ASSESSING GENDER BIAS IN ACUTE MEDICAL CARE IN CANADA

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Assessing Gender Bias in Acute Medical Care in Canada

by

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Abstract

Background: Gender bias has been explored extensively in the treatment of cardiovascular disease (CVD), particularly acute myocardial infarction (AMI). Previous research is inconsistent in suggesting that women who suffer an AMI are treated less optimally than men. To date, gender bias has not been well addressed in other CVDs, specifically cerebrovascular accident (CVA), coronary revascularization, or chronic kidney disease (CKD). In an attempt to get a clearer grasp of the problem, community acquired pneumonia (CAP) was also studied and served as a non-vascular disease control.

Methods: Using trained research nurses, retrospective chart reviews were completed for all patients admitted with AMI, CVA, for coronary revascularization, or CAP in 1995/6, 1998/9, and 2000/1 in two locations of Newfoundland (St. John's and Central Newfoundland). CKD care was analyzed using data from the STARRT (Study To Assess Renal Replacement Therapy) study, a Canadian multicentre retrospective chart review of incident dialysis patients followed for six months. All results were divided into three categories – access, intervention, and outcome – and, after controlling for baseline demographics, were explored for differences in care between men and women.

Results: Women were often older than men and suffered from more co-morbidities and more severe medical histories, except for CAP where men were more likely to have co-morbid illnesses. Women who had suffered an AMI had a significantly longer time to thrombolytics (70 vs. 45 mins.,

p=0.02) and were less likely to be admitted to the CCU (84% vs. 91%, p=0.02). Women with severe CAD were more likely to receive medical management (42% vs. 28%, p=0.005) and, of the women who did receive CABG, had longer wait times in one priority for CABG group (8.0 vs. 6.0 days, p=0.05). Women began dialysis with a lower eGFR level (8.6 vs. 10.1 mL/mins., p=0.006) after receiving less pre-dialysis care than men (>1 mth. vs. <1 mth.) (80% vs. 88%, p=0.05). There was no evidence of a gender bias against women in CVA patients, in fact women were more likely to be seen by a social worker than men (43% vs. 34%, p=0.01). Of the patients receiving treatment for CAP, women were less likely than men to receive the appropriate antibiotics (AB) when considering the 1993 guidelines for AB treatment (70% vs. 78%, p=0.03). While women received less optimal access and interventions, the proportion of death between men and women for all CVDs analyzed were similar.

Conclusions: Women are not treated with the same quality of care as men with regards to access and intervention for AMI's, coronary revascularization, and CKD. This bias was also found in a non-vascular control group. A potential gender bias in the treatment of these patients needs to be explored further.

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Table i Abbreviation Table

Term	Abbreviation
Cardiovascular Disease	CVD
Acute Myocardial Infarction	AMI
American Heart Association	AHA
National Institutes of Health	NIH
Newfoundland and Labrador	NL
Cerebrovascular Accident	CVA
Chronic Kidney Disease	CKD
Community Acquired Pneumonia	CAP
Electrocardiogram	ECG
ST-Segment Elevated Myocardial Infarction	STEMI
Acetylsalicylic Acid	ASA
Percutaneous Coronary Intervention	PCI
Coronary Artery Bypass Graft	CABG
Computed Tomography	CT
Magnetic Resonance Imaging	MRI
Coronary Artery Disease	CAD
Intravenous	IV
Antibiotic	AB
Glomerular Filtration Rate	GFR
Estimated Glomerular Filtrated Rate	eGFR
Renal Replacement Therapy	RRT
End-Stage Kidney Disease	ESKD
Hemodialysis	HD
Peritoneal Dialysis	PD
Arteriovenous	AV
Central Venous Catheters	CVC
Chronic Heart Failure	CHF
Chronic Obstructive Pulmonary Disease	COPD
Angiotensin Converting Enzyme	ACE
Body Mass Index	BMI
Study to Assess Renal Replacement Therapy	STARRT
Pneumonia Severity Index	PSI
Intensive Care Unit	ICU
Transient Ischemic Attack	TIA
Coronary Care Unit	CCU
Angiotensin Type 1 Receptor Blocker	ARB
Hormone Replacement Therapy	HRT
Canadian Cardiovascular Society	CCS
Left Ventricle	LV
World Health Organization	WHO
Modification of Diet in Renal Disease Study	MDRD

Chapter 1 Introduction

1.1 Cardiovascular Disease

Cardiovascular diseases (CVD), the class of diseases involving the heart or blood vessels, are among the leading causes of death throughout the world. CVD accounts for the death of more Canadians than any other disease [1]. Every seven minutes in Canada, someone dies from heart disease or stroke [1]. In 2004, 29% of the total deaths in the world and 32% in the Americas were caused by CVD [2]. In the same year in Canada, the age-standardized mortality per 100,000 was 131 – 165.6 for males and 101.7 for females [3]. The following year, diseases of the heart accounted for 31% of all deaths in Canada (30% male, 31% female) [1].

Not unexpectedly, CVD carries with it a large financial burden. In 2000, CVD associated costs in Canada exceeded $20 billion [4]. Of that, $7.6 billion were direct health care costs and $14.6 billion were felt indirectly through lost economic productivity [4]. In 2005, 57.4 million prescriptions for the treatment of CVD were written, up from 52.5 million in 2003 [4]. In the fiscal year 2005/6, CVD was accountable for the highest proportion of days (17%; 19% male, 15% female) spent in the hospital [4]. In 2007, 10% (34.6 million) of all visits to physicians were for the management of CVD [4].

Cardiovascular diseases are caused by atherosclerosis, a hardening of the arteries [5]. It is believed that atherosclerosis begins very early in life; everyone is born with healthy arteries but over time

blood flow becomes restricted [5]. This restriction has the potential to cause blood clots which may lead to heart attacks, strokes, or other deadly complications.

CVD touches a broad range of people. In Canada, people of all ages and backgrounds are affected. Today, CVD sufferers are more commonly female, younger, of lower socioeconomic status, less educated, of diverse races, and very often Aboriginal/Indigenous or South Asian Canadians [5].

The Public Health Agency of Canada provides a list of risk factors for CVD which include atherosclerosis, smoking, lack of exercise, unhealthy eating, obesity, high cholesterol, hypertension, stress, and diabetes [4]. Unbeknownst to many, nine out of 10 Canadians possess at least one of these risk factors and one in three Canadians have three or more risk factors [5]. Unfortunately, it is also not very widely known that many of these risk factors are preventable by altering dietary consumption and living an active lifestyle. There are also some non-modifiable risk factors for CVD which include age, ethnicity, sex, and family history [4]. Some risk factors are unique to women. Menopause, or any estrogen deficiency, is associated with an increased risk of CVD [6]. As well, studies on combined (estrogen and progestin) oral contraceptives with high (50-150μg/d) or medium (35-50 μg/d) estrogen doses have shown to be associated with increases in acute myocardial infarction (AMI) rates [6]. This risk is elevated further in women who also smoke.

CVD is a well researched topic and often the focus of Canadian health care. This is partially due to the fact that CVD is the number one killer of Canadians [1], but is also because of the preventable

nature of its risk factors [5]. When certain cardiovascular diseases are detected early and treated appropriately, they can be controlled [5]. Many of the causes, risk factors, and solutions of CVD are known (i.e. smoking, diet, exercise) yet most Canadians do little to prevent them.

1.2 A Man's Disease

In today's Western world, women have come to expect and demand equality in all areas. The last few decades have seen great progress in the fight for equal rights in many areas of women's daily lives. Unfortunately, medicine is not one of those areas; bias and inequality still exist in the way women are treated in today's health care system.

In 1960, the American Heart Association (AHA) sponsored a conference entitled "How I Can Help My Husband Cope with Heart Disease" [7]. Clearly at this time it was believed that heart disease predominantly affected men. Medical research involving women focused primarily on reproductive issues. Women of childbearing age were often excluded from trials of new drugs and treatments. This was partially due to potential for treatment associated birth defects and the concern that hormonal changes might alter the effects of the treatment being tested [8]. However, women of all ages were often excluded from clinical research. Investigators have claimed that normal variations in female hormone balance make the results of clinical studies too difficult to interpret. This logic does not explain every situation where women are left out of clinical trials and, unfortunately, exclusions such as this led to a lack of knowledge about optimal cardiac care for women.

1.3 Women and Research

In 1990 the Congressional Women's Caucus turned to legislative action and created the Women's Health Equity Act [9]. This was "designed to address some of the worst abuses in the disgraceful pattern of neglect regarding women's health" [10]. It also aimed to provide better healthcare for women into the next century. As a result, the National Institutes of Health (NIH) formed Research on Women's Health, an office dedicated to female health research. It is important to note that at this time American women comprised 53% of the population, made 25% more doctor visits than men, yet research involving women or their health issues received only 13% of the NIH research budget [10].

Overall, efforts to increase representation of women in clinical trials have been mildly successful, but this is primarily due to an increase in a few large single-sex trials; cancer trials (breast, cervical, or uterine), and the Women's Health Study [11-13]. Since 1990 there has been an increase in the number of women participating in clinical trials that involve both sexes, however this increase rarely produces trials with a 50/50 split of males to females [14]. Many studies use less than 35% female and more than 65% male subjects [15]. For example, a study published in the American Heart Journal in 2001 examined gender differences in chest pain in patients with coronary artery disease (CAD). The primary focus of the study was to access sex-based differences but only 13% of the patients were female [16]. A survey of studies published in 2006 found that only 37% of trial participants were women and only 13% of studies analyzed data by sex [17]. A regrettable result of such research is that it may lead to practice where women are given the same treatments as men even though female participation was limited in the clinical research. Biological differences affect

the way men and women respond to medications and therapeutics. Despite the obvious physical and physiological differences between men and women, medications are rarely prescribed with gender in mind. These studies may be less externally valid or generalizable to women. In addition, the use of results of studies that include limited female involvement further amplifies the gender inequity problem.

1.4 Yentl Syndrome

In 1991 Bernadine Healy, the first female director of the US NIH, recapped two studies that she believed established a gender bias in treatment of CVD [18]. In the first, women were less likely than men to be referred to diagnostic and therapeutic treatments when admitted for an acute coronary event [19]. In the second, women were equally as likely as men to undergo similar treatments if they were found to have significant coronary disease [20]. Healy used these studies to describe what she called the Yentl syndrome: "Once a woman showed that she was just like a man, by having severe coronary artery disease ..., then she was treated as a man would be." [18]. Yentl takes reference from a short story by Isaac Singer. In the story, Yentl had to pretend to be a boy in order to attend school and become educated in the Talmud – a text in mainstream Judaism that pertains to Jewish law, ethics, customs, and history [21]. In real life, Healy had just uncovered the phenomenon that women are only treated as equal to men when their symptoms are deemed to be equal. Since Healy's article, Yentl syndrome has been expanded beyond CVD and now includes any medical situation where a woman must show that she is equal to a man in terms of risk factors or disease severity to receive the same treatment a man would.

The aftermath of Healy's 1991 article sparked an intense and heated debate over gender differences in diagnostic and therapeutic treatments practiced around the world [22]. Healy's publication resulted in a marked increase in studies of gender differences in CVD treatment, particularly diagnostic and therapeutic policies [22]. The debate had a positive effect; the medical research community began to focus more research on women's cardiac health and raised the public's consciousness of the fact that CVD is not solely a man's disease and that women are equally at risk. Though the article and subsequent debate did raise public consciousness, the issue of gender bias in the treatment of CVD is still an overlooked and poorly researched area. To date, no consensus has been reached about the quality of care received by women suffering from heart disease.

1.5 Decision Delay

Cardiovascular diseases have a slightly worse prognosis for females than for males [1] because of higher short and long term mortality rates, particularly after an AMI [23, 24]. There are a few possible explanations for this.

Women's symptoms of certain CVDs are not always easily recognizable by the patients themselves or their health care providers. Using AMI as an example, the most frequently reported symptom for both genders is chest pain [24, 25]. Chest pain in women, however, is often more vague than the pain men experience; women tend to describe "twinges" of pain that come and go compared to men who report pain in the chest, neck , and arm [23]. In addition, women are more likely to report feeling more varied symptoms such as nausea, fatigue, or abdominal pain [6, 25-27]. These

symptoms, labeled "atypical" by health care professionals, may not immediately point to an AMI resulting in a longer diagnostic process for females [6, 15, 25]. Moreover, women themselves may not associate the symptoms they are having with a cardiac problem and may not seek treatment. Collectively, this is referred to as decision delay [23] and is a possible explanation for increased mortality among women suffering from a CVD.

Still using AMI as an example, the successful treatment of a heart attack is dependent on early intervention [15, 23, 26]. Women who are delaying their decision to seek care because of atypical symptoms are likely to take longer to receive a correct diagnosis and, as a result, will have longer wait times to treatment and an increased risk of death.

Another possible explanation for women having increased CVD mortality is a lack of appropriate treatment as highlighted in the Yentl syndrome. This gender bias hypothesis forms the basis of this thesis.

1.6 Significance

CVD is the number one killer in Canada and throughout most of the developed world [1]. In Newfoundland and Labrador (NL) the problem persists and is accentuated by increasing rates of obesity and diabetes. As the mean age of the population of both NL and Canada increases these

problems will compound, resulting in increasing numbers of the population that will suffer from, and die as a result of, CVD.

Historically, women have been seen as inferior to men. Though the rights of women have improved, women are still not always viewed as equals. A debate currently exists regarding the equality of treatment of men and women suffering from CVD. While much of the research into these deadly diseases focuses on men, equal numbers, if not more, women are dying from CVD. Health care in Canada must ensure that, regardless of gender, men and women are treated appropriately for their illnesses. Appropriate treatment may not mean they are given identical treatments but that they are provided with the same access to the appropriate treatments. Through research, including this study, we can assess if such access exists and thus guide future research, policy and practice change aimed at this important and deadly issue.

1.7 Purpose

The overall purpose of this thesis is to assess a potential gender bias in the treatment of acute care. All patients in this study were listed as either male or female based on self-identification of their sex. Sex was not genetically determined. As a result, I have chosen to refer to this study as one of a gender bias instead of a sex bias.

Previous research in the area of gender bias and CVDs has focused mainly on AMI yet the current study is one of more than just CVDs. Unfortunately, to date, research has not been conducted on gender bias in diseases other than CVDs. In this thesis I am extending this research to establish if a gender bias is in effect in CVDs other than AMI and in both a related and an unrelated disease. In particular, the focus will be on (AMI), cerebrovascular accident (CVA), and coronary revascularization. Chronic kidney disease (CKD) was also studied. While CKD is sometimes considered a vascular disease, it was included in this study because of its similar pathogenesis to CVDs, in particular AMI. In essence, CKD is a vascular control group. Community acquired pneumonia (CAP) was also included as an unrelated disease and serves as a non-vascular disease control group.

Chart reviews were conducted on thousands of patients suffering from each of these diseases and ailments to describe quality of treatment received and to ascertain if a gender bias was evident. This thesis will present a literature review on research conducted for all three cardiovascular diseases studied and both CKD and CAP. Data will be presented on acute care to assess whether there were differences in the treatment and quality of care received by men and women.

Chapter 2 Diagnoses and Treatment

In order to determine if men and women are receiving the same quality of medical care it is important to first have a greater understanding of the mechanisms used to diagnose and treat the specific diseases being studied.

2.1 Acute Myocardial Infarction

2.1.1 Diagnosis

A physician who suspects a patient has suffered an AMI, commonly known as a heart attack, will perform a number of diagnostic tests, including an electrocardiogram (ECG) and x-rays, and blood tests to determine the diagnosis and extent of the damage [6].

An examination of the ECG will determine the type of AMI suffered – either a ST-segment Elevated MI (STEMI) or a non-STEMI. A STEMI is a more severe heart attack than a non-STEMI. An AMI is caused by an interruption of blood supply to the heart. The location of the blockage, the length of time the heart is deprived of blood, and the amount of damage may determine which type of AMI the patient has suffered. A STEMI is caused by a prolonged period of blocked blood supply. As a result, it affects a large part of the heart muscle.

2.1.2 Treatment

Any patient who presents in the emergency room with a presumed AMI is given Acetylsalicylic acid (ASA; aspirin) immediately. Patients who have suffered a non-STEMI are normally treated with anticoagulant and continuing anti-platelet medication. For more severe STEMI cases, patients are given some form of reperfusion therapy, either thromobolysis or percutaneous coronary intervention (PCI), in addition to pharmacological treatment [6]. If both thromobolytics and PCI are unsuccessful, coronary artery bypass graft (CABG) surgery may sometimes be used. For the purpose of the current study, thromobolysis was studied; both PCI and CABG will be discussed in detail later. Thrombolysis refers to the breakdown of blood clots through the use of a class of drugs called thrombolytics. Thrombolytic agents work to break clots apart to restore the blood flow over the blocked blood vessels of the heart [6]. Thrombolytic agents should be administered within 30 minutes of patients' arrival in the emergency room when determined to be appropriate by an ECG indicating a STEMI [28, 29].

2.2 Cerebrovascular Accident

2.2.1 Diagnoses

A CVA, commonly referred to as a stroke, is a deterioration of brain function caused by a lack of blood supply to the brain. The shortage of blood supply may be due to a blocked or burst blood vessel [30]. This is likely caused by either ischemia or a hemorrhage which mirror the two classifications of stroke – ischemic stroke and hemorrhagic stroke [30]. Some common causes of stroke include a thrombus (blood clot) forming around atherosclerotic plaques, an embolus

(blocking an artery, or reduction of blood flow to all parts of the body as the result of cardiac arrest, AMI, or bleeding.

There are several techniques used to diagnose a stroke. Most commonly used are brain imaging (either computed tomography [CT] or magnetic resonance imaging [MRI]), neurological assessment, and laboratory tests [31]. When indicated, more specific tests, such as an echocardiography or toxicology screen, may be used [31].

2.2.2 Treatment

Patients who have suffered a stroke are admitted to the hospitals stroke unit. Treatment varies depending on the type of stroke suffered so determining the type of stroke is foremost. For the purpose of this study we focused on rehabilitation and care, so pharmacological interventions will not be discussed.

A stroke rehabilitation team is multidisciplinary as it includes many health care professionals with differing expertise [31], including nurses, speech language pathologists, dieticians, physiotherapists, etc. Stroke rehabilitation begins almost immediately and can last for many months depending on the severity of the injury [31]. Stroke teams' delivery of care and time to access the various aspects of care they provide are indicators of best quality of care [32-36].

2.3 Coronary Revascularization

2.3.1 Diagnoses

Coronary artery disease (CAD) results from the accumulation of plaques in the coronary arteries that supply the muscles of the heart with oxygen and nutrients. Many individuals can go decades without realizing they are developing CAD because the signs and symptoms of this disease are not displayed until the disease has progressed to an advanced stage. The build-up of plaques will eventually result in reduced blood flow to the heart causing ischemia, or a lack of oxygen, to the cells of the heart. The plaques may also rupture, partially or completely blocking off the coronary arteries. As the plaques grow and the arteries narrow, patients will begin to suffer from angina, or chest pain. Angina can be treated pharmacologically but unstable angina, resulting from changes in intensity or frequency in pain, can be deadly and requires immediate medical attention.

Patients who suffer from angina and seek medical attention will be given a variety of tests to confirm they have CAD. After reviewing family and medical history, physicians will likely perform an ECG, a stress test, an echocardiogram, chest x-ray, and a variety of blood tests [6]. There are many lifestyle changes that can be implemented to help alleviate angina pain and help treat CAD. These include healthy eating, increasing physical activity, losing weight, reducing stress and cessation of smoking.

2.3.2 Treatment

A patient with severe CAD and angina pain will be given a coronary angiogram, or cardiac catheterization, to assess their coronary circulation [6]. Based on the results, a physician will recommend one of three options: 1) PCI (also known as angioplasty). This is a procedure in which a balloon, with or without stent, is used to open the narrowed or blocked coronary arteries. 2) Medical management. Patients are given, among others, anti-anginal and anti-platelet drugs. 3) CABG surgery. In such a surgery, arteries or veins from other parts of the body are grafted to the coronary arteries to bypass atherosclerosis (cholesterol) build-up [6]. CABG can either be single, double, triple, or quadruple which simply refers to the number of coronary arteries that are bypassed during the surgery. PCI and CABG are more often effective than medical management at relieving symptoms [37]. CABG is superior to PCI in patients with multi-vessel CAD, low ejection fraction (how much blood is pumped out of the ventricles with each heart beat), or diabetes [38, 39].

2.4 Community Acquired Pneumonia

2.4.1 Diagnoses

CAP is a type of pneumonia that occurs in patients who have not recently been hospitalized and who are not residents of long term health care facilities. Pneumonia refers to an infection and inflammation of the lung. CAP occurs when the alveoli of the lungs (the areas that absorb oxygen) become filled with exudate induced by the infection and are unable to work correctly. The most common manifestations of CAP are shortness of breath, fever, chest pains, and cough [40].

A diagnosis of CAP requires a physical chest examination by a physician. Using a stethoscope a physician can determine a lack of normal breath sounds or the presence of crackling sounds – both indicators of CAP. Fever, increased respiratory rate, low blood pressure, and a fast heart rate may also be indicative of CAP. A chest x-ray and blood tests will also be performed on patients suspected of having CAP. A diagnosis of CAP may not be possible with a chest x-ray because the disease may be in its initial stages so a chest CT may be used in conjunction to reach a diagnosis [40].

2.4.2 Treatment

CAP is caused by microorganisms of which there are over 100 that may be involved [40]. The specific type of microorganism differs among different groups of people. For example, a healthy adult may be affected by a different group of microorganisms than an adult with a chronic disease would be. Several important groups of microorganisms are more common among people with certain risk factors. Determining people at risk for these organisms is an important part of the appropriate treatment of CAP.

CAP is treated by administering a type of antibiotic (AB) effective at killing the specific microorganism that caused the infection. Most people will be treated with oral AB's while some may need to be hospitalized with intravenous (IV) AB's. For the purpose of the current study, only patients who were hospitalized for CAP were included. In general, all therapies in older children and adults will include treatment for atypical bacteria.

In 1993 Canadian guidelines for the management of CAP were published by the Canadian Community Acquired Pneumonia Consensus Conference Group [41]. These guidelines were written to standardize the AB treatment of CAP in Canada. The guidelines list the organisms indentified as causing the disease, the age group and current health status of the patient, the clinical presentation, and the setting and provide guidance on the drugs that will appropriately treat each type of patient [41]. In 2000 these guidelines were updated by the Canadian Infectious Disease Society and the Canadian Thoracic Society [40]. The guidelines were updated due to the growing resistance of organisms to antimicrobial medications and the availability of new AB's [40].

2.5 Chronic Kidney Disease

2.5.1 Diagnoses

Chronic kidney disease (CKD) refers to the persistent loss of kidney function. CKD is defined as kidney damage for ≥3 months with or without decreased glomerular filtration rate (GFR) or GFR<60 mL/min/1.73m^2 for ≥3 months with or without kidney damage [42]. GFR reflects the flow rate of filtered fluid through a kidney [43]. Because CKD may be progressive, it is broken up into five stages to mirror the level of kidney malfunction. The stages are defined as either level of kidney failure or GFR and are outlined as follows:

Table 2.1 CKD Stages

Stage	Description	GFR (mL/min/1.73m^2)
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mildly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney failure	<15 (or dialysis)

GFR – glomerular filtration rate

As GFR levels decrease, the level of kidney function decreases and the stage of CKD increases. Once a patient reaches stage 5, they are considered to be eligible for renal replacement therapy (RRT) either by some form of dialysis or transplantation and are said to be in end-stage kidney disease (ESKD) [42].

Some patients with suspected kidney failure should be seen by a nephrologist. The first step for a nephrologist would be to ensure that appropriate tests have been performed to establish or confirm a diagnosis. The complete workup could include kidney biopsy or imaging, review of medications, review of family history, and a search for systemic disease, especially diabetes [44]. Patient education, awareness, and input into treatment are vital in CKD. It alleviates fear, improves quality of life, and is likely to produce more favorable outcomes if patients are involved in the decision making component of the treatment [44].

2.5.2 Treatment

The kidneys have an important role in maintaining health by maintaining equilibrium between water and minerals inside the body. Products the body cannot get rid of through respiration are removed

by the kidneys. Furthermore, the kidneys play a part in both the production of red blood cells and bone formation through the production of erythropoietin and calcitriol respectively. Dialysis is the passage of molecules in solution by diffusion across a semi-permeable membrane. Dialysis attempts to replace some of the functions of the kidneys through diffusion (waste removal) and ultrafiltration (fluid removal). Unfortunately, dialysis is not able to take over the endocrine functions of the kidney and, as a result, cannot produce erythropoietin or calcitriol. The two primary types of dialysis, hemodialysis (HD) and peritoneal dialysis (PD), work to filter fluids and remove wastes in different ways.

2.5.2.1 Hemodialysis

Hemodialysis literally means "dialysis of the blood" [45]. In 1944, Willem Kolff was the first to successfully perform HD, then called extracorporeal dialysis because it was performed outside the body [45]. Today, HD removes wastes and water by circulating blood outside the body through an external filter, a dialyzer, which contains a semi-permeable membrane [45]. The semi-permeable membrane works as follows: solutes with higher concentrations in the blood will diffuse through the membrane to the other side (often called the dialysate) and solutes with lower concentrations in the dialysate will diffuse through the membrane to the blood [45]. Hemodialysis is the most widely used dialysis modality worldwide [46]. It is normally administered three times a week anywhere from 2.5 to 5 hours in health care facilities, including hospitals, but can also take place at home or in an assisted-care setting [46]. Home based HD is not a popular treatment option and is currently only used in about 1-2% of cases in Canada and the USA [46].

The development of HD requires repeated access to blood circulation. In 1966 arteriovenous (AV) fistulas were developed and remain the popular access choice of today [47]. In the late 1970's synthetic grafts made of expanded polytetrafluoroethylene were introduced [47]. These synthetic grafts remain the most frequently used graft material today. Central venous catethers (CVC) are also used for HD access. The majority of catheter use is as bridging device to allow time for the maturation of more permanent access, such as grafts or fistulas, or for patients who only need temporary access [47]. Catheters can be used permanently for patients in whom all other types of permanent access have been exhausted and ruled out. AV fistulas are recognized as the preferred access method. Fistulas have many advantages, including lower infection rates, higher blood flow rates, and lower incidence of thrombosis (formation of blood clots) [47]. Fistulas have better access quality and survival than grafts or catheters. They have fewer complications and produce better patient survival than other access options [47].

Hospital-based HD reduces technical complexity for patients and caregiver burnout as it places all responsibility onto health care professionals instead of the patient and their family. However, there are limitations to HD. Dialysis units require specially trained nurses, physicians, and technicians and can only be done in certain areas [46]. As a result, transportation to a dialysis site may be complicated depending on the home location of the patient in reference to the nearest dialysis site. As well, there may be complications from vascular access and dietary restrictions often have to be placed on patients [46]. HD is generally well tolerated by patients but there are common side effects, including restless legs, nausea, vomiting, leg cramps, and headaches [46].

2.5.2.2 Peritoneal Dialysis

In PD a sterile solution that contains glucose is run through a tube into the peritoneal cavity, the abdominal cavity around the intestine, where the peritoneal membrane acts as a semi-permeable membrane [46]. The peritoneal membrane is a layer of tissue containing blood vessels that lines and surrounds the peritoneal cavity and the abdominal organs (stomach, spleen, liver, intestines) [46]. During PD treatment the dialysate is infused into the peritoneal cavity. It is left for a period of time to absorb waste and is then drained out and discarded [46]. The two principle techniques of PD are continuous ambulatory peritoneal dialysis and automated peritoneal dialysis. In CAPD the cycle is repeated manually every 6 hours and fluid is always present in the cavity [46]. APD is normally performed overnight and requires a machine to automate the fluid exchange [46].

Peritoneal dialysis is a simpler procedure than hemodialysis, is performed at home by the patient, and, thus, requires no travel and little technical expertise. It avoids the use of vascular access and associated complications [46]. PD patients are hospitalized at similar rates to HD patients but PD patients spend more days in hospital. Some common complications PD patients suffer include infection, abdominal distension, inadequate dialysis, and failure to thrive [46]. Such complications may lead patients to switch to hemodialysis. PD is less effective and durable, and therefore less popular, than hemodialysis.

Chapter 3 Literature Review

3.1 Acute Myocardial Infarction

While studies on gender differences in CVD did increase in the 1990's, the bulk of the research focused on AMI and the results were often mixed. Currently, research is inconsistent in suggesting that women who suffer an AMI are treated less optimally than men.

3.1.1 Demographics

The demographics of women who have an AMI are consistent. Women are almost always older [24, 25, 48-61] and more likely than men to have co-morbid conditions, especially hypertension [24, 25, 48, 49, 52-62], diabetes mellitus [49, 52-55, 57, 58, 60, 62], and chronic heart failure (CHF) [24, 25, 49, 54-60]. Women are normally less likely than men to be smokers [25, 48, 49, 53, 54, 58-61], or to have suffered a previous AMI [24, 49, 53-55, 57-59, 63]. Some studies have found that women are more likely to have had a previous CVA [48, 49] or chronic obstructive pulmonary disease (COPD) [55, 58]. It has been found that women are less likely [50, 57, 58, 60-62], more likely [63], or just as likely [24, 25, 59] than men to suffer a STEMI. A recent study has found that the gender gap, especially with regards to age, is changing for AMI patients [64]. Women are normally older than men when they suffer an AMI and this is partially due to the protective effects of estrogen [6] [65, 66]. However, more middle-aged women are found to have heart attacks. It is believed this change

is related to the increase in obesity coupled with high rates of blood pressure and cholesterol [64]. Moreover, middle-aged men seem to be suffering fewer heart attacks, further decreasing the gender difference previously found.

3.1.2 Symptoms and Decision Delay

Differences in the presentation of symptoms of AMI vary. Some studies do not provide information on presenting symptoms and their potential differences between the sexes [50, 53, 55]. While some researchers found that women are less likely than men to manifest chest pain [25, 54, 57], others found equal rates of chest pain in men and women [24, 52, 59, 67]. With regards to atypical symptoms, such as nausea, back pain, or weakness, it has been reported that women are more likely to experience them [25, 52, 67] but also equally likely as men to experience them [24]. It has also been noted that women are less likely to display ventricular arrhythmias [48, 56] and more likely to display atrial arrhythmias [48] than men. Furthermore, there is no consensus in the literature on decision delay to seek treatment; in some studies, it has been found that women are more likely to delay seeking treatment [51, 54], sometimes waiting more than 6 hours after symptom onset to present at the hospital or to seek attention [49, 60], while other authors have found no differences in time to presentation [24].

3.1.3 Clinical Care and Outcomes

With regards to diagnostics, women have been found to be less likely to receive exercise testing [48]. Women are often less likely to undergo diagnostic catheterization [24, 49, 54, 58, 59]. This

finding has held up when considering the gender of the treating physician [53]. Women are not always less likely to undergo catheterization [63]. In addition, one study suggests that the differences found are attributable to the older age of women and not simply gender [48].

Even after controlling for age, it has been often found that women are less likely than men to receive thrombolytics [24, 48, 49, 51]. Some researchers do not differentiate between types of reperfusion therapy and merely state that women are less likely to receive reperfusion [54, 58]. It has also been found that women are less likely than men to receive timely reperfusion therapy [58]. Other studies have found no differences in rates of thrombolysis [50, 60] or reperfusion [25].

There is no clear consensus on rates of revascularization (either PCI or CABG). While some studies have found that men and women have similar rates [25, 49, 61], others have found that women are less likely to be revascularized [55, 58], specifically with regards to CABG [24, 59].

Previous research has not focused much on the differences in treatment with regards to discharge medications. Studies have shown that women are less likely to receive ASA [49, 51] and beta blockers [51] at discharge. Other researchers have found no differences in the use of either of these drugs as secondary prevention [48, 54], as well as either angiotension converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) [25]. Women are less likely than men to receive in-hospital ASA [49, 58].

Death is another outcome that is debated in the literature. Some researchers found no differences in 30-day mortality between the sexes [48, 49] while others found that women were more likely to die in-hospital [24, 50, 51]. Women who suffered a STEMI were more likely to die [58], particularly in-hospital [62]. This did not hold up in all cases; one researcher found that younger women were more likely than men to die from either a STEMI or non-STEMI but older women fared similarly (with a STEMI) or better (with a non-STEMI) than men [57]. Other authors have also found that women who have suffered a STEMI are not more likely to die than men [61]. Death rates were also frequently analyzed based on age. One study found that women who were younger than 70 were more likely than men to die but for patients over 70 years there was no difference in death [60]. Similarly, women less than 60 years were more likely than men under 60 years to die [56]. Looking at post-hospital death rates, women are more likely than men to die within 5 years [55] or less likely to die after 3 years [58]. In summary, there is no consensus in the current literature about the differences between in-hospital and post-hospital mortality rates between men and women who have suffered an AMI.

3.1.4 Limitations

Of the research analyzed, a few studies have serious flaws, particularly with regards to statistical analysis. One study found differences in many aspects of treatment, with women being treated less optimally than men, but stated that when stratified for age the differences were no longer significant [50]. The authors of this article did not use multivariate techniques to come to this

conclusion. Instead, they merely divided the results up by age groups and performed the Students *t*-test. In their summary they stated that the differences they found were solely attributable to the older age of women at the time of presentation. While their conclusions may be correct, they cannot definitively rule out potential gender differences without the use of more appropriate statistical tests. Another problem is a lack of generalizability of the studies. One study in particular only used veterans in a veterans hospital as their study group [63]. The results of this study may not reach beyond the population studied.

Studies of treatment differences between the sexes for AMI rarely have equal numbers of male and female participants. In fact, many studies referenced include 18-39% female [24, 48, 50, 51, 55, 56, 58, 60-62, 67]. One study, entitled Women Veterans and Outcomes after Acute Myocardial Infarction, claimed its objective was to describe treatment and survival of women's veterans yet included only 236 women, or 1.7% of their study sample [63]. It is hard to determine differences in treatment between men and women when the majority of the patients studied are not women.

3.1.5 Summary

Women who have suffered an AMI are older and present with more co-morbidities than men. There is no consensus in symptom differences or delays to seeking treatment. Women are often less likely to receive diagnostic cardiac catheterization and less likely to receive reperfusion therapy. Neither of these findings hold up in all situations but appear in the majority of the published literature. Past

research is not in agreement with regards to any gender differences in revascularization, in-hospital and discharge medications, and in-hospital or long-term death.

3.2 Cerebrovascular Accident

Gender differences in CVA treatment are not as well researched as AMI. While treatment is not extensively covered, there is information about the demographics, severity, and outcomes of both men and women who have suffered a stroke. No consensus currently exists in the debate over treatment differences between the sexes for CVA.

3.2.1 Demographics

Women who have suffered a CVA are often significantly older than men [68-79]. Both men and women consistently present with co-morbidities but, unlike other CVDs, men often have more substantial medical histories. Women are more likely to have hypertension [68-71, 74-76, 78, 79] and more frequent atrial fibrillation [68-71, 73, 75, 78, 79], while men are often smokers [68-72, 74, 76-79] with CAD [68, 69, 72], dyslipidemia [68, 69, 72, 76], diabetes [68, 70, 71, 74-76], and previous AMI's [69, 70, 76, 79] and CVA's [70, 71, 74, 76]. Women are more likely than men to live at home alone and in assisted living care homes [70, 71, 74, 76, 79].

3.2.2 Diagnostics and Stroke Severity

There is little consensus in the literature into the severity of strokes suffered by males and females. It has been found that women are both more [69] and equally likely [76] as men to present to the hospital in an ambulance and both less [68, 71] and equally likely [74, 76, 80] to be admitted to and receive care on an acute stroke unit. Women are less likely to get brain imaging [79, 80], Doppler examination [79], echocardiogram [79], and angiography [79, 81], though it has also been found that there are no differences in such investigative methods [74, 76].

Women are more likely to present with a more severe manifestation of a CVA. They have more aphasic disorders [78], visual field disturbances [78], swallowing difficulties [78, 79], paralysis [79], and urinary incontinence [79]. Women are more likely than men to have difficulties maintaining consciousness upon admission [71, 74] and are likely to be in a coma [79]. Furthermore, using the Scandinavian Stroke Scale score, it was found that women are more likely to have a very severe or severe stroke while men are more likely to have a mild stroke [70]. Conversely, it has also been reported that there are no differences in level of consciousness or stroke severity in males and females [76].

3.2.3 Treatment

While previous literature has examined sex differences in both in-hospital and discharge pharmacological treatments for CVA, a review of that literature will not be discussed as the current study focused only on rehabilitation consultations.

Very few studies focused their research on gender differences in referral to and appointments with health care professionals that focused on rehabilitation. Of those that did include such treatments, there were no gender differences found [75, 79], specifically in physiotherapy, speech therapy, occupational health therapy [75], and transfer to a rehab facility [72]. Prior to discharge, women were less likely than men to receive life-style recommendations [68]. Women were found to be discharged to a long-term care, or chronic care, facility more often than men [68, 69, 74-76, 79].

There is no consensus on hospital length of stay; it has been found that there were no differences in length of stay between the sexes [69, 71], that women had shorter lengths of stay [68], or that women had longer hospital stays [78, 79]. Women had a significantly higher in-hospital mortality than men [68, 69], however no differences in in-hospital mortality were also reported [72, 74]. At 3-months post-stroke women were more likely to have died [71, 79]. At the 3-month check-up it was also found that women were more likely than men to be depressed [71, 74], to report poor health status [71, 74], to be less satisfied with their care [71], and to express the wish to have had more help during their hospital stay [74]. Moreover, female sex was a positive predictor of disability and handicap at 3-months [79]. At 6-months post-stroke it was found that women had greater disability than men, but showed no differences in mortality or quality of life at this time [76]. One year after their CVA women had a lower risk of death than men [75].

3.2.4 Limitations

A clear limitation of the CVA literature is the lack of gender research, especially compared to AMI. Patient profiles at presentation and outcomes have been researched but very little is known about rehabilitation treatment through the use of speech pathologists, occupational therapists, and other health care professionals. Another important limitation is generalizability; much of the present CVA research is conducted in Europe, particularly Sweden and Germany. It is possible that the patients participating in these studies and the results generated are not applicable to North America because healthcare systems are different.

3.2.5 Summary

Men who suffer a CVA often present with more co-morbidities and more extensive medical histories than women yet there is research that indicates that women suffer more severe strokes than men. Previous studies are inconsistent in suggesting that women are less likely to receive diagnostic tests but they do indicate a trend in this direction. There is no consensus in the literature about any gender differences in treatments, hospital length of stay, or both in-hospital and long-term death.

3.3 Coronary Revascularization

Compared to some CVDs, gender differences in the treatment of CAD through CABG surgery has been relatively well researched. This is likely due to the connection between CABG and AMI. CABG can be used as a treatment for certain patients who have suffered an AMI, depending on their response to other treatments. AMI treatment is a well researched gender bias topic and, as a result, CABG has also been examined for gender differences in quality of care.

3.3.1 Demographics

Women who have undergone cardiac catheterization are likely to be older than their male counterparts [19, 20, 82-91] with a higher body mass index (BMI) [83, 88]. Females are more likely to have co-morbid illnesses, especially hypertension [20, 84, 85], diabetes [19, 20, 83-85, 91], CHF [19, 83, 84, 91], and angina [19, 82, 86]. Women have been found to be less likely to have had a previous AMI [20, 83, 84, 86], yet one study found equal rates [82]. Females have been found to have both more [84, 85] and equal incidences [83] of cerebrovascular disease.

3.3.2 Disease Severity

Women were less likely to receive a coronary angiogram, or cardiac catheterization, to evaluate the extent of their CAD [19, 20, 87, 89, 91-93]. Of those who did receive an angiogram, men were more likely to have more significant CAD as noted by more multi-vessel disease [85, 86, 89, 94] or left main-stem stenosis [82], however this was not always the case; men and women were found to have equal rates of multi-vessel disease and CAD severity [90]. The sexes had similar ejection fractions [82, 83, 86, 94].

3.3.3 Revascularization Referral

In general, it was found that women and men were equally likely to receive PCI [90, 94, 95]. In some instances, however, it was noted that women were either more likely [85, 96] or less likely [87] to be referred for PCI.

It has been noted that women are less likely to receive CABG, regardless of age, co-morbidities, or disease severity [19, 82, 87, 88, 91, 94]. In one situation - one of the two articles that Healy based the Yentl syndrome on - the authors found that women were less likely than men to undergo CABG but, among the men and women who did receive a coronary angiogram and were found to have severe disease, there were no significant differences in the number of patients undergoing surgery [20]. One researcher found that women are less likely to receive CABG specifically if they have double vessel disease [85] but found no differences for single or triple vessel disease. Also, it has been reported that women are less likely to receive CABG if they are in a low-risk of cardiac death category [86]. In this situation, women are likely better off not receiving the surgery; they were more likely to be referred for surgery when surgery offered the least survival benefit relative to medical therapy. It has also been found that there are no differences in CABG between the sexes [89, 90, 95]. Of the women who did receive CABG, they were noted as having shorter wait times [82], likely due to their more severe medical histories.

3.3.4 Limitations

The studies referenced have several limitations. Two of the studies had no information on the results of noninvasive coronary tests, symptoms, severity of illness, or prior AMI [19, 91]. These variables will definitely contribute to the outcome studied and should have been included as

independent variables in the logistic regression. Misleading conclusions can be reached when extent of disease is not controlled for. A second study did not have access to any clinical data before cardiac catheterization [84]. As a result, they were unable to determine any gender differences in care prior to catheterization.

In general, many of these studies were conducted in one patient population in one health care system which may not reflect the rates of revascularization seen in the population of Newfoundland. As with most studies of this nature, they are open to the weaknesses that retrospective studies are prone to, including confounders caused by the inability to blind or randomize, missing or inadequate data, recall bias (relying on the accuracy of previous written word or recall of individuals), and the difficulty of establishing cause and effect [97].

3.3.5 Summary

Women with severe CAD were older than men and had more significant medical histories and risk factors, yet it is unknown if the severity of their CAD was more extensive than that of men because of a lack of consensus in the literature. Women were often less likely to receive diagnostic coronary angiograms and were less likely, in most instances, to undergo CABG. There is no agreement with regard to gender differences in the rates of patients who receive PCI as treatment.

3.4 Community Acquired Pneumonia

Based on review of literature, it appears that no studies have been conducted on any sex differences in quality of care in patients hospitalized with CAP.

3.5 Chronic Kidney Disease

To date, a potential gender bias has not been fully addressed in nephrology. Very few studies have been conducted to specifically look at treatment differences for CKD between the sexes. Most gender differences that have been found for CKD treatment have been uncovered in the results of a study and not as the result of analyzing gender differences directly.

3.5.1 Demographics

As a consequence of the lack of gender related CKD literature, there are very few known demographics describing men and women who require dialysis. There appears to be no difference in the age of patients requiring treatment [98, 99], although most studies only provide a mean age of the sample, not stratified for gender. As well, it has been noted that men are more likely than women to have an etiology of peripheral vascular disease [98], glomerulonephritis [98], or diabetes [98] and women are more likely to suffer from pyelonephritis and polycystic kidney disease [100, 101]. No other demographics are known.

3.5.2 Pre-Dialysis Care

Late patient referral to a nephrologist is associated with many negative outcomes that have been well documented, including sub-optimal treatment, in patients with CKD. Such patients often start dialysis later and unprepared and are thus at an increased risk of mortality [100, 102]. More specifically, it has been noted that late referrals result in patients starting dialysis with low levels of albumin, hemoglobin [102], calcium [103], and eGFR [102], and high levels of phosphate [100]. Moreover, late nephrologist referrals often result in a lack of permanent access [102, 104] and increased use of catheters [105]. A recent study has found a gender difference in diagnosing CKD. They found that women are more likely than men to have undiagnosed CKD, except in the latest stages of the disease [106]. This finding also highlights the importance of early nephrologist visits.

Conversely, early referral to a nephrologist has been known to be associated with many beneficial results. Patients with early referrals and earlier initiations of dialysis enjoyed increased input in their treatment, better patient education, [107], and spent fewer days in the hospital [108] compared to patients who required urgent referrals. These patients experienced more subjective benefits as well; pre-dialysis clinic attendance was a predictor of higher quality of life scores in four of eight domains in patients being treated with hemodialysis [108]. After controlling for baseline demographics, early referral was linked with higher scores in physical function, emotional role limitation, social function, and general health for the first six months after dialysis initiation [98].

Although the benefits and risks are well known and highly researched, there is no previous literature that examines any potential gender differences in the length of pre-dialysis care or timing of nephrology referral.

3.5.3 Dialysis Modality

Because most CKD patients are treated with HD, there is little literature describing gender differences in modality type. One Canadian study found that women are less likely than males to receive HD [109]. A follow-up study by the same researchers found that any differences in modality in the sexes is solely attributable to body size rather than sex [109]; women tend to have a lower body size and are, thus, more appropriately matched with PD which is more tolerable with smaller fill volumes of dialysate [110, 111].

Also, dialysis modality may reflect the level of care received by a CKD patient. Any patient who is receiving PD has obviously been seen by a nephrologist and made an informed and educated choice about their treatment modality. Therefore, patients receiving HD, in particular those with a catheter, are often given it as a default start and not through a decision researched and chosen by them and their nephrologist.

3.5.4 Dialysis Access

An important aspect of HD RRT is the type of access used. It has been found that patients who are older or female are less likely to have a fistula [99] and more likely to have a graft [112] or catheter [113, 114]. When women do receive a fistula, their gender is negatively associated with fistula success and an independent risk factor for fistula failure [99]. After controlling for age and medical history, women with fistulas had more early (2nd month of treatment) access-related procedures than their male counterparts [99]. Of patients with fistulas, men were found to experience significant benefits, including less access-related complications, than women, but this finding was only observed in younger men (≤72 yrs.) [99]. Similarly, women were less likely than men to have adequate fistulas because of technical failures, early thrombosis, or failure to mature [115]. These issues cannot be explained by differences in vascular diameter between males and females [116], although it is commonly believed that women have smaller vessels than men and this is often cited as a reason for the underutilization of fistulas in women [116]. Using Doppler ultrasonography, it has been found that while vessel diameters did differ between genders, the difference was not significant [117]. Despite all this, survival of a fistula is not always linked to female gender [118, 119].

3.5.5 Limitations

An obvious limitation of the CKD studies is the lack of research that directly examines gender differences in treatment. While some findings appear to support a theory of less optimal treatment of women, it must be noted that these results are based on the conclusions of only a few studies and could be disproven with more research. More exploration is needed in this area before any conclusions can be made.

3.5.6 Summary

Due to the small amount of literature that exists on sex bias in CKD care, very little is known about any gender differences in the treatment of this disease. It is unknown if there are any differences in age and medical risk factors of patients who require dialysis and no literature examining if men and women receive equal and appropriate amounts of pre-dialysis care. There is no agreement about gender differences in dialysis modality but the two studies that contradict each other are by the same researchers. It appears that women are less likely to receive optimal HD access, however this finding is based on a very small amount of literature and may not hold true.

3.6 Overall Limitations

The main limitation of the previous gender bias literature is that not enough exists. With the exception of AMI and coronary revascularization, the other conditions studied have received very little attention; CAP has been ignored. Of the studies that have been published, there is almost no agreement on the extent of the bias, or even exists.

Most of the studies referenced in this chapter originated from the United States or Europe. Consequently, a demographic bias may be in place when comparing these studies to the Canadian population studied in this thesis. The patients participating in these studies, in particular in the US,

may represent a sub-population of Americans who can afford health care. The results of such studies may not readily generalize to Canada.

3.7 Overall Summary

As previously mentioned, there is very little consistency in the results of the studies referenced, however a few themes do emerge. In general, women present at an older age than men and have more co-morbidities and extensive medical histories when compared to men.

Women were often less likely to receive diagnostic tests as readily as men and, in some cases, were less likely to receive the same treatments. These findings are not consistent. There is also no agreement on difference in the number of deaths for men and women for all conditions studied.

Chapter 4 Methods

The Human Investigation Committee of the Faculty of Medicine, Memorial University of Newfoundland, approved the study protocol.

4.1 Data Collection & Diagnoses

4.1.1 Acute Myocardial Infarction, Cerebrovascular Accident, Coronary Revascularization, Community Acquired Pneumonia

All data were collected from cases managed at regional secondary and tertiary care sites, specifically St. John's (Grace and St. Clare's Hospitals, and Health Sciences Center), Carbonear, and Grand Falls.

The specific diagnoses for each audit were as follows: AMI, acute CVA requiring admission, CABG, and CAP. All cases were identified using ICD-9/CMG discharge codes for the most responsible discharge diagnosis for the years 1995/96, 1998/99, and 2000/01. Audits were performed for all time periods except for AMI in 1995 and CABG in 2001.

Detailed patient admission and in-hospital data are recorded in patients' charts as per standard medical practice and hospital policies. As such, trained research nurses were able to abstract data retrospectively on demographics, clinical status, therapy, complications, and in-hospital mortality from medical records.

4.1.2 Chronic Kidney Disease

The STARRT study (Study To Assess Renal Replacement Therapy) is a Canadian multicentre retrospective chart review of incident dialysis patients followed for six months. At each of the ten participating centers, including St. John's, all patients starting RRT for 6 consecutive months from July 1 to September 31, 2006 were retrospectively identified. It was recorded whether patients started RRT as an outpatient or inpatient and, if starting as an inpatient, whether this was due to patient factors or because outpatient RRT was unavailable. Type of dialysis access, duration of nephrology care, demographic and laboratory parameters at the time of initiation were also collected. Patients were followed until death, transplant, transfer, or until six months after initiation of RRT.

4.2 Inclusion/Exclusion Criteria

4.2.1 Acute Myocardial Infarction, Cerebrovascular Accident, Coronary Revascularization, Community Acquired Pneumonia

Patients who died or were transferred to another institution were not included in the length of stay analysis. All patients 18 years of age and older were studied.

4.2.2 Chronic Kidney Disease

Inclusion criteria included subjects 18 years or older starting any form of HD or PD, both home or in center, or pre-emptive transplantation. Patients who required temporary RRT due to drug or environmental intoxication, suffered acute renal failure that was treated in the intensive care unit

(ICU), and those with a kidney transplant initiating temporary RRT due to rejection were excluded from the analyses.

4.3 Outcomes

Measurements included morbidity and mortality measures where appropriate. Where possible, quality of care was judged on measurable outcomes in relation to Canadian published statements of likely optimal care. Publications for respective years were used to benchmark care indicators where appropriate. All outcomes were explored for differences in care between men and women. In an attempt to clearly pinpoint the level at which a potential gender bias is at work, outcomes were divided into three categories: Access to care, Intervention, and Outcome as follows (Table 4.1):

Table 4.1 Categories of Outcomes

	Access	**Intervention**	**Outcome**
AMI	Thrombolytics Given Time to Thrombolytics Admission to CCU	Approp.Thrombolytics All Discharge Meds. All In-Hosp. Meds.	LOS Death
CVA	CT/MRI Time to CT/MRI Seen by Health Care Workers (OT, SW, etc.) Time to Health Care Workers (OT, SW, etc.)		LOS Death
Coronary Revascularization	Time to CABG	Post-Angio. Treatment Recommendations	
CAP		Approp. Antiobiotics (1993 & 2000)	LOS Death
CKD	Pre-Dialysis Care Lab Parameters	Modality Dialysis access	LOS Death

AMI – acute myocardial infarction; CCU – coronary care unit; Approp – appropriate; LOS – length of stay; CVA – cerebrovascular accident; CT/MRI – computed tomography/magnetic resonance imaging; OT – occupational therapist; SW – social workers; CABG – coronary artery bypass graft; Angio – angiography; CAP – community acquired pneumonia; CKD – chronic kidney disease.

In an attempt to differentiate from access as used in dialysis care, these results will be referred to as health care access, health care interventions, and health care outcomes from here on. In some instances, in particular death for coronary revascularization patients, outcomes were not explored because they were not available.

4.3.1 Acute Myocardial Infarction

Patients were only included in the time to thrombolytics analysis if time and date of both presentation to emergency department and thrombolytics given were recorded. Best quality of care indicators of AMI included administration of thrombolytic therapy within 30 minutes of patients' arrival in the emergency department [28, 29]and appropriateness of thrombolytics determined by electrocardiogram criteria [29]. More specifically, thrombolytics were deemed to be appropriate when a patient's EKGs indicated ST elevation (STEMI) were given thrombolytics.

4.3.2 Cerebrovascular Accident

Best quality of care indicators of CVA included care delivery and time to access the various aspects of care (neuro-imaging and stroke unit care/mobile stroke teams) [32-36]. Patients in hospitals without a CT scanner were transferred to St. John's for diagnostic imaging.

4.3.3 Coronary Revascularization

Quality of care indicators for surgery included blood utilization and mortality rates. Urgency was determined by pain syndrome and therapeutic response, severity of coronary artery disease defined by angiography and reversible ischemia on non-invasive tests. Optimal waiting times defined by priority were obtained from Naylor et al. [120].

Because of the flow of diagnostic events, the results for patients eventually referred for revascularization were analyzed in the following order: 1) the demographics of patients who underwent a coronary angiogram, then 2) the demographics of patients with critical CAD (CAD that has progressed and blood flow to the heart is severely limited), and finally, 3) the demographics of patients who were recommended for each form of coronary revascularization. The tables that display these results were formatted in the same way.

4.3.4 Community Acquired Pneumonia

Best quality of care was based on disease severity using a validated clinical predication rule (Pneumonia Severity Index [PSI]) that assesses the risk of death within 30 days [121] and appropriateness of AB use. Appropriateness of AB use was based on the 1993 Canadian CAP Consensus Guidelines [41]. In 2000, these guidelines were updated [40]. The 1993 guidelines were used to determine the appropriateness of AB prescriptions for all time periods. Treatments for patients admitted after October 1, 2000, which were deemed inappropriate by the 1993 guidelines, were reassessed using the new guidelines.

4.3.5 Chronic Kidney Disease

Optimal quality of care was based on 1) length of pre-dialysis care; 2) modality choice (PD/pre-emptive transplant, HD with graft or fistula vs. HD with catheter); 3) access (graft/fistula/PD catheter/pre-emptive transplant vs. catheter); 4) laboratory parameters at dialysis start; 5) clinical outcomes (hospitalizations, death).

4.4 Statistical Analysis

Descriptive analyses are presented as means ± standard deviations or median with 25-75th percentiles according to the normality of the distribution. Continuous variables were compared using the Students *t*-test or Mann Whitney U test depending on data distribution. Categorical variables were compared using the chi-square test.

Logistic regression models were created to assess a possible gender bias for dichotomous outcomes. The univariate models used demographics and baseline medical histories as predictors. In creating multivariable models, Hosmer and Lemeshow suggest using variables whose univariable test *p* values are less than 0.25 in an effort to identify all variables known to be important [122]. In order to include all relevant variables I followed their advice but chose a slightly stricter *p* value; univariate predictors with a *p* value of less than or equal to 0.1 were included in the exploration of the multivariate models. Gender and age were forced into all multivariate models. Multiple linear regression was used to explore parametric outcomes. A *p* value of less than 0.05 for all two-sided tests was considered significant. For all odds ratios and confidence intervals, the indicator variable used was female and this is reflected in both the data tables and text. All non-significant tables can be found in Appendix A.

Chapter 5 Results

5.1 Acute Myocardial Infarction

5.1.1 Demographics

Table 5.1 shows the results of the demographics and baseline characteristics for the AMI audits. There were a total of 1311 patients in the study. Almost 60% of the patients were male. The ages of the patients ranged from 18-95 years with an overall mean age of 68.3 years. Females were significantly older at 72.6 years (versus 65.5 years for males; $p<0.001$).

Women were more likely to present with a history of diabetes (40% vs. 26%, $p<0.001$), hypertension (57% vs. 39%, $p<0.001$), dyslipidemia (45% vs. 40%, $p=0.014$), angina (52% vs. 44%, p=0.026), and CHF (22%vs. 13%, $p<0.001$). Men were more likely to have a history of smoking (64% vs. 30%, $p<0.001$). There were no differences in family history of CAD, prior AMI, prior percutanueous transluminal coronary angioplasty, or history of CABG and transient ischemic attack/cerebrovascular accident (TIA/CVA). Men were more likely to have an STEMI than women (40% vs. 31%, $p=0.001$).

Table 5.1 Demographics and Baseline Characteristics (AMI)

	Total	Male	Female	*p* value
n (%)	1311	785 (59.9)	526 (40.1)	N/A
Age (mean ± SD; years)	68.3 ± 13.4	65.5 ± 13.8	72.6 ± 11.7	<0.001
Urban; *n* (%)	486 (37.1)	273 (34.8)	213 (40.5)	0.04
History of Diabetes; *n* (%)	423 (32.3)	202 (25.7)	211 (40.1)	<0.001
History of Hypertension; *n* (%)	611 (46.7)	309 (39.4)	302 (57.4)	<0.001
History of Smoking; *n* (%)	659 (50.4)	502 (63.9)	157 (29.8)	<0.001
History of Dyslipidemia; *n* (%)	549 (42.1)	311 (39.6)	238 (45.2)	0.01
Family History of CAD; *n* (%)	426 (32.6)	269 (34.3)	157 (29.8)	0.2
Prior Acute Myocardial Infarction; *n* (%)	399 (30.5)	233 (29.7)	166 (31.6)	0.4
History of Angina; *n* (%)	612 (46.7)	343 (43.7)	269 (51.1)	0.03
History of CABG; *n* (%)	80 (6.1)	49 (6.3)	31 (5.9)	0.3
History of CHF; *n* (%)	211 (16.1)	98 (12.5)	113 (21.5)	<0.001
Prior PTCA; *n* (%)	62 (4.7)	35 (4.5)	27 (5.1)	0.2
History of TIA/CVA; *n* (%)	110 (8.4)	61 (7.8)	49 (9.3)	0.5
STEMI vs. Non-STEMI; *n* (%)	478 (36.5)	313 (39.8)	165 (31.4)	0.001

p values represent comparisons between male and female

AMI – acute myocardial infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident; STEMI – ST elevated myocardial infarction

5.1.2 Health Care Access

Data outlining health care access are presented in Table 5.2. Women were less likely to be given thrombolytics (18% vs. 26%, p=0.001) but this difference did not remain significant in multivariate analysis. There was a significant difference in the time to thrombolytics, as measured from the time of arrival in the emergency department to the administration of thrombolytics. The median time to thrombolytics was significantly longer for women (70.0 mins.; 26.0, 150.0) than for men (45.0 mins.; 27.0, 73.3). This difference remained significant after multivariate analyses (OR=-0.15) (Table 5.3).

Women were also less likely to be admitted to the coronary care unit (CCU) (84% vs. 91%, $p<0.001$). After adjusting for age and baseline characteristics in the multivariate model, this difference persisted (OR=0.6, 95% CI=0.4-0.9) (Table 5.4).

Table 5.2 Health Care Access (AMI)

	Total	Male	Female	*p* value
Thrombolytics Given; *n* (%)	303 (23.1)	206 (26.2)	97 (18.4)	0.001
Time to Thrombolytics (median*; mins.)	47 [27, 84]	45 [27, 70]	70 [26, 150]	0.04
Admission to CCU; *n* (%)	1153 (87.9)	711 (90.6)	442 (84.0)	<0.001

p values represent comparisons between male and female

AMI – acute myocardial infarction; CCU – coronary care unit

*Median shown with [25th, 75th] percentiles

Table 5.3 Health Care Access: Time to Thrombolytics (AMI)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.16	0.03
Age	-1.40	0.08
Urban	-1.06	0.1
History of Diabetes	-0.016	0.8
History of Hypertension	-0.040	0.6
History of Smoking	0.11	0.1
History of Dyslipidemia	0.17	0.01
Family History of CAD	-0.011	0.9
Prior Acute Myocardial Infarction	0.021	0.8
History of Angina	-0.034	0.7
History of CABG	-0.049	0.5
History of CHF	0.022	0.7
Prior PTCA	0.010	0.9
History of TIA/CVA	-0.016	0.8
STEMI vs. Non-STEMI	-0.013	0.8
	Multivariate	
Gender (Female)	-0.15	0.02
Age	-0.10	0.1
History of Dyslipidemia	0.21	0.001

p values represent comparisons between male and female

AMI – acute myocardial infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident; STEMI – ST-Segment Elevated Myocardial Infarction

Table 5.4 Health Care Access: Admission to CCU (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.55	0.34-0.77	<0.001
Age	0.96	0.94-0.97	<0.001
Urban	2.50	1.82-3.57	<0.001
History of Diabetes	2.70	0.85-9.09	0.09
History of Hypertension	1.61	0.59-4.35	0.4
History of Smoking	1.37	0.88-2.13	0.2
History of Dyslipidemia	2.17	1.49-3.23	<0.001
Family History of CAD	1.30	0.88-1.92	0.2
Prior Acute Myocardial Infarction	1.92	0.60-6.25	0.3
History of Angina	1.32	0.37-4.55	0.7
History of CABG	1.28	0.32-5.26	0.7
History of CHF	1.02	0.33-3.23	1.0
Prior PTCA	2.86	0.60-13.51	0.2
History of TIA/CVA	1.14	0.41-3.13	0.8
STEMI vs. Non-STEMI	12.0	6.25-23.8	<0.001
	Multivariate		
Gender (Female)	0.63	0.44-0.93	0.02
Age	0.98	0.97-1.00	0.045
Urban	2.63	1.89-3.85	<0.001
History of Dyslipidemia	2.32	1.49-3.57	<0.001
STEMI vs. Non-STEMI	10.9	0.046-0.18	<0.001

p values represent comparisons between male and female

AMI – acute myocardial infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident; STEMI – ST-Segment Elevated Myocardial Infarction

5.1.3 Health Care Intervention

AMI interventions are listed in Table 5.5. For men and women who were thrombolyzed, there was no significant difference in the appropriateness of thrombolytics. Women were less likely to receive in-hospital medications, including adjunct ASA (15% vs. 24%, $p<0.001$) and adjunct heparin (16% vs. 23%, $p=0.004$). After controlling for age and medical history, these differences were no longer significant.

There were no statistically significant differences between the sexes for discharge prescriptions for anti-coagulant medications (including ASA), beta blockers, or statins. Men were more likely to receive an anti-lipid other than statin (5% vs. 3%, p=0.04). Women were more likely to receive a discharge prescription for angiotensin converting enzyme/angiotensin type 1 receptor blockers (ACE/ARB) (53% vs. 45%, p=0.001), digoxin (18% vs. 10%, p<0.001), a calcium antagonist (22% vs. 16%, p=0.002), a diuretic (35% vs. 21%, p<0.001), hormone replacement therapy (HRT) (3% vs. 0.1%, p<0.001), and a nitrate (48% vs. 40%, p<0.001). After controlling for age and baseline characteristics, the only significant differences remaining were for a diuretic (OR=1.4, 95% CI=1.1-1.9) (Table 5.6) and HRT (OR=33.3, 95% CI=2.8-250.0) (Table 5.7), both of which were more likely to be prescribed to women.

Table 5.5 Health Care Intervention (AMI)

	Total	Male	Female	*p* value
Appropriate Thrombolytics; *n* (%)	298 (22.7)	203 (25.9)	95 (18.1)	0.1
Adjunct Therapy; *n* (%)	293 (22.3)	202 (25.7)	91 (17.3)	<0.001
ASA Adjunct Therapy; *n* (%)	263 (20.1)	185 (23.6)	78 (14.8)	<0.001
Heparin Adjunct Therapy; *n* (%)	266 (20.3)	180 (22.9)	86 (16.3)	0.004
GP2b/3a Adjunct; *n* (%)	3 (0.23)	2 (0.25)	1 (0.19)	0.8
Discharge Medications				
Anti-Coagulant; *n* (%)	961 (73.3)	586 (74.6)	375 (71.3)	0.3
ASA; *n* (%)	888 (67.7)	542 (69.0)	346 (65.8)	0.3
Warfarin/Coumadin; *n* (%)	89 (6.8)	55 (7.0)	34 (6.5)	0.8
Plavix; *n* (%)	22 (1.7)	10 (1.3)	12 (2.3)	0.2
Ticlid; *n* (%)	9 (0.7)	6 (0.8)	3 (0.6)	0.7
Beta Blocker; *n* (%)	796 (60.7)	489 (62.3)	307 (58.4)	0.2
ACE/ARB; *n* (%)	633 (48.3)	355 (45.2)	278 (52.9)	0.001
Anti-Lipid; *n* (%)	241 (18.4)	152 (19.4)	89 (16.9)	0.3
Statin; *n* (%)	192 (14.6)	116 (14.8)	76 (14.4)	1.0
Other Anti-Lipid; *n* (%)	51 (3.9)	38 (4.8)	13 (2.5)	0.04
Vasodilator; *n* (%)	694 (52.9)	311 (39.6)	255 (28.5)	<0.001
Nitrate; *n* (%)	564 (43.0)	310 (39.5)	254 (48.3)	<0.001
Other Vasodilator; *n* (%)	5 (0.4)	3 (0.4)	2 (0.4)	1.0
Calcium Antagonist; *n* (%)	242 (18.5)	125 (15.9)	117 (22.2)	0.002
Diuretic; *n* (%)	353 (26.9)	168 (21.4)	185 (35.2)	<0.001
Digoxin; *n* (%)	172 (13.3)	77 (9.8)	95 (18.1)	<0.001
HRT; *n* (%)	14 (1.1)	1(0.1)	13 (2.5)	<0.001

p values represent comparisons between male and female

AMI – acute myocardial infarction; ASA – aspirin; ARB – angiotensin receptor blockers; ACE/ARB - angiotensin converting enzyme/angiotensin type 1 receptor blockers; HRT – hormone replacement therapy

Table 5.6 Health Care Intervention: Discharge Diuretic (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	2.08	1.59-2.70	<0.001
Age	1.08	1.06-1.09	<0.001
Urban	1.19	0.91-1.54	0.2
History of Diabetes	1.85	0.56-6.25	0.3
History of Hypertension	1.25	0.48-3.33	0.7
History of Smoking	0.50	0.36-0.67	<0.001
History of Dyslipidemia	0.57	0.42-0.77	<0.001
Family History of CAD	0.35	0.26-0.48	<0.001
Prior Acute Myocardial Infarction	5.56	0.83.20.05	0.08
History of Angina	2.21	0.46-10.00	0.3
History of CABG	2.50	0.46-12.46	0.3
History of CHF	9.81	2.43-24.55	<0.001
Prior PTCA	1.43	0.26-10.13	0.7
History of TIA/CVA	2.50	0.91-9.97	0.07
STEMI vs. Non-STEMI	0.40	0.29-1.11	<0.001
	Multivariate		
Gender (Female)	1.41	1.10-1.89	0.02
Age	1.06	1.04-1.08	<0.001
Family History of CAD	0.59	0.42-0.83	0.002
STEMI vs. Non-STEMI	0.60	0.42-0.77	<0.001

p values represent comparisons between male and female

AMI – acute myocardial infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident; STEMI – ST-Segment Elevated Myocardial Infarction

Table 5.7 Health Care Intervention: Discharge HRT (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	20.00	2.63-166.67	0.004
Age	1.00	0.98-1.10	0.4
Urban	0.56	0.20-1.67	0.3
History of Diabetes	0.0	0.0-0.0	1.0
History of Hypertension	0.0	0.0-0.0	1.0
History of Smoking	0.71	0.20-2.50	0.6
History of Dyslipidemia	1.67	0.44-5.00	0.4
Family History of CAD	2.50	0.77-9.98	0.1
Prior Acute Myocardial Infarction	0.0	0.0-0.0	1.0
History of Angina	0.0	0.0-0.0	1.0
History of CABG	0.0	0.0-0.0	1.0
History of CHF	0.0	0.0-0.0	1.0
Prior PTCA	0.0	0.0-0.0	1.0
History of TIA/CVA	0.0	0.0-0.0	1.0
STEMI vs. Non-STEMI	1.3	0.5-3.3	0.8
	Multivariate		
Gender (Female)	33.33	2.78-250.00	0.001
Age	0.95	0.92-100.00	0.03

p values represent comparisons between male and female

AMI – acute myocardial infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident; STEMI – ST-Segment Elevated Myocardial Infarction

5.1.4 Health Care Outcome

Outcomes are displayed in Table 5.8. There were no significant differences in the number of days spent in the CCU between males and females (3.0 days). Both genders spent the same number of days in the hospital (8.0 days) and did not differ significantly with regards to in-hospital death.

Table 5.8 Health Care Outcome (AMI)				
	Total	Male	Female	*p* value
CCU Length of Stay; median* (days)	3.0 [2.0, 5.0]	3.0 [2.0, 4.0]	3.0 [2.0, 5.0]	0.9
Hospital Length of Stay; median* (days)	8.0 [6.0, 11.0]	8.0 [6.0, 11.0]	8.0 [6.0, 12.0]	0.2
Death; *n* (%)	157 (12.0)	88 (11.2)	69 (13.1)	0.3

p values represent comparisons between male and female

AMI – acute myocardial infarction; CCU – coronary care unit

*Median shown with [25th, 75th] percentiles

5.2 Cerebrovascular Accident

5.2.1 Demographics

Table 5.9 shows the demographics and risk factors for the CVA audits. A total of 1000 patients were identified as having a diagnosis of CVA. Almost 56% of the patients were male. The ages of the patients ranged from 18-98 years with an overall mean of 70.6. Females were significantly older than males, however the actual age difference was minimal (72 vs. 70 years, p=0.002).

Men were more likely to have had a previous CVA (29 vs. 18%, p<0.001) and a previous MI (19 vs. 13%, p=0.01). Women were more likely to present with heart failure (14 vs. 9%, p=0.01).

Table 5.9 Demographics and Risk Factors (CVA)				
	Total	Male	Female	*p* value
n (%)	1000	558 (55.8)	442 (44.2)	N/A
Age; mean ± SD (years)	70.6 ± 13.3	69.5 ± 12.1	72.1 ± 14.5	0.002
Urban; *n* (%)	690 (69.0)	383 (68.6)	307 (69.5)	0.8
Previous CVA; *n* (%)	241 (24.1)	163 (29.2)	78 (17.6)	<0.001
Diabetes; *n* (%)	309 (30.9)	169 (30.3)	140 (31.7)	0.6
SPVD; *n* (%)	129 (12.9)	81 (14.5)	48 (10.9)	0.1
Prior MI; *n* (%)	162 (16.2)	105 (18.8)	57 (12.9)	0.01
Angina; *n* (%)	203 (20.3)	110 (19.7)	93 (21.0)	0.6
Heart Failure; *n* (%)	111 (11.1)	49 (8.8)	62 (14.0)	0.01
Chronic Renal Disease; *n* (%)	49 (4.9)	30 (5.4)	19 (4.3)	0.5
Cancer; *n* (%)	84 (8.4)	45 (8.1)	39 (8.8)	0.7

p values represent comparisons between males and females

CVA – cardiovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Males and females did not significantly differ in the severity of the stroke (Table 5.10).

Table 5.10 Severity (CVA)

	Total	Male	Female	*p* value
Confusion; *n* (%)	242 (24.2)	134 (24.0)	108 (24.4)	0.8
Coma; *n* (%)	128 (12.8)	63 (11.3)	65 (14.7)	0.1
Incontinence; *n* (%)	111 (11.1)	69 (12.4)	42 (10.0)	0.3
Arm Weakness; *n* (%)	664 (66.4)	366 (65.6)	298 (67.4)	0.3
Leg Weakness; *n* (%)	654 (65.4)	357 (64.0)	297 (67.2)	0.09
Gait Affected; *n* (%)	477 (47.7)	266 (47.7)	211 (47.7)	0.7
Cranial Nerve Paralysis; *n* (%)	514 (51.4)	286 (51.3)	228 (51.6)	0.6

p values represent comparisons between males and females
CVA – cardiovascular accident

5.2.2 Health Care Access

Health care access for CVA is shown in Table 5.11. There were no significant differences between the sexes for CT/MRI, or in the proportion seen by a dietician, speech language pathologist, physiotherapist, occupational therapist, or transferred to a rehabilitation center. Moreover, there were no differences in the time to access of any of these services. Females were more likely to be seen by a social worker (43 vs. 34%, p=0.006), a difference that persisted when controlling for risk factors and stroke severity (OR=1.4, 95% CI=1.1-1.9) (Table 5.12). However, there was no significant difference in the time to social worker assessment.

Table 5.11 Health Care Access (CVA)

	Total	Male	Female	*p* value
CT/MRI; *n* (%)	809 (80.9)	447 (80.1)	362 (81.9)	0.5
Time to 1st CT; median* (days)	2.10 [0.0-3.0]	2.03 [0.0-3.0]	2.19 [0.0-3.0]	0.3
Repeat CT/MRI; *n* (%)	191 (19.1)	115 (20.6)	76 (17.2)	0.2
>2 CT/MRI; *n* (%)	26 (2.6)	14 (2.5)	12 (2.7)	0.8
Seen by Dietician; *n* (%)	504 (50.4)	277 (49.6)	227 (51.4)	0.6
Time to Dietician; median* (days)	4.97 [2.0-6.0]	4.79 [2.0-6.0]	5.18 [2.0-6.0]	0.8
Seen by Speech Language Pathologist; *n* (%)	465 (46.5)	257 (46.1)	208 (47.1)	0.8
Time to Speech Language Pathologist; median* (days)	4.49 [1.0-5.0]	4.32 [1.0-2.0]	4.71 [1.0-2.0]	1.0
Seen by Physiotherapist; *n* (%)	700 (70.0)	387 (64.9)	313 (70.8)	0.6
Time to Physiotherapist; median* (days)	3.99 [1.0-5.0]	3.89 [2.0-4.0]	4.11 [1.0-5.0]	0.9
Seen by Social Worker; *n* (%)	379 (37.9)	190 (34.1)	189 (42.8)	0.006
Time to Social Worker; median* (days)	9.28 [3.0-11.25]	9.39 [3.0-11.0]	9.18 [3.50-12.0]	0.5
Seen by Occupational Therapist; *n* (%)	635 (63.5)	345 (61.8)	290 (65.6)	0.2
Time to Occupational Therapist; median* (days)	5.35 [2.0-6.0]	5.04 [2.0-6.0]	5.72 [2.0-7.0]	0.6
Transferred to Rehabilitation Center; *n* (%)	130 (13.0)	72 (12.9)	58 (13.1)	0.9
Time to Rehab Center Transfer; median* (days)	27.2 [11.0-35.0]	26.6 [10.0-32.0]	27.9 [14.0-37.5]	0.2

p values represent comparisons between males and females

CVA – cardiovascular accident; CT/MRI – computerized tomography scan/magnetic resonance imaging

*Median shown with [25th, 75th] percentiles

Table 5.12 Health Care Access: Seen by Social Worker (CVA)

	B	95% CI	*p* value
Univariate			
Gender (Female)	1.45	1.12-1.89	0.005
Age	1.02	1.01-1.03	<0.001
Confusion	1.75	1.30-2.38	<0.001
Coma	0.25	0.15-0.41	<0.001
Incontinence	1.25	0.83-1.85	0.3
Arm Weakness	2.04	1.49-2.86	<0.001
Leg Weakness	1.79	1.30-2.44	<0.001
Gait Affected	1.04	0.79-1.37	0.8
Cranial Nerve Paralysis	1.23	0.94-1.64	0.1
Previous CVA	1.06	0.79-1.43	0.7
Diabetes	1.43	1.08-1.85	0.01
SPVD	1.40	0.93-2.00	0.1
Prior MI	0.89	0.63-1.27	0.5
Angina	1.41	1.03-1.92	0.03
Heart Failure	1.33	0.89-2.00	0.2
Chronic Renal Disease	0.60	0.31-1.14	0.1
Cancer	1.01	0.64-1.59	1.0
Multivariate			
Gender (Female)	1.44	1.07-1.92	0.01
Age	1.03	1.01-1.04	<0.001
Confusion	1.82	1.32-2.50	<0.001
Arm Weakness	2.38	1.69-3.33	<0.001

p values represent comparisons between males and females

CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

5.2.3 Health Care Outcome

Outcomes are presented in Table 5.13. There was no significant difference for hospital length of stay. There was also no significant different in death but men were more likely than women to die after controlling for risk factors and stroke severity (OR=0.6, 95% CI=0.4-1.0) (Table 5.14).

Table 5.13 Health Care Outcome (CVA)

	Total	Male	Female	*p* value
Length of Stay; median* (days)	19.0 [5.0, 23.0]	17.9 [5.0, 22.0]	20.5 [5.0, 26.0]	0.06
Death; *n* (%)	209 (20.9)	116 (20.8)	93 (21.0)	0.9

p values represent comparisons between males and females

CVA – cardiovascular accident

*Median shown with [25th, 75th] percentiles

Table 5.14 Health Care Outcome: Death (CVA)

	B	95% CI	*p* value
Univariate			
Gender (Female)	1.01	0.75-1.39	0.9
Age	1.05	1.04-1.07	<0.001
Confusion	1.66	1.12-2.44	0.01
Coma	21.3	13.51-33.33	<0.001
Incontinence	5.24	3.37-8.13	<0.001
Arm Weakness	0.18	1.14-3.00	0.01
Leg Weakness	1.85	1.15-2.99	0.01
Gait Affected	1.25	0.85-1.85	0.3
Cranial Nerve Paralysis	2.40	1.54-3.75	<0.001
Previous CVA	1.19	0.84-1.69	0.3
SPVD	1.32	0.85-2.03	0.2
Diabetes	0.70	0.50-1.00	0.05
Prior MI	1.62	1.10-2.38	0.02
Angina	1.82	1.28-2.58	0.01
Heart Failure	3.37	2.22-5.10	<0.001
Chronic Renal Disease	2.13	1.16-3.92	0.02
Cancer	1.31	0.78-2.21	0.3
Multivariate			
Gender (Female)	0.63	0.40-1.00	0.05
Age	1.07	1.05-1.10	<0.001
Confusion	1.60	1.02-5.51	0.04
Incontinence	2.99	1.75-5.13	<0.001
Cranial Nerve Paralysis	2.11	1.31-3.38	0.002

p values represent comparisons between males and females

CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

5.3 Coronary Revascularization

5.3.1 Demographics

The clinical characteristics of patients given a coronary angiogram are displayed in Table 5.15. There were 1337 patients who were given an angiogram (34% female). Women were significantly older than men (62 vs. 61 yrs., $p<0.001$). Men were more likely to have had an AMI (20% vs. 15%, $p=0.003$)

and critical CAD (77% vs. 55%, $p<0.001$) while women were more likely to have chest pain of an uncertain origin (16% vs. 5%, $p<0.001$).

Table 5.15 Clinical Characteristics of Patients who had Coronary Angiography (Coronary Revascularization)

	Total	Male	Female	*p* value
n; %	1337	879 (65.7)	458 (34.3)	N/A
Age; mean ± SD (years)	60.8 ± 10.8	60.1 ± 10.7	62.1 ± 10.8	0.001
Indication for Heart Catheterization				
Stable Angina; *n* (%)	435 (32.5)	281 (32.0)	154 (33.6)	0.5
Unstable Angina; *n* (%)	262 (19.6)	181 (20.6)	81 (17.7)	0.2
MI; *n* (%)	230 (17.2)	171 (19.5)	59 (12.9)	0.003
Post-MI Angina; *n* (%)	113 (8.5)	76 (8.6)	37 (8.1)	0.7
Chest Pain of Uncertain Origin; *n* (%)	113 (8.5)	40 (4.6)	73 (15.9)	<0.001
CHF; *n* (%)	47 (3.5)	34 (3.9)	13 (2.8)	0.3
Critical CAD; *n* (%)	927 (69.3)	674 (76.7)	253 (55.2)	<0.001

p values represent comparisons between males and females

CABG – coronary artery bypass graft; MI – myocardial infarction; CHF – congestive heart failure; CAD – coronary artery disease

There were 927 patients who had critical CAD (27% female). Their demographics are presented in Table 5.16. Women were significantly older than men (65 vs. 61 yrs., $p<0.001$) and more likely to have diabetes (39% vs. 30%, $p=0.009$). Of these patients, women were more likely to have single vessel disease with no proximal left anterior descending stenosis (38% vs. 27%, $p=0.03$). Men were more likely to have unprotected left main disease (10% vs. 5%, $p=0.01$). The results of the angiogram showed that women were more likely to have grade 1 left ventricular function (77% vs. 65%, $p<0.01$) and men were more likely to have both grade 2 (17% vs. 11%, $p=0.02$) and grade 3 (8% vs. 3%, $p=0.05$) left ventricular function. Similarly, men were more likely than women to have ejection fractions of less than 35% (15% vs. 10%, $p=0.03$).

Table 5.16 Clinical Characteristics of Patients with Critical CAD (Coronary Revascularization)

	Total	Male	Female	*p* value
n; (%)	927	674 (72.7)	253 (27.3)	N/A
Age; mean ± SD	62.1 ± 10.3	61.2 ± 10.0	64.5 ± 10.7	<0.001
Diabetes; *n* (%)	298 (32.1)	200 (29.7)	98 (38.7)	0.009
Coronary Anatomy				
Single vessel, no PLAD; *n* (%)	277 (29.9)	183 (27.2)	94 (37.5)	0.003
Single vessel, PLAD; *n* (%)	55 (5.9)	38 (5.6)	17 (6.7)	0.5
Double vessel, no PLAD; *n* (%)	211 (22.8)	154 (22.8)	57 (22.5)	0.9
Double vessel, PLAD; *n* (%)	58 (6.3)	42 (6.2)	16 (6.3)	1.0
Triple vessel; *n* (%)	219 (23.6)	167 (24.8)	52 (20.6)	0.2
Unprotected left main disease; *n* (%)	78 (8.4)	66 (9.8)	12 (4.7)	0.01
Protected left main disease; *n* (%)	24 (2.6)	19 (2.8)	5 (2.0)	0.5
LV Angiogram				
Grade 1 Ventricle; *n* (%)	630 (68.0)	435 (64.5)	195 (77.1)	<0.001
Grade 2 Ventricle; *n* (%)	143 (15.4)	115 (17.1)	28 (11.1)	0.02
Grade 3 Ventricle; *n* (%)	74 (8.0)	56 (8.3)	18 (7.1)	0.6
Grade 4 Ventricle; *n* (%)	60 (6.5)	53 (7.9)	7 (2.8)	0.005
Ejection Fraction (<35%); *n* (%)	126 (13.6)	102 (15.1)	24 (9.5)	0.03
Very Positive Stress Test; *n* (%)	176 (19.0)	133 (19.7)	43 (17.0)	0.8
Maximal Medical Therapy; *n* (%)	377 (40.7)	264 (39.2)	113 (44.7)	0.1
CCS Angina Class				
Class 1-2; *n* (%)	188 (20.3)	140 (20.8)	48 (19.0)	0.5
Class 3; *n* (%)	201 (21.7)	145 (21.5)	56 (22.1)	0.8
Class 4; *n* (%)	481 (51.9)	347 (51.5)	134 (53.0)	0.7

p values represent comparisons between males and females

CABG – coronary artery bypass graft; PLAD – proximal left anterior descending; LV – left ventricle; CCS – Canadian Cardiovascular Society; MI – myocardial infarction; PCI – percutaneous coronary intervention

The clinical characteristics of the 285 patients (20% female) recommended for CABG are shown in Table 5.17. Women were significantly older than men (66 vs. 62 yrs., p=0.01) but there were no significant differences in co-morbidities. There were two differences in Canadian Cardiovascular Society (CCS) angina class – men were more likely than women to be in class 1 and 2 (18% vs. 7%, p=0.05) and women were more likely than men to be in class 4B (12% vs. 4%, p=0.008).

Table 5.17 Clinical Characteristics of Patients Recommended for CABG (Coronary Revascularization)

	Total	Male	Female	*p* value
n; (%)	285	228 (80.0)	57 (20.0)	N/A
Age; mean ± SD	62.8 ± 9.3	62.1 ± 9.0	65.6 ± 10.0	0.01
Co-morbidity Present; *n* (%)	137 (48.1)	107 (46.9)	30 (52.6)	0.4
Diabetes; *n* (%)	106 (37.2)	81 (35.5)	25 (43.9)	0.2
Recent MI; *n* (%)	71 (24.9)	52 (22.8)	19 (33.3)	0.1
Previous CABG; *n* (%)	6 (2.1)	4 (1.8)	2 (3.5)	0.4
High Ischemic Risk; *n* (%)	76 (26.7)	64 (28.1)	12 (21.1)	0.3
CCS Angina Class				
Class 1 & 2; *n* (%)	44 (15.4)	40 (17.5)	4 (7.0)	0.05
Class 3; *n* (%)	102 (35.8)	80 (35.1)	22 (38.6)	0.6
Class 4A; *n* (%)	32 (11.2)	27 (11.8)	5 (8.8)	0.5
Class 4B; *n* (%)	15 (5.3)	8 (3.5)	7 (12.3)	0.008
Class 4C; *n* (%)	32 (11.2)	24 (10.5)	8 (14.0)	0.5
Priority for CABG				
Very Urgent; *n* (%)	11 (3.9)	10 (4.4)	1 (1.8)	0.4
Urgent; *n* (%)	16 (5.6)	10 (4.4)	6 (10.5)	0.07
Semi-Urgent; *n* (%)	17 (6.0)	11 (4.8)	6 (10.5)	0.1
Short Wait; *n* (%)	35 (12.3)	29 (12.7)	6 (10.5)	0.7
Delayed Wait; *n* (%)	131 (46.0)	108 (47.4)	23 (40.4)	0.3

p values represent comparisons between males and females

CABG – coronary artery bypass graft; MI – myocardial infarction; CCS – Canadian Cardiovascular Society

5.3.2 Health Care Access

Health care access is presented in Table 5.18. While there were no significant differences in priority for CABG or days awaiting CABG, women in the priority category "short wait" had longer times to CABG than men in the same category (median 6.0 vs. 8.0 days, p=0.05). This difference remained significant after multivariate analysis (OR=-0.34) (Table 5.19).

Table 5.18 Health Care Access (Coronary Revascularization)

	Total	Male	Female	*p* value
Days Awaiting CABG by Priority				
Very Urgent; median* (days)	6.0 [0.0-9.0]	6.0 [0.0-0.25]	8.0	0.9
Urgent; median* (days)	5.0 [3.0-8.8]	6.5 [2.5-9.0]	3.5 [2.3-23.5]	0.3
Semi-Urgent; median* (days)	3.0 [1.0-7.0]	3.0 [1.0-4.0]	5.0 [1.8-9.3]	0.2
Short Wait; median* (days)	7.0 [2.0-27.5]	6.0 [2.0-28.5]	8.0 [4.5-29.2]	0.05
Delayed Wait; median* (days)	29.0 [9.0-85.0]	27.5 [8.0-77.5]	59.0 [13.0-344.0]	0.2
Days Awaiting CABG; median*	10 [3.8, 55.5]	10 [4.0, 48.0]	10 [6.0, 73.3]	0.3
Urgency Rating Score; median*	5.4 [4.2, 6.2]	5.5 [4.3, 6.2]	5.1 [3.9, 6.2]	0.5
Reco. Max. Wait Time; median*	49.0 [13.0, 10.6.0]	62.5 [19.5, 106.0]	64.0 [21.0, 105.8]	0.5

p values represent comparisons between males and females

CABG – coronary artery bypass graft

*Median shown with [25th, 75th] percentiles

Table 5.19 Health Care Access: Days Awaiting CABG for Patients with Short Wait Priority (Coronary Revascularization)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.34	0.05
Age	0.050	0.8
Diabetes	-0.20	0.3
Recent MI	0.12	0.5
Previous CABG	-0.12	0.5
Urgency Rating Score	0.14	0.4
Coronary Anatomy		
Single Vessel, no PLAD	0.027	0.9
Double Vessel, no PLAD	0.048	0.8
Double Vessel, PLAD	0.024	0.9
Triple Vessel	0.10	0.6
Unprotected Left Main Disease	-0.13	0.5
LV Angiogram		
Grade 1 LV	0.27	0.1
Grade 2 LV	-0.39	0.02
Grade 3 LV	0.063	0.7
Grade 4 LV	0.0090	1.0
Ejection Fraction (<35%)	0.061	0.7
Very Positive Stress Test	0.010	1.0
Maximal Medical Therapy	-0.19	0.3
CCS Angina Class 1-2	0.093	0.6
CCS Angina Class 3	-0.28	0.1
CCS Angina Class 4	0.21	0.2
	Multivariate	
Gender (Female)	-0.34	0.05
Age	0.0090	1.0

p values represent comparisons between males and females

CABG – coronary artery bypass graft; CAD – coronary artery disease; MI – myocardial infarction; PLAD - proximal left anterior descending; LV – left ventricle; CCS – Canadian Cardiovascular Society

5.3.3 Health Care Intervention

Women were more likely to be recommended for medical management of their CAD (42% vs. 28%, $p<0.001$) and men were more likely to be recommended for CABG (34% vs. 25%, $p=0.001$) (Table 5.20).

Table 5.20 Health Care Intervention (Coronary Revascularization)

	Total	Male	Female	*p* value
Recommendations for Treatment				
Medical Management; *n* (%)	297 (32.0)	191 (28.3)	106 (41.9)	<0.001
PCI; *n* (%)	315 (34.0)	232 (34.4)	83 (32.8)	0.6
Coronary Stent; *n* (%)	270 (85.7)	200 (86.2)	70 (84.3)	0.3
Drug Eluting Stent; *n* (%)	207 (65.7)	153 (65.9)	54 (65.1)	0.7
CABG; *n* (%)	285 (30.7)	228 (33.8)	57 (22.5)	0.001

p values represent comparisons between males and females

CABG – coronary artery bypass graft; PCI – percutaneous coronary intervention

After controlling for co-morbidity, CAD severity, and left ventricle (LV) class women were still more likely to be recommended for medical management (OR=1.7, 95% CI=1.2-2.5) (Table 5.21).

Table 5.21 Health Care Intervention: Medical Management (Coronary Revascularization)

	Univariate		
	B	95% CI	*p* value
Gender (Female)	1.82	0.40-0.74	<0.001
Age	1.01	0.99-1.02	0.2
Diabetes	1.02	0.75-1.39	0.9
Coronary Anatomy			
Single Vessel, no PLAD	2.58	1.93-3.47	<0.001
Single Vessel, PLAD	0.51	0.26-1.00	0.05
Double Vessel, no PLAD	1.27	0.92-1.75	0.1
Double Vessel, PLAD	0.48	0.24-0.93	0.03
Triple Vessel	0.53	0.37-0.76	0.001
Unprotected Left Main Disease	0.16	0.068-0.37	<0.001
Protected Left Main Disease	2.16	0.96-4.87	0.06
LV Angiogram			
Grade 1 LV	0.89	0.66-1.20	0.5
Grade 2 LV	1.13	0.77-1.64	0.5
Grade 3 LV	1.28	0.78-2.11	0.3
Grade 4 LV	0.84	0.47-1.50	0.6
Ejection Fraction (<35%)	1.06	0.71-1.58	0.8
Very Positive Stress Test	0.86	0.56-1.31	0.5
Maximal Medical Therapy	0.59	0.43-0.80	0.001
CCS Angina Class			
Class 1-2	2.43	1.74-3.39	<0.001
Class 3	0.60	0.41-0.86	0.60
Class 4	0.74	0.56-0.99	0.04
	Multivariate		
Gender (Female)	1.72	0.40-0.85	0.005
Age	1.01	0.99-1.02	0.4
Single Vessel, PLAD	0.29	0.13-0.64	0.002
Double Vessel, PLAD	0.27	0.12-0.61	0.002
Triple Vessel	0.38	0.24-0.59	<0.001
Unprotected Left Main Disease	0.094	0.033-0.27	<0.001
Maximal Medical Therapy	0.62	0.43-0.88	0.008
CCS Angina Class 4	1.92	1.26-2.90	0.002

p values represent comparisons between males and females

CABG – coronary artery bypass graft; CAD – coronary artery disease; PLAD - proximal left anterior descending; LV – left ventricle; CCS – Canadian Cardiovascular Society

After multivariate modeling, there were no differences between men and women who received CABG.

5.4 Community Acquired Pneumonia

5.4.1 Demographics

There were 1166 patients diagnosed with CAP (44% female). The demographics of these patients are in Table 5.22. There were no significant differences in age (69 vs. 68 yrs.). Men were more likely than women to have an adult caregiver at home (48% vs. 41%, p=0.01) and suffer from alcoholism (8% vs. 2%, p<0.001), CAD (36% vs. 30%, p=0.04), chronic renal failure (11% vs. 6%, p=0.02), COPD (35% vs. 25%, p<0.001) or another co-morbidity (33% vs. 28%, p=0.04). Women were more likely to have asthma (16% vs. 11%, p=0.01).

Table 5.22 Demographics and Risk Factors (CAP)

	Total	Male	Female	*p* value
n (%)	1166 (100)	656 (56.3)	510 (43.7)	N/A
Age; mean ± SD (years)	68.3 ± 17.6	68.8 ± 16.8	67.7 ± 18.6	0.3
Nursing Home Resident; *n* (%)	135 (11.6)	78 (11.9)	57 (11.2)	0.8
Adult Caregiver at Home; *n* (%)	519 (44.5)	312 (47.6)	207 (40.6)	0.01
Hospitalized in Past Year; *n* (%)	461 (39.5)	261 (39.8)	200 (39.2)	0.9
History of Alcoholism; *n* (%)	67 (5.7)	54 (8.2)	13 (2.5)	<0.001
History of CAD; *n* (%)	386 (33.1)	235 (35.8)	151 (29.6)	0.04
History of Neoplastic Disease; *n* (%)	197 (16.9)	121 (18.4)	76 (14.9)	0.2
History of Interstitial Disease; *n* (%)	66 (8.7)	44 (6.7)	22 (4.3)	0.1
Chronic Renal Failure; *n* (%)	101 (8.7)	69 (10.5)	32 (6.3)	0.02
Neurological Condition; *n* (%)	74 (6.3)	44 (6.7)	30 (5.9)	0.7
History of Smoking; *n* (%)	289 (24.8)	166 (25.3)	123 (24.1)	0.7
History Asthma; *n* (%)	154 (13.2)	73 (11.1)	81 (15.9)	0.01
COPD; *n* (%)	355 (30.4)	229 (34.9)	126 (24.7)	<0.001
Diabetes; *n* (%)	240 (20.6)	137 (20.9)	103 (20.2)	0.9
Chronic Liver Disease; *n* (%)	14 (1.2)	6 (0.9)	8 (1.6)	0.4
History of CHF; *n* (%)	242 (20.8)	142 (21.6)	100 (19.6)	0.5
CVD; *n* (%)	128 (11.0)	73 (11.1)	55 (10.8)	1.0
Other Comorbidity; *n* (%)	359 (30.8)	218 (33.2)	141 (27.6)	0.04
Oral Steroids; *n* (%)	127 (12.6)	89 (13.6)	58 (11.4)	0.4
Normal Mental Status; *n* (%)	932 (79.9)	513 (78.2)	419 (82.2)	0.2

p values represent comparisons between males and females

CAP – community acquired pneumonia; CAD – coronary artery disease; COPD – chronic obstructive pulmonary disease; CHF – congestive heart failure; CVD – cerebrovascular disease

Diagnostics and severity are presented in Table 5.23. Men were more likely to require mechanical ventilation (3% vs. 0.8%, p=0.006), have an abnormally high or low temperature (<35° or ≥40°) (3% vs. 1%, p=0.05) and have more than 1 lobe affected on a chest x-ray (24% vs. 18%, p=0.03). Women were more likely than men to be in lower PSI – class I and II (35% vs. 24%, p<0.001) and, as such, were more likely to be placed in a low risk group (60% vs. 44%, p<0.001). Men were more often in higher classes – class IV (40% vs. 32%, p=0.008) and class V (16% vs. 8%, p<0.001). Men presented with higher mean creatinine levels (139 vs. 108 µmol/L, p<0.001) and mean hemoglobin levels (130 vs. 123 g/L, p<0.001); in general, men tend to have higher hemoglobin than women so this

difference may simply be physiological. Women had higher urea levels than men (18 vs. 11 mmol/L, $p<0.001$).

Table 5.23 Disease Severity and Diagnostics (CAP)

	Total	Male	Female	*p* value
Dyspnea; *n* (%)	793 (68.0)	447 (68.1)	346 (67.8)	0.6
Cough; *n* (%)	882 (75.6)	493 (75.2)	389 (76.3)	1.0
Sputum Production; *n* (%)	628 (53.9)	351 (53.5)	277 (54.3)	1.0
Sputum Microbiology; *n* (%)	414 (35.5)	235 (35.8)	179 (35.1)	0.6
Positive Culture; *n* (%)	81 (6.9)	47 (7.2)	34 (6.7)	1.0
Pleuritic Chest Pain; *n* (%)	309 (26.5)	159 (24.2)	150 (29.4)	0.08
Pleural Fluid; *n* (%)	29 (2.5)	15 (2.8)	14 (2.7)	0.7
Maintain PO Intake; *n* (%)	783 (67.2)	452 (68.9)	331 (64.9)	0.2
Mechanical Ventilation; *n* (%)	24 (2.1)	20 (3.0)	4 (0.8)	0.006
Temperature <35° or ≥40°; *n* (%)	22 (1.9)	17 (2.6)	5 (1.0)	0.05
Respiratory Rate; *n* (%) (≥ 30/min.)	235 (20.2)	129 (19.7)	106 (20.8)	0.7
Pulse Rate; mean ± SD (per min.)	94.6 ± 19.1	94.1 ± 20.2	95.1 ± 17.7	0.4
Chest X-Ray; *n* (%)	1137 (97.5)	644 (98.2)	493 (96.7)	0.1
>1 lobe; *n* (%)	250 (21.4)	156 (23.8)	94 (18.4)	0.03
Was PO_2 Measured?; *n* (%)	583 (50.0)	326 (49.7)	257 (50.4)	0.9
PO_2; mean ± SD (mm Hg)	73.6 ± 33.3	72.7 ± 29.3	74.7 ± 37.9	0.5
Was O_2 Saturation Measured?; *n* (%)	580 (49.7)	323 (49.2)	257 (50.4)	0.7
O_2 Saturation; mean ± SD (%)	91.7 ± 9.7	91.4 ± 10.7	92.0 ±8.5	0.4
Systolic BP; mean ± SD (mm Hg)	130.3 ± 36.6	129.1 ± 26.1	131.8 ± 46.8	0.2
Diastolic BP; mean ± SD (mm Hg)	73.3 ± 13.8	73.7 ± 13.7	72.8 ± 14.0	0.3
Hematocrit; mean ± SD (%)	22.2 ± 145.9	25.2 ± 155.6	18.4 ± 132.5	0.4
Hemoglobin; mean ± SD (g/L)	126.8 ± 19.6	129.8 ± 20.6	123.0 ± 17.4	<0.001
White Blood Cell Count; mean ± SD	13.9 ± 15.8	14.2 ± 19.1	13.6 ±10.3	0.5
Urea; mean ± SD (mmol/L)	9.6 ± 11.2	10.9 ± 12.8	8.1 ± 8.2	<0.001
Creatinine; mean ± SD (μmol/L)	124.8 ± 104.7	138.4 ± 117.9	107.2 ± 81.3	<0.001
Blood Culture; *n* (%)	572 (49.1)	324 (49.4)	248 (48.6)	0.8
Positive Culture; *n* (%)	31 (2.7)	15 (2.3)	16 (3.1)	0.3
PSI Class I; *n* (%)	116 (9.9)	62 (9.5)	54 (10.6)	0.6
PSI Class II; *n* (%)	219 (18.8)	93 (14.2)	126 (24.7)	<0.001
PSI Class I & II; *n* (%)	335 (28.7)	155 (23.6)	180 (35.3)	<0.001
PSI Class III; *n* (%)	257 (22.0)	133 (20.3)	124 (24.3)	0.1
PSI Class IV; *n* (%)	425 (36.4)	261 (39.8)	164 (32.2)	0.008
PSI Class V; *n* (%)	149 (12.8)	107 (16.3)	42 (8.2)	<0.001
Low Risk; *n* (%)	595 (51.0)	290 (44.2)	305 (59.8)	<0.001

p values represent comparisons between males and females

CAP – community acquired pneumonia; BP – blood pressure; PSI – pneumonia severity index

5.4.2 Health Care Intervention

Using the 1993 guidelines (Table 5.24), women were less likely to receive appropriate antibiotics (70% vs. 78%, p=0.001).

Table 5.24 Health Care Intervention (CAP)

	Total	Male	Female	p value
Appropriateness of Antibiotic Choice (IV or Oral)				
1993 Guidelines				
Appropriate; *n* (%)	867 (74.4)	512 (78.0)	355 (69.6)	0.001
Yes; n (%)	768 (65.9)	453 (69.1)	315 (61.8)	0.009
With Extra Meds.; *n* (%)	99 (8.5)	59 (9.0)	40 (7.8)	0.5
Inappropriate; *n* (%)	299 (25.6)	144 (22.0)	155 (30.4)	0.001
Macrolide Only; *n* (%)	61 (5.2)	29 (4.4)	32 (6.3)	0.2
Wrong Drug; *n* (%)	219 (18.8)	101 (15.4)	118 (23.1)	0.001
No Meds. Ordered; *n* (%)	14 (1.2)	9 (1.4)	5 (1.0)	0.5
Lacking Macrolide; *n* (%)	5 (0.4)	5 (0.8)	0	0.05
2000 Guidelines				
Appropriate; n (%)	877 (75.2)	513 (78.2)	364 (71.4)	0.007
Yes; n (%)	778 (66.7)	454 (69.2)	324 (63.5)	0.05
With Extra Meds.; n (%)	99 (8.5)	59 (9.0)	40 (7.8)	0.5
Inappropriate; n (%)	289 (24.8)	143 (21.8)	146 (28.6)	0.007
Macrolide Only; n (%)	62 (5.3)	30 (4.6)	32 (6.3)	0.2
Wrong Drugs; n (%)	210 (18.0)	101 (15.4)	109 (21.4)	0.009
No Meds. Ordered; n (%)	14 (1.2)	9 (1.4)	5 (1.0)	0.6
Lacking Macrolide; n (%)	3 (0.3)	3 (0.5)	0	0.3

p values represent comparisons between males and females

CAP – community acquired pneumonia; IV - intravenous

This difference remained significant in multivariate analysis (OR=0.7, 95% CI=0.5-0.9) (Table 5.25). Women were significantly more likely than men to receive the wrong drug (23% vs. 15%, p=0.001). According to the 2000 guidelines (seen earlier in Table 5.24), women were also less likely to receive appropriate antibiotics (71% vs. 78%, p=0.007). Again, women were significantly more likely to receive the wrong drug (21% vs. 15%, p=0.009). However, this difference did not remain significant in multivariate analysis.

Table 5.25 Health Care Intervention: Appropriateness of Antibiotic Choice (1993 Guidelines) (CAP)

	B	95% CI	p value
	Univariate		
Gender (Female)	0.65	0.50-0.84	0.001
Age	1.04	1.03-1.04	<0.001
Nursing Home Resident	2.64	1.56-4.46	<0.001
Hospitalized in Past Year	1.04	0.79-1.37	1.0
Alcohol	0.64	0.38-1.09	0.1
CAD	2.44	1.78-3.36	<0.001
Neoplastic Disease	2.66	1.71-4.15	<0.001
Interstitial Disease	1.28	0.70-2.17	0.4
Chronic Renal Failure	3.75	1.87-7.52	<0.001
Neurological Condition	0.53	0.32-0.86	0.01
Smoker	0.66	0.49-0.89	0.006
Asthma	1.78	1.14-2.78	0.01
COPD	1.62	1.19-2.20	0.002
Diabetes	1.61	1.13-2.30	0.008
Liver Failure	2.05	0.46-9.26	0.3
CHF	3.11	2.04-4.72	<0.001
CVD	1.95	1.18-3.19	0.009
Low Risk	0.17	0.12-0.23	<0.001
Require Hospitalization	1.50	1.15-1.97	0.003
Dyspnea	1.43	1.08-1.90	0.01
Cough	0.98	0.71-1.34	0.9
Sputum	1.11	0.85-1.45	0.4
Chest Pain	0.65	0.49-0.87	0.003
AB Prior to Admission	0.67	0.38-1.18	0.2
	Multivariate		
Gender (Female)	0.72	0.53-0.94	0.03
Age	1.02	1.01-1.03	<0.001
Neoplastic Disease	1.68	1.03-2.72	0.04
Asthma	2.43	1.51-3.92	<0.001
Low Risk	0.28	0.19-0.41	<0.001

p values represent comparisons between males and females

CAP – community acquired pneumonia; CAD – coronary artery disease; COPD – chronic obstructive pulmonary disease; CHF – congestive heart failure; CVD – cerebrovascular disease

5.4.3 Health Care Outcome

There were no significant differences in hospitalization or length of stay (Table 5.26). Men were more likely than women to die (11% vs. 8%, p=0.03) but this difference did not remain significant after further multivariate analyses.

Table 5.26 Health Care Outcome (CAP)

	Total	Male	Female	*p* value
Require Hospitalization; *n* (%)	750 (64.3)	426 (64.9)	324 (63.5)	0.6
Prolonged LOS; *n* (%)	343 (29.4)	186 (28.4)	157 (30.8)	0.4
Time to Discharge; median* (days)	10.0 [2.0, 11.0]	9.7 [5.0, 11.0]	10.3[5.0, 11.5]	0.3
Death; *n* (%)	112 (9.6)	74 (11.3)	38 (7.5)	0.03

p values represent comparisons between males and females
CAP – community acquired pneumonia; LOS – length of stay
*Median shown with [25th, 75th] percentiles

5.5 Chronic Kidney Disease

5.5.1 Demographics

Table 5.27 describes data on the 339 patients starting RRT during the study period. Approximately 38% of the patients were female. The ages of patients ranged from 19-91 years, with an overall mean age of 63 years. There were no significant gender differences in baseline age, risk factors or etiology of kidney disease.

Table 5.27 Baseline Demographics and Medical History (CKD)

	Total	Male	Female	*p* value
n (%)	339	211 (62.2)	128 (37.8)	N/A
Age (mean ± SD; years)	63.0 ± 15.6	62.9 ± 15.7	63.1 ± 15.4	0.9
History of Diabetes; *n* (%)	163 (48.1)	106 (50.2)	57 (44.5)	0.3
History of Hypertension; *n* (%)	310 (91.4)	193 (91.5)	117 (91.4)	0.98
History of CHF; *n* (%)	62 (18.3)	39 (18.6)	23 (18.0)	0.9
History of Cancer; *n* (%)	61 (18.0)	39 (18.5)	22 (17.3)	0.8
History of Renal Disease; *n* (%)	75 (22.1)	47 (22.3)	28 (21.9)	0.9
Etiology of Renal Disease				
Diabetes; *n* (%)	139 (41.0)	88 (41.7)	51 (39.8)	0.9
GN/Auto-Immune; *n* (%)	53 (15.6)	34 (16.1)	19 (14.8)	0.8
Polycystic Kidneys; *n* (%)	21 (6.2)	15 (7.1)	6 (4.7)	0.4
Pyelonephritis; *n* (%)	10 (2.9)	5 (2.4)	5 (3.9)	0.4
Renal Vascular Disease; *n* (%)	75 (22.1)	47(22.3)	28 (21.9)	0.97
Unknown; *n* (%)	25 (7.4)	14 (6.6)	11 (8.6)	0.5
Other; *n* (%)	81 (23.9)	51 (24.2)	30 (23.4)	0.99

p values represent comparisons between males and females

CKD – chronic kidney disease; CHF – congestive heart failure; GN – glomerulonephritis

5.5.2 Health Care Access

Data in Table 5.28 shows men received significantly more pre-dialysis care (defined as greater than 1 month) than women (88 % vs. 79%, p=0.04).

Table 5.28 Health Care Access (CKD)

	Total	Male	Female	*p* value
Pre-Dialysis Care (>1 mth.); *n* (%)	282 (84.7)	182 (87.9)	100 (79.4)	0.04
Laboratory Parameters at Dialysis Start				
eGFR (mL/min.); mean ± SD	9.5 ± 5.1	10.1 ± 5.3	8.6 ± 4.5	0.01
Calcium (mmol/L); mean ± SD	2.1 ± 0.3	2.1 ± 0.3	2.1 ± 0.3	0.7
Phosphate (mmol/L); mean ± SD	1.9 ± 0.6	2.0 ± 0.7	1.9 ± 0.5	0.3
Hemoglobin (g/L); mean ± SD	102.6 ± 15.4	103.1 ± 15.3	101.8 ± 15.7	0.5
Ferritin (µg/L); mean ± SD	230.4 ± 258.4	240.8 ± 270.5	212.9 ± 237.2	0.4
Albumin (g/L); mean ± SD	32.9 ± 7.8	33.2 ± 7.8	32.3 ± 7.7	0.3
iPTH (ng/L); mean ± SD	120.0 ± 154.4	116.7 ± 150.4	125.8 ± 162.1	0.7

p values represent comparisons between males and females

CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate; iPTH – immunoreactive parathyroid hormone

Table 5.29 reveals that this difference remained significant after controlling for age and medical history risks (OR=0.5, 95% CI=0.3-1.0).

Table 5.29 Health Care Access: Pre-Dialysis Care (>1 mth.) (CKD)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.55	0.30-1.01	0.05
Age	1.00	0.98-1.02	0.9
History of Diabetes	1.60	0.86-2.96	0.1
History of Hypertension	2.36	0.98-5.68	0.06
History of CHF	0.46	0.23-0.90	0.02
History of Cancer	0.75	0.36-1.57	0.4
History of Renal Disease	1.37	0.63-2.97	0.4
	Multivariate		
Gender (Female)	0.54	0.29-1.00	0.05
Age	1.01	0.99-1.03	0.3
History of Hypertension	2.78	1.13-6.85	0.03
History of CHF	0.37	0.18-0.78	0.009

p values represent comparisons between males and females
CKD – chronic kidney disease; CHF – congestive heart failure

There were no differences between serum calcium, phosphate, albumin, hemoglobin or ferritin—all measured at dialysis start. Women had significantly lower eGFR levels at dialysis start (8.6 vs. 10 mL/min; p=0.01). After controlling for demographics, risk factors, access, and other laboratory values at dialysis start, this difference remained significant (OR=-1.41) (Table 5.30).

Table 5.30 Health Care Access: eGFR at Dialysis Start (CKD)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-1.41	0.02
Age	0.029	0.1
History of Diabetes	0.085	0.9
History of Hypertension	-2.10	0.05
History of CHF	1.65	0.02
History of Cancer	1.32	0.07
History of Renal Disease	0.76	0.3
Pre-Dialysis Care (>1 mth.)	-0.71	0.4
Optimal Access	0.68	0.2
Phosphate at Dialysis Start	-3.04	<0.001
Hemoglobin at Dialysis Start	0.067	<0.001
Ferritin at Dialysis Start	0.0017	0.2
Albumin at Dialysis Start	0.0031	0.9
	Multivariate	
Gender (Female)	-1.34	0.006
Age	0.012	0.4
History of CHF	1.47	0.02
Phosphate at Dialysis Start	-2.95	<0.001
Hemoglobin at Dialysis Start	0.034	0.03

p values represent comparisons between males and females

CKD – chronic kidney disease; CHF – congestive heart failure; eGFR – estimated glomerular filtration rate

5.5.3 Health Care Intervention

Interventions can be seen in Table 5.31. Although males were more likely to receive optimal modality (50% vs. 40%) and optimal access (50% vs. 40%) than females, these differences were not statistically significant. Women receiving HD took part in the same number of treatment sessions per week but experienced fewer hours (<4 hrs.) per treatment session than men (63 % vs. 81%, p=0.003).

Table 5.31 Health Care Intervention (CKD)

	Total	Male	Female	*p* value
Modality				
Optimal Choice; *n* (%)	155 (45.7)	104 (49.3)	51 (39.8)	0.09
HD Sessions per Week (≤3); *n* (%)	244 (98.7)	152 (98.0)	92 (100.0)	0.4
HD Hours per Session (4 hrs.); *n* (%)	184 (74.2)	125 (80.6)	59 (63.4)	0.003
Optimal Access; *n* (%)	156 (46.0)	105 (49.8)	51 (39.8)	0.08

p values represent comparisons between males and females

CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate; iPTH – immunoreactive parathyroid hormone

5.5.4 Health Care Outcome

There were no differences between hospitalization, hospitalization related to RRT, hospitalization after RRT, hospital length of stay, or death (Table 5.32).

Table 5.32 Health Care Outcome (CKD)

	Total	Male	Female	*p* value
Hospitalizations; *n* (%)	171 (50.4)	103 (48.8)	68 (53.1)	0.4
Hospitalizations Related to RRT; *n* (%)	64 (62.1)	37 (54.4)	101 (59.1)	0.3
Hospitalizations After RRT; *n* (%)	108 (31.9)	61 (28.9)	37 (54.4)	0.1
Hospital LOS (days); mean ± SD	14.4 (31.6)	13.8 (29.9)	15.4 (34.3)	0.6
Death; *n* (%)	23 (6.8)	13 (6.2)	10 (7.8)	0.6

p values represent comparisons between males and females

CKD- chronic kidney disease; RRT – renal replacement therapy; LOS – length of stay

5.6 Summary

In general, the women who presented in Newfoundland with either an AMI or CVA, or who were recommended for CABG, had very similar demographics. They were close in age (66-73 years) and experienced similar levels of diabetes (32-44%), congestive heart failure (14-22%), and prior CABG (4-6%). They did not differ greatly in any risk factor. The same risk factors were not recorded for each CVD so it is impossible to grasp the extent of their similarity but it is plausible that these women are more alike than we know.

With regards to the results being divided into health care access, interventions, and outcomes, the overall results were as follows (Table 5.33):

Table 5.33 Summary of Results

	Access	Intervention	Outcome
AMI	+ +		
CVA			
Coronary Revascularization	+	+	
CAP		+	
CKD	+ +		

*Each + represents one multivariate significant result

More often than men, women received less rigorous or appropriate health care access or interventions. Women were never more likely than men to die.

Chapter 6 Discussion

For all three CVDs studied, women were consistently older than men and, in all cases except CVA, had more co-morbid illnesses and more serious baseline medical histories and risk factors. This finding is consistent with previous literature, particularly with regards to AMI, that has found consistently that women suffer a cardiovascular incident at an older age when they are more likely to be in ill health [24, 25, 48-51, 57]. In CKD, there was no significant difference in either age or medical histories between the genders. In CAP, the non-vascular control group, there were no significant gender differences in age but men suffered from co-morbidities more often and presented with more severe cases of the disease.

6.1 Acute Myocardial Infarction

Women who suffered an AMI were less likely than men to be admitted to the CCU and, although they were thrombolyzed at an equal rate, they had longer thrombolysis wait times. These differences, both classified as health care access, remained significant after controlling for age, baseline medical history and co-morbidities, and severity of AMI, as indicated by STEMI. It has been suggested that women are less likely than men to receive timely reperfusion therapy [58] but past research has not examined differences in CCU admission. Having suffered a STEMI was found to be a significant predictor of admission to CCU so it is likely than severity of heart attack played a role in women being less likely to receive a CCU bed. Women suffered STEMIs less often than men and probably were admitted to CCU less as a result. However, having had a STEMI did not play a role in the time to thrombolytics analysis. Another possible explanation for the discrepancy in CCU

admission may be the atypical symptoms experienced by women. If a physician does not recognize that a woman is suffering from an AMI due to her ambiguous symptoms, it is foreseeable that she will experience a delay in receiving a correct diagnosis and will either be delayed in receiving a CCU bed or die before that opportunity arises.

With regards to interventions, women were more likely than men to receive two discharge medications, a diuretic and HRT. Despite women having less optimal access than men, in the form of admission to CCU and timely thrombolytics, they did not experience poorer outcomes as a result - women and men were equally likely to die.

An important point to add to the discussion of a gender bias in AMI is the inherent bias in the guidelines used to diagnose a myocardial infarction. The World Health Organization (WHO) requires at least two of the three following factors: 1) typical symptoms of myocardial ischemia for more than 30 minutes, 2) evolutionary changes on an ECG, or 3) increased levels of serum cardiac biomarkers [123]. While a bias may not appear obvious here, it has been noted in past research, and highlighted in Chapter 1 of this thesis, that women who are having a heart attack are more likely to experience atypical symptoms, including nausea, fatigue, or abdominal pain [6, 25-27] compared to typical symptoms of chest pain. How then is it possible for a woman experiencing the common atypical symptoms to be correctly diagnosed as suffering from an AMI when the WHO guidelines clearly state for her physician to look for ongoing typical symptoms? As a result, women may be subject to potentially life-threatening delays before crucial tests and treatments can be administered. In this situation, there is a prejudice against women simply because they do not

always experience the same symptoms as men – symptoms that are only deemed atypical because the diagnostic standards were established mainly from research on men [124, 125].

6.2 Cerebrovascular Accident

Patients who suffered a CVA did not differ significantly in baseline medical histories or stroke severity, but women were significantly older than men. One health care access result was found to be significant for a gender difference; women were more likely than men to be seen by a social worker. This difference remained significant after multivariate analysis. Although we do not have the data to support it, it is likely than women were referred to a social worker more often than men because the women did not have a spouse at home to return to upon hospital discharge. It has been well documented that women, on average, live longer than men [126-128]. Knowing this, it seems logical that a woman with a mean age of 72 who has suffered a stroke has outlived her husband and, as a result, needs to see a social worker to determine if she is fit to return home alone. A man in the same situation is, on average, younger and is more likely to have a partner at home to aid in his recovery.

One outcome result was also significant for a gender difference; men were more likely than women to die. This difference was not significant in the chi square test or univariate analysis but, after controlling for all other variables in multiple regression, it was found to be a significant difference. Men were more likely than women to have suffered a previous CVA which may have had an impact on their outcome, however, risk factors and medical histories were included in the multivariate analysis. There were no significant differences in CVA severity that may account for the difference in the number of deaths suffered.

6.3 Coronary Revascularization

Within the patients with severe CAD, who would eventually be assessed for CABG, women were significantly older than men and had more diabetes, the only co-morbidity measured. Men were more likely to have critical CAD. Women were less likely to receive CABG and more likely to receive medical management, however only medical management was significant in multiple regression. Since men had more severe CAD it would make sense for them to be referred for CABG more readily and medical management less readily than women. In this instance, severity of CAD does not account for the differences in treatment as critical CAD was included as an independent variable in the multivariate models and was not found to be a significant predictor. The symptom differences seen in AMI patients may also play a role in treatment differences seen in referrals for coronary revascularization. Similar to female AMI patients, in the early stages of CAD women often present with atypical symptoms, such as fatigue, abdominal and back discomfort, and jaw pain [124]. Consequently, it may take longer for a correct diagnosis to be obtained.

Women who were referred for CABG had longer wait times to receive the surgery if they were in the "short wait" priority group. Although small, this difference remained significant after further multivariate regression and, again, severity of CAD was accounted for. In this instance, gender was the only significant predictor of wait time and must be solely responsible for this two-day difference.

6.4 Chronic Kidney Disease

Female CKD patients were older than male patients but did not differ with regards to risk factors, medical histories, or etiology of disease. Women began dialysis unprepared with lower eGFR levels after receiving less pre-dialysis care than men. Both differences remained significant after controlling for baseline characteristics and other laboratory measures. The lower eGFR in women finding is consistent with previous research [103]. Low eGFR on dialysis initiation has also been linked to limited access to pre-dialysis care [103]. It is plausible then that the lack of pre-dialysis care received by women is related to the low eGFR levels at dialysis initiation in women. The mechanism of this relationship, however, is unknown. It is also important to note that there may be inaccuracies in the eGFR values used. These parameters were calculated using the Modification of Diet in Renal Disease Study (MDRD) 4 variable method which does not include weight [129]. Unfortunately, weight was either not recorded in patient charts or not extracted during the chart reviews and, therefore, unavailable for use. Due to body size not being taken into account eGFR levels may have been underestimated for heavy patients and overestimated for underweight patients. Moreover, eGFR is a relative measure and not an actual measure; it is an estimation of GFR normalized to an ideal body size as a body surface area of $1.73m^2$. Body weight differences by sex may affect true GFR differences at dialysis start but we have no way of measuring this definitively.

Previous research has not examined gender differences in pre-dialysis care. Despite women receiving less pre-dialysis care than men, there were no significant differences in optimal modality choice or optimal access choice. There were also no notable gender differences in hospitalizations, hospital length of stay, or death. While men and women received similar numbers of HD sessions per week, the sessions men took part in were significantly longer than sessions for women, likely due to body size.

6.5 Community Acquired Pneumonia

In this non-vascular control group, there was no significant age difference between men and women and men were found to have more co-morbidities than women. This finding differs from the CVDs studied in which women tended to be older and sicker upon presentation. Men were also less likely to be low risk patients and were more likely to be in PSI IV and V classes, indicating an increased risk of severe morbidity and mortality. Since previous research has yet to examine gender differences in CAP treatment it is unknown if this finding is unique to the current study population.

Women were less likely to receive the appropriate antibiotics according to both the 1993 and 2000 Canadian guidelines for the treatment of CAP. Upon further analysis, only the results from the 1993 guidelines remained significant, with the finding that women were less likely to be given an appropriate antibiotic. Of the four possible scenarios investigated (no medication ordered, macrolide only, no macrolide, wrong drug), it was determined that women most often were given the wrong drug. Level of risk was also found to be a predictor of appropriateness of antibiotic regime for the 1993 guidelines. It is possible that women were prescribed the wrong treatments more often than men because they were at a lower risk of death and perhaps deemed less critical to be treated correctly. On the other hand, being given the wrong drug may have put these women at further risk. Patients who were given the wrong antibiotic were likely then given a correct one meaning that these patients were over-treated. There are many negative outcomes that can result from being over-treated with antibiotics, including suffering side effects, building resistance to

organisms, and killing good bacteria in the body. Although we do not have the data to support it, these women who were given the wrong drug and over-treated may have suffered worse outcomes as a result.

While women were less likely to receive appropriate treatment they were not more likely to die because of it. In fact, men were slightly more likely than women to die, however this difference did not remain significant after multivariate analysis.

6.6 Explanations

The results of this study have found that women are receiving less optimal health care access (AMI, coronary revascularization, CKD) and interventions (coronary revascularization, CKD). There are a variety of reasons that might explain why men and women are being treated differently.

Firstly, perhaps the real issue is an underuse of procedures in women. Men may undergo more procedures than women if physicians view their symptoms or disease as more severe than women. It is still widely thought that men are more at risk, more likely to get, and more likely to die of CVDs; it is not inconceivable that there are physicians that believe this myth as well. In fact, a 2005 survey found that only one in five American primary care physicians was aware that more women than men die from CVD each year [130].

Secondly, the rates at which procedures are performed may be influenced by physicians' perceptions of sex-related differences in risk and efficacy. In general, women are older and have more co-morbidities than men when they present with CVD. Do they not receive the same treatments as men because the treatment is likely to kill them? Is it appropriate to treat a woman

with an invasive procedure, such as bypass surgery, knowing that she is old and unwell and may not survive this surgery? This study did find that women are normally older and in worse health than men; perhaps women received less optimal treatment because their physicians took these factors into account.

The rates at which procedures are performed also relates to the information the physicians are provided with. With regards to drug trials, it is still a reality that women are excluded or underrepresented in these studies [8]. As a result, many drug treatments end up being geared towards men and may not be appropriate for women or may be incorrectly generalized from one population to another. Physicians treating these women don't have the evidence highlighting what the best treatment options are since clinical trials have yet to show this.

Next, symptom differences and decision delay have been documented in female AMI patients [23, 131]; it is plausible that there are symptom differences between the genders for other CVDs that have not been explored. Decision delay has been found to be in effect in AMI patients when they attribute their atypical symptoms to something minor but also because of the characteristics of women in general. Women say they do not have time to visit a doctor, do not want to bother or disturb their family or a physician, or are embarrassed that they are making a big deal out of nothing [131]. These reasons are not unique to a heart attack and may result in decision delay in other CVDs. This phenomenon has also been documented in diseases that predominantly affect women, especially breast cancer [132, 133]. Decision delay leads to an increase in time to seek treatment and increases the likelihood of obtaining medical attention after a critical time period has passed. This critical period is especially true for thromolysis; for the current study, a quality of care indicator

for AMI was receiving thrombolysis within 30 minutes of arriving in the emergency room. A decision delay could easily compromise reaching this time limit.

Perhaps differences in patients' preferences are the reasons behind the treatment differences. Are women more willing than men to adapt their lifestyle and use medications to avoid more invasive procedures? Or if women are more averse to short-term risks, they may decline major procedures more often than men. Unfortunately, there is no way to support or reject this theory using the data that was available for the current study.

This study looked at secondary prevention – detecting the disease and attempting to prevent future events of a similar nature. Is the gender bias problem related to primary prevention? We have found that women are presenting when they are older and sicker than men. Is it that women receive better primary care than men that allows them to age, and thereby accumulate more co-morbidities? Ideally, primary care would be a protective factor against, for example, suffering an AMI. By the same logic, more extensive primary care would likely allow a patient to go longer without suffering an AMI perhaps explaining why women are older when they have their AMI. Age has been controlled for in the analyses of this study so this theory is unlikely. Is illness accelerated in women so that once they reach an older age the disease acts more rapidly than it does in a younger man? Research has noted that estrogen plays a protective role in women before menopause [6, 65, 66]. This likely also plays a role in the age and health of women who suffer from the CVDs studied. No definite explanation remains for why women are consistently older and sicker when they present. These questions can only be answered through a primary care study of family physicians aimed at any differences in care between men and women. In the present study our control group,

CAP, had more men who suffered co-morbidities – the opposite of the CVDs. With this in mind, future research into primary prevention should focus on prevention differences between men and women suffering from CVDs.

Finally, if none of these theories sufficiently explain the differences in care seen in the present study, the differences may represent a gender bias in the delivery of acute medical care. A gender bias has the potential to delay diagnostics in women and lead to delays in life-saving treatments or result in avoidable death. A gender bias can have devastating affects for men as well; men with more modest degrees of illness may undergo procedures that offer them no tangible benefit.

6.7 Implications for Practice

Upon exploring the history of gender bias in acute care it quickly became apparent that women have long been overlooked in research. One of the most important ways to overcome this inherent bias is through physician education. Family doctors, emergency room doctors, and cardiac specialists need to be aware of the atypical symptoms that female commonly experience in the hopes that women are diagnosed as quickly as men. Physicians also need to be aware of the possibility of a gender bias. In this situation, knowledge truly is power. Knowing that a bias may be at work will allow physicians to be more open-minded in their diagnosis and treatment of women.

Research has found that, even today, most clinical trials use male subjects but the results are extrapolated to include women. This needs to change. The number of women in multi-sex trials should be equal to the number of men. An increase in single-sex female trials is an improvement but is not enough to make the changes needed. When more women are studied, the differences between males and females should become clearer and, hopefully, the issues with symptoms and diagnoses of women will be resolved.

6.8 Limitations

This study is not without its weaknesses, many of which arise as a result of its retrospective nature. Relying on the accuracy of previously written charts may result in limitations such as data abstraction errors and incomplete or inadequate data. Some important information may not have been accessible or available. This study was not able to be blinded or randomized and, as such, is open to confounders and bias. As well, the results of any retrospective study have low external validity and are not easily generalizable. In a non-interventional study such as this one, relationships can only be inferred and causation cannot be proven. These results are hypothesis generating.

In addition, while all patients who were diagnosed with one of the five conditions studied were included in the analysis, it is still possible that patients were missed. Any patient who reached the emergency room but died before a diagnosis could be made would not have been included. To be included in the CAP portion of the study the patients had to be admitted to the hospital; any patient deemed not sick enough for hospitalization and was sent home would not have been included in the study. We have no way of knowing how sick the people sent home were; if the women sent home

were in worse condition than the men (or vice versa) this would have an effect on the study. Moreover, any patient who died en route to the hospital or in their own home would not have been included as they were not yet diagnosed.

It has been stated that, in this study, women received less optimal access and interventions but were never more likely to die. On the surface, it appears that women received less optimal treatment but did not suffer worse outcomes (i.e. were more likely to die) as a result of their poorer treatment. It is not correct to say this, however, as it points out a limitation of this study. Males and females are not equal and comparing the outcomes of the two sexes will not expose a true difference. If females would have done better than males with equally optimal care, then females actually would have suffered from suboptimal care even though, statistically, there were no significant differences in outcome. While comparing males to females is not necessarily an appropriate method for exploring a gender bias, it would be unethical to compare females with optimal care to females with suboptimal care. Therefore, although comparing males to females is not ideal, the method used in this study reflects the most appropriate way of studying differences in treatment and outcome.

6.9 Strengths

There are numerous strengths to this study. It would be impossible and unethical to design a randomized controlled trial in an attempt to examine a gender bias such as the one studied in this thesis; physicians could not be easily blinded to which group they were treating since the groups

were defined by gender, it would be unethical to create a control group of patients who received placebos for these serious medical problems, and only a fraction of the problem would be captured.

For the Newfoundland portion of this study, we included every patient in the study sites province who was diagnosed with an AMI, CVA, or CAP and every patient who was tested for coronary revascularization. The results do not need to be generalized to include other patients who suffered from these events – the results demonstrate the true results for Newfoundland during the years of the study. Because the Canadian health care system is one of national universal coverage where all care is provided by government services at no cost to individuals, we are confident that we included all patients irrespective of social status that otherwise would have had an impact on outcomes. This is a major strength of this study as we were able to remove any potential bias secondary to issues related to access to care that may be present in other studies. Cardiac nurses trained in chart abstraction were used to perform the chart audits. As a result, the data analyzed was of very high quality and the chart audits performed were thorough and resulted in a large number of outcomes to study. Studying gender bias was not an objective of the original data collectors. As such, they may not have added to any data biases that may affect the analysis of the present study.

6.10 Summary

This study has found that women received less appropriate treatment than men for AMI, coronary revascularization, CKD, and CAP. Fortunately, women did not appear to suffer worse outcomes as a

result of their less aggressive treatment. No evidence of a gender bias against women was found for patients suffering from a CVA.

There are possible explanations for this difference outside of a gender bias against women but the current study did not have the data to support or disprove these theories. Future research should focus on symptomology differences between the sexes in CVDs other than AMI. Decision delay in women should be explored further in AMI and in other CVDs to determine the extent of the role it plays in resulting treatment differences between the sexes.

Most importantly, research into gender differences in treatment for CVDs needs to increased. To date the majority of the published studies on this important topic focus solely on AMI. Women are just as likely as men to suffer from, and die of, CVDs yet do not appear to receive adequate treatments and are often left out of CVD research. Recently a group of authors made some important suggestions as a means to fill the gender gap in medical research. They propose funding agencies to insist on the appropriate representation of both sexes in trials and to consider sex differences in data analysis, scientific journals requiring authors to clearly label single-sex studies as such, and finally to ensure that the knowledge of sex differences is appropriately transmitted from research lab to a physicians clinic [124].

It has been 20 years since the NIH set up its Office of Research on Women's Health. Unfortunately, we have not come far enough in those two decades and may have even taken a few steps in the

wrong direction – one researcher believes that recruiting women to participate in clinical trials is no longer necessary [134]. They even go as far as to say that it is no men who are on the receiving end of the gender bias [134]. Women deserve equality in medical research and treatment. It is time for this gender bias to end.

References

1. *Mortality Summary List of Causes 2005*. 2009, Statistics Canada.

2. WorldHealthOrganization, *Estimated Deaths per 100,000 population by cause, and Member State 2004*. 2009, WHO, Department of Measurement and Health Information.

3. WorldHealthOrganization, *Age-Standardized Death Rates per 100,000 by cause, and Member State, 2004*. 2009, WHO Department of Measurement and Health Information.

4. *Tracking Heart Disease and Stroke in Canada*. 2009, Public Health Agency of Canada.

5. *Building a Heart Healthy Canada*. 2009, Canadian Heart Healthy Stategy Action Planning Committee.

6. von der Lohe, E., *Coronary Heart Disease in Women. Prevention, Diagnosis, Therapy*. 2003, Heidelberg, Germany: Springer-Verlag.

7. Hochman, J.S. and J.E. Tamis-Holland, *Acute coronary syndromes: does sex matter?* JAMA, 2002. **288**(24): p. 3161-4.

8. Miller, C.L. and C.R. Kollauf, *Evolution of information on women and heart disease 1957-2000: a review of archival records and secular literature.* Heart Lung, 2002. **31**(4): p. 253-61.

9. Merkatz, R.B., *Inclusion of women in clinical trials: a historical overview of scientific, ethical, and legal issues.* J Obstet Gynecol Neonatal Nurs, 1998. **27**(1): p. 78-84.

10. Sharp, N., *Women's Health Equity Act of 1990.* Nurs Manage, 1990. **21**(12): p. 21-2.

11. Lee, I.M., et al., *Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial.* JAMA, 2005. **294**(1): p. 56-65.

12. Lee, I.M., et al., *Beta-carotene supplementation and incidence of cancer and cardiovascular disease: the Women's Health Study.* J Natl Cancer Inst, 1999. **91**(24): p. 2102-6.

13. Cook, N.R., et al., *Low-dose aspirin in the primary prevention of cancer: the Women's Health Study: a randomized controlled trial.* JAMA, 2005. **294**(1): p. 47-55.

14. Harris, D.J. and P.S. Douglas, *Enrollment of women in cardiovascular clinical trials funded by the National Heart, Lung, and Blood Institute.* N Engl J Med, 2000. **343**(7): p. 475-80.

15. Efre, A.J., *Gender bias in acute myocardial infarction.* Nurse Pract, 2004. **29**(11): p. 42-55; quiz 56-7.

16. Sheps, D.S., et al., *Sex differences in chest pain in patients with documented coronary artery disease and exercise-induced ischemia: Results from the PIMI study.* Am Heart J, 2001. **142**(5): p. 864-71.

17. Geller, S.E., M.G. Adams, and M. Carnes, *Adherence to federal guidelines for reporting of sex and race/ethnicity in clinical trials.* J Womens Health (Larchmt), 2006. **15**(10): p. 1123-31.

18. Healy, B., *The Yentl syndrome.* N Engl J Med, 1991. **325**(4): p. 274-6.

19. Ayanian, J.Z. and A.M. Epstein, *Differences in the use of procedures between women and men hospitalized for coronary heart disease.* N Engl J Med, 1991. **325**(4): p. 221-5.

20. Steingart, R.M., et al., *Sex differences in the management of coronary artery disease. Survival and Ventricular Enlargement Investigators.* N Engl J Med, 1991. **325**(4): p. 226-30.

21. Singer, I., *Yentl the yeshiva boy.* An Isaac Bashevis Singer Reader. 1971, New York: Farrar, Straus, and Giroux. 135-166.

22. Orth-Gomer, K., *New light on the Yentl syndrome.* Eur Heart J, 2000. **21**(11): p. 874-5.

23. Rosenfeld, A.G., *Women's risk of decision delay in acute myocardial infarction: implications for research and practice.* AACN Clin Issues, 2001. **12**(1): p. 29-39.

24. Kudenchuk, P.J., et al., *Comparison of presentation, treatment, and outcome of acute myocardial infarction in men versus women (the Myocardial Infarction Triage and Intervention Registry).* Am J Cardiol, 1996. **78**(1): p. 9-14.

25. Nguyen, J.T., et al., *Gender disparity in cardiac procedures and medication use for acute myocardial infarction.* Am Heart J, 2008. **155**(5): p. 862-8.

26. Ting, H.H., et al., *Factors associated with longer time from symptom onset to hospital presentation for patients with ST-elevation myocardial infarction.* Arch Intern Med, 2008. **168**(9): p. 959-68.

27. McSweeney, J.C., et al., *Women's early warning symptoms of acute myocardial infarction.* Circulation, 2003. **108**(21): p. 2619-23.

28. Markel, K.N. and S.A. Marion, *CQI: improving the time to thrombolytic therapy for patients with acute myocardial infarction in the emergency department.* J Emerg Med, 1996. **14**(6): p. 685-9.

29. *Recommendations for ensuring early thrombolytic therapy for acute myocardial infarction. The Heart and Stroke Foundation of Canada, the Canadian Cardiovascular Society and the*

Canadian Association of Emergency Physicians for the Emergency Cardiac Care Coalition. CMAJ, 1996. **154**(4): p. 483-7.

30. Hossmann, K.A. and W.D. Heiss, *Neuropathology and pathophysiology of stroke*, in *Textbook of Stroke Medicine*, M. Brainin and W.D. Heiss, Editors. 2010, Cambridge University Press: Cambridge, United Kingdom. p. 1-27.

31. Roine, R.O. and M. Kaste, *Stroke units and clinical assessment*, in *Textbook of Stroke Medicine*, M. Brainin and W.D. Heiss, Editors. 2010, Cambridge University Press: Cambridge, United Kingdom. p. 219-229.

32. *How do stroke units improve patient outcomes? A collaborative systematic review of the randomized trials. Stroke Unit Trialists Collaboration.* Stroke, 1997. **28**(11): p. 2139-44.

33. *Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. Stroke Unit Trialists' Collaboration.* BMJ, 1997. **314**(7088): p. 1151-9.

34. *Organised inpatient (stroke unit) care for stroke.* Cochrane Database Syst Rev, 2007(4): p. CD000197.

35. Kalra, L., et al., *Alternative strategies for stroke care: a prospective randomised controlled trial.* Lancet, 2000. **356**(9233): p. 894-9.

36. Adams, R., et al., *Recommendations for improving the quality of care through stroke centers and systems: an examination of stroke center identification options: multidisciplinary consensus recommendations from the Advisory Working Group on Stroke Center Identification Options of the American Stroke Association.* Stroke, 2002. **33**(1): p. e1-7.

37. Rihal, C.S., et al., *Indications for coronary artery bypass surgery and percutaneous coronary intervention in chronic stable angina: review of the evidence and methodological considerations.* Circulation, 2003. **108**(20): p. 2439-45.

38. Serruys, P.W., et al., *Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease.* N Engl J Med, 2009. **360**(10): p. 961-72.

39. *Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial.* Lancet, 2002. **360**(9338): p. 965-70.

40. Mandell, L.A., et al., *Summary of Canadian guidelines for the initial management of community-acquired pneumonia: an evidence-based update by the Canadian Infectious Disease Society and the Canadian Thoracic Society.* Can Respir J, 2000. **7**(5): p. 371-82.

41. Mandell, L.A. and M. Neiderman, *Antimicrobial treatment of community acquired pneumonia in adults: A conference report.* Can J Infect Dis, 1993. **4**(1): p. 25-28.

42. Eustace, J.A. and J. Coresh, *Chronic Kidney Disease: Definition and Epidemiology*, in *Chronic Kidney Disease, Dialysis, and Transplantation. Companion to Brenner and Rector's The Kidney*, V.S. Balakrishnan, et al., Editors. 2005, Elsevier Saunders: Philadelphia, Pennsylania. p. 1-19.

43. Mohanram, A. and R.D. Toto, *Measurement of Kidney Function*, in *Chronic Kidney Disease, Dialysis, and Transplantation. A Companion to Brenner and Rector's The Kidney*, V.S. Balakrishnan, et al., Editors. 2005, Elsevier Saunders: Philadelphia, Pennslyvania. p. 20-30.

44. Curtis, B.M. and A. Levin, *The Role of the Chronic Kidney Disease Clinic*, in *Chronic Kidney Disease, Dialysis, and Transplantation. Companion to Brenner and Rector's The Kidney*, V.S. Balakrishnan, et al., Editors. 2005, Elsevier Saunders: Philadephia, Pennsylvania. p. 71-85.

45. Yeun, J.Y. and T.A. Depner, *Principles of Hemodialysis*, in *Chronic Kidney Disease, Dialysis, and Transplantation. Companion to Brenner and Rector's The Kidney*, V.S. Balakrishnan, et al., Editors. 2005, Elsevier Saunders: Philadephia, Pennsylvania. p. 307-340.

46. Nesrallah, G.E., P. Blake, and D. Mendelssohn, *Modality Options for End-Stage Renal Disease Care*, in *Chronic Kidney Disease, Dialysis, and Transplantation. A Companion to Brenner and Rector's The Kidney*, V.S. Balakrishnan, et al., Editors. 2005, Elsevier Saunders: Philadephia, Pennsylvania. p. 279-306.

47. Himmelfarb, J., L.M. Dember, and B.S. Dixon, *Vascular Access*, in *Chronic Kidney Disease, Dialysis, and Transplantation. A Companion to Brenner and Rector's The Kidney*, V.S. Balakrishnan, et al., Editors. 2005, Elsevier Saunders: Philadephila, Pennsylvania. p. 341-362.

48. Williams, R.I., A.G. Fraser, and R.R. West, *Gender differences in management after acute myocardial infarction: not 'sexism' but a reflection of age at presentation.* J Public Health (Oxf), 2004. **26**(3): p. 259-63.

49. Gan, S.C., et al., *Treatment of acute myocardial infarction and 30-day mortality among women and men.* N Engl J Med, 2000. **343**(1): p. 8-15.

50. Adams, J.N., et al., *Women and myocardial infarction: agism rather than sexism?* Br Heart J, 1995. **73**(1): p. 87-91.

51. Clarke, K.W., et al., *Do women with acute myocardial infarction receive the same treatment as men?* BMJ, 1994. **309**(6954): p. 563-6.

52. Goldberg, R.J., et al., *Sex differences in symptom presentation associated with acute myocardial infarction: a population-based perspective.* Am Heart J, 1998. **136**(2): p. 189-95.

53. Rathore, S.S., et al., *Sex differences in cardiac catheterization: the role of physician gender.* JAMA, 2001. **286**(22): p. 2849-56.

54. Vaccarino, V., et al., *Sex and racial differences in the management of acute myocardial infarction, 1994 through 2002.* N Engl J Med, 2005. **353**(7): p. 671-82.
55. Chang, W.C., et al., *Impact of sex on long-term mortality from acute myocardial infarction vs unstable angina.* Arch Intern Med, 2003. **163**(20): p. 2476-84.
56. Vaccarino, V., et al., *Sex differences in 2-year mortality after hospital discharge for myocardial infarction.* Ann Intern Med, 2001. **134**(3): p. 173-81.
57. Champney, K.P., et al., *The joint contribution of sex, age and type of myocardial infarction on hospital mortality following acute myocardial infarction.* Heart, 2009. **95**(11): p. 895-9.
58. Jneid, H., et al., *Sex differences in medical care and early death after acute myocardial infarction.* Circulation, 2008. **118**(25): p. 2803-10.
59. Herlitz, J., et al., *Treatment and outcome in acute myocardial infarction in a community in relation to gender.* Int J Cardiol, 2009. **135**(3): p. 315-22.
60. Zubaid, M., et al., *Differences in thrombolytic treatment and in-hospital mortality between women and men after acute myocardial infarction.* Jpn Heart J, 2001. **42**(6): p. 669-76.
61. Zimmermann, S., et al., *Short-term prognosis of contemporary interventional therapy of ST-elevation myocardial infarction: does gender matter?* Clin Res Cardiol, 2009. **98**(11): p. 709-15.
62. Lawesson, S.S., et al., *Gender perspective on risk factors, coronary lesions and long-term outcome in young patients with ST-elevation myocardial infarction.* Heart. **96**(6): p. 453-9.
63. Wheeler, S., et al., *Women veterans and outcomes after acute myocardial infarction.* J Womens Health (Larchmt), 2009. **18**(5): p. 613-8.
64. Towfighi, A., L. Zheng, and B. Ovbiagele, *Sex-specific trends in midlife coronary heart disease risk and prevalence.* Arch Intern Med, 2009. **169**(19): p. 1762-6.
65. Bairey Merz, C.N., et al., *Hypoestrogenemia of hypothalamic origin and coronary artery disease in premenopausal women: a report from the NHLBI-sponsored WISE study.* J Am Coll Cardiol, 2003. **41**(3): p. 413-9.
66. Moller-Leimkuhler, A.M., *Gender differences in cardiovascular disease and comorbid depression.* Dialogues Clin Neurosci, 2007. **9**(1): p. 71-83.
67. Berg, J., et al., *Symptoms of a first acute myocardial infarction in women and men.* Gend Med, 2009. **6**(3): p. 454-62.
68. Smith, D.B., et al., *Gender differences in the Colorado Stroke Registry.* Stroke, 2009. **40**(4): p. 1078-81.

69. Reeves, M.J., et al., *Quality of care in women with ischemic stroke in the GWTG program.* Stroke, 2009. **40**(4): p. 1127-33.

70. Palnum, K.D., et al., *Sex-related differences in quality of care and short-term mortality among patients with acute stroke in Denmark: a nationwide follow-up study.* Stroke, 2009. **40**(4): p. 1134-9.

71. Eriksson, M., et al., *Sex differences in stroke care and outcome in the Swedish national quality register for stroke care.* Stroke, 2009. **40**(3): p. 909-14.

72. Forster, A., et al., *Gender differences in acute ischemic stroke: etiology, stroke patterns and response to thrombolysis.* Stroke, 2009. **40**(7): p. 2428-32.

73. Niewada, M., et al., *Influence of gender on baseline features and clinical outcomes among 17,370 patients with confirmed ischaemic stroke in the international stroke trial.* Neuroepidemiology, 2005. **24**(3): p. 123-8.

74. Glader, E.L., et al., *Sex differences in management and outcome after stroke: a Swedish national perspective.* Stroke, 2003. **34**(8): p. 1970-5.

75. Holroyd-Leduc, J.M., et al., *Sex differences and similarities in the management and outcome of stroke patients.* Stroke, 2000. **31**(8): p. 1833-7.

76. Kapral, M.K., et al., *Sex differences in stroke care and outcomes: results from the Registry of the Canadian Stroke Network.* Stroke, 2005. **36**(4): p. 809-14.

77. Labiche, L.A., et al., *Sex and acute stroke presentation.* Ann Emerg Med, 2002. **40**(5): p. 453-60.

78. Roquer, J., A.R. Campello, and M. Gomis, *Sex differences in first-ever acute stroke.* Stroke, 2003. **34**(7): p. 1581-5.

79. Di Carlo, A., et al., *Sex differences in the clinical presentation, resource use, and 3-month outcomeof acute stroke in Europe: Data from a multicenter multinational hospital-based registry.* Stroke, 2003. **34**: p. 1114-19.

80. Rudd, A.G., et al., *Access to stroke care in England, Wales and Northern Ireland: the effect of age, gender and weekend admission.* Age Ageing, 2007. **36**(3): p. 247-55.

81. Patrick, S.J., et al., *Sex differences in the management of patients hospitalized with ischemic cerebrovascular disease.* Stroke, 1995. **26**(4): p. 577-80.

82. Naylor, C.D. and C.M. Levinton, *Sex-related differences in coronary revascularization practices: the perspective from a Canadian queue management project.* CMAJ, 1993. **149**(7): p. 965-73.

83. Butterworth, J., et al., *Female gender associates with increased duration of intubation and length of stay after coronary artery surgery. CABG Clinical Benchmarking Database Participants.* Anesthesiology, 2000. **92**(2): p. 414-24.

84. Ghali, W.A., et al., *Sex differences in access to coronary revascularization after cardiac catheterization: importance of detailed clinical data.* Ann Intern Med, 2002. **136**(10): p. 723-32.

85. Bell, M.R., et al., *Referral for coronary artery revascularization procedures after diagnostic coronary angiography: evidence for gender bias?* J Am Coll Cardiol, 1995. **25**(7): p. 1650-5.

86. Bickell, N.A., et al., *Referral patterns for coronary artery disease treatment: gender bias or good clinical judgment?* Ann Intern Med, 1992. **116**(10): p. 791-7.

87. Chandra, N.C., et al., *Observations of the treatment of women in the United States with myocardial infarction: a report from the National Registry of Myocardial Infarction-I.* Arch Intern Med, 1998. **158**(9): p. 981-8.

88. Dong, W., et al., *Gender differences in accessing cardiac surgery across England: a cross-sectional analysis of the health survey for England.* Soc Sci Med, 1998. **47**(11): p. 1773-80.

89. Miller, T.D., et al., *Gender differences and temporal trends in clinical characteristics, stress test results and use of invasive procedures in patients undergoing evaluation for coronary artery disease.* J Am Coll Cardiol, 2001. **38**(3): p. 690-7.

90. Roeters van Lennep, J.E., et al., *Gender differences in diagnosis and treatment of coronary artery disease from 1981 to 1997. No evidence for the Yentl syndrome.* Eur Heart J, 2000. **21**(11): p. 911-8.

91. Jaglal, S.B., V. Goel, and C.D. Naylor, *Sex differences in the use of invasive coronary procedures in Ontario.* Can J Cardiol, 1994. **10**(2): p. 239-44.

92. Shaw, L.J., et al., *Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease.* Ann Intern Med, 1994. **120**(7): p. 559-66.

93. Tobin, J.N., et al., *Sex bias in considering coronary bypass surgery.* Ann Intern Med, 1987. **107**(1): p. 19-25.

94. Krumholz, H.M., et al., *Selection of patients for coronary angiography and coronary revascularization early after myocardial infarction: is there evidence for a gender bias?* Ann Intern Med, 1992. **116**(10): p. 785-90.

95. Leape, L.L., et al., *Underuse of cardiac procedures: do women, ethnic minorities, and the uninsured fail to receive needed revascularization?* Ann Intern Med, 1999. **130**(3): p. 183-92.

96. Frishman, W.H., et al., *Differences between male and female patients with regard to baseline demographics and clinical outcomes in the Asymptomatic Cardiac Ischemia Pilot (ACIP) Trial.* Clin Cardiol, 1998. **21**(3): p. 184-90.

97. Hess, D.R., *Retrospective studies and chart reviews.* Respir Care, 2004. **49**(10): p. 1171-4.

98. Florakas, C., et al., *Differences in the treatment of male and female patients with end-stage renal disease.* CMAJ, 1994. **151**(9): p. 1283-8.

99. Astor, B.C., et al., *Relation between gender and vascular access complications in hemodialysis patients.* Am J Kidney Dis, 2000. **36**(6): p. 1126-34.

100. Curtis, B.M., et al., *Canadian survey of clinical status at dialysis initiation 1998-1999: a multicenter prospective survey.* Clin Nephrol, 2002. **58**(4): p. 282-8.

101. Khan, I.H., et al., *Chronic renal failure: factors influencing nephrology referral.* Qjm, 1994. **87**(9): p. 559-64.

102. Dogan, E., et al., *Effects of late referral to a nephrologist in patients with chronic renal failure.* Nephrology (Carlton), 2005. **10**(5): p. 516-9.

103. Obrador, G.T., et al., *Level of renal function at the initiation of dialysis in the U.S. end-stage renal disease population.* Kidney Int, 1999. **56**(6): p. 2227-35.

104. Stack, A.G., *Impact of timing of nephrology referral and pre-ESRD care on mortality risk among new ESRD patients in the United States.* Am J Kidney Dis, 2003. **41**(2): p. 310-8.

105. Innes, A., et al., *Early deaths on renal replacement therapy: the need for early nephrological referral.* Nephrol Dial Transplant, 1992. **7**(6): p. 467-71.

106. MacReady, N., *Sex Disparity Seen in Diagnosis of CKD*, in *Medscape Today*. 2009: New York.

107. Campbell, J.D., et al., *The Timing of Referral of Patients with End-Stage Renal Disease.* Dialysis & Transplantation, 1989. **18**(12): p. 660-686.

108. White, C.A., et al., *Pre-dialysis clinic attendance improves quality of life among hemodialysis patients.* BMC Nephrol, 2002. **3**: p. 3.

109. Florakas, C., et al., *Body size, not sex, is responsible for differences in type of dialysis.* CMAJ, 1999. **160**(6): p. 818-9.

110. Hirth, R.A., et al., *Predictors of type of vascular access in hemodialysis patients.* JAMA, 1996. **276**(16): p. 1303-8.

111. Dhingra, R.K., et al., *Type of vascular access and mortality in U.S. hemodialysis patients.* Kidney Int, 2001. **60**(4): p. 1443-51.

112. Di Iorio, B.R., et al., *Vascular access for hemodialysis: the impact on morbidity and mortality.* J Nephrol, 2004. **17**(1): p. 19-25.

113. Rayner, H.C., et al., *Creation, cannulation and survival of arteriovenous fistulae: data from the Dialysis Outcomes and Practice Patterns Study.* Kidney Int, 2003. **63**(1): p. 323-30.

114. Vernaglione, L., et al., *Comorbid conditions and gender impact the primary survival of distal radio-cephalic arteriovenous fistula inpatients on long-term hemodialysis.* J Nephrol, 2005. **18**(3): p. 276-81.

115. Miller, C.D., M.L. Robbin, and M. Allon, *Gender differences in outcomes of arteriovenous fistulas in hemodialysis patients.* Kidney Int, 2003. **63**(1): p. 346-52.

116. Marcus, R.J., et al., *Gender differences in vascular access in hemodialysis patients in the United States: developing strategies for improving access outcome.* Gend Med, 2007. **4**(3): p. 193-204.

117. Caplin, N., et al., *Venous access: women are equal.* Am J Kidney Dis, 2003. **41**(2): p. 429-32.

118. Puskar, D., et al., *Survival of primary arteriovenous fistula in 463 patients on chronic hemodialysis.* Croat Med J, 2002. **43**(3): p. 306-11.

119. Erkut, B., et al., *Primary arteriovenous fistulas in the forearm for hemodialysis: effect of miscellaneous factors in fistula patency.* Ren Fail, 2006. **28**(4): p. 275-81.

120. Naylor, C.D., et al., *Assessment of priority for coronary revascularisation procedures. Revascularisation Panel and Consensus Methods Group.* Lancet, 1990. **335**(8697): p. 1070-3.

121. Fine, M.J., et al., *A prediction rule to identify low-risk patients with community-acquired pneumonia.* N Engl J Med, 1997. **336**(4): p. 243-50.

122. Hosmer, D.W. and S. Lemeshow, *Applied Logistic Regression*. 2nd ed. 2000, Hoboken, New Jersey: John Wiley & Sons, Inc.

123. Alpert, J.S., et al., *Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction.* J Am Coll Cardiol, 2000. **36**(3): p. 959-69.

124. Kim, A.M., C.M. Tingen, and T.K. Woodruff, *Sex bias in trials and treatment must end.* Nature. **465**(7299): p. 688-9.

125. CBC, *Fill gender gap in medical research*. 2010, CBC News.
126. Santrock, J., *Life-Span Development*. 10th ed. 2006, New York, New York: McGraw Hill. 655.

127. Kinsella, K. and Y.I. Gist, *Gender and Aging: Mortality and Health*. 1998, U.S. Department of Commerce. Economics and Statistics Administration. Bureau of the Census. p. 7.

128. *Health - Life Expectancy at Birth*. 2005, Statistics Canada: Ottawa, Ontario. p. Indicators of well-being in Canada.

129. Levey, A.S. and e. al., *Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate.* Ann Intern Med, 1999. **145**: p. 247-254.

130. Mosca, L., et al., *National study of physician awareness and adherence to cardiovascular disease prevention guidelines.* Circulation, 2005. **111**(4): p. 499-510.

131. Rosenfeld, A.G., A. Lindauer, and B.G. Darney, *Understanding treatment-seeking delay in women with acute myocardial infarction: descriptions of decision-making patterns.* Am J Crit Care, 2005. **14**(4): p. 285-93.

132. Burgess, C., M.S. Hunter, and A.J. Ramirez, *A qualitative study of delay among women reporting symptoms of breast cancer.* Br J Gen Pract, 2001. **51**(473): p. 967-71.

133. Bish, A., et al., *Understanding why women delay in seeking help for breast cancer symptoms.* J Psychosom Res, 2005. **58**(4): p. 321-6.

134. Holden, C., *Women abound in NIH trials.* Science, 2008. **322**(5899): p. 219.

Appendix A Non-Significant Tables

Table 1 Health Care Access: Thrombolytics Given (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.64	0.48-0.83	0.001
Age	1.04	1.03-1.05	<0.001
Urban	1.03	0.79-1.35	0.8
History of Diabetes	1.11	0.31-3.98	0.9
History of Hypertension	0.56	0.17-1.92	0.4
History of Smoking	0.65	0.46-0.91	0.01
History of Dyslipidemia	0.80	0.58-1.10	0.8
Family History of CAD	0.64	0.48-0.87	0.003
Prior Acute Myocardial Infarction	1.16	0.32-4.20	0.8
History of Angina	1.61	0.52-5.05	0.4
History of CABG	1.97	0.47-8.35	0.4
History of CHF	3.19	1.14-8.98	0.03
Prior PTCA	0.66	0.17-2.64	0.6
History of TIA/CVA	2.45	0.82-7.30	0.1
STEMI vs. Non-STEMI	333.3	125-1000	<0.001
	Multivariate		
Gender (Female)	0.80	0.59-1.30	0.4
Age	1.03	1.0-1.03	0.06
STEMI vs. Non-STEMI	333.3	111.1-1000	<0.001

p values represent comparisons between male and female

STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 2 Health Care Intervention: Appropriateness of Thrombolytics (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	1.81	0.89-1.59	0.3
Age	1.01	0.99-1.02	0.4
Urban	1.31	0.98-1.77	0.07
History of Diabetes	0.64	0.20-2.06	0.5
History of Hypertension	0.68	0.26-1.75	0.4
History of Smoking	1.15	0.79-1.66	0.5
History of Dyslipidemia	0.59	0.43-0.82	0.001
Family History of CAD	0.79	0.57-1.10	0.2
Prior Acute Myocardial Infarction	0.37	0.12-1.13	0.08
History of Angina	0.33	0.12-0.91	0.03
History of CABG	0.16	0.041-0.64	0.009
History of CHF	0.79	0.28-2.28	0.7
Prior PTCA	0.36	0.10-1.30	0.1
History of TIA/CVA	0.84	0.31-2.22	0.7
STEMI vs. Non-STEMI	0.14	0.10-0.19	<0.001
	Multivariate		
Gender (Female)	1.3	0.80-1.67	0.3
Age	1.0	1.01-1.04	0.001
History of Dsylipdemia	0.6	0.40-0.90	0.008
STEMI vs. Non-STEMI	0.1	0.08-0.16	<0.001

p values represent comparisons between male and female

STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 3 Health Care Intervention: Adjunct ASA (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.57	0.42-0.76	<0.001
Age	1.04	1.03-1.05	<0.001
Urban	0.95	0.72-1.26	0.7
History of Diabetes	1.45	0.40-5.25	0.6
History of Hypertension	0.73	0.22-2.49	0.6
History of Smoking	0.65	0.46-0.93	0.02
History of Dyslipidemia	0.74	0.53-1.03	0.07
Family History of CAD	0.63	0.46-0.86	0.003
Prior Acute Myocardial Infarction	1.54	0.42-5.59	0.5
History of Angina	1.93	0.62-6.07	0.3
History of CABG	2.61	0.59-11.50	0.2
History of CHF	3.63	1.18-11.14	0.02
Prior PTCA	0.86	0.21-3.47	0.8
History of TIA/CVA	3.83	1.20-12.23	0.02
STEMI vs. Non-STEMI	500.0	111.1-1000	<0.001
	Multivariate		
Gender (Female)	0.70	0.50-1.05	0.08
Age	1.01	1.00-1.03	0.049
STEMI vs. Non-STEMI	500.0	100-1000	<0.001

p values represent comparisons between male and female

STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 4 Health Care Intervention: Adjunct Heparin (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.66	0.49-0.87	0.004
Age	0.96	0.95-0.98	<0.001
Urban	1.16	0.88-1.53	0.3
History of Diabetes	1.22	0.27-5.56	0.8
History of Hypertension	2.27	0.53-10.00	0.3
History of Smoking	1.56	1.09-2.22	0.02
History of Dyslipidemia	1.37	0.98-1.92	0.006
Family History of CAD	1.61	1.19-2.22	0.002
Prior Acute Myocardial Infarction	1.25	0.27-5.56	0.8
History of Angina	0.75	0.21-2.70	0.7
History of CABG	0.83	0.16-4.17	0.8
History of CHF	2.08	0.42-10.20	0.4
Prior PTCA	0.32	0.10-0.95	0.04
History of TIA/CVA	0.37	0.11-1.23	0.1
STEMI vs. Non-STEMI	250.00	83.33-500.00	<0.001
	Multivariate		
Gender (Female)	0.90	0.61-1.33	0.6
Age	0.99	0.97-1.00	0.08
STEMI vs. Non-STEMI	200.00	76.92-500.00	<0.001

p values represent comparisons between male and female

STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 5 Health Care Intervention: Discharge Anticoagulants (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.83	0.61-1.14	0.3
Age	1.00	0.99-1.02	0.5
Urban	2.5	1.7-3.6	<0.001
History of Diabetes	1.3	0.3-6.0	0.8
History of Hypertension	0.55	0.19-1.55	0.3
History of Smoking	0.65	0.44-0.95	0.03
History of Dyslipidemia	0.49	0.33-0.71	<0.001
Family History of CAD	0.58	0.40-0.84	0.003
Prior Acute Myocardial Infarction	0.91	0.19-4.34	0.9
History of Angina	1.06	0.23-4.97	0.9
History of CABG	0.75	0.14-3.99	0.7
History of CHF	1.39	0.38-5.08	0.6
Prior PTCA	0.89	0.16-4.84	0.9
History of TIA/CVA	0.97	0.25-3.81	1.0
STEMI vs. Non-STEMI	1.7	1.1-2.0	0.01
	Multivariate		
Gender (Female)	0.8	0.59-1.11	0.2
Age	1.0	1.0-1.01	0.7
Urban	2.8	1.9-4.1	<0.001
History of Dyslipidemia	0.5	0.4-0.8	0.002
STEMI vs. Non-STEMI	1.7	1.1-2.5	0.006

p values represent comparisons between male and female

STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 6 Health Care Intervention: Discharge Vasodilators (AMI)			
	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	1.43	1.20-2.00	<0.001
Age	0.96	0.95-0.97	<0.001
Urban	1.1	0.87-1.4	0.4
History of Diabetes	0.2	0.053-0.76	0.02
History of Hypertension	0.4	0.14-0.97	0.04
History of Smoking	1.6	1.2-2.2	0.001
History of Dyslipidemia	1.3	1.0-1.7	0.05
Family History of CAD	1.4	1.1-1.8	0.009
Prior Acute Myocardial Infarction	0.12	0.024-0.54	0.006
History of Angina	0.13	0.027-0.58	0.008
History of CABG	0.2	0.03-0.8	0.03
History of CHF	0.2	0.06-0.6	0.002
Prior PTCA	0.2	0.04-1.0	0.05
History of TIA/CVA	0.2	0.05-0.5	0.003
STEMI vs. Non-STEMI	0.4	0.32-0.5	<0.001
	Multivariate		
Gender (Female)	1.10	0.91-1.43	0.4
Age	0.96	0.95-0.97	<0.001
STEMI vs. Non-STEMI	0.5	0.4-0.7	<0.001

p values represent comparisons between male and female

STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 7 Health Care Intervention: Discharge Beta Blockers (AMI)			
	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.91	0.59-1.11	0.2
Age	1.02	1.01-1.03	<0.001
Urban	1.8	1.4-2.4	<0.001
History of Diabetes	1.3	0.38-4.3	0.7
History of Hypertension	0.31	0.12-0.77	0.01
History of Smoking	0.88	0.64-1.22	0.5
History of Dyslipidemia	0.44	0.33-0.60	<0.001
Family History of CAD	0.41	0.30-0.55	<0.001
Prior Acute Myocardial Infarction	1.5	0.38-5.64	0.6
History of Angina	1.4	0.37-5.42	0.6
History of CABG	1.1	0.25-4.53	0.9
History of CHF	1.9	0.68-5.44	0.2
Prior PTCA	0.80	0.18-3.51	0.8
History of TIA/CVA	1.0	0.33-3.20	1.0
STEMI vs. Non-STEMI	1.7	1.4-2.5	<0.001
	Multivariate		
Gender (Female)	0.91	0.70-1.20	0.5
Age	1.0	1.00-1.02	0.3
Urban	1.6	1.2-2.2	0.001
History of Hypertension	0.4	0.1-1.0	0.05
History of Dyslipidemia	0.6	0.4-0.8	<0.001
Family History of CAD	0.6	0.4-0.8	0.001
STEMI vs. Non-STEMI	1.7	1.3-2.5	<0.001

p values represent comparisons between male and female
STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 8 Health Care Intervention: Discharge ACE/ARB (AMI)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	1.43	1.20-1.89	0.001
Age	1.0	0.97-0.98	<0.001
Urban	1.8	1.4-2.3	<0.001
History of Diabetes	0.3	0.082-0.94	0.04
History of Hypertension	0.4	0.13-0.88	0.03
History of Smoking	1.1	0.81-1.5	0.5
History of Dyslipidemia	0.9	0.64-1.1	0.3
Family History of CAD	1.3	1.0-1.7	0.05
Prior Acute Myocardial Infarction	0.2	0.046-0.7	0.01
History of Angina	0.4	0.12-1.4	0.1
History of CABG	0.4	0.091-1.6	0.2
History of CHF	0.2	0.079-0.6	0.004
Prior PTCA	0.2	0.057-1.1	0.06
History of TIA/CVA	0.4	0.1-1.2	0.1
STEMI vs. Non-STEMI	1.1	0.83-1.42	0.5
	Multivariate		
Gender (Female)	1.30	1.00-1.59	0.07
Age	0.98	0.97-0.99	<0.001
Urban	1.7	1.4-2.2	<0.001

p values represent comparisons between male and female
STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 9 Health Care Intervention: Discharge Anti-Lipids (AMI)			
	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.91	0.59-1.20	0.3
Age	1.0	1.01-1.03	<0.001
Urban	2.4	1.8-3.1	<0.001
History of Diabetes	0.4	0.05-2.9	0.3
History of Hypertension	0.2	0.03-1.4	0.1
History of Smoking	0.6	0.4-0.9	0.01
History of Dyslipidemia	0.02	0.009-0.05	<0.001
Family History of CAD	0.5	0.4-0.7	<0.001
Prior Acute Myocardial Infarction	0.3	0.04-2.7	0.3
History of Angina	0.3	0.04-2.7	0.3
History of CABG	0.2	0.02-1.6	0.1
History of CHF	1.1	0.3-3.9	0.9
Prior PTCA	0.3	0.03-2.3	0.2
History of TIA/CVA	0.4	0.09-2.0	0.3
STEMI vs. Non-STEMI	1.3	0.9-1.7	0.1
	Multivariate		
Gender (Female)	0.77	0.59-1.20	0.3
Age	1.0	1.00-1.02	0.02
Urban	2.4	1.7-3.3	<0.001
History of Dyslipidemia	0.02	0.009-0.06	<0.001

p values represent comparisons between male and female
STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 10 Health Care Outcome: Death (AMI)			
	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	1.20	0.85-1.67	0.3
Age	0.93	0.91-0.95	<0.001
Urban	1.16	0.82-1.63	0.4
History of Diabetes	1.91	0.60-6.10	0.3
History of Hypertension	2.07	0.80-5.323	0.1
History of Smoking	2.44	1.64-3.62	<0.001
History of Dyslipidemia	4.11	2.71-6.26	<0.001
Family History of CAD	2.45	1.62-3.73	<0.001
Prior Acute Myocardial Infarction	2.47	0.83-7.36	0.1
History of Angina	2.90	1.05-8.02	0.04
History of CABG	3.50	0.99-12.36	0.05
History of CHF	1.30	0.49-3.49	0.6
Prior PTCA	3.93	1.04-14.87	0.04
History of TIA/CVA	2.00	0.79-5.07	0.1
STEMI vs. Non-STEMI	1.35	0.95-1.92	0.1
	Multivariate		
Gender (Female)	0.77	0.59-1.20	0.3
Age	0.9	0.92-0.95	<0.001
History of Dyslipidemia	3.0	1.9-4.7	<0.001
STEMI vs. Non-STEMI	2.0	1.35-2.94	<0.001

p values represent comparisons between male and female

STEMI – ST-Segment Elevated Myocardial Infarction; CAD – coronary artery disease; CABG – coronary artery bypass graft; CHF – congestive heart failure; PTCA – percutaneous transluminal coronary angioplasty; TIA/CVA – transient ischemic attack/cerebrovascular accident

Table 11 Health Care Access: CT/MRI (CVA)

	β	95% CI	*p* value
Univariate			
Gender (Female)	1.12	0.82-1.54	0.5
Age	0.94	0.93-0.96	<0.001
Confusion	1.35	0.89-2.04	0.2
Coma	0.47	0.31-0.72	<0.001
Incontinence	0.45	0.28-0.70	0.001
Arm Weakness	0.92	0.62-1.37	0.7
Leg Weakness	0.74	0.49-1.12	0.2
Gait Affected	0.87	0.60-1.27	0.5
Cranial Nerve Paralysis	0.73	0.51-1.05	0.09
Previous CVA	0.55	0.39-0.77	0.001
Diabetes	0.98	0.70-1.39	0.9
SPVD	0.74	0.47-1.15	0.2
Prior MI	0.78	0.52-1.16	0.2
Angina	0.83	0.56-0.56	0.3
Heart Failure	0.56	0.36-0.88	0.01
Chronic Renal Disease	0.56	0.30-1.06	0.08
Cancer	0.67	0.40-1.14	0.1
Multivariate			
Gender (Female)	1.41	1.00-1.92	0.06
Age	0.94	0.93-0.96	<0.001

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 12 Health Care Access: Time to 1st CT/MRI (CVA)		
	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.029	0.5
Age	0.060	0.2
Confusion	0.032	0.4
Coma	-0.0070	0.9
Incontinence	0.018	0.7
Arm Weakness	-0.12	0.03
Leg Weakness	0.045	0.4
Gait Affected	-0.025	0.6
Cranial Nerve Paralysis	-0.021	0.6
Previous CVA	-0.067	0.1
SPVD	-0.10	0.01
Diabetes	-0.35	0.4
Prior MI	0.0060	0.9
Angina	0.054	0.2
Heart Failure	-0.015	0.7
Chronic Renal Disease	0.0070	0.9
Cancer	-0.048	0.2
	Multivariate	
Gender (Female)	-0.011	0.8
Age	0.056	0.1
Arm Weakness	-0.098	0.008
Diabetes	-0.097	0.009

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 13 Health Care Access: Seen by Dietician (CVA)

	B	95% CI	*p* value
Univariate			
Gender (Female)	1.08	0.83-1.37	0.6
Age	1.00	0.99-1.01	0.7
Confusion	0.81	0.60-1.09	0.2
Coma	0.21	0.13-0.33	<0.001
Incontinence	0.83	0.56-1.23	0.3
Arm Weakness	1.30	0.96-1.75	0.09
Leg Weakness	1.35	1.00-1.82	0.05
Gait Affected	1.33	1.01-1.75	0.04
Cranial Nerve Paralysis	1.37	1.05-1.78	0.02
Previous CVA	0.92	0.68-1.22	0.5
Diabetes	1.67	1.27-2.17	<0.001
SPVD	0.90	0.63-1.32	0.6
Prior MI	0.81	0.58-1.14	0.2
Angina	0.83	0.61-1.12	0.2
Heart Failure	0.73	0.49-1.09	0.1
Chronic Renal Disease	0.66	0.37-1.19	0.2
Cancer	1.11	0.71-1.75	0.6
Multivariate			
Gender (Female)	1.09	0.83-1.45	0.5
Age	1.00	0.99-1.01	1.0
Cranial Nerve Paralysis	1.43	1.09-1.89	0.01
Diabetes	1.67	1.23-2.22	0.001

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 14 Health Care Access: Time to Dietician (CVA)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.063	0.2
Age	0.089	0.09
Confusion	-0.098	0.05
Coma	0.0010	1.0
Incontinence	-0.087	0.09
Arm Weakness	-0.059	0.4
Leg Weakness	0.11	0.1
Gait Affected	0.048	0.4
Cranial Nerve Paralysis	0.055	0.3
Previous CVA	-0.047	0.4
SPVD	0.013	0.8
Diabetes	-0.090	0.07
Prior MI	0.043	0.4
Angina	-0.10	0.05
Heart Failure	0.0090	0.9
Chronic Renal Disease	0.092	0.07
Cancer	-0.021	0.7
	Multivariate	
Gender (Female)	-0.036	0.4
Age	0.11	0.01
SPVD	-0.086	0.05

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 15 Health Care Access: Seen by Speech Language Pathologist (CVA)

	B	95% CI	*p* value
	Univariate		
Gender (Female)	1.04	0.79-1.35	0.8
Age	1.00	0.99-1.01	0.5
Confusion	0.92	0.67-1.27	0.6
Coma	0.17	0.10-0.27	<0.001
Incontinence	0.78	0.50-1.20	0.3
Arm Weakness	1.79	1.28-2.44	<0.001
Leg Weakness	1.72	1.27-2.38	0.001
Gait Affected	1.11	0.83-1.49	0.5
Cranial Nerve Paralysis	2.56	1.89-3.45	<0.001
Previous CVA	0.85	0.62-1.18	0.3
Diabetes	1.19	0.89-1.61	0.3
SPVD	0.84	0.57-1.25	0.4
Prior MI	0.77	0.53-1.11	0.2
Angina	1.15	0.82-1.61	0.4
Heart Failure	0.78	0.51-1.20	0.2
Chronic Renal Disease	0.37	0.19-0.70	0.003
Cancer	0.93	0.56-1.52	0.8
	Multivariate		
Gender (Female)	1.04	0.77-1.41	0.8
Age	1.01	1.00-1.02	0.1
Coma	0.22	0.065-0.71	0.01
Cranial Nerve Paralysis	2.63	1.96-3.57	<0.001
Chronic Renal Disease	0.41	0.20-0.83	0.01

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 16 Health Care Access: Time to Speech Language Pathologist (CVA)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.054	0.3
Age	-0.069	0.2
Confusion	-0.064	0.2
Coma	0.044	0.4
Incontinence	0.018	0.7
Arm Weakness	-0.088	0.2
Leg Weakness	0.022	0.8
Gait Affected	-0.079	0.1
Cranial Nerve Paralysis	-0.025	0.6
Previous CVA	-0.076	0.2
SPVD	-0.066	0.2
Diabetes	-0.10	0.06
Prior MI	-0.053	0.3
Angina	-0.020	0.7
Heart Failure	0.0020	1.0
Chronic Renal Disease	0.075	0.2
Cancer	-0.069	0.2
	Multivariate	
Gender (Female)	-0.052	0.3
Age	-0.066	0.2
SPVD	-0.091	0.05

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 17 Health Care Access: Seen by Physiotherapist (CVA)

	B	95% CI	*p* value
Univariate			
Gender (Female)	1.09	0.83-1.43	0.5
Age	1.00	0.99-1.01	0.6
Confusion	1.11	0.79-1.59	0.5
Coma	0.078	0.050-0.12	<0.001
Incontinence	0.60	0.39-0.92	0.02
Arm Weakness	2.94	2.08-4.00	<0.001
Leg Weakness	2.56	1.82-3.57	<0.001
Gait Affected	1.59	1.15-2.17	0.005
Cranial Nerve Paralysis	1.33	0.96-1.82	0.08
Previous CVA	0.98	0.71-1.35	0.9
Diabetes	1.56	1.15-2.13	0.005
SPVD	1.11	0.74-1.67	0.6
Prior MI	0.72	0.50-1.02	0.07
Angina	1.20	0.85-1.69	0.3
Heart Failure	0.82	0.53-1.25	0.3
Chronic Renal Disease	0.46	0.26-0.82	0.008
Cancer	0.87	0.54-1.41	0.6
Multivariate			
Gender (Female)	1.06	0.77-1.47	0.7
Age	1.01	1.00-1.02	0.5
Arm Weakness	3.03	2.17-4.17	<0.001
Diabetes	1.69	1.18-2.44	0.005
Prior MI	0.57	0.38-0.86	0.008

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 18 Health Care Access: Time to Physiotherapist (CVA)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.046	0.3
Age	0.0090	0.8
Confusion	-0.091	0.04
Coma	-0.017	0.7
Incontinence	-0.0050	0.9
Arm Weakness	0.056	0.3
Leg Weakness	-0.051	0.4
Gait Affected	-0.061	0.2
Cranial Nerve Paralysis	0.076	0.07
Previous CVA	-0.010	0.8
SPVD	0.0090	0.8
Diabetes	-0.076	0.07
Prior MI	0.028	0.5
Angina	-0.015	0.7
Heart Failure	-0.029	0.5
Chronic Renal Disease	-0.0070	0.9
Cancer	-0.027	0.5
	Multivariate	
Gender (Female)	-0.046	0.2
Age	0.042	0.3
Confusion	-0.081	0.04
SPVD	-0.080	0.04

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 19 Health Care Access: Time to Social Worker (CVA)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	0.015	0.8
Age	-0.039	0.5
Confusion	0.14	0.03
Coma	-0.049	0.4
Incontinence	-0.060	0.3
Arm Weakness	-0.13	0.07
Leg Weakness	0.035	0.6
Gait Affected	-0.088	0.1
Cranial Nerve Paralysis	-0.077	0.2
Previous CVA	-0.052	0.4
SPVD	-0.085	0.1
Diabetes	-0.020	0.7
Prior MI	0.058	0.3
Angina	0.013	0.8
Heart Failure	-0.0080	0.9
Chronic Renal Disease	0.032	0.6
Cancer	-0.051	0.4
	Multivariate	
Gender (Female)	-0.0050	0.9
Age	-0.019	0.7
Confusion	0.10	0.050
Arm Weakness	-0.13	0.01

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 20 Health Care Access: Seen by Occupational Therapist (CVA)

	B	95% CI	*p* value
Univariate			
Gender (Female)	1.18	0.91-1.54	0.2
Age	1.00	0.99-1.01	1.0
Confusion	1.03	0.75-1.43	0.8
Coma	0.072	0.043-0.12	<0.001
Incontinence	0.58	0.39-0.88	0.01
Arm Weakness	2.27	1.67-3.13	<0.001
Leg Weakness	1.96	1.45-2.70	<0.001
Gait Affected	1.25	0.93-1.69	0.1
Cranial Nerve Paralysis	1.09	0.81-1.45	0.6
Previous CVA	1.12	0.83-1.52	0.5
Diabetes	1.43	1.08-1.92	0.01
SPVD	0.97	0.66-1.43	0.9
Prior MI	0.89	0.63-1.27	0.5
Angina	1.08	0.78-1.49	0.7
Heart Failure	0.70	0.47-1.05	0.09
Chronic Renal Disease	0.44	0.25-0.68	0.006
Cancer	0.90	0.56-1.43	0.7
Multivariate			
Gender (Female)	1.28	0.95-1.75	0.1
Age	1.01	1.00-1.02	0.08
Coma	0.19	0.086-0.44	<0.001
Arm Weakness	2.38	1.72-3.33	<0.001
Chronic Renal Disease	0.48	0.25-0.92	0.03

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 21 Health Care Access: Time to Occupational Therapist (CVA)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.078	0.07
Age	-0.033	0.5
Confusion	-0.076	0.08
Coma	-0.043	0.3
Incontinence	0.026	0.6
Arm Weakness	-0.034	0.5
Leg Weakness	0.031	0.6
Gait Affected	-0.072	0.1
Cranial Nerve Paralysis	-0.022	0.6
Previous CVA	-0.17	<0.001
SPVD	-0.11	0.01
Diabetes	-0.026	0.5
Prior MI	0.065	0.1
Angina	-0.021	0.6
Heart Failure	-0.012	0.8
Chronic Renal Disease	0.015	0.7
Cancer	0.0070	0.9
	Multivariate	
Gender (Female)	-0.077	0.06
Age	0.0020	1.0
Previous CVA	-0.13	0.002

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 22 Health Care Access: Transferred to Rehabilitation Center (CVA)

	B	95% CI	*p* value
Univariate			
Gender (Female)	1.02	0.71-1.47	0.9
Age	1.00	0.99-1.02	0.8
Confusion	0.70	0.44-1.10	0.1
Coma	0.093	0.023-0.38	0.001
Incontinence	1.16	0.68-2.00	0.6
Arm Weakness	4.35	2.27-8.33	<0.001
Leg Weakness	4.35	2.33-8.33	<0.001
Gait Affected	1.47	0.98-2.17	0.06
Cranial Nerve Paralysis	1.47	0.99-2.17	0.05
Previous CVA	1.19	0.79-1.82	0.4
Diabetes	1.03	0.69-1.54	0.9
SPVD	1.03	0.60-1.79	0.9
Prior MI	0.59	0.33-1.05	0.08
Angina	0.88	0.55-1.43	0.6
Heart Failure	0.89	0.49-1.64	0.7
Chronic Renal Disease	1.33	0.61-2.94	0.5
Cancer	1.39	0.76-2.56	0.3
Multivariate			
Gender (Female)	1.04	0.71-1.54	0.8
Age	1.00	0.98-1.01	0.9
Arm Weakness	2.32	1.09-5.00	0.03
Leg Weakness	2.63	1.23-5.56	0.01

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 23 Health Care Access: Time to Rehabilitation Center (CVA)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	0.066	0.5
Age	0.15	0.2
Confusion	-0.10	0.3
Coma	0.084	0.4
Incontinence	0.058	0.6
Arm Weakness	-0.15	0.2
Leg Weakness	0.26	0.02
Gait Affected	0.031	0.8
Cranial Nerve Paralysis	-0.20	0.06
Previous CVA	-0.0040	1.0
SPVD	-0.18	0.08
Diabetes	-0.035	0.7
Prior MI	0.058	0.6
Angina	-0.017	0.9
Heart Failure	0.11	0.3
Chronic Renal Disease	0.050	0.6
Cancer	-0.070	0.5
	Multivariate	
Gender (Female)	0.0050	1.0
Age	0.073	0.4
Arm Weakness	0.22	0.02
Diabetes	-0.20	0.03

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 24 Health Care Outcome: Length of Stay (CVA)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.058	0.2
Age	0.13	0.04
Confusion	-0.030	0.5
Coma	0.22	<0.001
Incontinence	-0.072	0.2
Arm Weakness	-0.11	0.03
Leg Weakness	-0.086	0.08
Gait Affected	-0.039	0.5
Cranial Nerve Paralysis	-0.059	0.2
Previous CVA	-0.044	0.3
SPVD	-0.081	0.08
Diabetes	0.029	0.5
Prior MI	0.018	0.7
Angina	0.020	0.7
Heart Failure	-0.12	0.007
Chronic Renal Disease	0.030	0.5
Cancer	-0.077	0.09
	Multivariate	
Gender (Female)	-0.036	0.4
Age	0.11	0.02
Arm Weakness	-0.10	0.03

p values represent comparisons between males and females
CVA – cerebrovascular accident; SPVD – symptomatic peripheral vascular disease; MI – myocardial infarction

Table 25 Health Care Intervention: CABG (Coronary Revascularization)			
	Univariate		
	B	95% CI	*p* value
Gender (Female)	0.57	0.41-0.79	0.001
Age	1.01	1.00-1.02	0.2
Diabetes	1.31	0.97-1.78	0.08
Coronary Anatomy			
Single Vessel, no PLAD	0.010	0.059-0.16	<0.001
Single Vessel, PLAD	0.41	0.20-0.85	0.02
Double Vessel, no PLAD	0.38	0.25-0.56	<0.001
Double Vessel, PLAD	1.58	0.91-2.76	0.1
Triple Vessel	5.00	3.57-6.87	<0.001
Unprotected Left Main	22.22	10.87-45.45	<0.001
Disease			
Protected Left Main Disease	0.31	0.092-1.06	0.06
LV Angiogram			
Grade 1 LV	0.99	0.73-1.35	0.9
Grade 2 LV	0.85	0.58-1.27	0.4
Grade 3 LV	1.15	0.69-1.93	0.6
Grade 4 LV	1.26	0.69-2.29	0.5
Ejection Fraction (<35%)	1.16	0.77-1.77	0.5
Very Positive Stress Test	1.76	1.15-2.43	0.003
Maximal Medical Therapy	1.12	0.81-1.54	0.5
CCS Angina Class			
Class 1-2	0.61	0.42-0.89	0.009
Class 3	3.06	2.20-4.25	<0.001
Class 4	0.55	0.41-0.74	<0.001
	Multivariate		
Gender (Female)	0.76	0.50-1.16	0.2
Age	0.99	0.97-1.00	0.1
Double Vessel, PLAD	6.33	3.37-11.90	<0.001
Unprotected Left Main Disease	11.90	7.81-18.18	<0.001
CCS Angina Class 4	3.56	2.36-5.35	<0.001

p values represent comparisons between males and females

CABG – coronary artery bypass graft; CAD – coronary artery disease; PLAD - proximal left anterior descending; LV – left ventricle; CCS – Canadian Cardiovascular Society

Table 26 Health Care Access: Days Awaiting CABG for Patients with Very Urgent Priority (Coronary Revascularization)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.057	0.9
Age	-0.12	0.7
Diabetes	0.45	0.7
Recent MI	-0.094	0.8
Urgency Rating Score	0.24	0.5
Coronary Anatomy		
Double Vessel, no PLAD	-0.15	0.7
Triple Vessel	-0.10	0.8
Unprotected Left Main	0.19	0.6
Disease		
LV Angiogram		
Grade 1 LV	-0.35	0.3
Grade 2 LV	0.15	0.7
Grade 3 LV	0.41	0.2
Grade 4 LV	-0.19	0.6
Ejection Fraction (<35%)	0.22	0.5
Very Positive Stress Test	0.39	0.2
	Multivariate	
Gender (Female)	-0.12	0.8
Age	-0.17	0.7

p values represent comparisons between males and females
CABG – coronary artery bypass graft; CAD – coronary artery disease; MI – myocardial infarction; PLAD - proximal left anterior descending; LV – left ventricle

Table 27 Health Care Access: Days Awaiting CABG for Patients with Urgent Priority (Coronary Revascularization)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.27	0.3
Age	-0.046	0.9
Diabetes	-0.36	0.2
Recent MI	0.36	0.2
Previous CABG	0.033	0.9
Urgency Rating Score	-0.35	0.2
Coronary Anatomy		
Double Vessel, no PLAD	0.12	0.5
Double Vessel, PLAD	0.018	0.9
Triple Vessel	0.32	0.2
Unprotected Left Main	-0.45	0.08
Disease		
LV Angiogram		
Grade 1 LV	-0.16	0.6
Grade 2 LV	0.038	0.9
Grade 3 LV	0.17	0.5
Grade 4 LV	0.033	0.9
Ejection Fraction (<35%)	0.16	0.5
Very Positive Stress Test	-0.10	0.7
Maximal Medical Therapy	0.51	0.04
	Multivariate	
Gender (Female)	-0.45	0.06
Age	-0.065	0.8
Unprotected Left Main Disease	-0.53	0.02
Maximal Medical Therapy	0.51	0.02

p values represent comparisons between males and females
CABG – coronary artery bypass graft; CAD – coronary artery disease; MI – myocardial infarction; PLAD - proximal left anterior descending; LV – left ventricle

Table 28 Health Care Access: Days Awaiting CABG for Patients with Semi-Urgent Priority (Coronary Revascularization)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.36	0.2
Age	-0.086	0.8
Diabetes	0.15	0.6
Recent MI	-0.20	0.5
Previous CABG	0.072	0.8
Urgency Rating Score	0.50	0.05
Coronary Anatomy		
Double Vessel, no PLAD	0.23	0.4
Double Vessel, PLAD	-0.25	0.3
Triple Vessel	-0.16	0.6
Unprotected Left Main	0.21	0.4
Disease		
Protected Left Main Disease	0.072	0.8
LV Angiogram		
Grade 1 LV	-0.086	0.8
Grade 2 LV	0.39	0.1
Grade 3 LV	0.072	0.8
Grade 4 LV	-0.44	0.09
Ejection Fraction (<35%)	-0.33	0.2
Very Positive Stress Test	-0.018	0.9
Maximal Medical Therapy	-0.46	0.1
CCS Angina Class 3	-0.26	0.3
CCS Angina Class 4	0.26	0.3
	Multivariate	
Gender (Female)	-0.36	0.2
Age	-0.017	0.9

p values represent comparisons between males and females
CABG – coronary artery bypass graft; CAD – coronary artery disease; MI – myocardial infarction; PLAD - proximal left anterior descending; LV – left ventricle; CCS – Canadian Cardiovascular Society

Table 29 Health Care Access: Days Awaiting CABG for Patients with Delayed Wait Priority (Coronary Revascularization)

	Univariate	
	Parameter Estimate	*p* value
Gender (Female)	-0.13	0.2
Age	0.028	0.8
Diabetes	0.028	0.8
Recent MI	0.11	0.2
Previous CABG	0.030	0.7
Urgency Rating Score	0.072	0.4
Coronary Anatomy		
Single Vessel, no PLAD	0.025	0.8
Single Vessel, PLAD	0.073	0.4
Double Vessel, no PLAD	-0.12	0.2
Double Vessel, PLAD	0.018	0.8
Triple Vessel	-0.021	0.8
Unprotected Left Main	0.071	0.4
Disease		
Protected Left Main Disease	0.030	0.7
LV Angiogram		
Grade 1 LV	-0.022	0.8
Grade 2 LV	0.035	0.7
Grade 3 LV	0.022	0.8
Grade 4 LV	-0.042	0.6
Ejection Fraction (<35%)	-0.013	0.9
Very Positive Stress Test	0.077	0.4
Maximal Medical Therapy	-0.18	0.08
CCS Angina Class 1-2	-0.093	0.3
CCS Angina Class 3	0.0030	1.0
CCS Angina Class 4	0.11	0.2
	Multivariate	
Gender (Female)	-0.13	0.2
Age	-0.0030	1.0

p values represent comparisons between males and females
CABG – coronary artery bypass graft; CAD – coronary artery disease; MI – myocardial infarction; PLAD - proximal left anterior descending; LV – left ventricle; CCS – Canadian Cardiovascular Society

Table 30 Health Care Intervention: PCI (Coronary Revascularization)			
	Univariate		
	B	95% CI	*p* value
Gender (Female)	0.57	0.41-0.79	0.001
Age	1.01	1.00-1.02	0.2
Diabetes	1.32	0.97-1.78	0.08
Coronary Anatomy			
Single Vessel, no PLAD	0.097	0.059-0.16	<0.001
Single Vessel, PLAD	0.41	0.20-0.86	0.02
Double Vessel, no PLAD	0.38	0.26-0.56	<0.001
Double Vessel, PLAD	1.49	0.87-2.58	0.7
Triple Vessel	4.95	3.58-6.85	<0.001
Unprotected Left Main	22.22	10.87-45.45	<0.001
Disease			
Protected Left Main Disease	0.31	0.091-1.04	0.06
LV Angiogram			
Grade 1 LV	1.05	0.77-1.42	0.8
Grade 2 LV	0.88	0.60-1.31	0.5
Grade 3 LV	1.12	0.67-1.87	0.7
Grade 4 LV	0.97	0.55-1.72	0.9
Ejection Fraction (<35%)	1.03	0.69-1.56	0.9
Very Positive Stress Test	1.76	1.21-2.56	0.003
Maximal Medical Therapy	1.13	0.82-1.56	0.4
CCS Angina Class			
Class 1-2	0.61	0.42-0.89	0.009
Class 3	3.04	2.19-4.22	<0.001
Class 4	0.59	0.44-0.78	<0.001
	Multivariate		
Gender (Female)	0.79	0.52-1.20	0.3
Age	0.98	0.96-1.00	0.07
Single Vessel, PLAD	0.049	0.027-0.089	<0.001
Single Vessel, no PLAD	0.13	0.060-0.30	<0.001
Double Vessel, no PLAD	0.15	0.093-0.23	<0.001
Unprotected Left Main Disease	16.13	2.91-13.16	0.01
Protected Left Main Disease	0.11	0.030-0.39	<0.001
CCS Angina Class 3	3.50	2.31-5.26	<0.001

p values represent comparisons between males and females
CABG – coronary artery bypass graft; CAD – coronary artery disease; PLAD - proximal left anterior descending; LV – left ventricle; CCS – Canadian Cardiovascular Society

Table 31 Health Care Intervention: Optimal Modality Choice (CKD)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.68	0.44-1.06	0.1
Age	0.99	0.98-1.01	0.3
History of Diabetes	0.81	0.52-1.24	0.3
History of Hypertension	1.44	0.66-3.14	0.4
History of CHF	0.45	0.25-0.81	0.008
History of Cancer	0.85	0.48-1.48	0.6
History of Renal Disease	0.97	0.58-1.62	0.9
Pre-Dialysis Care (>1 mth.)	28.28	6.74-118.62	<0.001
eGFR at Dialysis Start	1.03	0.98-1.08	0.2
Phosphate at Dialysis Start	0.40	0.27-0.61	<0.001
Hemoglobin at Dialysis Start	1.05	1.03-1.06	<0.001
Ferritin at Dialysis Start	1.00	0.99-1.01	0.5
Albumin at Dialysis Start	1.14	1.09-1.19	<0.001
	Multivariate		
Gender (Female)	0.63	0.35-1.11	0.1
Age	0.99	0.97-1.01	0.3
History of CHF	0.46	0.21-0.99	0.05
Pre-Dialysis Care (<1 mth.)	21.48	4.58-100.78	0.001
Phosphate at Dialysis Start	0.53	0.33-0.85	0.008
Hemoglobin at Dialysis Start	1.02	1.00-1.04	0.03
Albumin at Dialysis Start	1.13	1.08-1.19	<0.001

p values represent comparisons between males and females

CHF – congestive heart failure; eGFR – estimated glomerular filtration rate

Table 32 Health Care Intervention: Optimal Access Choice (CKD)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	0.67	0.43-1.05	0.08
Age	0.99	0.98-1.01	0.2
History of Diabetes	0.83	0.45-1.27	0.4
History of Hypertension	1.46	0.67-3.18	0.3
History of CHF	0.45	0.25-0.80	0.007
History of Cancer	0.83	0.48-1.46	0.5
History of Renal Disease	0.95	0.57-1.59	0.9
Pre-Dialysis Care (>1 mth.)	28.69	6.84-120.34	<0.001
eGFR at Dialysis Start	1.03	0.98-1.08	0.2
Phosphate at Dialysis Start	0.41	0.27-0.61	<0.001
Hemoglobin at Dialysis Start	1.05	1.03-1.06	<0.001
Ferritin at Dialysis Start	1.00	1.00-1.01	0.4
Albumin at Dialysis Start	1.14	1.09-1.19	<0.001
	Multivariate		
Gender (Female)	0.60	0.33-1.08	0.08
Age	0.99	0.97-1.01	0.2
History of CHF	0.45	0.21-0.99	0.05
Pre-Dialysis Care (<1 mth.)	22.26	4.71-105.32	<0.001
Phosphate at Dialysis Start	0.53	0.33-0.85	0.008
Hemoglobin at Dialysis Start	1.02	1.00-1.04	0.03
Albumin at Dialysis Start	1.14	1.08-1.19	<0.001

p values represent comparisons between males and females

CHF – congestive heart failure; eGFR – estimated glomerular filtration rate

Table 33 Health Care Outcome: Hospitalization after RRT (CKD)

	Univariate		
	Exp β	95% CI	*p* value
Gender (Female)	2.56	0.87-2.22	0.2
Age	1.02	1.00-1.03	0.03
History of Diabetes	1.36	0.86-2.15	0.2
History of Hypertension	0.87	0.39-1.95	0.7
History of CHF	1.03	0.57-1.86	0.9
History of Cancer	1.51	0.85-2.68	0.2
History of Renal Disease	1.28	0.75-2.20	0.4
Pre-Dialysis Care (>1 mth.)	0.87	0.46-1.65	0.7
eGFR at Dialysis Start	1.01	0.96-1.06	0.7
Phosphate at Dialysis Start	0.93	0.64-1.36	0.7
Hemoglobin at Dialysis Start	0.10	0.98-1.01	0.7
Ferritin at Dialysis Start	1.00	1.00-1.02	0.2
Albumin at Dialysis Start	0.99	0.95-1.02	0.4
	Multivariate		
Gender (Female)	1.37	0.86-2.22	0.2
Age	1.02	1.00-1.03	0.03

p values represent comparisons between males and females

CHF – congestive heart failure; eGFR – estimated glomerular filtration rate

Table 34 Health Care Outcome: Death (CKD)

	Exp β	95% CI	*p* value
Univariate			
Gender (Female)	1.28	0.55-3.03	0.6
Age	1.04	1.00-1.07	0.3
History of Diabetes	0.55	0.23-1.34	0.2
History of Hypertension	0.30	0.10-0.88	0.03
History of CHF	1.66	0.62-4.39	0.3
History of Cancer	3.95	1.64-9.52	0.002
History of Renal Disease	1.61	0.63-4.07	0.3
Pre-Dialysis Care (> 1 mth.)	0.42	0.15-1.13	0.08
eGFR at Dialysis Start	1.01	0.93-1.09	0.8
Phosphate at Dialysis Start	1.07	0.54-2.09	0.9
Hemoglobin at Dialysis Start	0.95	0.92-0.98	0.001
Ferritin at Dialysis Start	1.00	1.00-1.01	0.08
Albumin at Dialysis Start	0.94	0.88-0.99	0.03
Multivariate			
Gender (Female)	1.41	0.57-3.45	0.5
Age	1.03	1.00-1.07	0.08
History of Cancer	3.70	1.41-10.00	0.008
Hemoglobin at Dialysis Start	0.94	0.91-0.97	<0.001

p values represent comparisons between males and females

CHF – congestive heart failure; eGFR – estimated glomerular filtration rate

Table 35 Health Care Intervention: Appropriateness of Antibiotic Choice (2000 Guidelines) (CAP)

	B	95% CI	p value
	Univariate		
Gender (Female)	0.69	0.53-0.99	0.008
Age	1.04	1.03-1.04	<0.001
Nursing Home Resident	2.92	1.68-5.10	<0.001
Hospitalized in Past Year	1.03	0.78-1.36	0.8
Alcohol	0.61	0.36-1.04	0.07
CAD	2.49	1.80-3.44	<0.001
Neoplastic Disease	2.80	1.77-4.42	<0.001
Interstitial Disease	1.22	0.66-2.23	0.5
Chronic Renal Failure	4.08	1.95-8.47	<0.001
Neurological Condition	0.54	0.33-0.88	0.01
Smoker	0.64	0.48-0.87	0.004
Asthma	1.78	1.13-2.79	0.01
COPD	1.68	1.23-2.29	0.001
Diabetes	1.75	1.21-2.52	0.003
Liver Failure	1.96	0.44-8.77	0.4
CHF	3.08	2.01-4.72	<0.001
CVD	2.11	1.26-3.55	0.005
Low Risk	0.16	0.12-0.23	<0.001
Require Hospitalization	1.53	1.17-2.02	0.002
Dyspnea	1.50	1.13-2.00	0.005
Cough	0.99	0.72-1.36	0.9
Sputum	1.12	0.86-1.47	0.4
Chest Pain	0.65	0.48-0.86	0.003
AB Prior to Admission	0.72	0.40-1.29	0.3
	Multivariate		
Gender (Female)	0.79	0.59-1.06	0.1
Age	1.02	1.01-1.03	<0.001
Neoplastic Disease	1.75	1.06-2.87	0.03
Asthma	2.39	1.48-3.89	<0.001
Low Risk	0.27	0.18-0.39	<0.001

p values represent comparisons between males and females

CAD – coronary artery disease; COPD – chronic obstructive pulmonary disease; CHF – congestive heart failure; CVD – cerebrovascular disease

Table 36 Health Care Outcome: Death (CAP)

	B	95% CI	p value
	Univariate		
Gender (Female)	0.63	0.42-0.95	0.03
Age	1.05	1.03-1.06	<0.001
Nursing Home Resident	1.90	1.14-3.18	0.01
Hospitalized in Past Year	1.61	1.09-2.39	0.02
Alcohol	1.55	0.74-3.23	0.2
CAD	2.56	1.72-3.81	<0.001
Neoplastic Disease	1.74	1.10-2.76	0.02
Interstitial Disease	1.13	0.50-2.55	0.7
Chronic Renal Failure	2.63	1.54-4.49	<0.001
Neurological Condition	2.20	1.17-4.16	0.02
Smoker	0.66	0.40-1.09	0.7
Asthma	0.78	0.42-1.45	0.4
COPD	1.11	0.73-1.69	0.6
Diabetes	1.27	0.80-2.01	0.3
Liver Failure	2.62	0.72-9.53	0.1
CHF	2.42	1.59-3.69	<0.001
CVD	2.69	1.64-4.39	<0.001
Low Risk	0.17	0.10-0.28	<0.001
Require Hospitalization	2.77	1.68-4.56	<0.001
Dyspnea	1.16	0.74-1.81	0.5
Cough	0.48	0.32-0.74	0.001
Sputum	0.67	0.45-0.99	0.05
Chest Pain	0.29	0.15-0.55	<0.001
AB Prior to Admission	0.92	0.35-2.40	0.9
	Multivariate		
Gender (Female)	0.65	0.42-1.02	0.06
Age	1.04	1.02-1.06	<0.001
CAD	2.08	1.35-3.22	0.001
Neurological Condition	2.74	1.34-5.59	0.006
Require Hospitalization	2.58	1.50-4.41	0.001
Cough	0.59	0.37-0.93	0.02

p values represent comparisons between males and females

CAD – coronary artery disease; COPD – chronic obstructive pulmonary disease; CHF – congestive heart failure; CVD – cerebrovascular disease