| | Within AnxS Category (%) | 100.0 | 100.0 | 100.0 | 100.0 | |

**Missing Data*
*†Scores 3 or greater are recognized in clinical settings as a positive screen for symptoms of anxiety and depression*
*Abbreviations for Table 7 above: AnxS, anxiety sensitivity*

Univariate associations between AnxS and symptoms of depression were assessed using a Chi-Square test. The associations presented in **Table 8**, reported that associations between AnxS and depression approached statistical significance (0.078).

Table 8: Associations between Anxiety Sensitivity and Symptoms of Depression

| | | Anxiety Sensitivity Category * | | | | **Significance** (Pearson Chi-Square, P-value) |
|---|---|---|---|---|---|---|
| **Depression Category *** | | **Low** (<17 pts) | **Moderate to High** (17-22 pts) | **High** (>22 pts) | **Total** | NSS (5.105, 0.078) |
| **Low** (0-2 pts) | Count | 28 | 5 | 8 | 41 | |
| | Within Depression Category (%) | 68.3 | 12.2 | 19.5 | 100.0 | |
| | Within AnxS Category (%) | 87.5 | 55.6 | 66.7 | 77.4 | |
| **High** (3-6 pts) † | Count | 4 | 4 | 4 | 12 | |
| | Within Depression Category (%) | 33.3 | 33.3 | 33.3 | 100.0 | |
| | Within AnxS Category (%) | 12.5 | 44.4 | 33.3 | 22.6 | |
| **Total** | Count | 32 | 9 | 12 | 53 | |
| | Within Depression Category (%) | 60.4 | 17.0 | 22.6 | 100.0 | |
| | Within AnxS Category (%) | 100.0 | 100.0 | 100.0 | 100.0 | |

**Missing Data*
*†Scores 3 or greater are recognized in clinical settings as a positive screen for symptoms of anxiety and depression*
*Abbreviations for Table 8 above: AnxS, anxiety sensitivity; NSS, not statistically significant*

The implications of creating a new variable to investigate the interrelationships among the three constructs and their impact of patient outcomes in CR can be found in the discussion section of this thesis. A new variable was created with three categories representing the extent to which participants had 1,2, or 3 of high AnxS, high symptoms of anxiety, and high symptoms of depression. The "null group" were those participants with low AnxS, symptoms of anxiety, or symptoms of depression. The "all group" were those who presented with high AnxS and high symptoms of anxiety and high symptoms of depression. The "some group" were those who presented with a mix of some high and some low levels of AnxS, symptoms of anxiety, or

symptoms of depression. Of the 53 participants that had complete data for all 3 scores, there were 4 participants in the "All Group" (7.5%), 36 were in the "Some Group" (67.9%), and 13 participants were in the "Null Group" (21.7%).

Univariate associations between this new variable, representing the impact of overlapping AnxS, symptoms of anxiety, and symptoms of depression were assessed using a Chi-Square test, with the results presented in **Table 9**. There were statistically significant associations ($p<0.05$) between this category and diastolic blood pressure, suggesting that individuals in the "Null" group met the guideline recommended target significantly more frequently than individuals in the "All" group. It is worth noting that only 1 participant in the "All" group reported not being within target. No additional associations were found between this new variable, physical activity, exercise capacity, Mediterranean diet adherence, resting systolic blood pressure, non-HDL-c, and HbA1c ($p>0.05$).

Table 9: Associations between High Levels of Anxiety Sensitivity, Anxiety, Depression and Clinical Characteristics at Initial Assessment

| **Dependent Variable** | **All Group:** High AnxS, Anxiety and Depression (n, % within ASI category) | **Some Group:** Mix of High and/or low AnxS, Anxiety, and Depression (n, % within ASI category) | **Null Group:** Low AnxS, Anxiety, and Depression (n, % within ASI category) | **Significance** (Pearson Chi-Square test statistic, p-value) |
|---|---|---|---|---|
| **Clinical Characteristics** | | | | |
| Physical Activity * | Active (24+ pts): 3, 75.0<br><br>Moderately Active (14-23 pts): 0,0<br><br>Sedentary (<14 pts): 1, 25.0 | Active (24+ pts): 25, 83.3<br><br>Moderately Active (14-23 pts): 4, 13.3<br><br>Sedentary (<14 pts): 1, 3.3 | Active (24+ pts): 8, 66.7<br><br>Moderately Active (14-23 pts): 2, 16.7<br><br>Sedentary (<14 pts): 2, 16.7 | NSS (4.046, 0.400) |
| Exercise Capacity * | Excellent (10+ METs): 0,0 | Excellent (10+ METs): 0,0 | Excellent (10+ METs): 0,0 | NSS (2.994, 0.559) |

| **Dependent Variable** | **All Group:** High AnxS, Anxiety and Depression (n, % within ASI category) | **Some Group:** Mix of High and/or low AnxS, Anxiety, and Depression (n, % within ASI category) | **Null Group:** Low AnxS, Anxiety, and Depression (n, % within ASI category) | **Significance** (Pearson Chi-Square test statistic, p-value) |
|---|---|---|---|---|
| | Good (7-10 METs): 1, 25.0<br><br>Moderate (4-7 METs): 3, 75.0<br><br>Poor (1-4 METs): 0,0 | Good (7-10 METs): 19, 57.6<br><br>Moderate (4-7 METs): 12, 36.4<br><br>Poor (1-4 METs): 2, 6.1 | Good (7-10 METs): 7, 58.3<br><br>Moderate (4-7 METs): 5, 41.7<br><br>Poor (1-4 METs): 0,0 | |
| Mediterranean Diet Adherence * | High (10+ pts): 1, 25.0<br><br>Moderate (6-9 pts): 1, 25.0<br><br>Low (5 or less pts): 2, 50.0 | High (10+ pts): 9, 25.0<br><br>Moderate (6-9 pts): 21, 58.3<br><br>Low (5 or less pts): 6, 16.7 | High (10+ pts): 4, 36.4<br><br>Moderate (6-9 pts): 4, 36.4<br><br>Low (5 or less pts): 3, 27.3 | NSS (3.844, 0.427) |
| Resting Diastolic Blood Pressure * | Within Target (<90mmHg): 2, 66.7<br><br>At Risk (>90mmHg): 1, 33.3 | Within Target (<90mmHg): 27, 100.0<br><br>At Risk (>90mmHg): 0,0 | Within Target (<90mmHg): 13, 100.0<br><br>At Risk (>90mmHg): 0,0 | Significant (13.651, 0.001) |
| Resting Systolic Blood Pressure * | Within Target (<140mmHg): 1, 33.3<br><br>At Risk (>140mmHg): 2, 66.7 | Within Target (<140mmHg): 21, 77.8<br><br>At Risk (>140mmHg): 6, 22.2 | Within Target (<140mmHg): 11, 84.6<br><br>At Risk (>140mmHg): 2, 15.4 | NSS (3.635, 0.162) |
| Non-HDL-c * | Within Target (<2.6mmol/L): 1, 25.0<br><br>At Risk (>2.6mmol/L): 3, 75.0 | Within Target (<2.6mmol/L): 15, 48.4<br><br>At Risk (>2.6mmol/L): 16, 51.6 | Within Target (<2.6mmol/L): 3, 25.0<br><br>At Risk (>2.6mmol/L): 9, 75.0 | NSS (2.397, 0.302) |
| HbA1c * | Within Target (<7.0%): 3, 75.0 | Within Target (<7.0%): 26, 83.9 | Within Target (<7.0%): 11, 91.7 | NSS (0.767, 0.681) |

| Dependent Variable | All Group: High AnxS, Anxiety and Depression (n, % within ASI category) | Some Group: Mix of High and/or low AnxS, Anxiety, and Depression (n, % within ASI category) | Null Group: Low AnxS, Anxiety, and Depression (n, % within ASI category) | Significance (Pearson Chi-Square test statistic, p-value) |
|---|---|---|---|---|
| | At Risk (>7.0%): 1, 25.0 | At Risk (>7.0%): 5, 16.1 | At Risk (>7.0%): 1, 8.3 | |

**Missing Data*
*Abbreviations for Table 9 above: MET, Metabolic Equivalent; HbA1c, hemoglobin A1c; NSS, not statistically significant (p>0.05)*

## 4.3. Results: Investigating Anxiety Sensitivity as a Predictor of Change in Physical Activity, Exercise Capacity, and Adherence to the Mediterranean Diet

In this section, the results of analyses addressing specific aim 3 are presented. Of the 59 participants who completed baseline questionnaires, 31 (52.5%) completed 6-week follow-up measures.

**Specific Aim 3:** To determine if anxiety sensitivity at initial assessment predicts change in exercise capacity, physical activity, and diet at 6-week follow-up.

**Hypothesis 3:** Individuals with higher levels of anxiety sensitivity will have smaller increases in exercise capacity, physical activity, and diet after 6-week follow-up.

Univariate associations between AnxS, physical activity, exercise capacity, and adherence to the Mediterranean diet at 6-week follow-up were assessed using a Chi-Square test, with results presented in **Table 10**. Clinical variables presented in the table were measured once at the 6-week period. No significant associations were reported (p>0.05).

Table 10: Associations between Anxiety Sensitivity and Clinical Characteristics at 6-week Follow-up Assessment

| **Dependent Variable** | **ASI Category:** Low (Score <17) (n, %) | **ASI Category:** Moderately High (Score 17-22) (n, %) | **ASI Category:** High (Score>22) (n, %) | **Significance** (Pearson Chi-Square test statistic, p-value) |
|---|---|---|---|---|
| **Clinical Characteristics** | | | | |
| Physical Activity * | Active (24 pts+): 13, 76.5<br><br>Moderately Active (14-23 pts): 2, 11.8<br><br>Sedentary (<14pts): 2, 11.8 | Active (24 pts+): 2, 100.0<br><br>Moderately Active (14-23 pts): 0,0<br><br>Sedentary (<14pts): 0,0 | Active (24 pts+): 6, 66.7<br><br>Moderately Active (14-23 pts): 1, 11.1<br><br>Sedentary (<14pts): 2, 22.2 | NSS (1.246, 0.870) |
| Exercise Capacity * | Excellent (10+ METs): 0,0<br><br>Good (7-10 METs): 6, 46.2<br><br>Moderate (4-7 METs): 7, 53.8<br><br>Poor (1-4 METs): 0,0 | Excellent (10+ METs): 0,0<br><br>Good (7-10 METs): 2, 66.7<br><br>Moderate (4-7 METs): 1, 33.3<br><br>Poor (1-4 METs): 0,0 | Excellent (10+ METs): 0,0<br><br>Good (7-10 METs): 7, 77.8<br><br>Moderate (4-7 METs): 1, 11.1<br><br>Poor (1-4 METs): 1, 11.1 | NSS (5.394, 0.249) |
| Mediterranean Diet Adherence * | High (10+ pts): 5, 26.3<br><br>Moderate (6-9 pts): 10, 52.6<br><br>Low (5 or less pts): 4, 21.1 | High (10+ pts): 1, 33.3<br><br>Moderate (6-9 pts): 2, 66.7<br><br>Low (5 or less pts): 0,0 | High (10+ pts): 0,0<br><br>Moderate (6-9 pts): 5, 71.4<br><br>Low (5 or less pts): 2, 28.6 | NSS (3.148, 0.533) |

**Missing Data*

*Abbreviations for Table 10 above: MET, Metabolic Equivalent; NSS, not statistically significant (p>0.05)*

## 4.4. Identified Stakeholders with Potential to Reduce Burden Associated with Anxiety Sensitivity in Cardiac Rehabilitation

In this section, the results of analyses addressing specific aim 4 are presented.

> **Specific Aim 4**: To identify key stakeholders within different disciplines who have the power, influence, and potential to assist in investigating, preventing, and mitigating the burden associated with anxiety sensitivity in CR.

After conducting a comprehensive "snowball sample" of relevant stakeholders, 21 were identified within the academic (n=10), advocacy (n=8), government (n=1), and non-for-profit (n=2) sectors (See **Table 11** below). Identified stakeholders with an estimated rank of influence equal to 1 were then grouped with a reporting of their potential impact of reducing the burden associated with AnxS in CR.

Table 11: Identified Multidisciplinary Stakeholders with Potential to Reduce Risk of Burden Associated with Anxiety Sensitivity in Cardiac Rehabilitation

| Stakeholder | Location | Regional Jurisdiction | Field of Activity/Role | Rank of Influence |
|---|---|---|---|---|
| **Sector: Academia** | | | | |
| Medical Director of CRSP at St. Joseph's Health Care London | London, Ontario | Local, provincial, national, global | Works clinically and academically to reduce burden, and improve clinical outcomes associated with CR | 1 (High) |
| Director of CPRP at Toronto Rehabilitation, UHN | Toronto, Ontario | Local, provincial | An expert on the impact of exercise in CR. Works clinically and academically to reduce burden, and improve clinical outcomes associated with CR | 1 (High) |
| Director of Research, CR, Peter Munk Center, UHN | Toronto, Ontario | Local, provincial, national, global | Works academically to optimize patient outcomes in post-acute cardiovascular care | 1 (High) |

| Stakeholder | Location | Regional Jurisdiction | Field of Activity/Role | Rank of Influence |
|---|---|---|---|---|
| Clinical Psychologist involved in CR | London, Ontario | Local, provincial, national | Extensive knowledge in Cardiovascular health and the influence of psychology | 2 (Moderate) |
| Beryl and Richard Ivey Research Chair in aging, mental health, rehabilitation, and recovery | London, Ontario | Local, provincial, national, global | Contributed academically to the use of mental health technology for individuals with depression | 2 (Moderate) |
| Beryl Ivey Chair of One Health | London, Ontario | Local, provincial, national, and global | One Health Advocate | 3 (Low) |
| Western University | London, Ontario | Local, provincial, national, and global | Encourages One Health through academic research and student-led committees | 3 (Low) |
| One Health Institute | Guelph, Ontario | Local, provincial, national, and global | Promotes academic, research, and outreach programs related to One Health | 3 (Low) |
| Ontario Veterinary College | Guelph, Ontario | Local, provincial, national | Works clinically and academically with animal health. Potential to advance translational research on the influence of AnxS on cardiovascular disease | 3 (Low) |
| Guelph University | Guelph, Ontario | Local, provincial, national, and global | Encourages One Health through academic research and student-led committees | 3 (Low) |
| **Sector: Advocacy Groups** | | | | |
| Senior Vice President of CorHealth Ontario | Toronto, Ontario | Provincial | Primary focus on healthcare policy and planning improvement. Facilitated collaboration between CCN and OSN organizations, leading to the founding of CorHealth | 1 (High) |
| President of the CACPR | Saskatoon, Saskatchewan | National | Enhances knowledge, clinical care, and | 1 (High) |

| Stakeholder | Location | Regional Jurisdiction | Field of Activity/Role | Rank of Influence |
|---|---|---|---|---|
| | | | research within the scope of CR | |
| Interim Chair of CRNO | Ottawa, Ontario | Local, provincial, national | Focuses on care provided by CR program. | 1 (High) |
| Vice President of CorHealth Ontario | Toronto, Ontario | Provincial | Works to fulfill CorHealth mandate of improving the healthcare system by leading the clinical and digital teams. | 2 (Moderate) |
| Clinical Neuropsychologist staff member on OPA | St. Catherine's, Ontario | Provincial | Works on psychotherapy treatments on range of mental health disorders. Potential to investigate the targeting of AnxS | 2 (Moderate) |
| Director-general of WHO | Geneva, Switzerland | Global | Launched Mental Health Initiative for Universal Coverage | 3 (Low) |
| One Health Club | London, Ontario | Local | One Health Advocate | 3 (Low) |
| One Health Student Committee | Guelph, Ontario | Local | Student-led committee advocating for the importance of One Health | 3 (Low) |
| **Sector: Government** | | | | |
| Minister of Health in Ontario | Toronto, Ontario | Provincial | Responsible for governing and managing the healthcare system on Ontario population-level | 1 (High) |
| **Sector: Non-Profit/Voluntary Organizations** | | | | |
| National Chief Executive Officer of CMHA | Toronto, Ontario | Local, provincial, national | Acknowledge the influence of social determinants of health on mental health outcomes. Has 7 years of experience working on a multi-stakeholder. | 1 (High) |
| CEO of Heart and Stroke Foundation | Ottawa, Ontario | National | Leading funder for cardiovascular related research. Potential to invest in research targeting AnxS for treatment in CR | 2 (Moderate) |

*Abbreviations for Table 11 above: AnxS, Anxiety sensitivity; CACPR, Canadian Association of Cardiovascular Prevention and Rehabilitation; CCN, Cardiac Care Network; CMHA, Canadian Mental Health Association; CPRP, Cardiovascular Prevention and Rehabilitation Program; CR, Cardiac rehabilitation; CRNO, Cardiac Rehabilitation Network of Ontario; CRSP, Cardiac Rehabilitation and Secondary Prevention; NGO, Non-governmental organization; OPN, Ontario Psychological Association; OSN, Ontario Stroke Network; UHN, University Health Network; WHO, World Health Organization*

Table 12: Identified Stakeholders with the Highest Estimated Potential Power and Influence

| **Stakeholder** | **Regional Jurisdiction** | **Potential Impact of Direct Influence** |
|---|---|---|
| Health Minister of Ontario | Provincial | Potential to administer funding and provide access to support psychological services aimed to treat AnxS in CR. |
| Medical Director of CRSP Program at St. Joseph's Health Care London | Local, provincial | Ability to conduct a collaborative clinical trial with Toronto Rehabilitation on the efficacy of treating AnxS in CR. This stakeholder also has established relationships with members of the CACPR. This may help with implementing changes to the CACPR guidelines if AnxS treatment provides clinical benefit. |
| Director of CPRP at Toronto Rehabilitation, UHN | Local, provincial | Ability to conduct a collaborative clinical trial with CRSP program at St. Joseph's Health Care London on the efficacy of treating AnxS in CR. |
| Director of Research, CR, Peter Munk Center, UHN | Local, provincial | This stakeholder is an active member of the CACPR. They have the potential to communicate the efficacy of AnxS treatment to board members, with efforts to modify guidelines where applicable. |
| Senior Vice President of CorHealth Ontario | Provincial | Potential to advocate for guideline modifications, communicating evidence- |

| | | |
|---|---|---|
| | | based recommendations of treating AnxS to the CACPR. |
| President of the CACPR | National | Potential to lead and implement changes to the CACPR on the burden associated with AnxS, grounded by evidence-based research conducted by clinical trials. |
| Interim Chair of CRNO | Local, provincial | Potential advocate to the CACPR on guideline modifications relating to treatment of AnxS. |
| National Chief Executive Officer of CMHA | Local, provincial, national | Potential to guide engagement of stakeholders involved. |

# Chapter 5

## 5.0. Discussion

This longitudinal cohort study, despite being curtailed by the COVID-19 pandemic to 59 participants, provides a novel evaluation of relationships between AnxS and patient outcomes in CR.

## 5.1. Characteristics of the Study Sample

Due to COVID-19, CR was completed virtually by patients. Subsequently, participation in this study was also completed virtually, making this group of participants a unique "COVID-19 cohort". As a direct consequence to delays in clinical care due to COVID-19, research activities were also delayed, impacting the number of participants enrolled in this study. Therefore, it is important that enrollment continues beyond the completion of this thesis to increase the statistical power of this study. Of eligible patients, about 38% consented to participate in the study. Of the participants who consented, 87% completed questionnaires at initial assessment, and of the participants who completed questionnaires at initial assessment, about 53% completed follow-up surveys. This data speaks to study performance of this cohort. Despite a low sample size, clinical characteristics (i.e., age and reason for referral) of this cohort were consistent with similar studies done in CR.[83,84] However, this cohort was more physically active and presented with a good level of exercise capacity at initial assessment than anticipated. This may have been due to this cohort being a relatively younger sample compared to other CR samples, as approximately 20% of the cohort was under the age of 50. Results also suggested that a vast majority of participants (75%), moderately adhered to the Mediterranean diet. Results also suggested that about half of the participants (50.8%) did not meet the guideline recommended target for blood lipid control (non-

HDL-c), while most participants (72.9%) attained the guideline recommended target for blood glucose control (HbA1c) at baseline. This suggests that this cohort may be healthier than other CR cohorts but needs further investigation to support this claim.

## 5.2. Anxiety Sensitivity and Patient Outcome Characteristics

Previous studies have reported associations between gender and AnxS, suggesting that women report significantly higher AnxS compared to men. Inconsistent with those findings and our hypothesis, sex and physical activity were not significantly associated with AnxS in this study. This may be due to the current study investigating these relationships in CR in which previous studies did not. Additionally, the sample size reporting sex was low (n=58), creating implications for statistical power. Future studies should re-test this association with a larger sample size to ensure these findings are accurate. Previous studies have also reported associations between physical activity and AnxS, suggesting that individuals more physical active report significantly lower AnxS compared to those who are sedentary. Based on our cohort being more active than anticipated, we did expect to detect an association. However, physical activity was not associated with AnxS. This may be due to much of the literature reporting associations in a younger and non-clinical population. It may also be due to a low sample size of those reporting level of physical activity (n=47). Future studies should re-test this association with a larger sample size to ensure these findings are accurate. Interestingly, results indicate that individuals with high AnxS may have low adherence to the Mediterranean diet, however it does warrant further study and additional sample size to ensure that this was not a spurious observation. No other associations between AnxS and the remaining socio-environmental and clinical characteristics were found, which were not expected. This may also be due to lack of statistical power, therefore, these associations merit further investigation with a larger sample size to ensure these findings are accurate. If significant

associations are found with a larger sample size, this may suggest the need to target AnxS for treatment, as individuals with high AnxS will be less likely to report favourable patient outcomes in CR.

## 5.3. Anxiety Sensitivity, Anxiety, and Depression

Previous studies have reported associations between AnxS, anxiety, and depression. Consistent with the findings from the literature, results from this study reported 2 key relationships. Significant associations between symptoms of depression and symptoms and anxiety were observed in this cohort as expected, and consistent with previously reported observations.[117] More importantly, reported significant associations between AnxS and symptoms of anxiety in this study may provide clinical implications in CR. Based on the literature, we expected significant associations between AnxS and symptoms of depression, however, this association only approached significance likely due to low statistical power. With symptoms of anxiety and depression being routinely screened and treated in CR, the need to understand whether routine screening and treatment of AnxS in CR is beneficial merits further investigation. With insufficient sample size to investigate the interrelationships among AnxS, symptoms of anxiety, symptoms of depression, and their impact on patient outcomes in CR, the creation of a new variable was a preliminary step used to address this question with the data obtained. Additionally, associations between AnxS, the "All", "Some", and "Null" groups, suggest that individuals with high AnxS, and positive PHQ-4 screens on symptoms of anxiety and depression, reported a resting diastolic blood pressure outside of the recommended target range. No other associations between AnxS, symptoms of anxiety and depression, and additional CR clinical characteristics were found. Based on the findings of association between AnxS, depression, and anxiety, we expected to see more associations between AnxS and the study outcomes. However, we did not observe these

associations potentially due to lack of statistical power. Future studies should evaluate the same associations with a larger sample size to ensure the relationships observed are accurate.

## 5.4. Anxiety Sensitivity and Clinical Progress in Cardiac Rehabilitation

Currently, the literature suggests that AnxS is a predictive marker for change in exercise behaviour.[68] We expected that AnxS at initial assessment would be a predictive marker for change in physical activity at 6-week follow-up, however no significant associations were found. Moshier's study involving a much younger cohort[68] may explain why no relationship was observed as the cohort in this thesis was significantly older than that of Moshier's. Secondly, only 31 participants completed follow-up questionnaires, indicative of low statistical power. Additionally, AnxS at initial assessment did not predict physical activity, exercise capacity, and adherence to the Mediterranean diet at 6-week follow-up.

Strong evidence suggests that CR improves patient outcomes and reduces burden related to CVD.[4] Despite the efficacy of CR, individuals with high AS have reported fear or exercise which may be related to CR dropout.[83] If AnxS at baseline is proven to be a predictive marker for clinical characteristics at 6-week follow-up, this may provide a better a predictor for CR dropout, supporting the need to treat AnxS. The evaluation of this relationship with a larger sample size merits further investigation which may provide clinical implications.

## 5.5. Stakeholder Implications

Stakeholders play an essential role both independently and collaboratively in improving patient outcomes associated with AnxS in CR. The RECARE approach has been an effective framework for identifying stakeholders in a systematic and collaborative style as indicated with the RECARE project.[116] The RECARE project was applied to a large transdisciplinary research project, where a

broad network of stakeholders was created.[116] This approach allowed for stakeholder identification to be directly part of the research methodology by establishing criteria for stakeholder identification and allowing identified stakeholders to recruit potential stakeholders who could positively impact the outcomes of the study. Using this process, stakeholder implications in this thesis were more applicable to the research question.

Research, advocacy, and policy modifications are common themes seen across many key stakeholders that aim to effectively support the healthcare needs of patients enrolled in CR. Academia has proven to be essential in conducting research relevant to cardiovascular health. To reduce the burden associated with AnxS, clinicians and researchers are on the forefront of conducting clinical trials to target AnxS for treatment within CR. Additionally, provincial healthcare providers with executive roles provide population-level benefit as they often are involved in overseeing the clinical and economic decisions related to improving the healthcare system. The provincial government is another example of a potential stakeholder that carries high power and influence. Resource allocation to support clinical trials and possible changes to routine care in CR is one way they can make a clinical impact.

Based on these findings, categorizing identified stakeholders based on level of influence, interest, and power is both an efficient and effective way to reduce the burden associated with AnxS in CR, as those with higher influence, interest, and power, will likely provide substantial impact.

## 5.6. Strengths and Limitations

The strengths of this study include its novelty along with its prospective study design – information obtained from this study will be relevant for individuals that have been recently diagnosed with or that currently suffer from a cardiac condition. The prospective aspect of the study will allow us to

draw casual inferences about the potential to target AnxS for treatment for those enrolled in a CR program. By observing the impact of AnxS on socio-environmental, sociodemographic, and clinical characteristics, this study is novel in applying a One Health approach to investigate a research problem specific to CR. Identification of multisectoral stakeholders highlighted an additional key element of the One Health approach and may allow future studies to test the efficacy of stakeholder engagement in improving patient outcomes in CR. Due to the impact of COVID-19, the findings from this study should be interpreted with a few limitations in mind. Firstly, selection bias may have impacted this study in the following ways: a. the pandemic may have been related to why the cohort was relatively younger compared to previous CR cohorts – this may have played a role in higher than expected fitness of the sample; b. a long delay of intake into CR had an unknown effect on patients who agreed to wait to enroll in CR – this may have impacted associations reported in Chapter 4; c. virtual care in CR may have added unknown implications of enrolled patients as prescribed exercises, for example, were not routinely monitored; and d. lower enrollment of those eligible to participate in CR directly impacted the number of eligible patients for this study. Psychological measurements during this study may have also been affected by conditions caused by COVID-19 – this could include feelings of hopelessness, anxiousness, and little to no interest in doing things, which are characteristics evaluated through the PHQ-4. Future analysis of this study should aim to compare PHQ-4 scores from this cohort to a previous "non-COVID" cohort. Additionally, this study did not account for participants who could have been undergoing CBT treatment for AnxS. Future analysis should take this into consideration when interpreting the results. A stakeholder limitation was the use of the snowball sampling method. All stakeholders were identified from one source as opposed to obtaining them from initially identified

stakeholders. Future research should aim to include direct involvement of stakeholders when creating a multidisciplinary network of stakeholders.

## 5.7. Contributions and Future Directions

To date, this is one of the first prospective studies to investigate the relationships between AnxS and patient outcomes in CR, and the first study to investigate this relationship during the COVID-19 era, as previous studies have investigated similar relationships cross-sectionally. Benefits to this study design allowed for changes in characteristics to be evaluated in the target population. However, based on the findings of this study, repeating this study with a larger sample size post-pandemic may provide more substantial support for the need to routinely assess AnxS in CR if significant associations are reported.

This study is also one of the first studies to identify transdisciplinary stakeholders with high power, influence, and interest in investigating, preventing, and mitigating the burden associated with AnxS in this study population. While evidence supports the effectiveness of using the One Health approach to implement change within the realm of infectious disease, many aspects of the approach can be transferred to non-communicable diseases. Future studies should directly engage with identified stakeholders to conduct clinical trials on treating AnxS in CR, translating the results of the clinical trial to the appropriate stakeholders, and implementing system-level changes to routine care, allowing for AnxS to be routinely evaluated alongside symptoms of anxiety and depression.

# Chapter 6

## 6.0. Conclusion

This study provides some evidence for the importance of evaluating AnxS in CR. Although no significant associations were reported between AnxS, sociodemographic, socio-environmental, or clinical characteristics, we were able to provide some evidence of association between AnxS and adherence to the Mediterranean diet. We were also able to provide evidence consistent with the literature of significant associations between symptoms of anxiety and symptoms of depression, significant associations between AnxS and anxiety, and some evidence of association between AnxS and depression. We were also able to provide evidence of the associations between resting diastolic blood pressure and the combined presence of high AnxS, a positive screen for symptoms of depression, and a positive screen for symptoms of anxiety as reported by the PHQ-4. This association was based on a small sample size and must be re-evaluated using a larger sample. Important to the One Health approach, we were able to provide evidence of powerful and influential stakeholders that may assist in reducing the burden associated with AnxS in CR.

Unfortunately, due to a small sample size, most analyses lacked the statistical power to be thoroughly investigated. As a result of these findings, we propose that a larger sample size is needed to observe more accurate findings of this study. Additionally, the significant associations reported in this study also lacked statistical power and should also be re-analysed with a larger sample size and with different parametric tests (i.e., t-test and regression) to ensure reported results are accurate. We also propose that snowball sampling of stakeholders be obtained directly from previously identified stakeholders as potentially stronger collaborations and networks may exist.

# Citations


1. American Heart Association. What is Cardiovascular Disease? | American Heart Association. American Heart Association. Published 2017. Accessed June 12, 2021. https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease#.WRG85mnyt0w
2. Amini M, Zayeri F, Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: results from global burden of disease study 2017. *BMC Public Health*. 2021;21(1):1-12. doi:10.1186/s12889-021-10429-0
3. Joseph P, Leong D, McKee M, et al. Reducing the global burden of cardiovascular disease, part 1: The epidemiology and risk factors. *Circ Res*. 2017;121(6):677-694. doi:10.1161/CIRCRESAHA.117.308903
4. Sandesara PB, Lambert CT, Gordon NF, et al. Cardiac Rehabilitation and Risk Reduction: Time to "Rebrand and Reinvigorate." *J Am Coll Cardiol*. 2015;65(4):389-395. doi:https://doi.org/10.1016/j.jacc.2014.10.059
5. Savage PD, Sanderson BK, Brown TM, Berra K, Ades PA. Clinical research in cardiac rehabilitation and secondary prevention: looking back and moving forward. *J Cardiopulm Rehabil Prev*. 2011;31(6):333-341. doi:10.1097/HCR.0b013e31822f0f79
6. Stone JA, Arthur HM, Suskin N, Austford L, Carlson J, Cupper L. Canadian guidelines for cardiac rehabilitation and cardiovascular disease prevention: translating knowledge into action. *Winnipeg, Canada Can Assoc Card Rehabil*. 2009;3.
7. Grace SL, Bennett S, Ardern CI, Clark AM. Cardiac rehabilitation series: Canada. *Prog Cardiovasc Dis*. Published online 2014. doi:10.1016/j.pcad.2013.09.010
8. HM A, N S, M B, et al. The Canadian Heart Health Strategy and Action Plan: Cardiac rehabilitation as an exemplar of chronic disease management. *Can J Cardiol*. 2010;26(1):37-41. doi:10.1016/S0828-282X(10)70336-6
9. Mitchell BL, Lock MJ, Davison K, Parfitt G, Buckley JP, Eston RG. What is the effect of aerobic exercise intensity on cardiorespiratory fitness in those undergoing cardiac rehabilitation? A systematic review with meta-analysis. *British Journal of Sports Medicine*. 2018.
10. Grace SL, Chessex C, Arthur H, et al. Systematizing inpatient referral to cardiac rehabilitation 2010: Canadian association of cardiac rehabilitation and canadian cardiovascular society joint position paper. *Can J Cardiol*. Published online 2011. doi:10.1016/j.cjca.2010.12.007
11. Thomas RJ, King M, Lui K, Oldridge N, Piña IL, Spertus J. AACVPR/ACC/AHA 2007 performance measures on cardiac rehabilitation for referral to and delivery of cardiac rehabilitation/secondary prevention services. *Circulation*. Published online 2007. doi:10.1161/CIRCULATIONAHA.107.185734
12. Grace SL, Parsons TL, Duhamel TA, Somanader DS, Suskin N. The Quality of Cardiac Rehabilitation in Canada: A Report of the Canadian Cardiac Rehab Registry. *Can J Cardiol*. 2014;30:1452-1455. doi:10.1016/j.cjca.2014.06.016
13. Sagar VA, Davies EJ, Briscoe S, et al. Exercise-based rehabilitation for heart failure: systematic review and meta-analysis. *Open Hear*. 2015;2(1):e000163. doi:10.1136/openhrt-2014-000163
14. Candido E, Richards JA, Oh P, et al. The relationship between need and capacity for multidisciplinary cardiovascular risk-reduction programs in Ontario. *Can J Cardiol*.

Published online 2011. doi:10.1016/j.cjca.2011.01.008
15. Tran M, Pesah E, Turk-Adawi K, et al. Cardiac Rehabilitation Availability and Delivery in Canada: How Does It Compare With Other High-Income Countries? *Can J Cardiol*. 2018;34(10, Supplement 2):S252-S262. doi:https://doi.org/10.1016/j.cjca.2018.07.413
16. SL G, K T-A, C S de AP, DA A. Ensuring Cardiac Rehabilitation Access for the Majority of Those in Need: A Call to Action for Canada. *Can J Cardiol*. 2016;32(10 Suppl 2):S358-S364. doi:10.1016/J.CJCA.2016.07.001
17. Swabey T, Suskin N, Arthur HM, Ross J. The Ontario cardiac rehabilitation pilot project. Canadian Journal of Cardiology. doi:10.1097/00008483-200201000-00001
18. Cortés O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: A systematic review. *Am Heart J*. 2006;151(2):249-256. doi:10.1016/J.AHJ.2005.03.034
19. Suaya JA, Shepard DS, Normand S-LT, Ades PA, Prottas J, Stason WB. Use of Cardiac Rehabilitation by Medicare Beneficiaries After Myocardial Infarction or Coronary Bypass Surgery. Published online 2007. doi:10.1161/CIRCULATIONAHA.107.701466
20. Rolfe DE, Sutton EJ, Landry M, Sternberg L, Price JAD. Women's experiences accessing a women-centered cardiac rehabilitation program: A qualitative study. *J Cardiovasc Nurs*. Published online 2010. doi:10.1097/JCN.0b013e3181c83f6b
21. Lemstra ME, Alsabbagh W, Rajakumar RJ, Rogers MR, Blackburn D. Neighbourhood Income and Cardiac Rehabilitation Access as Determinants of Nonattendance and Noncompletion. *Can J Cardiol*. 2013;29(12):1599-1603. doi:10.1016/j.cjca.2013.08.011
22. TJ C, S G, S M, et al. Sex bias in referral of women to outpatient cardiac rehabilitation? A meta-analysis. *Eur J Prev Cardiol*. 2015;22(4):423-441. doi:10.1177/2047487314520783
23. L S, SL G, S G, LB S, S M, TJ C. Sex differences in cardiac rehabilitation enrollment: a meta-analysis. *Can J Cardiol*. 2014;30(7):793-800. doi:10.1016/J.CJCA.2013.11.007
24. Feola M, Garnero S, Daniele B, et al. Gender differences in the efficacy of cardiovascular rehabilitation in patients after cardiac surgery procedures. *J Geriatr Cardiol*. 2015;12(5):575. doi:10.11909/J.ISSN.1671-5411.2015.05.015
25. SL G, S G-W, S K, J B, N S, DE S. A multisite examination of sex differences in cardiac rehabilitation barriers by participation status. *J Womens Health (Larchmt)*. 2009;18(2):209-216. doi:10.1089/JWH.2007.0753
26. Marzolini S, Colella TJF. Factors That Predispose Women to Greater Depressive Symptoms: A Sex-, Age-, and Diagnosis-Matched Cardiac Rehabilitation Cohort. *Can J Cardiol*. 2021;37(3):382-390. doi:10.1016/j.cjca.2020.08.019
27. Suskin NG, Huitema AA, Hartley T, McKelvie RS. Sex, Depression, and More in Cardiac Rehabilitation. *Can J Cardiol*. 2021;37(3):357-358. doi:10.1016/j.cjca.2020.12.001
28. Smits JAJ, Otto MW, Powers MB, Baird SO. Anxiety sensitivity as a transdiagnostic treatment target. In: *The Clinician's Guide to Anxiety Sensitivity Treatment and Assessment*. ; 2019. doi:10.1016/b978-0-12-813495-5.00001-2
29. American Psychiatric Association. No Title. *Diagnostic Stat Man Ment Disord*. 2013;Fifth Edit.
30. Dhar AK, Barton DA. Depression and the Link with Cardiovascular Disease. *Front Psychiatry*. 2016;7(MAR):1. doi:10.3389/FPSYT.2016.00033
31. Levine GN, Cohen BE, Commodore-Mensah Y, et al. Psychological Health, Well-Being, and the Mind-Heart-Body Connection: A Scientific Statement from the American Heart Association. *Circulation*. 2021;143:E763-E783. doi:10.1161/CIR.0000000000000947

32. Towfighi A, Ovbiagele B, El Husseini N, et al. Poststroke Depression: A Scientific Statement for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke*. 2017;48(2):e30-e43. doi:10.1161/STR.0000000000000113
33. Lichtman JH, Froelicher ES, Blumenthal JA, et al. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: Systematic review and recommendations: A scientific statement from the american heart association. *Circulation*. 2014;129(12):1350-1369. doi:10.1161/CIR.0000000000000019
34. Dunbar SB, Dougherty CM, Sears SF, et al. Educational and psychological interventions to improve outcomes for recipients of implantable cardioverter defibrillators and their families: A scientific statement from the american heart association. *Circulation*. 2012;126(17):2146-2172. doi:10.1161/CIR.0b013e31825d59fd
35. Gan Y, Gong Y, Tong X, et al. Depression and the risk of coronary heart disease: a meta-analysis of prospective cohort studies. *BMC Psychiatry 2014 141*. 2014;14(1):1-11. doi:10.1186/S12888-014-0371-Z
36. Q W, JM K. Depression and the Risk of Myocardial Infarction and Coronary Death: A Meta-Analysis of Prospective Cohort Studies. *Medicine (Baltimore)*. 2016;95(6). doi:10.1097/MD.0000000000002815
37. Hare DL. Depression and cardiovascular disease. *Curr Opin Lipidol*. 2021;32(3):167-174. doi:10.1097/MOL.0000000000000749
38. T T, D C, HE T, K S, AL P, JL R. Sex differences in psychosocial and cardiometabolic health among patients completing cardiac rehabilitation. *Appl Physiol Nutr Metab*. 2019;44(11):1237-1245. doi:10.1139/APNM-2018-0876
39. McGrady A, McGinnis R, Badenhop D, Bentle M, Rajput M. Effects of depression and anxiety on adherence to cardiac rehabilitation. *J Cardiopulm Rehabil Prev*. 2009;29(6):358-364. doi:10.1097/HCR.0b013e3181be7a8f
40. Mayo Clinic Staff. Anxiety disorders - Symptoms and causes - Mayo Clinic. May 4. Published 2018. Accessed July 11, 2021. https://www.mayoclinic.org/diseases-conditions/anxiety/symptoms-causes/syc-20350961
41. Celano CM, Daunis DJ, Lokko HN, Campbell KA, Huffman JC. Anxiety Disorders and Cardiovascular Disease. *Curr Psychiatry Rep*. 2016;18(11):101. doi:10.1007/s11920-016-0739-5
42. Portegies MLP, Bos MJ, Koudstaal PJ, Hofman A, Tiemeier HW, Arfan Ikram M. Anxiety and the risk of stroke the Rotterdam study. *Stroke*. 2016;47(4):1120-1123. doi:10.1161/STROKEAHA.115.012361
43. Kubzansky LD, Davidson KW, Rozanski A. The clinical impact of negative psychological states: Expanding the spectrum of risk for coronary artery disease. *Psychosom Med*. 2005;67(SUPPL. 1). doi:10.1097/01.psy.0000164012.88829.41
44. Pan Y, Cai W, Cheng Q, Dong W, An T, Yan J. Association between anxiety and hypertension: A systematic review and meta-analysis of epidemiological studies. *Neuropsychiatr Dis Treat*. 2015;11:1121-1130. doi:10.2147/NDT.S77710
45. SL G, SE A, J I, ZM S, DE S. Prospective examination of anxiety persistence and its relationship to cardiac symptoms and recurrent cardiac events. *Psychother Psychosom*. 2004;73(6):344-352. doi:10.1159/000080387
46. TA H, JE N, GE E, I B, B R. Anxiety and depression after acute myocardial infarction: an 18-month follow-up study with repeated measures and comparison with a reference population. *Eur J Cardiovasc Prev Rehabil*. 2009;16(6):651-659.

doi:10.1097/HJR.0B013E32832E4206
47. Naragon-Gainey K, Watson D. Personality, Structure. *Encycl Hum Behav Second Ed*. Published online January 1, 2012:90-95. doi:10.1016/B978-0-12-375000-6.00275-5
48. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association; 2013. doi:10.1176/appi.books.9780890425596
49. Taylor S. Treating anxiety sensitivity in adults with anxiety and related disorders. In: *The Clinician's Guide to Anxiety Sensitivity Treatment and Assessment*. ; 2019:55-75. doi:10.1016/b978-0-12-813495-5.00004-8
50. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Behav Res Ther*. Published online 1986. doi:10.1016/0005-7967(86)90143-9
51. Taylor S, Cox BJ. An expanded anxiety sensitivity index: Evidence for a hierarchic structure in a clinical sample. *J Anxiety Disord*. Published online 1998. doi:10.1016/S0887-6185(98)00028-0
52. Olatunji BO, Wolitzky-Taylor KB. Anxiety Sensitivity and the Anxiety Disorders: A Meta-Analytic Review and Synthesis. *Psychol Bull*. Published online 2009. doi:10.1037/a0017428
53. Taylor S, Zvolensky MJ, Cox BJ, et al. Robust Dimensions of Anxiety Sensitivity: Development and Initial Validation of the Anxiety Sensitivity Index-3. *Psychol Assess*. Published online 2007. doi:10.1037/1040-3590.19.2.176
54. Farris SG, DiBello AM, Allan NP, Hogan J, Schmidt NB, Zvolensky MJ. Evaluation of the Anxiety Sensitivity Index-3 among Treatment-Seeking Smokers. *Psychol Assess*. 2015;27(3):1123. doi:10.1037/PAS0000112
55. Roushani K, Bassak Nejad S, Arshadi N, Mehrabizadeh Honarmand M, Fakhri A. The Effects of Cognitive Behavioral Therapy Based on Hofmann's Model on Anxiety Sensitivity and Positive and Negative Affects Among Undergraduate Female Students with Social Anxiety Symptoms in Ahvaz Jundishapur University of Medical Sciences. *Jentashapir J Heal Res*. 2017;8(1). doi:10.5812/jjhr.40231
56. Naragon-Gainey K. Meta-Analysis of the Relations of Anxiety Sensitivity to the Depressive and Anxiety Disorders. *Psychol Bull*. Published online 2010. doi:10.1037/a0018055
57. Khakpoor S, Saed O, Shahsavar A. The concept of "Anxiety sensitivity" in social anxiety disorder presentations, symptomatology, and treatment: A theoretical perspective. *Cogent Psychol*. 2019;6(1):1617658. doi:10.1080/23311908.2019.1617658
58. Mantar A, Yemez B, Alkin T. Anxiety sensitivity and its importance in psychiatric disorders. *Turk Psikiyatr Derg*. 2011;22(3):187-193. Accessed June 21, 2021. https://europepmc.org/article/med/21870308
59. Farris SG, Abrantes AM. Anxiety sensitivity in smokers with indicators of cardiovascular disease. *Psychol Heal Med*. 2017;22(8):961-968. doi:10.1080/13548506.2017.1300672
60. Pagotto U, Fallo F, Fava GA, Boscaro M, Sonino N. Anxiety sensitivity in essential hypertension. *Stress Med*. 1992;8(2):113-115. doi:10.1002/smi.2460080210
61. Chiaie RD, Iannucci G, Paroli M, et al. Symptomatic subsyndromal depression in hospitalized hypertensive patients. *J Affect Disord*. 2011;135(1-3):168-176. doi:10.1016/j.jad.2011.07.008
62. Alcántara C, Edmondson D, Moise N, Oyola D, Hiti D, Kronish IM. Anxiety sensitivity

and medication nonadherence in patients with uncontrolled hypertension. *J Psychosom Res*. 2014;77(4):283-286. doi:10.1016/j.jpsychores.2014.07.009
63. Seldenrijk A, Van Hout HPJ, Van Marwijk HWJ, et al. Sensitivity to depression or anxiety and subclinical cardiovascular disease. *J Affect Disord*. 2013;146(1):126-131. doi:10.1016/j.jad.2012.06.026
64. Delle Chiaie R, Baciarello G, Villani M, et al. Cardiovascular reactivity of mitral valve prolapse patients during experimental stress exposure: Evidence for a functional nature of cardiovascular symptoms. *Acta Psychiatr Scand*. 1996;93(6):434-441. doi:10.1111/j.1600-0447.1996.tb10674.x
65. Alcántara C, Qian M, Meli L, et al. Anxiety Sensitivity and Physical Inactivity in a National Sample of Adults with a History of Myocardial Infarction. *Int J Behav Med*. 2020;27(5):520-526. doi:10.1007/s12529-020-09881-w
66. Hearon BA, Harrison TJ. Not the exercise type? Personality traits and anxiety sensitivity as predictors of objectively measured physical activity and sedentary time. *J Health Psychol*. Published online 2020. doi:10.1177/1359105320906242
67. Moshier SJ, Hearon BA, Calkins AW, et al. Clarifying the link between distress intolerance and exercise: Elevated anxiety sensitivity predicts less vigorous exercise. *Cognit Ther Res*. 2013;37(3):476-482. doi:10.1007/s10608-012-9489-9
68. Moshier SJ, Szuhany KL, Hearon BA, Smits JAJ, Otto MW. Anxiety Sensitivity Uniquely Predicts Exercise Behaviors in Young Adults Seeking to Increase Physical Activity. *Behav Modif*. 2016;40(1-2):178-198. doi:10.1177/0145445515603704
69. Horenstein A, Potter CM, Heimberg RG. How does anxiety sensitivity increase risk of chronic medical conditions? *Clin Psychol Sci Pract*. 2018;25(3). doi:10.1037/h0101753
70. McWilliams LA, Asmundson GJG. Is there a negative association between anxiety sensitivity and arousal-increasing substances and activities? *J Anxiety Disord*. 2001;15(3):161-170. doi:10.1016/S0887-6185(01)00056-1
71. DeWolfe CEJ, Watt MC, Romero-Sanchiz P, Stewart SH. Gender differences in physical activity are partially explained by anxiety sensitivity in post-secondary students. *J Am Coll Heal*. 2020;68(3):219-222. doi:10.1080/07448481.2018.1549048
72. Hearon BA, Quatromoni PA, Mascoop JL, Otto MW. The role of anxiety sensitivity in daily physical activity and eating behavior. *Eat Behav*. 2014;15(2):255-258. doi:10.1016/j.eatbeh.2014.03.007
73. Smits JAJ, Tart CD, Presnell K, Rosenfield D, Otto MW. Identifying potential barriers to physical activity adherence: Anxiety sensitivity and body mass as predictors of fear during exercise. *Cogn Behav Ther*. 2010;39(1):28-36. doi:10.1080/16506070902915261
74. LeBouthillier DM, Asmundson GJG. A Single Bout of Aerobic Exercise Reduces Anxiety Sensitivity But Not Intolerance of Uncertainty or Distress Tolerance: A Randomized Controlled Trial. *Cogn Behav Ther*. 2015;44(4):252-263. doi:10.1080/16506073.2015.1028094
75. Broman-Fulks JJ, Storey KM. Evaluation of a brief aerobic exercise intervention for high anxiety sensitivity. *Anxiety, Stress Coping*. 2008;21(2):117-128. doi:10.1080/10615800701762675
76. Jacquart J, Dutcher CD, Freeman SZ, et al. The effects of exercise on transdiagnostic treatment targets: A meta-analytic review. *Behav Res Ther*. 2019;115:19-37. doi:10.1016/j.brat.2018.11.007
77. Broman-Fulks JJ, Berman ME, Rabian BA, Webster MJ. Effects of aerobic exercise on

anxiety sensitivity. *Behav Res Ther*. 2004;42(2):125-136. doi:10.1016/S0005-7967(03)00103-7
78. Medina JL, Deboer LB, Davis ML, et al. Gender moderates the effect of exercise on anxiety sensitivity. *Ment Health Phys Act*. 2014;7(3):147-151. doi:10.1016/j.mhpa.2014.08.002
79. Sabourin BC, Hilchey CA, Lefaivre MJ, Watt MC, Stewart SH. Why do they exercise less? Barriers to exercise in high-anxiety-sensitive women. *Cogn Behav Ther*. 2011;40(3):206-215. doi:10.1080/16506073.2011.573572
80. Zvolensky MJ, Rosenfield D, Garey L, et al. Does exercise aid smoking cessation through reductions in anxiety sensitivity and dysphoria? *Heal Psychol*. 2018;37(7):647-657. doi:10.1037/hea0000588
81. Sabourin BC, Watt MC, Krigolson OE, Stewart SH. Two interventions decrease anxiety sensitivity among high anxiety sensitive women: Could physical exercise be the key? *J Cogn Psychother*. 2016;30(2):131-146. doi:10.1891/0889-8391.30.2.131
82. Smits JAJ, Berry AC, Rosenfield D, Powers MB, Behar E, Otto MW. Reducing anxiety sensitivity with exercise. *Depress Anxiety*. 2008;25(8):689-699. doi:10.1002/da.20411
83. Farris SG, Bond DS, Wu WC, Stabile LM, Abrantes AM. Anxiety sensitivity and fear of exercise in patients attending cardiac rehabilitation. *Ment Health Phys Act*. 2018;15:22-26. doi:10.1016/j.mhpa.2018.06.005
84. Kraemer KM, Carroll AJ, Clair M, Richards L, Serber ER. The role of anxiety sensitivity in exercise tolerance and anxiety and depressive symptoms among individuals seeking treatment in cardiopulmonary rehabilitation. *Psychol Heal Med*. Published online 2020. doi:10.1080/13548506.2020.1776889
85. Mackenzie JS, Jeggo M. The one health approach-why is it so important? *Trop Med Infect Dis*. 2019;4(2). doi:10.3390/tropicalmed4020088
86. CDC. One Health Basics | One Health | CDC. Centers for Disease Control and Prevention. Published 2018. Accessed June 19, 2021. https://www.cdc.gov/onehealth/basics/index.html
87. Khan MS, Rothman-Ostrow P, Spencer J, et al. Articles The growth and strategic functioning of One Health networks: a systematic analysis. Published online 2018. doi:10.1016/S2542-5196(18)30084-6
88. Health Canada and Public Health Agency of Canada. Evaluation of the Public Health Agency of Canada's Non-Enteric Zoonotic Infectious Disease Activities List of Acronyms. Published 2010. Accessed July 10, 2021. https://www.canada.ca/content/dam/canada/health-canada/migration/healthy-canadians/department-ministere/public-health-sante-publique/transparency-transparence/corporate-reporting-rapports-gestion/evaluation/2016-2017/zoonotic-zoonoses/alt/pub-eng.pdf
89. Kimani T, Ngigi M, Schelling E, Randolph T. One Health stakeholder and institutional analysis in Kenya. *Infect Ecol Epidemiol*. 2016;6(1):31191. doi:10.3402/IEE.V6.31191
90. Armitage R, Nellums LB. Emerging from COVID-19: Prioritising the burden of loneliness in older people. *Br J Gen Pract*. 2020;70(697):382. doi:10.3399/bjgp20X711869
91. Hwang TJ, Rabheru K, Peisah C, Reichman W, Ikeda M. Loneliness and social isolation during the COVID-19 pandemic. *Int Psychogeriatrics*. 2020;32(10):1217-1220. doi:10.1017/S1041610220000988

92. Lee EE, Depp C, Palmer BW, et al. High prevalence and adverse health effects of loneliness in community-dwelling adults across the lifespan: role of wisdom as a protective factor. *Int psychogeriatrics*. 2019;31(10):1447-1462. doi:10.1017/S1041610218002120
93. Steptoe A, Shankar A, Demakakos P, Wardle J. Social isolation, loneliness, and all-cause mortality in older men and women. *Proc Natl Acad Sci U S A*. 2013;110(15):5797-5801. doi:10.1073/pnas.1219686110
94. Camacho P, Fan H, Liu Z, He JQ. Small mammalian animal models of heart disease. *Am J Cardiovasc Dis*. 2016;6(3):70-80. Accessed June 21, 2021. www.AJCD.us/
95. Bernhardt JM, Mays D, Kreuter MW. Dissemination 2.0: Closing the gap between knowledge and practice with new media and marketing. *J Health Commun*. 2011;16(SUPPL. 1):32-44. doi:10.1080/10810730.2011.593608
96. (No Title). Accessed July 6, 2021. https://www.corhealthontario.ca/resources-for-healthcare-planners-&-providers/cath-&-pci/referral-forms/Code-Definitions-10-31-2017.pdf
97. Guidance from the CCS COVID-19 Rapid Response Team and CCS Affiliate organizations - Canadian Cardiovascular Society. Accessed July 6, 2021. https://ccs.ca/guidance-from-the-ccs-covid-19-rapid-response-team-and-ccs-affiliate-organizations/
98. Rehabilitation. CA of C. *Canadian Guidelines for Cardiac Rehabilitation and Cardiovascular Disease Prevention : Translating Knowledge into Action.* 3rd ed. Canadian Association of Cardiac Rehabilitation; 2009.
99. Godin G, Shephard RJ. A simple method to assess exercise behavior in the community. *Can J Appl Sport Sci*. Published online 1985.
100. Godin G. *Number 1 COMMENTARY Health & Fitness Journal of Canada*. Vol 4.; 2011. doi:10.14288/HFJC.V4I1.82
101. Hlatky MA, Boineau RE, Higginbotham MB, et al. A brief self-administered questionnaire to determine functional capacity (The Duke Activity Status Index). *Am J Cardiol*. Published online 1989. doi:10.1016/0002-9149(89)90496-7
102. Coutinho-Myrrha MA, Dias RC, Fernandes AA, et al. Duke Activity Status Index for Cardiovascular Diseases: Validation ofthe Portuguese Translation. *Arq Bras Cardiol*. 2014;102(4):383. doi:10.5935/ABC.20140031
103. Duke Activity Status Index in Coronary Patients Undergoing Abdominal Nonvascular Surgery. *Internet J Cardiol*. 2012;9(1). doi:10.5580/16b
104. Martínez-González MA, García-Arellano A, Toledo E, et al. A 14-item mediterranean diet assessment tool and obesity indexes among high-risk subjects: The PREDIMED trial. *PLoS One*. Published online 2012. doi:10.1371/journal.pone.0043134
105. Olveira C, Olveira G, Espildora F, et al. Mediterranean diet is associated on symptoms of depression and anxiety in patients with bronchiectasis. *Gen Hosp Psychiatry*. Published online 2014. doi:10.1016/j.genhosppsych.2014.01.010
106. Zito FP, Polese B, Vozzella L, et al. Good adherence to mediterranean diet can prevent gastrointestinal symptoms: A survey from Southern Italy. *World J Gastrointest Pharmacol Ther*. Published online 2016. doi:10.4292/wjgpt.v7.i4.564
107. Nerenberg KA, Zarnke KB, Leung AA, et al. Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. *Can J Cardiol*. Published online 2018. doi:10.1016/j.cjca.2018.02.022

108. Pearson GJ, Thanassoulis G, Anderson TJ, et al. 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. *Can J Cardiol*. 2021;0(0). doi:10.1016/j.cjca.2021.03.016
109. Committee DCCPGE. Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes*. Published online 2018. doi:10.1080/00945718308059306
110. Imran SA, Agarwal G, Bajaj HS, Ross S. Targets for Glycemic Control. *Can J Diabetes*. 2018;42:S42-S46. doi:10.1016/j.jcjd.2017.10.030
111. Allan NP, Raines AM, Capron DW, Norr AM, Zvolensky MJ, Schmidt NB. Identification of anxiety sensitivity classes and clinical cut-scores in a sample of adult smokers: Results from a factor mixture model. *J Anxiety Disord*. 2014;28(7):696-703. doi:10.1016/j.janxdis.2014.07.006
112. Löwe B, Wahl I, Rose M, et al. A 4-item measure of depression and anxiety: Validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord*. Published online 2010. doi:10.1016/j.jad.2009.06.019
113. Kroenke K, Baye F, Lourens SG. Comparative validity and responsiveness of PHQ-ADS and other composite anxiety-depression measures. *J Affect Disord*. Published online 2019. doi:10.1016/j.jad.2018.12.098
114. Tools for Pain Treatment & Management | OPG. Accessed July 11, 2021. https://www.oregonpainguidance.org/tools/
115. SPSS Statistics - Canada | IBM. Accessed July 11, 2021. https://www.ibm.com/ca-en/products/spss-statistics
116. Leventon J, Fleskens L, Claringbould H, Schwilch G, Hessel R. An applied methodology for stakeholder identification in transdisciplinary research. *Sustain Sci*. 2016;11(5):763-775. doi:10.1007/s11625-016-0385-1
117. Gorman JM. COMORBID DEPRESSION AND ANXIETY SPECTRUM DISORDERS. *DEPR 190 Depress Anxiety*. 1996;4:160-168.

# Appendices

## Appendix A

Western Research

**Date:** 24 February 2021

**To:** Dr. Neville Suskin

**Project ID:** 115679

**Study Title:** Investigating Relationships among Anxiety Sensitivity, Depression, Anxiety and Clinical Outcomes in Patients Enrolled in a Cardiac Rehabilitation Program

**Reference Number/ID:** N/A

**Application Type:** HSREB Amendment Form

**Review Type:** Delegated

**Full Board Reporting Date:** 09/March/2021

**Date Approval Issued:** 24/Feb/2021

**REB Approval Expiry Date:** 26/Jan/2022

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Dear Dr. Neville Suskin ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

**Documents Approved:**

| Document Name | Document Type | Document Date |
|---|---|---|
| 115679_studyprotocol_v2021-02-23 | Protocol | 23/Feb/2021 |
| 115679_voicemail_initial_contact_v2021-02-23 | Other Materials | 23/Feb/2021 |
| 115679_Email_Mailout_Script_LOI_v2021-02-23 | Other Materials | 23/Feb/2021 |

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Karen Gopaul , Ethics Officer on behalf of Dr. Philip Jones, HSREB Chair

***Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).***

Page 1 of 1

*Western University Health Sciences Research Ethics Board Approval Letter*

**LAWSON APPROVAL**

**LAWSON APPROVAL NUMBER:** R-21-046

PROJECT TITLE: Investigating the Relationship Between Anxiety Sensitivity, Depression, Anxiety and Clinical Outcomes in Patients Enrolled in a Cardiac Rehabilitation Program

PRINCIPAL INVESTIGATOR: Dr. Neville Suskin

LAWSON APPROVAL DATE: Tuesday, 26 January 2021

ReDA ID: 9812

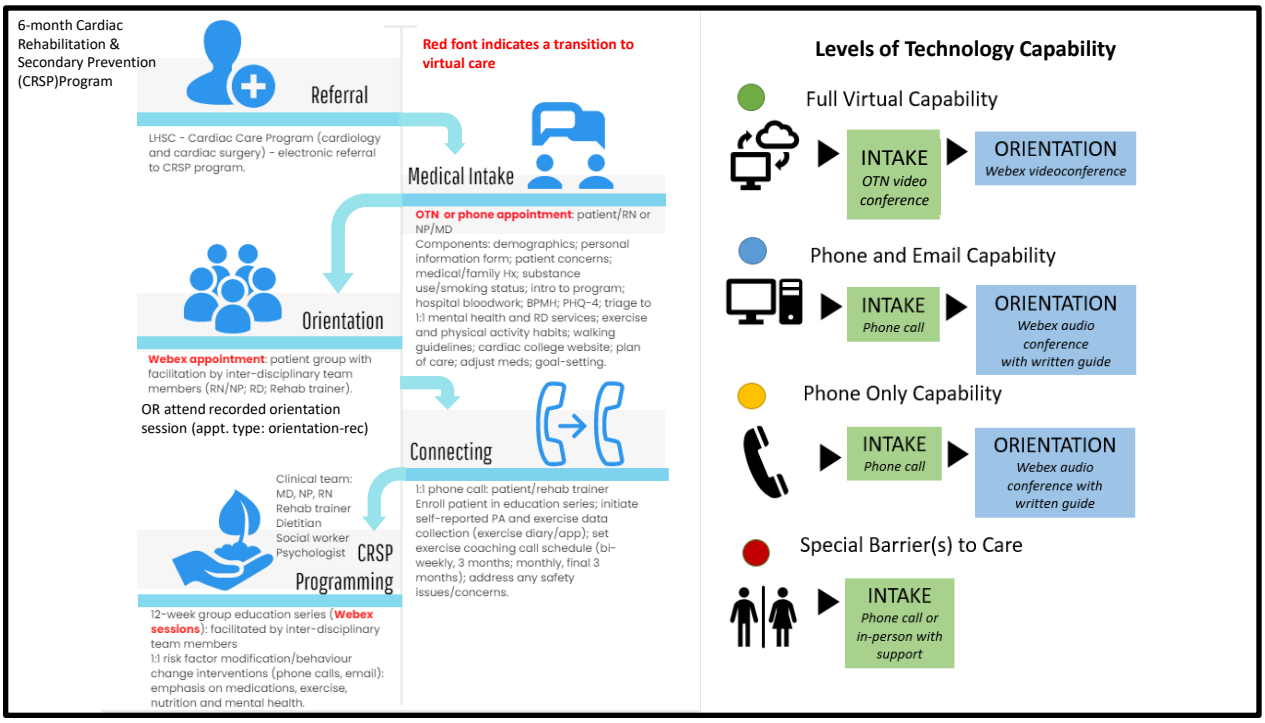
Overall Study Status: Active

Please be advised the above project was reviewed by Lawson Administration and the project was approved. Your official approval document can be found in the documents section of your study in ReDA.

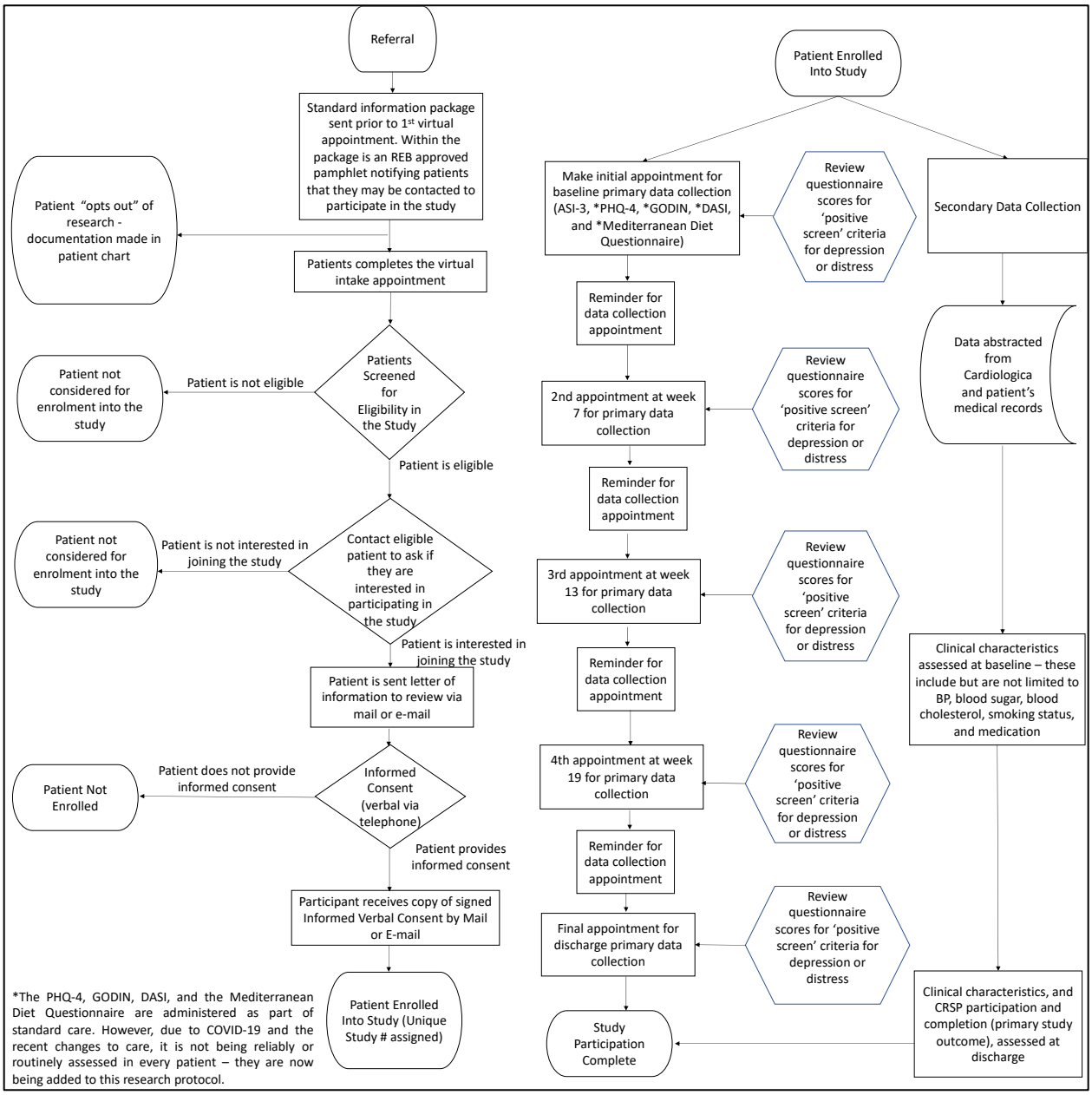


*Lawson Health Research Institute/ReDA Approval Email*

# Appendix B



Flow Diagram of Virtual Care Process for CR and Levels of Technology Capability




Flow Diagram of Patient Enrollment and Data Collection Methodology

**Graduate Student:** Good morning/afternoon/evening, am I speaking with Mr or Mrs.*** or May I please speak with Mr. or Mrs. *** (ensure you have the correct name and salutation before continuing)

**Preferred Name and Salutation: _____**

My name is Ebuka, and I am a master's student calling on behalf of the Cardiac Rehabilitation program at St. Joseph's Hospital about a new study we are conducting. You have been contacted to see if you would be willing to participate in one of the research studies that we are conducting in our program.

Participation in research is always voluntary. You may refuse to participate in research and your decision does not affect your patient care.

Are you interested in learning more about this study?

**If yes: then continue as below**

**If response is No:** Ok, thank you very much for your time! If you change your mind at any time you can contact us at (*telephone #).* Have a good day/evening.

Is now a good time to talk to you about this?

**If Yes:** then continue as below

**If response is No**: ask the individual when a good time might be to call him/her back

**Date: _____**

**Time: _____**

**Graduate Student:** The purpose of this study is to investigate mental health factors such as anxiety sensitivity. The results of this study help us understand how they may impact your progress during cardiac rehabilitation.

In participating for the study, you will be asked to complete five different surveys every six weeks while enrolled into Cardiac Rehabilitation, completing each individual survey a total of 5 times. Completing the surveys will take approximately 30 minutes and you will have the option to complete it via phone call or video conference with me, have a secure link sent to your email to be completed online, or to send it in by mail.

Does this sound like something you would be interested in participating in?

Version Date: 21/01/2021

Copy of Initial Call Script (Page 1)

**If response is No:** Ok, thank you very much for your time! If you change your mind at any time you can contact us at (*telephone #).* Have a good day/evening.

**If response is Yes**: Thank you very much for donating your time and energy!

The next step is that I am required to send you the Letter of Information which includes much more information about the study. You will have time to review this Letter on your own and I will make a follow-up appointment with you to review it and complete informed consent if you decide to join the study.

I can send you this Letter of Information through email or by mail. Which do you prefer?

(Circle preference): Mail Email

Email address: _____

Mailing address: _____

No problem [insert salutation], I will be sending you this form today. When would you be available to review the Letter of Information together and complete informed verbal consent if you want to join the study?

Great! What day and time work best for you?

**Date:** _____

**Time:** _____

Thank you [insert name and salutation], and can I call you with the same number?

**Number to call**: _____

Fantastic, I really look forward to contacting you by [insert date]

Do you have any other questions [answer any questions the patient may have]

Have a nice day!

Version Date: 21/01/2021

Copy of Initial Call Script (Page 2)

**Investigating Relationships among Anxiety Sensitivity, Depression, Anxiety and Clinical Outcomes in Patients Enrolled in a Cardiac Rehabilitation Program**

**LETTER OF INFORMATION**

**Principal Investigator**
Dr. Neville Suskin
Medical Director of the Cardiac Rehabilitation and Secondary Prevention Program, SJHC

**Co-Investigators**
Dr. Stephanie Frisbee, Pathology and Laboratory Medicine, Western University

Dr. Peter Prior, Cardiac Rehabilitation and Secondary Prevention, SJHC

Tim Hartley, Cardiac Rehabilitation and Secondary Prevention, SJHC

**Graduate Student Investigator**
Ebuka Osuji, One Health, Department of Pathology and Laboratory Medicine, Western University

**CONTACT**
If you have questions about this study, please contact a member of the Cardiac Rehabilitation and Secondary Prevention Program.

If you have a medical concern, please speak to a member of the Cardiac Rehabilitation and Secondary Prevention Program's clinical team.

If you need immediate medical assistance, please call 911 or visit the closest Emergency Department for immediate care.

**CONFLICT OF INTEREST**
There are no conflicts of interest to declare related to this study.

**PURPOSE OF THE STUDY**
The purpose of this study is to investigate mental health factors, such as anxiety sensitivity in cardiac rehabilitation patients. The results of this study will help us to understand how to better support patients during cardiac rehabilitation.

**HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?**
We plan to enroll around 325 people in this study.

**WHAT DOES THIS STUDY INVOLVE?**
This study involves completing questions about your mental health, your exercise and activity, and your diet. These questions are completed at 5 different time points. Completing the questions will take around 30 minutes each time.

You will have the choice to answer these questions by phone, by videocall, through the mail, or online using a program called REDCap. If you choose:



Copy of Letter of Information (Page 1)

**A. Phone call** – The student researcher will call you and go through all questions. The phone call will not be recorded.

**B. Videocall** – The student researcher will use WebEx, a hospital approved program, to videocall you and go through all questions. The videocall will not be recorded.

**C. Mail** – The student researcher will send you a prepaid postage envelope with all the questions. You will complete the questions and then mail them back to us.

**D. Online using REDCap** – REDCap is a hospital approved computer program that lets participants directly answer questions. The student researcher will email you a secure link that will bring you to the questions that you need to answer.

We will be using questions that have been developed by different researchers:

1. Anxiety Sensitivity Index (ASI-3): 18 questions measuring symptoms of anxiety sensitivity.

2. Patient Health Questionnaire (PHQ-4): 4 questions measuring symptoms of anxiety and depression.

3. The Godin Leisure-Time Exercise Questionnaire (GODIN): 2 questions about how often you exercise.

4. The Duke Activity Status Index (DASI): 12 questions about how much exercise you can do.

5. The Mediterranean Diet Questionnaire: 14 questions about what your weekly diet.

**CLINICAL AND SURVEY INFORMATION USE**

For this study we will be using information about your progress in cardiac rehabilitation. This information is recorded in your health record at the Cardiac Rehabilitation and Secondary Prevention Program. This information will be linked with your responses to the questions we ask you.

**RISKS OR HARMS OF PARTICIPATION**

The risks of participating in this study are minimal. You do not need to answer questions that you do not want to answer or that make you feel uncomfortable. When you participate in research there is always an increased risk that your information might be accidently shared with others. The research team does their best to prevent this from happening. We describe these steps in the "HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL" section.

**BENEFITS**

You will not receive any direct benefits from participating in this study. The results of this study will help us to understand how to better support patients during cardiac rehabilitation.

**POSSIBLE UNEXPECTED FINDINGS**

All the questions asked in this study are for research only. Results from the questions are not enough to diagnose you. If your responses to any of the questions are outside a normal range, a member of the clinical team at the Cardiac Rehabilitation and Secondary Prevention Program will



Copy of Letter of Information (Page 2)

be contacted. The clinical team may then make a referral to a psychologist. If it is determined to be more serious, 911 may be called.

**CAN I CHOOSE TO LEAVE THE STUDY?**
Your participation in this study is voluntary. This means it is your choice to be part of the study or not. If you decide to leave the study, you can withdraw and stop completing the questions. Even if you have signed the consent form, you may leave the study. If you decide to leave, it is important you understand your healthcare will not be affected. If you do leave from the study, we will still use the information you have provided.

**ALTERNATIVES TO PARTICIPATION**
The alternative to participation in this research is to not participate in the study. Your healthcare will not be affected in any way.

**WHAT ARE MY RIGHTS AS A RESEARCH PARTICIPANT?**
If you are harmed as a direct result of being in this study, all necessary medical treatment will be made available to you at no cost. You do not waive any legal rights by signing the consent form.

**WHAT ARE THE COSTS TO PARTICIPANTS?**
There are no costs to participating in this study.

**IS THERE ANY COMPENSATION FOR PARTICIPATING IN THIS STUDY?**
You will not receive any payment for taking part in this study.

**HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?**
Your answers to the questions will be entered into REDCap by you or by a member of the research team. REDCap is a hospital approved computer program that lets participants directly answer questions. REDCap stores information following the hospital security guidelines and policies. All information collected in REDCap and from your health record will be kept on safe servers at Western University and St. Joseph's Hospital.

Your data will be collected and stored under the supervision of Dr. Neville Suskin, Dr. Peter Prior, and Dr. Stephanie Frisbee. Your responses to the questions will be linked to the information in your health record using a unique study number. A list that links your study number with your name will be kept in a secure place, separate from the information collected from you as part of this research study. This study number will only be used for the purposes of this study. All other ways to identify you will be removed. Western University's Health Sciences Research Ethics Board (HSREB) and Lawson's Quality Assurance Education Program (QAEP) will have access to study data throughout the study. The research team will keep any personal health information about you in a secure and confidential location for 15 years. You will not be named in any journals, reports, or publication that come from this study.

Email may be used as a form of communication for this study; please note that it is not a secure form of communication.

**OPEN ACCESS DATA**
After all identifying information has been removed, the data collected as part of this study will be accessible to the research team as well as the broader scientific community. Data will be analyzed in different ways to gain knowledge and understanding for different research questions. The data may also be made available to other researchers so that it can be inspected and analyzed in different ways.



Copy of Letter of Information (Page 3)

**WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?**
For questions about the study, a research-related injury, or if you have problems, concerns, questions or suggestions about the research, please contact:

**Principal Investigator**
Dr. Neville Suskin MBChB, MSc
Cardiologist and Medical Director of the SJHC CRSP Program
Scientist, Lawson Health Research Institute
Associate Professor of Medicine, Western University

If you have concerns or questions about your rights as a participant or about the way the study is conducted, please contact:

Patient Relations
St Joseph's Healthcare London

If you have any further questions about the study or if you did not understand any of the information, please ask the research team before continuing with Informed Consent. If you would like more time to think about your decision to participate, you should not sign the Informed Consent Form and notify the research team.



Copy of Letter of Information (Page 4)

ST JOSEPH'S HEALTH CARE LONDON

S

**Documentation of Verbal Consent**

**Study Title:** Investigating Relationships among Anxiety Sensitivity, Depression, Anxiety and Clinical Outcomes in Patients Enrolled in a Cardiac Rehabilitation Program

**Principal Investigator:** Dr. Neville Suskin, MBChB, MSc, Cardiologist and Medical Director of the St Joseph's CRSP Program

Name of Participant: _____

Date of Discussion: _____

Duration of Discussion: _____

| | | |
|---|---|---|
| I want to confirm that you received the LOI from us and that you have had a chance to review it. | ☐ Yes | ☐ *No |
| Do you have any questions about the procedures associated with participating in this study (i.e. the surveys) | ☐ Yes | ☐ No |
| Do you have any questions about the risks associated with participating in this study? | ☐ Yes | ☐ No |
| Do you understand that your participation in this study is voluntary, and that your healthcare will not be affected in any way? | ☐ Yes | ☐ No |
| Do you have any questions for me? | ☐ Yes | ☐ No |
| Has this study been explained to you and have all your questions been answered? | ☐ Yes | ☐ No |
| Do you allow the study team to access your paper and electronic hospital chart? | ☐ Yes | ☐ No |
| Do you agree to take part in this study? | ☐ Yes | ☐ No |

***If the answer is No, the LOI will be reviewed during this time with the participant**

| Signature of Person Conducting the Consent Discussion | Printed Name and Role | Date |
|---|---|---|



Copy of Verbal Consent Documentation (Page 1)

Next Step after Informed Verbal Consent has been contained:

Thank you for agreeing to participate in this study. The next step is for you decide how you would like to complete the surveys. You will need to complete them 5 different times.

Would you like to complete these surveys by:
☐ Mail. [document mailing address below]
☐ Email.* [document email address below]
☐ Video conference.* [document email address below]
☐ Phone [document phone number below]

Mailing address: _____

Email Address: _____

Phone Number: _____

***Remind participants:** We will be sending you information via email. Please remember that the security of information sent by email cannot be guaranteed. Please do not communicate personal or sensitive information by email.

We would like to provide you with a copy of what we've talked about today. This will include your name, the study title, and the other information you have provided over the phone. Can we send this to you by email or mail? If you choose not to be sent a copy of your consent by mail or email, you may pick up a copy of your consent at St. Joseph's Health Care London in the future when the pandemic is over.

☐Mail. Confirm mailing address if not confirmed previously:

☐Email. Confirm email address if not confirmed previously:

If you have questions, you can contact the student researcher in charge of that study. If you have questions about your rights as a research participant or want to speak with someone who is not involved in this study, you can call the Office of Human Research Ethics (OHRE)



Copy of Verbal Consent Documentation (Page 2)

# Appendix C

Anxiety Sensitivity Index – 3 (ASI-3) Questions and Factor Categories

Table 1

*Study 1: U.S.–Canadian Subsample 1 (n = 2,361)—Loadings (and Standard Errors) for Final, Multigroup Three-Factor Solution of the ASI–3*

| Item no. | Item | Factor 1: Physical Concerns | Factor 2: Cognitive Concerns | Factor 3: Social Concerns |
|---|---|---|---|---|
| 4 | When my stomach is upset, I worry that I might be seriously ill.[a] | .79 (.02) | | |
| 12 | When I notice my heart skipping a beat, I worry that there is something seriously wrong with me. | .76 (.02) | | |
| 8 | When I feel pain in my chest, I worry that I'm going to have a heart attack. | .69 (.02) | | |
| 7 | When my chest feels tight, I get scared that I won't be able to breathe properly. | .68 (.02) | | |
| 15 | When my throat feels tight, I worry that I could choke to death. | .67 (.02) | | |
| 3 | It scares me when my heart beats rapidly.[a] | .66 (.02) | | |
| 14 | When my thoughts seem to speed up, I worry that I might be going crazy. | | .87 (.01) | |
| 18 | When my mind goes blank, I worry there is something terribly wrong with me. | | .84 (.01) | |
| 10 | When I feel "spacey" or spaced out I worry that I may be mentally ill. | | .83 (.02) | |
| 16 | When I have trouble thinking clearly, I worry that there is something wrong with me. | | .83 (.01) | |
| 2 | When I cannot keep my mind on a task, I worry that I might be going crazy.[a] | | .77 (.02) | |
| 5 | It scares me when I am unable to keep my mind on a task.[a] | | .62 (.02) | |
| 9 | I worry that other people will notice my anxiety. | | | .85 (.01) |
| 6 | When I tremble in the presence of others, I fear what people might think of me. | | | .79 (.01) |
| 11 | It scares me when I blush in front of people. | | | .75 (.02) |
| 13 | When I begin to sweat in a social situation, I fear people will think negatively of me. | | | .70 (.02) |
| 17 | I think it would be horrible for me to faint in public. | | | .59 (.02) |
| 1 | It is important for me not to appear nervous.[a] | | | .54 (.02) |

*Note.* Factor model was simultaneously fitted to the samples of women and men, matching loadings, item errors, and factor correlations. ASI–3 = Anxiety Sensitivity Index–3.

[a] Items from the original Anxiety Sensitivity Index.

# PHQ-4: THE FOUR-ITEM PATIENT HEALTH QUESTIONNAIRE FOR ANXIETY AND DEPRESSION

| Over the last two weeks, how often have you been bothered by the following problems? | Not at all | Several days | More than half the days | Nearly every day |
|---|---|---|---|---|
| Feeling nervous, anxious or on edge | 0 | 1 | 2 | 3 |
| Not being able to stop or control worrying | 0 | 1 | 2 | 3 |
| Feeling down, depressed or hopeless | 0 | 1 | 2 | 3 |
| Little interest or pleasure in doing things | 0 | 1 | 2 | 3 |
| TOTALS | | | | |

Total score is determined by adding together the scores of each of the 4 items.
Scores are rated as normal (0-2), mild (3-5), moderate (6-8), and severe (9-12).
Total score ≥3 for first 2 questions suggests anxiety.
Total score ≥3 for last 2 questions suggests depression.

Reprinted with permission from Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. Psychosomatics. 2009;50(6):613-21. From Principles of Neuropathic Pain Assessment and Management, November 2011.

*The PHQ-4 and other tools are available online at www.oregonpainguidance.org/clinical-tools.*

## Godin Leisure-Time Exercise Questionnaire

**INSTRUCTIONS**

In this excerpt from the Godin Leisure-Time Exercise Questionnaire, the individual is asked to complete a self-explanatory, brief four-item query of usual leisure-time exercise habits.

**CALCULATIONS**

For the first question, weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. Total weekly leisure activity is calculated in arbitrary units by summing the products of the separate components, as shown in the following formula:

Weekly leisure activity score = (9 × Strenuous) + (5 × Moderate) + (3 × Light)

The second question is used to calculate the frequency of weekly leisure-time activities pursued "long enough to work up a sweat" (see questionnaire).

**EXAMPLE**

Strenuous = 3 times/wk

Moderate = 6 times/wk

Light = 14 times/wk

Total leisure activity score = (9 × 3) + (5 × 6) + (3 × 14) = 27 + 30 + 42 = 99

Godin, G., Shephard, R. J.. (1997) Godin Leisure-Time Exercise Questionnaire. Medicine and Science in Sports and Exercise. 29 June Supplement: S36-S38.

Godin Leisure-Time Questionnaire – Instructions for Scoring

**Godin Leisure-Time Exercise Questionnaire**

1. During a typical **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

| | Times Per Week |
|---|---|
| a) **STRENUOUS EXERCISE** **(HEART BEATS RAPIDLY)** (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling) | _____ |
| b) **MODERATE EXERCISE** **(NOT EXHAUSTING)** (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing) | _____ |
| c) **MILD EXERCISE** **(MINIMAL EFFORT)** (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking) | _____ |

2. During a typical **7-Day period** (a week), in your leisure time, how often do you engage in any regular activity **long enough to work up a sweat** (heart beats rapidly)?

| OFTEN | SOMETIMES | NEVER/RARELY |
|---|---|---|
| 1. ☐ | 2. ☐ | 3. ☐ |

Godin Leisure-Time Questionnaire – Items included

time
make it count

# The DASI Score Sheet (to be used by staff)

## DUKE ACTIVITY STATUS INDEX
### Score sheet

| Can you: | Scores are only given for 'yes' replies | |
|---|---|---|
| 1. Take care of yourself, that is, eat, dress, bathe or use the toilet? | 2.75 | Yes/No |
| 2. Walk indoors, such as around your house? | 1.75 | Yes/No |
| 3. Walk a block or two on level ground? | 2.75 | Yes/No |
| 4. Climb a flight of stairs or walk up a hill? | 5.50 | Yes/No |
| 5. Run a short distance? | 8.00 | Yes/No |
| 6. Do light work around the house like dusting or washing dishes? | 2.70 | Yes/No |
| 7. Do moderate work around the house like vacuuming, sweeping floors or carrying groceries? | 3.50 | Yes/No |
| 8. Do heavy work around the house like scrubbing floors or lifting or moving heavy furniture? | 8.00 | Yes/No |
| 9. Do garden work like raking leaves, weeding or pushing a lawn mower? | 4.50 | Yes/No |
| 10. Have sexual relations? | 5.25 | Yes/No |
| 11. Participate in moderate recreational activities like golf, bowling, dancing, doubles tennis or throwing a ball? | 6.00 | Yes/No |
| 12. Participate in strenuous sports like swimming, singles tennis, football, basketball or skiing? | 7.50 | Yes/No |

**(To be completed by staff) Duke Activity Status Index** (DASI) = ☐

The higher the score is, the more physically active a person is according to this set of activities of daily living. The DASI score should be completed every three months and the score entered into the back of the exercise diary to monitor progress.

Supported by the NKF.
www.kidney.org.uk

Supported by ANSA.
www.anaemianurse.org

Duke Activity Status Index (DASI) – Questions and Scoring

Mediterranean Diet Questionnaire - Questions and Scoring

| Questions | Criteria for 1 point |
|---|---|
| 1. Do you use olive oil as main culinary fat? | Yes |
| 2. How much olive oil do you consume in a given day (including oil used for frying, salads, out-of-house meals, etc.)? | ≥4 tbsp |
| 3. How many vegetable servings do you consume per day? (1 serving : 200 g [consider side dishes as half a serving]) | ≥2 (≥1 portion raw or as a salad) |
| 4. How many fruit units (including natural fruit juices) do you consume per day? | ≥3 |
| 5. How many servings of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? (1 serving: 100–150 g) | <1 |
| 6. How many servings of butter, margarine, or cream do you consume per day? (1 serving: 12 g) | <1 |
| 7. How many sweet or carbonated beverages do you drink per day? | <1 |
| 8. How much wine do you drink per week? | ≥7 glasses |
| 9. How many servings of legumes do you consume per week? (1 serving : 150 g) | ≥3 |
| 10. How many servings of fish or shellfish do you consume per week? (1 serving 100–150 g of fish or 4–5 units or 200 g of shellfish) | ≥3 |
| 11. How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard? | <3 |
| 12. How many servings of nuts (including peanuts) do you consume per week? (1 serving 30 g) | ≥3 |
| 13. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage? | Yes |
| 14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomato and onion, leek, or garlic and simmered with olive oil)? | ≥2 |

# Appendix D

## Original Aims and Hypotheses

**Specific Aim 1:** To investigate the associations between anxiety sensitivity and cardiac rehabilitation and secondary prevention clinical outcomes for patients participating in the cardiac rehabilitation and secondary prevention program.

***Hypothesis 1a:*** Individuals with higher levels of anxiety sensitivity at the beginning of a cardiac rehabilitation and secondary prevention program will have lower levels of participation and will be less likely to complete the program.

***Hypothesis 1b***: Individuals with higher levels of anxiety sensitivity at the beginning of a cardiac rehabilitation and secondary prevention program will be less likely to attain the expected therapeutic targets for the program, including exercise capacity, blood pressure control, and blood lipid control.

**Specific Aim 2:** To investigate changes in anxiety sensitivity during the course of a cardiac rehabilitation and secondary prevention program, and how these changes in anxiety sensitivity are associated with clinical outcomes for patients participating in a cardiac rehabilitation and secondary prevention program.

***Hypothesis 2a:*** Anxiety sensitivity will decrease during the course of a cardiac rehabilitation and secondary prevention program.

***Hypothesis 2b:*** Individuals with higher reductions in anxiety sensitivity will have higher levels of participation and will be more likely to complete a cardiac rehabilitation and secondary prevention program.

***Hypothesis 2c:*** Individuals with higher reductions in anxiety sensitivity will be more likely to attain the expected therapeutic targets for a cardiac rehabilitation and

secondary prevention program including, exercise capacity, blood pressure control, and blood lipid control.

**Specific Aim 3:** To investigate the interrelationships between anxiety sensitivity, symptoms of anxiety, and symptoms of depression, and how these interrelationships are associated with clinical outcomes for patients participating in a cardiac rehabilitation and secondary prevention program.

***Hypothesis 3a:*** In some individuals, anxiety sensitivity will be present, fully independent of symptoms of anxiety and symptoms of depression

***Hypothesis 3b*:** Individuals with higher levels of anxiety sensitivity will be more likely to report symptoms of anxiety and symptoms of depression

***Hypothesis 3c*:** Individuals with the concurrent presence of anxiety sensitivity, symptoms of anxiety, and symptoms of depression, will have the lowest levels of participation and completion

***Hypothesis 3d***: Individuals with the concurrent presence of anxiety sensitivity, symptoms of anxiety, and symptoms of depression will be less likely to attain the expected therapeutic targets for a cardiac rehabilitation and secondary prevention program including increased exercise capacity, blood pressure control, and blood lipid control.

**Specific Aim 4**: To identify key stakeholders, individuals or groups who have an interest in or the ability to act upon the results of the study in order to optimize the health of Cardiac Rehabilitation and Secondary Prevention patients.

**Specific Aim 5**: To create a map of identified stakeholders that assists in visualizing the relationships between stakeholders, their organization affiliations, and their relative influence.

# Curriculum Vitae

# Ebuka Osuji

## SUMMARY OF QUALIFICATIONS

- Trained researcher with 3 years of clinical experience
- Exceptional written and oral communication skills applied across various styles, topics, and target audiences
- Analytic and critical thinker, skilled in both abstract and detail-oriented work
- Passionate about mentorship and leadership developmental programs
- Exceptional organizational and management skills
- Resilient to unique academic and research experiences

## EDUCATION

**Master of Science**, Pathology and Laboratory Medicine, One Health September 2019-Present
*Western University, London, ON*

- Thesis: A One Health Approach Investigating Relationships between Anxiety Sensitivity, Depression, Anxiety and Clinical Outcomes in Patients Enrolled in a Cardiac Rehabilitation and Secondary Prevention Program
- Demonstrating research, organization, and communication skills

**Bachelor of Science**, Honours Life Science, Minor in Biology June 2019
*McMaster University, Hamilton, ON*

## AWARDS AND ACCOMPLISHMENTS

- Awarded Ontario Graduate Scholarship (OGS) of $15,000 (2021)
- Awarded *Western Graduate Research Scholarship* of $6,000 for high academic standing (2019-2021)
- Maintained a 3.98 GPA during graduate studies (2019-2021)
- Recognized in the *Dean's Honour List* for high academic standing (2017-2019)
- Awarded *McMaster Entrance Scholarship* of $1,000 for high academic standing (2015)

## RESEARCH EXPERIENCE

**MSc. Candidate** September 2019-Present

*The University of Western Ontario, London, ON*

- Research Assistant in the Cardiac Rehabilitation and Secondary Prevention (CRSP) Program at St. Joseph's Healthcare London
- First MSc. Cohort of One Health Program: One Health considers human health, animal health (translational methods), and environmental health (social determinants) to achieve optimal outcomes associated with non-infectious disease. Relevant stakeholders are identified and mapped as part of the study objectives
- Created 50-page study protocol comprised of background information and the materials and methods of my study
- Initiated and completed the "Research Ethics Approval" (REB) process for my study
- Experience with working with hospital approved, REDCap platform, used to set-up survey tools and collect both clinical data and survey data
- Experience with performing literature searches across multiple health-related databases
- Developed the ability to critique high and low impact research papers in order to gain the skills and understanding to create and develop my own manuscript
- Attended monthly seminars under the Pathology and Laboratory Medicine Department, tuning into guest speakers discuss clinical research relevant to the field of Pathology
- Attended weekly research meetings with the CRSP research team to discuss progress with my research project and other research projects being conducted in the program
- Advisory Committee meetings held every 6-months to update members of my research team with project milestones.

**Summer Research Student**

May 2017-August 2017

Microbiology Department

*Mount Sinai Health System, Toronto, ON*

- Created standard operating procedures with superiors
- Collected data in Excel to validate the ACCELERATE PHENO System to detect susceptibility of hospital bacteria to various antimicrobial agents
- Ran the BioFire FilmArray Multiplex PCR System on blood samples to detect for Candida species
- Used SHIGA TOXIN QUIK CHEK to detect Shiga toxins in *E. coli* species via agglutination techniques

- Created Validation report for QUIK CHEK
- Practiced technical skills such as streaking, plating, creating 0.5 McFarlan, and using selective agars
- Exposed to microbiology related lab instruments such as the MALDI-TOF and VITEK machinery
- Gave mini presentation to supervisors and employees of the department summarizing the projects and work done over the course of my employment

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**VOLUNTEER EXPERIENCE**

**Outpatient Physiotherapy Volunteer** May 2016 – August 2016

William Osler Health System

*Etobicoke General Hospital*

Duties included:

- Reviewed patient charts prior to their arrival in order to set and prep the following item(s):
  - Preparing patient beds
  - Prepping heat/cooling pads
  - Prepping exercise stretch bands based on incoming patient schedule
- Talked to patients as they completed their designated exercise routines
- Demonstrated leadership when new volunteers came to the clinic – assisted them in becoming more familiar with how the clinic is run
- Worked in collaboration with physiotherapists, physiotherapist assistance and other volunteers in order to deliver standard of care

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**INTERPERSONAL AND TEACHING EXPERIENCE**

**Graduate Teaching Assistant** September 2020-Present

Department of Pathology and Laboratory Medicine

*The University of Western Ontario, London, ON*

- Course: One Health 3300 – Foundations to One Health
- Objective was to mark weekly quizzes related to conceptual frameworks, socialism, environmental health, animal health, human health, and their interconnectedness
- Course: One Health 3600 – One Health in Action

- Objective is to continue working on the well-developed proposals from the One Health 3300 class and assist students to work on and finalize an "action-plan" project to implement the One Health approach to a non-infectious or infectious disease related case.

**Undergraduate Teaching Assistant** September 2018-December 2018
School of Interdisciplinary Science (SIS)
*McMaster University, Hamilton, ON*

- Course: Science 1A03 – Investigating Science: Opportunities & Experiences
- Objective was to help first year university students prepare for the university career through different avenues
- Lead in class sessions three times a week on applying basic research skills to analyzing scientific articles, working on mini-projects, and creating reflections
- Shed insight on my own experiences as an undergraduate as a way to facilitate discussion

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## COMMUNICATIONS EXPERIENCE

**Pathology and Laboratory Medicine Research Day**
April 2021
Department of Pathology and Laboratory Medicine
*Western University, London, ON*

- Conducted a 3-minute poster presentation of my master's thesis followed by a 2-minute Q&A period

**Health & Rehabilitation Sciences Graduate Research Conference**
February 2021
Western Health Sciences
*Western University, London, ON*

- Conducted a 5-minute oral presentation of my master's thesis

**One Health Poster Day**
November 2020
The Centre for Public Health and Zoonoses and the One Health Institute at the University of Guelph, in collaboration with the One Health Program in the Department of Pathology and Laboratory Medicine at the Schulich School of Medicine & Dentistry at Western University
*The University of Guelph*

- Conducted a 2-minute live oral presentation via Microsoft Teams of my master's thesis
- Had the opportunity to gain constructive feedback regarding my study and gain insight on other research projects relevant to One Health

**One Health Poster Day**
November 2019

The Centre for Public Health and Zoonoses and the One Health Institute at the University of Guelph, in collaboration with the One Health Program in the Department of Pathology and Laboratory Medicine at the Schulich School of Medicine & Dentistry at Western University

*The University of Guelph*

- Conducted In-Person Poster Presentation of my master's thesis
- Had the opportunity to gain constructive feedback regarding my study and gain insight on other research projects relevant to One Health

**Physician Observership** September 2018-December 2018

Oncology

*Juravinski Cancer Centre, Hamilton, Ontario*

- Visited patient rooms with Dr. Dhesy and observed her role as a medical oncologist
- Observed breast exams, body CT's, and patient history
- Shadowed the work of the current medical residents in the department
- Examined the roles of other practitioners that worked alongside Dr. Dhesy
- Completed a placement project summing everything learned over the 4-month span

**Summer Student Research Day** August 2017

Mount Sinai Health System, Department of Microbiology

*Toronto, Ontario*

- Conducted a 15-minute oral presentation to supervisors and employees of the department summarizing the projects and work done over the course of my employment at Mount Sinai Hospital

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## PUBLICATIONS

**Scoping Review – 1st Author**

Present

Pathology and Laboratory Medicine Department

*The University of Western Ontario, London, ON*

- **Manuscript (In Progress):** The Relationship Between Anxiety Sensitivity and Outcomes in Cardiac Rehabilitation – A Scoping Review

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## LEADERSHIP

**Mentor for Pathology and Laboratory Medicine Program** September 2020-Present

Western University

*London, Ontario*

- Currently a mentor in the PaLM Program at Western University as a graduate student. I meet

with a 1st year MSc. student monthly to discuss any questions or advice he might need as well as providing social support, advocating for the importance of mental health especially during these uncertain times.

**Mentor and Alumnus of MOTION Basketball Association**
September 2014-Present
*Rexdale, Ontario*

- Attend yearly events to speak to at-risk youth about relatable experiences and how to go about making a change in the community

**Summer Science Camp Counsellor**
June 2019-August 2019
*YMCA (GTA), Mississauga, Ontario*

- Ran Camps for 7 weeks, running science activities for junior (ages 5-8) and senior (ages 9-12) children. Science experiments range from making "slime" and other hands-on activities to performing chemical reactions for the older and more advanced groups. I was not only a teacher but learned to become a mentor for both kids and other staff.

**Member of the Black Aspiring Physicians of McMaster Association**
September 2016-April 2019
McMaster University
Hamilton, Ontario

- Being part of the Black Aspiring Physicians of McMaster Association, I was able to both receive and give mentorship to fellow undergraduate students who identify as Black, hoping to pursue a career in healthcare.

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SKILLS & CERTIFICATIONS

- Certified in Standard First Aid & CPR/AED Level C – Canadian Red Cross
- Certified in WHMIS Training – Western University
- Certified in Tri-Council Policy Statement (TCPS 2: Core): Ethical Conduct for Research Involving Humans Course on Human Ethics
- Certified in Animal Ethics and Regulation – Western University
- Certified in Supervisor Health and Safety Awareness – Western University
- Certified in AODA: Accessibility and Service – Western University
- Proficient in all Microsoft applications