Depression Symptoms in Older Adults with Coronary Artery Disease: A Population Based Study

By

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Abstract

Coronary artery disease (CAD) is the leading cause of mortality in developed countries, followed by depression. Recent literature supports a bidirectional relationship between depression and CAD, which adversely affects the quality of life. Although there is a high prevalence of co-occurring CAD and depression, there is limited research on relationship of depression and aging in individuals with CAD. This study employs analytical cross sectional design to identify the relationships between depressive symptoms and aging and identifies factors predicting higher scores on depression screening scales in individuals with CAD. The analyses revealed that older adults reported significantly higher scores on *Hospital Anxiety and Depression Scale* (HADS) in comparison to younger adults. Moreover female sex, age ≥75 years, smoking, physical limitation, anxiety and social support were independent predictors of depression in individuals with CAD. There is a need to further study the dynamics of depression in older adults with CAD and the effect of depression treatment on morbidity, mortality and quality of life.

Preface

This thesis is an original work by Fahreen Rajani. The research project received research ethics approval from the University of Alberta Research Ethics Board, Project Name "DEPRESSION SYMPTOMS IN OLDER ADULTS WITH CORONARY ARTERY DISEASE: A POPULATION BASED STUDY", Study ID Pro00047661

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CHAPTER 1

INTRODUCTION

The world's population is rapidly changing. A feature of this change is the increasing proportion of older adults, which is expected to double from 12% in 2015 to 22% by 2050 (World Health Organization [WHO], 2016a). According to the Public Health Agency of Canada (2011), the average life expectancy for Canadians is 80.9 years. The first wave of Canadian 'baby boomers' turned 65 in 2011 (Smith, 2012) and it is estimated that by 2021, older adults will comprise 18% of Canada's population of 6.7 million (Rivard & Buchanan, 2006; Smith, 2012). It is also estimated that 74-90% Canadian seniors suffer from at least one chronic condition (Smith, 2012) with associated healthcare costs of $190 billion, of which $90 billion represents direct expenditure on treatment (Public Health Agency of Canada, 2011). This increasing life expectancy and changing demographics demands particular attention to the health status and quality of life of older adults in Canada.

Coronary artery disease (CAD) is the most common form of cardiovascular disease in Canada (Public Health Agency of Canada, 2009) and the leading cause of death worldwide (WHO, 2016b). Approximately 3.8 million men and 3.4 million women around the world die from CAD each year (WHO, 2004). In Europe, 4 million people die of cardiovascular diseases every year. This represents half of all deaths in Europe and includes 1.8 million deaths are attributable to CAD (Nichols, Townsend, Scarborough & Rayner, 2014). The United States also has a major burden of disease due to cardiovascular diseases, which affect 85.6 million adults, 43.7 million of whom are $\geq$ 60 years of age (Mozaffarian, et. al., 2015). By 2020, CAD will responsible for 11.1 million deaths globally (Mathers & Loncar, 2006). Mortality related to cardiovascular diseases is also very high with an average of one death every 40 seconds.

Almost 5% of Canadians suffer from heart diseases and 6.5% of all hospitalizations are attributed to CAD (Public Health Agency of Canada, 2009). People over 65 years account for 54% of the total number of individuals affected by heart diseases and 68.8% of those with heart disease report having activity restrictions (Public Health Agency of Canada, 2009). This has major economic implications for health care systems and for society in general. The cost associated with treating individuals who live with cardiovascular diseases is highest among those 65 years of age and older (Public Health Agency of Canada, 2009). CAD accounts for the largest proportion of the health cost related to cardiovascular diseases (Public Health Agency of Canada, 2009). The hospitalization rates for older adults (≥ 65 years of age) are $21,506.7 per 100,000 population, which is more than any other age group (Public Health Agency of Canada, 2009).

Another major health concern experienced by older adults in developed countries is depression. The prevalence of depression among older adults is 20% in the general population and 90% among those living in long-term care facilities in Canada (Rivard & Buchanan, 2006). Despite its high prevalence and adverse effects on quality of life (QoL), depression is underdiagnosed and undertreated. Depressive symptoms in older adults are often overlooked and misdiagnosed as they often co-occur with other age related problems (WHO, 2016a). Although frailty, depression, social withdrawal, chronic diseases, and impaired functional status are commonly associated with aging (WHO, 2016a), these are not a normal part of aging.

Depressive symptoms are higher among people with CAD and clinically significant depression is an independent risk factor for mortality in patients with CAD (Van der Kooy, Van Hout, Marwijk, Marten, Stehouwer, & Beekman, 2007). Moreover, cardiovascular disease and depression are strongly associated with mortality in high and middle-income countries (WHO, 2006; Swardfager Herrmann, Dowlati, Oh, Kiss, & Lanctot, 2008). There is an increased vulnerability of depression among elders diagnosed with CAD and vice versa (Ondria, Aaron,

Ashley, & Julia, 2013; Whooley & Wong, 2013). Depressive symptoms predict adverse clinical outcomes and hospital readmissions in patients diagnosed with CAD (Mallik, Krumholz, Lin, Kasl, Mattera, Roumains & Vaccarino, 2005). Major depressive disorder secondary to CAD is associated with 3.5-fold increase in mortality (Glassman, Bigger, & Gaffney, 2009). There is also increasing evidence of depressive symptoms prevalence among people with CAD (Ondria, Aaron, Ashley, & Julia, 2013; Whooley & Wong, 2013). A national Canadian study (Gilmour, 2008) reported a statistically significant association between depression and incident heart diseases in women (hazards ratio=1.8 95% CI=1.3, 2.7). In that study, the incidence of a heart disease event in patients with no history of heart disease was 81.6% for men and 86.8% for women (Gilmour, 2008).

Study Purpose

There have been multiple efforts to explain the relationship between depression and CAD. However, there is dearth of knowledge about the dynamics of this relationship in older adults. Therefore, this study aims to explore the relationship between age and depressive symptoms among older adults (i.e., those ≥ 75 years of age) diagnosed with CAD and to examine that relationship in light of related factors such as gender, smoking status, quality of life, anxiety scores, social support, and co-morbidities.

Research Questions

1. What is the prevalence of depression among older adults with CAD?
2. Is there a statistically significant difference in the depression scores of individuals ≥ 75 years of age and those younger than 75?
3. What factors predict depression in older adults with CAD?

Significance to Nursing

The results from this study has implications for nursing practice including planning care for older adults with CAD, depression screening in community and cardiac rehabilitation settings, and timely detection and treatment of depression in individuals with CAD. Detection and treatment of depression at earlier stages will help reduce the associated morbidity, mortality and improve quality of life. Findings from this study may improve our understanding of treatments options that will improve the quality of life for elders living with CAD.

Operational Definitions

Depressive symptoms refers to scores >11 on the *Hospital Anxiety and Depression Scale* (HADS; Zigmond & Snaith, 1983).

CAD refers to coronary artery disease (CAD) diagnosed per coronary artery catheterization.

Old age refers to individuals ≥ 75 years of age.

CHAPTER 2

LITERATURE REVIEW

Search Strategies

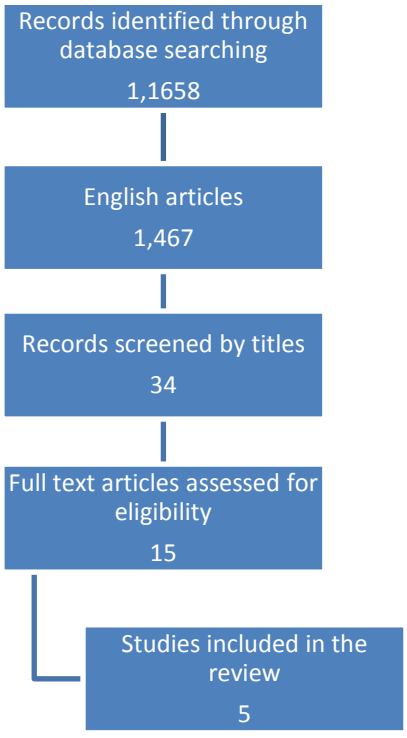
This chapter surveys recent literature on coronary artery disease (CAD) and depressive symptoms in older adults. PubMed, Medline, and EBSCO databases were searched using the following terms individually and in various combinations: coronary artery disease (CAD), coronary heart disease, ischemic heart disease (IHD), older adults, age 65 and above, Canada, cardiac catheterization, mental health, mental illness, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), major depressive disorder, and depression.

The articles for this literature review were selected on the following predetermined inclusion and exclusion criteria: results of quantitative research studies focusing on depression and CAD among older adults (≥ 65 years); published in the English language between 2000 and 2014. Only one study was found to be from Canada therefore, studies from other developed countries in North America and Europe were also included in the literature review. Since there is limited literature on the population of interest (i.e. older adults), the age limit was also not strictly followed and the studies that matched the scope of the search were included in the review despite of not meeting the criteria for age group (≥65 years).

There were no limitations placed on the gender, culture and ethnic background of the study participants. However, cardiac diseases other than ischemic heart disease (IHD) and CAD were not included in the study. Mental illness other than depression and quality of life studies were also excluded. Systematic reviews, concept analyses, and ecological studies were also excluded. Only research studies close to the problem statement were included in the literature review.

In total 1,658 articles were found. After the language of article was limited to English, 1,467 articles remained. Thirty-four articles were identified to be related to the topic after screening the titles for relevance to the topic. The articles excluded based on non-research articles, systematic reviews, review articles, descriptive papers, and randomized controlled trails. Some articles did not have depression as outcome variable and was used to predict outcomes in patients with CAD. After reading the abstracts of the shortlisted articles, 15 research studies were identified to be relevant to the research problem. Based on the above mentioned criteria 5 articles were chosen to guide the literature review for the stated problem. A critical analysis of the selected articles was done utilizing Loiselle and Profetto-McGrath's guide to critiquing quantitative research to identify the strengths and limitations of the studies utilized for literature review (Profetto-McGrath, Polit, & Beck, 2010). In addition to these five articles, literature was included to support the background information on CAD, depression and associated factors.

Fig 2A: PRISMA Flow Diagram for selection of articles shortlisted for review



Coronary Artery Disease (CAD)

Coronary artery disease (CAD) is disorder characterized by episode of myocardial oxygen demand/supply mismatch due to ischemia or hypoxia (Montalescot, et al., 2013). It can be classified as stable or unstable (Fihn, et al., 2014). Stable CAD is characterized by reversible hypoxia or ischemia, associated by transient chest discomfort often induced by exercise, emotional or other stress (Fihn, at al., 2014; Montalescot, et al., 2013). On the other hand, unstable CAD is due to the persistent ischemia characterized by irreversible myocardial damage typically exhibited as pain or discomfort in chest, near sternum, epigastrium, lower jaw, between the shoulder blades, either arm or wrist, shortness of breath and ST segment changes on electrocardiogram (Montalescot, et al., 2013). Ischemia is most commonly caused by atherosclerosis, a condition caused by plaque formation in coronary arteries (Marzilli, et al., 2012). Ischemia can also be caused by vasospasms (narrowing of coronary arteries; Stillman, Stillman, Tepper¸Cho, 2013) or spontaneous coronary dissection (Lakhter, et al., 2016; Nakai, et al., 2016; Eleid, et al., 2014).

Prevalence

CAD is a common health problem and accounts for 7.7 million disability-adjusted life years (DALYs; WHO, 2006). It is the leading cause of death in developed countries (WHO, 2006) and is the cause of 17.3% of all deaths in Canada (Public Health Agency of Canada, 2009).

Diagnosis

The assessment and diagnosis of the CAD involves comprehensive history taking and clinical assessment for the presence of risk factors including dyslipidemia (Valensi, Avignon, Sultan, Chanu, Nguyen & Cosson, 2016; Martin, et al., 2014); diabetes (Rydén, 2013); smoking (Farkouh, et al., 2013); hypertension; positive family history; and alcohol abuse (Deloukas, et al.,

2013). Diagnostic tests to identify CAD or myocardial ischemia include electrocardiogram (Montalescot, et al., 2013), stress test (Zimarino, et al., 2016), computed tomography coronary angiography (Nørgaard, et al., 2014; Arbab-Zadeh, et al., 2012) and coronary artery catheterization.

Risk Factors

Factors that contribute to increased risk of CAD include hypertension, hyperlipidemia, diabetes, smoking, insulin resistance, obesity, age, gender, sedentary life style, family history and depression (Farkouh, et al., 2013; Deloukas, et al., 2013; Yusuf et al., 2004; Saleheen & Frossard, 2004). CAD is caused by atherosclerosis, spasm, plaque formation in the coronary arteries blocks the arteries and hinders blood flow to the heart (Lerman, Kwon & Lerman, 2015). Spasm and inflammation causes vasospasm mediated by release of histamine, serotonin and catecholamines thus reducing blood flow to heart (Shiomi, et al., 2013; Choudhury, Fuster, Fayad, 2005).

Old Age and CAD

CAD is the most common form of cardiovascular diseases (Public Health Agency of Canada, 2009). Almost 5% of Canadians suffer from heart diseases and 6.5% of all hospitalizations are attributed to CAD (Public Health Agency of Canada, 2009). The death rate secondary to cardiovascular diseases 8,122.1 per 100,000 population and 17.3% of all deaths in Canada are attributed to CAD (Public Health Agency of Canada, 2009). People over 65 years account for 54% of the total number of individuals affected by heart diseases and 68.8% of people with heart disease report having activity restrictions (Public Health Agency of Canada, 2009) Moreover, CAD has economic implications. The cost associated with treating individuals who live with cardiovascular diseases is highest among those 65 years of age and older (Public Health Agency of Canada, 2009). CAD accounts for the largest proportion of the cost related to

cardiovascular diseases (Public Health Agency of Canada, 2009). The hospitalization rates for older adults (aged more than 65 years) are 21,506.7 per 100,000 population which more than other age groups (Public Health Agency of Canada, 2009).

Depression/Depressive Symptoms

Depression makes the largest contribution to the global burden of disease. Depression is associated with highest rate of DALYs in middle and high income countries and is projected to be the leading cause of disease burden in middle and high income countries by the year 2030 (WHO, 2006).

Depressive disorders are a group of mental disorder characterized by depressed mood, anhedonia (diminished sense of pleasure), weight change, disturbed sleep, psychomotor agitation, fatigue, decreased libido, feeling of worthlessness, diminished ability to think or concentrate, and recurrent thoughts of death or suicide (American Psychiatric Association [APA], 2013). The presence of depressive symptoms is highly co-related with impaired functioning (Kurdyak, Chong, Gnamn Goering, & Alter, 2011) and lower quality of life (Kugler, Bara, Waldthausen, Einhom, Haastert, Fegbeutel & Haverich, 2014). The most common depressive disorder is major depressive disorder (MDD), however it is important to note that symptoms of depression may exist without meeting the criteria described in the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM 5, APA). Most screening tools, including the *Hospital Anxiety and Depression Scale* (HADS; Zigmond & Snaith, 1983) are used to screen for the presence of depressive symptoms and it severity.

Etiology

Although the exact mechanisms are not known, depression likely caused by an interaction of biological, social and psychological factors (Kupfer, Brent, Lewis, Reynolds & Thase, 2008). Factors thought to precipitate or perpetuate depression include genetic

predisposition, personality traits, social stressors, major loss, physical illness and adverse life events. Females are more prone to be depressed than males (Semple & Smyth, 2013).

Symptoms and Diagnosis

The DSM 5 (APA, 2013) outlines the following diagnostic criteria for MDD, the classic disorder in this group. MDD is diagnosed based on report of ≥5 of the following symptoms in the past 2-weeks and represents a change from previous functioning. At least one of the symptoms must be either (1) depressed mood or (2) loss of interest or pleasure in usual activities:

- Depressed mood
- Markedly diminished interest or pleasure in all, or almost all, activities
- Significant weight loss when not dieting or weight gain
- Insomnia or hypersomnia nearly every day.
- Psychomotor agitation or retardation nearly every day
- Fatigue or loss of energy nearly every day.
- Feelings of worthlessness or excessive or inappropriate guilt
- Diminished ability to think or concentrate, or indecisiveness, nearly every day
- Recurrent thoughts of death

The diagnosis of MDD and other depressive disorders relies primarily on good history taking and mental state examination (Semple & Smyth, 2013). There are also several scales used to detect the presence of depressive symptoms including the *Hamilton Depression Rating Scale* (HAM-D; Hamilton, 1960); the *Beck Depression Inventory* (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Aben, Verhey, Lousberg, Lodder & Honig, 2002), the *Zung Self-Rating Depression Scale* (Zung, 1965) and the *HADS* (Zigmond & Snaith, 1983).

Depressive Symptoms in Old Age

Depressive symptoms among older adults are more frequent, last longer, have a worse prognosis, and have a tendency to become chronic or relapse (Sutin, Terracciano, Milaneschi, An, Ferrucci & Zonderman, 2013; Mitchell & Subramaniam, 2005). There are no vivid differences in depressive symptoms between young and older adults (Goldberg, Breckenridge and Sheikh, 2003). However, some features are more remarkable in old age such as the presence of psychomotor retardation or agitation, cognitive impairment, depressive delusions, and paranoia (Corcoran, et al., 2013; Cahoon, 2012; Murray, Banerjee, Byng, Tylee, Bhugra & Macdonald, 2006). Depression may also present as pseudo-dementia in older patients exhibited as marked difficulty in concentrating and memory (Semple & Smyth, 2013; Alexopoulos, 2005). Depression may also present as pseudo-dementia in older patients exhibited as marked difficulty in concentrating and affected memory (Semple & Smyth, 2013).

There are discrepancies in the literature concerning the relationship of age and depression. Some authors suggest a U-shaped relationship between depression and age, with the prevalence of depression being higher in young and old age groups and lower in middle age (Sutin, et al., 2013; Mirowsky & Ross, 1992). Others report an age related increase in the prevalence of depression (Stordal, Mykletun & Dahl, 2003; Pálsson, Östling & Skoog, 2001). A meta-regression done by Ferrari et al., (2013) reported that 55% of the variability in the prevalence of depression is explained by sex, depression subtype, survey instrument, year of study, prevalence period and region. In addition to these factors, mobility problems, chronic illness, and living in a long-term care setting can also precipitate depressive symptoms in older adults. According to one systematic review, depression is the most common psychiatric problem among both community-dwelling older adults and those living in long-term care settings where the prevalence may be as high as 90% (Djernes, 2006).

Links between CAD and Depression/Depressive Symptoms

CAD and Depression/Depressive Symptoms

There is an increased vulnerability for depression among elders diagnosed with CAD and vice versa (Ondria, Aaron, Ashley, & Julia, 2013; Whooley & Wong, 2013). Depressive symptoms predict adverse clinical outcomes and hospital readmissions in patients diagnosed with CAD (Mallik et al., 2005). Major depressive disorder secondary to CAD is associated with 3.5 fold increase in mortality (Glassman, Bigger, & Gaffney, 2009). There is an increasing evidence of depressive symptomatology prevalence among people with CAD.

Pasca, Ardelean, Rus & Cioara (2013) studied the prevalence of depression in 231 patients (mean age 60.6 ±7.8) diagnosed with different types of ischemic heart disease, which includes CAD. Participants were screened for depression using the 2-item *Patients' Health Questionnaire* (*PHQ*; Kroenke, Spitzer, & Williams, 2003) and those who screened positive for depression were evaluated by a psychiatrist. Severity of depression was assessed using the 26-item *Cardiac Depression Scale* (Hare & Davis, 1996) at baseline and every three months for two years. Chi square, Fisher, Student, Mann Whitney, ANOVA and multiple logistic regression was performed to analyze the data. After the 24 month follow up period, the prevalence of depression was 33.8% among the study participants. There was a significant positive linear relationship between depression, age ($p<0.01$) and severity of symptoms ($p<0.001$). The time of depression onset after the diagnosis of IHD was 5-8 months. Prevalence of depression is also found to be increasing with age ($r^2=0.06$, $p<0.05$). This study provides valuable insights regarding depression in patients with CAD and its association with age. However the choice of the statistical tests mentioned in the report lacks justification. Using both parametric and nonparametric tests in the single study for the same variables raises doubts on the reliability of the results.

Another study done by Sunbul et al. (2013) studied the relationships among CAD, anxiety, and depression. A total of 116 participants were enrolled in the study and classified into 'normal' (age 54.5±10.5) and 'abnormal' (age 52.2 ± 11.1) groups based on the findings of coronary angiography (CAG). The *BDI (*Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), *Beck Anxiety Inventory (*Beck, Epstein, Brown, & Steer, 1988), and *State-Trait Anxiety Inventory* (Spielberger, Gorsuch, & Lushene, 1970) were administered before CAG. There were no significant between-group difference in demographic variables and associated risk factors (hypertension, diabetes, hyperlipidemia, smoking, and family history of CAD). Univariate analysis showed that a score > than 12 on the *BDI* predicted CAD. There was also a significant difference ($p<0.001$) in *BDI* scores among the two groups with patients in abnormal group (15.0±9.8) reporting higher scores on BDI than those in normal group (9.2±7.6). However the prevalence of depression among the participants was not reported.

Koivula, Halme and Astedt-Kurki (2010) studied 152 patients (age 69.7 ±8.9) nine years after coronary artery bypass graft (CABG) surgery to determine the incidence of depression and its association with demographics, lifestyle, perceived health, perceived symptoms, and social support variables. Depression and social support were measured using the *Zung Self-Rated Depression Scale* (Zung, 1965) and *Social Support from the Network Scale* (Koivula, Kaunonen & Tarkka, 2005) respectively. In this cross-sectional study, 24% of the participants reported to be depressed whereas, incidence of depression was 30% in participants aged 65 and above years.

A cross-sectional cohort study conducted by Swardfager, Herrmann, Dowlati, Oh, Kiss and Lanctot, (2008) aimed to determine the incidence of depression and identify the predictors of depressive symptoms in patients with CAD in cardiac rehabilitation centre. Three hundred and thirty six participants (age 63.6 ±10.7) were enrolled in the study from the *Toronto Rehabilitation Institute Cardiac Rehabilitation and Secondary Prevention Program* 3-8 weeks

post percutaneous coronary intervention (PCI, formerly known as angioplasty with stent), myocardial infarction, or coronary artery bypass graft (CABG). The *Center for Epidemiological Studies Depression Scale* (CES-D; Radloff, 1977) was administered to measure depression among participants. Analysis revealed that 22.3% of the participants had mild depressive symptoms and 10.4% had significant depressive symptoms. Only 6.3% of the participants were taking anti-depressant medications and 9.3% were using anxiolytic medications. Eighty-two percent of those with significant depressive symptoms were not talking any anti-depressant medication.

Gravely-Witte, Gucht, Heiser, Grace and Elderen (2007) studied the impact of angina and cardiac history on health-related quality of life and depression in CAD patients. Patients (age 53.98 ±8.39) were recruited 45 days post cardiac event including PCI, CABG or MI. Depression was assessed through 90 item symptom checklist in 171 patients aged less than 70 years at base line and 6 months follow-up. The analysis showed that at six months follow up, cardiac history and angina were significantly predictive of higher scores of depression in patients with PCI, myocardial infarction or CABG.

The sample size in the studies reviewed above range from 116-336. Small sample size has important implications for power of the study (Chow, Wang & Shao, 2007). Higher sample size decreases the variability and also decreases the likelihood of type 1 error which is rejecting the null hypothesis when is true (Chow, et al., 2007). Only one study by Koivula, Halme and Astedi-Kurki (2010) reported their sampling strategy, which was convenience sampling. The other four studies did not explicitly mention the sampling technique, however it is presumed that convenient sampling was used in those studies based on their description of participant selection method. According to Bornstein, Jager & Putnick, (2014), convenience sampling is the least effective sampling design in quantitative study as it limits generalizability and external validity.

Gravely, et al. (2007) did not consider the comorbidities which might have an effect on depression in addition to CAD. Moreover, the sample contained more men than women. These factors are also threat to the internal validity and reliability of the findings (Polit & Beck, 2010).

Depressive symptoms were identified as an independent risk factor for cardiac mortality and morbidity over two decades ago (Frasure-Smith, Lespérance & Talajic, 1993). Since then, there have been many studies exploring the links between depression and CAD with the aim of developing interventions to reduce the mortality and morbidity in patients with CAD. Wellenius, Mukamal, Kulshreshtha, Asonganyi & Mittleman, (2008) identified that depressive symptoms are associated with high risk of progression of atherosclerotic changes in patients with CAD. A meta-analysis of 25 years of research on the association of CAD and depression reveals that depression is associated with 1.6-2.7 fold increase in the risk of adverse outcomes in patients with a previous history of myocardial infarction (Meijer, Conradi, Bos, Thombs, van Melle, & de Jonge, 2011).

Hypothesized Etiology for the Association between CAD and Depression/Depressive Symptoms

Factors that explain the link between CAD and depression can be classified as behavioural and biological (Whooley & Wong, 2013). Behavioural factors include physical inactivity, medication non-adherence, smoking, dietary indiscretion, and social isolation. Biological factors include autonomic nervous system activation, systemic inflammation, and activation of hypothalamic-pituitary-adrenal axis, mental stress induced ischemia, platelet activation and serotonergic dysfunction, endothelial dysfunction and common genetic vulnerability.

Behavioural Factors

Physical inactivity. There are clear associations among physical inactivity, depression, cardiovascular disease, and old age (Blumenthal, et al., 2012). Anhedonia, the inability to feel pleasure, is a common depressive symptom and contributes to decreased physical activity. Physical inactivity is prevalent in patients with depression and conversely, depressed people have higher odds of physical inactivity (Abu-Omar, Rütten & Lehtinen, 2004; Ströhle, 2009). Physical inactivity due to depression accounts for a major proportion of cardiovascular mortality risk (Win, Parakh, Eze-Nliam, Gottdiener, Kop and Ziegelstein, 2011) and physical inactivity and depression are independent risk factors for mortality secondary to cardiac events (Win, et al., 2011).

Physical activity is an important lifestyle factor in management and prevention of cardiovascular disease and also reduces the likelihood of depression (Herring, Puetz, O'Connor, & Dishman, 2012; Krogh, Nordentoft, Sterne, & Lawlor, (2011); Abu-Omar, Rütten & Lehtinen, 2004). The *Heart and Soul Study* is a prospective cohort study examining ways that depression and other mental health problems affect outcomes of persons living with CAD (Ruo, Rumsfeld, Hlatky, Lui, Browner, & Whooley, 2003). The authors of the study report that physical activity is strong mediator in the relationship of depression and future cardiac events in patients with known CAD (Whooley, et al., 2008). Physical inactivity in patients with known cardiovascular diseases increases the risk of morbidity and mortality (Blumenthal et al. 2012; Brummett, Babyak, Siegler, Mark, Williams, & Barefoot, 2003; Whooley et al. 2008; Win, et al., 2011).

Old age is also an important predictor of an individual's mobility (Nilsson, Siersma, Manty, Avlund, Vass, & Lund, 2014; Rantakokko, Manty, & Rantanen, 2013). Immobility and function often decline with age and when immobility accompanies depression, there are often marked reductions in physical activity.

Medication non-adherence. Medication non-adherence is another behavioural factor contributing to the relationship between depression and CAD. Patients with depressive symptoms are more likely to be non-adherent to medication including cardio-protective medications (Gehi, Hass, Pipkin, & Whooley, 2005; Lin, et al., 2012; Rieckmann et al., 2006). Medication noncompliance is highly associated with future cardiac events and increased mortality in patients with known cardiovascular disease (Baroletti & Dell'Orfano, 2010). In the Heart and Soul Study, medication non-adherence was a mediator in the relationship of depressive symptoms and cardiovascular mortality (Whooley et al, 2008).

Smoking. Smoking is a maladaptive coping mechanism adopted by majority of depressed patients (Breslau, Peterson, Schultz, Chilcoat, & Andreski, 1998). The literature suggests a bidirectional relationship between smoking and depression (Breslau, et al., 1998; Taylor, Fluharty, & Munafo, 2014). Smoking is associated with two-fold increase in risk of new onset MDD and depressed patients are three times more likely to progress to daily smoking (Breslau, et al., 1998; Luger, Suls, & Vander Weg, 2014). There is also evidence that current and former smokers have greater odds of being depressed, anxious, and of experiencing psychological distress than those who have never smoked (Taylor, et al., 2014). One plausible explanation for this is that depressed individuals self-medicate by smoking in order to activate the dopaminergic reward system (Brody, et al., 2004).

Smoking cessation has also been associated with decreased mortality in patients with CAD (Critchley & Capewell, 2003). However, patients with depression have lower success rates with smoking cessation efforts (Hitsman, et al., 2013). Smoking can be a confounder and a mediator in the relationship of depression and CAD because of its bidirectional relationship with depression (Whooley & Wong, 2013).

In the *Heart and Soul Study*, adjusting for smoking weakened the association between depression and future cardiac events by more than 10% (Whooley, et al., 2008). The strength of the association between depression and future cardiac events decreased by an additional 5% and 32% after adjusting for medication noncompliance and physical inactivity respectively. Moreover, adjusting for all three variables eliminated the association between depression and cardiac events (Whooley, et al., 2008)

Social Isolation. Social isolation has also been found to increase mortality secondary to CAD (Brummett, et al., 2003; Friedmann, Thomas, Liu, Morton, Chapa, & Gottlieb, 2006). Socially isolated individuals are less likely to receive regular medical attention, are less compliant with medication regimes, and are less physically active (Horsten, Mittleman, Wamla, Schenck-Gustafsson, & Orth-Gomer, 2000). Social isolation is also linked to depression (Friedmann, et al., 2006), low socio-economic status, high smoking, rates and high hostility ratings (Brummett, et al., 2003).

Biological Factors

In addition to behavioural factors, there are also biological factors that help to explain the relationship between CAD and depression. These biological factors include autonomic nervous system activation (Curtis and O'Keefe, 2002); systemic inflammation (Rocha and Libby 2009; Frasure-Smith, Lespérance, Irwin, Sauve, Lespérance and Théroux, 2007); activation of hypothalamic-pituitary-adrenal axis (Brown, Varghese and McEwen, 2004); mental stress induced ischemia (Ziegelstein, et al., 2007); platelet activation and serotonergic dysfunction (Schins, et al., 2004); endothelial dysfunction (Cooper, Tomfohr, Milic, Natarajan, Bardwell, Ziegler, & Dimsdale, 2011); and genetic vulnerability (Bozzini, et al., 2009, McCaffery, et al., 2009).

Gaps in Literature

The relationship between CAD and depression has been of interest to researchers since early 1990s. However, only a few studies have focused on the relationship of CAD and depression in older adults. Given the aging in the population, it is important to identify problems that interfere with the health, functional status, and quality of life of older adults.

Existing research examining the relationship between CAD and depression in the elderly has several methodological problems including small sample size, convenience sampling, a failure to control for comorbidities, and a lack of focus on persons aged 75 or older. The mean age for the participants ranged from 52.2 years to 69.7 years. None of the studies reported the relationship of depressive symptomatology with old age. Albeit, Pasca et al. (2013) reported significant linear relationship of depression with age but the study participants were not exclusively older adults. Koivula, Halme and Astedi-Kurki, (2010) in their study reported the prevalence of depression for participants over 65 years to be 30%, which is higher than the study population i.e. 24%. This demands a further exploration of depressive symptomatology among older age people living with CAD. Only three of five studies reported the prevalence of depression among study participants. The prevalence ranges from 22.3% to 33.8% with a reported significant association with age and severity of the disease. Depression was also found to be an independent risk factor of CAD in the study sample. Based on the literature review and identified gaps in the literature, there is a need to study depressive symptomatology and its associated factors in old population.

CHAPTER 3

METHOD

Data Source

Data for the present study was drawn from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH®) database (Ghali & Knudtson, 2000). Started in January 1995, APPROACH is an ongoing prospective data collection initiative that enrolls all persons undergoing cardiac catheterization in Alberta, Canada. Those who agree to be contacted are followed longitudinally to assess long term clinical, economic, and QoL outcomes (Ghali & Knudtson, 2000). Baseline and subsequent data are collected through structured questionnaires and include demographics, health history, *HADS* (Zigmond & Snaith, 1983); *Euroqol Index* (EQ-5D; The Euroquol Group, 1990)*, Medical Outcome Study Social Support Survey* (MOS-SS; Sherbourne & Stewart, 1991)*,* and the *Seattle Angina Questionnaire* (SAQ; Spertus, Winder, Dewhurst, Deyo, Prodzinski, McDonnell, & Fihn, 1995).

Participants

The cohort enrolled in the APPROACH database between July 2006 and January 2014 who met the following inclusion criteria were included in the present study: (1) underwent cardiac catheterization in Alberta; (2) diagnosed with CAD; (3) enrolled in the APPROACH database; and (4) responded to follow-up questionnaires. The response rate at one-year follow up for the APPROACH database was 64-68%. Age was defined as the age at first cardiac catheterization.

Ethical Oversight

This study was approved by the Health Research Ethics Board, University of Alberta, Edmonton, Canada. Permission to use data for research purpose was also obtained from Alberta Health Services, Cardiovascular Health and the Stroke Strategic Clinical Network.

Measurement Tools

The *Seattle Angina Questionnaire* (SAQ) is a 19 item self-administered disease specific QOL questionnaire that employs 5-6 point Likert scales to assess five dimensions of CAD including physical limitation, angina stability, angina frequency, treatment satisfaction and disease perception (Spertus et al., 1995). Scores on each dimension are transformed to a score of 0 to 100 and increasing score indicates better functioning. The internal consistency reliability coefficients in women with chronic stable angina were 0.91, 0.69, 0.72 and 0.67 for physical limitation, angina frequency, treatment satisfaction and disease perception respectively (Kimble, Dunbar, Weintraub, McGuire, Fazio, De & Strickland, 2002). The SAQ also has good test retest reliability and is sensitive to change in clinical condition (Spertus et al., 1995).

Health related quality of life (HRQOL) was measured using the *Euorqol Index 5D* (The Euroquol Group, 1990). The EQ-5D measures HRQOL in the preceding 4 weeks based on the 5 dimensions of health (mobility, self-care, family and leisure activities, pain, and mood) and yields a single score. Each dimension of health is scored from 1 to 5; higher scores on the EQ-5D indicate poorer HRQOL (De Smedt, 2013). The tool's reliability, expressed as Cronbach's alpha, is 0.73 demonstrating an acceptable internal consistency (De Smedt, 2013).

The *HADS* (Zigmond & Snaith, 1983) is used to screen for depressive symptoms. It is widely used in clinical settings to identify clinically significant symptoms of anxiety and depression in patients with chronic disease. The HADS is a 14-item questionnaire containing 7 questions each for depression and anxiety. Responses are scored on a scale of 0–3, with 3 indicating higher symptom frequency (Whelan-Goodinson, Ponsford & Schonberger, 2009). Scores for each subscale can range from 0 to 21; scores greater than 7 are suggestive of depression. Scores for the entire scale (emotional distress) range from 0 to 42, with higher scores indicating more distress, indicating a need for further assessment. Bjelland, Dahl, Haug and

Neckelmann (2002) reviewed 747 studies, which used the HADS and determined that the Cronbach's alpha for the anxiety and depression subscales ranged from 0.68-0.93 and 0.67-0.90 respectively. The sensitivity and specificity of HADS for both subscales was 0.80 (Bjelland, et al., 2002). Cronbach's alpha is a measure of internal consistency of the tool and a Cronbach's alpha of 0.70-0.80 are considered satisfactory and for clinical application with values higher than 0.90 being desirable (Bland & Altman, 1997).

Social support was assessed using the *Medical Outcome Study Social Support Survey* (Sherbourne & Stewart, 1991). The survey yields an overall social support index and scores on four separate functional subscales measuring: (1) emotional/informational social support; (2) tangible social support; (3) affectionate social support; and (4) positive social interaction. Scores are calculated as continuous variables and analyzed on a transformed percentage scale (potential range of 0% –100%), with higher scores indicating greater support (Sherbourne & Stewart, 1991). Internal consistency for the overall support index is 0.97 (Sherbourne & Stewart, 1991).

Data Analysis

Data analysis was performed using the *Statistical Package for the Social Science* (SPSS, version 22.0 ®). Descriptive statistics and frequencies were calculated. Categorical data was presented as percentages whereas numerical data were presented as mean and standard deviation (SD). All the variables were compared in between the two age groups i.e. young (aged <75) and old (aged ≥75) using t-test and chi square. Depression scores were dichotomized into normal (scores < 8) and abnormal (scores > 7) to determine the prevalence of depressive symptoms in the two age groups. Linear regression modelling was employed to evaluate the relationship between age and depression in individuals with coronary artery disease. Predictor variables for the models were selected based on their correlation with the outcome variable (i.e., depression scores). Age was treated as categorical variable (older adults and younger adults) and depression

scores were treated as continuous variable. Age and female were included in the first model followed by the comorbidities in model 2 and, quality of life, anxiety and social support variables in the third model. Alpha was set at 0.05 for all the tests and p value less than 0.05 was considered statistically significant. Normality of the distribution for variables and linearity for relationships were checked with QQ plot and scatter plot respectively. Moreover, post-hoc Chronbach's alpha was also computed to assess internal consistency of the scales used in the study.

CHAPTER 4

RESULTS

There were 5,888 participants enrolled in the APPROACH database in the period under review, with older adults (age ≥75 years) accounting for 20.8% of the cohort. One year after cardiac catheterization, 13.1% and 15.07% of the older adults (age ≥75 years) reported abnormal depressive and anxiety symptoms on HADS respectively. The depression scores of older adults aged ≥75 years (3.88) were statistically significantly higher than those aged less than 75 years (3.51) ($p<0.001$).

Sample Characteristics

The sample was comprised of 1262 women (21.4%) and 4626 men (78.6%) and the age ranged from 30 -94 years. 13.14% of the total sample screened positive for depressive symptoms whereas 22.1% reported anxiety scores >7. There was a higher proportion of women aged ≥75 years (27.4%) compared with the younger adults (19.9%). Older adults (age ≥75 years) had higher proportion of hypertension (78.5%), cerebrovascular disease (6.5%), Malignancy (7%), prior myocardial infarction (13.9%), prior coronary artery bypass grafting (4.2%), gastrointestinal disease (7.8%), pulmonary disease (15.8%), renal disease (5.1%), and congestive heart failure (14%). Whereas, younger adults had higher body mass index (BMI; 29.05) and higher proportion of co-morbid diseases including hyperlipidemia (75.5%), and acute coronary syndrome (53.1%). The proportion of former smokers was higher (41%) in older adults (age ≥75 years) whereas proportion of current smokers was higher (23.4%) in young adults.

Table 4A: Sample Characteristics

	<75 years of age	≥ 75 years of age	P value
N (%)	4661 (79.1)	1227 (20.8)	
Depressed (%)	613 (13.2)	161 (13.1)	1.0
Mean Depression Scores (SD)	3.51 (3.24)	3.88 (3.01)	0.000
Anxious (%)	1117 (23.6)	185 (15.07)	0.000
Mean Anxiety Scores (SD)	5.05 (3.75)	4.22 (3.40)	0.000
Women (%)	926 (19.9)	336 (27.4)	0.000
Mean BMI (SD)	29.05 (4.93)	27.17 (4.42)	0.000
Dialysis (%)	17 (0.4)	6 (0.5)	0.342
Diabetes Mellitus (%)	1021 (21.9)	282 (23)	0.220
Malignancy (%)	140 (3.0)	86 (7)	0.000
Prior CABG (%)	80 (1.7)	52 (4.2)	0.000
Prior PCI (%)	154 (3.3)	47 (3.8)	0.206
Cerebrovascular disease (%)	166 (3.6)	80 (6.5)	0.000
Peripheral Vascular Disease (%)	341 (7.3)	82 (6.7)	0.243
Pulmonary Disease (%)	535 (11.5)	194 (15.8)	0.000
Renal Disease (%)	107 (2.3)	63 (5.1)	0.000
Congestive Heart Failure (%)	296 (6.4)	172 (14)	0.000
Prior MI (%)	398 (8.5)	171 (13.9)	0.000
Hypertension (%)	3216 (69)	963 (78.5)	0.000
Hyperlipidemia (%)	839 (75.5)	839 (68.4)	0.000
GI disease (%)	252 (5.4)	96 (7.8)	0.001
Liver Disease (%)	16 (0.3)	3 (0.2)	0.419
ACS (%)	2747 (58.9)	652 (53.1)	0.000
Family History (%)	1887 (40.5)	292 (23.8)	0.000
Current smoker (%)	1091 (23.4)	83 (6.8)	0.000
Former smoker (%)	1741 (37.4)	503 (41)	0.011

Quality of Life Indicators

Two dimensions of SAQ (Spertus et al., 1995), namely *Physical Limitation* and *Quality of Life (QoL)* were significantly different among the two age groups with older adults (age ≥75 years) reporting better *QoL* ($p<0.001$) and poor *Physical Limitation* scores ($p<0.001$). There were no significant differences in emotional ($p=0.487$), tangible ($p=0.081$) and social support ($p=0.383$) scores among the two groups. Scores on components of *EuroQol index* (The Euroquol Group,

1990) were statistically significantly (p< 0.001) higher in young adults than in older adults (age ≥75 years) except *pain and discomfort* (p= 0.057).

Table 4B: Quality of Live Indicators

	<75 years of age	≥ 75 years of age	P value
Mean SAQ physical limitation (SD)	84.77 (19.13)	72.24 (23.64)	0.000
Mean SAQ Angina Frequency (SD)	91.85 (14.93)	91.10 (15.70)	0.129
Mean SAQ Treatment Satisfaction (SD)	90.52 (15.09)	90.80 (13.88)	0.538
Mean SAQ Quality of Life (SD)	77.97 (19.98)	80.35 (90.40)	0.000
Mean Emotional Support (SD)	70.53 (26.29)	71.13 (26.23)	0.487
Mean Tangible Support (SD)	78.18 (28.42)	76.55 (28.88)	0.081
Mean Affectionate Support (SD)	80.02 (28.57)	82.02 (25.75)	0.021
Mean Social Support (SD)	77.15 (26.23)	76.41 (25.96)	0.383
Mean EQ Mobility (SD)	1.17 (0.37)	1.33 (0.47)	0.000
Mean EQ Self-care (SD)	1.03 (0.19)	1.09 (0.29)	0.000
Mean EQ Usual Activities (SD)	1.23 (0.45)	1.38 (0.53)	0.000
Mean EQ Pain and Discomfort (SD)	1.28 (0.48)	1.31 (0.49)	0.057
Mean Anxiety and Depression (SD)	1.31 (0.50)	1.25 (0.45)	0.000

Depression

An independent t-test was used to determine if there was a difference in depression scores among the two age groups (i.e., younger [<75years] and older [> 75 years]) adults. A two tailed independent t-test with alpha set at 0.05 showed that the depression scores among older adults aged≥75 years (3.88) were statistically significant higher (t_{5886}= -3.572, p < 0.001) than those of participants aged < 75 years (3.51).

Regression Analysis

Model 1 with age ≥75 years and female sex as predictors, explained 0.3% of the variability of depression scores (p<0.001). Model 2 explained 2.6% of the variability of the depression scores when comorbidities were added in the second model. In model 3 with the addition of quality of life measures, smoking status and anxiety scores R squared increased to

0.582, predicting 58.2% of variability of the depression scores. P values in model 3 indicated that age, female sex, current smokers, EQ- self-care, EQ- Usual Activities, EQ- pain and discomfort, EQ- anxiety and depression, SAQ- physical limitation score, SAQ- angina frequency domain,

Table 4C: Regression Analysis

	Model 1	Model 2	Model 3
R Squared	0.003	0.026	0.582
Variables	Standardized coefficients		
Age ≥75 years	0.052***	0.040**	0.049***
Women	-0.018	-0.017	0.092***
BMI		0.050**	0.016
Malignancy		0.000	0.012
Prior CABG		0.027	-0.005
Cerebrovascular disease		0.034*	0.011
Pulmonary disease		0.089***	0.018
Renal disease		0.031*	0.012
Congestive heart failure		0.037*	0.014
Prior MI		0.058***	0.017
Hypertension		0.007	0.007
Hyperlipidemia		-0.012	-0.007
GI Disease		0.000	-0.002
ACS		-0.009	-0.012
Family History		0.007	0.002
Current Smoker			0.025*
Former Smoker			-0.005
EQ 5D Mobility			0.024
EQ 5D Self Care			0.030**
EQ 5D Usual Activities			0.099***
EQ 5D Pain and discomfort			0.037**
EQ 5D Anxiety and depression			0.137***
SAQ Physical Limitation			-0.150***
SAQ Angina Frequency			0.031*
SAQ Treatment Satisfaction			-0.049***
SAQ – quality of life			-0.012
HADS Anxiety Scores			0.412***
Emotional Support Scores			-0.081***
Tangible Support Scores			0.011
Affectionate Support Scores			0.004
Social Support Scores			-0.100***

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

SAQ- treatment satisfaction domain, HADS anxiety scores, emotional support scores and social support scores remained independently predictive of depression scores. As well age ≥75 years was independently predictive of depression scores in all three models. However, female sex was only significant in the third model with the addition of quality of life indicators. None of the comorbidities significantly predicted depression scores in the final model suggesting that age≥75 years, female sex, quality of life determinants, anxiety scores and being a current smoker predicts 58.2% of the variability of depression scores on HADS.

The HADS anxiety score was the most important predictor of depression score followed by physical limitation score, EQ- anxiety and depression score, social support, SAQ- usual activities, female sex, emotional support, age and SAQ- treatment satisfaction. Age ranked eighth in predicting depression scores with present smokers being the weakest after, SAQ- angina frequency, pain and discomfort and current smokers.

Reliability and Power Analysis

Internal reliability for the scales used in the study, measured using Cronbach's alpha resulted in the following. HADS (0.793), SAQ (0.796), EQ index, (0.728) and total support scale (0.877). The power of the study computed using the G* Power version 3.1® is 1.0 with effect size of 1.427. The high power of the study suggests that the study doesn't fail to reject the null hypothesis when it is false. Since a large sample size was used for the study, the probability of Type I error is low with alpha set as 0.05.

CHAPTER 5

DISCUSSION

The study presents two major findings. The first finding is related to the differences in HADS depression scores. There was a significant difference ($p<0.001$) in depression scores among older adults aged ≥ 75 years (3.88) and young adults aged <75 years (3.55) in the cohort. The second finding is related to the factors that were independently significantly predictive of higher scores on the HADS depression scale such as smoking, anxiety, physical inactivity, and social support.

There is evidence that supports a relationship between old age and depression. (Mirowsky & Ross, 1992; Wade and Cairney, 1997; Stordal, Mykletun and Dahl, 2003). In the current study, the prevalence of depressive symptoms was 13.1% in contrast to a study conducted by Koivula, Halme and Astedt-Kurki (2010) in which the prevalence of depression among individuals ≥ 65 years of age with CAD was reported to be 30%. Possible explanations for this two-fold difference are the variances in method. Koivula and colleagues followed participants nine years after CABG surgery using, *Zung Self-Rated Depression Scale* (Zung, 1965). Another factor to consider is their sample size, which is only 2.5% of the current study sample. Koivula and colleagues did not include participants who were medically managed or had a percutaneous intervention as was done in the current study. Prevalence estimates of depression come from cross-sectional studies which often lack sufficient sample size and power. It also lacks discrimination between community older adults and those from residential homes (Kessler et al., 2010; O'Connor, 2006; Chong, et al., 2001; Jorm, 2000; Beekman, et al., 1999; Lyness, et al., 1995)

The difference in depression rates between the two age groups can be explained by factors associated with aging. Since depression is caused by the interaction of biological, social

and psychological factors (Kupfer, Brent, Lewis, Reynolds & Thase, 2008), we have a reason to believe that the symptoms of depression differ in older adults when compared to young people. This may explain why depression is under diagnosed and under treated in older adults (Gathuru, Odukoya & Thorpe, 2016; Halfin, 2007; Lyness, et al. 1995). Older adults tend to exhibit severe psychomotor retardation or agitation, cognitive impairment, depressive delusions, and paranoia as depressive symptoms (Semple & Smyth, 2013). They are known to report more somatic symptoms than mood symptoms. Moreover, some studies reported that depressive symptoms (e.g. loneliness, low mood, changes in sleep and appetite etc.) are perceived as normal part of aging by the health care professionals resulting in under recognition and under treatment of depression (Murray, Banerjee, Byng, Tylee, Bhugra & Macdonald, 2006; Burroughs, Lovell, Morley, Baldwin, Burns & Chew-Graham, 2006). However, it is important to note that there is an increased emphasis on not considering these symptoms as normal part of aging and any such symptom should be ruled out by a clinician. Difference in symptoms also emphasizes the importance of using modified tool with established reliability and validity to screen depression in older adults such as *Geriatric Depression Scale* (Parmelee & Katz, 1990) or *CES-D* (Radloff, 1977).

The second major finding is related to the factors contributing to depression. Factors that significantly predict higher depressive symptoms in the current study can be divided into modifiable factors (e.g., smoking status, activity, anxiety, depression, treatment satisfaction and, social and emotional support) and non-modifiable factors (e.g., age and sex). Modifiable factors are of prime interest in the current study because of their role in preventing and/or minimizing the risk of disease. Results in the current study are significant in the light of a review done by Whooley and Wong (2013) in which they identified biological and behavioural factors explaining the bidirectional relationship between depression and cardiac disorders. The

behavioural factors that significantly predict depressive symptoms in patients with coronary disease include physical limitation scores, smoking, social support and anxiety. Whooley and Wong (2013) didn't include anxiety as a behavioural factor in their review however; it was the most important factor predicting depressive symptoms in our population.

Anxiety

Anxiety was the most important predictor of depressive symptoms in the current study. Anxiety commonly co-occurs with depression (Rivas-Vazquez et al., 2004; Rapaport, 2001), particularly in CAD populations (Chang, Chen, Lee, Chen, Yang, & Chen, 2016; José, et al., 2016). A study of the latent structure of HADS and the links between the anxiety and depression revealed that there is an underlying affective state common for anxiety and depression which represents overall emotional distress (Spurgeon, James & Sackley, 2016). The study also reported decreasing differentiation between the anxiety and depression when the symptom severity increases (Spurgeon, James & Sackley, 2016). Moreover the validity studies on HADS reports high correlation between anxiety and depression suggesting a relationship between the two (Zigmond & Snaith, 1983; Bjelland, 2002). Cardiac events such as myocardial infarction or angina are sudden and may result in serious consequences therefore, patients experience anxiety. Anxiety could be related to catheterization procedure, lifestyle changes, management of heart attack or physical limitations (Sheps & Sheffield, 2001) and is associated with adverse outcomes (Januzzi, Stern, Pasternak & DeSanctis, 2000). Anxiety is also found to be associated with increased mortality especially when it co-occurs with depression (Watkins, L. L., Koch, G. G., Sherwood, Blumenthal, Davidson, O'Connor and Sketch, 2013).

Physical Inactivity

Another predictor in the current study was physical limitation scores. Older adults reported more physical limitation than younger participants. There are clear associations among

physical inactivity (Warburton, Nicol & Bredin, 2006), depression (Strawbridge et al., 2006), cardiovascular disease (Lee, Shiroma, Lobelo, Puska, Blair, Katzmarzyk & Lancet Physical Activity Series Working Group, 2012), and old age (Wannamethee, Shaper & Walker, 1998). Anhedonia, the inability to feel pleasure, is a common depressive symptom and contributes to decreased physical activity (Leventhal, 2012; Thompson, 2003). Physical inactivity is prevalent in patients with depression and conversely, depressed people have higher odds of physical inactivity (Abu-Omar, Rütten & Lehtinen, 2004; Ströhle, 2009; Vance, Marson, Triebel, Ball, Wadley, & Cody, 2016).

Smoking

Current smokers typically report higher scores on the HADS (Luger, et al., 2014). According to a review of epidemiological studies, depressed individuals reportedly are more likely to smoke and less likely to quit smoking than people who do not exhibit depressive symptoms (Weinberger et al., 2016). They also have high rates of relapse if they quit smoking and are more likely to meet the criteria for nicotine dependence. The literature suggests a bidirectional relationship between smoking and depression (Breslau, et al., 1998; Taylor, et al., 2014). Smoking is associated with increase in risk of new onset major depressive disorder (MDD) and depressed patients are more likely to progress to daily smoking (Breslau, et al., 1998; Luger, et al., 2014). Similar associations were found in the present study. There is also evidence that current and former smokers have greater odds of being depressed, anxious, and of experiencing psychological distress than those who have never smoked (Taylor, 2014). One plausible explanation of this finding is that depressed individuals self-medicate by smoking in order to activate the dopaminergic reward system (Brody, et al., 2004).

Being a former smoker did not predict depression scores. This finding is consistent with the literature. Smoking cessation was reported to be associated with decreased mortality in

patients with CAD (Critchley & Capewell, 2003). However, patients with depression have lower success rates with smoking cessation efforts (Hitsman, et al., 2013). Smoking can be a confounder and a mediator in the relationship of depression and CAD because of its bidirectional relationship with depression (Whooley & Wong, 2013).

Social Support

Another important group of factors identified in the present study are tied to social support. Social support has been found to mediate the relationship between depression and CAD (Uchino, 2006). Since, older adults are more vulnerable to social isolation (Cornwell & Waite, 2009); CAD and depression are more likely to cause devastating effects in late life (Simning, Seplaki & Conwell, 2016). Social isolation is found to increase mortality secondary to CAD (Brummett, et al., 2003; Friedmann, 2006; Simning et al., 2016). Socially isolated individuals are less likely to receive regular medical attention, are less compliant with medication regimes, and are less physically active (Horsten, et al., 2000). Social isolation is also linked to depression (Friedmann, et al., 2006), low socio-economic status, high smoking, rates and high hostility ratings (Brummett, et al., 2003).

Limitations

The limitations of the present study findings are tied to the use of secondary data. As the objective of primary data collection was different from the present study, variables such as past psychiatric history, use of psychotropic medications and medication adherence were not captured. Individuals with psychiatric history or those on psychotropic drugs may contribute to false negative or false positive results on HADS. Therefore, it is recommended to consider these factors in future studies to isolate depression cases and avoid outliers. Another limitation is related to study participants' cardiac diagnosis. All patients undergoing cardiac catheterization may not have CAD which can interfere with the findings. Nonetheless, it is important to note that

patients who undergo cardiac catheterization must exhibit symptoms mimicking myocardial ischemia affecting their overall health. Another important factor is the time at which depression scores are assessed and the mode of treatment received by the patient. Depression may take longer to unveil as the coping mechanisms are exhausted with time. For instance, Koivula, Halme and Astedt-Kurki (2010) found higher prevalence of depressive symptoms in patients nine years after CABG surgery. Moreover, mode of treatment sometimes determines the severity of the disease. Patients who are managed medically may not have as much blockage as those who are treated with PCI or CABG. Additionally, CABG patients also deal with post-surgery complications such as limitations in activity, pain at surgical site etc.

Conclusion

The relationship of depressive symptomatology and CAD has been studied in the general population for over two decades now but the present study is among the first to focus on older adults and CAD. It presents magnitude of depressive symptoms and its predictors among individuals with CAD. Older adults (over 75 years of age) exhibit significantly higher severity of depressive symptoms than younger people diagnosed with CAD. Anxiety, physical inactivity, smoking and social support are the most important predictors of depressive symptoms in patients with CAD.

Findings from this study have implications for nursing practice, research and education. The identified predictors of depressive symptoms are modifiable factors and play an important role in the prevention and treatment of depression in the population of interest. Since depression and CAD have a bidirectional relationship and are associated with increased morbidity and mortality, it is vital to address these factors at primary care and rehabilitation programs. Hospital stay for patients with myocardial infarction is often short with hemodynamic stability and

restoration of myocardial perfusion as priority goal. In such a case psychological well-being is often overlooked leaving patients vulnerable to anxiety and depression as evidenced by high rates of depressive and anxiety symptoms in the study population. Therefore it is important to integrate psychological component in nursing care of patients with cardiac diseases. Psychological assessment and depression screening should be made a part of routine assessment at primary care level and in cardiac rehabilitation programs. Cardiac patients in general and older adults in particular, should be routinely screened for depression at all levels of care and symptoms suggestive of depression should be ruled out by appropriate health care professional. Depressive symptoms should not be considered as normal part of aging and patients should be encouraged to seek psychological help for depressive symptoms. This can be achieved by introduction of short versions of depression screening tools such as *PHQ-2* (Löwe, Kroenke & Gräfe, 2005). *PHQ-2* is a 2 item questionnaire which makes it easy and quick to use in busy health care settings. The score of 3 or more was found to have sensitivity of 83% and a specificity of 92% for major depression (Löwe, Kroenke & Gräfe, 2005). *PHQ-2* is also recommended by American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research and endorsed by the American Psychiatric Association (Lichtman, et al., 2008). Implications for integrating psychological care as part of cardiac rehabilitation program include increasing awareness among health care professionals about the scope and magnitude of problem, educating patients about the increased risk of developing depressive symptomatology, increased mortality and morbidity with pre-existing CAD.

Another important consideration to promote depression active depression screening is healthcare professional training. As discussed earlier, majority of healthcare professionals see

depressive symptoms as normal part of aging and fail to address psychological needs of older patients. Training of health care professionals and integrating psychological assessment such as *PHQ-2* will ensure timely screening, diagnosis and treatment of depression and improve quality of life of the affected individuals. Nurse-led interventions in the area will help in promoting health, alleviate morbidity and mortality, and improve quality of life of older adults which is core to nursing practice. In addition to screening and diagnosis of depression in older adults, there is a need to identify effective treatment options for depression.

Identification of effective treatment modalities can be made possible through nursing research. Future implications for research include qualitative inquiry of depressive symptoms in older adults with CAD to determine the course of depression and its effects on their quality of life. This will provide the healthcare professionals with understanding of the depression and depressive symptoms experienced by older adults which may not be same as younger adults. Moreover, identifying tools with high specificity and sensitivity to screen older adults for depression and depressive symptoms, exploring knowledge, skills and attitudes of healthcare professionals towards late life depression in CAD and most importantly designing intervention and evaluating its effectiveness to prevent and treat depression in individuals with CAD. Moreover, it is also important to study the effects of interventions such as integrated care model for cardiac depression and role of antidepressants in effective treatment of depression. The research findings will further inform nursing practice and education. It will promote evidenced based practice in clinical settings and play a role in curriculum designing with focus on psychological assessment in cardiac patients. Moreover teaching nursing students easy to use screening tools to help in early detection of depressive symptoms and provision of holistic care.

In conclusion, depressive symptoms are prevalent in patients with CAD. Factors such as anxiety, physical inactivity, smoking and social support are important predictors of depressive

symptoms and should be addressed at all care levels to improve quality of life and promote wellness in older adults with CAD.

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APPENDIX A

Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983))

This questionnaire will help your physician know how you are feeling. Read every sentence. Place an "X" on the answer that best describes how you have been feeling during the LAST WEEK. You do not have to think too much to answer. In this questionnaire, spontaneous answers are more important. Mark only one answer for each question.

A (1) I feel tense or wound up:
- 3 ( ) Most of the time
- 2 ( ) A lot of times
- 1 ( ) From time to time
- 0 ( ) Not at all

D (2) I still enjoy the things I used to:
- 0 ( ) Definitely as much
- 1 ( ) Not quite so much
- 2 ( ) Only a little
- 3 ( ) Hardly at all

A (3) I get a sort of frightened feeling as if something awful is about to happen:
- 3 ( ) Very definitely and quite badly
- 2 ( ) Yes, but not too badly
- 1 ( ) A little, but it doesn't worry me
- 0 ( ) Not at all

D (4) I can laugh and see the funny side of things:
- 0 ( ) As much as I always could
- 1 ( ) Not quite as much now
- 2 ( ) Definitely not so much now
- 3 ( ) Not at all

A (5) Worrying thoughts go through my mind:
- 3 ( ) Most of the time
- 2 ( ) A lot of times
- 1 ( ) From time to time
- 0 ( ) Only occasionally

D (6) I feel cheerful:
- 0 ( ) Most of the time
- 1 ( ) Usually
- 2 ( ) Not often
- 3 ( ) Not at all

A (7) I can seat at ease and feel relaxed:
- 0 ( ) Definitely
- 1 ( ) Usually
- 2 ( ) Not often
- 3 ( ) Not at all

D (8) I feel as I am slowed down:
- 3 ( ) Nearly all the time
- 2 ( ) Very often
- 1 ( ) From time to time
- 0 ( ) Not at all

A (9) I get a sort of frightened feeling like butterflies in the stomach:
- 0 ( ) Not at all
- 1 ( ) From time to time
- 2 ( ) Quite often
- 3 ( ) Very often

D (10) I have lost interest in my appearance:
- 3 ( ) Definitely
- 2 ( ) I don't take so much care as I should
- 1 ( ) I may not take quite as much care
- 0 ( ) I take just as much care as ever

A (11) I feel restless, as if I had to be on the move:
- 3 ( ) Very much indeed
- 2 ( ) Quite a lot
- 1 ( ) Not very much
- 0 ( ) Not at all

D (12) I look forward with enjoyment to things:
- 0 ( ) As much as I ever did
- 1 ( ) A little less than I used to
- 2 ( ) Definitely less than I used to
- 3 ( ) Hardly at all

A (13) I get a sudden feeling of panic:
- 3 ( ) Very often indeed
- 2 ( ) Quite often
- 1 ( ) From time to time
- 0 ( ) Not at all

D (14) I can enjoy a good TV or radio program or book:
- 0 ( ) Often
- 1 ( ) Sometimes
- 2 ( ) Not often
- 3 ( ) Hardly at all

APPENDIX B

Seattle Angina Questionnaire (Spertus et al., 1995)

Seattle Angina Questionnaire

1. The following is a list of activities that people often do during the week. Although for some people with several medical problems it is difficult to determine what it is that limits them, please go over the activities listed below and indicate how much limitation you have had **due to chest pain, chest tightness, or angina over the past 4 weeks.**

Place an x in one box on each line.

Activity	**Severely Limited**	**Moderately Limited**	**Somewhat Limited**	**A Little Limited**	**Not Limited**	**Limited, or did not do for other reasons**
Dressing yourself	❑	❑	❑	❑	❑	❑
Walking indoors on level ground	❑	❑	❑	❑	❑	❑
Showering	❑	❑	❑	❑	❑	❑
Climbing a hill or a flight of stairs without stopping	❑	❑	❑	❑	❑	❑
Gardening, vacuuming, or carrying groceries	❑	❑	❑	❑	❑	❑
Walking more than a block at a brisk pace	❑	❑	❑	❑	❑	❑
Running or jogging	❑	❑	❑	❑	❑	❑
Lifting or moving heavy objects (e.g. furniture, children)	❑	❑	❑	❑	❑	❑
Participating in strenuous sports (e.g. swimming, tennis)	❑	❑	❑	❑	❑	❑

2. Compared with 4 weeks ago, how often do you have **chest pain, chest tightness, or angina** when doing your **most strenuous** level of activity?
I have had **chest pain, chest tightness,** or **angina**...

Much more often	**Slightly more** often	About **the same**	**Slightly less** often	**Much less** often
❑	❑	❑	❑	❑

3. Over the past 4 weeks, on average, how many times have you had **chest pain, chest tightness, or angina?**
I get **chest pain, chest tightness,** or **angina**...

4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks
❑	❑	❑	❑	❑	❑

4. Over the past 4 weeks, on average, how many times have you had to take nitros (nitroglycerin tablets) for your **chest pain, chest tightness,** or **angina?**
I take nitros...

4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks
❑	❑	❑	❑	❑	❑

5. How bothersome is it for you to take your pills for **chest pain, chest tightness** or **angina** as prescribed?

Very bothersome	**Moderately** bothersome	**Somewhat** bothersome	**A little** bothersome	**Not** bothersome at all	My doctor has **not prescribed** pills
❑	❑	❑	❑	❑	❑

6. How satisfied are you that everything possible is being done to treat your **chest pain, chest tightness, or angina**?

Not satisfied at all	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Highly satisfied
❑	❑	❑	❑	❑

7. How satisfied are you with the explanations your doctor has given you about your **chest pain, chest tightness, or angina**?

Not satisfied at all	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Highly satisfied
❑	❑	❑	❑	❑

8. Overall, how satisfied are you with the current treatment of your **chest pain, chest tightness, or angina**?

Not satisfied at all	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Highly satisfied
❑	❑	❑	❑	❑

9. Over the past 4 weeks, how much has your **chest pain, chest tightness, or angina** interfered with your enjoyment of life?

It has **severely** limited my enjoyment of life	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **barely** limited my enjoyment of life	It has **not** limited my enjoyment of life
❑	❑	❑	❑	❑

10. If you had to spend the rest of your life with your **chest pain, chest tightness, or angina** the way it is right now, how would you feel about this?

Not satisfied at all	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Highly satisfied
❑	❑	❑	❑	❑

11. How often do you worry that you may have a heart attack or die suddenly?

I can't stop worrying about it	**I often** think or worry about it	**I occasionally** worry about it	**I rarely** think or worry about it	**I never** think or worry about it
❑	❑	❑	❑	❑

APPENDIX C

Euroqol Index (The Euroquol Group, 1990)

APPENDIX D

Medical Outcome Study Social Support Survey (Sherbourne & Stewart, 1991)

Social Support Survey Instrument

People sometimes look to others for companionship, assistance, or other types of support. How often is each of the following kinds of support available to you if you need it? Choose one number from each line.

Social Support Survey Resources

Scoring Instructions for MOS Social Support Survey Instrument

Emotional/informational support	None of the time	A little of the time	Some of the time	Most of the time	All of the time
Someone you can count on to listen to you when you need to talk	1	2	3	4	5
Someone to give you information to help you understand a situation	1	2	3	4	5
Someone to give you good advice about a crisis	1	2	3	4	5
Someone to confide in or talk to about yourself or your problems	1	2	3	4	5
Someone whose advice you really want	1	2	3	4	5
Someone to share your most private worries and fears with	1	2	3	4	5
Someone to turn to for suggestions about how to deal with a personal problem	1	2	3	4	5
Someone who understands your problems	1	2	3	4	5

Tangible support	None of the time	A little of the time	Some of the time	Most of the time	All of the time
Someone to help you if you were confined to bed	1	2	3	4	5
Someone to take you to the doctor if you needed it	1	2	3	4	5
Someone to prepare your meals if you were unable to do it yourself	1	2	3	4	5
Someone to help with daily chores if you were sick	1	2	3	4	5

Affectionate support	None of the time	A little of the time	Some of the time	Most of the time	All of the time
Someone who shows you love and affection	1	2	3	4	5
Someone to love and make you feel wanted	1	2	3	4	5
Someone who hugs you	1	2	3	4	5

Positive social interaction	None of the time	A little of the time	Some of the time	Most of the time	All of the time
Someone to have a good time with	1	2	3	4	5
Someone to get together with for relaxation	1	2	3	4	5
Someone to do something enjoyable with	1	2	3	4	5

Additional item	None of the time	A little of the time	Some of the time	Most of the time	All of the time
Someone to do things with to help you get your mind off things	1	2	3	4	5

APPENDIX E

APPROACH access request form

APPROACH
Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease

REQUEST for ACCESS to APPROACH ONLINE

Fax completed form to: 403-210-9837 or Email: support@approach.org

***Please print clearly to avoid delays in receiving your User Account Access**

Date: _____ Date Access Required: _____

Circle one: **CREATE** **Name Change** **Deactivate account** **Site Change**

Name (please print): **Last Name:** _____ **First Name:** _____

If Name change: **Previous Last Name:** _____

AHS username: _____

Primary Site: _____ **Unit:** _____

Secondary Site: _____ Unit: _____

Job Title: _____

Describe what Position and Role you have? (i.e. Admission Nurse, Physician (type), Unit Clerk, Cath Lab, Admin Secretary, Nuclear Tech, CT Tech, Researcher etc.) _____

Will you ENTER Data into APPROACH? Circle One **Yes** **No**

If YES, please tick beside the modules you'll enter.

- ☐ Patient
- ☐ CathLab Referral ☐ Cath Procedure ☐ PCI Procedure ☐ CARAT
- ☐ Surgery Referral ☐ Surgery Procedure
- ☐ Admission ☐ Navigation ☐ Cardiac Function Clinic ☐ Survey
- ☐ CT Referral ☐ CT ☐ Nuclear Test Referral ☐ Nuclear Test
- ☐ Heart Rhythm Devices Referral ☐ Heart Rhythm Devices
- ☐ THV Referral ☐ THV

Work Phone: _____

Work Email: _____

Your password will be sent to the email address provided

Site Authorizing Personnel:

Name: _____ Title: _____

Phone: _____ Email: _____

Authorized Signature: _____

FOR APPROACH USE ONLY

Approval Granted by:

Date of Approval:

APPROACH ID#: COP ID#: Staff ID:

APPENDIX F

APPROACH database patient questionnaire (Ghali & Knudtson, 2000)

University of Alberta Hospitals - Cath Report

[redacted] v1.09

TESTING, APPROACH
8111 ABC, 1st Floor
8440-112st
EDMONTON, AB T6G2B7
(780) 407-7504

PHN: 5556-5678
Hosp Nr: 87654321

Height: 165.0 cm
Weight: 70.0 kg
BMI: 25.7

Gender: Male
Birth Date: Oct 20,1938
Cath Date: Feb 29,2000

Priority: *Urgent - In Hospital*

Printed on Fri, Mar 03,2000

Cath Date: Feb 29,2000
Refer Physician: Dr. JANE ANDERSON
Perform Cardio: Dr. RICK JONES
Assist Cardio: Dr. JOHN SMITH

CINE #: **CLN:**
Tech #1: Approach Admin
Tech #2: None

Work Status: Full Time
Admission CCS Class: IVa
Protocol: None
Access Site: Right Radial

Indication: **Acute Coronary Syndrome**
ECG(worst): ST elevation
Peak CK: 650 **Peak Troponin I:** 2
Ischemia: Ongoing
Peak Troponin T: 0
C Reactive Protein: 0.0
Antithrombotic -> ReoPro ->
Fibrinolytic -> nPA ->
CHF-> ☐ Yes ☑ No **Hemodynamic Instability->** ☑ Yes ☐ No **Cardiogenic Shock->** ☐ Yes ☑ No

TESTS (Less Than Three Months)

- ☐ Treadmill
- ☐ Thallium
- ☐ Echo

Electrocardiogram

	Q	ST↑	ST↓	T↓
I, aVL	☐	☐	☐	☐
V_{1-3}	☐	☐	☑	☐
V_{4-6}	☐	☑	☐	☐
II, III, aVF	☐	☑	☐	☐

ECG Not Avail: ☐ Yes
ECG Normal: ☐ Yes
Atrial Fibrillation: ☑ Yes ☐ No
Pacemaker: ☐ Yes ☑ No
LBBB: ☐ Yes ☑ No
LVH: ☐ Yes ☑ No

OutCome Determinants/Relevant Data

	?	Yes	No
Hypertension	☐	☑	☐
Hyperlipidemia	☐	☑	☐
-Cholesterol mmol/L: 6.200			
-Triglycerides mmol/L: 1.950			
-HDL mmol/L: 0.650			
-LDL mmol/L: 3.700			

Diabetes Mellitus	Yes	No
Type I	☐	☑
Type II (Insulin)	☐	☑
Type III (No Insulin)	☑	☐
HGA1C	0.70	

	?	Yes	No
Prior Infarction	☐	☐	☑
Prior PTCA	☐	☑	☐
Prior CABG	☐	☐	☑
Congestive Heart Failure	☐	☐	☑
Peripheral Vascular Disease		☐	☑
Cerebrovascular Disease		☐	☑

Renal Insufficiency	Yes	No
-Dialysis	☐	☑
-Creatinine Level: 87		

Co-morbidity Factors	Yes	No
Pulmonary	☐	☑
Liver GL	☐	☑
Malignancy	☐	☑

Smoking: ☐ Never ☑ Current ☐ Former
Date Quit:

Meds:
- ☑ Beta-Blocker
- ☐ IV Nitro
- ☐ LA Nitrates
- ☐ Ca Channel Blocker
- ☑ Lipid-Lowering
- ☐ ACE
- ☑ ASA (Aspirin)
- ☐ Oral IIb/IIIa Recep Blockers
- ☐ Ticlopidine/Clopidogrel
- ☑ Oral Hypoglycemics
- ☐ Hormone Rep Therapy
- ☐ Anticoagulants
- ☐ Antidepressants

LV EF - Angiography:
Calc: 38% Estimate: 30-50% Reason: Not Entered
LV EF - Non-invasive Methods:
Based On: Not Entered Calc: 0% Estimate: Not Entered

Angiographer's Initial Recommendations:
PTCA
Extent Coronary Artery Disease: 2- VD(>75% prox LAD)
Duke Jeopardy Score: 66.67%

Complications:
- ☑ Prolonged Angina
- ☐ Myocardial Infarction
- ☐ Cerebral Vascular Accident
- ☐ None
- ☐ Pulmonary Edema
- ☐ Emergency Surgery
- ☐ VT/VF Converted
- ☐ Death
- ☐ Access Site Complications
- ☐ Anaphylactic Reaction
- ☐ Contrast Allergy
- ☐ Acute Closure During Cath
- ☐ Other

Note: See attached Heartview Diagram

Submitted By: _____
Dr. RICK JONES

APPENDIX G

University of Alberta, Health Ethics Research Board Ethics Approval

UNIVERSITY OF ALBERTA

Fahreen Rajani <fahreeni@ualberta.ca>

HERO: Your Ethics Application is Approved Pro00047661

hero@ualberta.ca <hero@ualberta.ca>
Reply-To: DoNotReply@ais.ualberta.ca
To: fahreeni@ualberta.ca

Wed, May 6, 2015 at 7:02 PM

UNIVERSITY OF ALBERTA

Ethics Application has been Approved

ID:	Pro00047661
Title:	Predictors of Depressive Symptoms in Older Adults with Coronary Artery Disease (CAD)
Study Investigator:	Geraldine Lasiuk
Description:	This is to inform you that the above study has been approved. Click on the link(s) above to navigate to the HERO workspace. Note: Please be reminded that the REMO system works best with Internet Explorer or Firefox. Please do not reply to this message. This is a system-generated email that cannot receive replies.

University of Alberta
Edmonton Alberta
Canada T6G 2E1