Long Term Functional Survival After Surgery on the Thoracic Aorta in Manitoba

by

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A Thesis submitted to the Faculty of Graduate Studies of
The University of Manitoba
in partial fulfilment of the requirements of the degree of

MASTER OF SCIENCE

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Abstract

Problem: The epidemiology of thoracic aortic disease (TAD) in Manitoba is currently unknown. Additionally, it is unclear whether minimally invasive thoracic endovascular aortic repair (TEVAR) is associated with improved functional (ie. non-institutionalized) survival compared to open surgery.

Methods: Data housed at the Manitoba Centre for Health Policy and the Manitoba Thoracic Aortic Diseases clinic were used to examine the epidemiology and functional survival of patients with TAD.

Results: The incidence and prevalence of TAD is increasing, especially in women and the Winnipeg region. There was no difference between TEVAR and open surgery in functional survival (HR 1.509; p=0.3565) however, a small sample size makes it difficult to interpret these results.

Conclusion: Resources should be allocated to ensure appropriate monitoring, treatment and follow up for the growing number of patients with TAD. Multicenter collaboration is necessary to make definitive conclusions regarding functional survival in TEVAR and open surgery patients.

Acknowledgements

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List of Abbreviations

AAA	Abdominal Aortic Aneurysm
ACP	Antegrade Cerebral Perfusion
AD	Aortic Dissection
AIDS	Acquired Immunodeficiency Syndrome
AKI	Acute Kidney Injury
AR	Aortic Rupture
ATC	Anatomical Therapeutic Chemical
AVR	Aortic Valve Replacement
BSA	Body Surface Area
CCI	Charlson Comorbidity Index
CI	Confidence Interval
CM	Centimeter
CPB	Cardiopulmonary Bypass
CSF	Cerebrospinal Fluid
CT	Computed Tomography
CTAC	Canadian Thoracic Aortic Collaborative
DHCA	Deep Hypothermic Circulatory Arrest
DPIN	Drug Program Information Network
DSM	Diagnostic Services Manitoba
EDIS	Emergency Department Information System
EIA	Employment Income Assistance
FDA	Food and Drug Administration
HIPC	Health Information Privacy Committee
HIV	Human Immunodeficiency Virus
HRQoL	Health Related Quality of Life
ICD	International Classification of Diseases
ICU	Intensive Care Unit
ICULOS	Intensive Care Unit Length of Stay
IMH	Intramural Hematoma

IPTW	Inverse Probability of Treatment Weighting
IQR	Interquartile Range
IRAD	International Registry for Acute Aortic Dissections
KG	Kilogram
MaCS	Manitoba Cardiac Surgery
MCHP	Manitoba Centre for Health Policy
MTAD	Manitoba Thoracic Aortic Diseases
NIS	National Inpatient Sample
OMT	Optimal Medical Therapy
OR	Odds Ratio
PAU	Penetrating Atherosclerotic Ulcer
PHIN	Personal Health Information Number
prICULOS	Prolonged Intensive Care Unit Length of Stay
V/Q	Ventilation / Perfusion
VQI	Vascular Quality Initiative
RHA	Regional Health Authority
RR	Risk Ratio
SAMIN	Social Assistance Management Information Network
SD	Standard Deviation
SMD	Standardized Mean Difference
TAA	Thoracic Aortic Aneurysm
TAAA	Thoracoabdominal Aneurysm
TAD	Thoracic Aortic Disease
TEVAR	Thoracic Endovascular Aortic Repair
TTR	Talent Thoracic Retrospective
WRHA	Winnipeg Regional Health Authority

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Introduction

Disease of the Descending Thoracic Aorta

Diseases of the descending thoracic aorta represent a spectrum of pathology that often goes undetected until a catastrophic event such as aneurysm rupture or acute dissection occurs. Descending thoracic aortic aneurysms (TAA) develop primarily due to degeneration within the aortic wall, resulting in a loss of wall strength and progressive dilation over time [1]. The general consensus on the true incidence and prevalence of thoracic aortic disease (TAD) has not yet been determined [1]. The available literature is heterogeneous with early studies publishing data on small patient cohorts, and more contemporary studies including a recent publication from Ontario [2], using a wide variety of hospital based data not necessarily representative of an entire population. Screening studies using computed tomography (CT) estimate the prevalence of TAA to be between 160 to 260 per 100 000 population, however this is difficult to determine as many asymptomatic aneurysms go undiagnosed [3, 4].

Descending TAA's can be isolated to the descending intra-thoracic aorta, or extend from the thoracic cavity past the diaphragm into the abdominal aorta and are known as thoracoabdominal aneurysms (TAAA). Two potentially lethal complications associated with descending TAA are acute aortic rupture (AR) or acute aortic dissection (AD) [1]. Continued aneurysm expansion is the most common reason for rupture or dissection [1]. At a mean size of 6 cm or greater, the yearly risk of rupture, dissection or death is approximately 14% [5]. The presence of acute symptoms, bicuspid aortic valve associated aortopathy, and connective tissue disease are important patient related factors that increase the risk of acute complications [1].

Surgical Repair of the Descending Thoracic Aorta

Traditionally, repair of descending aortic pathology requires an open chest and/or chest + abdomen (i.e. thoracoabdominal) surgical procedure which, while life-saving, is associated with significant morbidity primarily due to the invasiveness of the procedure. The major causes of morbidity associated with open repair of descending TAA or TAAA are stroke (ranging from 2 to 8% [6-8]), paraplegia (as high as 14% depending on the extent of repair and the status of the artery of Adamkiewicz [6]) and acute kidney injury (AKI) (12.3%[6]), with 4 to 5% of these patients deteriorating to dialysis dependent renal failure [6, 9]). The average 30 day in-hospital

mortality for patients undergoing open surgical intervention has been reported to be approximately 12% in single center studies [7], while previous large database studies describe an elective mortality of up to 19%[10].

Advances in Operative Technology for Descending Repair

In the mid-1990's, Dake et al published a landmark report describing the successful use of thoracic endovascular aortic repair (TEVAR) for the treatment of descending aortic pathology [11]. A TEVAR procedure is a less invasive technique for the operative management of thoracic aortic disease. In contrast to the traditional open surgical approach involving a thoracotomy (or thoracoabdominal) incision, the femoral vessels are accessed either directly using a small cut down or with a percutaneous Seldinger technique. Wires and catheters are used to deploy a stent graft within the lumen of the diseased aorta which markedly decreases the invasiveness of the procedure [12]. A TEVAR approach is particularly useful in older frail patients with complex co-morbid conditions and increased susceptibility to in-hospital and post-discharge complications. There are now multiple studies demonstrating that TEVAR can successfully treat descending thoracic aortic disease with a markedly reduced perioperative risk to the patient. A systematic review of eleven studies examining outcomes of patients with descending TAA reported a pooled 30 day in-hospital mortality of 4%, paraplegia rate of 3.2% and stroke rate of 2.7%[13]. Despite these encouraging perioperative results, the long-term outcomes associated with TEVAR, particularly in patients who would be eligible for open repair are not well known.

Why is this study needed now?

At present, there is a paucity of contemporary information comparing the long-term (greater than 5 year) outcomes of endovascular versus open surgery for repair of the descending thoracic aorta. Given the increasing focus on patient centered outcomes, identification of factors affecting quality of life beyond crude survival rates is important. Our group has previously reported on the patient centred outcome of "functional survival", defined as patients who are alive and not living in an institutionalized setting (i.e. non-institutional survival) [14]. The functional survival for patients undergoing TEVAR and open surgery for descending aortic pathology is not yet known, and represents important information which could be utilized by surgeons during patient-caregiver counselling, and the shared operative decision making process.

Unique Manitoba Resource to Address Current Gap in Knowledge

In September 2011, the Manitoba Thoracic Aortic Diseases (MTAD) database was established in conjunction with the newly formed Thoracic Aortic Diseases Clinic. For the past 6 years, our centre has utilized the clinic to facilitate data collection on all patients presenting with thoracic aortic diseases. The MTAD database is unique in that it contains individual information on all patients assessed in the clinic regardless of their management strategy (i.e. both the medically and surgically treated patient populations).

The Manitoba Centre for Health Policy (MCHP) is a provincial data repository which houses healthcare, education, social, justice and registry data for all residents of Manitoba [15]. Linkage of the MTAD database with the MCHP data repository allows for the use of robust in-hospital and post-discharge administrative data for the examination of long term functional survival in patients undergoing endovascular and open descending aortic repair.

Literature Search

Epidemiology of Degenerative Thoracic Aortic Disease

The true incidence and prevalence of TAA and AD is difficult to determine because many patients remain asymptomatic for long periods of time [1]. Often, diagnosis is either made during later stages of the disease when symptoms arise or incidentally on imaging tests done for other reasons.

Early Literature

In 1982, Bickerstaff et al published a seminal paper examining the incidence of TAA and found 72 patients diagnosed over a period of 30 years [16]. Age and sex adjusted incidence was 5.9 per 100 000 person years with no difference noted between sexes [16]. One of the first major studies using population level data was done in Minnesota and examined in-patient and out-patient diagnoses of TAA from 1980 to 1994 [17]. They found an overall incidence of 10.4 per 100 000 person years, and contrary to the Bickerstaff study it was apparent that the incidence in males was significantly greater than in females [17]. The disparity in diagnosis by sex has also been

shown to be increasing over time. Olsson et al reported the incidence or TAA in males increasing by 52% from 10.7 per 100 000 to 16.3 per 100 000, and the incidence in females increasing 28% from 7.1 per 100 000 to 9.1 per 100 000 over 15 years [18].

The epidemiology of aortic dissection was described in a population based study published in 2000 for a region in western Hungary [19]. Between 1972 and 1998, they identified 84 patients with a diagnosis of AD with an incidence of 2.9 per 100 000[19]. In a follow-up study using data from Minnesota, the age and sex stratified incidence of AD was significantly higher in males than in females (5.2 per 100 000 vs 2.2 per 100 000), with a similar overall incidence of 3.5 per 100 000 [20]. These findings have been corroborated in early publications from Asia which report an incidence of roughly 4 per 100 000 during a similar time period [21, 22].

Contemporary Literature

Since the 1980's, improvements in imaging technology and the widespread use of high quality CT scans and echocardiography have increased the likelihood of detecting thoracic aortic disease. The early literature is now considered outdated, as much of the data was collected prior to or during these technological advancements. Population demographics have also changed over time, with patients now older and sicker than they were in previous decades. Additionally, contemporary reports have focused on aortic dissection and have found variable results compared to previous publications. A study using Medicare data from 2000 to 2011 found an incidence of 10 per 100 000 hospitalized patients and this was stable over the reported time period [23]. In contrast, Melvinsdottir et al. published data using the entire Icelandic population from 1998 to 2013 and found the age and sex adjusted incidence to be 2.5 per 100 000 [24]. Similar to the Medicare report, they also found that the incidence of AD was stable to over the course of the study [24].

While the above-mentioned studies primarily used retrospective data including both asymptomatic and symptomatic patients, two publications have examined incidence and prevalence of strictly asymptomatic thoracic aortic disease based on CT scan screening programs [3, 4]. Itani et al evaluated scans from 6791 patients who were part of a screening program for lung cancer and tuberculosis and has been one of few groups who have reported a prevalence of

TAA with158 per 100 000 [3]. Using data from the Heinz Nixdorf Recall Study in Germany, Kalsch et al used CT scans from 4609 asymptomatic patients evaluated for the presence of coronary artery calcification [4]. They found an TAA incidence of 41 per 100 000, which is significantly higher than early reports although the data is not adjusted for age or sex [4].

The Canadian Experience

Up until a publication by McClure et al in February 2018 [2], there had been no studies examining the epidemiology of thoracic aortic disease in Canada. The Canadian healthcare system operates under a publicly funded organizational structure where diagnoses on physician billings and hospital records are usually available via International Classification of Diseases (ICD) coding. McClure reports the incidence of thoracic aortic disease in Ontario, a province of 13.5 million people, using all available hospital records including emergency department and hospital based ambulatory care visits [2]. They found the overall incidence of AD to be 4.6 per 100 000, or 5.5 per 100 000 for males and 3.7 per 100 000 for females [2], which is in line with the results of previous studies on AD [19-22, 24]. The total incidence of TAA was 7.6 per 100 000, or 10.8 per 100 000 for males and 5.5 per 100 000 for females, again similar to early reports [18].

While these results are interesting, important and novel in the context of the Canadian population, they are not necessarily generalizable to Manitoba. Challenges in diagnosis and management arise in this province due to the remote nature of many communities which may affect the incidence and prevalence figures. Additionally, a single referral center is responsible for the medical and surgical care of patients with diagnosed thoracic aortic disease, therefore provincial epidemiology plays an important part of resource utilization planning.

Aneurysms of the Descending Thoracic Aorta

Natural History

Descending TAA and TAAA develop slowly over time, however due to their insidious nature it is estimated that only 5% are symptomatic and diagnoses are usually made incidentally on unrelated imaging tests [25]. Degenerative aneurysms expand at a rate of 0.1cm to 0.3 cm per year depending on their location and etiology [1]. Larger aneurysms also have a correspondingly

higher rate of yearly growth which increases the risk of acute aneurysm related complications [26]. Coady et al. found that asymptomatic patients with a descending aneurysm greater than 7.0 cm had a 43% increase in the risk of dissection or rupture [27]. Without open surgical repair, the prognosis for patients with large or symptomatic TAA/TAAA is poor, with a 5-year survival between 20 and 65% [16, 28, 29].

Open Surgical Repair

Open resection and replacement of a descending TAA with a homograft was first reported in 1951 by Conrad Lam [30]. The advent of cardiopulmonary bypass (CPB) and the use of hypothermia, spinal cord protection and distal perfusion techniques developed by Cooley and DeBakey in the 1950's and 1960's expanded the surgical repertoire for the treatment descending aneurysms [31]. With the evolution of surgical techniques has come significant improvement in morbidity and mortality. Thirty years ago, mortality rates for open descending aneurysm replacement were as high as 44% depending on the extent of the surgery [7]. Coselli and colleagues recently published their experience with 3309 TAAA repairs in which they report an operative mortality of 7.5% and 30 day mortality of 7.2%[6]. Isolated descending TAA require replacement of a smaller segment of the aorta and are generally thought to be less risky than TAAA repair. Contemporary reports of 30-day mortality following isolated descending replacement range from 3-12% [32-35].

Complications Associated with Open Repair

Open repair of the descending aorta requires a large thoracotomy incision and single lung ventilation to facilitate surgical exposure. Additionally, renal artery perfusion may be affected by aortic cross clamping and the variable use of distal perfusion techniques. Replacement of the aneurysmal section of the aorta inevitably involves sacrifice of spinal arteries, potentially decreasing spinal cord perfusion causing acute ischemia and reperfusion injury [36]. Therefore, the most common causes of morbidity following open repair are pulmonary complications, acute kidney injury and paraplegia [7].

Paraplegia: The rate of post-operative paraplegia has been declining over time with the increasing use of spinal cord protection strategies. Cerebrospinal fluid (CSF) drainage, moderate

hypothermia, optimization of arterial perfusion pressure and neurochemical protection including steroid and naloxone administration are now considered standard of care in descending operations [36]. These techniques allow for the monitoring and adjustment of spinal cord perfusion pressure, as well as tolerance of ischemia during periods of circulatory arrest and have contributed significantly to improved outcomes [7]. The rates of paraparesis and permanent paraplegia for patients undergoing descending TAA and TAAA repair range from 2 to 5% in contemporary reports [6, 32, 33, 37-39].

Kidney Injury: Renal failure remains a significant concern following both isolated descending and TAAA replacement. Several studies have reported post-operative AKI to be an independent risk factor for mortality [37, 40-42]. Selective renal perfusion and renal cooling are used to mitigate the risk of AKI, however the incidence remains 2-12%[6, 32, 33, 38, 39, 43]. .

Pulmonary Complications: Open descending aneurysm repair involves a left thoracotomy incision and single lung ventilation. Given the extensive incisions and selective ventilation, pulmonary complications are among the most common following these cases. Data from studies involving both TAAA and TAA repairs indicate the incidence of respiratory complications ranges from 20-50%[6, 32, 37, 40, 44, 45]. Approximately 8% of these patients will go on to require a tracheostomy to facilitate ventilator weaning [6, 32, 38]. Respiratory failure was also found to be an independent predictor of mortality [42].

Durability and Mortality Outcomes After Open TAA Repair
Despite the associated perioperative risk of morbidity and mortality, patients surviving the first 30 days postoperatively have excellent long term graft durability. Coselli reports a freedom from repair failure, wherein the reason for repair is specifically related to the implanted graft, of 94% at 15 years [6]. This result is independent of any intervention for degeneration of the aorta proximal or distal to the repair site[6].

Long-term survival following open descending repair has been extensively reported in the literature with estimates at 1, 3, 5, 10 and 15 years of approximately 85%, 80%, 70%, 60% and 20% respectively [6, 32, 38]. 10 year mortality rates in these studies are similar to the age, sex

and race matched population suggesting that deaths were likely unrelated to their aortic disease and further supports the durability of open repair [46].

Evolution of Endovascular Repair of Descending Thoracic Aneurysms

After nearly 40 years of experience with open repair of descending TAA, it was widely recognized that despite advances in patient management and operative techniques, open repair would always carry significant perioperative risk. Following a report of the first successful endovascular exclusion of an abdominal aortic aneurysm in 1991 [47], Dake et al. published their series of 13 patients who had undergone endovascular repair of descending TAA in 1994 [11]. The procedure was successful in all 13 patients, with no patient experiencing death, stroke or paraplegia during the 12 month follow up period [11]. After these encouraging preliminary results, the Gore TAG device became the first commercially manufactured stent graft to undergo feasibility and pivotal trials in the United States in 1998-1999 [48]. The results of the pivotal trial were published in 2005 [49], with subsequent U.S. Food and Drug Administration approval for the use of the Gore TAG device in the treatment of descending TAA.

Early Clinical Trials:

As other devices emerged onto the market, several studies including the VALOR trial [50] and Talent Thoracic Retrospective (TTR) trial [51] were published illustrating a wide experience with endovascular aneurysm repair. The endovascular stents used in this era were primarily Gore TAG or Medtronic Talent, and 30-day mortality ranged from 5 to 19% [50-54]. The incidence of major morbidity was low, with spinal cord injury, stroke and AKI in the 3-6% range [50-54]. While the perioperative mortality and major morbidity rates were not inferior to open surgery at the time, there was significant concern regarding the incidence of post-operative endoleak with implanted stent grafts. Endoleaks have been classified into five different types and typically occur due to an inadequate exclusion of the aneurysm following endograft placement [55]. This allows persistent blood flow into the aneurysm sac and places the patient at continued risk of aneurysm expansion and rupture. Approximately 20-43% of patients had some type of endoleak in the first 30 days after their procedure, with 10-26% requiring repeat intervention for repair [50-54]. Complications related to vascular access were also as high as 27% in the early post-operative period [50, 51, 53, 54]. Given the early experience with endovascular techniques in

these studies, long term survival projections did not extend beyond 5 years and ranged from 53 to 75% [51, 53, 54].

Contemporary Clinical Trials:

Since this early period, advances in device technology have allowed for expanded use of TEVAR. Smaller delivery systems and improved deployment mechanisms have made endografts easier to use and more feasible when faced with challenging anatomy. Despite this, there have been surprisingly few contemporary studies dedicated solely to investigating outcomes in descending TAA. Three small studies have shown that the 30-day mortality following TEVAR for descending TAA has decreased compared to the early experience with rates of 3 to 5% [56-58]. The incidence of stroke, kidney injury and paraplegia remain similar to the initial clinical experience, with rates consistently reported at less than 5% [56-58].

Despite improvement in stent graft design and delivery system optimization, endoleaks and vascular complications continue to be an issue in both the perioperative and extended post operative period. Following surgery, 10 to 20% of patients will have a type I endoleak with up to 39% requiring repeat intervention, and 5% will have issues related to vascular access [57, 58]. Survival at one and two years post operatively ranged from 70 to 100% with a freedom from aortic related events greater than 80% [57, 58]. Ranney et al report a long term survival of just 45.7% at 12 years post operatively illustrating the effect of age and comorbidity burden on this population, however aortic specific survival was 96.2% [56].

Endovascular Repair of Thoracoabdominal Aneurysms

Thoracoabdominal aneurysms pose significant challenges when it comes to endovascular repair, and as such, the evolution of materials and techniques has been slower than for isolated descending pathology.

Given the extent of aorta that TAAA's encompass, finding a suitable landing zone and excluding the aneurysm while maintaining patency of visceral vessels can be difficult [59]. Open repair of the thoracoabdominal aorta is still considered the gold standard however, many patients presenting with TAAA are older adults (>65 years of age) with a significant comorbidity burden and are often not candidates for an open procedure [59]. Two minimally invasive techniques

have been developed to address TAAA pathology in this vulnerable patient population. The first is a hybrid procedure involving open abdominal surgery to "debranch" and bypass the paravisceral vessels, which serves to increase the available landing zone on the paravisceral aorta [59]. Following the bypass, endovascular stent grafts are inserted to complete the repair. Despite initial expectations, the rates of morbidity and mortality following hybrid repair are similar to that of open surgery and the procedure is now infrequently performed [60].

To improve upon the results of hybrid procedures, complex total endovascular techniques using custom fenestrated, multi-branched, parallel or physician modified endografts are now being used for the treatment of TAAA. While total endovascular procedures are less invasive and potentially reduce the incidence of type III endoleaks, the grafts can be difficult to implant which nearly doubles the average procedure time [61] as well as the radiation dose [62]. Additionally, it is impossible to re-implant large intercostal arteries as one normally would during an open procedure and consequently rates of spinal cord injury have been reported as high as 17% [61, 62]. Consistent with the results seen in hybrid procedures, the morbidity and mortality associated with total endovascular repair is still significant despite the minimally invasive approach.

Endovascular Versus Open Repair for Descending Thoracic Aortic Aneurysms
Since the introduction and subsequent Food and Drug Administration (FDA) approval of endovascular stent grafts for the treatment of thoracic aortic disease, there have been many observational studies comparing outcomes of open and endovascular aneurysm repair. Given the speed with which TEVAR technology has developed and the favourable early observational results, a lack of equipoise between the two therapies has developed making randomization unethical [63]. Therefore, no RCTs have been completed to date, resulting in a paucity of high quality literature especially related to long term outcomes [64]. Given the lack of equipoise it is unlikely any randomized trials will be completed in the future, making robust observational studies essential in evaluating the long-term efficacy of TEVAR.

The short term (30 day) outcomes of studies comparing endovascular and open repair have been recently summarized in a systematic review and meta-analysis by Alsawas et al [65]. The

included studies represent a variety of data sources with nine single center studies, two hospital data base studies, three multicenter studies, three Medicare studies and four studies using the National Inpatient Sample (NIS). When the results for 30 day all-cause mortality were pooled, they found that TEVAR reduced the odds of death by 44% (OR, 0.56; 95% CI, 0.4-0.74; $I^2 =$ 69%) [65]. Additionally, endovascular repair significantly reduced the odds of paraplegia/spinal cord injury (OR, 0.35; 95% CI, 0.2-0.61; $I^2 = 0$), pulmonary complications (OR, 0.41; 95% CI, 0.37-0.46; $I^2 = 0$%), ICU and hospital length of stay (pooled mean difference (PMD), -5.89 days; 95% CI -9.65 to -2.12; $I^2 = 65$% and PMD, -5.17 days; 95% CI, -7.77 to -2.57; $I^2 = 91$%) [65]. There was no difference between groups in the odds of stroke at 30 days. The authors conclude that TEVAR results in decreased mortality, morbidity and hospital/ICU length of stay at 30 days when compared to open surgery, however they acknowledge that the quality of evidence is low [65].

Many studies published to date have reported mid-term follow up, with outcome results between 1 and 5 years following the index aortic procedure. Several have noted that on average, TEVAR patients are older and have a higher burden of cardiovascular, respiratory and renal co-morbidities than their open counterparts [66-68]. The survival advantage seen with TEVAR at 30 days disappears during mid-term follow up with all but one study reporting no significant difference between the two groups [63, 66-72]. Two large industry sponsored trials have reported an equivalent survival rate of 60-70% at 5 years however [63, 73] Von Allmen et al. used administrative hospital data and found a survival benefit in patients undergoing open surgery [74]. The Authors suspect this result may have been impacted by the quality of data reporting, and limitation of open repair to centres of excellence, whereas TEVAR is conducted more widely and by a variety of practitioners [75]. There was no difference in the freedom from aneurysm related deaths or freedom from re-intervention beyond one year of follow up despite an increased incidence of major pulmonary, renal, cardiovascular and neurological complications in the open surgery group [63, 67, 75]. The incidence of any endoleak at longest midterm follow up was between 5% and 15% and aneurysm sacs were noted to either remain stable or decrease in size throughout the follow up period [63, 72, 73]. Therefore, despite increased age and comorbidity burden, the mid-term survival of TEVAR patients is not significantly different compared to patients undergoing open surgery. Additionally, the decrease in adverse events seen

during the early post-operative period persist to 5 years of follow up. There is very little data extending beyond 10 years of follow up in this population of patients.

Dissection of the Descending Aorta

Natural History of Aortic Dissection:

Dissection within the descending thoracic aorta can arise either from extension of a Stanford type A dissection past the aortic arch, or as a primary Stanford type B dissection with the entry tear distal to the left subclavian artery. Acute type A dissections are life threatening and require emergency repair. It is estimated that 50% of patients with acute type A dissection will die within 48 hours of symptom onset, a mortality rate of approximately 1% per hour [76]. Surgical repair of acute type A dissections is focused on exclusion of the entry tear in the ascending aorta, and often patients with DeBakey Type I dissections are left with a chronically dissected descending aorta which requires medical management and long term follow up.

Acute type B dissection can be classified as complicated or uncomplicated. A complicated dissection is defined by refractory pain, uncontrolled hypertension, organ malperfusion syndromes, progressive aortic dilatation or rupture and necessitates urgent repair. Medical therapy has been the primary treatment for uncomplicated acute type B dissection, as most patients do well with blood pressure and heart rate control. The risk of mortality with open surgery in this setting is approximately 30% compared to 10% for medical management, therefore the risk of surgery outweighs any procedural benefit [77]. While optimization of medical therapy in uncomplicated type B dissection is successful in many, a proportion of patients will require future intervention on their chronically dissected descending aorta due to progressive aneurysmal dilatation, malperfusion syndromes or rupture.

Open Repair of Descending Aortic Dissections

Open repair of chronic dissection carries perioperative risk of morbidity and mortality similar to that of open descending aneurysm repair. There has been some speculation however that patients undergoing chronic dissection repair represent a more complex population as they have already in some way failed medical management [78]. Additionally, repairing a chronic type B dissection is more technically challenging than repairing an aneurysm. Despite this, the 30-day mortality rates range from 5-10%, and the rate of paraplegia, AKI and respiratory complications

are consistent with what has been reported for descending aneurysm repair [9, 78-80]. The durability of repair is also excellent in this population with 80-95% freedom from re-intervention up to 10 years post operatively [9, 78-80].

Endovascular Repair of Acute Aortic Dissection

Uncomplicated Type B Dissection:

Two randomized trials have been conducted to examine the use of TEVAR and optimal medical therapy (OMT) versus OMT alone, in patients with uncomplicated type B dissection. The ADSORB trial investigated the freedom from a composite of aortic related events (incomplete/no false lumen thrombosis, aortic dilatation and rupture) in acute uncomplicated type B dissection at 1 year and found improvement in the TEVAR group compared to medical therapy alone [81]. While the results are encouraging, the trial was not powered to examine other clinical endpoints, including mortality, and long term data has yet to be published [82]. The INSTEAD trial included patients in the subacute and early chronic period (2 to 52 weeks) following acute type B dissection. After two years of follow up, there was no difference between groups in all cause death, aortic related death and freedom from progressive aortic disease despite improved aortic remodelling in the TEVAR group [83]. In 2013, the 5 year results of the INSTEAD trial (termed "INSTEAD XL") were published. In contrast to the original paper, subacute TEVAR induced better aortic remodelling and decreased aortic specific mortality during the 2 to 5 years of follow up after the procedure [84]. Additionally, patients in the OMT group had an increased crossover to TEVAR after 2 years, usually requiring an emergency procedure which was more likely to result in poor outcomes [84]. While the utility of TEVAR in the acute period is still questionable, the results of the INSTEAD XL trial support endovascular repair of uncomplicated type B dissections during the subacute phase. In clinical practise across centres, there is still conflicting opinions regarding subacute TEVAR however these results have led to a IIa recommendation for consideration of TEVAR in uncomplicated type B dissection by the 2014 European Society of Cardiology Guidelines on the Diagnosis and Treatment of Thoracic Aortic Diseases [85].

Complicated Type B Dissection:

Complicated type B dissection requires urgent surgical repair either by an endovascular or open approach [86]. TEVAR is generally considered to be first line therapy in patients requiring intervention as the risk of in hospital mortality is significantly lower than open surgery [77]. When compared to OMT, mortality rates are decreased at 5 years of follow up in International Registry of Aortic Dissection (IRAD) for patients undergoing TEVAR [87].

Endovascular Repair of Chronic Aortic Dissection
Chronic type B dissection is complicated by progressive intimal flap thickening and multiple entry tears which result in persistent false lumen flow [12, 88]. Residual false lumen flow contributes to false lumen expansion and continuing aortic dilatation, which has been shown to negatively impact patient outcomes [89]. Intimal flap thickening can make deployment of endovascular stent grafts challenging, and multiple entry tears may mean a large segment of aorta must be covered to try and prevent persistent false lumen flow. Consequently, endovascular repair of chronic type B dissection is only recommended if the aorta is greater than 60 mm in diameter, there is growth greater than 10 mm per year, uncontrolled hypertension, malperfusion, persistent pain or signs of impending rupture [85]. There is a paucity of literature regarding the efficacy of TEVAR for chronic dissection, especially at long term follow up. A recent study by Conway et al using the Vascular Quality Index (VQI) registry reported technical success in 96.8% of patients with acceptable perioperative mortality rate of 2.4%, consistent with other small contemporary studies [90-92]. In hospital re-intervention was required in 10.4% of patients and the incidence of perioperative paraplegia was 2.4% [90]. Perhaps one of the most feared complications following TEVAR of chronic type b dissection is retrograde dissection into the ascending aorta. This occurred in 1.6% of patients and is thought to be associated with damage of the fragile aorta from proximal bare metal stents, metal barbs or balloon dilatation [90]. Positive aortic remodelling following TEVAR of chronic type B dissection has been reported with a decrease in false lumen diameter and an increase in true lumen diameter in 79% and 66% of patients respectively [88]. A decrease in false lumen diameter was found in 79.4% of patients, and true lumen diameter was increased in 66.1%. Despite promising short term results, the use of TEVAR for repair of chronic type b dissection is still controversial and long term data is required to inform clinical decision making.

Endovascular Versus Open Repair for Descending Aortic Dissection

Several studies have been done comparing the outcomes of TEVAR and open repair for complicated acute type B dissection. The in-hospital/ 30-day mortality for TEVAR patients ranged from 4 to 11%, which was significantly lower than patients undergoing open repair [93-96]. Results for postoperative morbidity were variable, however generally TEVAR patients had shorter ICU and hospital length of stay, fewer respiratory complications, less bleeding and decreased incidence of AKI [93, 95] [97]. Similar to the results for aneurysm repair, the rate of late mortality, and freedom from re-intervention was not significantly different between groups [93, 94, 98] [99]. Approximate survival projections at 1, 3 and 5 years following endovascular or open procedure are 90%, 80% and 60-70% respectively [93, 94, 96]. Given the superior perioperative outcomes found in TEVAR patients, endovascular repair is now a class I indication in patients presenting with acute complicated type B dissection [85].

There are few studies that have directly compared open and endovascular therapy for chronic type B dissection repair, as most of the literature examines outcomes of each modality separately. In a recent report by van Bogerijen et al encompassing twenty years of treatment experience, there was no difference in the rate of early mortality, spinal cord injury, AKI or respiratory complications between the two groups [100]. Similarly, Nozdrzykowski et al found no difference in mortality and morbidity between medically treated, endovascular and open surgical cohorts for in hospital, 1 and 3 year follow up [101]. In both studies however, patients undergoing TEVAR had a higher rate of late re-intervention. Van Bogerijen et al found the treatment efficacy of open repair at three years to be significantly higher than TEVAR (96.7% vs 87.5%, p = 0.026) and TEVAR was an independent predictor of treatment failure [100]. In the Nozdrzykowski study, 28.9% of patients required re-intervention following TEVAR compared to none in the open surgery group [101]. The authors have postulated that the increased incidence of delayed complications in this population may be due to the thicker chronic dissection intimal flap that prevents optimal true lumen expansion and subsequent aortic remodelling, while variable perfusion of residual flap fenestrations contributes to ongoing perfusion of the false lumen and aneurysm expansion [100]. Subsequently, the role of endovascular therapy in the treatment of chronic type b dissection remains controversial. While periprocedural results are not

inferior to open, TEVAR patients are at higher risk of late complications and require close monitoring for signs of progressive disease.

Examining a Patient Centered Outcome - Functional Survival

Over the last decade, perioperative morbidity and mortality have improved as operative techniques have been refined and technology advanced. With this has come an increased focus on patient centered outcomes including not only long-term survival but also health related quality of life (HRQoL). A recent systematic review illustrated that despite several studies examining HRQoL in patients undergoing surgery on the aortic root and ascending aorta, there are relatively few reports in those undergoing descending aortic procedures [102]. Only one study has directly compared HRQoL between TEVAR and open surgery patients for descending aortic pathology and they found no significant difference, although the follow up period was short and the patient population was small [70]. The importance of disposition at the time of hospital discharge has been highlighted in three other studies that found patients undergoing TEVAR were more likely to be discharged home (i.e. have a "routine" discharge), whereas patients were more frequently discharged to alternative care facilities following open surgery [103-105].

In 2015, Manji et al published the first report describing "*functional survival*" in cardiac surgery patients following prolonged ICU length of stay (prICULOS) [14]. Functional survival refers to patients who are alive and not institutionalized and represents a key metric in determining the quality of survival following cardiac surgery [14]. Following the 2016 study, 4 additional papers have utilized functional survival as an outcome, examining its role in not only prICULOS patients, but also with frailty and octogenarians undergoing aortic valve replacement (AVR) [106-109].

In the original ICU based study, despite increasing age and co-morbidities in the prICULOS group, they found the 1 and 5 year functional survival to be 73.9% and 53.8% respectively, which was similar to the crude survival of all patients in the cardiac surgery cohort (prICULOS and non-prolonged ICULOS) [14]. In a subsequent study examining functional survival in the octogenarians of the prICULOS group, 1 and 5 year outcomes were again reasonable at 81% and

57% however these rates were lower than what was found in the non-prICULOS (91.7% and 70.1%) [106]. Authors of both studies concluded that knowledge of functional survival as an outcome plays an important role in informed consent discussions and surgical decision making for patients and their families [14, 106].

A third report was published this year in the same cohort of cardiac surgery patients examining the effect of early re-hospitalization on functional survival. They found that the mortality rate for patients who were re-hospitalized following prICULOS was higher than for the non-prICULOS (15.6% vs 7.6%), and re-hospitalization within 30 days of the index procedure was an independent predictor of poor functional survival 1 year post operatively (OR, 2.29; p <0.001) [107]. Despite this discouraging result, the authors also identified several modifiable patient risk factors (access to physicians, mental health issues and social service availability) which could potentially be targeted to decrease the frequency of re-hospitalization in this patient group [107].

When functional survival was examined in the context of octogenarians undergoing AVR, results were similar to survival in age and sex matched controls at 1 and 5 years despite higher incidence of perioperative morbidity and mortality than the younger cohort [108]. This emphasized that appropriately selected octogenarians can indeed under major cardiac surgery with acceptable long term outcomes.

Finally, Lytwyn et al modified the original definition of functional survival to include patients who were alive and had a score greater than 60 on the EuroQol – Visual Analogue Scale, a widely used measure of health related quality of life [109]. They found that the addition of a validated frailty score to the Euro II risk prediction model improved the prognostic value for functional survival in frail patients [109]. Any diagnosis of preoperative frailty also led to a 2 to 3.5 times increased risk of poor functional survival at 1 year following cardiac surgery [109].

Clinical Importance of this Study
The epidemiology of thoracic aortic disease has yet to be described for the Manitoba population. The MTAD Clinic is the only centre in the province that manages patients with diagnosed thoracic aortic disease. Understanding the incidence and prevalence, as well as changing trends

over time is important in determining optimal resource utilization strategies especially given the current era of heightened fiscal responsibility.

Functional survival has become a useful tool in evaluating the quality of survival following cardiac surgery in a variety of settings, however it has yet to be used in patients undergoing thoracic aortic surgery. Open surgery on the thoracic aorta is almost always classified as a complex procedure, involving long CPB times and unique adjuncts such as deep hypothermic circulatory arrest, partial CPB, left heart bypass, single lung ventilation and extensive incisions. Intuitively, one would think that functional survival following open surgery would be worse given the invasiveness of the procedure, especially compared to endovascular repair. However, in the current era open surgery patients tend to be younger and healthier, with endovascular repair used more frequently in those who would not be candidates for open repair due to age or significant comorbidity burden. Thus, the impact of functional survival on open surgery compared to endovascular repair of the descending thoracic aorta remains to be seen.

The goals of this study were two-fold: First we sought to determine the incidence and prevalence of diagnosed degenerative thoracic aortic disease and characterize the distribution of patients in Manitoba, and second we planned to compare the long term functional survival in patients with descending thoracic aortic disease treated with either an endovascular or open surgical approach.

Materials and Methods

Study Design

We conducted a retrospective cohort study using linked administrative data to characterize the epidemiology of TAD in Manitoba, examine the long term functional survival of patients undergoing endovascular repair of the descending thoracic aorta and compare to those who have open surgical repair.

Data Sources

Data for the entire population of Manitoba was obtained using selected databases at the MCHP. Information regarding patients undergoing TEVAR and open thoracic aortic surgery was collected using the MTAD database which had been linked to selected databases at the MCHP. Data housed at MCHP has been de-identified and linked using a scrambled personal health information number (PHIN) to ensure patient privacy.

The following data sources were used, with a detailed description of each found in Appendix 1:

1. Manitoba Cardiac Surgical Database (MaCS)
2. Drug Program Information Network (DPIN)
3. Emergency Department Information System (EDIS)
4. Home Care Utilization (MH MSSP)
5. Hospital Abstracts
6. Long Term Care Utilization
7. Medical Claims / Medical Services
8. Manitoba Health Insurance Registry
9. Employment/ Income Assistance (SAMIN)
10. Vital Statistics Mortality

Epidemiology of Degenerative Thoracic Aortic Disease

Case Identification

All adult patients (older than 18 years) who were residents of Manitoba from 1994 (the earliest available MCHP data) to December 31, 2016 were included in this portion of the study. Any patient who had diagnosis of descending aortic aneurysm or dissection in the MTAD database was considered a case. Hospital abstracts were queried for degenerative thoracic aortic pathology using four digit ICD-9 and ICD-10 codes and patients were considered a case if there were one or more relevant diagnoses (Appendix 2).

For patients with an outpatient diagnosis only, the three digit ICD-9 code '441' in the Medical Services database was used to identify anyone with "Aortic Disease". This included both thoracic and abdominal diagnoses. Due to the nature of the three digit ICD-9 code, alternative methods were required to exclude patients with isolated abdominal pathology from our outpatient cohort. Using the Medical Services claims for CT scans of the chest, any patient with

a diagnosis of '441' and subsequent chest CT within 1 year of the diagnosis was retained. The accuracy of this criteria was verified by examining both the inclusion of patients with known thoracic diagnoses from the MTAD database, as well as the number of patients with confirmed abdominal aortic aneurysms (AAA) who underwent thorax or cardiac CT scans in the hospital abstracts. Medical Services claims were then used to identify patients where the diagnosis of '441' was assigned by a vascular surgeon only, and these were subsequently excluded. Any patients with a diagnosis by a cardiac surgeon alone or in conjunction with a vascular surgeon, or another specialty besides Cardiac or Vascular Surgery were retained. Following this, any patients with a confirmed abdominal diagnosis but no concomitant thoracic diagnosis in the hospital abstracts were excluded. Additionally, any patients who were from out of province, had diagnoses of aortic coarctation or aortic trauma were also excluded.

The final study cohort was determined by combining diagnoses from the MTAD database, hospital abstracts and medical services claims, accounting for overlap between data sources. A diagram outlining the process for case identification is found in Figure 1.

Figure 1. Case identification flow diagram
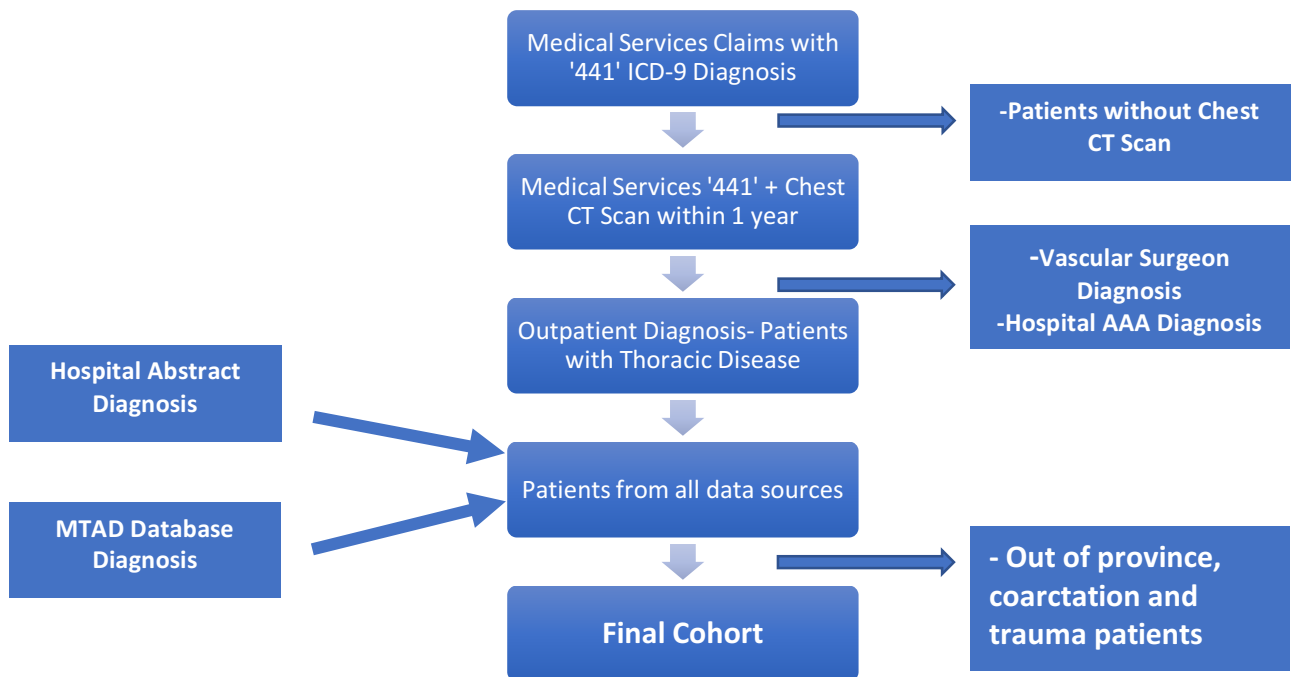
ICD, Incernational Classification of Diseases; CT, Computed Tomography; AAA, Abdominal Aortic Aneurysm; MTAD, Manitoba Thoracic Aortic Diseases

Baseline Characteristics

General patient characteristics including age and sex were determined using non-missing values from the Manitoba Health Insurance Registry. The number of patients diagnosed with hypertension, dyslipidemia and variables within the Charlson Comorbidity Index was determined for the entire study period from 1994 to 2016. Patients were considered to have the comorbidity in question if it was identified using ICD-9/10 codes, tariffs and anatomical therapeutic classification (ATC) codes in at least one of the following data sources: Drug Program Information Network database, Hospital Abstracts and Medical Services Claims (Table 1, Appendix 3, Table 2).

Table 1. Components of the Charlson Comorbidity Index

Myocardial Infarction	Diabetes Without Complications
Congestive Heart Failure	Diabetes With Complications
Peripheral Vascular Disease	Paraplegia and Hemiplegia
Dementia	Renal Disease
Chronic Pulmonary Disease	Cancer
Connective Tissue/Rheumatic Disease	Metastatic Carcinoma
Peptic Ulcer Disease	HIV/AIDS
Mild Liver Disease	Sum of Charlson Comorbidity Groups
Moderate or Severe Liver Disease	Weighted Sum of Charlson Comorbidity Groups

Table 2. Anatomical Therapeutic Classification Codes for Antihypertensives and Lipid-Lowering Medication

Comorbidity	Drug Type	ATC Code
Hypertension	Antiadrenergic agents centrally acting, Antiadrenergic agents ganglion-blocking, Antiadrenergic agents peripherally acting, arteriolar smooth muscle agents, other antihypertensives, antihypertensives and diuretics in combination, combinations of antihypertensives in ATC-GR.C02	C02
Hypertension	Low-ceiling diuretics thiazides, Low-ceiling diuretics excluding thiazides, High-ceiling diuretics, Potassium-sparing agents, Diuretics and potassium-sparing agents in combination, Other diuretics	C03
Hypertension	Beta blocking agents, Beta blocking agents and thiazides, Beta blocking agents and other diuretics, Beta blocking agents/thiazides and other diuretics, Beta blocking agents and vasodilators, Beta blocking agents other combinations	C07
Hypertension	Selective calcium channel blockers with vascular effects, Selective calcium channel blockers with direct cardiac effects, Non-selective calcium channel blockers, Calcium channel blockers and diuretics	C08
Hypertension	ACE Inhibitors plain, ACE inhibitors combinations, Angiotensin II Antagonists plain, Angiotensin II antagonists combinations, Other agents acting on the renin-angiotensin system	C09
Dyslipidemia	Lipid modifying agents plain, Lipid modifying agents combinations	C10

ATC, Anatomical Therapeutic Classification.

Incidence and Prevalence of Degenerative Thoracic Aortic Disease

For each patient in the final epidemiology cohort, the date of first diagnosis with any TAD was considered the earliest chest CT scan, hospital abstract or medical services claim. The year of first diagnosis was counted as the incident year from 1994 to 2016 inclusive. Data on mortality was obtained using the Vital Statistics Mortality registry and location of residence was determined using six digit postal codes found in the Manitoba Health Insurance Registry. Annual population figures were obtained from the MCHP mid-year population estimates.

A 'washout period' from 1994 to 1997 was used to compute the baseline prevalence of TAD (patients alive and living in Manitoba) as of January 1, 1998. Yearly prevalence was then calculated for patients with previous incident diagnoses who remained alive and living in Manitoba until December 31, 2016. To account for known sex and age related differences in the occurrence of thoracic aortic aneurysms, incidence and prevalence for each year was age

standardized and stratified by sex per 100 000 population. Six digit postal codes were used for stratification by region of residence based on the current regional health structure in Manitoba: Interlake Eastern Regional Health Authority (RHA), Northern-Health Region, Prairie Mountain Health, Southern Health-Sante Sud., and Winnipeg RHA. To examine geographical variation in TAD, the annual incidence and prevalence was mapped by RHA. RHA boundaries and the location of health care facilities was provided by the Medical Transportation Coordination Center in Brandon, Manitoba. A color-coded scale was used to illustrate the total age standardized incidence and prevalence in each region per year with blue representing smaller numbers and red larger. Dark grey dots denote the presence of a health care facility (hospital, nursing station or other regional health care site), and those highlighted with a yellow circle indicate the presence of a CT scanner. The Winnipeg region is magnified to allow for improved visualization. All maps were generated using ArcGIS® software by Esri. The ArcGIS Online World Topo Map was used as a basemap (Sources: Esri, DeLorme, HERE, TomTom, Intermap, increment P Corp., GEBCO, USGS, FAO, NPS, NRCAN, GeoBase, IGN, Kadaster NL, Ordnance Survey, Esri Japan, METI, Esri China (Hong Kong), swisstopo, MapmyIndia, and the GIS User Community). ArcGIS® and ArcMap™ are the intellectual property of Esri and are used herein under license. Copyright © Esri. All rights reserved. For more information about Esri® software, please visit www.esri.com.

The age specific incidence and prevalence per 100 000 was also determined and compared to trends in the general Manitoba population using pyramids constructed from the mid-year population estimates for 1998 and 2016. The average annual incidence and prevalence stratified by age and sex was determined using a Poisson distribution with 95% confidence limits.

To further explore trends in age specific incidence, the total number of yearly chest and cardiac CT scans were examined from 1998 to 2016 using medical services claims.

The incidence and prevalence of thoracic aortic aneurysm, aortic dissection and thoracic aortic could only be investigated using hospital abstracts, which capture the more specific four digit ICD-9/ICD-10 code (Appendix 2). Thoracic aortic rupture was examined primarily using ICD-9/10 codes within the hospital abstracts, however many patients with rupture die prior to

reaching hospital. ICD9/10 codes for the primary cause of death were queried for a diagnosis of aortic rupture in Vital Statistics registry to provide any additional cases. Patients were classified as aneurysm, dissection or rupture based on the earliest ICD code specific for either disease. A washout period from 1994 to1997 was used to determine the baseline prevalence of patients with for all three pathologies as of January 1, 1998. The age standardized incidence and prevalence of TAA, aortic dissection and aneurysm rupture in hospitalized patients was then calculated in a similar manner to that of the entire cohort mentioned above.

Long Term Functional Survival in Endovascular versus Open Descending Aortic Repair
Population
To examine functional survival, we identified all patients over the age of 18 who underwent a TEVAR or open surgical procedure for descending aortic pathology in Manitoba from January 1, 2005 to December 31, 2016 using diagnostic information provided in the MTAD database. Any patients who had a TEVAR procedure during this time but had a previous index open surgical repair prior to January 1, 2005 were also included. Any patients who were not residents of Manitoba at the time of their procedure, who had incomplete data, or underwent surgery for coarctation, traumatic aortic injury or total arch repair were excluded. Individuals were considered a "TEVAR patient" if their first aortic procedure was a TEVAR, irrespective of the type of subsequent procedure. "Open patients" were those whose first descending aortic procedure was done via open surgery, irrespective of the type of subsequent procedure. Patients who underwent an open type A dissection repair of the ascending aorta and subsequently had a TEVAR of their residual type B dissection were classified as a TEVAR patient, as this represents the first procedure on the descending aorta.

Baseline Characteristics
General patient characteristics such as age and sex were determined using the Manitoba Health Registry data with missing values supplemented using the MTAD database. Height, weight and body surface area (BSA) were obtained from the MTAD database and missing values were calculated using multiple imputation procedures.

Comorbidities were assessed up to three years prior to the index procedure date. Relevant ICD-9/ICD-10 codes from the hospital abstracts and medical services claims was collated using the Charlson Comorbidity Index (CCI) (Table 1). Additional conditions relevant to aortic disease were also examined. Patients were considered to have hypertension or dyslipidemia if at least one relevant ICD-9/ICD-10 code, tariff code or drug ATC code was found in the hospital abstracts and medical services claims (Table 2). Smoking history (current smoker or ever smoked) and a history of previous cardiac surgery was obtained from the MTAD database.

The MTAD database was used to determine the type of aortic pathology diagnosed in each patient. This included both acute and chronic type B dissection, thoracic aortic aneurysm, thoracoabdominal aneurysm, penetrating atherosclerotic ulcer (PAU), intramural hematoma (IMH), acute aortic syndrome (including any dissection, PAU or IMH) and rupture. The aorta was divided using the eleven landing zones for aortic interventions [110] to calculate the number of segments covered or replaced.

Evaluation of socioeconomic status was completed using three different surrogate measures. Region of residence was determined using six digit postal codes found in the Health Insurance Registry. Patients were classified based on the eleven region structure implemented in 2002 by Manitoba Health with Winnipeg and Brandon considered 'urban' and all other areas considered 'rural'.

To calculate income quintiles, urban and rural residence population categories were broken down into five quintiles containing roughly 20% of the population [111]. The quintiles were then ordered from lowest to highest with the first and second quintiles in each category considered 'low income', and quintiles 4, 5 and 6 considered 'high income'.
Pre-operative and post-operative employment and income assistance (EIA) was examined using the Social Assistance Management Information Network (SAMIN).

Outcomes
To assess our primary and secondary outcomes, patient data was examined from the date of the index procedure to December 2017.

Primary Outcome: Functional survival was determined using information regarding mortality from the Vital Statistics registry, and institutionalization from the Long Term Care Utilization database. Any long term care admission either at the time of discharge from hospital or in the period following discharge home was considered along with mortality rates to provide an estimate of functional survival (alive and not institutionalized) post operatively.

Secondary Outcomes: The incidence of post-operative major adverse events (death, myocardial infarction, stroke, kidney failure, paralysis, repeat intervention), hospital and ICU length of stay, and 30 day in hospital mortality was assessed using hospital abstracts, the MaCS database and the MTAD database. The incidence of repeat hospitalization in the first year following the index procedure will be determined for each cohort along with the primary reason for readmission using hospital abstracts. Hospital abstracts were also used to determine the discharge disposition, i.e. whether patients were discharged home without support or required additional inpatient, rehabilitation, personal care home or home care services.

Statistical Analysis

All patient cohorts were examined using descriptive statistics. Continuous variables were tested for normality using the Kolmogorov-Smirnov test and are reported as a mean with standard deviation or median with interquartile range (IQR) where appropriate. Categorical variables are reported as a frequency with percentage. Continuous variables were compared using a t test or a Mann Whitney U test if medians are reported. Categorical variables were compared using the Chi-Square test, or the Fisher's Exact test if the sample sizes are small. A p value less than or equal to 0.05 was considered statistically significant. Outcomes with five or fewer individuals or events were suppressed in accordance with the MCHP guidelines for small data values.

To adjust for confounding, a logistic regression model incorporating the following baseline characteristics: age, gender, height, weight, body surface area, hypertension, dyslipidemia, smoking, history of prior cardiac surgery, weighted Charlson comorbidity score and pathology: aneurysm, acute and chronic type B dissection, rupture, PAU and IMH. Propensity scores were generated for each patient based on the probability of undergoing an open surgical repair. Propensity score overlap assessment was done using a kernel density plot and patients with

scores in top and bottom 5% of the distribution were trimmed. The propensity scores were then used to create a weight for each patient through inverse probability of treatment weighting (IPTW).

Weight in the treatment (open surgery) condition = $1 / P (Z=1 \mid X)$

Weight in the control (TEVAR) condition = $1 / (1 - P (Z = 1 \mid X))$

To control for large IPTW values, stabilized weights were calculated:

Stabilized weight in the treatment condition = $P (Z=1) / P (Z=1 \mid X)$

Stabilized weight in the control condition = $1 - P (Z=1) / (1 - P (Z=1 \mid X))$

A balance assessment using weighted standardized differences was conducted for all covariates in the model. Covariates with weighted standardized differences less than or equal to 0.2 were included in the model. Any continuous covariates with weighted differences greater than 0.2 were transformed using the square function, and the propensity scores were re-calculated to see if the differences then met the inclusion criteria. Categorical covariates with weighted standardized differences greater than 0.2 were assessed for clinical relevance, and were either used as a stratification variable or excluded from the model if stratification was not possible.

Following identification of the appropriate propensity score model, a weighted time to event analysis was done for functional survival (a composite of death and institutionalization) using a Cox proportional hazards model. The proportional hazards assumption was assessed using Schoenfeld residuals. Results have been reported as hazard ratios with 95% confidence intervals (CI). A follow up analysis was done to examine the effect of era on functional survival. Eras were determined based on temporal trends in TEVAR use at our institution. Patients who had procedures prior to 2012 were considered part of the 'early era', while patients who had procedures from 2012 to the end of 2016 were classified as 'late era'.

All data management, programming and analysis was performed using SAS® version 9.4.

Ethics

Approval for this project was granted by the University of Manitoba Health Research Ethics Board (Ethics # HS 19617 (H2016:134)), the St. Boniface Hospital Research Review Committee (RRC Reference Number RRC/2016/1585) and the Health Sciences Center Department of Research (RIC #RI2017:092).

Approval for data access was granted by the MCHP and the Manitoba Health Information Privacy Committee (HIPC) (HIPC No. 2016/2017-01), Diagnostic Services of Manitoba (DSM), Department of Families (FAMLSP16-00111), Vital Statistics Agency and the Winnipeg Regional Health Authority (WRHA) Research Access and Approval Committee.

Results

Epidemiology of Degenerative Thoracic Aortic Disease

Case Identification

Using our case identification method 4264 patients were diagnosed with degenerative thoracic aortic disease from 1998 to 2016 in Manitoba (Figure 2). Notably, all patients from the MTAD database (ie. those with confirmed diagnosis of TAD) were captured when the medical services data was restricted using chest CT scans, indicating our method was not overly exclusive. When the hospital abstracts were queried, only 16% of patients with a known diagnosis of AAA had a chest CT scan within 12 months which indicates we aren't being over-inclusive.

Figure 2. Patient flow using case identification method
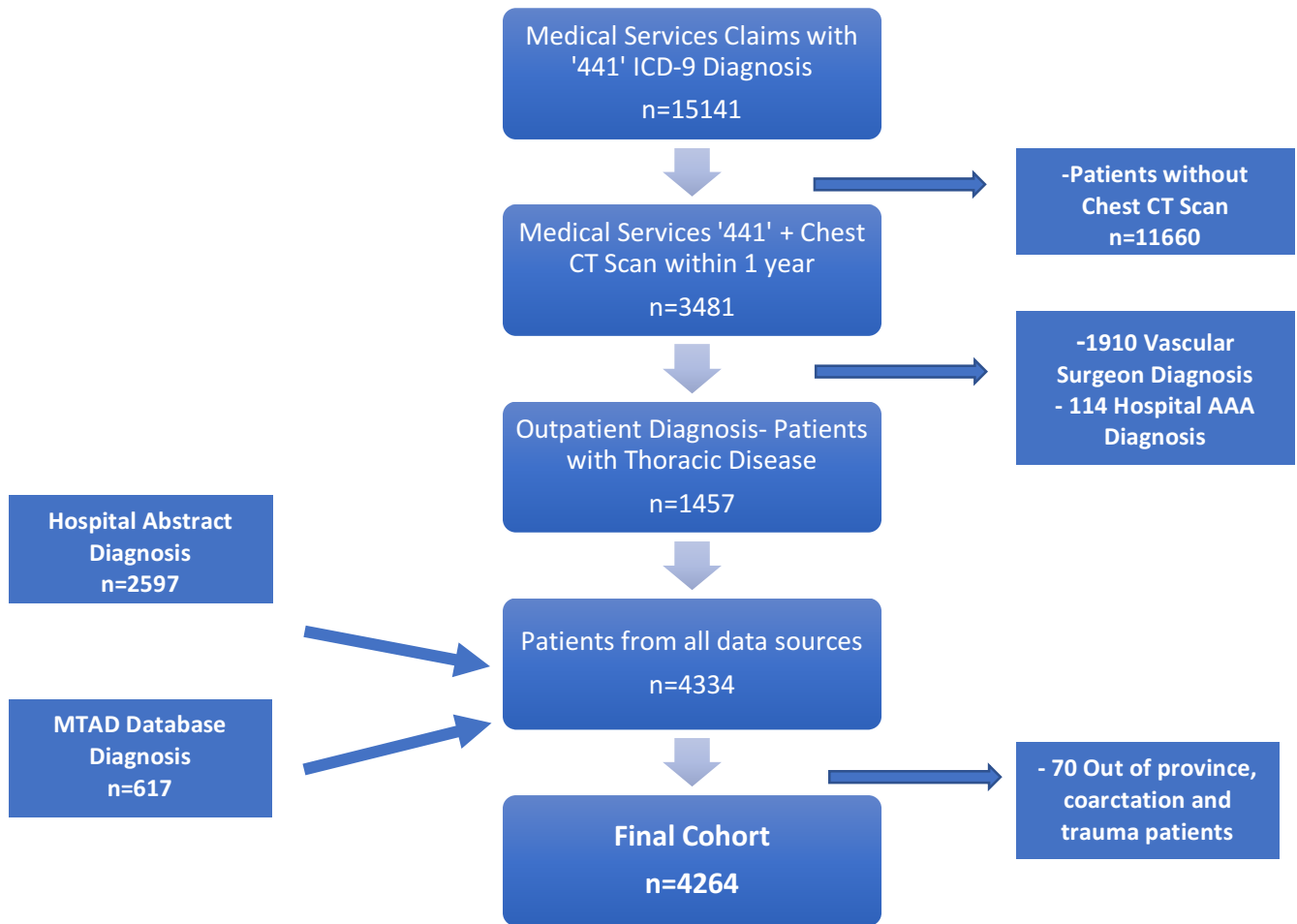

```
┌─────────────────────────────┐
│ Medical Services Claims with│
│   '441' ICD-9 Diagnosis     │
│         n=15141             │
└─────────────────────────────┘
              │                          ┌──────────────────────┐
              │──────────────────────────▶│ -Patients without    │
              ▼                          │  Chest CT Scan        │
┌─────────────────────────────┐          │  n=11660             │
│ Medical Services '441' + Chest│         └──────────────────────┘
│  CT Scan within 1 year      │
│         n=3481              │           ┌──────────────────────┐
└─────────────────────────────┘          │ -1910 Vascular       │
              │──────────────────────────▶│  Surgeon Diagnosis   │
              ▼                          │ - 114 Hospital AAA   │
┌─────────────────────────────┐          │  Diagnosis           │
│ Outpatient Diagnosis- Patients│         └──────────────────────┘
│  with Thoracic Disease      │
│         n=1457             │
└─────────────────────────────┘

┌──────────────────────┐
│ Hospital Abstract    │
│    Diagnosis         │
│    n=2597           │
└──────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ Patients from all data sources│
│         n=4334             │
└─────────────────────────────┘
┌──────────────────────┐
│ MTAD Database        │
│    Diagnosis         │
│    n=617            │
└──────────────────────┘
              │                          ┌──────────────────────┐
              ▼                          │ - 70 Out of province,│
┌─────────────────────────────┐──────────▶│  coarctation and     │
│        Final Cohort         │          │  trauma patients     │
│         n=4264             │          └──────────────────────┘
└─────────────────────────────┘
```

ICD, Incernational Classification of Diseases; CT, Computed Tomography; AAA, Abdominal Aortic Aneurysm; MTAD, Manitoba Thoracic Aortic Diseases

Baseline Characteristics

The median age was 70 and 63% of patients were male. Most patients had a diagnosis of hypertension or dyslipidemia (88% and 72%), and a 26% had a history of myocardial infarction. Congestive heart failure was present in nearly half of patients and 30% had diabetes without complications. Diabetes with complications was less frequent with only 12% of patients identified. The median weighted sum of CCI (CCI score) was 5 (IQR 3, 8) (Table 3).

Table 3. Baseline Characteristics of All Patients With Degenerative Thoracic Aortic Disease in Manitoba.

	Summary Measure n=4264
Age (n=4261)*	70 (60, 78)
Sex, male (n= 4260)	2703 (63.45%)
Hypertension	3770 (88.41%)
Dyslipidemia	3066 (71.9%)
Charlson Comorbidity Index:	
Myocardial Infarction	1105 (25.91%)
Congestive Heart Failure	1905 (44.68%)
Peripheral Vascular Disease	-
Cerebrovascular Disease	1657 (38.86%)
Dementia	702 (16.46%)
Pulmonary Disease	2792 (65.48%)
Connective Tissue Disease	496 (11.63%)
Peptic Ulcer Disease	756 (17.73%)
Mild Liver Disease	361 (8.47%)
Moderate to Severe Liver Disease	108 (2.53%)
Diabetes – No Complications	1284 (30.11%)
Diabetes- Complications	495 (11.61%)
Paraplegia or Hemiplegia	320 (7.5%)
Renal Disease	813 (19.07%)
Cancer	1666 (39.07%)
Metastatic Cancer	387 (9.08%)
HIV/AIDS	7 (0.16%)
Sum of Charlson Scores*	4 (3, 6)
Weighted Sum of Charlson Scores*	5 (3, 8)

* indicates median (IQR); - indicates value was suppressed; HIV, Human Immuno-deficiency Virus; AIDS, Acquired Immune Deficiency Syndrome

Incidence of Degenerative Thoracic Aortic Disease

The overall age standardized incidence of degenerative TAD in Manitoba has increased by 45% over 19 years to 24.4 cases per 100 000 population (Figure 3). When stratified by gender the annual age standardized incidence was consistently two times higher in males, peaking at 42 cases per 100 000 in 2013. The lowest incidence in men was seen between 2001 and 2003, where cases hovered around 19 per 100 000. From 2014 to 2016, incidence has been relatively stable

with between 31 and 24 per 100 000 new male cases. Females have seen a gradual increase over time with fewer drastic fluctuations than in men. Peak age standardized incidence was 18.2 per 100 000 in 2007, with relative stability since then around approximately 16 per 100 000. Although their overall incidence rate was lower, women had a greater rate of increase in incident cases from 1998 to 2016, growing 68% compared to 27% in men.

Figure 3. Age Standardized Incidence of Degenerative Thoracic Aortic Disease per 100 000 Population in Manitoba
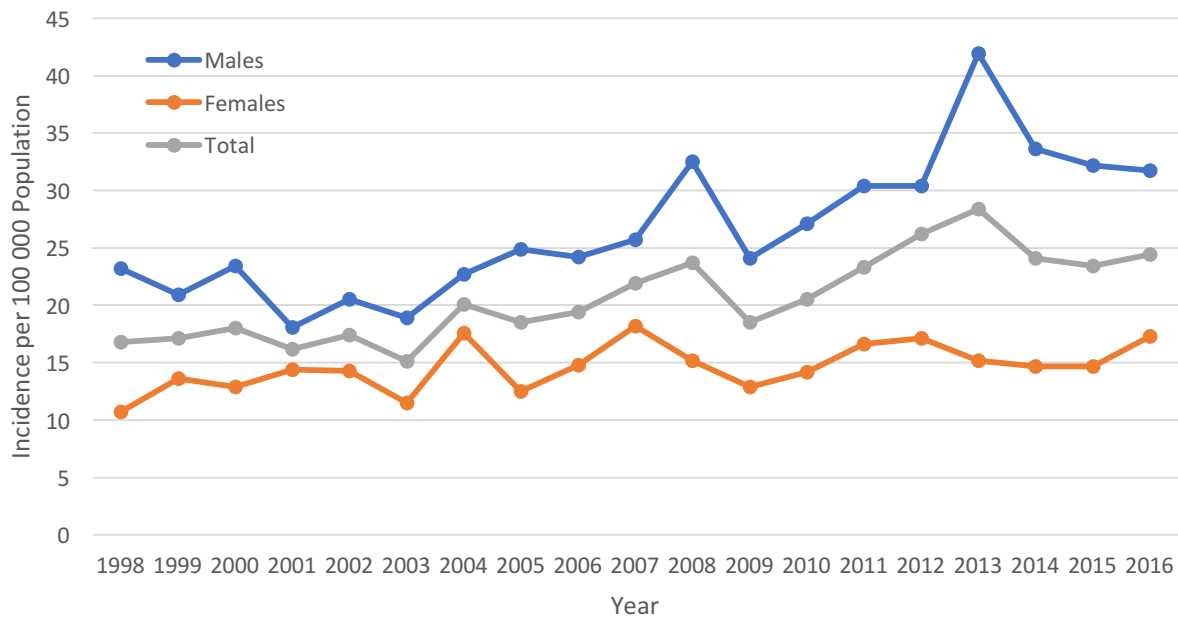
To facilitate comparisons with age standardized incidence, the total number of yearly chest and cardiac CT scans was examined. As expected, the number of scans has increased exponentially over the study period, with 5702 scans were done in 1998 compared to 37165 in 2016. Cardiac CT scans became available in 2008, and while the number of these scans is also increasing they still represent a very small portion of the total number of scans done per year (0.9% in 2016) (Figure 4).

Figure 4. Total Number of Thorax and Cardiac CT Scans Per Year, 1998 to 2016
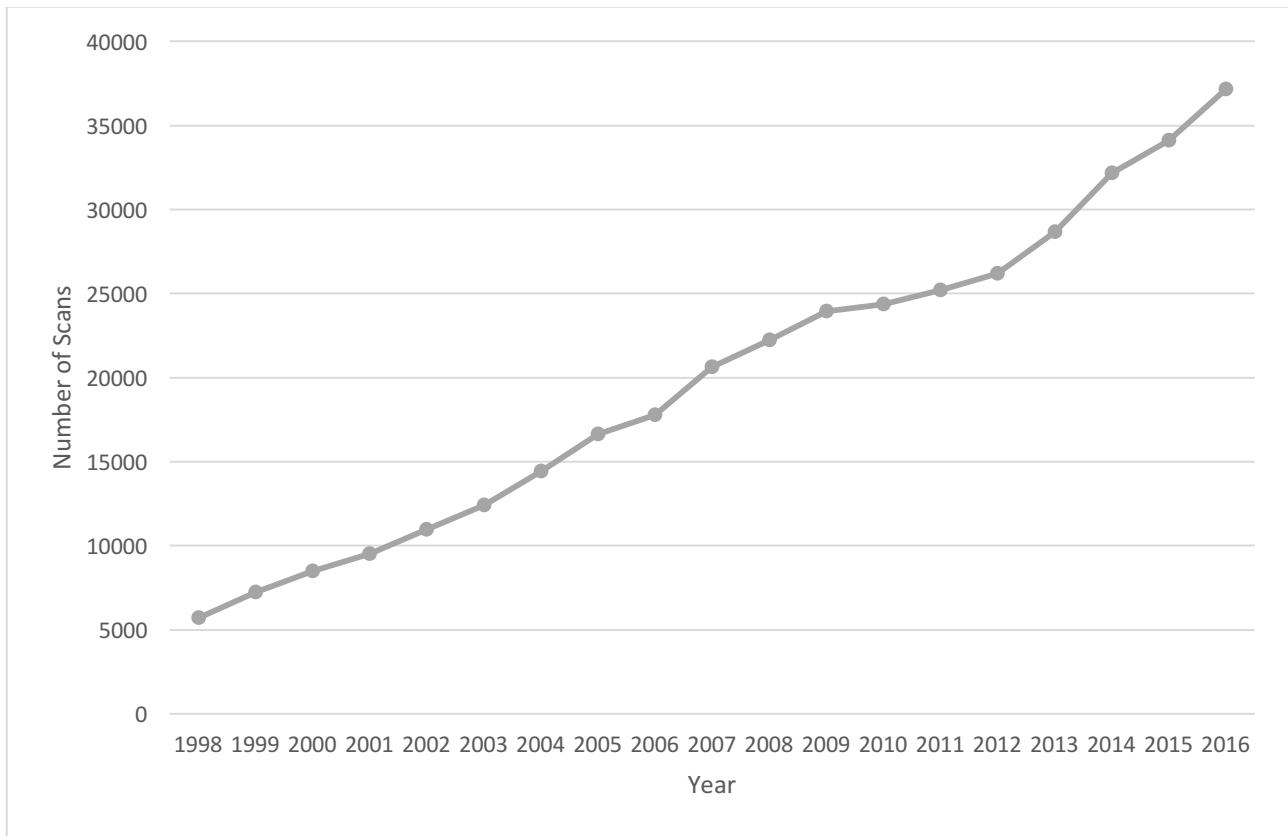
The age specific incidence per 100 000 was highest in the 70 to 79 age category until 2014 (Figure 5). Between 2014 and 2016, incidence has been highest in the 60 to 69 age category. Annual population pyramids for Manitoba in 1998 and 2016 were constructed for comparative purposes to see if the changing trends in incidence by age were reflective of trends within the whole population. In 1998, the baby boomer generation is evident in the 30-55 age range while in 2016, this has moved up to ages 50 to 70. The number of people older than 75 has decreased since 1998 from 5% to 2.7% of the population in males and 8.1% to 7.7% of the population in females (Figure 6)

Figure 5. Age Specific Incidence per 100 000 Population, 1998 to 2016
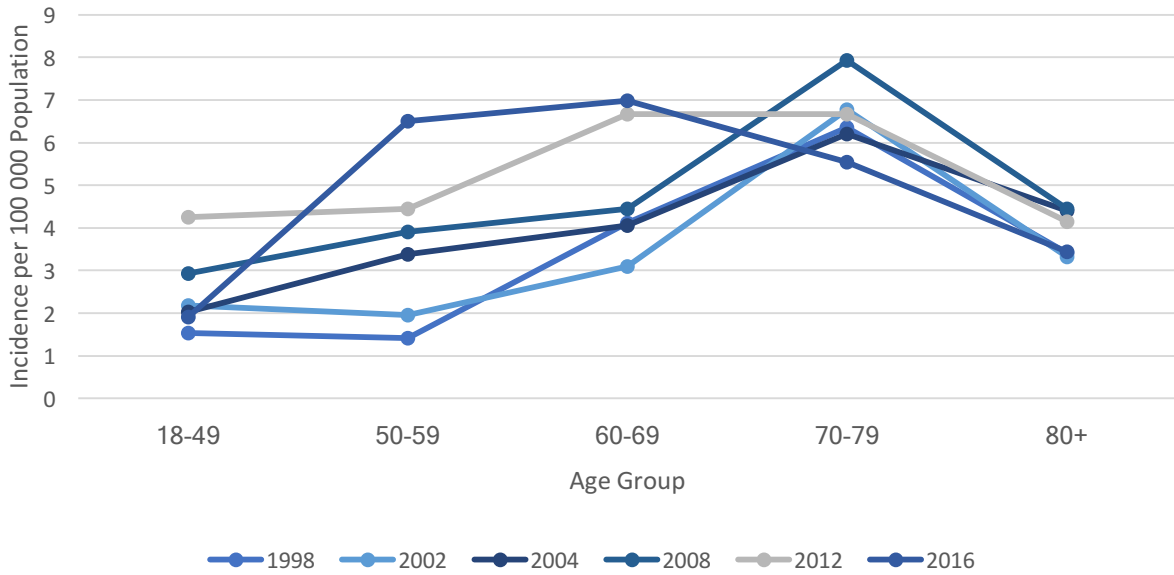
Figure 6. Annual Population Statistics for the Province of Manitoba

A. 1998

B. 2016

Percent of Population

Males　Females
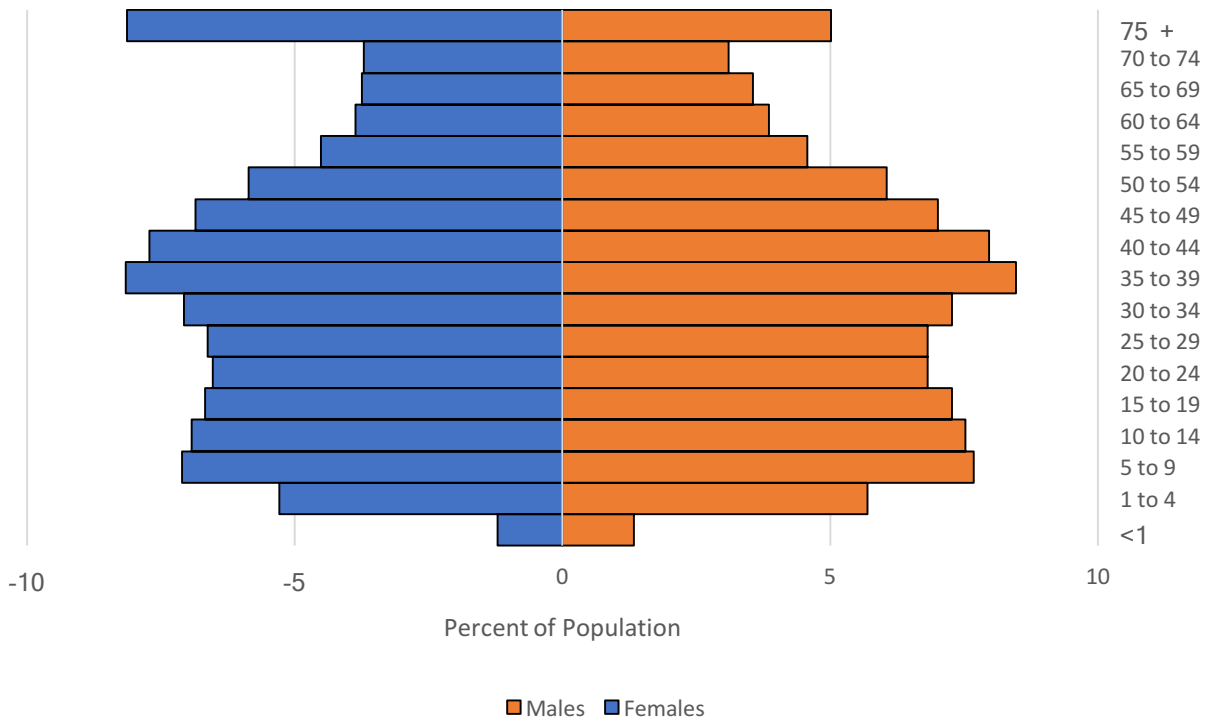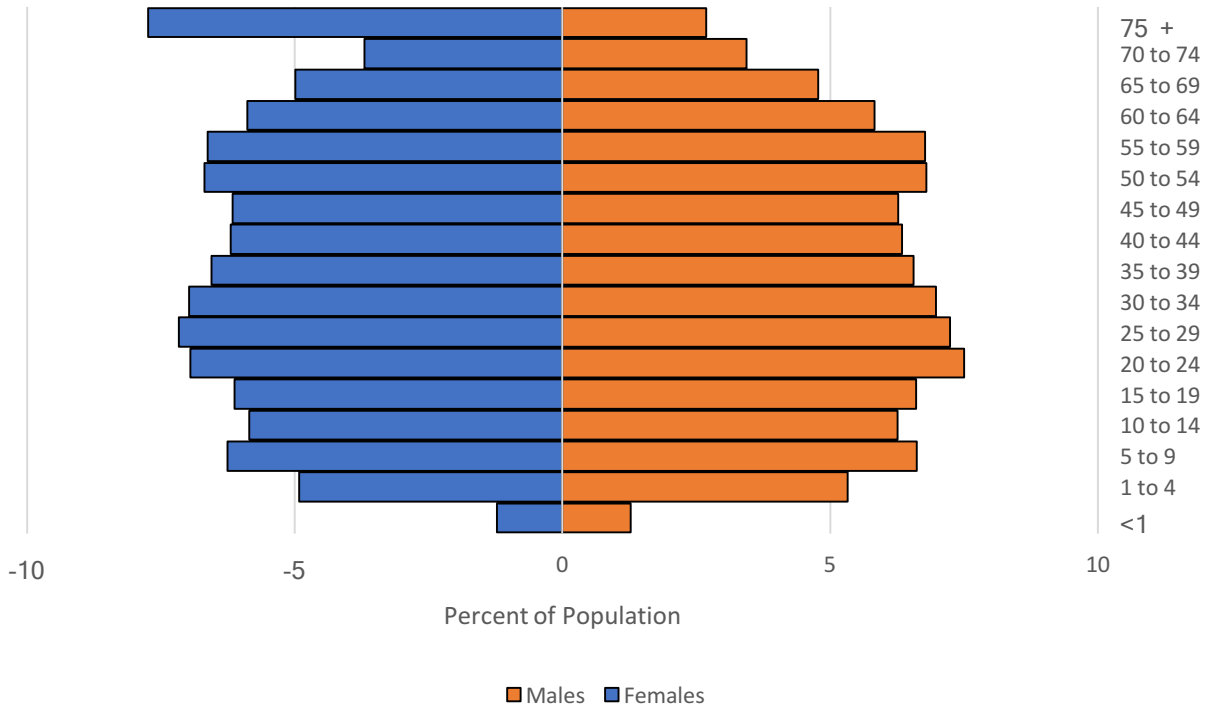
When stratified by age and sex, the average annual incidence of TAD in Manitoba increased with age and was higher in men than in women across all age categories (Table 4). The difference was more pronounced in the younger age groups where male patients aged 30 to 39 and 40 to 49 had a rate three times higher than women (RR 3.3; 95% CI, 2.1 to 5.4; RR 3.3; 95% CI, 2.4 to 4.5). The total average annual incidence was nearly two times higher in men (RR 1.9; 95% CI, 1.8 to 1.9).

Table 4. Average Annual Incidence of Thoracic Aortic Disease in Manitoba per 100 000 Population by Age and Sex, 1998 to 2016

Age, yr	Women			Men				
	No. of Cases	Average annual incidence (95%CI)		No. of Cases	Average annual incidence (95%CI)		Rate Ratio (95% CI)	
18-29	17	0.9	(0.56 to 1.4)	41	2.1	(1.6 to 2.9)	2.3	(1.3 to 4.2)
30-39	23	1.5	(0.97 to 2.2)	78	5.0	(4.0 to 6.2)	3.3	(2.1 to 5.4)
40-49	53	3.2	(2.4 to 4.2)	177	10.6	(9.1 to 12.3)	3.3	(2.4 to 4.5)
50-59	140	9.4	(7.9 to 11)	433	29	(26.4 to 31.9)	3.1	(2.6 to 3.8)
60-69	269	25.6	(22.7 to 28.8)	621	61.7	(57 to 66.8)	2.4	(2.1 to 2.8)
70-79	440	59	(53.7 to 64.8)	638	103	(95.3 to 111.3)	1.7	(1.5 to 2.0)
80+	386	59	(53.7 to 64.8)	363	107.2	(96.7 to 118.8)	1.8	(1.5 to 2.0)
Total	1328	14.7	(13.9 to 15.5)	2351	27.3	(26.2 to 28.4)	1.9	(1.8 to 1.9)

Yr, Years; No, Number; CI, Confidence Interval.

When stratified by region, Winnipeg has a significantly higher age standardized incidence with a peak of 16.6 per 100 000 in 2012 (Figure 7). While variable from year to year, the incidence in Winnipeg has increased 45% overall since 1998. The remaining four regions have seen relatively stable figures over the 19 year time period an incidence of 0.2 to 5.1 per 100 000 population. The Prairie Mountain region, which includes the city of Brandon (Manitoba's second largest city) has the highest incidence in this region cluster, with the Northern region consistently the lowest.

Figure 7. Age Standardized Incidence of Degenerative Thoracic Aortic Disease per 100 000 Population by Region
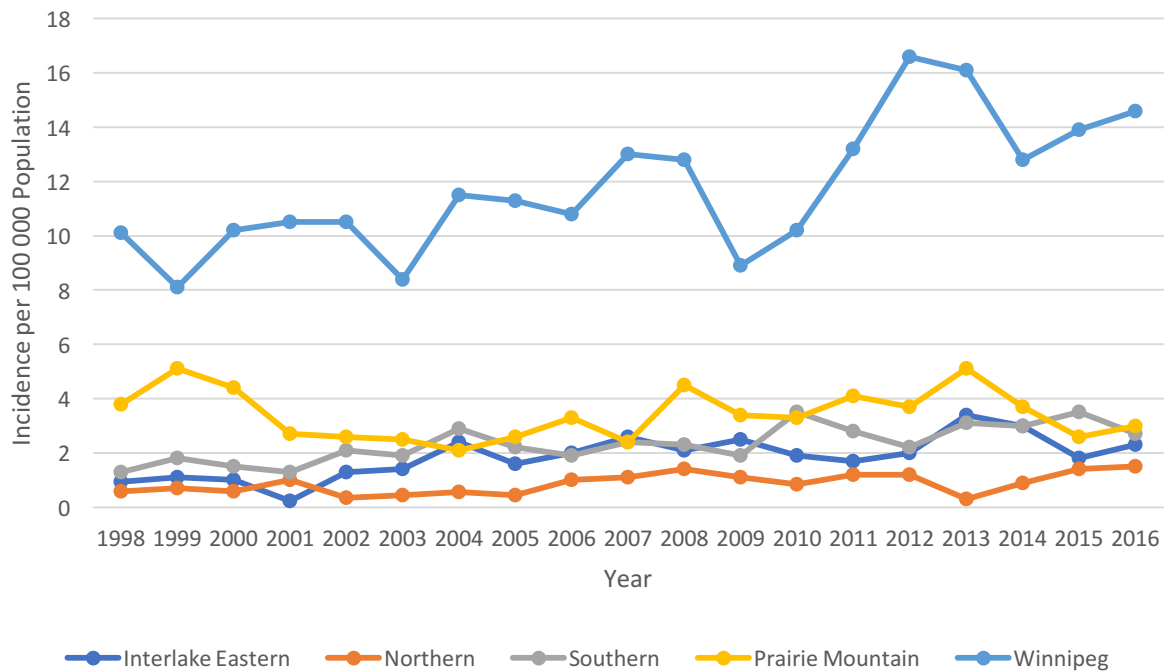
Prevalence of Degenerative Thoracic Aortic Disease

During the 'washout period' from 1994 to 1997, 537 patients were identified with a diagnosis of degenerative TAD. By the end of 1997, 350 patients were alive and living in Manitoba to form our baseline prevalence cohort going into 1998. The total age standardized prevalence of degenerative TAD has quadrupled from 58 per 100 000 in 1998 to 243 per 100 000 in 2016 (Figure 8). When stratified by sex, prevalence is significantly higher in men although the number of prevalent cases has increased four times in both sexes over the study period. There was an isolated decrease in prevalence in 2005 in both sexes, however the corresponding incidence that year decreased in females but increased in males. The age specific prevalence has increased in every age category from 1998 to 2016 (Figure 9). The prevalence was highest in the 60 to 69 age group with a peak of 65 per 100 000 in 2016. After age 79, the prevalence rapidly drops, presumably related to an increased number of deaths in these elderly patients.

Figure 9. Age Standardized Prevalence of Degenerative Thoracic Aortic Disease per 100 000 Population in Manitoba
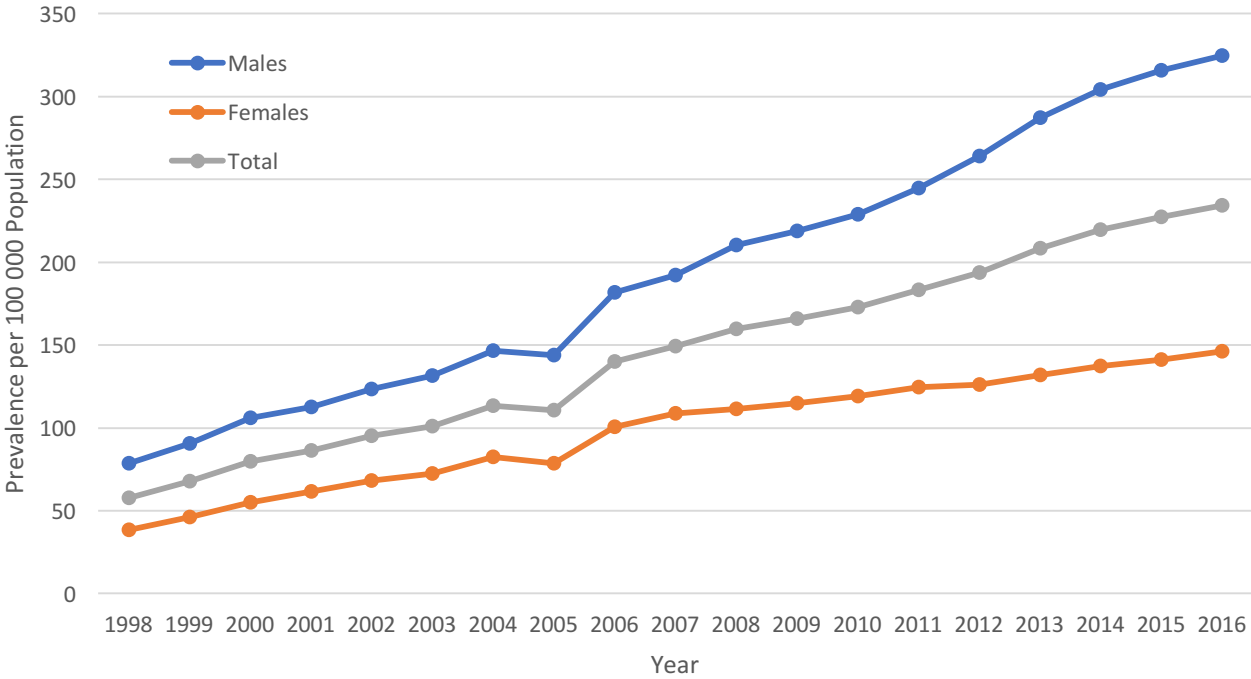
Figure 8. Age Specific Prevalence per 100 000 Population by Year, 1998 to 2016
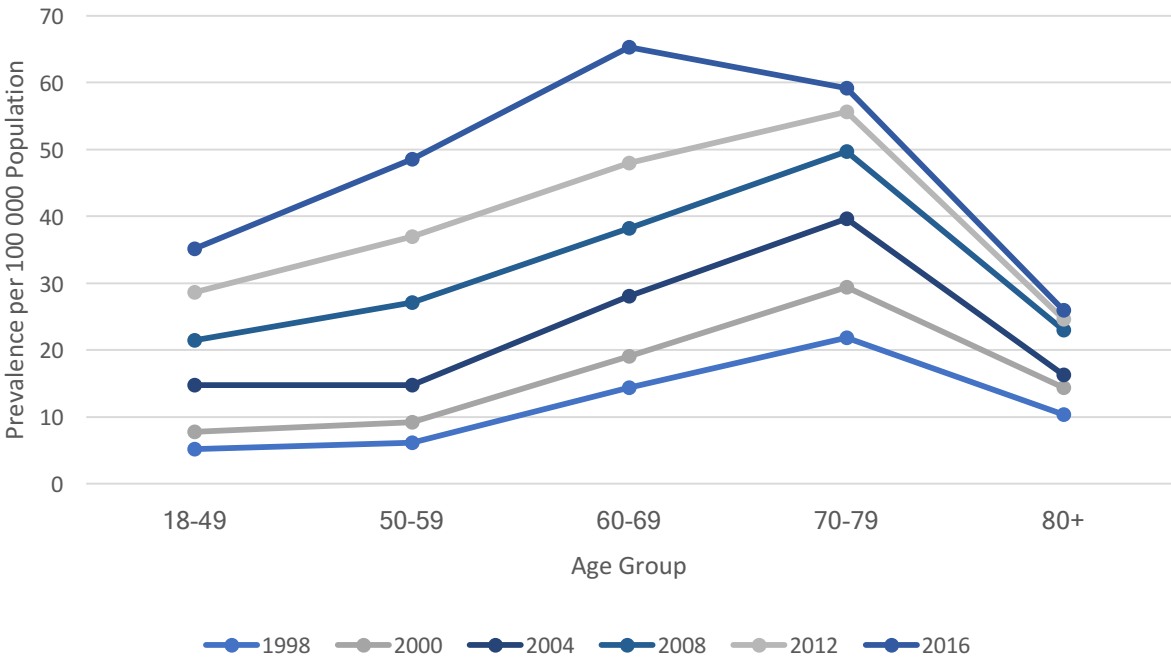
The age standardized prevalence of TAD has increased drastically in the Winnipeg region, quadrupling since 1998 (Figure 10). Trends in the other four regions are similar to what was found for incidence, with the Prairie Mountain region having the highest prevalence and Northern having the lowest. While the overall prevalence in these regions is much lower than Winnipeg, it has increased over time in each region. In the Northern region, the prevalence was 1.8 per 100 000 in 1998 and had climbed up to 10.4 per 100 000, nearly a 6-fold increase in 19 years. Prevalence in the Interlake Eastern region was not far behind with a 5.6 fold increase to 22 per 100 000 in 2016. The Prairie Mountain region showed the least amount of growth with a prevalence 2.9 times higher by 2016, and the Southern region was in the middle with an increase from 6.1 to 27.7 per 100 000 (2.9- fold) from 1998 to 2016.

Figure 10. Age Standardized Prevalence of Degenerative Thoracic Aortic Disease per 100 000 Population by Region
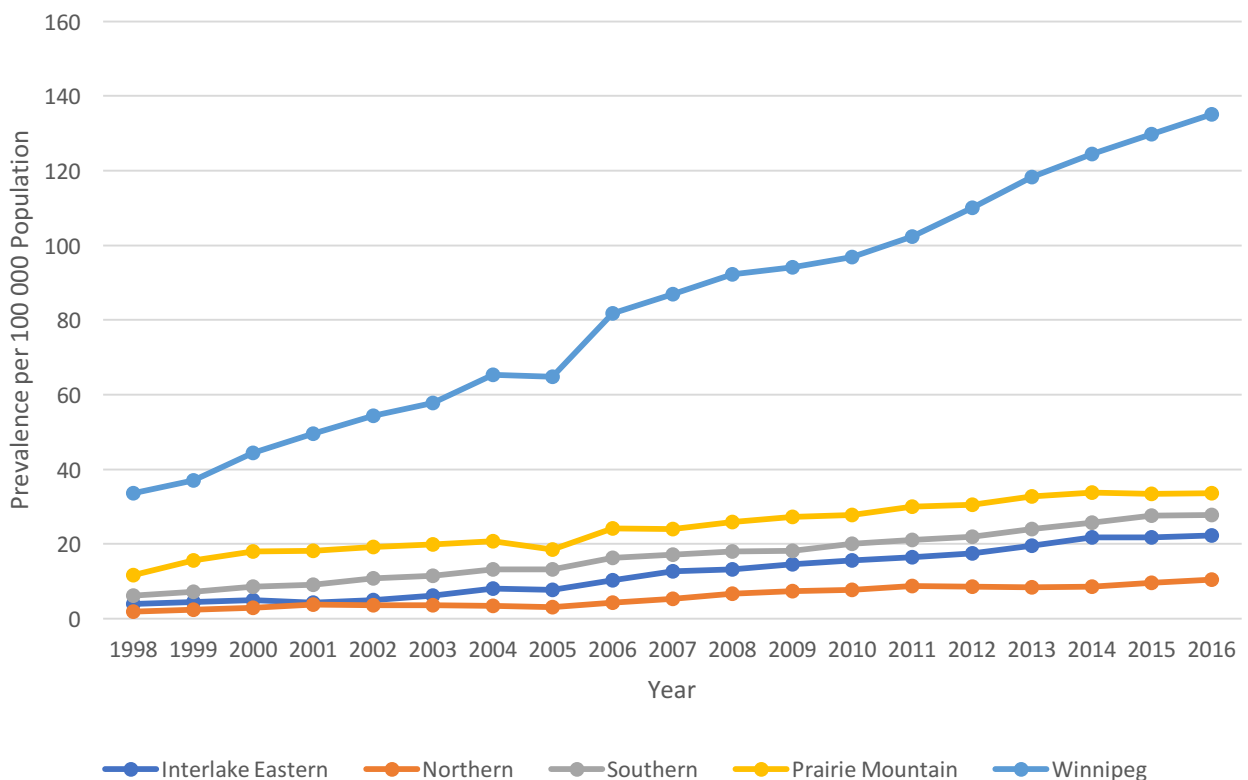
Geographical Trends in Incidence and Prevalence Across Regions

When examined geographically, Winnipeg occupies the smallest land mass of all five regions but also has the largest population, seven CT scanners, 16 health care centres, and the highest incidence and prevalence across all study years (Table 5, Figure 11 and 12). The population of the Southern region is the second largest at approximately 200 000 people, and they are serviced by three CT scanners (1 scanner per 66 000 people) and 18 health care centres. Despite this, the incidence and prevalence in the Southern region is consistently lower than the Prairie Mountain region which has a smaller population and only two scanners. Of note, there are 36 health care centres within the Prairie Mountain region, which is the most out of any region in the province. Greater than half of the total provincial land mass is occupied by the Northern region however it contains only 6% of the population. Thirty health care centres and two CT scanners service this vast region where the incidence and prevalence of TAD is the lowest in the province. While the Interlake- Eastern region occupies the second largest land mass, it's population is only greater than the Northern region, and it contains only one CT scanner. This results in a scanner to resident ratio of 1 per 128 000 and the second lowest incidence and prevalence. Overall, as illustrated by the changing colors from cold (blue) to hot (red), the incidence and prevalence is increasing in each region over the course of this study. This is especially true in Winnipeg which contains the highest number of scanners in the smallest geographical region, and the Prairie Mountain region where there is one health care centre per 4700 residents.

Table 5. Population Statistics, Health Care Centres and CT Scan Availability in the Manitoba Health Regions

	Population-2016	Geographical Area Km^2	Number of CT Scanners	Scanners per Population	Health Care Centres	Centres per Population
Winnipeg	767 543	570	7	1/110 000	16	1/48 000
Prairie Mountain	169 760	67 000	2	1/85 000	36	1/ 4716
Interlake-Eastern	128 105	61 000	1	1/128 000	17	1/7535
Southern	197 476	27 025	3	1/ 65 700	18	1/10 971
Northern	76 424	396 000	2	1/ 38 200	30	1/2558

Figure 11. Geographical Change in the Age Standardized Incidence of Thoracic Aortic Disease per 100 000 Population Across Health Regions Over 19 Years

A.

B.

Aortic Disease Age-Adjusted Incidence per 100,000 Population - 2004

C.

Aortic Disease Age-Adjusted Incidence per 100,000 Population - 2010

Annual Incidence per 100,000 Population
- ≤ 1.0
- 1.0 - 2.0
- 2.0 - 3.0
- 3.0 - 4.0
- ≥ 4.0
- Health Care Facility
- CT Facility

D.

Aortic Disease Age-Adjusted Incidence per 100,000 Population - 2016
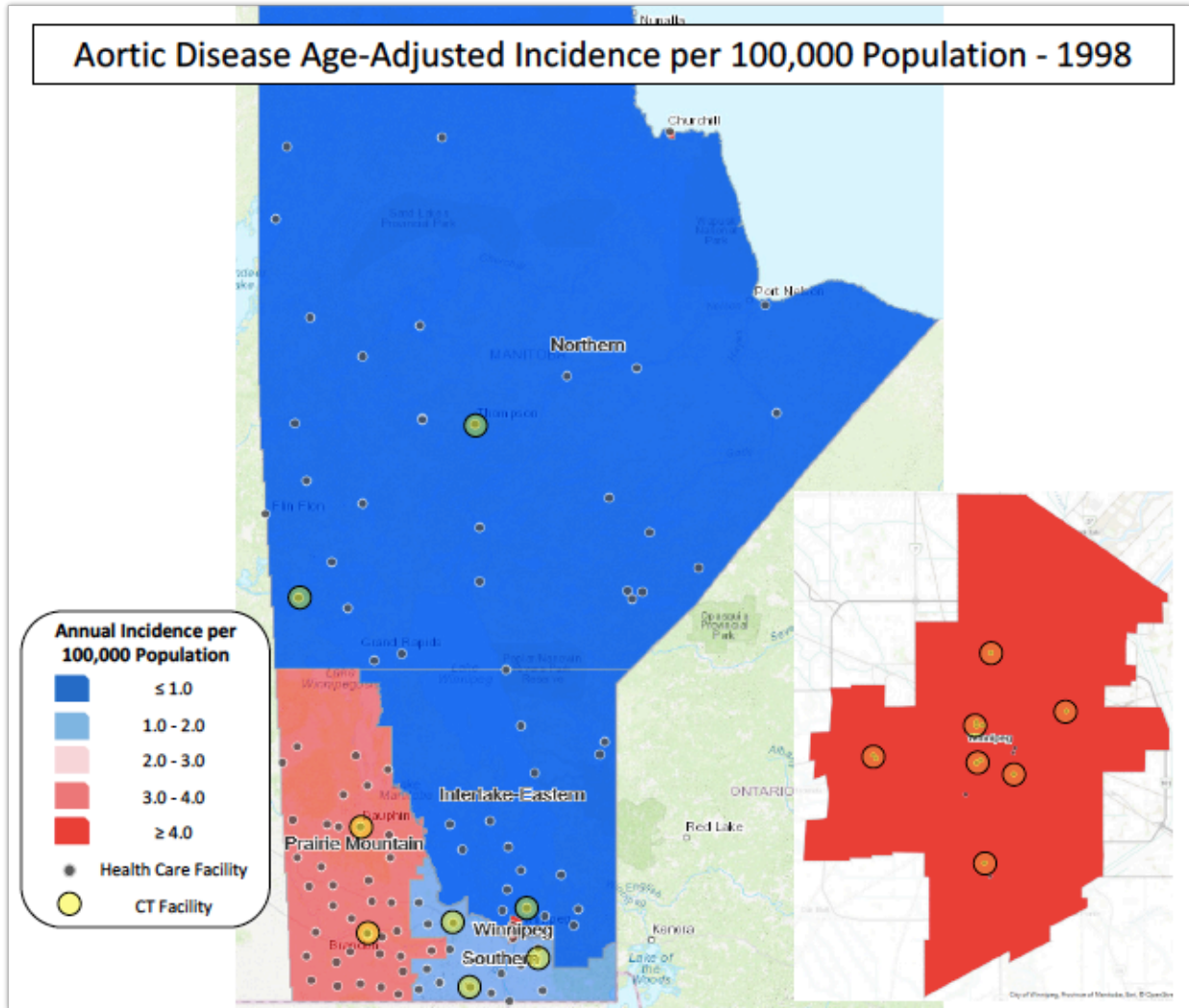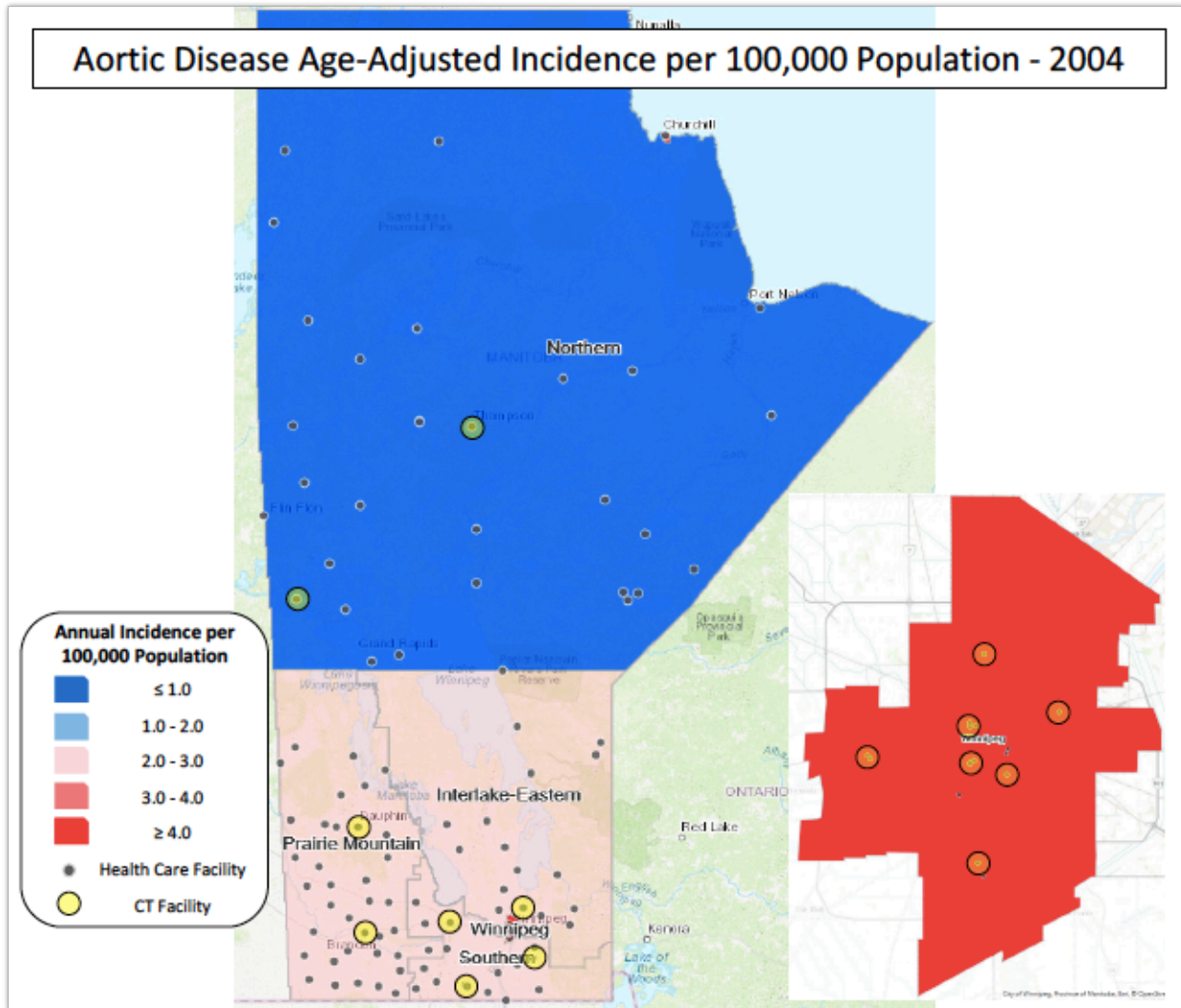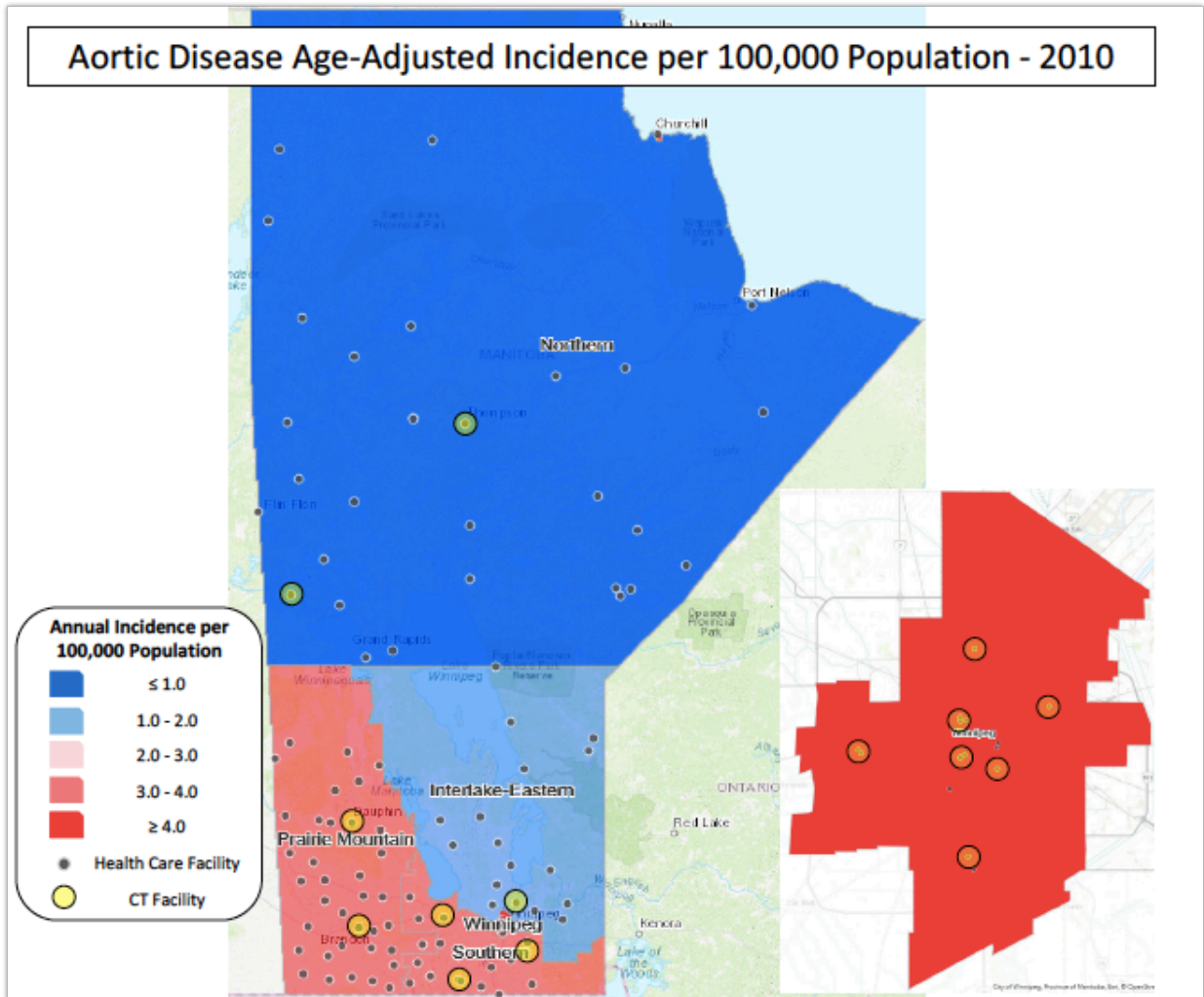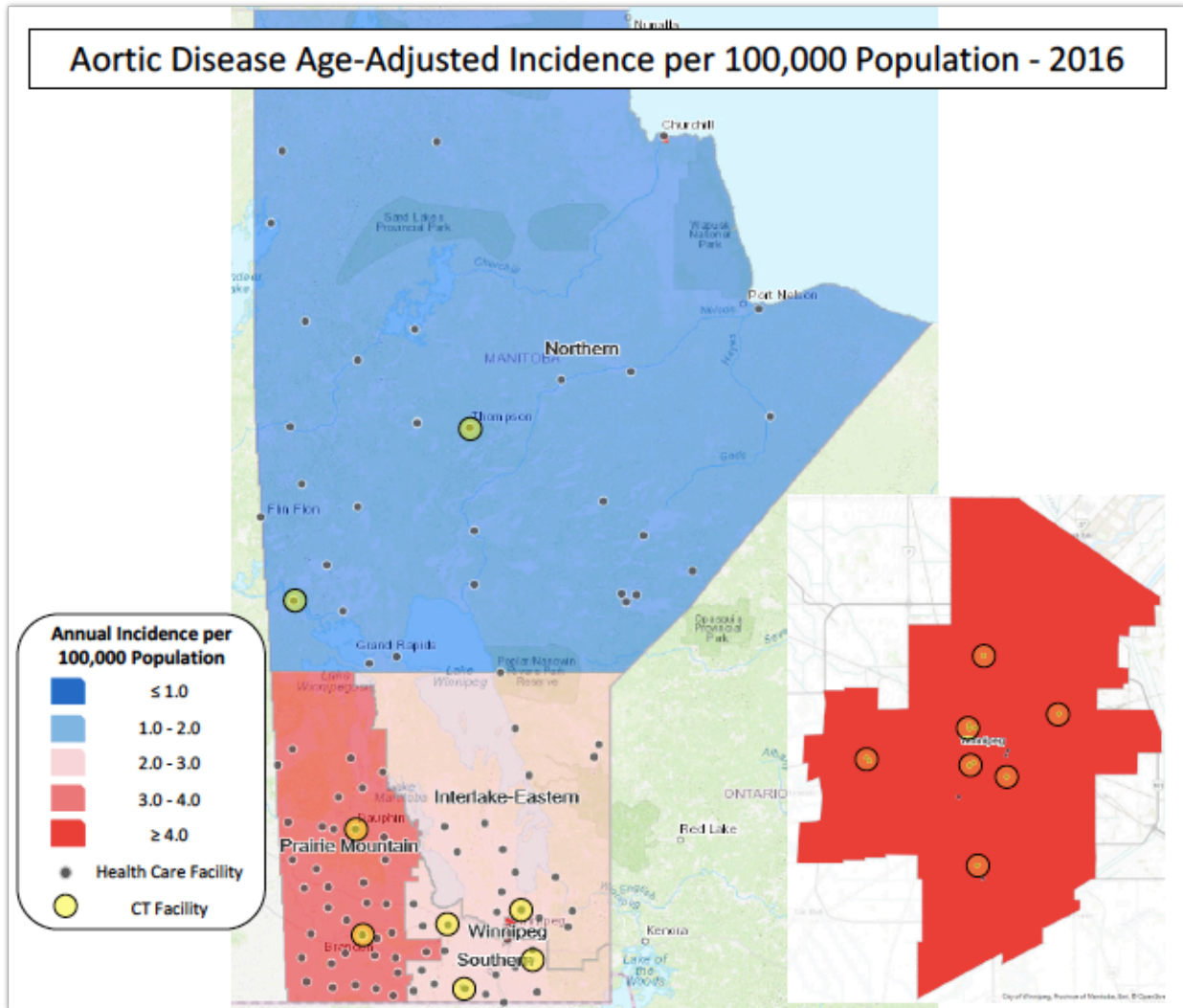
Figure 12. Geographical Change in the Age Standardized Prevalence of Thoracic Aortic Disease per 100 000 Population Across Health Regions Over 19 Years

A.

B.

Aortic Disease Age-Adjusted Prevalence per 100,000 Population - 2004

C.

Aortic Disease Age-Adjusted Prevalence per 100,000 Population - 2010
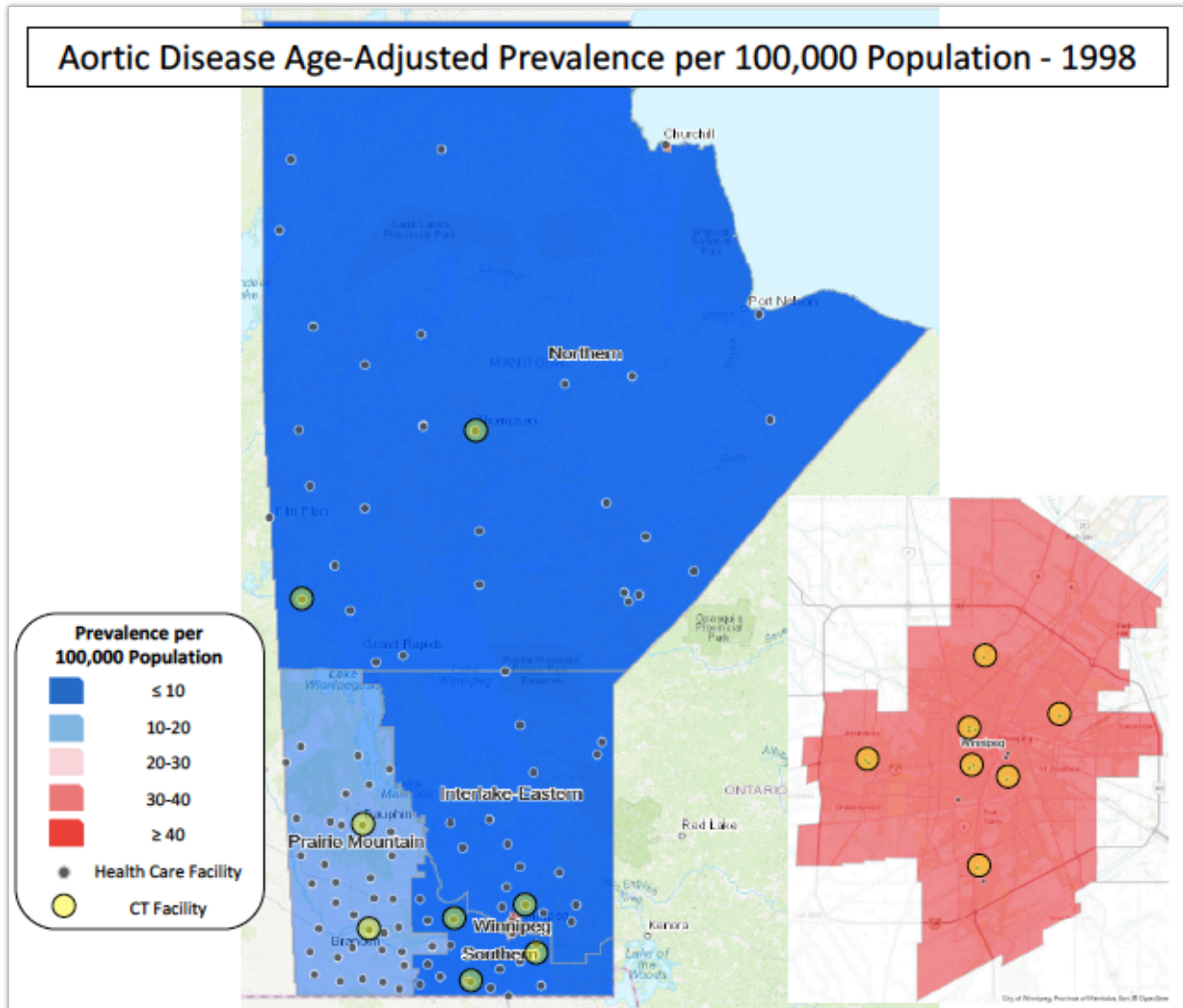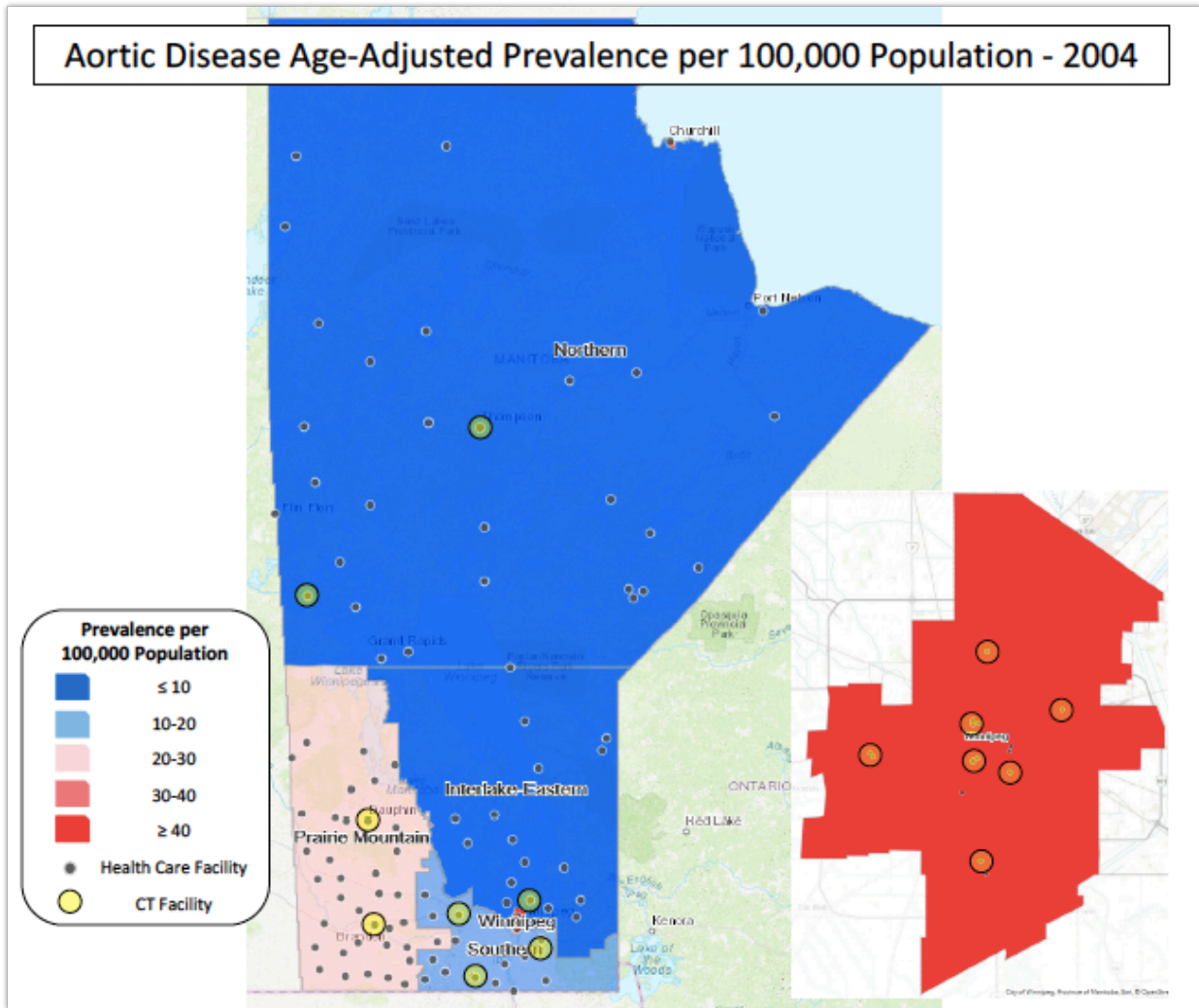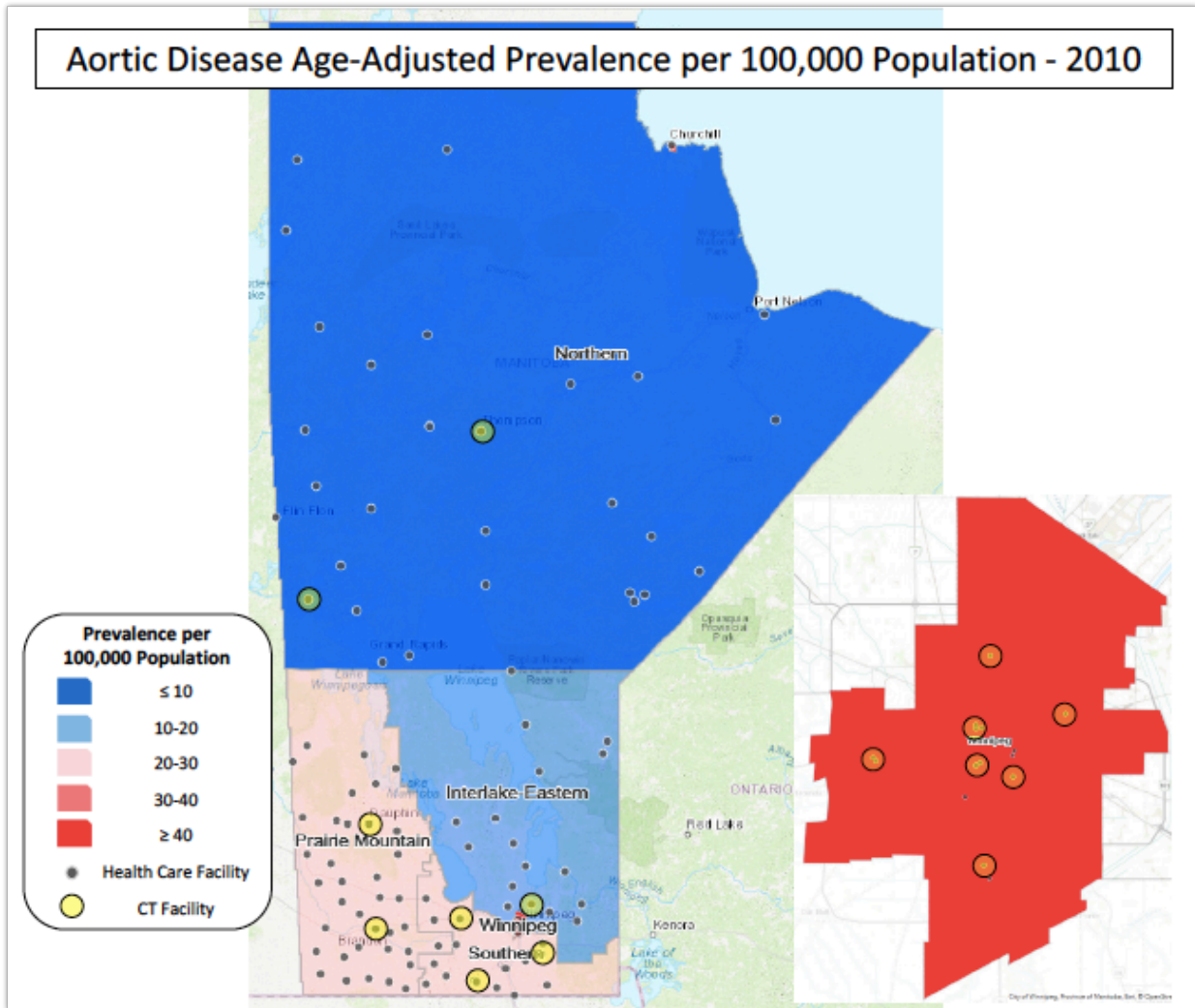
D.
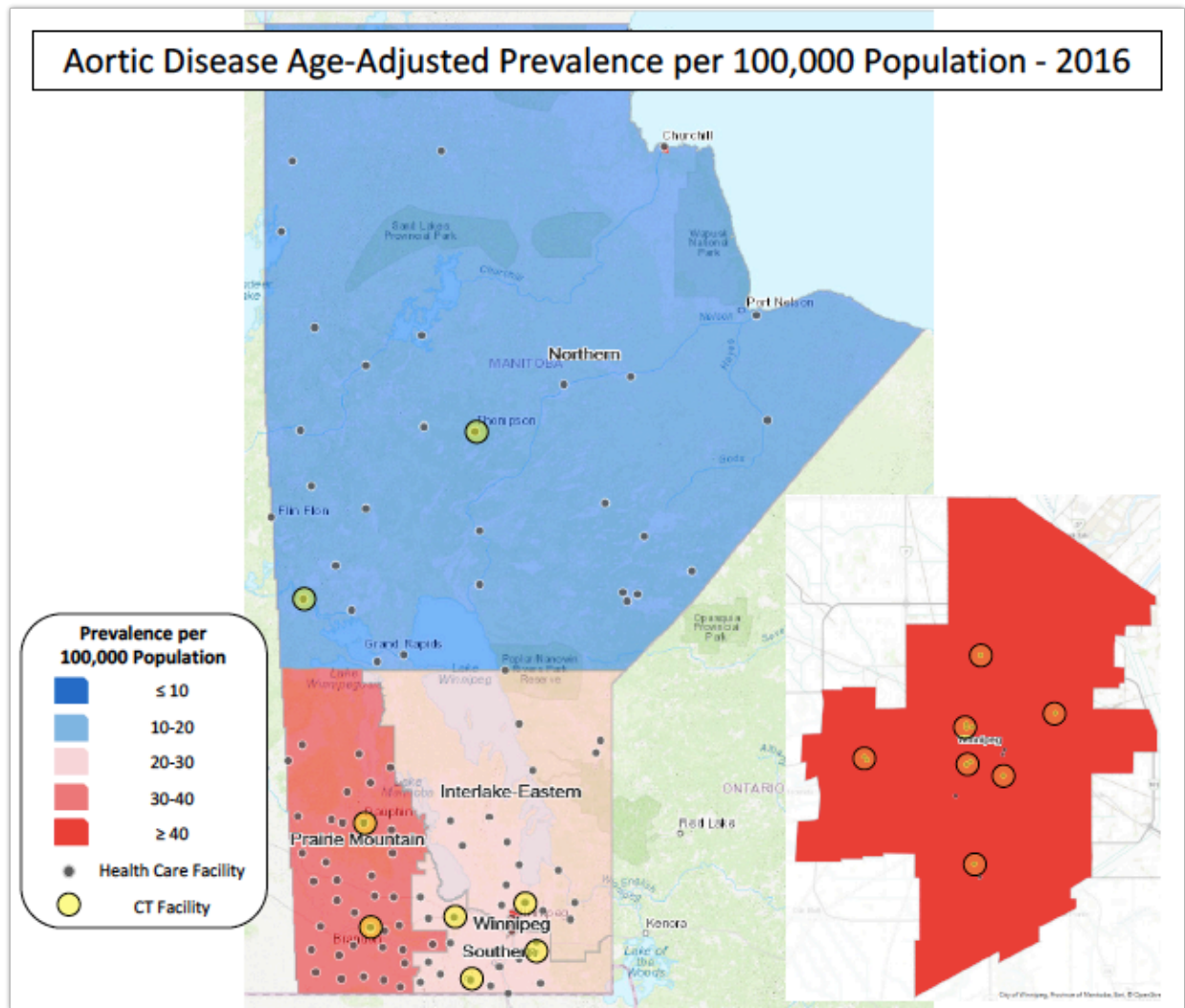
Epidemiology of Specific Thoracic Aortic Pathology

Epidemiological trends were examined for thoracic aortic aneurysm, dissection and rupture using hospital abstracts. The age standardized incidence of aneurysms increased by 28% from 8.5 to 10.9 per 100 000 (Figure 13). The incidence of dissection has remained relatively constant with figures hovering around 3 per 100 000 over the study period.

A total of 199 patients with aneurysm or dissection were identified as being alive and living in Manitoba at the end of 1997. This constituted the baseline prevalence entering the first year of study. The age standardized prevalence of was higher for aneurysms and increased 3-fold to a peak of 97 per 100 000 in 2016 (Figure 14). Although overall the prevalence of dissection was lower, there was a 5-fold increase over time from 5 to 26 per 100 000.

Figure 13. Age Standardized Incidence of Thoracic Aortic Aneurysm and Dissection in Hospitalized Patients per 100 000 Population
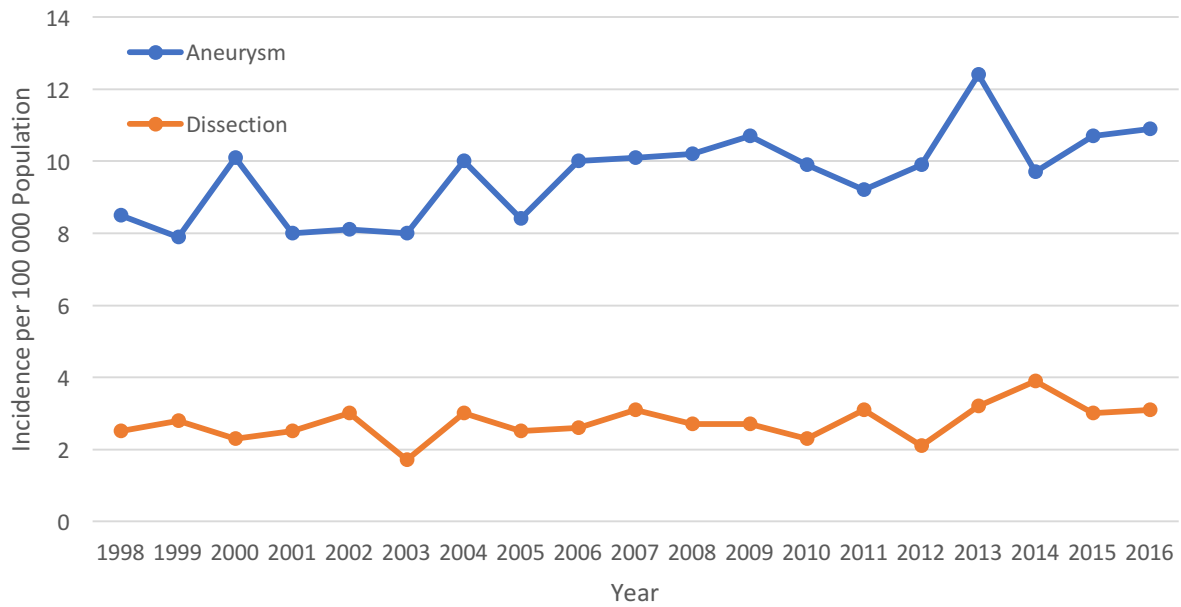
Figure 14. Age Standardized Prevalence of Thoracic Aortic Aneurysm and Dissection in Hospitalized Patients per 100 000 Population
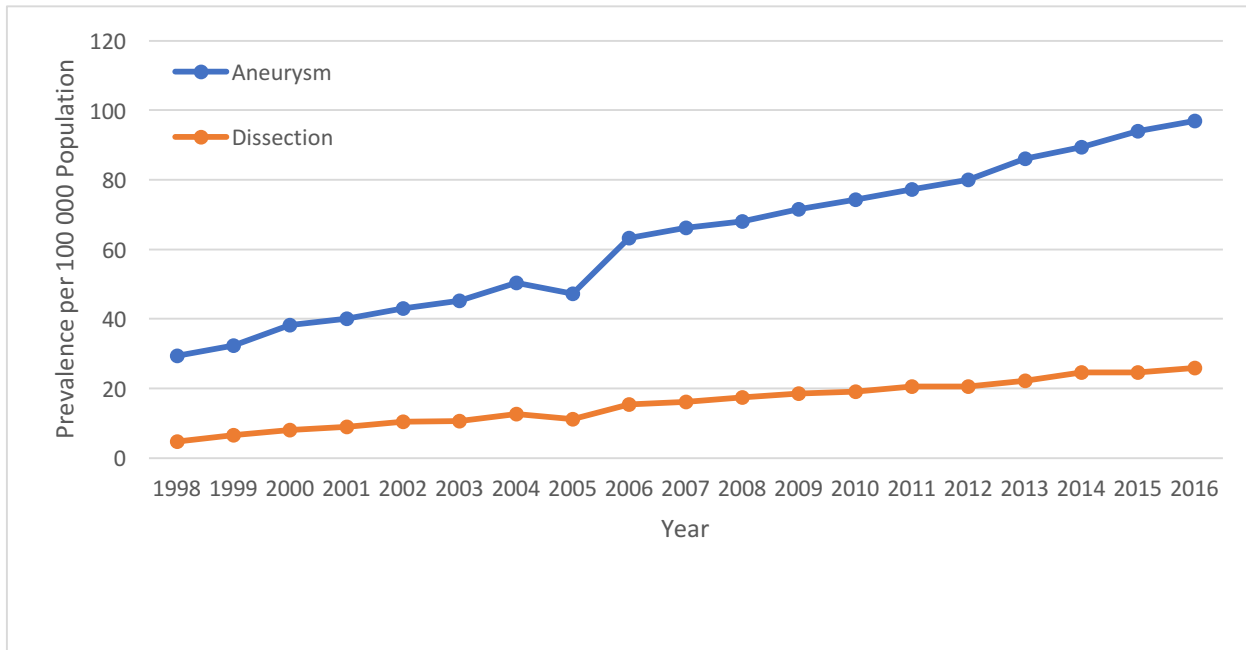
Thoracic aortic rupture is a relatively rare, and often lethal event. The crude incidence has been stable over time with approximately 10 to 20 diagnosed cases per year (Figure 15). When calculating the 'washout' period for rupture, 17 patients were identified as alive and living in Manitoba at the end of the 1997 year. This formed our baseline prevalence cohort beginning in 1998. Overall, the crude prevalence of aortic rupture has increased since 1998, with a notable jump between 2005 to 2007. The total number of prevalent cases has remained relatively stable in more recent years with 85 cases in 2016. When age standardized per 100 000 population, the incidence and prevalence of aortic rupture show similar trends (Figure 16). While the incidence was variable from 1998 to 2010 with 1.1 to 2.6 cases per 100 000, it has been since then between 1 and 1.5 per 100 000. The prevalence has increased, again with a significant rise between 2005 and 2007. This time period corresponds with the introduction and rapid growth of TEVAR as a therapy for TAD in Manitoba. Since 2008, the prevalence has remained constant around 7 per 100 000.

Figure 15. Crude Incidence and Prevalence of Thoracic Aortic Rupture in Manitoba, 1998 to 2016
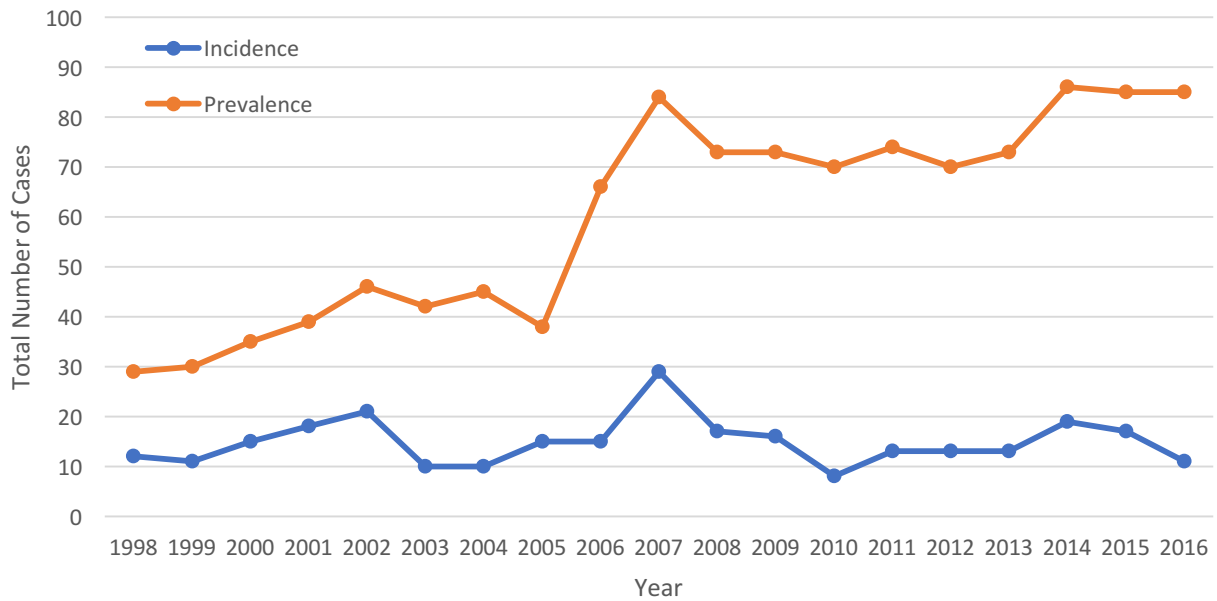
Figure 16. Age Standardized Incidence and Prevalence of Thoracic Aortic Rupture per 100 000 Population, 1998 to 2016
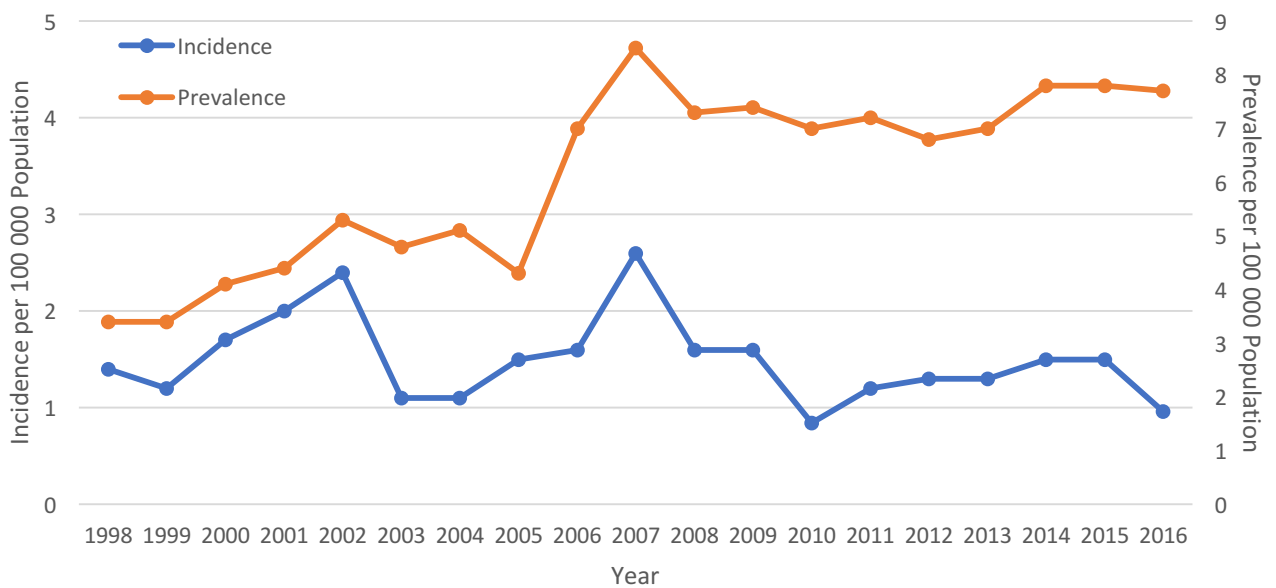
Long Term Functional Survival in Endovascular versus Open Descending Aortic Repair

Population

At the beginning of the period of investigation, 198 TEVAR procedures and 53 open surgical procedures were identified within the MTAD database. Several factors, however, have impacted our final patient cohort sample size: 1) there was significant patient overlap amongst treatment groups, ie. many patients underwent multiple procedures, either TEVAR or open, and numbers were reduced when patients were placed into a treatment group according to the type of their first procedure; 2) 16 patients were not residents of Manitoba, and therefore no data was available for them through the MCHP; 3) We excluded patients with an aortic coarctation (n=10) and those who had undergone repair for aortic trauma (19 patients) as these populations are inherently different than patients with degenerative TAD; 4) our primary outcome analysis required exclusion of patients who had IMH (17), a further trimming of 12 patients during the propensity score overlap assessment and exclusion of 2 patients who had underwent procedures beyond Dec 31, 2016, where vital statistics data was not yet available. In total, we were left with a total cohort of 119 patients, 84 in the TEVAR and 35 in the open surgery group (Figure 17)

Figure 17. Patient Flow Diagram for the TEVAR and Open Surgery Cohorts

198 TEVAR Procedures **53 Open Procedures**	→	**-30 Patients had multiple TEVARS** **-4 Patients had multiple open procedures** **-6 Patients who had both TEVAR and open procedures**
↓		
200 TOTAL PATIENTS **FIRST PROCEDURE:** 154 TEVAR 46 Open	→	**- 16 Out of province patients** **- 10 Coarctation patients** **- 19 trauma patients**
↓		
155 Patients: 113 TEVAR 42 Open	→	**Other Data Clean UP:** **- 4 Patients who had TEVAR for total arch** **- 1 Patients who did not have data**
↓		
150 Patients : 108 TEVAR 42 Open	→	**- 17 IMH patients (16 TEVAR, 1 Open)** **- 12 patients trimmed during propensity score overlap analysis** **- 2 patients with procedures after Dec 31, 2016**
↓		
119 Patients: 84 TEVAR 35 Open		

TEVAR, thoracic endovascular aortic repair; IMH, intramural hematoma

Baseline Characteristics

In the initial cohort for the analysis of functional survival there were 134 patients, including those with IMH. Ninety-nine patients were in the TEVAR group and 35 patients were in the open group. Patients undergoing open surgery had a median age that was significantly lower than those who had TEVAR (64 years, IQR (49, 71) vs 72 years, IQR (65, 80); p=0.0001). About 75% of the patients were male in each group. Open surgery patients were significantly heavier, with a mean weight of 87.8kg compared to 77.2kg in TEVAR patients (p=0.0017). They also had a higher mean body surface area (2.06, SD 0.29 vs 1.91, IQR, SD 0.28; p=0.009) (Table 6).

There was no difference between the open surgery and TEVAR groups in the incidence of cerebrovascular disease (23% vs 32%, p=0.21, chronic pulmonary disease (34% vs 44%, p=0.29), diabetes (29% vs 32%, p=0.4) or smoking (66% vs 71%, p=0.58). Despite the significantly older TEVAR cohort, the weighted sum of Charlson comorbidity groups was not significantly different between groups (TEVAR, median 3 IQR (2, 6); Open, median 2 (IQR 2,5); p=0.15). Results for many of the comorbidity variables relevant to aortic disease and cardiac surgery had to be suppressed due to small values including hypertension, dyslipidemia, history of previous cardiac surgery, myocardial infarction, congestive heart, peripheral vascular and renal disease (Table 6).

In the TEVAR group, majority of patients were treated for aneurysmal disease (62.6%) whereas only 40% of open surgery patients had aneurysm repair (p=0.02). In contrast, 49% of open patients had an aortic dissection repair compared to 28% of TEVAR patients (p=0.03). The number of individual patients with PAUs and IMHs could not be reported due to small values however, when these patients were combined with aortic dissection patients under the umbrella term 'acute aortic syndrome' there was no difference between the treatment groups (51% Open vs 48% TEVAR; p=0.69). The incidence of thoracic aortic rupture was suppressed due to small values. The median number of segments of aorta that were covered with stent graft (TEVAR) or replaced with Dacron graft (open surgery) was slightly higher in the TEVAR cohort, but this difference was not statistically significant (3, IQR (2, 4) vs 2, IQR (2, 3); p=0.17) (Table 6).

Socio-economic data was available for 92 TEVAR patients and 34 open patients. Majority of the patients in both treatment groups were living in an urban setting at the time of their first procedure (77% open vs 77% TEVAR; p=0.9). There was no difference between groups in the number of patients stratified by income level. 41% of patients were considered low income and 59% high in the open surgery group, and 39% were low and 61% were high income in the TEVAR group. The results for pre- and post- procedure EIA use were suppressed due to small values (Table 6).

Table 6. Baseline Characteristics of the Study Cohort Including IMH Patients

	TEVAR (n=99)	Open Surgery (n=35)	p value
Age Median (IQR)	72 (65, 80)	64 (49, 71)	0.0001
Gender, male n (%)	74 (75%)	27 (77%)	0.9
Height, cm Mean (SD)	169.8 (9.4)	172.8 (12.6)	0.2
Weight, kg Mean (SD)	77.2 (19.2)	87.8 (22.2)	0.0077
BSA Mean (SD)	1.91 (0.28)	2.06 (0.29)	0.009
Hypertension	-	-	-
Dyslipidemia	-	-	-
Previous Cardiac Surgery	-	-	-
Smoking History- Current or former	70 (71%)	23 (66%)	0.58
Charlson Comorbidity Index n (%)			
Myocardial Infarction	-	-	-
Congestive Heart Failure	-	-	-
Peripheral Vascular Disease	-	-	-
Cerebrovascular Disease	34 (34%)	8 (23%)	0.21
Dementia	-	-	-
Chronic Pulmonary Disease	44 (44%)	12 (34%)	0.29
Connective Tissue/Rheumatic Disease	-	-	-
Peptic Ulcer Disease	-	-	-
Mild Liver Disease	-	-	-
Moderate or Severe Liver Disease	-	-	-
Diabetes (With and Without Complications)	32 (32%)	10 (29%)	0.68
Paraplegia and Hemiplegia	-	-	-

Renal Disease	-	-	-
Cancer	21 (21%)	7 (20%)	0.88
Metastatic Carcinoma	-	-	-
HIV/AIDS	-	-	-
Sum of Charlson Comorbidity Groups Median (IQR)	3 (2, 5)	2 (2, 4)	0.08
Weighted sum of Charlson Comorbidity Groups Median (IQR)	3 (2, 6)	2 (2, 5)	0.15
Pathology n (%)			
Dissection	28 (28%)	17 (49%)	0.029
Acute Type B	-	-	-
Chronic/Residual Type B	-	-	-
Descending Aneurysm	62 (62.6%)	14 (40%)	0.02
Thoracoabdominal:			
I	-	-	-
II	-	-	-
III	-	-	-
IV	-	-	-
V	-	-	-
PAU	-	-	-
IMH	-	-	-
Acute Aortic Syndrome (Dissection, PAU or IMH)	47 (47.5%)	18 (51%)	0.69
Rupture	-	-	-
Number of segments covered/replaced Median (IQR)	3 (2, 4)	2 (2, 3)	0.17
Socioeconomic Measures n (%)	n=92	n=34	p value
Area of residence at time of procedure, urban/rural	71 (77%) / 21 (23%)	26 (76.5%) / 8 (23.5%)	0.93
Income Quintile			
U1	-	-	-
U2	-	-	-
U3	-	-	-
U4	-	-	-
U5	-	-	-
R1	-	-	-
R2	-	-	-
R3	-	-	-
R4	-	-	-
R5	-	-	-

Low Income (U1, U2, R1, R2)	36 (29%)	14 (41%)	0.83
High Income **(U3, U4, U5, R3, R4, R5)**	56 (61%)	20 (59%)	0.83
Income Assistance	-	-	-
Pre-Operative	-	-	-
Post-Operative	-	-	-

IQR, Interquartile range; cm, centimeter; kg, kilogram; SD, standard deviation; BSA, body surface area; HIV, human immuno-deficiency virus; AIDS, acquired immune deficiency syndrome; PAU, penetrating atherosclerotic ulcer; IMH, intramural hematoma; U, urban; R, rural; - indicates suppressed value.

Primary Outcome

To control for confounding, a propensity score model was developed on the probability of undergoing an open descending repair for all patients. The initial cohort included patients that had a diagnosis of IMH. The kernel density plot for the first model displayed an area of non-overlap for open surgery patients with high propensity scores (Figure 18). There was a high density of TEVAR patients with propensity scores between 0 and 0.5, with relatively small density of patients between 0.5 and 1.0. The distribution of propensity scores in the open patients was more bimodal with the highest density of patients having propensity scores between 0.5 and 1.0, and a second smaller peak between 0 and 0.5. Fourteen patients with propensity scores in the top and bottom 5% of the distribution were trimmed, improving the overlap between groups (Figure 19). Inverse probability of treatment weights were calculated for each patient. The median IPTW was 1.23 with a minimum value of 1.01 and maximum of 17.9. Stabilization of the IPTWs was successful in reducing the number of extreme weights, with the stabilized median coming down to 0.83, minimum to 0.31 and maximum to 5.26 (Table 7). When a weighted standardized mean differences (SMD) were analyzed to assess covariate balance, the difference was greater than ± 0.2 for 'Weighted Charlson Comorbidity Score', 'Aneurysm' and 'IMH' (Table 8). The SMD was the highest for the IMH variable at -0.3677. When exploring this result, it was found that 16 out of 17 patients with IMH underwent a TEVAR procedure. This meant that it would be impossible to adjust for this categorical variable via stratification and it was decided to exclude the IMH patients entirely from the analysis.

Figure 18. Kernel Density Plot of Propensity Scores for Patients Undergoing TEVAR and Open Surgery
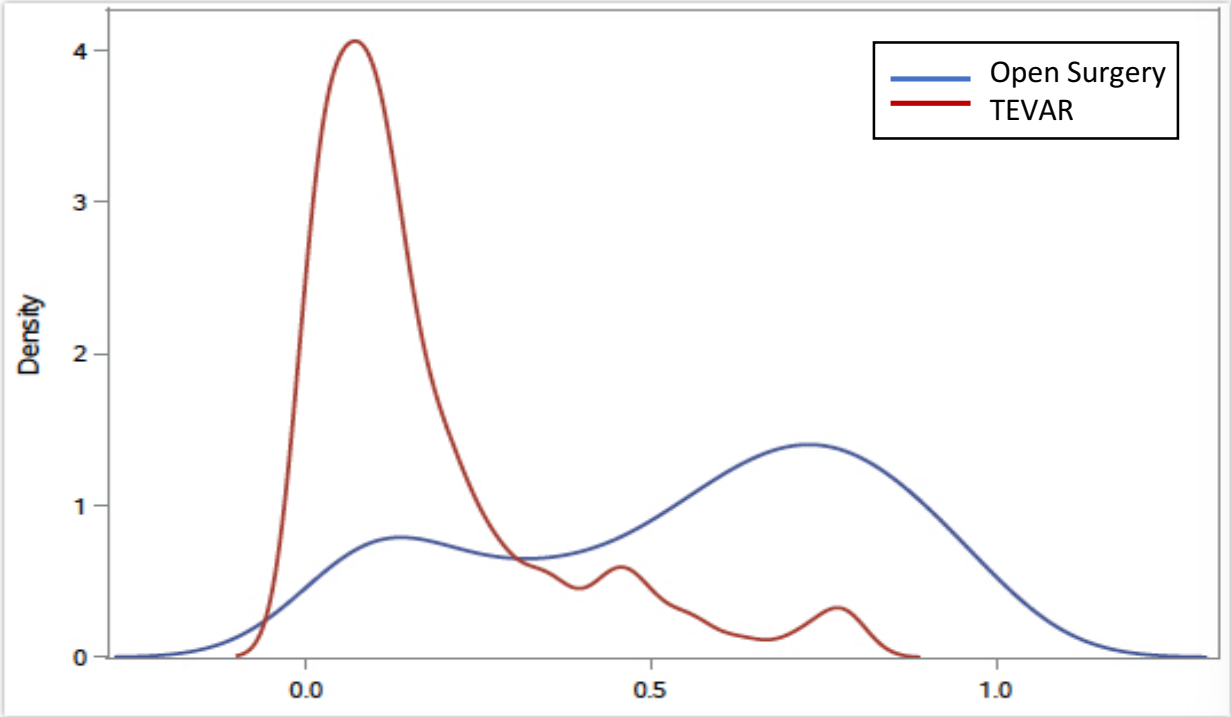
Figure 19. Kernel Density Plot of Propensity Score Following Trimming of Outliers
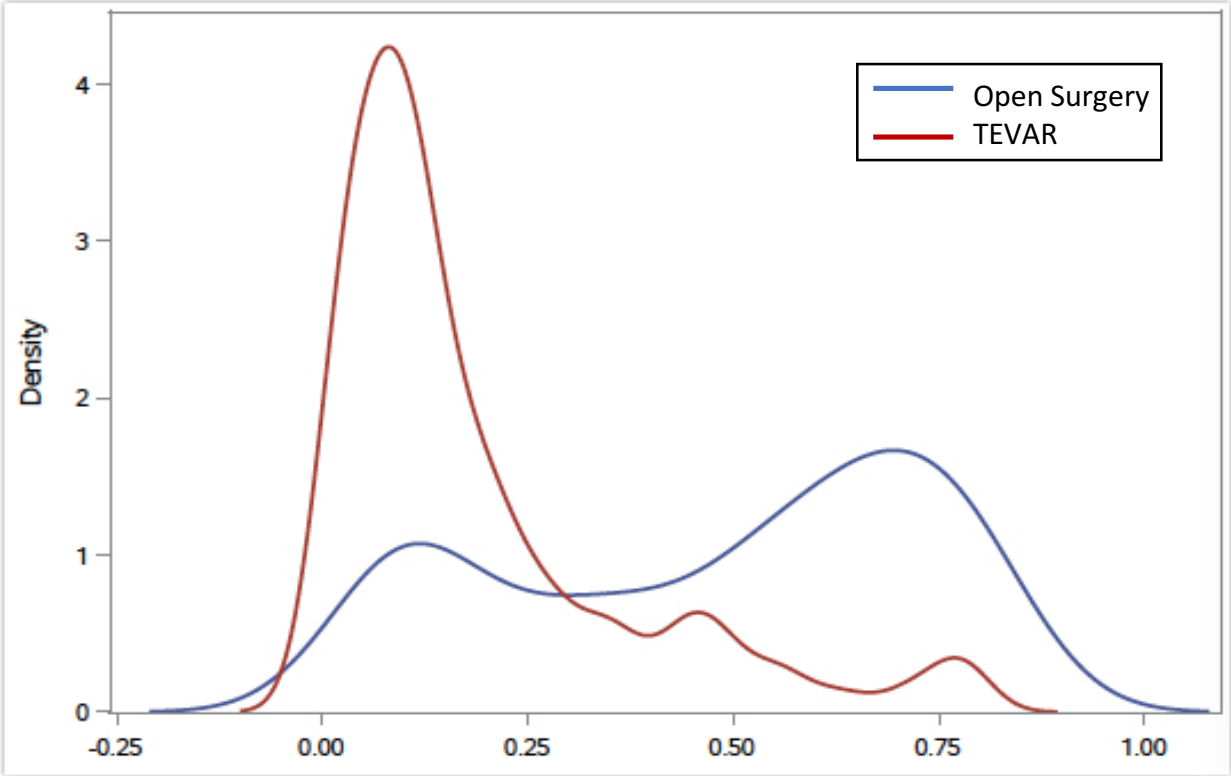
Table 7. Inverse Probability of Treatment Weights

	First Model	
	IPTW	sIPTW
Median	1.23	0.83
IQR	(1.10, 1.63)	(0.76, 0.98)
Minimum Value	1.01	0.31
Maximum Value	17.9	5.26
Range	16.9	4.94

IQR, Interquartile Range; IPTW, inverse probability of treatment
weighting; sIPTW, stabilized inverse probability of treatment weights.

Table 8. Weighted Standardized Mean Difference of Variables

	First Model Weighted SMD
Age, years	0.1238
Sex	0.1533
Height, cm	-0.1160
Weight, kg	0.0897
BSA	0.0740
Hypertension	0.0893
Dyslipidemia	0.1835
Smoking	0.1984
Weighted Charlson Comorbidity Score	0.2402
Prior Cardiac Surgery	-0.0434
Aneurysm	0.2204
Acute Type B Dissection	-0.2195
Chronic Type B Dissection	0.0142
PAU	-0.1609
IMH	-0.3677

SMD, Standardized Mean Difference; cm, centimetre; kg, kilogram; PAU, penetrating
atherosclerotic ulcer; IMH, intramural hematoma.

After removing the IMH patients from the cohort, baseline characteristics were examined again to see if patient exclusion had resulted in any significant changes (Table 9). Open patients were still significantly older (median age 63 vs 71, p=0.0003), larger (mean weight 88.1kg vs 78.1kg, p=0.017) and had a higher BSA (2.03 vs 1.94, p=0.021). There was no difference in the reportable components of the Charlson Comorbidity Index. The incidence of dissection however is no longer significant with 46% of open patients and 30% of TEVAR patients undergoing treatment for this pathology (p=0.095). There was still a significantly higher number of patients in the TEVAR group who had a thoracic aortic aneurysm (70% vs 43%, p=0.005). While the number of segments covered or replaced was not significant, there is now a trend towards significance with a higher median and IQR in the TEVAR group (3 (2, 4) vs 2 (2, 3); p=0.076). Measures of socio-economic status are essentially unchanged.

Table 9. Baseline Characteristics of the Study Cohort Excluding IMH Patients

	TEVAR (n=84)	Open Surgery (n=35)	p value
Age Median (IQR)	71 (64, 78)	63 (47, 71)	0.0003
Gender, male n (%)	63 (75%)	27 (77%)	0.8
Height, cm Median (IQR)	170.8 (164, 177)	173.2 (163, 183)	0.15
Weight, kg Mean (SD)	78.1 (19.7)	88.1 (22.1)	0.017
BSA Median (IQR)	1.94 (1.74, 2.13)	2.03 (1.8, 2.2)	0.021
Hypertension	-	-	-
Dyslipidemia	-	-	-
Previous Cardiac Surgery	-	-	-
Smoking History- Current or former	63 (75%)	23 (66%)	0.30
Charlson Comorbidity Index n (%)			
Myocardial Infarction	-	-	-
Congestive Heart Failure	-	-	-
Peripheral Vascular Disease	-	-	-

Cerebrovascular Disease	26 (31%)	8 (23%)	0.37
Dementia	-	-	-
Chronic Pulmonary Disease	37 (44%)	12 (34%)	0.32
Connective Tissue/Rheumatic Disease	-	-	-
Peptic Ulcer Disease	-	-	-
Mild Liver Disease	-	-	-
Moderate or Severe Liver Disease	-	-	-
Diabetes (With and Without Complications)	23 (33%)	9 (26%)	0.41
Paraplegia and Hemiplegia	-	-	-
Renal Disease	-	-	-
Cancer	14 (17%)	7 (20%)	0.66
Metastatic Carcinoma	-	-	-
HIV/AIDS	-	-	-
Sum of Charlson Comorbidity Groups Median (IQR)	3 (2, 4)	2 (1, 4)	0.13
Weighted sum of Charlson Comorbidity Groups Median (IQR)	2 (2, 6)	2 (1, 5)	0.24
Pathology n (%)			
Dissection	25 (30%)	16 (46%)	0.095
Acute Type B	-	-	-
Chronic/Residual Type B	-	-	-
Descending Aneurysm Thoracoabdominal:	59 (70%)	15 (43%)	0.005
I	-	-	-
II	-	-	-
III	-	-	-
IV	-	-	-
V	-	-	-
PAU	-	-	-
IMH	-	-	-
Acute Aortic Syndrome (Dissection, PAU or IMH)	32 (38%)	17 (49%)	0.29
Rupture	-	-	-
Number of segments covered/replaced Median (IQR)	3 (2, 4)	2 (2, 3)	0.076
Socioeconomic Measures n (%)	n=79	n=34	p value
Area of residence at time of procedure, urban/rural	61 (77%) / 18 (23%)	27 (79%) / 7 (21%)	0.8

Income Quintile			
U1	-	-	-
U2	-	-	-
U3	-	-	-
U4	-	-	-
U5	-	-	-
R1	-	-	-
R2	-	-	-
R3	-	-	-
R4	-	-	-
R5	-	-	-
Low Income (U1, U2, R1, R2)	33 (42%)	15 (44%)	0.82
High Income (U3, U4, U5, R3, R4, R5)	46 (58%)	19 (56%)	0.82
Income Assistance	-	-	-
Pre-Operative	-	-	-
Post-Operative	-	-	-

IQR, Interquartile range; cm, centimeter; kg, kilogram; SD, standard deviation; BSA, body surface area; HIV, human immuno-deficiency virus; AIDS, acquired immune deficiency syndrome; PAU, penetrating atherosclerotic ulcer; IMH, intramural hematoma; U, urban; R, rural; - indicates suppressed value.

The propensity score model for functional survival was then repeated using the final cohort without IMH patients. Kernel density estimations assessing propensity score overlap showed a similar trend as the plot including IMH patients (Figure 20). During trimming procedures, 12 patients with scores in the top or bottom 5% of the distribution were removed and the plot was updated (Figure 21). The IPTW's for the second model had a similar median value (1.29), but the maximum value and range were reduced. The weights further improved with stabilization, with maximum stabilized IPTW of 4.6 (Table 10). The weighted SMD's also showed significant improvement in covariate balance, with only the weighted Charlson comorbidity score greater than 0.2 (Table 11).

Figure 20. Kernel Density Plot of Propensity Scores Excluding IMH Patients

Figure 21. Kernel Density Plot of Propensity Scores Excluding IMH Patients Following Trimming of Outliers
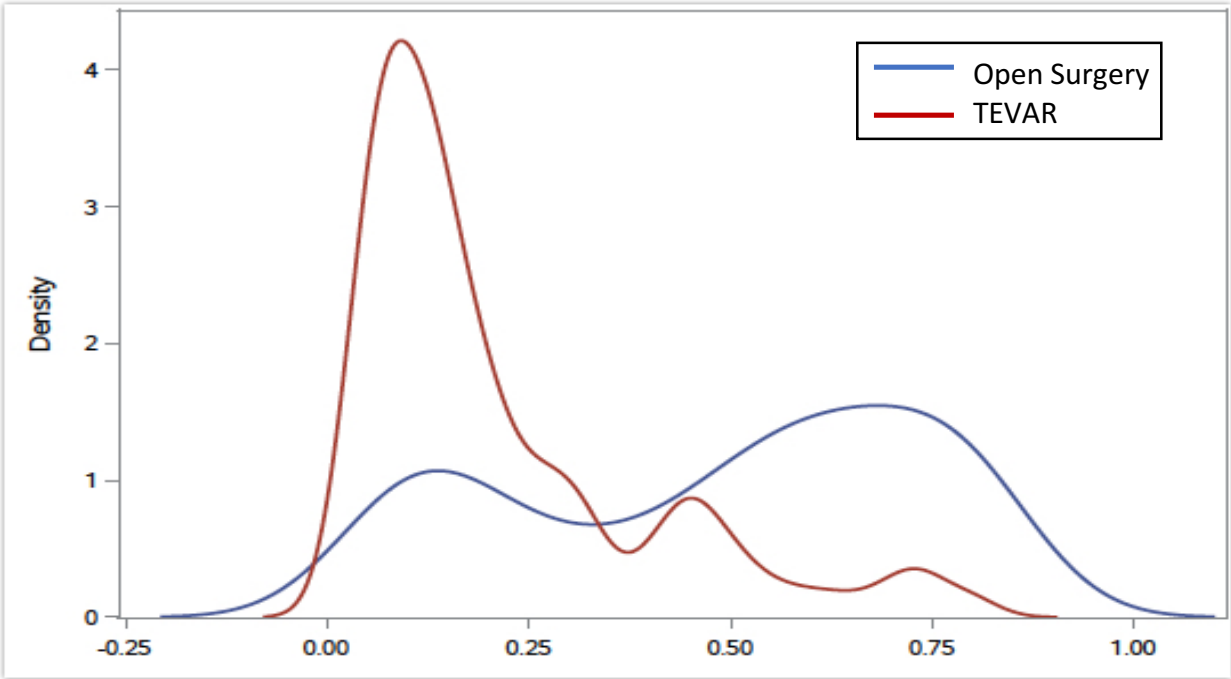
Table 10. Inverse Probability of Treatment Weights Excluding IMH Patients

	First Model		Second Model - no IMH Patients	
	IPTW	sIPTW	IPTW	sIPTW
Median	1.23	0.83	1.29	0.82
IQR	(1.10, 1.63)	(0.76, 0.98)	(1.13, 1.82)	(0.74, 1.01)
Minimum Value	1.01	0.31	1.03	0.35
Maximum Value	17.9	5.26	13.3	4.6
Range	16.9	4.94	12.3	4.26

IQR, Interquartile Range; IPTW, inverse probability of treatment weighting; sIPTW, stabilized inverse probability of treatment weights.

Table 11. Weighted Standardized Mean Difference of Variables Excluding IMH Patients

	First Model Weighted SMD	Second Model Weighted SMD- no IMH
Age, years	0.1238	0.1211
Sex	0.1533	0.1074
Height, cm	-0.1160	-0.1460
Weight, kg	0.0897	0.0427
BSA	0.0740	0.0275
Hypertension	0.0893	0.1066
Dyslipidemia	0.1835	0.1459
Smoking	0.1984	0.1082
Weighted Charlson Comorbidity Score	0.2402	0.2297
Prior Cardiac Surgery	-0.0434	-0.0444
Aneurysm	0.2204	0.1158
Acute Type B Dissection	-0.2195	-0.1815
Chronic Type B Dissection	0.0142	-0.0483
PAU	-0.1609	0.0287
IMH	-0.3677	-

SMD, Standardized Mean Difference; cm, centimetre; kg, kilogram; PAU, penetrating atherosclerotic ulcer; IMH, intramural hematoma.

The propensity score model was revised a third time, including the square of the weighted Charlson Comorbidity score. Propensity scores in both treatment groups were again assessed for overlap with minimal change in trends from the first iteration (Figure 22). Twelve outlying patients were removed again in the trimming procedures to improve the distribution overlap (Figure 23). The median IPTW matched that of the second model at 1.29, while the maximum value was slightly lower (12.6 vs 13.3). Stabilization resulted in the best model of the three with the lowest maximum value at 4.25 and the smallest range (3.91) (Table 12). Weighted SMDs showed that the transformation of the weighted Charlson Comorbidity score variable was successful and all variables now had an acceptable SMD under our cut off of 0.2 (Table 13).

Figure 22. Kernel Density Plot of Propensity Scores Using Transformed Variable
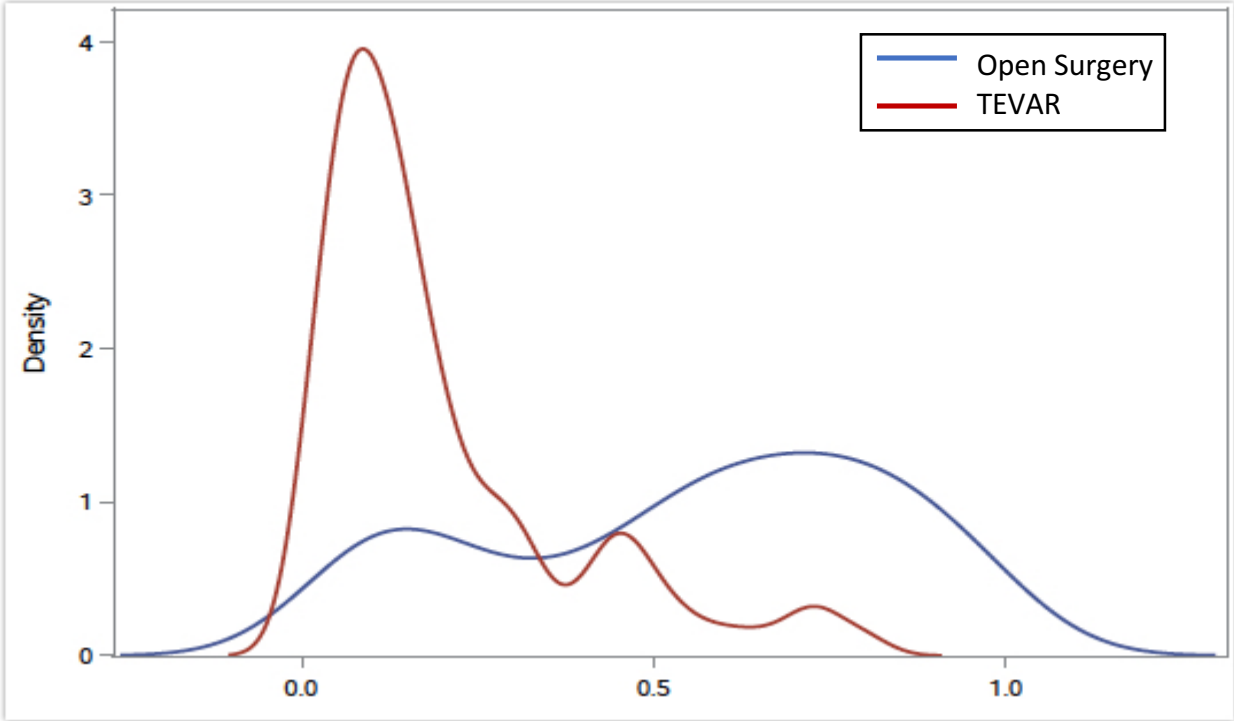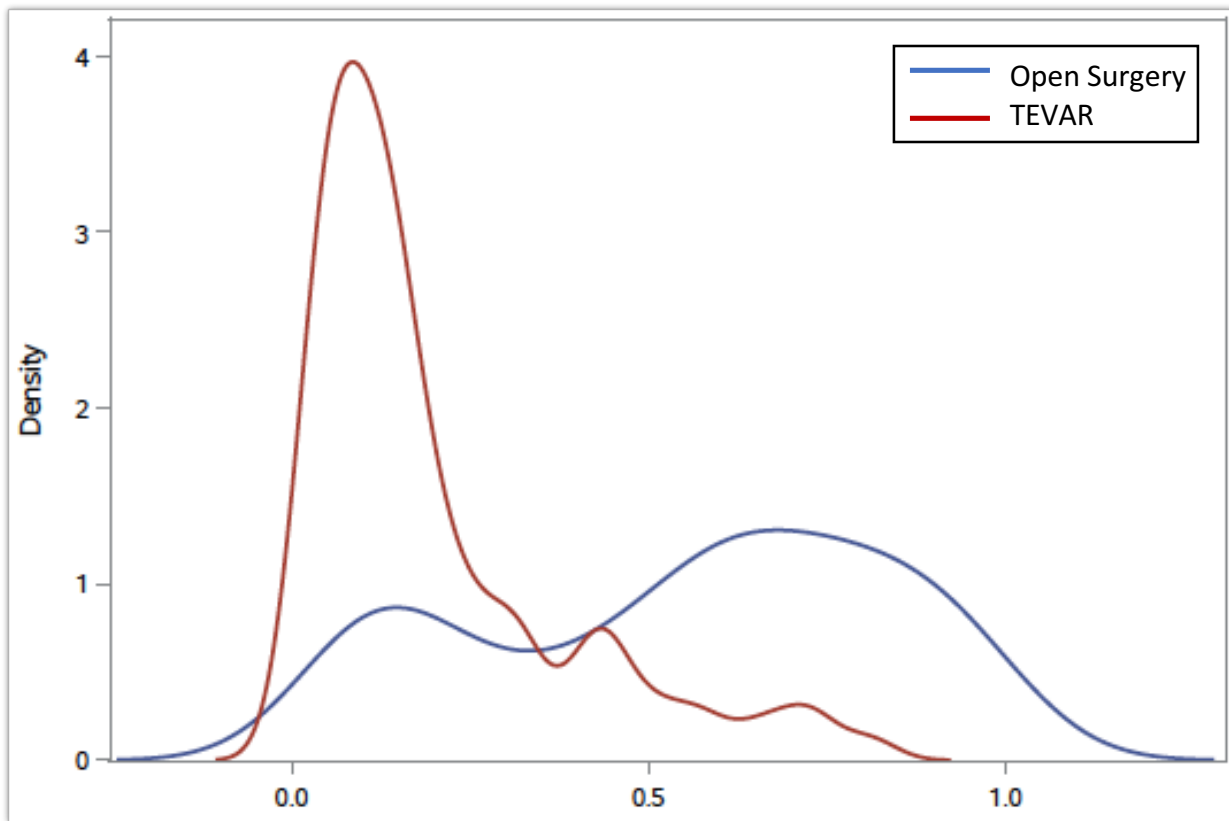
Figure 23. Kernel Density Plot of Propensity Scores Using Transformed Variable Following Trimming of Outliers
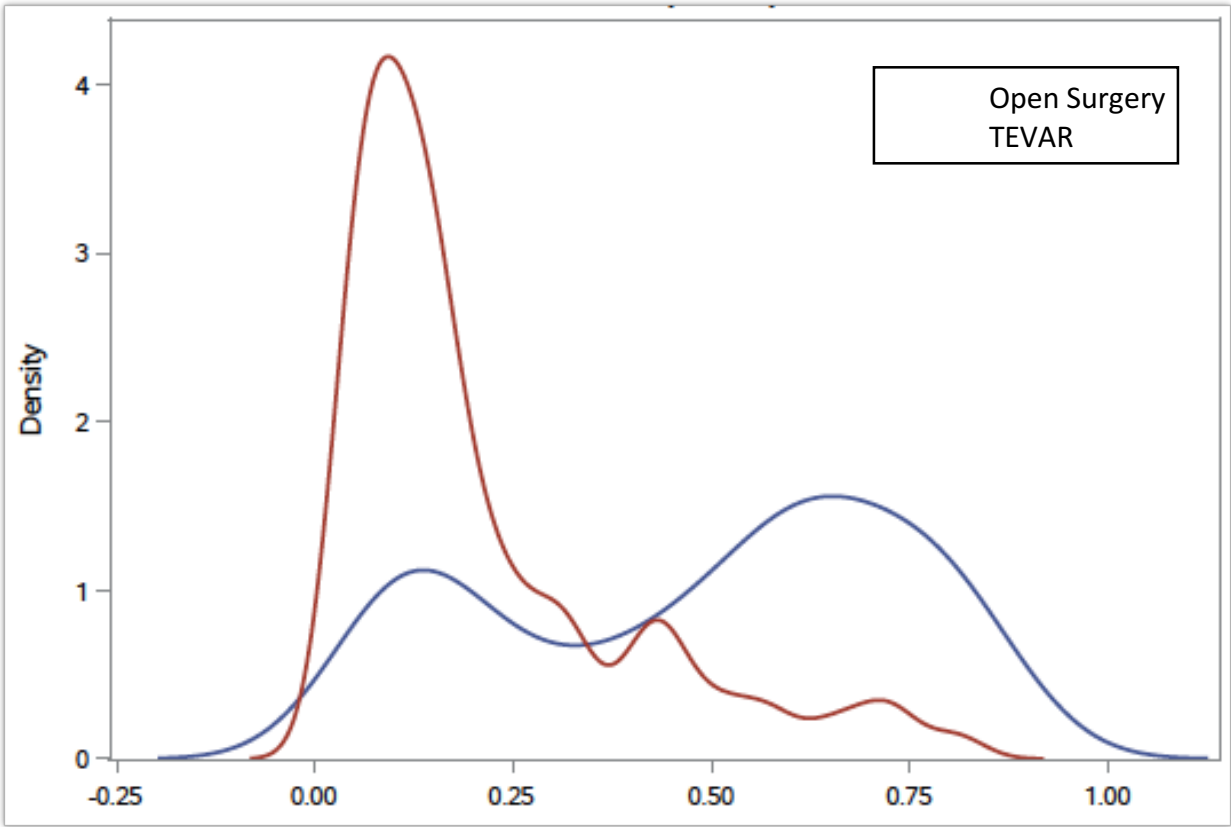
Table 12. Inverse Probability of Treatment Weights Including Transformed Variable

	First Model		Second Model - no IMH Patients		Third Model - transformed variable	
	IPTW	**sIPTW**	**IPTW**	**sIPTW**	**IPTW**	**sIPTW**
Median	1.23	0.83	1.29	0.82	1.29	0.82
IQR	(1.1, 1.6)	(0.76, 0.98)	(1.13, 1.82)	(0.74, 1.01)	(1.13, 1.77)	(0.75, 1.02)
Minimum Value	1.01	0.31	1.03	0.35	1.03	0.34
Maximum Value	17.9	5.26	13.3	4.6	12.6	4.25
Range	16.9	4.94	12.3	4.26	11.6	3.91

IQR, Interquartile Range; IPTW, inverse probability of treatment weighting; sIPTW, stabilized inverse probability of treatment weights.

Table 13. Weighted Standardized Mean Difference Including Transformed Variable

	First Model Weighted SMD	Second Model Weighted SMD- no IMH	Third Model Weighted SMD- Transformed variable
Age, years	0.1238	0.1211	0.0678
Sex	0.1533	0.1074	0.0536
Height, cm	-0.1160	-0.1460	-0.1269
Weight, kg	0.0897	0.0427	0.0497
BSA	0.0740	0.0275	0.0356
Hypertension	0.0893	0.1066	0.0967
Dyslipidemia	0.1835	0.1459	0.1324
Smoking	0.1984	0.1082	0.0592
(Weighted Charlson Comorbidity Score)^2	0.2402	0.2297	0.0852
Prior Cardiac Surgery	-0.0434	-0.0444	-0.0297
Aneurysm	0.2204	0.1158	0.0898
Acute Type B Dissection	-0.2195	-0.1815	-0.1714
Chronic Type B Dissection	0.0142	-0.0483	-0.0287
PAU	-0.1609	0.0287	0.0477
IMH	-0.3677	-	-

SMD, Standardized Mean Difference; cm, centimetre; kg, kilogram; PAU, penetrating atherosclerotic ulcer; IMH, intramural hematoma.

After establishment of the propensity score model and stabilized weights, the Cox Proportional Hazards Model was carried out for functional survival. There was a total of 25 functional survival events (death and or long term care admission) and 94 censored events in 119 patients. The median follow up time was significantly longer for the open surgery group (4.3 years vs 2.3 years, p = 0.0001). The proportional hazards assumption tested using Schoenfeld residuals was satisfied. There appeared to be no significant difference between TEVAR and open groups in functional survival out to 15 years (HR 1.509; 95% CI 0.629, 3.617; p=0.3565) (Figure 24).

Due to small numbers of included patients, exploration of the effect of era and socioeconomic status on functional survival was not possible.

Figure 24. Cox Proportional Hazards Model for Long Term Functional Survival After Surgery on the Descending Aorta
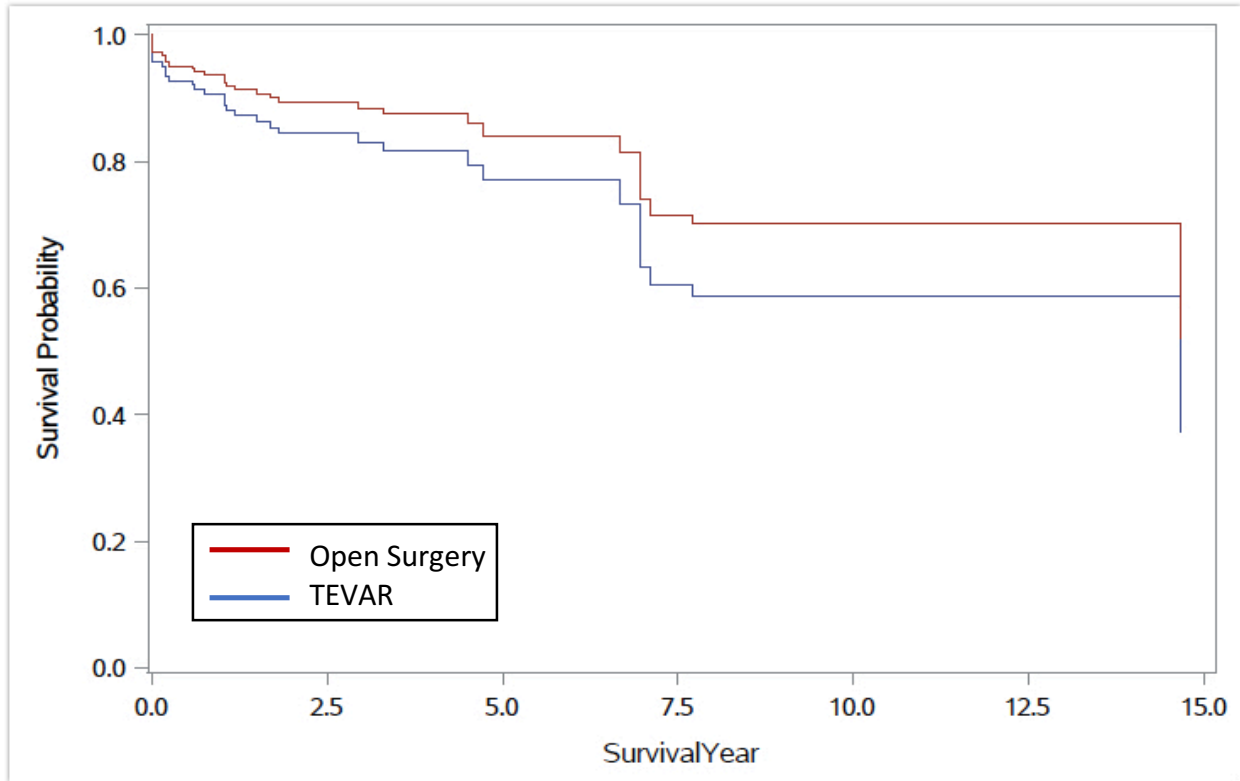
Post Hoc Power Analysis

Following a significant reduction in the number of patients included in our cohort, an exploratory sample size calculation was carried out. With our sample size of 119 patients, and 25 events (death or long term care admission), we would require a hazard ratio of at least 3.4 to make a definitive conclusion regarding this outcome (Table 14).

Table 14. Exploratory Power Calculation Given Sample Size and Event Rate

α (2 tailed)	0.05	
β	0.2	
q1	0.3	Proportion of patients in open surgery group
q0	0.7	Proportion of patients in TEVAR group
Total Events in Study	25	
Relative Hazard Required to Conclude Significance	3.4	

Secondary Outcomes

Due to small values, it was not possible to report data for death, long term care admissions and all but one of the post-operative major adverse event variables. The incidence of respiratory failure was significantly higher in the open surgery group (23%) compared to 2% in the TEVAR group (p=0.026) (Table 15). The median hospital length of stay was also significantly longer in open surgery patients at 17 days compared to 6 days in TEVAR patients (p<0.0001). The ICU length of stay is not reported due to insufficient data. There were 91 hospitalizations in 41 TEVAR patients, and 33 hospitalizations in 20 open surgery patients within the first year following the initial procedure. The total number of patients with readmission (49% TEVAR vs 57% open, p=0.073) and the median number of readmissions per patient was not significantly different between groups (TEVAR: median 0, IQR (0, 2); Open: median 1, IQR (0, 1); p=0.89). In open surgery patients, 75% of the readmissions were unrelated to post-operative complications, cardiac or vascular issues whereas in TEVAR patients 49% of the readmissions were post operative/cardiac/vascular and 51% were due to other causes (p=0.0122). In both treatment groups, approximately two thirds of patients were discharged home with no support post operatively, while 20 to 30% required transfer to another acute inpatient institution, continuing care (personal care home or rehabilitation facility), home care with support or death prior to discharge.

Table 15. Summary of Secondary Outcomes

	TEVAR n=84	Open Surgery n=35	p value
Post Operative Major Adverse Events:			
In hospital mortality	-	-	-
Myocardial Infarction	-	-	-
Stroke	-	-	-
Kidney Failure Requiring Dialysis	-	-	-
Paraplegia	-	-	-
Paraparesis	-	-	-
Respiratory Failure	6 (7.14%)	8 (22.9%)	0.026
Hemorrhage	-	-	-
Reoperation	-	-	-
Hospital Length of Stay, days Median (IQR)	6 (4, 11)	17 (10, 26)	<0.0001
ICU Length of Stay	-	-	-
30 Day Mortality	-	-	-
All Cause Death	-	-	-
Long Term Care Admissions	-	-	-
Repeat Hospitalization Within 1 Year of Procedure:			
Total Hospitalizations	91	33	-
Number of Patients Hospitalized	41 (48.8%)	20 (57.1%)	0.073
Readmissions per Patient (median, (IQR))	0 (0, 2)	1 (0, 1)	0.89
Reason For Repeat Hospitalization:			
Post op/Cardiac/Vascular	45 (49.5%)	8 (24.2%)	
Other	46 (50.55%)	25 (75.8%)	0.0122
Discharge Disposition:			
Home with no Support	58 (79.45%)	20 (68.8%)	
Transfer/Continuing Care/Home with Support/Death	15 (20.55%)	9 (31%)	0.26

IQR, InterQuartile Range; ICU, Intensive Care Unit; -, value suppressed

Discussion

During our characterization of degenerative TAD in Manitoba, we found that the age standardized incidence and prevalence has been steadily increasing over the last 19 years. Sex disparity remains, with men having twice the average annual incidence compared to women. While men have a higher yearly incidence and prevalence, the age standardized incidence appears to be rising faster in women. Both the age standardized incidence and prevalence were significantly higher in the Winnipeg region, however prevalence in all five Manitoba regions is increasing with time most notably in the North. In hospitalized patients, the incidence of aneurysm has increased while the incidence of dissection and rupture has been stable over time. Although, overall prevalence of all three conditions continues to increase.

Our comparison of functional survival in patients undergoing TEVAR and open surgery to repair the descending aorta was challenging due to the decrease in sample size. Despite development of a weighted propensity score model, we were unable to draw any conclusions from our results regarding the functional survival outcome.

Epidemiology of Degenerative Thoracic Aortic Disease

Case Identification

Until very recently [2], there had yet to be an epidemiological description of TAD in a Canadian patient population. In this study published in February 2018, McClure et al used de-identified administrative data housed at the Institute of Clinical Evaluative Sciences in Ontario. Despite their robust cohort including more than 13.5 million people, only trends in the yearly incidence were examined and data was restricted to hospital admissions and hospital based ambulatory visits [2]. Our study encompasses all inpatient and outpatient diagnoses as well as changes in the prevalence of TAD over time which provides a more complete picture of the province wide burden of disease. McClure also describes a novel algorithm for the stratification of type A versus type B dissections as well as a cross referencing method using multiple databases for case identification however, no formal validation procedures utilizing a gold standard or reference population have been included in the manuscript. Unlike other conditions such as chronic kidney disease [112], there has yet to be a universally accepted and appropriately validated case

identification method published for TAD. This is likely related to challenges associated with the use of administrative data and method of ICD coding for TAD.

As a publicly funded health care system, data from a variety of sources is routinely collected in each province, which can provide a wealth of information regarding the health of its citizens and function of the system as a whole. One of the downfalls in utilizing administrative data for research is as the name implies; the data is gathered primarily for administrative purposes which can make translation for use in a research setting difficult. This became apparent when developing a strategy to identify patients with degenerative thoracic aortic disease in Manitoba. The ICD coding system specific for aortic disease requires four digits to distinguish thoracic aortic pathology from abdominal aortic pathology. The medical services claims data uses a three digit ICD-9 code ('441') which meant we were unable to exclude the patients with abdominal aortic disease using ICD coding alone. Identifying patients within the hospital abstracts was not an issue, as the diagnoses are recorded using a four digit ICD-10 code. Additionally, patients in the MTAD database had all been assigned a diagnosis upon assessment in the clinic. Therefore, for patients who only had an outpatient diagnosis (ie. had no hospital diagnosis of TAD and had never been seen in clinic) we had to develop a method to exclude patients with abdominal disease using other available data in conjunction with the medical services claims.

Regardless of the method of initial detection, the gold standard in diagnosis of thoracic aortic disease is a CT scan of the thorax or a cardiac CT scan. As a first step, we conducted an exploratory analysis to determine the effect of limiting patients with a '441' diagnosis code in the medical services claims to those who also had a thorax or cardiac CT scan 3, 6 or 12 months before or after their diagnosis. To validate this method, we used patients from the MTAD database with a confirmed TAD diagnosis as our reference population. When using the criteria of a 441 diagnosis in medical services plus a cardiac or thorax CT within 12 months, we correctly captured all patients in our reference (MTAD) population. This validation step ensures we are less likely to exclude patients with thoracic versus abdominal disease.

When developing the criteria for case identification, it was acknowledged that patients with abdominal aortic aneurysms and thoracic disease have much in common and there is the

potential for overlap between pathologies. Therefore, it was important to determine whether patients with abdominal disease were as likely to get a chest CT scan as those with thoracic disease. In other words, was the proposed methodology over inclusive of AAA patients? To accomplish this, the incidence of chest CT scan within twelve months of AAA diagnosis in hospitalized patients was examined and only 16% of them had a scan. While this is reassuring, two additional methods were used to further refine the method for case identification and avoid erroneous inclusion of AAAs:

1) For each medical services claim, it is possible to identify the specialty of the physician who has submitted the claim and made the diagnosis. Using this code, 1910 patients were excluded who had only been assigned a '441' diagnosis by a vascular surgeon. This represents approximately 55% of the cohort prior to exclusion, an important step in making sure we are capturing the correct pathology. Any patient with a diagnosis by a cardiac surgeon, in addition to a vascular surgery diagnosis or alone was retained. Patients who had been diagnosed with aortic disease by a physician other than a vascular or cardiac surgeon were also retained. These patients are important, as they represent outpatients followed in the community primarily by family doctors or internal medicine specialists, who have not yet been seen by a cardiac surgeon. It is only possible to speculate as to the reason why these patients have not been referred. Perhaps the aneurysm is relatively small and the family doctor feels comfortable with management, or maybe the patient lives in a remote location and has been unable to travel to Winnipeg for consultation. Regardless, treatment and follow up patterns in the community are an important part of the management of TAD and will be the focus of future study.

2) From the remaining cohort, 114 patients (8%) with a hospital diagnosis of AAA alone, with no associated thoracic diagnosis were excluded. At this point, we were confident we had established an outpatient cohort as specific for thoracic aortic disease as possible using the data we had available. Further omission criteria were not employed for fear of over exclusion.

Overall, it is felt that the final cohort of 4264 patients using data from available three sources is an appropriate representation of all diagnosed TAD in Manitoba. Given the nature of

administrative data and the ICD coding, it is still possible that there are errors in diagnostic coding, misclassification or over inclusion. In addition, certain radiology groups in Manitoba are paid by salary not fee for service and therefore do not provide CT scan data billing data to the MCHP, so this portion of patients may not be captured however this is a system level issue over which we had little control.

Incidence and Prevalence of Thoracic Aortic Disease

Baseline characteristics for patients in our cohort are consistent with known risk factors for vascular disease. The population was primarily male, with high rates of hypertension, dyslipidemia and diabetes. Sixty-five percent of patients had a diagnosis of pulmonary disease, perhaps reflecting the association of smoking with degenerative aortic pathology. A significant number of patients also had cardiac comorbidities including 46% with congestive heart failure and 26% with myocardial infarction. Overall the burden of comorbidities was high, with a median weighted Charlson comorbidity score of 5. This equates to a projected 10 year survival of only 21% using Charlson's prediction model [113]. With the exception of gender, all of the comorbidities mentioned are potentially modifiable, highlighting the importance of preventative medicine and risk factor management in the treatment of aortic disease.

Overall, the total age standardized incidence and prevalence of degenerative TAD in Manitoba is increasing. We suspect that the increasing incidence is primarily related to improvements in imaging technology and a corresponding increase in the number of imaging tests done, as most asymptomatic aneurysms and dissections are diagnosed incidentally on imaging. This theory is supported by data presented in Figure 4 which shows that the number of thorax and cardiac CT scans done in the province has also increased significantly over time. The correlation between trends in imaging and incidental diagnosis has also been described for adrenal masses, where the prevalence has increased from a mean of 0.64% in the 1980's and early 90's to 4.4% in 2006 [114, 115]. Presumably, the more scans that are done for whatever reason, the more likely an incidental diagnosis is to be made. Additionally, in the early to mid-2000's, CT pulmonary embolism (PE) studies essentially replaced ventilation/perfusion (V/Q) testing to become the standard imaging modality used for diagnosis of PE[116], which has most certainly contributed to the growth in CT scan rates.

Notably, the total prevalence as well as the prevalence stratified by sex has quadrupled over the course of the study. In 2016, the incidence and prevalence peaked in males at 32 per 100 000 and 325 per 100 000 population, and in females at 17 per 100 000 and 146 per 100 000 respectively. These numbers are significantly higher than what has been previously reported in the literature, however most studies present data on specific aortic pathologies (ie. dissection or aneurysm)[2, 3, 16, 17] rather than all TAD combined.

Perhaps the best comparative study is one published by Olsson et al describing the age and sex adjusted incidence for all TAD in Sweden from 1987 to 2002 [18]. Similar to our data, they found that the incidence of TAD in both males and females was increasing over time (52% and 28% respectively) [18]. However, the overall incidence of TAD in Manitoba was still approximately double what Olsson found in both genders. It is hard to know for sure what might account for these differences, although the baseline characteristics of the Swedish cohort were not published. Presumably there are inherent differences in the Swedish population that may make development of TAD less likely. Manitoba residents are known to have a relatively high burden of disease, including established risk factors for the development of vascular disease. Nearly 30% of Manitoban's over the age of 20 are hypertensive, 9% of people over the age of 1 have diabetes, and 54% of people live with one or more chronic conditions [117], all of which could contribute to the increased results in our study.

The Swedish study also only used diagnoses found in hospital abstracts, which excludes anyone who had an isolated outpatient diagnosis, and effectively decreases their reported incidence. This is a common issue when evaluating the literature on the epidemiology of TAD. Inconsistencies in available data sources and the prolonged asymptomatic progression of TAD makes it difficult to establish a true incidence and prevalence. Studies using hospital abstracts make up the bulk of the literature providing a description primarily of symptomatic TAD, without capturing the large outpatient population living with the disease [2, 21-24, 118]. Our study now presents one of the largest cohorts reflecting both inpatient and outpatient diagnoses, providing a more representative estimate of the diagnosed incidence and prevalence of TAD.

Interestingly, there is an isolated decrease in the prevalence of TAD during the 2005 year. The total age standardized incidence is also decreased, although when examined by gender the incidence actually increased in males. To our knowledge, there was no significant change in radiology services at this time that would cause such a solitary decrease in diagnosed cases. Conversion to digital imaging services did not occur until 2007 and does not seem to have affected incidence or prevalence data. It is possible that a systematic change in administrative data collection may have occurred resulting in this trend. Perhaps the largest change in data coding and collection occurred with the implementation of ICD-10 coding, which took place in Canada starting in the year 2000. This is unlikely to have contributed to what we observe in 2005, therefore the cause is still unclear.

Given the disproportional number of men affected by TAD, we anticipated the age standardized incidence and prevalence to be higher than in women. Interestingly, over the 19-year study period the incidence in women actually increased to a greater extent compared to men. The reasons for this are unclear. There has been an growing awareness of the severity of female vascular disease in the literature surrounding AAA epidemiology and pathophysiology. While estrogen has been shown to provide protective effect against the development of AAA, women who end up with abdominal aneurysms have a faster rate of growth and an increased incidence of rupture [119, 120]. While routine screening for AAA is not currently recommended in women [117], physicians and patients may be more aware of symptoms and risk factors for aortic disease leading to an increase in investigation and diagnoses.

Evidence of the protective effect of estrogen may be apparent in our data when comparing the average annual incidence of TAD between men and women. During pre-menopausal years (age 30-59), the average annual incidence was over three times higher in men than in women. Between the ages of 60 and 80, the average annual incidence in women increases six-fold, narrowing the rate ratio to 1.7 per 100 000 from age 70 to 79. Currently there is no validated screening program in place for TAD, however identifying and treating risk factors for aortic disease is important for both men and women, especially over the age of 60.

The age specific incidence and prevalence has followed an interesting trend over the study period. The incidence of TAD was highest in the 70 to 79 age category until 2014, when the 60 to 69 category saw the highest number of new cases. In 2016, both the incidence and prevalence were higher in the 60 to 69 age group with a significant decline from 60 to 80 years. These results can be explained in the context of changing trends in the Manitoba population over the same period (Figure 5). In 1998, the baby boomer generation can be seen on the population pyramid between ages 30 and 50. Degenerative TAD, especially aneurysms take some time to develop and at younger ages this cohort of people is less likely to be affected. The population of people over the age of 70 in 1998 is relatively small, however they are more likely to have disease and thus the age specific incidence and prevalence in this category is higher. By 2016, the baby boomer generation is now older and there is a larger population existing at an age when TAD is more likely to develop.

When examined by region, the age standardized incidence and prevalence of TAD was significantly higher in Winnipeg. We suspect this result is driven by differential access to health care and radiology services as many diagnoses of TAD are made incidentally on imaging. Winnipeg is the smallest of all five regions, but has the largest population and the highest concentration of CT scanners. People living in large urban centers like Winnipeg have greater access to health care providers and are closer to imaging services, and therefore are more likely to undergo CT scans, chest X rays and echocardiograms for any reason. The Prairie Mountain region which has the second highest incidence and prevalence includes Brandon, Manitoba's second largest city. Within this region there are only two CT scanners for 170 000 people, however the region is also serviced by the most health care centres at 36. The Northern region also has two CT scanners, although the region encompasses a far greater area than Prairie Mountain. Despite 30 health care centres, the incidence and prevalence of TAD in the North is consistently the lowest amongst all five regions. This may reflect ongoing difficulty accessing healthcare over such a large geographical area resulting in relative under diagnosis compared to other regions. While access to CT scans is important, patients must first see a physician to obtain an imaging referral therefore, the availability and proximity of health care services is an important factor in diagnosis of asymptomatic TAD.

Interestingly, the overall incidence of TAD in Winnipeg has increased 45% over the study period, while incidence in the remaining four regions has been relatively stable. As reported by the Manitoba government, the percentage of people over the age of 65 is increasing in all five regions, so these findings are not likely related to a regional difference in aging trends [121]. It could possibly be due to a greater expansion of imaging services and primary care access across Winnipeg compared to the other four regions however this is difficult to confirm.

The increase in the prevalence of TAD from 1998 to 2016 is quite striking, with the Winnipeg region prevalence quadrupling over the 19-year period. While the Northern region continues to have the lowest overall prevalence amongst the five Manitoba regions, it has seen the largest growth, increasing nearly 6-fold from 1.8 per 100 000 to 10.4 per 100 000 population. The significant growth in prevalence is a bit surprising, especially in regions other than Winnipeg which have seen a relatively stable incidence over time. If the number of new cases is not increasing in each region per year, perhaps fewer people are dying. During the study period, significant advances have been made in the operative management of thoracic aortic disease including the adoption of deep hypothermic circulatory arrest (DHCA), ACP and endovascular therapies, and in general surgical outcomes have improved. Additionally, the importance of medical therapy and risk factor management in the prevention and treatment of cardiac and vascular disease has been emphasized since the mid-1990's by major policy development groups including the Canadian Task Force on Preventive Health Care and the United States Preventive Services Task Force. There have also been significant improvements in the delivery of health care in remote regions in Manitoba, which may account for the large increase in prevalence in the Northern health region. The J.A. Hildes Northern Medical Unit has been expanded since its inception in 1970 to serve 3 northern hospitals, 12 rural nursing stations and 8 health care centers in Nunavut [122]. The use of telehealth services to facilitate specialist consultation and follow up care, has also improved access to the health care system for those living in remote areas. When taking these factors into consideration, it is possible to explain the increasing prevalence by improved survivorship.

When examining the epidemiology of TAD broken down by pathology, we found the age standardized incidence of TAA in hospitalized patients increased 28% to 10.9 per 100 000

population in 2016. Available literature provides a wide variety of estimates from 3.5 per 100 000 population to 10.4 per 100 000 person years [2, 16, 17, 20]. The most recent study using administrative data from Ontario, Canada reported a TAA incidence of 7.6 per 100 000 population [2]. Although this is lower than our incidence estimate, there was less morbidity amongst the Ontario patients particularly in conditions considered risk factors for the development of TAD, with approximately 20% diagnosed with diabetes, 75% with hypertension and 30% with dyslipidemia [2]. In the Manitoba cohort, 30% had diabetes without diabetes related complications, 88% were hypertensive and 72% had dyslipidemia. Despite these differences, this contemporary data is probably a better representation of the true incidence of TAA in hospitalized patients in Canada compared to what has been reported in older international studies.

The incidence of thoracic aortic dissection in hospitalized patients was constant during our study at approximately 3 per 100 000 population per year. This is consistent with several previous reports that place the incidence of dissection between 2.5 and 5 per 100 000 [2, 19, 20, 22, 24]. Interestingly, two previous authors have also reported a stable incidence of AD during their study period. Thoracic aortic dissection and aortic rupture often result as a complication of TAA. Despite an increasing incidence of TAA in our study, the number of newly diagnosed aortic dissections and ruptures has been relatively unchanged. This suggests perhaps that the management of TAA, both medical and surgical has improved with time, preventing a corresponding increase in the incidence of AD and rupture.

Prevalence estimates for thoracic aortic pathology are infrequently reported in the literature. Two studies using CT scans from screening trials found an unadjusted TAA prevalence of 158 to 260 per 100 000 population, which is significantly higher than our reported prevalence of 97 per 100 000 in 2016. Based on their methods, these estimates represent more of a 'point prevalence' than an annual prevalence as we have reported. Due to the robust nature of our data source at the MCHP, we incorporated both patient death as well as relocation into our annual prevalence calculation. It is unclear as to whether the previous authors considered these important factors, which could account for the higher numbers reported in their studies.

Long Term Functional Survival in Endovascular versus Open Descending Aortic Repair

Study Population

The comparison of functional survival in patients undergoing TEVAR and open surgery for descending thoracic aortic repair was challenging. Several unanticipated events occurred resulting in a significant reduction in our sample size. When considering patients for inclusion in the study, we did not account for the degree of overlap between the two procedures. Therefore, patients who had an open surgery and then subsequently a TEVAR (or vice versa) were included in the preliminary counts for both the open surgery and TEVAR groups. Upon development of our final cohorts, patients were classified based on their first procedure type and we realized our total patient number was lower than initially expected.

Upon linkage of our MTAD data with the MCHP, we had to exclude another 16 patients who were from out of province, as the MCHP only provides administrative data for residents of Manitoba with a Manitoba Health card number. This is one of the major drawbacks of using MCHP data, especially for projects related to the Manitoba Cardiac Sciences Program. The St. Boniface Hospital in Winnipeg is the only tertiary care centre offering specialized cardiac care in the province. In addition to serving nearly 1.3 million Manitobans, patients from northwestern Ontario, western Saskatchewan and Nunavut often come to Winnipeg for treatment as it may be the closest centre to their area of residence. This is an important consideration for future studies related to Cardiac Surgery as there are a significant number of patients within our complete MTAD database as well as the Manitoba Cardiac Surgery database for which long term data at MCHP will not be available.

Our initial data collection included all patients who underwent a TEVAR or open procedure on the descending thoracic aorta regardless of pathology. Upon stratification by pathology it became clear that we could not include patients who had undergone repair for coarctation of the aorta or thoracic aortic trauma in the same study as those with degenerative disease. Traumatic aortic injury (TAI) or aortic rupture primarily occurs due to motor vehicle accidents. The sudden deceleration forces upon collision pull the mobile ascending, arch and proximal descending aorta against the fixed descending aorta which can cause a tear or frank rupture. Patients with TAI tend to be younger, with a median age of approximately 40 to 55 years, and have fewer

comorbidities than those with aneurysms or dissections [123-125]. Coarctation is a genetic condition causing narrowing of the lumen of the aorta is usually diagnosed in childhood or early adulthood depending on the severity of symptoms. Like the trauma population, patients who undergo coarctation repair are therefore much younger and healthier than those with degenerative disease [126]. Given the differences in baseline characteristics between the trauma/coarctation population and degenerative population, we could not feasibly combine the two and expect to reasonably control for confounding.

During the study planning phase, the decision to include patients with thoracoabdominal aneurysms (TAAA) in our cohort was entertained. The treatment of TAAAs requires more extensive procedures with a higher degree of complexity than aneurysms isolated to the thoracic aorta. Surgical repair is extremely invasive with an increased risk of complications including, respiratory complications, paraplegia and renal failure than TAA repair [6, 33, 39, 127]. Similarly, endovascular repair with TEVAR usually requires use of fenestrated graft techniques and potentially staged procedures. This not only increases procedure time and radiation dose, but also the potential for spinal cord injury as spinal arteries are not re-implanted. However, the underlying process of aortic degeneration is similar for all three major pathologies (TAAA, TAA and AD). In light of our already small patient numbers, we elected to keep the TAAA patients in the cohort despite these potential differences.

Outcome Analysis

To mimic the effect of randomization and control for confounding variables we used a propensity score analysis for the functional survival outcome. We initially explored propensity score matching, however it quickly became clear that we would lose well over half of our remaining sample size as unmatched patients were discarded. Inverse probability of treatment weighting was instead employed to try and maintain as many patients within our sample size as we could. A kernel density plot was used to assess the degree of propensity score overlap. Patients with extreme propensity scores in areas where the curves do not overlap are inherently different from the rest of the cohort, therefore trimming improves the balance of baseline covariates. An additional 12 patients with propensity scores in the top and bottom 5% required exclusion following the propensity score overlap assessment.

Finally, during model development we found that the weighted standardized mean difference for the IMH variable was exceedingly high. Seventeen patients in our cohort had a diagnosis of IMH and 16 out of 17 had treatment with TEVAR. Clinically, IMH of the descending aorta is thought to be less serious than a type B dissection as there is no entry tear in the intima of the vessel. Management is primarily with medical therapy, and then TEVAR if complications arise. As evidenced by treatment assignment in our patients, open repair of IMH in the endovascular era is uncommon. As only one patient in our cohort with IMH had open repair, we were unable to stratify our analysis on this variable to try and control for the variable imbalance. We then elected to exclude the IMH patients from our analysis all together, further reducing our already limited sample size.

The reduced cohort of patients impacted the project in two ways. First, the primary outcome analysis was a challenge. Due to the small number of patients, the likelihood of achieving acceptable covariate balance in the weighted SMD calculation was much lower than if using a more robust cohort. A range of acceptable SMD's from 0.1 to 0.25 have been reported by various authors in the literature, with 0.1 generally acknowledged as the conventional cut off [128-133]. In the first iteration of the model, only 5 out of 15 variables were under a cut off of 0.1. Removal of the IMH patients reduced the SMD values to some extent however there were still 9 variables over the cut off. An exploratory analysis was done to see if direct adjustment within the cox proportional hazards model for the variables with SMD greater than 0.1 would account for the residual imbalance. The results were similar to the analysis done without direct adjustment for these variables (HR 1.7 vs 1.5, p=0.28 vs p=0.35), and we questioned the utility of including 15 variables in the propensity score model only to direct adjust for 9 of them again in the Cox model. While it is ideal to strive for an SMD less than 0.1, in small observational studies such as ours it may not be realistic. In light of this, we decided to use a more conservative SMD cut off of $\pm$ 0.2 [130, 131], accepting the fact that we are unlikely to achieve ideal variable balance in this small population. In doing this, the only variable with a SMD greater than 0.2 was the weighted Charlson comorbidity score. Running the model again with this variable transformed using a square function significantly improved the covariate balance in the entire model with all variables less than 0.2, and 11 out of 14 less than 0.1.

The third iteration of our weighted propensity score model was used to complete the time to event Cox proportional hazard analysis. With very small number of included patients, there was also a small number of events with 25 patients dying or admitted to long term care facilities. Technically, this meets the 'events per predictor variable' criteria with greater than 10 events per predictor, however lack of precision is evidenced in our results. The hazard of poor functional survival in patients undergoing TEVAR was 50% higher than for open surgery but this difference was not significant (p value = 0.36). The confidence interval was very wide, from 0.629 to 3.6 indicating uncertainty as to the true treatment effect. In an exploratory 'backwards' power calculation, we determined that with our sample size, and number of events we would require a hazard ratio of 3.4 to make a meaningful conclusion about the treatment effect, which is more than double what we actually observed. To claim significance with a hazard ratio of 1.5, we would require 227 events in a sample population with similar distribution to ours (30% of patients in the open surgery group and 70% in the TEVAR group). Therefore, we are unable to make any definitive conclusions regarding the impact of treatment type on long term functional survival after surgery on the descending thoracic aorta.

In addition to difficulty with the primary outcome analysis, our limited sample size also affected our ability to report several key baseline characteristics and secondary outcomes. To ensure patient privacy, the MCHP requires suppression of any values less than 6 or those where a value less than 6 could be deduced using the presented data. Consequently, the number of patients in our cohort with a history of hypertension, dyslipidemia, peripheral vascular disease, myocardial infarction, congestive heart failure, renal disease and previous cardiac surgery had to be suppressed, limiting our ability to thoroughly compare the two treatment groups. Additionally, we were not able to examine the proportion of patients with acute versus chronic type B dissection. This is an important distinction as the pathology, treatment and overall risk profile for these patients is very different. Death and long term care admission, the individual components of our functional survival outcome were not reportable, which again contributes to the difficulty in interpreting our primary outcome. Finally, several perioperative outcomes including in hospital mortality, myocardial infarction, stroke, kidney failure, paraplegia, paraparesis and reoperation for bleeding were suppressed. These are important variables in the comparison of

endovascular and open therapies for pathology of the descending aorta as much of the argument for using TEVAR centers around reducing the risk of morbidity and mortality following open surgery.

We were still able to report important outcome variables that impact both physical health as well as quality of life. The incidence of post-operative respiratory failure was three times higher and the hospital stay 11 days longer in patients who underwent open repair, as one would expect with a more invasive procedure. Fewer TEVAR patients required readmission to hospital within the first year following their procedure, however this result only trended towards significance (p=0.07). TEVAR patients were more likely to require readmission for post-operative complications, cardiac or vascular reasons than open surgery patients. Unlike open repair of the descending aorta where the segment of diseased vessel is physically removed, the aneurysm or dissection in endovascular repair remains. In aortic dissection, stents are usually only placed to cover the entry tear which often leaves a large segment of residual dissection. This can progress to aneurysmal dilatation of the chronic dissection or rupture, requiring further hospitalization and intervention which may account for the results we see here.

Despite significant challenges with our analysis, the question of functional survival in these patient populations remains an important one. The bottom line is, we require a much larger sample size to make any reasonable conclusions. In completing this project, we have established appropriate methods and SAS coding which could potentially be used at other centres to examine functional survival in a larger cohort. The Canadian Thoracic Aortic Collaborative (CTAC) group is an organization made up of aortic surgeons from across Canada who are involved in outcomes and guidelines base research. Several collaborative projects involving data collected and analyzed from multiple centers have already been completed. The next step in this research will involve engagement of the CTAC group to assess the feasibility of proceeding with a multi-centre study looking at long term functional survival in thoracic aortic disease on a national level.

Limitations

Our research has several limitations, primarily related to working with retrospective administrative data. While the data housed at MCHP is robust, it was not collected specifically for use in this project therefore the data was not always available in the format we required. The three digit ICD codes provided in the medical services data made development of our case identification method more difficult. While we are confident it appropriately captures the population of interest, misclassification of patients may have occurred despite our best efforts. Additionally, the data available in each dataset is collected by many people in different settings across the province, and is susceptible to data entry, classification and coding errors over which we have no control.

The completeness of medical services claims for thorax and cardiac CT scans is dependent on the Radiology funding arrangement across the province. Only scans done by radiologists who are fee for service, or who shadow bill will be captured in the medical services claims. Certain groups use an alternate funding plan whereby radiologists are paid a set salary, without shadow billing. If this is the case, information on specific scans does not get transferred to MCHP. This primarily occurs at the HSC Women's Pavilion, St Boniface, Brandon, Selkirk and Dauphin Hospitals although the agreement between scans done at each centre and the availability at MCHP has improved over time.

The data sets housed at MCHP do not include First Nations residents living on reserve, out of province patients who received treatment in Manitoba for whatever reason, and those not registered with Manitoba Health. So while the data generated is at a population level, we can't say it encompasses every resident of Manitoba.

When examining the epidemiology of thoracic aortic disease, we are determining the *diagnosed* incidence and prevalence from 1998 to 2016. This does not capture every single person who is living with aortic disease. Due to its insidious nature, many people remain asymptomatic and go undiagnosed for years, therefore it is likely impossible to calculate a *true* incidence and prevalence. In addition, the mortality for patients who experience type A dissection and thoracic aortic rupture is very high with up to 50% of patients dying prior to reaching the hospital [19,

134]. Any study examining outcomes in dissection or rupture patients is faced with this dilemma. Autopsy results are often used to try and estimate the out of hospital incidence but depending on the jurisdiction, autopsies may not be completed on every patient who dies outside of a health care facility.

Finally, the size of the final cohort used in the functional survival comparison was very small. This significantly affected our model development and made it difficult to control for confounding variables. We also were unable to report several baseline characteristics and secondary outcomes in accordance with the MCHP's policy on small values reporting. Ultimately, the small numbers rendered our time to event analysis comparing functional survival in TEVAR and open surgery patients inconclusive.

Conclusion

In our population level study, we found the incidence and prevalence of TAD increased significantly over the 19-year study period, especially in women and the Winnipeg region. We suspect that this growth is related to a corresponding increase in the use of advanced imaging techniques, resulting in a higher number of incidental diagnoses. The growing number of women diagnosed with TAD may be related to an increased awareness amongst practitioners of the risk and mortality associated with aortic disease in women. Regional trends appear to be associated with the patient's proximity to an urban centre, which provide greater access to imaging facilities.

With the aging baby boomer population, we expect the number of people affected by TAD will only continue to increase. The MTAD clinic is the only center responsible for the management of patients with TAD, serving a very large geographical area including all of Manitoba, Northwestern Ontario, western Saskatchewan and parts of Nunavut. To maintain the high level of medical, surgical and follow up care provided in the MTAD clinic in the current era of increased patient demand, improvements in infrastructure, funding and support services are required.

Unfortunately, the impact of endovascular versus open surgical treatment on functional survival after repair of the descending thoracic aorta remains to be seen. Multi-centre collaboration with other aortic surgery groups across Canada is required to provide enough data to complete this important analysis.

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Appendix 1: Description of Data Sources

Database	Data Years	Specific Variables and Rationale
Hospital Separations Abstracts	1994/95 to 2016/17	Hospital admission date, discharge date, all ICD 10 diagnosis codes, tariff codes (if available), fields related to outpatient/inpatient definition, costing data (RIWs). This information will allow for characterization of patient comorbidities, and post operative outcomes.
Medical Claims (Physician Billings)	1994/95 to 2016/17	Service date, diagnosis code, tariff codes (if available). Coding to differentiate between family practitioner and specialist. Data will be used to identify comorbidities, as well as post operative care requirements.
Drug Program Information Network	1995/96 to 2016/17	DIN codes (drug type and name), date of fill, dosage. Prescribing records will be used as part of the diagnosis and verification of pre-operative comorbidities such as hypertension, diabetes and dyslipidemia.
Long Term Care – Utilization History	1994/95 to 2016/17	Date of entry to or exit from a long term care facility (if available). Information on all long term care admissions, discharges and level of care is provided and is a critical component of determining our primary outcome
Home Care – MSSP and VON Home Care – MDS Assessment	1994/95 to 2016/17 2000 to 2016/17	Dates of homecare assistance (if available) duration of homecare assistance. Home care claims will be analyzed to determine if there is any difference between requirements of care pre and post-operatively
Manitoba Health Insurance Registry	1994/95 to 2016/17	Date of death (if available), end of coverage date (if available), any other fields related to Manitoba Health coverage definition, Postal Code of residence. Allows for the identification of all individuals who have been registered under Manitoba Health including migration in and out of the province as well as date and reason for coverage cancellation. This will be useful in determining the reason for patient censorship during our follow up period.
Income/Employment Assistance (SAMIN)	1995/96 to 2016/17	Start date of income assistance receipt, duration of income assistance receipt.

		We will use this data as an indicator of socioeconomic status within our patient population
Publically Available Census Data	1996, 2001, 2006, 2011, 2016 Census Years	Define average neighbourhood family income based on dissemination area level income from census data. We will use this data as an indicator of socioeconomic status within our patient population
Vital Statistics Mortality	1994/95 to 2016/17	Cause of death (where available) and date of death. This will be an integral part of determining our primary outcome.
Emergency Care - ADT and E-Triage	1999/00 to 2009/10	Date of ER visit, diagnosis for ER visit. Information will be used to examine the incidence and etiology of repeat patient presentation to hospital following their index procedure
Emergency Department Information System	2007/08 to 2016/17	Date of ER visit, diagnosis for ER visit. Information will be used to examine the incidence and etiology of repeat patient presentation to hospital following their index procedure
Manitoba Cardiac Surgical Database	1994/95 to 2016/17	All fields in database. This data will provide diagnostic information, preoperative comorbidities, procedural details and post operative complications.

Appendix 2: ICD- 9 and ICD – 10 Codes for Aortic Diseases

Pathology	ICD-9 Code	ICD-10 Code
Coarctation of aorta	747.10	Q25.1
Dissection of aorta, unspecified site	441.00	I71.00
Injury to thoracic aorta	901.0	S25.0
Dissection of thoracic aorta	441.01	I71.01
Dissection of thoracoabdominal aorta	441.03	I71.03
Rupture thoracic aneurysm	441.1	I71.1
Thoracic aortic aneurysm without rupture	441.2	I71.2
Ruptured aortic aneurysm unspecified site	441.5	I71.8
Thoracoabdominal aneurysm rupture	441.6	I71.5
Thoracoabdominal aneurysm without rupture	441.7	I71.6
Aortic Aneurysm unspecified site without rupture	441.9	I71.9
Thoracic Aortic Ectasia	447.71	I77.810
Thoracoabdominal aortic ectasia	447.73	I77.812

Appendix 3: ICD – 9 and ICD -10 Codes for Relevant Comorbidities

Comorbidity	ICD-9 Code	ICD-10 Code
Charlson Comorbidity Index:		
Myocardial Infarction	410, 412	I21, I22, I25.2
Congestive Heart Failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93	I43, I50, I09.9, I11.0, I13.2, I25.5, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9, P29.0
Peripheral Vascular Disease	093.0, 437.3, 440, 441, 443.1, 443.2, 443.8, 443.9, 447.1, 557.1, 557.9, V434	I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular Disease	362.34, 430, 431, 432, 433, 434, 435, 436, 437, 438	G45, G46, I60, I61, I63, I64, I65, I66, I67, I68, I69, H34.0
Dementia	290, 294.1, 331.2	F00, F01, F02, F03, G30, F05.1, G31.1
Chronic Pulmonary Disease	416.8, 416.9, 490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505, 506.4, 508.1, 508.8	J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J63, J64, J65 J67, I27.8, I27.9, J68.4, J70.1, J70.3
Connective Tissue Disease-Rheumatic Disease	446.5, 710.0, 710.1, 710.2, 710.3, 710.4, 714.1, 714.2, 714.8, 725	M05, M32, M33, M34, M06, M31.5, M353, M360
Peptic Ulcer Disease	531, 532, 533, 534	K25, K26, K27, K28
Mild Liver Disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570, 571, 573.3, 573.4 573.8, 573.9, V427	B18, K73, K74, K70.0, K70.1, K70.2, K70.3, K70.9, K71.7, K71.3, K71.4, K71.5, K76.0, K76.2, K76.3, K76.4, K76.8, K76.9, Z94.4
Diabetes without complications	250.0, 250.1, 250.2, 250.3, 250.8, 250.9	E10.0, E10.1, E10.6, E10.8, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9
Diabetes with complications	250.4, 250.5, 205.6, 250.7	E10.2, E10.3, E10.4, E10.5, E10.7, E11.2, E11.3, E11.4, E11.5, E11.7, E12.2, E12.3, E12.4, E12.5, E12.7, E13.2, E13.3, E13.4, E13.5, E13.7, E14.2, E14.3, E14.4, E14.5, E14.7
Paraplegia and Hemiplegia	334.1, 342, 343, 344.0, 344.1, 344.2, 344.3, 344.4, 344.5, 344.6, 344.9	G81, G82, G04.1, G11.4, G80.1, G80.2, G83.0, G83.3, G83.4, G83.9

Renal Disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582, 583.0, 583.1, 593.2, 583.4, 583.6, 583.7, 585, 586, 588.0, V420, V451, V56	N18, N19, N05.2, N05.3, N05.4, N05.5, N05.6, N05.7, N25.0, I12.0, I13.1, N03.2, N03.3, N03.4, N03.5, N03.6, N03.7, Z49.0, Z49.1, Z49.2, Z94.0, Z99.2
Cancer	140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157 ,158, 159, 160, 161, 162, 163, 164, 165, 170, 171, 172, 174, 175, 176, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 200, 201, 202, 203, 204, 205, 206, 207, 208, 2386	C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C11, C12, C13, C14, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24, C25, C26,C30, C31, C32, C33, C34, C37, C38, C39, C40, C41, C43, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C60, C61, C62, C63, C64, C65, C66, C67, C68, C69, C70, C71, C72, C73, C74, C75, C76, C81, C82, C83, C84, C85, C88, C90, C91, C93, C94, C95, C96, C97
Moderate or Severe Liver Disease	456.0, 456.1, 456.2, 572.2, 572.3, 572.4, 572.8	K70.4, K71.1, K72.1, K72.9, K76.6, K76.7, I85.0, I85.9, I86.4, I98.2
Metastatic Carcinoma	196, 197, 198, 199	C77, C78, C79, C80
AIDS/HIV	042, 043, 044	B20, B21, B22, B24
Other Comorbidities:		
Hypertension	401, 402, 403, 404, 405	I10, I11, I12, I13, I15, I16
Dyslipidemia	272	E78