Hospitalization and Readmission among Congenital Heart Disease Patients in Canada

by

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Abstract

The prevalence of congenital heart disease (CHD) is rising, particularly among adults. The rise is particularly prominent for CHD with complex lesions. The impact of these changes on the healthcare system/resource is not known.

The first part of this thesis used the hospital discharge abstract data from the Canadian Institute for Health Information and assessed temporal changes in hospitalizations of CHD patients in Canada from 2003 to 2009. Poisson regression analysis was performed to assess temporal changes in the hospitalization rate, stratified by age, sex, and severity of CHD. Increasing inpatient service utilization over time was observed among adult CHD patients particularly in older patients and those with complex CHD.

The second part of this thesis focused on determining the readmission rate among CHD patients and identifying risk factors associated with readmission. Poisson regression was used to analyze the readmission rates by age, sex, and severity of CHD. Logistic regression analysis was performed to identify risk factors associated with readmission within two weeks and one month after discharge. The hospital readmission was common among CHD patients particularly among patients aged 40 years or older, males and those with complex CHD.

The pattern of inpatient health service utilization by CHD patients in Canada presented in this study would help policy makers to adopt appropriate strategies to meet the increasing demands of this expanding population. In addition, findings on readmission and associated risk factors from our study would facilitate clinicians to identify high-risk patients. We need further studies focusing on the healthcare cost of hospital admissions as well as unplanned readmission among CHD patients.

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List of abbreviations

CHD	Congenital heart disease
CCASS	Canadian Congenital Anomalies Surveillance System
CIHI	Canadian Institute for Health Information
DAD	Discharge Abstract Data
ICD	International classification of disease
CCP	Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures
CCI	Canadian Classification of Health Interventions
TOF	Tetralogy of Fallot
TGA	Transposition of great arteries
VSD	Ventricular septal defect
ASD	Atrial septal defect
HLHS	Hypoplastic left heart syndrome
IE	Infective endocarditis
CAD	Coronary artery disease
CVA	Cerebrovascular accidents

Chapter 1

Introduction

1.1 Literature review

1.1.1 Congenital heart disease

Congenital heart disease (CHD) is the most common birth defect leading to infant mortality (1, 2) and disability in youth and adult life (3). Congenital heart disease is defined as "a gross structural abnormality of the heart or intra-thoracic great vessels that is actually or potentially of functional significance" (4). Over the past two decades, survival of children with CHD to adolescence and adulthood has increased due to improvements in medical and surgical management in early childhood - resulting in a rapidly growing adult CHD population (5).

1.1.1.1 Prevalence

Incidence is defined as the number of new cases developed in a defined population over a period of time. Given the definition of incidence, incidence for CHD would be the number of new cases of CHD in utero since CHD is a developmental defect occurring during the gestational period. However, because of termination of pregnancy or spontaneous abortion, the number of cases in-utero cannot be readily measured. Therefore, birth prevalence is the most practical measure of expressing disease burden at birth for CHD (6).

Hoffman *et al.* reviewed 44 international articles that measured the birth prevalence of CHD. In most of the literature, the birth prevalence rate was approximately 8/1,000 live births varying between 4/1,000 live births and 50/1,000 live births (7). The prevalence of moderate and severe forms of CHD was about 6/1,000 live births and increased to 19/1,000 live births if bicuspid aortic valve was included (7). The prevalence of CHD including all forms increases to 75/1,000 live births when tiny muscular ventricular septal defect (VSD) and other trivial lesions are considered (7).

An English study found 1,942 cases of CHD in a population of 377,310 live births after reviewing all births in one health region (Newcastle) between 1985 and 1994 resulting in an incidence of 5.2 per 1,000 live births (8). However, in most population-based studies from the end of the 1990s onward, the reported prevalence of CHD ranges from 8 to 13 per 1,000 live births. In the US from 1998 to 2005, a study using data from a population based birth defects surveillance system in Atlanta reported a CHD prevalence of 8 per 1,000 live births and that of critical CHD (includes cyanotic defect, hypolastic left heart syndrome and pulmonary atresia) of 1.6 per 1,000 live births (9). Using EUROCAT registry, a total 26,598 cases with CHD were reported in 16 European countries from 2000 to 2005 with a prevalence of 13/1,000 live births (10). Moos *et al*. conducted a population based study in Belgium using hospital based data and followed 111,225 children born in 2000 for 5 years. The documented prevalence of CHD was 8.3 per 1000 live births in Belgium and 51% of them were girls (11). In the Netherlands, the prevalence of CHD increased from 7.3 to 11.3 per 1000 live births between 1977 and 2005. The prevalence started increasing in the early 1980s, and then became stable during the late 1990s (12). The underlying reasons for variation in reported birth prevalence in different studies include variations in case ascertainment, type of CHD lesions included, inclusion of term or preterm babies and geographic areas included.

In Canada, the Canadian Congenital Anomalies Surveillance System (CCASS) is an ongoing and passive population-based surveillance system established in 1996. The source of data for CCASS is the hospital Discharge Abstract Data (DAD) obtained from the Canadian

Institute for Health Information (CIHI). CHD cases are ascertained up to the first 30 days of life. In Canada the birth rate of CHD showed a decreasing trend from 1998 onwards. The reported birth rate of CHD was 11 per 1,000 total births in 1998, 9.5 per 1,000 total births in 2003 and 8.5 per 1,000 total births in 2009 in Canada except the province of Quebec, including both live births and stillbirths (13). The rate of CHD was found to be different in different provinces; Newfoundland and Labrador, Quebec and Alberta showed approximately 1.2 to1.5 times higher birth rate of CHD than the Canadian average. Nunavut had almost two times increase in birth rate of CHD than the Canadian average. However, the estimates for Nunavut, Newfoundland and Labrador were not stable. British Columbia showed approximately 0.8 times lower rate and the rate was slightly lower in Manitoba and Newbrunswick than the Canadian average. (13). However, there are some limitations of the CCASS report: it uses only inpatient data. Consequently, cases diagnosed on an ambulatory basis are not captured. As well, some cases of CHD are not discovered in the first month of life. Prenatal diagnosis of congenital anomalies before 20 weeks of gestation that resulted in termination of pregnancy would not be captured (http://www.apheo.ca/index.php?pid=202).

1.1.2 Changing Epidemiology of congenital Heart Disease

1.1.2.1 Advances in diagnostic and therapeutic management

Surgical procedures to repair congenital heart defects have been evolving over seven decades first starting back in 1938 with ligation of a patetnt ductus arteriosus (PDA) (14). Newer techniques are introduced to treat complex lesions (14). Availability of more effective diagnostic tools for example fetal echocardiography as well as better therapeutic and postoperative management of CHD patients have resulted in improved survival of CHD patients (15-19). In the current era, patients with CHD are living longer leading to an increasing prevalence of CHD; pediatric patients now become postoperative adult survivors (20).

1.1.2.2 Trends in mortality and improvement in survival

Mortality of patients with CHD declined significantly over the past two decades. Whereas in the 1950s only 20% of infants or newborns with moderate or complex lesions survived their first year of life (21), more recent studies showed that 85% to 90% children with CHD survive to adulthood (22, 23). In Finland, a population-based retrospective analysis of 6,336 CHD children who underwent pediatric surgery showed a 45-year (1953 to 1998) survival rate of 85% after excluding operative mortality (22). A study of 7,497 CHD patients born between 1970 and 1992 showed that among patients who were born between 1990 and 1992, approximately 90% survived to adulthood which was significantly higher than the preceding decade (23).

Two studies using CDC data reported reduced mortality in CHD patients over time in the US. The annual mortality among all ages of CHD patients decreased in the US by about 39% from 2.5 to 1.5/ 100,000 population between 1979 and 1997 (24). The decline in mortality was even more profound during a more recent time period; a 50 to 75% reduction in mortality was found (depending on the CHD lesion) between 1980 and 2005 (25).

In addition, mortality due to arrhythmia and heart failure has been decreasing over time irrespective of age and type of lesion. Arrhythmia was the primary cause of death before 2000, while myocardial infarction was a more common cause after 2000 (25).

In England between 1995/1996 and 2003/2004, a hospital-based study showed that the age-standardized population mortality rate with CHD reduced by 26% across all ages in patients with CHD as the primary diagnosis (26). The mortality reduction reported in this study was lower than those published in other studies. The lower reduction may have been due to the fact that the study population was hospitalized patients, i.e., more complicated patients.

Although mortality rate reduced in all ages, disproportionate reduction in mortality was observed across the age groups. In the English study, the largest proportionate decrease was in children between 1 to 4 years followed by children aged 5 to 14 years. Among all deaths, 40% of deaths occurred in adults aged 45 years and older (26). Similar to this finding, in Quebec the largest reduction in mortality was in children with CHD; the mortality rate in children with CHD reduced by 59% exceeding that of children in the general population. By contrast, the reduction in mortality rate of adult CHD patients was 16%, very similar to that of the general adult population. However, in patients aged 65 years and above the mortality rate remained stable. Moreover, survival of CHD patients improved more (37% mortality reduction) in later period (2002 to 2005) than that observed in the first period of study (1987 to 1990) (27).

In addition, median age at death increased indicating that most patients are surviving to adolescence and adulthood (24). Marelli *et al.* found that the median age at death increased in CHD patients from 2 years to 23 years during the observation period of 1987 to 2005 (27). Mortality rate was consistently higher in males than females over the period of study (26). This is consistent with the fact that complex cyanotic lesions like transposition of great arteries and hypoplastic left heart syndrome are more common in male patients and patients with complex CHD are vulnerable to develop more complications.

Survival patterns also differ by type of lesions. A longitudinal follow up for 43 to 54 years of a total of 1,000 children with CHD, having the first initial cardiac consultation at the

University of Minnesota between 1952 and 1963 showed normal survival of patients with ventricular septal defect (VSD), atrial septal defect (ASD) and patent ductus arteriosus (PDA) but lower survival in patients with aortic stenosis and cyanotic defects such as transposition of great arteries (TGA) and tetralogy of Fallot (TOF). However, survival was lower if VSD, ASD and PDA are associated with other conditions (28).

Now more effective interventions are available for moderate and complex CHD leading to significant improvement in survival with time among patients with moderate and severe defects. The mortality rate declined substantially in TGA (71%) and TOF (40%) for all age patients in the US between 1979 and 2005 (25). In Quebec 67% reduction in mortality has been observed in children with severe CHD between 1987 and 2005 (27).

Though birth prevalence of CHD has been falling in Canada over time, improvement of survival of these patients would contribute to the increasing prevalence of CHD patients, particularly in adults. Also the distribution of types of CHD is changing over time. Therefore, there will be more adult CHD patients as well as more patients with complex CHD seen in foreseeable future.

1.1.2.3 Demographic shift and increasing burden

Improvement in survival of CHD children to adulthood leads the epidemiology of congenital heart disease to change over time with emergence of a new expanding population of adults with CHD. Congenital heart disease should be considered now a life-long condition spanning from fetal life to advanced age.

A systematic review of 10 studies revealed the worldwide prevalence of CHD in adults to be approximately 3 per 1,000; 3% and 15% of them accounted for severe and moderate lesions, respectively (29). The data should be interpreted cautiously as the review did not depict the regional differences and substantial heterogeneity existed across the studies in terms of different case definitions and data collection methods.

A population-based study showed increasing prevalence of CHD both in children and adults in Quebec. Over a 15-year period of study, the prevalence of CHD increased by 73% in children whereas in adults it increased by 14%. The largest increase in prevalence over time was in 13 to 18 years of age followed by those in 18 to 25 years. In addition, the prevalence of severe CHD increased more in adults compared to that in children (85% vs. 22%). Though the prevalence of CHD was higher in children, the absolute number of adults with CHD was higher than that of children and the number of adults and children with severe CHD was nearly equal by the year 2000 (5). Another study conducted in Quebec reported that, among the adult general population, a 37% increase in the prevalence of CHD in 18 to 64 years age from 1990 to 2005; but constant in the population of 65 years old and above (30).

A study conducted in one health region of UK predicted that each year there would be more than 1,600 cases added to the existing adult CHD population. This number was predicted to continue to increase linearly over time and with increasing complexity (8).

In the year of 2000, the prevalence of CHD was 11.9 per 1,000 children, 4.1 per 1,000 adults and 5.78 per 1,000 in the general population in Quebec. Extrapolating these observed prevalence to the Canadian population of 24 million, the authors estimated around 96,000 of the Canadian adult population would have CHD in the year 2000, and 9,000 of them would have severe lesions (5). According to Task Force 1 of the 32nd Bethesda conference, by the end of 2006 the number of adult survivors with CHD would increase to 124,000 (21). In 2000, the total number of adults living with CHD in the United States was estimated to be 800,000; 47% of them had simple CHD, 38% with moderate CHD and 15% with simple CHD (21). It is estimated, using the data from an English study (8) to the population of 280 million in the U.S that in the U.S, there would be 8,960 new adult CHD cases each year. Extrapolating the Canadian data to the US population, in 2010 there would be approximately 2 to 3 million CHD patients in US; among them the estimated number of children would be between 975,000 and 1.4 million and that of adult would be between 959,000 and 1.5 million (31).

1.1.3 Impact of congenital heart disease

1.1.3.1 Impact on patients' health

In patients with CHD, the physiology of the body's system is compensated due to the presence of long standing heart defects and most of the therapeutic interventions are reparative or palliative leading to residual injuries, sequelae or complications later on (32). Problems arising in CHD patients may be electrophysiologic disturbances, valve disease, persistent intracardiac shunting, myocardial dysfunction, lesions of the pulmonary or systemic circulation, problems associated with prosthetic materials, infectious complications, thromboembolic event or extravascular disturbances affecting multiple organs and systems. The problems may arise due to defect itself, effect of therapeutic procedures, hemodynamic abnormalities or complications (33).

Infective endocarditis

Infective endocarditis (IE) is one of the most important complications occurring in CHD patients particularly in patients with valvular lesions and postoperative patients such as shunt, prosthetic valve or conduit (34, 35). The most frequent complications leading to death in IE patients are valvular regurgitation (30%), cardiac failure (23%) and systemic emboli (23%) (36).

In CHD patients who had surgical repair before 19 years of age, 25-year cumulative incidence of IE following surgery varied between 1 and 11.5 cases per 1,000 patient years (37). In a large population-based cohort of children with CHD, who were followed up to 18 years of age since birth, the cumulative incidence of IE was 6.1 per 1,000 children or 4.1 per 10,000 patient years (38). On the hand, the incidence of IE was 3 times higher in adult CONCOR (CONgenital CORvitia) CHD patients (11 per 10,000 person years) compared to that of children reported in earlier study (39). Moreover, the incidence of endocarditis has increased with the growing population of patients with CHD (40).

Risk of IE depends on the type of CHD present; defects that lead to high velocity or turbulent flow of blood such as VSD, aortic stenosis, coarctation of the aorta are found to be associated with higher risk of IE (41, 42). In children, cyanotic defects, endocardial cushion defects and left sided lesions predispose to IE more frequently than ASD (38). The cumulative incidence of IE after 25 years post surgery was 1.3% for TOF, 2.7% for isolated VSD, 3.5% for coarctation of aorta, 13.3% for valvular aortic stenosis and 2.8% for premium atrial septal defect (37). The pattern of IE has changed over time; target being transitioned to corrective surgery with prosthetic valve, complex cyanotic CHD, small VSD and dental cause (43). It can be expected as rising number of adult CHD patients and patients with complex lesions resulting in increased incidence of IE in these patients than before.

Arrhythmia

Electrophysiological disturbances like arrhythmias are the most frequent long-term complication of CHD leading to morbidity (44) and sudden cardiac death (26%) in adulthood (45). Patients with CHD are 8 times more likely to experience atrial fibrillation in comparison to their age and sex matched control (46). It remains the most common cause of hospitalization in adult CHD patients (47, 48) and 37% of emergency admissions in CHD patients are due to arrhythmia, particularly supraventricular tachyarrhythmias including atrial fibrillation and atrial flutter (49).

Arrhythmia may occur in any type of CHD lesions; but the risk is high in moderate and complex defects (50, 51). Patients with TOF, TGA and patients having Fontan procedure, atrial switch procedure mostly experience arrhythmia. About one third of patients with repaired TOF developed symptomatic atrial tachycardia (52). Among patients with single ventricle who had undergone a right atrial to pulmonary artery Fontan procedure, 50% developed atrial tachycardia within approximately 15 years of surgery (53). There are several underlying mechanisms for developing arrhythmia in CHD patients such as extensive suture line, damage to atria during performing atrial switch procedure and underlying hemodynamic abnormality (54).

Heart failure

Heart failure occurs in a considerable proportion of adults with congenital heart disease in their life time and is one of the major important causes of death in adult CHD patients (55). Patients with single or systemic right ventricles are particularly at risk (56, 57).

Unlike infective endocarditis, which is more common in left sided heart defects, heart failure in patients with congenital heart disease is predominantly caused by right-sided heart disease (58-61). Moderate to severe heart failure is present in approximately 40% of adult patients who underwent the Fontan procedure and in over 20% of those having the Mustard procedure (56, 62).

Coronary artery disease and cerebrovascular accident

With aging the adult with CHD experienced the added risk of acquiring the coronary artery disease (CAD) and cerebrovascular accident which further increases the burden of the disease. Recent evidence suggests that coronary artery intimal proliferation, a precursor of atherosclerosis responsible for development of CAD, is common among young children with CHD, particularly among those who underwent congenital heart surgery (63). CAD was present in about 9.2% of 250 adult CHD patients who selectively underwent coronary angiography (64). Retrospective analysis of 208 patients with TOF revealed similar prevalence of cardiovascular disease as in the general population. However, in 29 to 39 years and 40 to 59 years old male patients, the prevalence were significantly higher than that of age and gender matched general population (30% vs. 14%; 63% vs. 29%) (65). However, in cyanotic CHD patients, cyanosis play protective role against the development of the atherogenesis of coronary artery by causing hypocholesterolemia, hypoxemia, upregulated nitric oxide, hyperbilirubinemia and low platelet counts (66).

A study using aggregated European and Canadian CHD population found 10 to 100 times higher incidence of cerebrovascular accident (CVA) in CHD patients compared to the general population. One in 50 adult patients may develop CVA through his or her mid-life. Patients with cyanotic lesions have 10 times higher risk than average to develop CVA. The types of CHD that lead to arrhythmia or thromboembolic event more frequently are associated with increased risk of CVA (67).

Other comorbid conditions or complications

Beside the cardiovascular system, CHD also affects other organs or systems of body and may result in complications like glomerulopathy, proteinuria, hyperuricemia, brain abscess, respiratory tract infection, and pulmonary hypertension (68-72). Some of them are rare conditions, but may pose serious life threatening effect.

1.1.3.2 Impact on the health care system

Because of the increasing prevalence of CHD particularly in adults, the healthcare service utilization has been rising throughout the lifespan of CHD patients. A U.S study found more than two times increase in the annual number of hospitalization among adult CHD patients between 1998 and 2005 which account for 357% increase in total national charges for adult CHD admissions. Moreover, patients having complex CHD had more comorbid conditions than those having simple CHD. The number of comorbid conditions increased leading to increase hospital costs (73). Another study conducted in Belgium observed higher expenditure in health care for patients with CHD compared to the age and gender corrected expenditures for the general population (74). In England, 16% increase in the age-standardized hospitalization rate has been found in CHD patients over a 10-year period; mostly among the older patients of 45 to 64 years old. In the UK, patients with CHD showed higher care resource utilizations than patients with no CHD in terms of more referral to specialist care, higher number of prescription issued and increased number of GP consultations (26, 46).

Investigation of CONCOR (CONgenital CORvitia) CHD populations showed that the hospital admission rate in the year 2005 was high in all age groups, ranging between 11% in the youngest age group and 68% in oldest age groups. Moreover, the hospital admission rate was 2 to 3 times higher in CONCOR CHD patients above 30 years of age than that of the Dutch CHD population; with a more prominent increase in older age patients. Majority of the hospital admissions were cardiovascular origin (61%) especially arrhythmia (75).

In Canada, data regarding the healthcare service utilization in CHD patients are scarce. A Quebec study observed a higher rate of healthcare service utilization in adults with CHD patients between 1996 and 2004. Among adult CHD patients, 91% had GP visits, 87% received outpatient specialist care, 68% visited emergency room and around half of the patients needed hospitalization over eight years period of study. Hospitalization rate and mean length of hospital stay were higher in CHD patients relative to that in the general population (76). Another population-based study found a higher readmission rate among children with CHD especially in severe lesion over a 15-year period in Quebec (77). There has been 44% and 269% increase in patients receiving ambulatory care in the Toronto Congenital Cardiac Centre for adults between 1987 to 1992 and 1992 to 1997, respectively (78). However, none of these studies showed how the healthcare burden has been changing among CHD patients in Canada across different age groups.

1.2 Knowledge gap and justification of this study

From the above discussion, the prevalence of CHD is rising particularly in adults as most patients born with CHD now survive to adulthood. There are now more adult CHD patients than children and the number of adults with CHD would continue to increase. Majority of the patients have reparative or at least palliative surgery in their early life. Therefore, survivors of CHD are mostly postoperative patients. These patients are at increased risk of developing sequelae due to intrinsic defect, secondary to therapeutic intervention or hemodynamic abnormality. In addition, CHD patients acquire other comorbid conditions in their adulthood. As a result, burden on the healthcare system by CHD patients is increasing, particularly with increasing age, complexity of the disease. The epidemiology of healthcare utilization by CHD patients is expected to be changing over time with changing epidemiology of CHD. There are several studies showing increase in healthcare service utilization in CHD patients in different countries. However, data is lacking in Canada.

This thesis used hospital discharge abstract data from 2003 to 2009 obtained from CIHI. The dataset contains demographic and clinical information of patients receiving inpatient care in Canada except Quebec. This study will help us to understand the extent and pattern of healthcare service utilization by CHD patients and identify any preventable factor leading to excess use of resources. Moreover, we can also have better ideas regarding the effective allocation of healthcare resources in order to provide the unique services for the benefits of the patient.

1.3 Objectives and hypotheses

In my first paper presented in Chapter 2, I aimed to measure the extent of hospitalizations among CHD patients in Canada and to determine temporal changes over time from 2003 through 2009. It is important to identify the characteristics of patients who are utilising the services the most. Therefore, the objective was to determine the hospitalization rate of CHD patients by age, sex, and severity of CHD. I hypothesized that with time the hospitalization of CHD patients would be increasing with more increase in adult patients and patients with complex CHD.

The length of stay is also an important indicator of healthcare burden as occupying hospital beds for longer duration is associated with increased resources use. Some patients might require multiple admissions; therefore the total length of hospital stay per patient will best reflect inpatient resource utilization. I calculated the median length of stay per hospitalization and median total length of stay (over the study period) for CHD patients and describe by age, sex, and severity of CHD.

In Chapter 3, my second paper focusing on the readmission of CHD patients after hospitalization is presented. Readmission is defined as a hospital admission following the first (index) admission during the study period. Patients requiring readmission pose significant burden on h ealthcare systems. Understanding the characteristics of readmitted patients has both clinical and public health implications. Therefore, I intended to determine the readmission rate in CHD patients at 2-week (14 days), 1-month (31 days), 3-month (90 days) and 1-year (365 days) following discharge from the index hospitalization. Our second objective was to identify the factors predisposing to readmission in CHD patients.

References

1. Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. Lancet. Feb 20;375(9715):649-56.

2. Dastgiri S, Stone DH, Le-Ha C, Gilmour WH. Prevalence and secular trend of congenital anomalies in Glasgow, UK. Arch Dis Child. 2002 Apr;86(4):257-63.

3. van der Bom T, Zomer AC, Zwinderman AH, Meijboom FJ, Bouma BJ, Mulder BJ. The changing epidemiology of congenital heart disease. Nat Rev Cardiol. Jan;8(1):50-60.

4. Mitchell SC, Korones SB, Berendes HW. Congenital heart disease in 56,109 births. Incidence and natural history. Circulation. 1971 Mar;43(3):323-32.

5. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. Circulation. 2007 Jan 16;115(2):163-72.

6. Mason CA, Kirby RS, Sever LE, Langlois PH. Prevalence is the preferred measure of frequency of birth defects. Birth Defects Res A Clin Mol Teratol. 2005 Oct;73(10):690-2.

7. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002 Jun 19;39(12):1890-900.

8. Wren C, O'Sullivan JJ. Survival with congenital heart disease and need for follow up in adult life. Heart. 2001 Apr;85(4):438-43.

9. Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. J Pediatr. 2008 Dec;153(6):807-13.

10. Dolk H, Loane M, Garne E. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. Circulation. Mar 1;123(8):841-9.

11. Moons P, Sluysmans T, De Wolf D, Massin M, Suys B, Benatar A, et al. Congenital heart disease in 111 225 births in Belgium: birth prevalence, treatment and survival in the 21st century. Acta Paediatr. 2009 Mar;98(3):472-7.

12. Oyen N, Poulsen G, Boyd HA, Wohlfahrt J, Jensen PK, Melbye M. National time trends in congenital heart defects, Denmark, 1977-2005. Am Heart J. 2009 Mar;157(3):467-73 e1.

13. PHAC. Congenital Anomalies in Canada 2013, A perinatal health surveillance report. Public Health Agency Canada; 2013.

14. Guleserian KJ. Adult congenital heart disease: surgical advances and options. Prog Cardiovasc Dis. Jan-Feb;53(4):254-64.

15. Burch M. Congenital heart disease. Medicine. 2010;38(10):561-8.

16. Walsh EP. Interventional electrophysiology in patients with congenital heart disease. Circulation. 2007 Jun 26;115(25):3224-34.

17. Janousek J, Tomek V, Chaloupecky VA, Reich O, Gebauer RA, Kautzner J, et al. Cardiac resynchronization therapy: a novel adjunct to the treatment and prevention of systemic right ventricular failure. J Am Coll Cardiol. 2004 Nov 2;44(9):1927-31.

18. Dubin AM, Janousek J, Rhee E, Strieper MJ, Cecchin F, Law IH, et al. Resynchronization therapy in pediatric and congenital heart disease patients: an international multicenter study. J Am Coll Cardiol. 2005 Dec 20;46(12):2277-83.

19. Reitz BA, Wallwork JL, Hunt SA, Pennock JL, Billingham ME, Oyer PE, et al. Heart-lung transplantation: successful therapy for patients with pulmonary vascular disease. N Engl J Med. 1982 Mar 11;306(10):557-64.

20. Perloff JK. Pediatric congenital cardiac becomes a postoperative adult. The changing population of congenital heart disease. Circulation. 1973 Mar;47(3):606-19.

21. Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, et al. Task force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol. 2001 Apr;37(5):1170-5.

22. Nieminen HP, Jokinen EV, Sairanen HI. Late results of pediatric cardiac surgery in Finland: a population-based study with 96% follow-up. Circulation. 2001 Jul 31;104(5):570-5.

23. Moons P, Bovijn L, Budts W, Belmans A, Gewillig M. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. Circulation. Nov 30;122(22):2264-72.

24. Boneva RS, Botto LD, Moore CA, Yang Q, Correa A, Erickson JD. Mortality associated with congenital heart defects in the United States: trends and racial disparities, 1979-1997. Circulation. 2001 May 15;103(19):2376-81.

25. Pillutla P, Shetty KD, Foster E. Mortality associated with adult congenital heart disease: Trends in the US population from 1979 to 2005. Am Heart J. 2009 Nov;158(5):874-9.

26. Billett J, Majeed A, Gatzoulis M, Cowie M. Trends in hospital admissions, in-hospital case fatality and population mortality from congenital heart disease in England, 1994 to 2004. Heart. 2008 Mar;94(3):342-8.

27. Khairy P, Ionescu-Ittu R, Mackie AS, Abrahamowicz M, Pilote L, Marelli AJ. Changing mortality in congenital heart disease. J Am Coll Cardiol. Sep 28;56(14):1149-57.

28. Moller JH, Anderson RC. A 43- to 54-year follow-up of 1,000 patients with congenital heart disease. Am J Cardiol. May 15;111(10):1496-500.

29. van der Bom T, Bouma BJ, Meijboom FJ, Zwinderman AH, Mulder BJ. The prevalence of adult congenital heart disease, results from a systematic review and evidence based calculation. Am Heart J. Oct;164(4):568-75.

30. Afilalo J, Therrien J, Pilote L, Ionescu-Ittu R, Martucci G, Marelli AJ. Geriatric congenital heart disease: burden of disease and predictors of mortality. J Am Coll Cardiol. Sep 27;58(14):1509-15.

31. Marelli A. The Future of ACHD Care Symposium: Changing demographics of congenital heart disease. Progress in Pediatric Cardiology. 2012;34(2):85-90.

32. Perloff JK, Warnes CA. Challenges posed by adults with repaired congenital heart disease. Circulation. 2001 May 29;103(21):2637-43.

33. Oliver RJM. Congenital heart disease in adults: residua, sequelae, and complications of cardiac defects repaired at an early age. Rev Esp Cardiol. 2003;56(1):73-88.

34. Knirsch W, Nadal D. Infective endocarditis in congenital heart disease. Eur J Pediatr. Sep;170(9):1111-27.

35. Perloff JK. Congenital heart disease in adults. A new cardiovascular subspecialty. Circulation. 1991 Nov;84(5):1881-90.

36. Niwa K, Nakazawa M, Tateno S, Yoshinaga M, Terai M. Infective endocarditis in congenital heart disease: Japanese national collaboration study. Heart. 2005 Jun;91(6):795-800.

37. Morris CD, Reller MD, Menashe VD. Thirty-year incidence of infective endocarditis after surgery for congenital heart defect. JAMA. 1998 Feb 25;279(8):599-603.

38. Rushani D, Kaufman JS, Ionescu-Ittu R, Mackie AS, Pilote L, Therrien J, et al. Infective endocarditis in children with congenital heart disease: cumulative incidence and predictors. Circulation. Sep 24;128(13):1412-9.

39. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Veen G, et al. Turning 18 with congenital heart disease: prediction of infective endocarditis based on a large population. Eur Heart J. Aug;32(15):1926-34.

40. Li W, Somerville J. Infective endocarditis in the grown-up congenital heart (GUCH) population. Eur Heart J. 1998 Jan;19(1):166-73.

41. de Gevigney G, Pop C, Delahaye JP. The risk of infective endocarditis after cardiac surgical and interventional procedures. Eur Heart J. 1995 Apr;16 Suppl B:7-14.

42. Michel PL, Acar J. Native cardiac disease predisposing to infective endocarditis. Eur Heart J. 1995 Apr;16 Suppl B:2-6.

43. Di Filippo S, Delahaye F, Semiond B, Celard M, Henaine R, Ninet J, et al. Current patterns of infective endocarditis in congenital heart disease. Heart. 2006 Oct;92(10):1490-5.

44. Engelfriet P, Boersma E, Oechslin E, Tijssen J, Gatzoulis MA, Thilen U, et al. The spectrum of adult congenital heart disease in Europe: morbidity and mortality in a 5 year follow-up period. The Euro Heart Survey on adult congenital heart disease. Eur Heart J. 2005 Nov;26(21):2325-33.

45. Oechslin EN, Harrison DA, Connelly MS, Webb GD, Siu SC. Mode of death in adults with congenital heart disease. Am J Cardiol. 2000 Nov 15;86(10):1111-6.

46. Billett J, Cowie MR, Gatzoulis MA, Vonder Muhll IF, Majeed A. Comorbidity, healthcare utilisation and process of care measures in patients with congenital heart disease in the UK: cross-sectional, population-based study with case-control analysis. Heart. 2008 Sep;94(9):1194-9.

47. Somerville J. Management of adults with congenital heart disease: an increasing problem. Annu Rev Med. 1997;48:283-93.

48. Grown-up congenital heart (GUCH) disease: current needs and provision of service for adolescents and adults with congenital heart disease in the UK. Heart. 2002 Sep;88 Suppl 1:i1-14.

49. Kaemmerer H, Bauer U, Pensl U, Oechslin E, Gravenhorst V, Franke A, et al. Management of emergencies in adults with congenital cardiac disease. Am J Cardiol. 2008 Feb 15;101(4):521-5.

50. Walsh EP, Cecchin F. Arrhythmias in adult patients with congenital heart disease. Circulation. 2007 Jan 30;115(4):534-45.

51. Triedman JK. Arrhythmias in adults with congenital heart disease. Heart. 2002 Apr;87(4):383-9.

52. Roos-Hesselink J, Perlroth MG, McGhie J, Spitaels S. Atrial arrhythmias in adults after repair of tetralogy of Fallot. Correlations with clinical, exercise, and echocardiographic findings. Circulation. 1995 Apr 15;91(8):2214-9.

53. Fishberger SB, Wernovsky G, Gentles TL, Gauvreau K, Burnett J, Mayer JE, Jr., et al. Factors that influence the development of atrial flutter after the Fontan operation. J Thorac Cardiovasc Surg. 1997 Jan;113(1):80-6.

54. Curtis SL, Stuart AG. Outcome in congenital heart disease. Current Paediatrics. 2005;15(7):549-56.

55. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, van Dijk AP, et al. Mortality in adult congenital heart disease. Eur Heart J. May;31(10):1220-9.

56. Norozi K, Wessel A, Alpers V, Arnhold JO, Geyer S, Zoege M, et al. Incidence and risk distribution of heart failure in adolescents and adults with congenital heart disease after cardiac surgery. Am J Cardiol. 2006 Apr 15;97(8):1238-43.

57. Winter MM, Bouma BJ, Groenink M, Konings TC, Tijssen JG, van Veldhuisen DJ, et al. Latest insights in therapeutic options for systemic right ventricular failure: a comparison with left ventricular failure. Heart. 2009 Jun;95(12):960-3.

58. Tulevski, II, Dodge-Khatami A, Groenink M, van der Wall EE, Romkes H, Mulder BJ. Right ventricular function in congenital cardiac disease: noninvasive quantitative parameters for clinical follow-up. Cardiol Young. 2003 Oct;13(5):397-403.

59. Tulevski, II, Zijta FM, Smeijers AS, Dodge-Khatami A, van der Wall EE, Mulder BJ. Regional and global right ventricular dysfunction in asymptomatic or minimally symptomatic patients with congenitally corrected transposition. Cardiol Young. 2004 Apr;14(2):168-73.

60. Winter MM, van der Plas MN, Bouma BJ, Groenink M, Bresser P, Mulder BJ. Mechanisms for cardiac output augmentation in patients with a systemic right ventricle. Int J Cardiol. Aug 20;143(2):141-6.

61. Tulevski, II, Hirsch A, Dodge-Khatami A, Stoker J, van der Wall EE, Mulder BJ. Effect of pulmonary valve regurgitation on right ventricular function in patients with chronic right ventricular pressure overload. Am J Cardiol. 2003 Jul 1;92(1):113-6.

62. Piran S, Veldtman G, Siu S, Webb GD, Liu PP. Heart failure and ventricular dysfunction in patients with single or systemic right ventricles. Circulation. 2002 Mar 12;105(10):1189-94.

63. Guerri-Guttenberg RA, Castilla R, Francos GC, Muller A, Ambrosio G, Milei J. Transforming growth factor beta1 and coronary intimal hyperplasia in pediatric patients with congenital heart disease. Can J Cardiol. Jul;29(7):849-57.

64. Giannakoulas G, Dimopoulos K, Engel R, Goktekin O, Kucukdurmaz Z, Vatankulu MA, et al. Burden of coronary artery disease in adults with congenital heart disease and its relation to congenital and traditional heart risk factors. Am J Cardiol. 2009 May 15;103(10):1445-50.

65. Bradley E, Parker J, Novak E, Ludbrook P, Billadello J, Cedars A. Cardiovascular disease in late survivors of tetralogy of fallot: a tertiary care center experience. Tex Heart Inst J.40(4):418-23.

66. Fyfe A, Perloff JK, Niwa K, Child JS, Miner PD. Cyanotic congenital heart disease and coronary artery atherogenesis. Am J Cardiol. 2005 Jul 15;96(2):283-90.

67. Hoffmann A, Chockalingam P, Balint OH, Dadashev A, Dimopoulos K, Engel R, et al. Cerebrovascular accidents in adult patients with congenital heart disease. Heart. Aug;96(15):1223-6.

68. Dittrich S, Haas NA, Buhrer C, Muller C, Dahnert I, Lange PE. Renal impairment in patients with long-standing cyanotic congenital heart disease. Acta Paediatr. 1998 Sep;87(9):949-54.

69. Ghafari S, Malaki M. Truncus arteriosus: A major cause of proteinuria in children. J Cardiovasc Dis Res. Oct;2(4):237-40.

70. Hayabuchi Y, Matsuoka S, Akita H, Kuroda Y. Hyperuricaemia in cyanotic congenital heart disease. Eur J Pediatr. 1993 Nov;152(11):873-6.

71. Andres S, Bauer G, Rodriguez S, Novali L, Micheli D, Farina D. Hospitalization due to respiratory syncytial virus infection in patients under 2 years of age with hemodynamically significant congenital heart disease. J Pediatr (Rio J). May;88(3):246-52.

72. Silversides CK, Salehian O, Oechslin E, Schwerzmann M, Vonder Muhll I, Khairy P, et al. Canadian Cardiovascular Society 2009 Consensus Conference on the management of adults with congenital heart disease: complex congenital cardiac lesions. Can J Cardiol. Mar;26(3):e98-117.

73. Opotowsky AR, Siddiqi OK, Webb GD. Trends in hospitalizations for adults with congenital heart disease in the U.S. J Am Coll Cardiol. 2009 Jul 28;54(5):460-7.

74. Moons P, Siebens K, De Geest S, Abraham I, Budts W, Gewillig M. A pilot study of expenditures on, and utilization of resources in, health care in adults with congenital heart disease. Cardiol Young. 2001 May;11(3):301-13.

75. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Sieswerda GT, et al. The emerging burden of hospital admissions of adults with congenital heart disease. Heart. Jun;96(11):872-8.

76. Mackie AS, Pilote L, Ionescu-Ittu R, Rahme E, Marelli AJ. Health care resource utilization in adults with congenital heart disease. Am J Cardiol. 2007 Mar 15;99(6):839-43.

77. Mackie AS, Ionescu-Ittu R, Pilote L, Rahme E, Marelli AJ. Hospital readmissions in children with congenital heart disease: a population-based study. Am Heart J. 2008 Mar;155(3):577-84.

78. Gatzoulis MA, Hechter S, Siu SC, Webb GD. Outpatient clinics for adults with congenital heart disease: increasing workload and evolving patterns of referral. Heart. 1999 Jan;81(1):57-61.

Chapter 2

Epidemiology of hospitalization of Congenital Heart Disease patients in Canada from 2003 to 2009

2.1 Abstract

Background: The impact of rising populations of congenital heart disease on the inpatient care is not known in Canada. This paper aimed to assess temporal changes in hospitalizations of CHD patients.

Methods: We identified all patients with CHD diagnosis, receiving inpatient care during the fiscal years 2003 to 2009 in Canada from hospital discharge abstract data of the Canadian Institute for Health Information. Poisson regression analysis was performed to assess temporal changes in the annual hospitalization rate. The analysis was also stratified by patients' characteristics including age, sex and severity of CHD.

Results: In Canada, a total 68,099 hospitalizations occurred in 43,182 patients with CHD from fiscal years 2003 to 2009, with an average increase of the number of hospitalizations of 1.1% per year. The number of hospitalizations increased by 3% per year in adults but there was no change in children: the greatest increase was in the patients aged 40-64 years followed by those 65+. The annual hospitalization rate was stable during the study period varying between 38 and 40 per 100,000 persons (p=0.52). The total length of stay was longest among infants, age 65+, males and complex CHD patients.

Conclusion: We found high inpatient service utilization among CHD patients, particularly adults ≥ 40 years, infants, males and complex CHD patients. The number of hospitalizations with CHD increased over time particularly among adults ≥40 years. The growing patient population and their increasing number of hospitalizations have implication on the adult cardiology programs and their inpatient health care resources.

2.2 Introduction

Congenital heart disease (CHD) is the most common birth defect with a birth prevalence of 8 to 10 per 1,000 livebirths (1). With improving survival (2), the prevalence of CHD is rising rapidly in adults, and adults with CHD now outnumber children with CHD. In addition, the distribution of different types of CHD has also changed with an increasing prevalence of severe CHD among adults compared to children (3, 4). Adult patients with CHD are at risk of developing late consequences related to CHD and associated interventions (5, 6). Moreover, they may acquire other co-morbid conditions with aging. The impact of this changing demographic on the number of adult CHD clinic visits has been previously described in Canada (7). However, the impact of this changing demographic on inpatient care is not known. Therefore, objectives of this paper are: a) to determine temporal changes in the hospitalization rate among CHD patients in Canada; b) to assess temporal changes in the hospitalization rate by patients' characteristics including age, sex, and severity of CHD; and c) to determine temporal changes in length of hospital stay and compare by patients' characteristics.

2.3 Methods

2.3.1 Study design and data source

We conducted an observational retrospective cohort study using administrative hospital discharge abstract data from the Canadian Institute for Health Information (CIHI) in order to examine the hospitalization of CHD patients in Canada. CIHI is a national database that contains demographic and clinical information of patients who come into contact with inpatient services. Acute care facilities from all provinces except Quebec submit their data to CIHI. Patients' health care numbers and names were not provided to ensure the privacy of information.

2.3.2 Study population

Inclusion criteria: Our study population consisted of all patients, irrespective of their age, with a diagnosis of CHD receiving inpatient care during the fiscal years of 2003 to 2009 in Canada. CHD was identified based on *International Classification of Disease, Ninth (ICD9) and Tenth (ICD10) Revision*, from any of 25 diagnostic fields. The first diagnostic field was the most responsible (principal) diagnosis for a particular hospitalization and the remaining 24 diagnostic fields were secondary diagnoses.

Exclusion criteria: We excluded patients with isolated patent ductus arteriosus (PDA) and those who lived in Yukon, Northwest Territories, Nunavut or Quebec even if they received care in hospitals of other provinces. We also excluded patients who were discharged alive on the same day of admission, assuming they were admitted for a day procedure. Hospitalizations within 24 hours of discharge were considered hospital-to-hospital transfers and therefore counted as single hospitalizations.

2.3.3 Outcome measures

Our primary outcome of interest was the annual number and rate of hospitalizations with CHD as a primary or secondary diagnosis and the annual number and rate of hospitalizations by age group, sex, severity of CHD and therapeutic intervention. For each year, we calculated the hospitalization rate by dividing the number of hospitalizations by the population size of Canada (less Yukon, Northwest Territories, Nunavut and Quebec) in the given year. The same procedure stratified by age, sex, and severity of CHD was applied to the calculation of annual hospitalization rates by age, sex, and severity of CHD.

Length of stay (LOS) was the secondary outcome. In the event of a hospitalization within 24 hours of a discharge, the length of stay was measured as the duration between the first admission date and the second discharge date. We also assessed the total length of stay, defined as the total duration of hospital days (over multiple hospitalizations) per person over the seven year study period. For the total length of stay variable, age was defined as the age at first hospitalization during the study period (index hospitalization).

2.3.4 Independent variables

CHD lesions were grouped into three complexities: simple, moderate and complex, as previously defined (8). We classified patients with multiple CHD diagnoses based on the hierarchies of complexities. For example, if a patient had complex lesions and moderate or simple lesions, s/he was classified as a complex CHD patient. Similarly, patients with moderate and simple CHD lesions were categorised as moderate CHD patients. Age was categorized into six categories: infants (<1 year); 1-4 years; 5-17 years; 18-39 years; 40-64 years; and 65+ years.

We used the Canadian Classification of Health Interventions (CCI) codes corresponding to ICD 10 codes and the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) codes corresponding to ICD9 codes to identify the therapeutic cardiovascular intervention performed during hospitalizations. The hospitalizations were grouped into 4 categories based on the intervention procedure performed: no cardiac intervention; cardiac surgery only; cardiac catheterization only; or both cardiac surgery and catheterization.

2.3.5 Statistical analysis

Characteristics of index hospitalizations (i.e., characteristics of patients) and all hospitalizations were described by frequency distributions and continuous variables such as length of stay (LOS) were described with median with interquartile range (IQR). Ten most common principal diagnoses during index and all hospitalizations were described by frequency distributions for children and adults separately. We expressed the annual hospitalization rate per 100,000 persons. Poisson regression analysis was performed to assess temporal changes in the annual hospitalization rate. The numbers and rates of annual hospitalizations were also analyzed stratifying by age group, sex and severity of CHD. Length of stay and total length of stay were compared using Kruskal Wallis and Wilcoxon rank sum tests across the categories of age, sex and severity of CHD. Two sided p-values <0.05 were considered statistically significant. All analyses were performed using SAS statistical software (Version 9.3 SAS Institute, Cary, NC).

2.3.6 Ethics

All procedures of the study were approved by the Health Research Ethics Board at the University of Alberta.

2.4 Results

A total 43,182 patients with CHD were hospitalized in Canada from fiscal years 2003 to 2009, accounting for a total 68,099 inpatient admissions over these years. During this period, 31,449 (72.8%) patients had a single hospitalization; 6,377 (14.8%) had 2 hospitalizations; and 5,356 (12.4%) had 3 or more hospitalizations. In-hospital death occurred in 2,487 (5.8%) patients and 1,431 (58%) of all deaths occurred at the time of index hospitalization. In Table 2.1, the characteristics of patients during the index hospitalization and all hospitalizations they experienced during the study period are described. The principal diagnoses responsible for hospitalizations are reported in Table 2.2A for children and in Table 2.2B for adult patients.

Among all hospitalizations, infants contributed to 41.5% followed by 40-64 years (17.6%) and patients age 65+ (14.9%). Male patients were predominantly (52.9%) hospitalized. Of all hospitalizations, 55.5% were for simple CHD and 32.8% were for moderate CHD patients. Among children, ventricular septal defect, atrial septal defect (ostium secundum) and respiratory illness were major principal diagnoses. On the other hand, acquired cardiovascular disease was mostly associated with hospitalizations in adults.

The overall number of hospitalizations increased from 9,503 in 2003 to 10,142 in 2009, an average increase of 1.1% per year. However, the annual hospitalization rate was stable during the study period varying between 38 and 40 per 100,000 persons (p=0.52).

The number of hospitalizations increased in adults with the highest increase in the 40-64 years old, followed by the patient age 65+. The number of hospitalizations increased per year by 3.1% from 1,315 to 1,562 for the patient age 65+, 3.5% from 1,543 to 1,870 for 40-64 years old and 1.1% from 926 to 988 for 18-39 years old. In contrast, the number of hospitalizations did not change significantly in other age groups (<1 year, 1-4 years and 5-17 years).

From 2003 through 2009, the number of hospitalizations increased per year by 1.1% from 5,000 to 5,337 for male and by 1.1% from 4,503 to 4,805 for female.

Over the same period, the number of hospitalizations increased per year by 1.8% from 5,107 to 5,661 among simple CHD patients and by 2.1% from 1,166 to 1,316 for complex CHD patients. No significant change was found over time for moderate CHD patients, however.

Infants consistently had the highest annual hospitalization rate over the seven year-period followed by 1-4 year olds and the patient age 65+ (Figure 2.1). The annual hospitalization rate was consistently higher for males with 41 to 43 per 100,000 persons; for females, the rate was 35 to 37 per 100,000 persons. The annual hospitalization rate was higher for simple CHD patients ranging from 21 to 22 per 100,000 persons, followed by 12 to 13 per 100,000 persons for moderate CHD patients and 4 to 5 per 100,000 persons for complex CHD patients.

With respect to changes in hospitalization rates, the hospitalization rate in infants decreased by a factor of 0.978 per year (95% CI 0.972 to 0.983, $p<0.001$). There was a small but statistically significant increase in the annual hospitalization rate observed per year for patients aged 40-64 years (Rate ratio 1.012, 95% CI 1.003 to 1.021, $p=0.010$) and for patients age 65+ (Rate ratio 1.014, 95% CI 1.004 to 1.024, $p=0.005$). In all other age groups, there were no significant changes in the annual hospitalization rate over the study period. There was no statistically significant change in the hospitalization rates over the study period for male or female patients, and for patients of any CHD severity.

Length of stay

The median LOS during the index hospitalization was 6 (IQR: 3-14) days. In Table 2.3, the LOS of index hospitalization is shown by patient characteristics including the 10 most common index hospitalization principal diagnoses. Index hospitalizations with diagnosis of hypoplastic left heart syndrome (HLHS) followed by transposition of great arteries (TGA) had longer duration of median LOS. The median total LOS per person over the 7-year study period was greatest in infants and the patient age 65+ at index hospitalization, males, and in those with complex CHD (Table 2.4).

2.5 Discussion

To our knowledge, this is the first study to assess temporal trends of hospitalizations among CHD patients in Canada. We found that the inpatient service utilization was high particularly in infants, patients age 40+, males, and those with complex CHD among our study population. The absolute number of annual hospitalizations increased an average of 1.1% per year from 2003 to 2009. Hospitalizations with CHD in Canada increased more than that observed among all-cause hospitalizations which increased annually by 0.6%, 0.4% and 0.2% over three consecutive years from 2003/2004 to 2005/6 (9).

A population based study in the UK reported a 9.7% increase in the number of hospitalizations with a primary diagnosis of CHD between 1995/1996 and 2003/2004, which is an average increase of 1.2% per year (10). This is similar to the observed increase in the number of hospitalizations among our study population. However, the annual number of hospitalizations in adults with CHD in the U.S. more than doubled between 1998 and 2005, with an average increase of 14.6% per year (11). The larger increase in hospitalizations, relative to our findings, observed in the U.S study might be due to the difference in study methods. Hospitalizations with admission and discharge on the same date were excluded from our study. In contrast, the U.S study included hospitalizations with day procedures, which may have been performed with increasing frequency during their study period (1998-2005). In addition, these authors included PFO which may have been increasingly recognized during their study period.

The annual hospitalization rate with CHD in our study was stable between 38 and 40 per 100,000 persons including all age groups. The Canadian population experienced an average of 1.1% growth per year from 2003 to 2009 which is the likely explanation of the increase in hospitalization numbers with the stable annual hospitalization rates during the period studied (12).

Using the CONCOR (CONgenital CORvitia) Dutch national registry, a two to three times higher hospitalization rate was observed in adult CHD patients compared to that of the general Dutch population from 2001 to 2006 (13). In Quebec, the hospitalization rate among CHD children was higher than that of general population from 1996 to 2000 (14). All these studies investigated hospitalizations among specific age groups. However, we investigated hospitalizations among all age groups.

In our study, the number of annual hospitalizations increased in adults (3% per year), but not in children. The greatest increase was observed in 40- 64 years old (3.5% per year) followed by patients age 65+ (3.1%). This is consistent with the growing population of adult CHD survivors (3). In contrast, the number of hospitalizations for infants and the other children remained stable over time.

The annual hospitalization rate in infants, however, reduced by approximately 2.2% per year from 2003 to 2009. This is consistent with, but more than, the decreasing trend of birth prevalence of CHD in Canada, an average 1.7% decrease of prevalence per year (15). The annual hospitalization rate increased by 1.2% per year in 40-64 years old patients and by 1.4% per year in those 65+ years.

In our study, we found consistently higher number and rate of annual hospitalization with males across the fiscal years compared to females. In a population based study, the prevalence of CHD was more common in female than male patients (3). However, there were more males among hospitalized patients, which might imply that male patients developed more complications or comorbid conditions compared to females (16). Female patients have milder lesions (17) and experience lower mortality compared to male patients (18). Males with CHD are more likely to undergo surgery in infancy and adulthood and, have a worse outcome after reoperations in adulthood compared with females (18, 19).

Our study showed more hospitalizations with simple CHD followed by moderate CHD patients. The annual number of hospitalizations increased per year in patients with simple (1.8%) and complex CHD (2.1%). Although the proportion of patients with complex CHD was less than those with simple or moderate CHD, there were disproportionately more admissions and more total hospital days among complex CHD patients. Complex CHD patients are more likely to develop late complications and require re-intervention than those with simple or moderate CHD (8).

The principal diagnosis associated with hospitalization differed by age. In adults, cardiac events such as congestive heart failure, ischaemic heart disease, atrial fibrillation and atrial flutter were the most common reasons for hospitalization. Existing literature suggested that cardiac arrhythmia had been the most leading cause of hospitalization in adult CHD patients (13); however our data demonstrates that ischemic heart disease is resulting in hospitalizations among adults with CHD, and is consistent with other studies demonstrating that ischemic heart disease is an emerging problem in this population (20). On the other hand, in children, respiratory illnesses including pneumonia and acute bronchiolitis were more common diagnoses associated with hospitalization.

The median LOS among our study population was 6 (IQR: 3-14) days which is consistent with the findings of 5 days (IQR: 2-13) reported among adult CHD patients in Belgium (21).

Complex CHD patients had the highest duration of total LOS, consistent with the findings of a population based study among Quebec CHD patients which reported a longer mean LOS in patients with severe lesions compared to other lesions (14).

Strengths and limitations of the study

The most important strength of our study is the use of a large nationally representative study population. The hospital discharge abstract database from CIHI captures all patients with congenital heart disease receiving inpatient care in Canada except Quebec, Nunavut, Yukon and the North West Territories. We examined CHD patients from all age groups which allowed us to compare inpatient resource utilization across age groups. This provided understanding of the extent of inpatient service utilization by age group which could be utilized for implementing appropriate strategies in allocating age-appropriate resources.

An important drawback of using an administrative database is that it was not being constructed for research purposes; for example, the CIHI discharge abstract database is lacking demographic information such as socioeconomic status as well as information about the characteristics of hospitals including type and number of hospitals (tertiary vs. community hospital). Moreover, there exists hospital-to-hospital as well as across-province variation in recording health data. There may be a chance of misclassification of CHD as we relied on administrative data to identify CHD patients. Moreover, we used both ICD 9 and ICD 10 diagnostic codes. Some CHD lesions have no unique ICD 9 code but have a unique ICD 10 code. However, only 5% of hospitalizations had a diagnosis with ICD 9 coding.

We used the general population as a denominator in calculating the hospitalization rate. If there is disproportionate growth between the general population and the CHD population over time, the hospitalization rate expressed per 100,000 persons in the general population might not show the actual trend of hospitalization rates among subjects with CHD.

Our study population is limited to patients receiving inpatient care. This study does not represent the complete burden of CHD on health care systems as many CHD patients receive only outpatient care.

We may have missed some patients with CHD receiving inpatient care if the CHD diagnosis was not coded in any of the diagnostic fields (misclassification). Many congenital heart defects are corrected or repaired during childhood and many patients survive to adulthood with a misconception of being "cured". Therefore, when these patients are admitted for reasons other than CHD, there is a possibility that the CHD might not be coded as a diagnosis. Similarly, diagnosis of simple CHD might be missed if a patient with simple CHD was hospitalized due to a reason not related to CHD, such as injury. On the other hand, complex CHD patients were more likely to be admitted with complications of CHD, which might lead to a greater likelihood of their CHD diagnosis being coded. This might result in differential misclassification of CHD hospitalizations; consequently our results might underestimate hospitalizations with simple CHD.

2.6 Conclusion

The number of hospitalizations with CHD increased over time particularly in 40+ years patients. Though there were more hospitalizations associated with simple CHD, patients with complex lesions had disproportionately more admissions. This study will help us to understand the extent and pattern of inpatient health care service utilization by CHD patients. Adult cardiology programs require greater allocation of inpatient health care resources for this growing population.

References

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002 Jun 19;39(12):1890-900.

2. Moons P, Bovijn L, Budts W, Belmans A, Gewillig M. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. Circulation. Nov 30;122(22):2264-72.

3. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. Circulation. 2007 Jan 16;115(2):163-72.

4. Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Lifetime Prevalence of Congenital Heart Disease in the General Population from 2000 to 2010. Circulation. Jun 18.

5. Somerville J. Management of adults with congenital heart disease: an increasing problem. Annu Rev Med. 1997;48:283-93.

6. Perloff JK. Adults with surgically treated congenital heart disease. Sequelae and residua. JAMA. 1983 Oct 21;250(15):2033-6.

7. Gatzoulis MA, Hechter S, Siu SC, Webb GD. Outpatient clinics for adults with congenital heart disease: increasing workload and evolving patterns of referral. Heart. 1999 Jan;81(1):57-61.

8. Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, et al. Task force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol. 2001 Apr;37(5):1170-5.

9. CIHI. Trends in inpatient hospitalization and day surgery in Canada from 1995/1996 to 2005/2006.; 2007.

10. Billett J, Majeed A, Gatzoulis M, Cowie M. Trends in hospital admissions, in-hospital case fatality and population mortality from congenital heart disease in England, 1994 to 2004. Heart. 2008 Mar;94(3):342-8.

11. Opotowsky AR, Siddiqi OK, Webb GD. Trends in hospitalizations for adults with congenital heart disease in the U.S. J Am Coll Cardiol. 2009 Jul 28;54(5):460-7.

12. Statistics Canada. Population Census data from Stat Canada.

13. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Sieswerda GT, et al. The emerging burden of hospital admissions of adults with congenital heart disease. Heart. Jun;96(11):872-8.

14. Mackie AS, Pilote L, Ionescu-Ittu R, Rahme E, Marelli AJ. Health care resource utilization in adults with congenital heart disease. Am J Cardiol. 2007 Mar 15;99(6):839-43.

15. Joseph KS, Liu S. Congential Anomalies In Canada 2013 A Perinatal Health Surveillence Report. 2013 p. 33-41.

16. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Vliegen HW, et al. Gender and outcome in adult congenital heart disease. Circulation. 2008 Jul 1;118(1):26-32.

17. Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. J Pediatr. 2008 Dec;153(6):807-13.

18. Marelli A, Gauvreau K, Landzberg M, Jenkins K. Sex differences in mortality in children undergoing congenital heart disease surgery: a United States population-based study. Circulation. Sep 14;122(11 Suppl):S234-40.

19. Zomer AC, Verheugt CL, Vaartjes I, Uiterwaal CS, Langemeijer MM, Koolbergen DR, et al. Surgery in adults with congenital heart disease. Circulation. Nov 15;124(20):2195-201.

20. Giannakoulas G, Dimopoulos K, Engel R, Goktekin O, Kucukdurmaz Z, Vatankulu MA, et al. Burden of coronary artery disease in adults with congenital heart disease and its relation to congenital and traditional heart risk factors. Am J Cardiol. 2009 May 15;103(10):1445-50.

21. Moons P, Siebens K, De Geest S, Abraham I, Budts W, Gewillig M. A pilot study of expenditures on, and utilization of resources in, health care in adults with congenital heart disease. Cardiol Young. 2001 May;11(3):301-13.

Tables and Figures

Table 2.1: Demographic and clinical characteristics of study subjects

Characteristics	**Index hospitalizations, n (%)**	**All Hospitalizations, n (%)**
Fiscal year		
2003	7,497 (17.4)	9,503 (14.0)
2004	6,340 (14.7)	9,327 (13.7)
2005	6,215 (14.4)	9,732 (14.3)
2006	6,048 (14.0)	9,765 (14.3)
2007	5,669 (13.1)	9,503 (14.0)
2008	5,855 (13.6)	10,127 (14.9)
2009	5,558 (12.9)	10,142 (14.9)
Age groups		
<1 year	21,714 (50.3)	28,233 (41.5)
1-4 years	2,041 (4.7)	5,862 (8.6)
5-17 years	3,128 (7.2)	5,125 (7.5)
18-39 years	4,463 (10.3)	6,760 (9.9)
40-64 years	7,220 (16.7)	11,992 (17.6)
65+ years	4,616 (10.7)	10,127 (14.9)
Sex		
Female	20,356 (47.1)	32,069 (47.1)
Male	22,826 (52.9)	36,030 (52.9)
Length of stay, Median (IQR)	6 (3 - 16)	6 (3 - 14)
Severity of CHD		
Simple	26,881 (62.3)	37,810 (55.5)
Moderate	13,265 (30.7)	22,329 (32.8)
Complex	3,036 (7.0)	7,960 (11.7)
Cardiac intervention		
No intervention	30,513 (70.7)	47,773 (70.2)
Cardiac surgery	9,180 (21.3)	14,456 (21.2)
Cardiac catheterization	2,808 (6.5)	4,572 (6.7)
Both cardiac surgery and catheterization	681 (1.6)	1,298 (1.9)

Table 2.2A: Most frequent principal diagnosis in children (<18 years old)

Index hospitalisations N= 26,883		**All hospitalisations N=39,220**	
Principal diagnosis	**n (%)**	**Principal diagnosis**	**n (%)**
Ventricular septal defect	1,839 (6.8)	Ventricular septal defect	2,347 (6.0)
Ostium secundum atrial septal defect	1,294 (4.8)	Ostium secundum atrial septal defect	1,489 (3.8)
Coarctation of the aorta	680 (2.5)	Pneumonia	1,086 (2.8)
Other specified anomalies of heart	621 (2.3)	Tetralogy of Fallot	985 (2.5)
Other anomalies of heart	594 (2.2)	Acute bronchiolitis	912 (2.3)
Tetralogy of Fallot	516 (1.9)	Coarctation of the aorta	858 (2.2)
Transpositon of the great arteries	482 (1.8)	Other specified anomalies of heart	785 (2.0)
Down's syndrome	469 (1.7)	Transposition of the great arteries	753 (1.9)
Acute bronchiolitis	425 (1.6)	Endocardial cushion defect	727 (1.9)
Endocardial cushion defect	406 (1.5)	Other anomalies of the heart	632 (1.6)

Table 2.2B: Most frequent principal diagnosis among adults

Index hospitalisations N=16,299		**All hospitalisations N=28,879**	
Principal diagnosis	**n (%)**	**Principal diagnosis**	**n (%)**
Non rheumatic aortic valve disorder	2,085 (12.8)	Non rheumatic aortic valve disorder	2,570 (8.9)
Ostium secundum atrial septal defect	1,493 (9.2)	Congestive heart failure	2,457 (8.5)
Ischaemic heart disease	1,055 (6.5)	Ostium secundum atrial septal defect	1,853 (6.4)
Aortic valve abnormality	789 (4.8)	Ischaemic heart disease	1,740 (6.0)
Congestive heart failure	691 (4.2)	Atrial fibrillation and flutter	1,596 (5.5)
Atherosclerosis of coronary artery without angina	644 (4.0)	Atherosclerosis of coronary artery without angina	1,023 (3.5)
Atrial fibrillation and flutter	592 (3.6)	Aortic valve abnormality	928 (3.2)
Non rheumatic mitral valve disorder	381 (2.3)	Non rheumatic mitral valve disorder	546 (1.9)
Infective endocarditis	301 (1.8)	Infective endocarditis	476 (1.6)
Pneumonia	201 (1.2)	Pneumonia	472 (1.6)

Table 2.3: Length of stay during index hospitalization

Variables	Length of stay (days) Median (IQR)	p-values
Age groups		
<1 year	8 (3 – 26)	<0.0001
1-4 years	4 (2 – 6)	
5-17 years	3 (1 – 5)	
18-39 years	4 (2 – 7)	
40-64 years	6 (3 – 10)	
65+ years	8 (5 – 15)	
Sex		
Female	5 (3 – 15)	<0.0001
Male	6 (3 – 16)	
Severity of CHD		
Simple	6 (3 – 14)	<0.0001
Moderate	6 (3 – 16)	
Complex	9 (3 – 25)	
Principal diagnosis* (frequency >100) by highest length of stay		
Hypoplastic left heart syndrome (266)	20 (7 – 41)	
Transposition of great arteries (493)	16 (7– 26)	
Infective endocarditis (335)	15 (9 – 30)	
Total anomalous pulmonary venous connection (107)	14 (9 – 26)	
Down syndrome (472)	10 (5 – 22)	
Pulmonary artery atresia (106)	10 (4 – 23)	
Cardiomyopathy (128)	9 (5 – 20)	
Ischaemic heart disease (1,066)	8 (4 – 18)	
Atherosclerosis of coronary artery without angina (645)	8 (5 – 14)	
Congestive heart failure (821)	8 (4 – 16)	

*In order to present the maximum resource utilization, the principal diagnoses with frequency >100 were chosen.

Table 2.4: Total length of stay between 2003-2009 inclusive

Characteristics of patients	**Total length of stay (days) Median (IQR)**	**p-values**
Age groups at index hospitalization		
<1 year	11.0 (3.6 – 32.0)	<0.0001
1-4 years	4.4 (2.4 – 10.1)	
5-17 years	4.3 (1.6 – 7.8)	
18-39 years	5.2 (2.5 – 10.5)	
40-64 years	8.1 (5.0 – 18.0)	
65+ years	15.3 (7.3 – 34.0)	
Sex		
Female	7.5 (3.2 – 23.1)	<0.0001
Male	9.1 (4.2 – 24.5)	
Severity of CHD		
Simple	7.3 (3.3 – 20.8)	<0.0001
Moderate	9.2 (4.0 – 25.8)	
Complex	19.2 (6.8 – 47.0)	

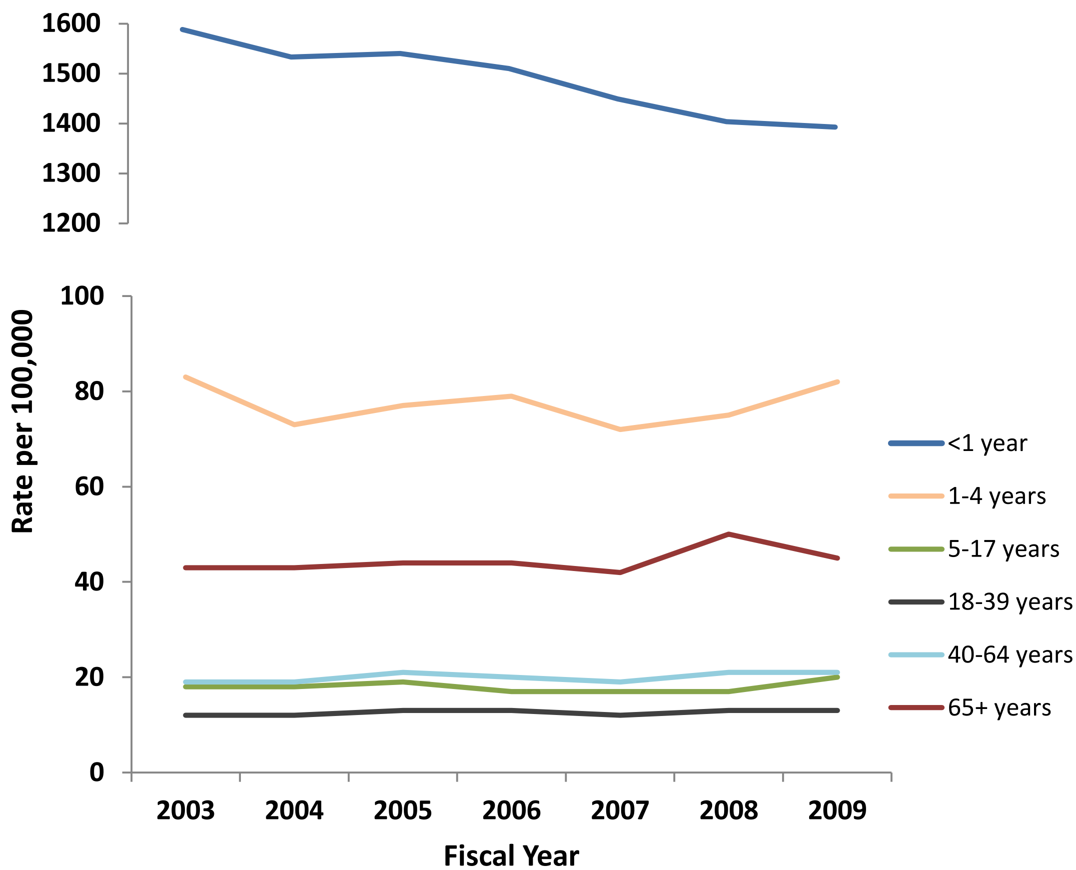


Figure 2.1: Age-specific annual hospitalization rate in Congenital Heart Disease patients in Canada (2003 – 2009)

Appendices

Supplementary Table 2.1: Characteristics of all hospitalizations (CHD as primary and secondary diagnosis) by fiscal year from 2003-2009

Characteristics	**2003 N=9,503 14.0%**	**2004 N=9,327 13.7%**	**2005 N=9,732 14.3%**	**2006 N=9,765 14.3%**	**2007 N=9,503 14.0%**	**2008 N=10,127 14.9%**	**2009 N=10,142 14.9%**
Age groups							
<1 year	4,073 (42.9)	4,017 (43.1)	4,047 (41.6)	4,086 (41.8)	3,994 (42.0)	4,008 (39.6)	4,008 (39.5)
1-4 years	892 (9.4)	774 (8.3)	821 (8.4)	848 (8.7)	779 (8.2)	828 (8.2)	920 (9.1)
5-17 years	754 (7.9)	732 (7.9)	759 (7.8)	702 (7.2)	686 (7.2)	698 (6.9)	794 (7.8)
18-39 years	926 (9.7)	896 (9.6)	973 (10.0)	1,002 (10.3)	944 (9.9)	1,031 (10.2)	988 (9.7)
40-64 years	1,543 (16.2)	1,560 (16.7)	1,750 (18.0)	1,706 (17.5)	1,704 (17.9)	1,859 (18.4)	1,870 (18.4)
65+ years	1,315 (13.8)	1,348 (14.5)	1,382 (14.2)	1,421 (14.6)	1,396 (14.7)	1,703 (16.8)	1,562 (15.4)
Sex							
Female	4,503 (47.4)	4,410 (47.3)	4,575 (47.0)	4,578 (46.9)	4,441 (46.7)	4,757 (47.0)	4,805 (47.4)
Male	5,000 (52.6)	4,917 (52.7)	5,157 (53.0)	5,187 (53.1)	5,062 (53.3)	5,370 (53.0)	5,337 (52.6)
Length of stay, Median (IQR)	6 (3 – 14)	6 (3 – 13)	6 (3 – 13)	6 (3 – 13)	6 (3 – 13)	6 (3 – 14)	6 (3 – 14)
Severity of CHD							
Simple	5,107 (53.7)	5,086 (54.5)	5,444 (55.9)	5,505 (56.4)	5,310 (55.9)	5,697 (56.3)	5,661 (55.8)
Moderate	3,230 (34.0)	3,174 (34.0)	3,187 (32.8)	3,192 (32.7)	3,081 (32.4)	3,300 (32.6)	3,165 (31.2)
Complex	1,166 (12.3)	1,067 (11.4)	1,101 (11.3)	1,068 (10.9)	1,112 (11.7)	1,130 (11.2)	1,316 (13.0)
Cardiac Intervention							
No intervention	6,754 (71.1)	6,707 (71.9)	6,865 (70.5)	6,831 (70.0)	6,641 (69.9)	7,058 (69.7)	6,917 (68.2)
Cardiac surgery	2,049 (21.6)	1,955 (21.0)	2,013 (20.7)	2,025 (20.7)	1,947 (20.5)	2,172 (21.5)	2,295 (22.6)
Cardiac catheterization	565 (6.0)	508 (5.5)	660 (6.8)	698 (7.2)	718 (7.6)	719 (7.1)	704 (6.9)
Both cardiac surgery and catheterization	135 (1.4)	157 (1.7)	194 (2.0)	211 (2.2)	197 (2.1)	178 (1.8)	226 (2.2)

Principal diagnosis							
Atrial septal defect (Ostium secundum)	398 (4.2)	359 (3.8)	519 (5.3)	539 (5.5)	499 (5.3)	488 (4.8)	540 (5.3)
Congestive heart failure	353 (3.7)	428 (4.6)	423 (4.4)	409 (4.2)	388 (4.1)	438 (4.3)	453 (4.5)
Non rheumatic aortic valve disorder	356 (3.8)	319 (3.4)	339 (3.5)	366 (3.8)	362 (3.8)	436 (4.3)	440 (4.3)
Ventricular Septal Defect	386 (4.1)	362 (3.9)	359 (3.7)	309 (3.2)	357 (3.8)	328 (3.2)	331 (3.3)
Ischaemic Heart Disease	263 (2.8)	265 (2.8)	265 (2.7)	261 (2.7)	218 (2.3)	277 (2.7)	208 (2.1)
Atrial fibrillation and flutter	224 (2.4)	242 (2.6)	251 (2.6)	245 (2.5)	240 (2.5)	230 (2.3)	240 (2.4)
Pneumonia	235 (2.5)	219 (2.4)	245 (2.5)	232 (2.4)	189 (2.0)	193 (1.9)	245 (2.4)
Aortic valve abnormalities	204 (2.2)	197 (2.1)	194 (2.0)	169 (1.7)	163 (1.7)	185 (1.8)	229 (2.3)
Tetralogy of Fallot	149 (1.6)	150 (1.6)	146 (1.5)	163 (1.7)	162 (1.7)	137 (1.4)	135 (1.3)
Atherosclerosis of coronary artery without angina	159 (1.7)	161 (1.7)	173 (1.8)	167 (1.7)	131 (1.4)	118 (1.2)	117 (1.2)

Supplementary table 2.2: Proportion of patients with most frequent single CHD diagnosis

Congenital heart defects	**n (%)**
Ostium secundum atrial septal defect	9,719 (22.5)
Aortic valve abnormality	4,660 (10.8)
Ventricular septal defect	4,368 (10.1)
Other specified anomalies of heart	2,584 (6.0)
Pulmonary artery stenosis	1,917 (4.4)
Unspecified anomalies of heart and circulatory system	1,575 (3.6)
Coarctation of aorta	942 (2.2)
Specified and other anomalies of great veins	842 (1.9)
Transposition of great arteries	566 (1.3)
Anomalies of aorta	501 (1.2)
Endocardial cushion defect	486 (1.1)

Supplementary table 2.3: Proportion of patients with most frequent combination of two CHD diagnoses

Combination of two congenital heart defects	**n (%)**
Ostium secundum atrial septal defect and Patent ductus arteriosus	2,246 (5.2)
Ostium secundum atrial septal defect and Ventricular septal defect	993 (2.3)
Ventricular septal defect and Patent ductus arteriosus	526 (1.2)
Ostium secundum atrial septal defect and Aortic valve abnormality	130 (0.3)
Other congenital malformation of pulmonary and tricuspid valve and Patent ductus arteriosus	110 (0.3)

Chapter 3

Hospital Readmission of Congenital Heart Disease Patients in Canada

3.1 Abstract

Background: Little is known about hospital readmission in children or adults with congenital heart disease (CHD). We assessed readmission rates among CHD patients stratified by age, sex, and severity of CHD from 2003 to 2009 in Canada and identified risk factors associated with hospital readmission in CHD patients.

Methods: A retrospective cohort study was conducted among CHD patients identified from the hospital discharge abstract database of the Canadian Institute for Health Information from 2003 to 2009. Poisson regression was used to analyze the readmission rates by age, sex, and severity of CHD. Logistic regression analysis was performed to identify risk factors associated with readmission within 2-week and 1-month after discharge.

Results: The readmission rates of CHD patients were 49 per 1,000 patients within 2-week, 84 per 1,000 patients within 1-month, 164 per 1,000 patients within 3-month, and 352 per 1,000 patients within 1-year. The 65+ patient had an approximately 1.4 to 1.8 times higher readmission rate compared to infants ($p<0.001$). The readmission rates of complex CHD patients were 2.4 to 4.5 times higher than those of simple CHD patients ($p<0.001$), and moderate CHD patients had 1.4 to 1.9 times higher readmission rates than simple CHD patients ($p<0.001$). CHD patients age

40+ years, males, and those with complex CHD were more likely to be readmitted within 2-week and 1-month.

Conclusion: Hospital readmission was common in CHD patients, particularly adults aged 40+ years, males and those with complex lesions. Further studies are required to investigate the mechanism for unplanned readmission.

3.2 Introduction

The number of adults with congenital heart disease (CHD) is rapidly increasing, particularly those with complex lesions (1). In Canada, it was estimated that the number of survivors with adult CHD increased by 70% from 96,324 in 2000 to 166,428 in 2010 (2). This growing population poses a significant burden on the health care system. Though many of these patients undergo reparative surgery in early stage of life, the potential of developing haemodynamic residua and other cardio-pulmonary complications are high in later life in these patients, particularly among those with complex defects (3, 4). A population-based case-control study showed a higher prevalence of comorbid conditions such as atrial fibrillation, heart failure, stroke, and chronic renal failure in CHD patients compared to age-sex-matched controls (5).

Hospital admissions and readmissions represent a vast burden on health care resources and are more common in the CHD population compared to the age-sex-matched general population (7). In Canada, hospital readmissions cost approximately $1.8 billion in 2010 (6). Readmissions are in many cases avoidable and therefore warrant further investigation. However, little is known about hospital readmission in children or adults with CHD. Increasing hospitalizations with CHD over time, reported in several studies (7-9), warrants evaluation of risk factors for readmission in these patients. In this paper, we investigated CHD patients from all ages: (1) to assess the readmission rate among CHD patients from 2003 to 2009; and (2) to identify risk factors for hospital readmission in CHD patients.

3.3 Methods

3.3.1 Study design and data source

We conducted a retrospective cohort study to assess readmission of children and adults with CHD. We identified hospitalizations with a primary or secondary diagnosis of CHD between fiscal years 2003 and 2009 inclusive from the hospital discharge abstract database (DAD) of the Canadian Institute for Health Information (CIHI). This national database includes all acute care hospitalizations in Canada except the province of Quebec.

3.3.2 Study population

Patients with CHD regardless of their age who received inpatient care in Canada between fiscal years 2003 and 2009 were included. Exclusion criteria were patients with isolated patent ductus arteriosus (PDA), patients residing in Quebec, Nunavut, Yukon or the Northwest Territories, and hospitalizations with discharge dates being the same as the admission dates. We also excluded patients who died during the index hospitalization (i.e., the first hospitalization of each patient in the study period) as they were not at risk of readmission. Hospitalizations within 24 hours of discharge were considered hospital-to-hospital transfers and therefore a single hospitalization event. In order to assess the proportion readmitted within a given time length (e.g., 2-week) after the day of discharge of the index hospitalization, we excluded index hospitalizations for which discharge dates were within the given time length (e.g., 2-week) to the end of 2009 fiscal year: for these hospitalizations, readmissions within the given time length were not fully recorded in our database.

3.3.3 Outcome measures

Our primary outcome was the rate of readmission within a given time length after discharge from the index hospitalization. Readmission was defined as all hospital admissions within the 2-week (14 days), 1-month (31 days), 3-month (90 days) and 1-year (365 days) intervals following the index-hospitalization's discharge date. For calculating the readmission rate within one of the specific time intervals, which is a cumulative outcome, we included all readmissions after the discharge from the index hospital admission.

The secondary outcome was first readmission within 2-week and 1-month after discharge from index hospitalization: this was used to identify factors associated with readmission.

3.3.4 Independent variables

The independent variables examined were age, sex, neighborhood median household income, severity of CHD, Charlson co-morbidity index, length of stay, and day of week at discharge. Age, length of stay, Charlson co-morbidity index, and day of week at discharge were defined at the time of index hospitalization. Age was categorized into six categories: infants (<1 year); 1-4 years; 5-17 years; 18-39 years; 40-64 years; and 65+ years. CHD lesions were grouped into three complexities: simple, moderate and complex, as previously defined (10). We classified patients with multiple CHD diagnoses based on the hierarchies of complexities. For example, if a patient had complex lesions and moderate or simple lesions, s/he was classified as a complex CHD patient. Similarly, patients with moderate and simple CHD lesions were categorised as moderate CHD patients. Length of stay was divided into 3 groups: ≤2-week, >2-week to 1-month, and >1-month. For adult patients, we used the Charlson co-morbidity index to define the comorbid conditions (11, 12). Median household income in the forward sortation area (FSA) of the patient's residence was recorded as an indicator of socioeconomic status: this information was obtained from Statistics Canada. We divided our study population into four quartiles of neighborhood (FSA) median household income. Therefore, each quartile represents 25% of the study population. Days of week of discharge were grouped into two categories: Friday or Saturday and other days (Sunday to Thursday).

3.3.5 Statistical analysis

The readmission rate was reported per 1,000 patients (or 1,000 index hospitalizations). The numerator of the readmission rate was the number of readmissions within a given time period (e.g., 2-week), including multiple readmissions of a patient, after the discharge from the index hospitalization. The denominator was the number of index hospitalizations (which is the number of patients as well) in the study period with a sufficient follow-up time to allow the length of the given time period for readmission. Categorical variables were described by frequency distributions.

Poisson regression analysis was performed to assess temporal changes in the readmission rate. The readmission rate was compared across the age groups, sex, and severity of CHD.

We performed two separate multivariable logistic regression analyses to identify factors associated with readmissions within 2-week and 1-month following the index hospitalization. The independent variables we examined were age, sex, severity of CHD, length of stay, median household income, and days of week of discharge. We also assessed readmission in adults adjusting for the Charlson co-morbidity index in addition to other variables in a separate multivariable logistic regression model. Two sided p-values <0.05 were considered statistically significant. All analyses were performed using SAS statistical software (Version 9.3 SAS Institute, Cary, NC).

3.3.6 Ethics

All procedures of the study were approved by the Health Research Ethics Board at the University of Alberta

3.4 Results

Among 68,099 hospitalizations during the study period, we identified 43,182 index hospitalizations, the first hospitalization of a subject during the study period. Total 1,431 (3.3%) patients died during index hospitalization and therefore, were excluded from the analysis. Among 41,540 subjects with a follow up of at least 2-week, 1,985 (4.8%) were readmitted with a readmission rate within 2-week of 49 per 1,000 patients. Among 41,261 patients with a follow up of at least 1-month, 3,195 (7.7%) were readmitted yielding a readmission rate within 1-month of 84 per 1,000 patients. Among 40,425 patients with a follow up of at least 3-month, 5,291 (13.1%) were readmitted with a readmission rate within 3-month of 164 per 1,000 patients. Of 36,315 patients with a follow up of at least a year, 7,923 (21.8%) were readmitted within 1-year with a readmission rate within a year of 352 per 1,000 patients (Table 3.1).

Supplementary Figure 3.1 shows that readmission rate within 2-week, 1-month, 3-month and 1-year decreased slightly but similarly from 2003 to 2009 (Rate ratio 0.97, 95% CI 0.9 to 1.0, p=0.004).

Readmission rates are shown by age group in Figure 3.1. Among all age groups, the patient age 65+ had approximately 1.4 to 1.8 times higher readmission rate for all time periods following the initial discharge, compared to infants ($p<0.001$). Readmission rates in 5-17 years old and 18-39 years old patients were significantly lower in 1-month, 3-month and 1-year than infants ($p<0.001$). In addition, 1-4 year old children had a 0.8 times lower readmission rate than infants but statistically significant at 1-month ($p=0.008$) and 3-month ($p=0.004$).

Figure 3.2 shows the readmission rate by severity of CHD. Patients with complex CHD experienced 2.4 to 4.5 times higher readmission rates following the initial discharge ($p<0.001$); and those with moderate CHD had 1.4 to 1.9 times higher readmission rates than those with simple CHD ($p<0.001$).

The readmission rate was 1.1 times higher in male compared to females in 2-week ($p=0.004$), 1-month and 3-month ($p<0.001$).

In adults, congestive heart failure, atrial fibrillation and flutter, and ischemic heart disease were the most common principal diagnoses at the time of readmission. On the other hand, in children, congestive heart failure and respiratory illnesses were the most common principal non-CHD diagnoses during readmission (Supplementary table 3.1-3.4).

Result of Logistic regression analysis for readmission within 2-week and 1-month

In total 41,540 patients and 41,261 patients were analyzed to determine the odds ratio for readmission within 2-week and 1-month after the discharge from index hospitalizations, respectively. In Table 3.2 and Table 3.3, the characteristics of patients readmitted within 2-week and 1-month and adjusted odds ratios for readmission are presented.

The 65+ and 40-64 years old patients were more likely to be readmitted compared to infants. The odds of readmission within 2-week was 1.3 times higher (95% CI 1.2 to 1.5, p<0.001) in 40-64 years old patients and 2.3 times higher (95% CI 2.0 to 2.6, p<0.001) in the 65+ patients than infants, after adjusting for sex, severity of CHD, neighborhood median income, index hospitalization length of stay, and day of week of discharge. Similar results were found for readmission within 1-month of discharge from index hospitalization (Table 3.3).

The adjusted odds of readmission were slightly higher for male patients with CHD than female counterparts (OR 1.1, 95% CI 1.0 to 1.3, p=0.005) within 2-week, adjusting for age, severity of CHD, neighborhood median income, index hospitalization length of stay, and day of week of discharge: the result for 1-month was identical.

Among CHD patients, odds of readmission increased with increasing severity of CHD. Within 2-week of discharge, the odds of readmission was 1.6 times higher for moderate CHD patients (95% CI 1.5 to 1.8, p<0.001) and 3.3 times higher for complex CHD patients (95% CI 2.8 to 3.8, p<0.001) compared to simple CHD patients. The odds ratios of readmission within 1-month was 4.0 for complex CHD patients (95% CI 3.5 to 4.5, p<0.001) and 1.7 for moderate CHD patients (95% CI 1.6 to 1.9, p<0.001), compared to simple CHD patients.

Patients who stayed in hospital for '>2-week to 1-month' or '>1-month' had higher odds of readmission within one month compared to patients with hospital stay '≤2-week' during index hospitalizations (OR 1.2, 95% CI 1.0 to 1.3, p=0.005 and OR 1.2, 95% CI 1.1 to 1.3, p=0.001, respectively).

Patients from the lowest quartile of neighborhood median household income showed slightly higher; but statistically insignificant odds of readmission within 1-month compared to patients from the highest quartile (Table 3.3). There was no difference in odds of readmission within 2-week among patients who were discharged on Friday or Saturday compared to those who were discharged on Sunday to Thursday (OR 1.0, 95% CI 0.9 to 1.1, p=0.63). A similar result was found for 1-month readmission with no difference by day of the week.

Adults with 1-2 comorbidity index showed 1.4 times higher odds of readmission within 2 weeks (95% CI 1.2 to 1.7, p<0.001) and those with 3+ comorbidity index had 2.0 times higher odds of readmission (95% CI 1.5 to 2.7, p<0.010) compared to adults with no comorbid condition adjusting for other variables. Similar result was found for readmission within 1-month. In supplementary table 3.5 and 3.6, odds of readmission in adults were presented adjusting for the Charlson co-morbidity index in addition to other variables.

3.5 Discussion

In this study, we investigated hospital readmission of CHD patients from all ages in Canada from 2003 to 2009. Approximately 5%, 8%, 13% and 22% of patients were readmitted within 2-week, 1-month, 3-month and 1-year respectively following the index hospitalization. Readmissions were more common in adults 40 years or older, males, longer index hospitalization stay and among those with complex lesions.

The readmission rate observed in our study population was lower than that reported in a study conducted in children with CHD (≤17 years) in Quebec which reported the cumulative readmission of 9% (vs. 3.7%-4.6% in this study) within 14 days and 14% (vs. 6.7%-8.4% in this study) within 31days (13). A case control study showed readmission rate within of 3.8% after the arterial switch procedure and 11.4 % after the Norwood procedure in neonate in children's hospital in Boston (14). In a population of 334,959 children largely without CHD discharged from hospitals in Ontario, around 3.4% of children were readmitted within one month of discharge (15). An American study conducted in 72 children's hospitals in 34 States reported an all-cause unplanned readmission rate within 30 days of 6.5%, also largely among children without CHD (16). Contrary to U.S, Canada has publicly funded universal healthcare systems which might have resulted in lower readmission rate in the Ontario study than that observed in the U.S study. There is a paucity of data on readmission of adult CHD patients.

In this study, we investigated both children and adult CHD patients for the readmission and compared the readmission across the age groups. Among children (<18 year), the readmission rate was significantly higher in infants at all-time points except 2-week. However, Mackie *et al*. in Quebec found 22% of infants were readmitted within one month compared to 11% of older children (13). Among adults (>18 years) in the current study, the readmission rate increased with increasing age at all-time points, with the highest readmission rate in 65+ years patients. This may reflect a greater burden of cardiac complications or co-morbid conditions in adults relative to the other age groups. It has been estimated that approximately 55% of adult CHD patients are at significant risk of premature death, re-operation and complications (10). Over the past six decades, the management of CHD has evolved significantly because of the provision of newer techniques (3). Many older patients with simple lesions may need to undergo surgery in adulthood (17). In addition, many adult CHD patients require re-intervention or revision of prior surgical procedures (17). At the time of transition from pediatric to adult cardiology care, many young adult patients become lost to follow up from specialist care and present later with overt symptoms of complications requiring multiple admissions (18-20).

Readmission was slightly more common in male than female patients. Male patients may develop more complications or comorbid conditions requiring hospitalizations or interventions compared to females. Study using CONCOR (CONgenital CORvitia) Dutch national registry showed that adult females with CHD were at lower risk of developing infective endocarditis (47%), aortic outcomes (33%) and arrhythmia (22%) than male (21).

Patients in the lowest quartile had slightly higher odds of readmission within 1-month than that of patients in the highest quartile after adjusting for age, sex, severity of CHD, LOS, and day of week of discharge. Lower SES has been found to be a predictor of readmission among patients with heart failure; patients from the lowest quartile were 1.2 times more likely to be readmitted than those form highest quartile (22). SES might influence utilization of health care services even in a universal health care system in Canada. A study using data of a national population health survey done in 1994 in Canada showed that, although patients from lower SES had more visits to primary care providers, those with higher SES had more specialist visits (23).

We found a substantial effect of CHD complexity on readmission. The readmission rate was appreciably higher in patients with complex CHD followed by those with moderate and simple CHD patients. Data from Quebec is consistent with these observations, where the readmission rate within 31 days was approximately 1.5 times higher was among children with severe lesions (13). Patients with complex CHD are more likely to develop complications due to the disease itself or associated with prior surgical or catheter interventions (24).

We hypothesized that patients, who stayed in hospital for longer duration, might be sicker relative to other patients and therefore, required more readmission. We found that longer duration of hospital stay was significantly associated with readmission within 1-month. Our finding is parallel to that reported among children with CHD in Quebec (13).Days of discharge has been shown to be important an predictor for readmission (13). However, days of discharge had no significant effect on readmission in our study.

Adult patients develop comorbid conditions like diabetes, cardiovascular events or renal disease with aging (5). We used the Charlson co-morbidity index to measure the burden of comorbidity on readmission in adult CHD patients. In our study, adults with more comorbid conditions were more likely to be readmitted.

Strengths and limitations of study

We did not have any data on outpatient management or clinical events among study subjects. Out of hospital death and migration to other countries or provinces were not included in the study. We assumed patients who were not readmitted were alive throughout the study period and censored at one year: this might not be a valid assumption. We were unable to distinguish planned from unplanned hospital readmissions, though both represent a burden on health care systems and affected individuals.

We used an administrative database which has limited clinical information and is prone to misclassification. We did not have any information on the location or type of hospital (tertiary care vs. community). We used neighbourhood median household income in FSA, which is an aggregate measure, as a proxy of patients' socioeconomic status. Substantial heterogeneity was observed across individual income within the same FSA in Alberta (25). Using Statistics Canada Census data from 1996, authors found that FSA-based income level misclassified over 50% of the subjects compared to income quintiles based on enumeration area (EA) (26). Since EA is a smaller unit than FSA, there is less variation in income level within the same EA.

Despite these limitations, use of a national-level administrative database allowed us to capture a large sample from all hospitals in all provinces of Canada except Quebec and the territories. We included all age groups, unlike prior studies, which allowed a broad perspective as the number of adults with CHD is increasing and CHD is a lifelong condition.

3.6 Conclusion

In summary, hospital readmission was common in CHD patients, particularly among adults age 40+, males, and among patients with complex lesions. These data support the need for adults with CHD to be followed in specialized adult CHD programs with personnel experienced in the management of CHD. Further studies are needed to determine the mechanisms responsible for unplanned readmissions.

References

1. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. Circulation. 2007 Jan 16;115(2):163-72.

2. Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Lifetime Prevalence of Congenital Heart Disease in the General Population from 2000 to 2010. Circulation. Jun 18.

3. Guleserian KJ. Adult congenital heart disease: surgical advances and options. Prog Cardiovasc Dis. Jan-Feb;53(4):254-64.

4. Webb G, Williams RG, editors. Care of the Adult With Congenital Heart Disease. 32nd Bethesda Conference; 2001. Journal of American College of Cardiology.

5. Billett J, Cowie MR, Gatzoulis MA, Vonder Muhll IF, Majeed A. Comorbidity, healthcare utilisation and process of care measures in patients with congenital heart disease in the UK: cross-sectional, population-based study with case-control analysis. Heart. 2008 Sep;94(9):1194-9.

6. McKesson Canada. Reducing Avoidable Hospital Readmissions: A Strategic Approach to Better Management of Costs and Clinical Outcomes. ; 2013 Contract No.: Document Number|.

7. Mackie AS, Pilote L, Ionescu-Ittu R, Rahme E, Marelli AJ. Health care resource utilization in adults with congenital heart disease. Am J Cardiol. 2007 Mar 15;99(6):839-43.

8. Opotowsky AR, Siddiqi OK, Webb GD. Trends in hospitalizations for adults with congenital heart disease in the U.S. J Am Coll Cardiol. 2009 Jul 28;54(5):460-7.

9. Billett J, Majeed A, Gatzoulis M, Cowie M. Trends in hospital admissions, in-hospital case fatality and population mortality from congenital heart disease in England, 1994 to 2004. Heart. 2008 Mar;94(3):342-8.

10. Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, et al. Task force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol. 2001 Apr;37(5):1170-5.

11. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.

12. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol. 2004 Dec;57(12):1288-94.

13. Mackie AS, Ionescu-Ittu R, Pilote L, Rahme E, Marelli AJ. Hospital readmissions in children with congenital heart disease: a population-based study. Am Heart J. 2008 Mar;155(3):577-84.

14. Mackie AS, Gauvreau K, Newburger JW, Mayer JE, Erickson LC. Risk factors for readmission after neonatal cardiac surgery. Ann Thorac Surg. 2004 Dec;78(6):1972-8; discussion 8.

15. Beck CE, Khambalia A, Parkin PC, Raina P, Macarthur C. Day of discharge and hospital readmission rates within 30 days in children: A population-based study. Paediatr Child Health. 2006 Sep;11(7):409-12.

16. Berry JG, Toomey SL, Zaslavsky AM, Jha AK, Nakamura MM, Klein DJ, et al. Pediatric readmission prevalence and variability across hospitals. JAMA. Jan 23;309(4):372-80.

17. Warnes CA. The adult with congenital heart disease: born to be bad? J Am Coll Cardiol. 2005 Jul 5;46(1):1-8.

18. Dearani JA, Connolly HM, Martinez R, Fontanet H, Webb GD. Caring for adults with congenital cardiac disease: successes and challenges for 2007 and beyond. Cardiol Young. 2007 Sep;17 Suppl 2:87-96.

19. Gatzoulis MA. Adult congenital heart disease: a cardiovascular area of growth in urgent need of additional resource allocation. Int J Cardiol. 2004 Dec;97 Suppl 1:1-2.

20. Curtis SL, Stuart AG. Outcome in congenital heart disease. Current Paediatrics. 2005;15(7):549-56.

21. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Vliegen HW, et al. Gender and outcome in adult congenital heart disease. Circulation. 2008 Jul 1;118(1):26-32.

22. Philbin EF, Dec GW, Jenkins PL, DiSalvo TG. Socioeconomic status as an independent risk factor for hospital readmission for heart failure. Am J Cardiol. 2001 Jun 15;87(12):1367-71.

23. Dunlop S, Coyte PC, McIsaac W. Socio-economic status and the utilisation of physicians' services: results from the Canadian National Population Health Survey. Soc Sci Med. 2000 Jul;51(1):123-33.

24. Hoffmann A, Chockalingam P, Balint OH, Dadashev A, Dimopoulos K, Engel R, et al. Cerebrovascular accidents in adult patients with congenital heart disease. Heart. Aug;96(15):1223-6.

25. Sin DD, Svenson LW, Man SF. Do area-based markers of poverty accurately measure personal poverty? Can J Public Health. 2001 May-Jun;92(3):184-7.

26. Southern DA, Ghali WA, Faris PD, Norris CM, Galbraith PD, Graham MM, et al. Misclassification of income quintiles derived from area-based measures. A comparison of enumeration area and forward sortation area. Can J Public Health. 2002 Nov-Dec;93(6):465-9.

Tables and Figures

Table 3.1: Readmission rate within 2-week, 1-month, 3-month and 1-year

Time since discharge date of initial hospitalization	Index hospitalizations (D)#	Patients readmitted N (%)	Readmission hospitalizations (R)	Readmission rate per 1,000 patients*
2-week	41,540	1,985 (4.8)	2,026	49
1-month	41,261	3,195 (7.7)	3,461	84
3-month	40,425	5,291 (13.1)	6,623	164
1-year	36,315	7,923 (21.8)	12,795	352

Number of patients with first hospitalization

*Readmission rate per 1,000 patients=(R/D) × 1,000

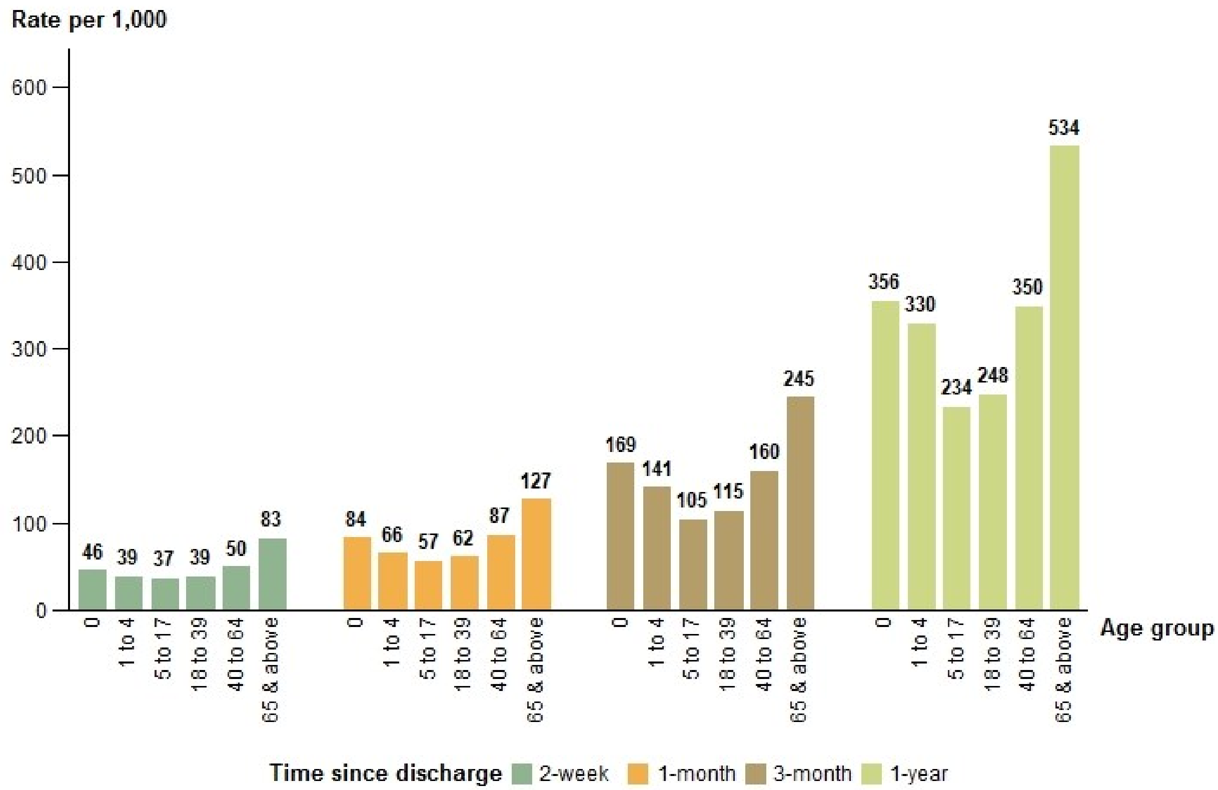


Figure 3.1: Readmission rate across age groups

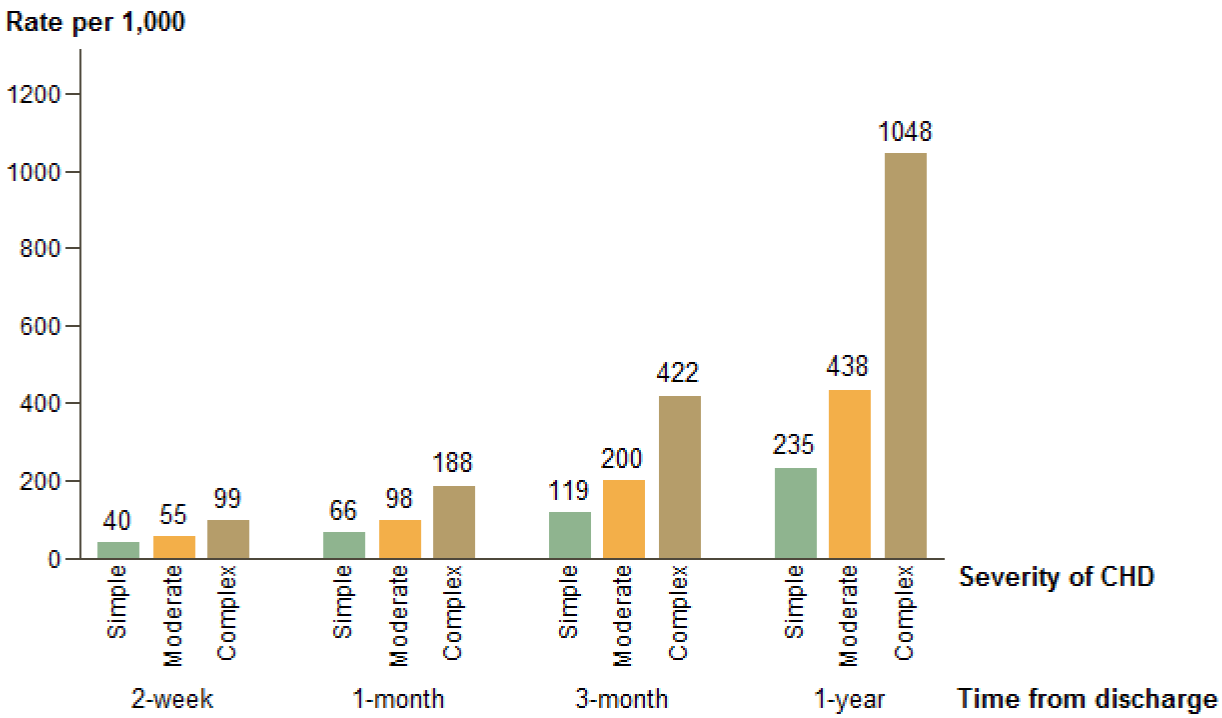


Figure 3.2: Readmission rate by severity of CHD

Table 3.2: Baseline characteristics of 41,540 patients and adjusted odds ratios for readmission within 2-week

Characteristics	Patients readmitted N=1,985	Patients not readmitted N= 39,555	Adjusted* odds ratios with 95% confidence interval	p-values
Age groups				
<1 year	921 (4.5)	19,690 (95.5)	1.0	
1-4 years	75 (3.7)	1,949 (96.3)	0.7 (0.6 to 0.9)	0.010
5-17 years	114 (3.7)	2,980 (96.3)	0.7 (0.6 to 0.9)	0.001
18-39 years	171 (3.9)	4,218 (96.1)	0.9 (0.8 to 1.1)	0.38
40-64 years	350 (5.0)	6,663 (95.0)	1.3 (1.2 to 1.5)	<0.001
65+ years	354 (8.0)	4,055 (92.0)	2.3 (2.0 to 2.6)	<0.001
Sex				
Female	868 (4.4)	18,726 (95.6)	1.0	
Male	1,117 (5.1)	20,829 (94.9)	1.1 (1.0 to 1.3)	0.005
Neighborhood median household income (CAD)				
≤ 47,453	492 (4.8)	9,747 (95.2)	1.0 (0.9 to 1.1)	0.94
47,454-55,365	493 (4.8)	9,777 (95.2)	1.0 (0.9 to 1.1)	0.91
55,368-69,622	495 (4.9)	9,715 (95.1)	1.0 (0.9 to 1.2)	0.72
69,711-169,666	486 (4.6)	10,030 (95.4)	1.0	
Length of stay				
≤2-week	1,380 (4.5)	28,992 (95.5)	1.0	
>2-week-1-month	334 (5.7)	5,528 (94.3)	1.1 (1.0 to 1.3)	0.048
>1-month	271 (5.1)	5,035 (94.9)	1.1 (0.9 to 1.2)	0.29
Severity of CHD				
Simple	1,035 (4.0)	25,035 (96.0)	1.0	
Moderate	690 (5.4)	12,039 (94.6)	1.6 (1.5 to 1.8)	<0.001
Complex	260 (9.5)	2,481 (90.5)	3.3 (2.8 to 3.8)	<0.001
Days of week of discharge				
Sunday to Thursday	1,421 (4.8)	27,983 (95.2)	1.0	
Friday or Saturday	564 (4.7)	11,572 (95.4)	1.0 (0.9 to 1.1)	0.58

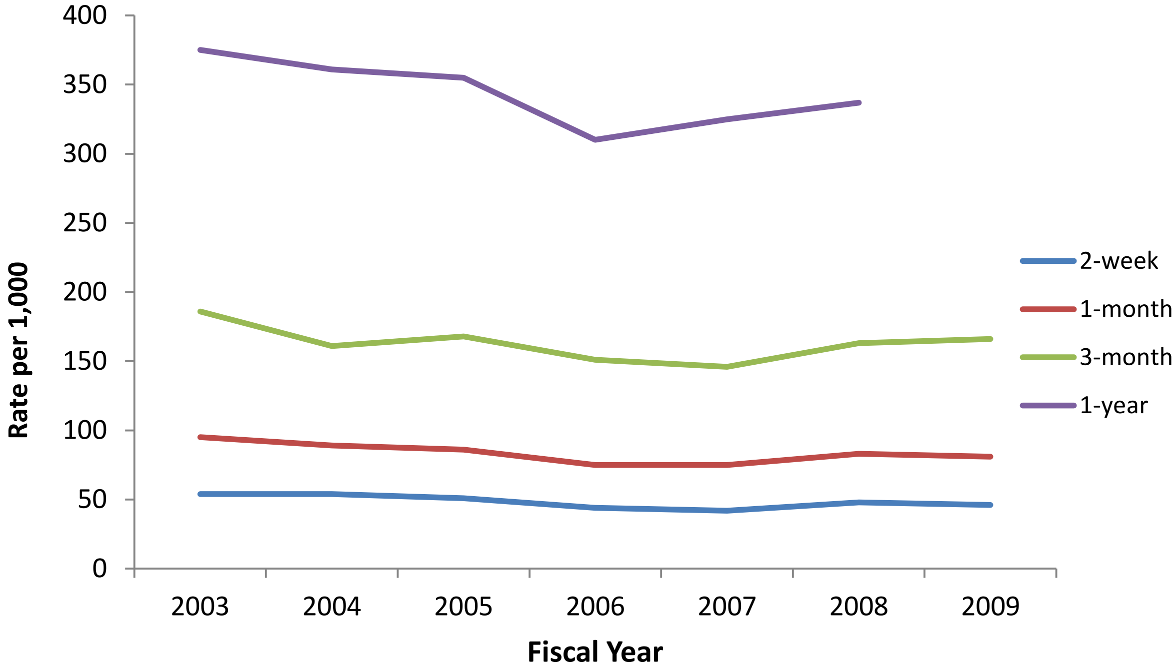
*Adjusted for variables listed in table

Table 3.3: Baseline characteristics of 41,261 patients and adjusted odds ratios for readmission within 1-month

Characteristics	Patients readmitted N=3,195	Patients not readmitted N=38,066	Adjusted* odds ratios with 95% confidence interval	p-values
Age groups				
<1 year	1,562 (7.6)	18,885 (92.4)	1.0	
1-4 years	120 (6.0)	1,892 (94.0)	0.7 (0.6 to 0.8)	<0.001
5-17 years	167 (5.4)	2,914 (94.6)	0.6 (0.5 to 0.7)	<0.001
18-39 years	253 (5.8)	4,110 (94.2)	0.8 (0.7 to 1.0)	0.005
40-64 years	572 (8.2)	6,400 (91.8)	1.4 (1.2 to 1.5)	<0.001
65+ years	521 (11.9)	3,865 (88.1)	2.1 (1.9 to 2.4)	<0.001
Sex				
Female	1,410 (7.2)	18,060 (92.8)	1.0	
Male	1,785 (8.2)	20,006 (91.8)	1.1 (1.0 to 1.2)	0.003
Neighborhood median household income (CAD)				
≤ 47,453	830 (8.2)	9,350 (91.8)	1.1 (1.0 to 1.2)	0.26
47,454-55,365	783 (7.7)	9,419 (92.3)	1.0 (0.9 to 1.1)	0.83
55,368-69,622	780 (7.7)	9,355 (92.3)	1.0 (0.9 to 1.1)	0.71
69,711-169,666	771 (7.4)	9,668 (92.6)	1.0	
Length of stay				
≤2-week	2,163 (7.2)	28,009 (93.8)	1.0	
>2-week-1-month	542 (9.3)	5,280 (90.7)	1.2 (1.0 to 1.3)	0.005
>1-month	490 (9.3)	4,777 (90.7)	1.2 (1.1 to 1.3)	0.001
Severity of CHD				
Simple	1,598 (6.2)	24,294 (93.8)	1.0	
Moderate	1,136 (9.0)	11,501 (91.0)	1.7 (1.6 to 1.9)	<0.001
Complex	461 (16.9)	2,271 (83.1)	4.0 (3.5 to 4.5)	<0.001
Days of week of discharge				
Sunday to Thursday	2,276 (7.8)	26,913 (92.2)	1.0	
Friday or Saturday	919 (7.6)	11,153 (92.4)	1.0 (0.9 to 1.1)	0.78

*Adjusted for variables listed in table

Appendices



Supplementary Figure 3.1: Temporal changes in CHD readmission rate

Supplementary Table 3.1: Principal diagnoses at time of readmission within 2-week

Children	n (%)	Adult	n (%)
Total readmissions	1,137	**Total readmissions**	889
Principal diagnoses		**Principal diagnoses**	
Ventricular septal defect	46 (4.0)	Congestive heart failure	102 (11.5)
Acute bronchiolitis	30 (2.6)	Atrial fibrillation and flutter	86 (9.7)
Congestive heart failure	30 (2.6)	Ischaemic heart disease	50 (5.6)
Tetralogy of Fallot	29 (2.6)	Non rheumatic aortic valve disorder	44 (4.9)
Upper respiratory tract infection	28 (2.5)	Atherosclerosis of coronary artery without angina	30 (3.4)
Pneumonia	26 (2.3)	Infective endocarditis	23 (2.6)
Other specified anomalies of heart	20 (1.8)	Pneumonia	20 (2.2)
Transposition of the great arteries	20 (1.8)	Supraventricular tachycardia	18 (2.0)
Endocardial cushion defect	20 (1.8)	Ostium secundum atrial septal defect	15 (1.7)
Coarctation of the aorta	17 (1.5)	Pleural effusion	14 (1.6)

Supplementary Table 3.2: Principal diagnoses at time of readmission within 1-month

Children	n (%)	Adult	n (%)
Total readmissions	2,023	**Total readmissions**	1,438
Principal diagnoses		**Principal diagnoses**	
Ventricular septal defect	84 (4.2)	Congestive heart failure	181 (12.6)
Acute bronchiolitis	75 (3.7)	Atrial fibrillation and flutter	134 (9.3)
Congestive heart failure	70 (3.5)	Ischaemic heart disease	84 (5.8)
Tetralogy of Fallot	65 (3.2)	Non rheumatic aortic valve disorder	81 (5.6)
Upper respiratory tract infection	50 (2.5)	Atherosclerosis of coronary artery without angina	51 (3.5)
Pneumonia	45 (2.2)	Infective endocarditis	30 (2.1)
Endocardial cushion defect	43 (2.1)	Ostium secundum atrial septal defect	30 (2.1)
Coarctation of the aorta	36 (1.8)	Pneumonia	29 (2.0)
Transposition of the great arteries	36 (1.8)	Non rheumatic mitral valve disorder	27 (1.9)
Other specified anomalies of heart	27 (1.3)	Supraventricular tachycardia	25 (1.7)

Supplementary Table 3.3: Principal diagnoses at time of readmission within 3-month

Children	n (%)	Adult	n (%)
Total readmissions	3,983	**Total readmissions**	2,640
Principal diagnoses		**Principal diagnoses**	
Ventricular septal defect	200 (5.0)	Congestive heart failure	336 (12.7)
Acute bronchiolitis	158 (4.0)	Atrial fibrillation and flutter	218 (8.3)
Congestive heart failure	155 (3.9)	Non rheumatic aortic valve disorder	164 (6.2)
Tetralogy of Fallot	145 (3.6)	Ischaemic heart disease	130 (4.9)
Pneumonia	130 (3.3)	Atherosclerosis of coronary artery without angina	119 (4.5)
Upper respiratory tract infection	103 (2.6)	Ostium secundum atrial septal defect	86 (3.3)
Endocardial cushion defect	101 (2.5)	Non rheumatic mitral valve disorder	57 (2.2)
Coarctation of the aorta	97 (2.4)	Infective endocarditis	50 (1.9)
Transposition of the great arteries	87 (2.2)	Supraventricular tachycardia	46 (1.7)
Hypoplastic left heart syndrome	76 (1.9)	Aortic valve abnormality	41 (1.6)

Supplementary Table 3.4: Principal diagnoses at time of readmission within 1-year

Children	**n (%)**	**Adult**	**n (%)**
Total readmissions	7,624	**Total readmissions**	5,171
Principal diagnoses		**Principal diagnoses**	
Ventricular septal defect	402 (5.3)	Congestive heart failure	704 (13.6)
Tetralogy of Fallot	401 (5.3)	Atrial fibrillation and flutter	390 (7.5)
Acute bronchiolitis	350 (4.6)	Non rheumatic aortic valve disorder	263 (5.1)
Pneumonia	331 (4.3)	Ischaemic heart disease	250 (4.8)
Endocardial cushion defect	239 (3.1)	Atherosclerosis of coronary artery without angina	214 (4.1)
Congestive heart failure	228 (3.0)	Ostium secundum atrial septal defect	207 (4.0)
Upper respiratory tract infection	214 (2.8)	Non rheumatic mitral valve disorder	109 (2.1)
Transposition of the great arteries	178 (2.3)	Supraventricular tachycardia	99 (1.9)
Hypoplastic left heart syndrome	149 (2.0)	Pneumonia	91 (1.8)
Coarctation of the aorta	133 (1.7)	Infective endocarditis	90 (1.7)

Supplementary Table 3.5: Baseline characteristics of 15,811 adult patients and adjusted odds ratios for readmission within 2-week

Characteristics	Patients readmitted N=875	Patients not readmitted N= 14,936	Adjusted* odds ratios with 95% confidence interval	p-values
Age groups				
18-39 years	171 (3.9)	4,218 (96.1)	1.0	
40-64 years	350 (5.0)	6,663 (95.0)	1.2 (1.0 to 1.5)	0.064
65+ years	354 (8.0)	4,055 (92.0)	1.9 (1.6 to 2.4)	<0.001
Sex				
Female	384 (5.1)	7,150 (94.9)	1.0	
Male	491 (5.9)	7,786 (94.1)	1.1 (1.0 to 1.3)	0.17
Neighborhood median household income (CAD)				
≤ 47,453	225 (5.7)	3,759 (94.4)	1.2 (1.0 to 1.5)	0.066
47,454-55,365	235 (5.9)	3,718 (94.1)	1.3 (1.0 to 1.6)	0.021
55,368-69,622	229 (5.9)	3,664 (94.1)	1.3 (1.0 to 1.5)	0.028
69,711-169,666	174 (4.5)	3,705 (95.5)	1.0	
Length of stay				
≤2-week	703 (5.4)	12,327 (94.6)	1.0	
>2-week-1-month	134 (6.9)	1,798 (93.1)	1.0 (0.8 to 1.2)	0.76
>1month	38 (4.5)	811 (95.5)	0.6 (0.4 to 0.9)	0.005
Severity of CHD				
Simple	643 (5.5)	11,043 (94.5)	1.0	
Moderate	204 (5.4)	3,563 (94.6)	1.1 (1.0 to 1.4)	0.11
Complex	28 (7.8)	330 (92.2)	2.1 (1.4 to 3.1)	<0.001
Charlson comorbidity score				
0	390 (4.4)	8,501 (95.6)	1.0	
1-2	420 (6.8)	5,792 (93.2)	1.4 (1.2 to 1.7)	<0.001
3+	65 (9.2)	643 (90.8)	2.0 (1.5 to 2.7)	<0.001
Days of week of discharge				
Sunday to Thursday	632 (5.6)	10,675 (94.4)	1.0	
Friday or Saturday	243 (5.4)	4,261 (94.6)	1.0 (0.8 to 1.2)	0.87

*Adjusted for variables listed in tables

Supplementary Table 3.6: Baseline characteristics of 15,721 adult patients and adjusted odds ratios for readmission within 1-month

Characteristics	**Patients readmitted N=1,346**	**Patients not readmitted N= 14,375**	**Adjusted* odds ratios with 95% confidence interval**	**p-values**
Age groups				
18-39 years	253 (5.8)	4,110 (94.2)	1.0	
40-64 years	572 (8.2)	6,400 (91.8)	1.3 (1.1 to 1.6)	<0.001
65+ years	521 (11.9)	3,865 (88.1)	1.9 (1.6 to 2.3)	<0.001
Sex				
Female	574 (7.7)	6,922 (92.3)	1.0	
Male	722 (9.4)	7,453 (90.6)	1.2 (1.0 to 1.3)	0.009
Neighborhood median household income (CAD)				
≤ 47,453	348 (8.8)	3,615 (91.2)	1.2 (1.0 to 1.4)	0.079
47,454-55,365	348 (8.9)	3,584 (91.1)	1.2 (1.0 to 1.4)	0.075
55,368-69,622	351(9.1)	3,516 (90.9)	1.2 (1.0 to 1.4)	0.031
69,711-169,666	281(7.3)	3,576 (92.7)	1.0	
Length of stay				
≤2-week	1,062 (8.2)	11,897 (91.8)	1.0	
>2-week-1-month	211 (11.0)	1,707 (89.0)	1.1 (0.9 to 1.3)	0.25
>1month	73 (8.7)	771 (91.4)	0.8 (0.6to 1.1)	0.11
Severity of CHD				
Simple	973 (8.4)	10,648 (91.6)	1.0	
Moderate	329 (8.8)	3,414 (91.2)	1.2 (1.1 to 1.4)	0.002
Complex	44 (12.3)	313 (87.7)	2.3 (1.6 to 3.1)	<0.001
Charlson comorbidity score				
0	587 (6.6)	8,250 (93.4)	1.0	
1-2	667 (10.8)	5,509 (89.2)	1.5 (1.3 to 1.7)	<0.001
3+	92 (13.0)	616 (87.0)	1.8 (1.4 to 2.3)	<0.001
Days of week of discharge				
Sunday to Thursday	952 (8.5)	10,286 (91.5)	1.0	
Friday or Saturday	394 (8.8)	4,089 (91.2)	1.1 (0.9 to 1.2)	0.31

*Adjusted for variables listed in tables

Supplementary methods for time to event analysis

For the purpose of determining time to first readmission after the initial discharge, we did multivariable Cox proportional hazard regression analysis on the sample followed for 1-year. There was no information regarding out of hospital death and migration of patients. We assumed patients who were not readmitted within 1-year were censored at 1-year. In addition, we also checked whether the hazard of readmission differed at different time intervals.

Supplementary Table 3.7: Baseline characteristics of 36,315 patients and adjusted hazard ratios for readmission within 1-year

Characteristics	**Patients readmitted N=7,923**	**Patients not readmitted N= 28,392**	**Adjusted* hazard ratios with 95% confidence interval**	**p-values**
Age groups				
<1 year	3,535 (19.8)	14,347 (80.2)	1.0	
1-4 years	369 (20.1)	1,468 (79.9)	0.8 (0.7 to 0.9)	<0.001
5-17 years	471 (17.1)	2,286 (82.9)	0.7 (0.6 to 0.8)	<0.001
18-39 years	682 (17.7)	3,169 (82.3)	0.9 (0.9 to 1.0)	0.15
40-64 years	1,490 (24.6)	4,565 (75.4)	1.7 (1.6 to 1.8)	<0.001
65+ years	1,376 (35.0)	2,557 (65.0)	2.6 (2.5 to 2.8)	<0.001
Sex				
Female	3,609 (21.1)	13,501 (78.9)	1.0	
Male	4,314 (22.5)	14,891 (77.5)	1.1 (1.0 to 1.1)	0.020
Neighborhood median household income (CAD)				
≤ 47,453	2,028 (22.5)	6,984 (77.5)	1.0 (1.0 to 1.1)	0.39
47,454 to 55,365	1,930 (21.5)	7,056 (78.5)	1.0 (0.9 to 1.1)	0.94
55,368 to 69,622	2,004 (22.4)	6,947 (77.6)	1.1 (1.0 to 1.1)	0.09
69,711 to 169,666	1,904 (20.9)	7,198 (79.1)	1.0	
Length of stay				
≤2-week	5,389 (20.2)	21,249 (79.8)	1.0	
>2-week-1-month	1,325 (26.0)	3,771 (74.0)	1.2 (1.1 to 1.3)	<0.001
>1month	1,209 (26.4)	3,372 (73.6)	1.3 (1.2 to 1.4)	<0.001
Severity of CHD				
Simple	3,741(16.5)	18,924 (83.5)	1.0	
Moderate	2,953 (26.3)	8,259 (73.7)	2.0 (1.9 to 2.1)	<0.001
Complex	1,229 (50.41)	1,209 (49.6)	5.1 (4.8 to 5.5)	<0.001
Days of weeks of discharge				
Sunday to Thursday	5,535 (21.6)	20,140 (78.4)	1.0	
Friday or Saturday	2,388 (22.4)	8,252 (77.6)	1.1 (1.0 to 1.1)	0.017

*Adjusted for variables listed in table

Supplementary Table 3.8: Adjusted hazard ratio for readmission at different time periods after initial discharge across age groups* and severity of CHD**

Variables	**2-week or less**		**2-week-1-month**		**1-month-3-month**		**3-month-1-year**	
	Hazard Ratios with 95% CI	p-values	Hazard Ratios with 95% CI	p-values	Hazard Ratios with 95% CI	p-values	Hazard Ratios with 95% CI	p-values
Age groups								
<1 year	1.0		1.0		1.0		1.0	
1-4 years	0.7 (0.6 to 0.9)	0.012	0.6 (0.4 to 0.8)	0.002	0.7 (0.6 to 1.0)	0.016	1.0 (0.9 to 1.2)	0.89
5-17 years	0.7 (0.6 to 0.9)	0.004	0.5 (0.3 to 0.6)	<0.001	0.6 (0.4 to 0.7)	<0.001	0.9 (0.8 to 1.0)	0.06
18-39 years	1.0 (0.8 to 1.2)	0.68	0.7 (0.6 to 0.9)	0.003	0.8 (0.7 to 1.0)	0.049	1.1 (1.0 to 1.2)	0.15
40-64 years	1.6 (1.4 to 1.8)	<0.001	1.4 (1.2 to 1.7)	<0.001	1.4 (1.2 to 1.6)	<0.001	2.0 (1.8 to 2.2)	<0.001
65+ years	2.6 (2.3 to 3.0)	<0.001	1.7 (1.5 to 2.1)	<0.001	2.3 (2.0 to 2.6)	<0.001	3.2 (2.9 to 3.6)	<0.001
Severity of CHD								
Simple	1.0		1.0		1.0		1.0	
Moderate	1.7 (1.5 to 1.9)	<0.001	1.9 (1.7 to 2.2)	<0.001	2.2 (2.0 to 2.5)	<0.001	2.1 (1.9 to 2.2)	<0.001
Complex	3.3 (2.8 to 3.8)	<0.001	4.8 (4.1 to 5.8)	<0.001	5.8 (5.1 to 6.6)	<0.001	6.3 (5.7 to 7.0)	<0.001

*Adjusted for sex, neighborhood median income, severity of CHD, LOS and days of week of discharge

** Adjusted for age, sex, neighborhood median income, LOS and days of week of discharge

Chapter 4

Summary, implications and future directions

4.1 Summary

4.1.1 Summary findings from Chapter 2

This is the first study in Canada to document temporal trends in hospitalization of CHD patients. We observed higher inpatient service utilization in CHD patients with an average of 1.1% increase per year from 2003 to 2009. The relative increase in the number of admissions with CHD was higher than that of all cause admissions in Canada during the same time period (1). The number of hospitalizations increased in adults particularly in 40 years or older patients but there was no change in children. Infants, the patient age 65+, males, and patients with complex CHD had the greatest duration of total hospital stay over the study periods.

Higher inpatient service utilization was reported among CHD patients in other countries which support our findings. A population based study of patients from all age groups with CHD as primary diagnosis found a 9.7% increase (an average of 1.2% per year) in the number of hospital admissions from 1995/1996 to 2003/2004 in England (2). In the U.S, the annual number of hospitalizations in adults with CHD increased more than double between 1998 and 2005, with an average increase of 14.6% per year (3). Unlike this U.S study, we excluded hospitalizations with day procedures and we excluded subjects with a PFO, which might have resulted in lower increases in hospitalization in our study population than that observed in the U.S. The authors used ICD9 codes for CHD diagnosis while only 5% of our hospitalizations had diagnosis with ICD9 coding. Several other studies showed significantly increased healthcare resource utilization among CHD patients using ICD 9 coding. Another possible explanation might be the difference in the healthcare system between Canada and U.S. In Canada, due to its publicly funded universal healthcare system, people are more likely to visit outpatient or emergency departments which might have resulted in lower hospitalization in Canada.

The annual hospitalization rate remained relatively stable varying between 38 and 40 per 100,000 persons. The Canadian population experienced an average of 1.1% growth per year from 2003 to 2009 (4) which is consistent with the constant annual hospitalization rates, while the admission number increased by 1.1% per year during the period studied. In terms of planning for healthcare resources, the absolute number of hospitalizations would be more relevant than the hospitalization rates. Mackie *et al.* found the hospitalization rate among adult CHD patients was 214 per 1,000 person-years in Quebec (5). The annual hospitalization rate among CONCOR (CONgenital CORvitia) adult CHD patients in Netherlands was 308 per 1,000 patient-years (6). The difference in hospitalization rate reported in our study is due to the different denominators. We measured the hospitalization rate of CHD patients per general population. In contrast, the denominator used in the Quebec and Dutch studies was the 'CHD patients'.

The number of hospitalization increased significantly in adults particularly in 40-64 years old and patients age 65+: in the 40-64 years age group, the increase was by 3.5% per year and in the patient 65+, it was by 3.1% per year. Similar to our findings, increased hospitalization among adult CHD patients have been reported in other countries (3, 7). Evidence suggests that the number of adults with CHD have been rising rapidly, even more so than children with CHD (8, 9). Moreover, the adult survivors of CHD have increased risk of co-morbidity like infective endocarditis (10, 11), arrhythmia (12), heart failure (13) and coronary heart disease (14) predisposing to more frequent hospitalizations.

The age-specific annual hospitalization rate showed a significant decreasing trend for infants (by 2.2% per year) over the study period. The number of infants increased in the general population with an average of 2.0% per year (4), more than the increase in the number of hospitalizations with CHD in infants, an average increase of 0.3% per year. However, the annual hospitalization rate increased by 1.2% per year for 40-64 years old patients and by 1.4% per year for patients 65+. Small amount of increase in the annual hospitalization rate for the older patients relative to the increase in the number of hospitalization might be explained by the increase in the number of people in the general population. For example, the number of the persons age 65+ in the general population increased by 2.4% per year compared to 3.1% increase in the number of hospitalizations per year. For 40-64 years age group, the number of people increased in the general population by 2.2% per year compared to 3.5% per year increase in the number of hospitalizations. In the other age groups (1- 4 years, 5-17 years and 18-39 years), there has been no significant change in the number of hospitalizations as well as the number of people in the general population (4). The reason for the non-increase in the infant hospitalization in spite of the population increase is at least partially explained by the decrease in the birth prevalence of CHD in Canada, an average 1.7% decrease in the birth prevalence during the same period of study (15).

Contrary to the prevalence of CHD which is more common in female (8), we found more hospitalizations with male, representing 53% of hospitalizations, compared to female. The complex CHD is more prevalent in male patients and studies suggest that complex CHD patients have late complications or co-morbid conditions (16, 17). Cardiovascular disease is more prevalent in male with tetralogy of Fallot (TOF) (18). Females are at lower risk of infective endocarditis (47%), aortic complications (33%) and arrhythmias (22%) compared to male patients (19).

The annual hospitalization rate per 100,000 persons varied between 21 and 22 for simple CHD, between 12 and 13 for moderate, and between 4 and 5 for complex CHD patients. Our study found that the number of hospitalizations increased with simple (1.8% per year) and complex CHD (2.1%), while it did not change significantly with moderate CHD over the study period. This may be partly explained by the fact that complex CHD is associated with late complications (20).

In children, respiratory illness like pneumonia, acute bronchiolitis were the most common non-cardiac principal diagnoses. For adults, cardiac complications including congestive heart failure (CHF), ischemic heart disease (IHD) and atrial arrhythmia were the most responsible diagnoses associated with hospitalizations in addition to the diagnosis of CHD. This suggests the growing recognition of acquired cardiovascular disease in the CHD population such as heart disease that is common in the general population now being seen in CHD survivors.

We also showed higher resource utilization in CHD patients in terms of length of stay (LOS). The median LOS observed in our study population was 6 days (IQR: 3-14) parallel to that published by Moon *et al.* (7) and higher than that in heart failure patients (varying between 3.5 and 3.7 days) (21). The patient age 65+ followed by infants have longer durations of total hospital stay independent of other factors. These patients have greater burden of co-morbidity due to the disease as well as aging (11-14). On the other hand, infants are at risk of infections since earlier period of life is very critical to develop adaptive process (22). As discussed above, males and patients with complex CHD are at greater risk of developing complications.

Therefore, these patients have more frequent hospitalization resulted in longer duration of total LOS.

4.1.2 Summary findings from Chapter 3

The readmission rates observed in this study including patients of all age groups were 49 per 1,000 patients in 2-week, 84 per 1,000 patients in 1-month, 164 per 1,000 patients in 3-month and 352 per 1,000 patients in 1-year. Risk factors for readmission among our study population were age 40 years old or older, males, longer hospital stay and complex CHD.

Approximately 8% of our study population were readmitted within 1-month following initial discharge. Our finding is close to that reported with unplanned readmission rate of 8.5% among patients with any diagnosis in Canada (23).

The readmission rate in children varied between 3.7% and 4.6% within 2-week and between 5.7% and 8.4% within 1-month in our study. A study of children (≤17 years) in Quebec, between 1990 and 2005, found a higher readmission rate than that reported in our study; 9% within 14 days and 14% within 31 days (24). A study conducted at 72 children hospitals in 34 states of the US reported that all-cause unplanned readmission rate in 30 days was 6.5% for all hospitalized children (25). This rate is similar to the readmission rate observed in our study population. Readmission rate is higher among CHD children after surgery except for arterial switch procedure which is physiologically corrective procedure. A case-control study showed readmission rate of 3.8% after the arterial switch procedure and 11.4% after the Norwood procedure in neonates in Children's Hospital in Boston (26). In a retrospective cohort study among 685 patients who underwent congenital heart surgery in a pediatric hospital, 74 re-admissions occurred in 70 patients (10%) within 30 days following surgery (27).

Among children, infants had significantly higher readmission rates within 1-month, 3-month and 1-year. Mackie *et al.* also found more readmission within 31 days in infants (1 in 5 infants) than other children (1 in 9 children) in Quebec (24). Infants with CHD have respiratory compromise due to altered anatomy and physiologic hemodynamic abnormality (22). As a result, infants are vulnerable to viral infection such as respiratory syncytial virus infection, which have serious consequences among infants with CHD than those without CHD (28). In addition, it has been hypothesized that there might be a tendency on the part of physicians to hospitalize infants having complications more often than other children (24).

While readmission of adults with other diseases such as heart failure has been studied, readmission among adults CHD has not been examined previously. Around 16% of adults discharged with heart failure had unplanned readmissions within 30 days of discharge (29). Among adults, 8.6% were readmitted within 1-month following discharge from the index hospitalization. Moreover, we observed that patients aged 40 years or older were more likely to be readmitted compared to infants; with the greatest risk in patients age 65+ years. This is consistent with the fact that older age patients develop the complications or comorbid conditions more than those who are younger. Around 9% of 250 adult CHD patients who underwent angiography were reported with coronary artery disease (CAD) and one in 50 adult patients developed cerebrovascular accident (CVA) through his or her mid-life (14, 30). The incidence of infective endocarditis (IE) was 3 times higher in adult CONCOR (CONgenital CORvitia)-study CHD patients (11 per 10,000 person years) compared to that of children reported in the earlier study (10). It has been estimated that approximately 55% of adult congenital heart disease (ACHD) patients are at significant risk of premature death, re-operation and complications (31). Over the past six decades, the management of CHD has evolved significantly because of the provisions of newer techniques (32). Many older patients with simple lesions may need to undergo surgery in adulthood and the age of operation also plays an important role in the development of complications. For instance, late events like arrhythmia or heart failure are more common in patients with atrial septal defect (ASD) repaired in adulthood. In addition, many of the adult CHD patients require re-intervention or revision of the surgery as they might have oldest style surgery in their childhood (33, 34). At the time of transition from pediatric care to adult care, approximately 50% of the adult CHD patients became lost to follow up from specialist care for extended periods and presented later with the overt symptoms of complications requiring multiple admissions (35, 36).

Our findings support that risk of readmission increases with increasing complexity of CHD; complex CHD and moderate CHD patients were more likely to be readmitted than simple CHD patients. Congenital heart defect patients have significant burdens of comorbidity due to the disease itself, interventions performed, and/or hemodynamic abnormalities (20). The risk of these complications increases with increasing severity of CHD. About one third of patients with repaired TOF developed symptomatic atrial tachycardia (37). Patients with cyanotic lesions have 10 times higher risk than average to develop CVA (30).

Readmission was slightly more common in male than female patients. Male patients may develop more complications or comorbid conditions requiring hospitalizations or interventions compared to female patients. Study using the CONCOR (CONgenital CORvitia) Dutch national registry showed that adult females with CHD were at lower risk of developing infective endocarditis (47%), aortic outcomes (33%) and arrhythmia (22%) than males (19).

Patients from the lowest quartile of median neighborhood household income have slightly higher risk of readmission in 1-month than those in the highest quartile. Socioeconomic status (SES) was found to play a significant role in readmission of heart failure patients (38). In a national survey in Canada in 1994, it was demonstrated that people from lower SES may have lower utilization of specialized care compared to those from higher SES (39).

We also observed that patients with longer duration of hospital stay were more likely to be readmitted within 1-month. Our findings parallel that reported among children with CHD in Quebec (24). Patients who stayed in hospital for longer duration are likely more complex and thereby required readmission more often relative to other patients.

Discharge planning is a very important component of inpatient care; discharging patients early might be associated with worse outcomes (24). In the current study, however, we did not find any elevated risk of readmission within 2-week and 1-month among patients discharged on Friday or Saturday, the days of week when there may be a tendency for early discharge for weekend, compared to those discharged other days of week (Sunday to Thursday).

Co-morbidity was an important predictor of readmission among adults with CHD in our study. Adult CHD patients have a greater risk of developing comorbid conditions like diabetes, chronic renal disease than their age and sex matched control (40). Adults with higher comorbid conditions were more likely to be readmitted and odds of readmission increased with increasing number of comorbid conditions.

4.2 Implication of findings and relevance to public health

Our study provides a broad view on the pattern of inpatient health service utilization by CHD patients in Canada. As the number of CHD patients, particularly adult CHD patient are rising due to the improvement in the survival of CHD patients, the burden on healthcare systems are expected to be growing further with these patients. Therefore, healthcare systems must be prepared to meet increasing demands of this expanding population. Availability of these findings will facilitate policy makers to make evidence-based decisions to improve allocations of healthcare resources.

Readmission has significant public health importance, since national healthcare costs can be reduced by reducing readmission. Findings from our study would help clinicians to identify high-risk patients and prevent their readmission. We did not investigate other factors that might lead to readmissions such as continuity of follow up after discharge, adherence to medication, distance of residence from hospital. Moreover, this study did not provide any information regarding specific details of underlying reasons for readmission such as complications associated with disease or for intervention procedures. Patients could have planned readmissions to prevent unwanted consequences and these were not distinguished in this study.

4.3 Future directions

Increasing hospitalisations and longer duration of hospital stay impose significant resource burdens. Further study should be designed at estimating the healthcare cost of hospital admissions in CHD patients. Unplanned readmissions are mostly associated with events occurring as complications associated with disease itself and interventions, and therefore, can be preventable if we could anticipate or predict who would develop complications. Future study should focus on differentiating planned and unplanned readmission and identifying patients at risk of unplanned readmission, and evaluating methods for preventing unplanned readmission. For example, methods such as intensive home care, potential co-management of these patients with nurse practitioners, and use of telemedicine as an adjunct in the evaluation of patients who live in remote locations far from specialized CHD clinics may be considered.

References

1. CIHI. Trends in inpatient hospitalization and day surgery in Canada from 1995/1996 to 2005/2006.; 2007.

2. Billett J, Majeed A, Gatzoulis M, Cowie M. Trends in hospital admissions, in-hospital case fatality and population mortality from congenital heart disease in England, 1994 to 2004. Heart. 2008 Mar;94(3):342-8.

3. Opotowsky AR, Siddiqi OK, Webb GD. Trends in hospitalizations for adults with congenital heart disease in the U.S. J Am Coll Cardiol. 2009 Jul 28;54(5):460-7.

4. Statistics Canada. Population Census data from Stat Canada.

5. Mackie AS, Pilote L, Ionescu-Ittu R, Rahme E, Marelli AJ. Health care resource utilization in adults with congenital heart disease. Am J Cardiol. 2007 Mar 15;99(6):839-43.

6. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Sieswerda GT, et al. The emerging burden of hospital admissions of adults with congenital heart disease. Heart. Jun;96(11):872-8.

7. Moons P, Siebens K, De Geest S, Abraham I, Budts W, Gewillig M. A pilot study of expenditures on, and utilization of resources in, health care in adults with congenital heart disease. Cardiol Young. 2001 May;11(3):301-13.

8. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. Circulation. 2007 Jan 16;115(2):163-72.

9. Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Lifetime Prevalence of Congenital Heart Disease in the General Population from 2000 to 2010. Circulation. Jun 18.

10. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Veen G, et al. Turning 18 with congenital heart disease: prediction of infective endocarditis based on a large population. Eur Heart J. Aug;32(15):1926-34.

11. Li W, Somerville J. Infective endocarditis in the grown-up congenital heart (GUCH) population. Eur Heart J. 1998 Jan;19(1):166-73.

12. Somerville J. Management of adults with congenital heart disease: an increasing problem. Annu Rev Med. 1997;48:283-93.

13. Norozi K, Wessel A, Alpers V, Arnhold JO, Geyer S, Zoege M, et al. Incidence and risk distribution of heart failure in adolescents and adults with congenital heart disease after cardiac surgery. Am J Cardiol. 2006 Apr 15;97(8):1238-43.

14. Giannakoulas G, Dimopoulos K, Engel R, Goktekin O, Kucukdurmaz Z, Vatankulu MA, et al. Burden of coronary artery disease in adults with congenital heart disease and its relation to congenital and traditional heart risk factors. Am J Cardiol. 2009 May 15;103(10):1445-50.

15. Joseph KS, Liu S. Congential Anomalies In Canada 2013 A Perinatal Health Surveillence Report. 2013 p. 33-41.

16. Moons P, Sluysmans T, De Wolf D, Massin M, Suys B, Benatar A, et al. Congenital heart disease in 111 225 births in Belgium: birth prevalence, treatment and survival in the 21st century. Acta Paediatr. 2009 Mar;98(3):472-7.

17. Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. J Pediatr. 2008 Dec;153(6):807-13.

18. Bradley E, Parker J, Novak E, Ludbrook P, Billadello J, Cedars A. Cardiovascular disease in late survivors of tetralogy of fallot: a tertiary care center experience. Tex Heart Inst J.40(4):418-23.

19. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Vliegen HW, et al. Gender and outcome in adult congenital heart disease. Circulation. 2008 Jul 1;118(1):26-32.

20. Oliver RJM. Congenital heart disease in adults: residua, sequelae, and complications of cardiac defects repaired at an early age. Rev Esp Cardiol. 2003;56(1):73-88.

21. Chen J, Dharmarajan K, Wang Y, Krumholz HM. National trends in heart failure hospital stay rates, 2001 to 2009. J Am Coll Cardiol. Mar 12;61(10):1078-88.

22. Zachariah P, Simoes EA. Respiratory syncytial virus infection and congenital heart disease. South Afr J Epidemiol Infect. 2008;23(2):17-9.

23. CIHI. All Cause Readmission to the Acute Care and Return to the Emergency Department.

24. Mackie AS, Ionescu-Ittu R, Pilote L, Rahme E, Marelli AJ. Hospital readmissions in children with congenital heart disease: a population-based study. Am Heart J. 2008 Mar;155(3):577-84.

25. Berry JG, Toomey SL, Zaslavsky AM, Jha AK, Nakamura MM, Klein DJ, et al. Pediatric readmission prevalence and variability across hospitals. JAMA. Jan 23;309(4):372-80.

26. Mackie AS, Gauvreau K, Newburger JW, Mayer JE, Erickson LC. Risk factors for readmission after neonatal cardiac surgery. Ann Thorac Surg. 2004 Dec;78(6):1972-8; discussion 8.

27. Kogon B, Jain A, Oster M, Woodall K, Kanter K, Kirshbom P. Risk factors associated with readmission after pediatric cardiothoracic surgery. Ann Thorac Surg. Sep;94(3):865-73.

28. MacDonald NE, Hall CB, Suffin SC, Alexson C, Harris PJ, Manning JA. Respiratory syncytial viral infection in infants with congenital heart disease. N Engl J Med. 1982 Aug 12;307(7):397-400.

29. Au AG, McAlister FA, Bakal JA, Ezekowitz J, Kaul P, van Walraven C. Predicting the risk of unplanned readmission or death within 30 days of discharge after a heart failure hospitalization. Am Heart J. Sep;164(3):365-72.

30. Hoffmann A, Chockalingam P, Balint OH, Dadashev A, Dimopoulos K, Engel R, et al. Cerebrovascular accidents in adult patients with congenital heart disease. Heart. Aug;96(15):1223-6.

31. Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, et al. Task force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol. 2001 Apr;37(5):1170-5.

32. Guleserian KJ. Adult congenital heart disease: surgical advances and options. Prog Cardiovasc Dis. Jan-Feb;53(4):254-64.

33. Warnes CA. The adult with congenital heart disease: born to be bad? J Am Coll Cardiol. 2005 Jul 5;46(1):1-8.

34. Curtis SL, Stuart AG. Outcome in congenital heart disease. Current Paediatrics. 2005;15(7):549-56.

35. Dearani JA, Connolly HM, Martinez R, Fontanet H, Webb GD. Caring for adults with congenital cardiac disease: successes and challenges for 2007 and beyond. Cardiol Young. 2007 Sep;17 Suppl 2:87-96.

36. Gatzoulis MA. Adult congenital heart disease: a cardiovascular area of growth in urgent need of additional resource allocation. Int J Cardiol. 2004 Dec;97 Suppl 1:1-2.

37. Roos-Hesselink J, Perlroth MG, McGhie J, Spitaels S. Atrial arrhythmias in adults after repair of tetralogy of Fallot. Correlations with clinical, exercise, and echocardiographic findings. Circulation. 1995 Apr 15;91(8):2214-9.

38. Philbin EF, Dec GW, Jenkins PL, DiSalvo TG. Socioeconomic status as an independent risk factor for hospital readmission for heart failure. Am J Cardiol. 2001 Jun 15;87(12):1367-71.

39. Dunlop S, Coyte PC, McIsaac W. Socio-economic status and the utilisation of physicians' services: results from the Canadian National Population Health Survey. Soc Sci Med. 2000 Jul;51(1):123-33.

40. Billett J, Cowie MR, Gatzoulis MA, Vonder Muhll IF, Majeed A. Comorbidity, healthcare utilisation and process of care measures in patients with congenital heart disease in the UK: cross-sectional, population-based study with case-control analysis. Heart. 2008 Sep;94(9):1194-9.