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CONGENITAL HEART DISEASE

Changing Mortality in Congenital Heart Disease

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Objectives This study sought to characterize temporal trends in all-cause mortality in patients with congenital heart disease (CHD).

Background Historically, most deaths in patients with CHD occurred in early childhood. Notable advances have since been achieved that may impact on mortality trends.

Methods We conducted a population-based cohort study of patients with CHD in Quebec, Canada, from July 1987 to June 2005. A total of 8,561 deaths occurred in 71,686 patients with CHD followed for 982,363 patient-years.

Results The proportion of infant and childhood deaths markedly declined from 1987 to 2005, with a reduction in mortality that exceeded that of the general population. Distribution of age at death transitioned from a bimodal to unimodal, albeit skewed, pattern, more closely approximating the general population. Overall, mortality decreased by 31% (mortality rate ratio: 0.69, 95% confidence interval [CI]: 0.61 to 0.79) in the last (2002 to 2005) relative to the first (1987 to 1990) period of observation. Mortality rates decreased in all age groups below 65 years, with the largest reduction in infants (mortality rate ratio: 0.23, 95% CI: 0.12 to 0.47). In adults 18 to 64 years, the mortality reduction (mortality rate ratio: 0.84, 95% CI: 0.73 to 0.97) paralleled the general population. Gains in survival were mostly driven by reduced mortality in severe forms of CHD, particularly in children (mortality rate ratio: 0.33, 95% CI: 0.19 to 0.60), and were consistent across most subtypes.

Conclusions Deaths in CHD have shifted away from infants and towards adults, with a steady increase in age at death and decreasing mortality. (J Am Coll Cardiol 2010;56:1149–57) © 2010 by the American College of Cardiology Foundation

Congenital heart disease (CHD) is the most common form of major birth defects, affecting over 1% of newborns (1). Historically, most patients with CHD died in early childhood. However, the past 4 decades have witnessed extraordinary advances in this field (2–7). Indeed, population prevalence studies indicate that the number of adults now rivals the number of children with severe defects (1). Changing patterns of death in this growing population must be investigated to adequately plan allocation of health care resources. We established a unique population-based database that includes over 70,000 patients with CHD followed for nearly 1 million patient-years and that captures all deaths from 1987 to 2005. Our objective was to characterize temporal trends in all-cause mortality in patients with CHD.

Methods

Data sources and collection. Quebec is the second most-populated province in Canada, with over 7.6 million inhabitants. A unique Medicare number is assigned to every individual, and all diagnoses and health services provided are systematically recorded over a lifespan (1). The physician's services and claims database contains demographic data and records on all patients who contacted the health care system, as inpatients or outpatients, and includes diagnostic and therapeutic procedures performed since 1982. Diagnostic codes adhere to the International Classification of Disease-Ninth Revision (ICD-9). As physician remuneration is based on these claims, there is a strong incentive to divulge all professional activities. The hospital

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Abbreviations and Acronyms

CHD = congenital heart disease

CI = confidence interval

ICD-9 = International Classification of Disease-9th Revision

IQR = interquartile range

discharge summary database contains records on all hospital admissions and captures demographic data, diagnostic codes, and therapeutic procedures. All diagnoses are linked with specialty-specific provider codes.

Data on all patients with a diagnosis of CHD between January 1, 1983, and June 30, 2005, who were alive on or born after July 1, 1987, were obtained from the Quebec Health Insurance Board. To protect patient confidentiality, information was transmitted with encrypted identifiers. Using the same encrypted numbers, the Quebec Ministry of Health provided additional hospitalization discharge data. These source databases were linked for each individual, thereby generating a comprehensive record of health care coverage for patients with CHD. The study was approved by the McGill University Health Center ethics board and the Quebec government agency responsible for privacy of access to information.

Study population. A hierarchical categorization scheme, summarized in Table 1, was used to classify patients with CHD (1). We identified all patients with at least 1 diagnostic code for CHD and/or surgical procedure specific to these codes who came into contact with the health care system. The 24 ICD-9 diagnostic codes and corresponding surgical codes were grouped into 5 categories of decreasing specificity (Table 1) and cross-referenced between source administrative databases.

Using provider codes, physicians reporting diagnostic codes or procedures were classified as cardiovascular specialist (pediatric, medical, or surgical), primary care physician (general or family physician, pediatrician, or internist), echocardiographer, or other (1). When more than 1 ICD-9 code was recorded, the most frequent diagnosis in the diagnostic hierarchical block in Table 1 with the lowest numerical value was retained, prioritizing diagnoses by cardiovascular specialists. We adhered to the guiding principle of minimizing, to the greatest extent possible, subjective opinion in categorizing lesions. Thus, each diagnostic category encompasses a spectrum of severity, with no judgment as to physiologic or clinical ramifications. Lesions included in block 1 of Table 1 were considered "severe," because these diagnoses were most likely to be associated with cyanosis or require surgical intervention in early life (1). To minimize misclassification errors, this systematic algorithmic approach was subject to sensitivity analyses of randomly selected samples within each diagnostic category (1,8). All discrepancies were reviewed and adjudicated by 2 independent CHD specialists.

Study design. A retrospective open-cohort study was conducted, with a maximum follow-up of 18 years, by identifying all patients with CHD alive each year from July 1, 1987, to June 30, 2005. Given that congenital disease is present at birth, patients with any diagnostic code for CHD between January 1, 1983, and June 30, 2005, entered the study cohort on July 1, 1987, if alive and born prior to that date, or at birth if born after that date.

Mortality data. In Quebec, death certificates must contain nominal and demographic data, along with the individual's unique and unvarying Medicare number. By law, the attestation of death must be sent to the registrar of civil status who then forwards this information to the Quebec Health Insurance Board. Further validation of mortality data occurs by cross-referencing vital status information provided by other Quebec institutions. Documentation of death is theoretically complete in this database, whether it occurs in or out of hospital. In addition, the hospital discharge database was used to cross-reference in-hospital deaths. Since this database was initiated in 1987, the beginning of follow-up was defined as July 1, 1987, to optimize data accuracy and allow fiscal years to be compared with general Quebec population data. With this strategy, originally developed to maximize reliability of vital status information for patients without CHD, death could be confirmed in 99.75% of cases (9).

Statistical analysis. In descriptive analyses, the distribution of age at death among subjects with CHD who died in a given fiscal year, starting from July 1, 1987, was characterized by histogram plots and medians and interquartile ranges (IQRs) (25th, 75th percentiles). Median ages at death in selected years were compared with Kruskal-Wallis tests.

Table 1 Hierarchical Classification of Congenital Heart Disease

Block	Diagnostic Codes	ICD-9 Code
1	Endocardial cushion defect	745.6
	Tetralogy of Fallot	745.2
	Univentricular heart	745.3
	Transposition complex	745.1
	Truncus arteriosus	745.0
	Hypoplastic left heart syndrome	746.7
2	Atrial septal effect	745.5
	Ventricular septal defect	745.4
	Patent ductus arteriosus	747.0
	Aortic coarctation	747.1
	Ebstein's anomaly	746.2
3	Unspecified defect of septal closure	745.9
4	Anomalies of the pulmonary artery	747.3
	Anomalies of the pulmonary valve	746.0
	Congenital tricuspid valve disease	746.1
	Congenital aortic stenosis	746.3
	Congenital aortic insufficiency	746.4
	Congenital mitral stenosis	746.5
	Congenital mitral insufficiency	746.6
	Anomalies of great veins	747.4
5	Other unspecified anomalies of the heart	746.8/9
	Other unspecified anomalies of the circulation	747.9
	Other unspecified anomalies of the aorta	747.2

ICD-9 = International Classification of Disease-9th Revision.

Statistical analyses focused on changes in mortality rates across six 3-year time intervals, from 1987 to 1990, to 2002 to 2005. These analyses accounted for the fact that some subjects were identified only at time of death and, thus, similar subjects who did not die in the same period were not identified, or were identified only much later in the database. To avoid resulting biases in estimating mortality rates, statistical analyses were, therefore, limited to restricted cohorts. Restricted cohorts were defined as the population of subjects indentified prior to the beginning of each 3-year interval who remained alive (i.e., "at risk") at the beginning of the interval. For every subject in a given restricted cohort, death within the corresponding 3-year period was modeled as a binary dependent variable. Adjusted mortality rates in the periods 1990 to 1993, to 2002 to 2005 were compared with the earliest period (1987 to 1990) with multivariate Poisson regression models that controlled for age at the beginning of the period, sex, and subtype of CHD categorized as severe, simple shunt, and other. Since individual patients may have been included in more than 1 restricted cohort, analyses were performed with and without the generalized estimating equations (GEE) extension of Poisson regression (10) to account for the dependence of within-subject observations (11). Since the 2 approaches yielded similar results, we report adjusted mortality rate ratios and their 95% confidence intervals (CIs) without GEE. Poisson regression analyses of all CHD lesions were performed separately for 6 age groups. For each age group, adjusted mortality rate ratios were likewise estimated from general Quebec population data using Poisson regression adjusted for sex and age within each group (except infants). In lesion-specific analyses, to ensure sufficient statistical power, patients were regrouped as children (age <18 years) or adults (age 18 to 65 years), and less frequent CHD subtypes were not considered.

Two-tailed p values <0.05 were considered statistically significant. All analyses were performed using SAS software version 9.1 (SAS Institute, Cary, North Carolina).

Results

Study population. The full cohort was comprised of 71,686 patients with CHD followed for 982,363 patient-years. The general Quebec population varied between 6.8 and 7.5 million people during the first (1987 to 1988) and final (2004 to 2005) years of follow-up, respectively. Characteristics of the full and restricted cohorts are summarized in Table 2.

Distribution of age at death in CHD. A total of 8,561 (11.9%) deaths occurred during follow-up. As portrayed by the histogram on the left of Figure 1, the distribution of age at death during the first year of observation (1987 to 1988) displayed a bimodal pattern, with the highest mortality peak in infancy and a lower peak in later adulthood. In contrast, by the last year (2004 to 2005), the distribution shifted toward deaths at older ages, becoming nearly unimodal (right-hand graph in Fig. 1). In 1987 to 1988, 49.0% of deaths in patients with CHD occurred under the age of 20, whereas by 2004 to 2005, only 9.3% of deaths occurred under age 20 years. Although in 2004 to 2005, deaths at ages 0 to 4 years remained somewhat more frequent than in later childhood, the distribution of age at death after 4 years of age approximated that of the general Quebec population (bold curve).

Temporal changes in mortality. Overall, the median age at death increased by 15 years, from 60 years (IQR: 3 to 76 years) in 1987 to 1993, to 75 years (IQR: 60 to 83 years) in 1999 to 2005 ($p < 0.001$). In patients with severe forms of CHD, the median age at death increased from 2 years (IQR: 1 to 13 years) in 1987 to 1993, to 23 years (IQR: 1 to 56 years) in 1999 to 2005 ($p < 0.001$). Table 3 summarizes the number of deaths in each restricted cohort and the proportion of deaths that occurred in patients with severe versus other forms of CHD, and in children versus adults.

Figure 2 shows how adjusted mortality rates varied over time for each age category, relative to the first 3 years of observation. The mortality reduction in children with CHD was greatest in infants, became smaller with increasing age, and exceeded that of the general population. Infants with CHD experienced a 77% reduction in mortality (mortality rate ratio: 0.23, 95% CI: 0.12 to 0.47, $p < 0.001$), in comparison to a 52% decline (mortality rate ratio: 0.48, 95% CI: 0.38 to 0.60, $p < 0.001$) in the general infant population. For children 5 to 17 years of age, the mortality reduction was 66% (mortality rate ratio: 0.34, 95% CI: 0.21 to 0.54, $p < 0.001$) in the CHD cohort compared with 50% (mortality rate ratio: 0.50, 95% CI: 0.45 to 0.55, $p < 0.001$) in the general population.

In all but the oldest age group, adults with CHD experienced statistically significant reductions in mortality that paralleled general population trends. Mortality rate ratios for adults 18 to 34 years of age with CHD and in the general population were 0.60 (95% CI: 0.40 to 0.90, $p = 0.02$) and 0.64 (95% CI: 0.61 to 0.67, $p < 0.001$), respectively. For adults 35 to 64 years of age, corresponding mortality rate ratios were 0.72 (95% CI: 0.55 to 0.93, $p = 0.02$) and 0.70 (95% CI: 0.69 to 0.71, $p < 0.001$). Mortality rates declined in the general population of adults age ≥65 years (mortality rate ratio: 0.78, 95% CI: 0.77 to 0.78, $p < 0.001$), but not in the CHD cohort (Fig. 2).

Table 4 provides adjusted mortality rate ratios, according to CHD subtype, separately for all patients, children, and adults 18 to 64 years old. Gains in survival were mostly driven by decreased mortality in severe forms of CHD, particularly in children who experienced a 67% reduction in mortality (mortality rate ratio: 0.33, 95% CI: 0.19 to 0.60, $p < 0.001$).

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Table 2 Characteristics of the Full and Restricted Cohorts of Patients With Congenital Heart Disease

	Full Cohort (n = 71,686)	Restricted Cohort* (n = 57,663)
Deaths, n (%)	8,561 (11.9)	5,967 (10.3)
Age category on July 1, 1987, yrs		
<1	1,154 (1.6)	1,054 (1.8)
1–4	4,451 (6.2)	4,238 (7.3)
5–17	10,129 (14.1)	9,092 (15.8)
18–34	9,320 (13.0)	8,168 (14.2)
35–64	14,944 (20.8)	11,999 (20.8)
≥65	4,881 (6.8)	3,897 (6.8)
Born after July 1, 1987	26,807 (37.4)	19,215 (33.3)
Sex		
Females	38,031 (53.0)	30,824 (53.5)
Males	32,563 (45.4)	26,232 (45.5)
Missing†	1,092 (1.5)	607 (1.0)
Congenital heart disease diagnosis		
Severe congenital heart disease		
Endocardial cushion defect	2,204 (3.1)	1,946 (3.4)
Tetralogy of Fallot	2,084 (2.9)	1,804 (3.1)
Transposition of the great arteries	1,011 (1.4)	810 (1.4)
Univentricular heart‡	669 (0.9)	499 (0.9)
Truncus arteriosus	301 (0.4)	236 (0.4)
Other forms of congenital heart disease		
Atrial septal defect	17,186 (24.0)	13,194 (22.9)
Ventricular septal defect	14,550 (20.3)	12,315 (21.4)
Patent ductus arteriosus	2,070 (2.9)	1,527 (2.6)
Aortic coarctation	1,385 (1.9)	1,131 (2.0)
Ebstein's anomaly	191 (0.3)	143 (0.2)
Other	30,005 (41.9)	24,058 (41.7)

Values are presented as n (%). *Six restricted cohorts were created for each of the 3-year intervals from 1987 to 1990, to 2002 to 2005 by identifying congenital heart disease subjects who were alive and, therefore, "at risk" at the beginning of the respective 3-year period. Restricted cohorts were used for the analyses of mortality rates (see Statistical Analysis section). †Sex was not available for infant deaths that were captured by a temporary administrative database prior to allocation of the permanent unique identifier. ‡Includes hypoplastic left heart syndrome.

Discussion

Heart defects are the most common form of congenital disease, with an estimated prevalence of 11.9 per 1,000 children in 2000 (1). Three decades ago, CHD was considered a predominantly pediatric condition, as patients with complex forms seldom survived beyond childhood. However, patient care markedly improved, resulting in a growing and aging population. Indeed, adults now outnumber children with both severe and other types of CHD (1).

One may expect that these observed population trends should be reflected in changing mortality patterns. However, estimation of population-based mortality in CHD is challenging. Prior studies have largely been restricted to lesion-specific retrospective cohort studies or surgical series, with a few population-based analyses based on birth defects or death registries (5,12–16). Birth registry studies are limited to subjects diagnosed within the first year of life (17,18). Milder forms of CHD may escape detection until later years, thereby potentially skewing such results towards more severe subtypes. In contrast, mortality studies relying on death registries have focused on subjects in whom CHD was considered the main cause of demise (13,19). Yet, in older patients with CHD, sudden (14,20) and heart failure–related (5,21) deaths are common. Restricting deaths to those attributed to CHD may exclude most fatalities, particularly among adults, thereby biasing the resulting distribution of age at death towards younger years (13).

The comprehensiveness of administrative databases in Quebec provided us with a unique opportunity to assemble a population-based cohort with CHD that was not restricted to those diagnosed in infancy. "All cause mortality," which encompasses deaths that may or may not have been related to CHD, was deliberately selected as the primary outcome, given its indisputable clinical relevance, previously validated high degree of accuracy (9), and applicability to general population data for comparative purposes. Our systematic algorithmic approach, with sensitivity analyses of randomly selected samples, was developed to minimize diagnostic misclassification errors (1,8), whereas our multivariate analyses of restricted cohorts were designed to minimize selection bias and confounding by type of CHD. Using this methodology, we found that age at death increased over time. Adjusted mortality rates declined in all age categories under 65 years. From 1987 to 1990, to 2002

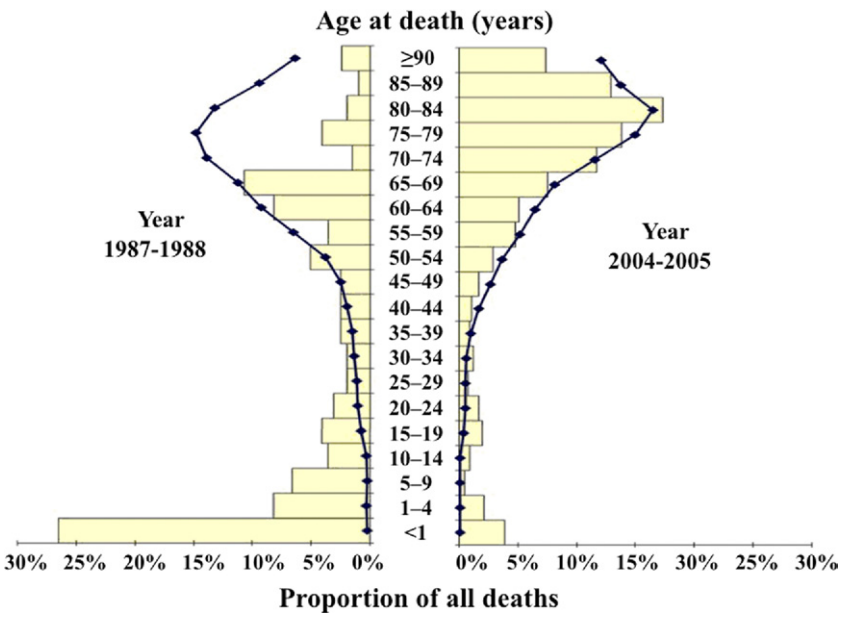

Figure 1 Distribution of Age at Death in Patients With Congenital Heart Disease in 1987 to 1988 and 2004 to 2005

Histogram bars depict the proportion of all deaths (x-axis) according to age at death (y-axis) in our cohort of patients with congenital heart disease in the first (1987 to 1988; **left**) and final (2004 to 2005; **right**) years of observation. **Bold black curves with diamonds** represent the corresponding age at death distribution in the general Quebec population during the same periods of observation.

to 2005, mortality decreased by 59% in children, exceeding general population trends, and by 16% in adults 18 to 64 years of age, matching the general population. Children with severe forms of CHD experienced a 67% reduction in mortality, with a consistent effect across most subtypes. Although comparable U.S. data are not available, these observations are consistent with a report from the federal interagency forum on child and family statistics, which captures representative data on large segments of the population (22). During a similar period of observation, death rates from birth defects and heart disease declined by 50% and nearly 60%, respectively (22).

Changing mortality in CHD is likely multifactorial, reflecting major strides in patient care and improvements in survival in the population as a whole. Changing mortality rates in CHD must, therefore, be interpreted within the context of general population data. A rapid decline in fetal and infant mortality rates in the general population of industrialized nations has been previously reported. Indeed, infant mortality is considered one of the most important indicators of the health of a nation, and has been associated with a variety of factors such as maternal health, quality and access to medical care, socioeconomic conditions, and public health practices (23). Factors specific to the decline in infant

Table 3 Deaths in the 6 Restricted Cohorts of Patients With CHD

	1987–1990	1990–1993	1993–1996	1996–1999	1999–2002	2002–2005
Total population with CHD						
Number of deaths	303	591	927	1,176	1,425	1,545
Number of patients	13,772	22,652	30,886	38,372	45,747	53,241
Severe vs. other forms of CHD						
Number of deaths in severe CHD	61 (20)	78 (13)	77 (8)	105 (9)	89 (6)	84 (5)
Number of patients with severe CHD	2,387	2,994	3,426	3,958	4,410	4,887
Number of deaths in other forms of CHD	242 (80)	513 (87)	850 (82)	1,071 (91)	1,336 (94)	1,461 (95)
Number of patients with other forms of CHD	11,385	19,658	27,460	34,414	41,337	48,354
Children vs. adults with CHD						
Number of deaths in children with CHD	89 (29)	78 (13)	95 (10)	78 (7)	79 (5)	62 (4)
Number of children with CHD*	7,568	10,943	14,087	16,392	19,566	22,228
Number of deaths in adults with CHD	214 (71)	513 (87)	832 (90)	1,098 (93)	1,346 (95)	1,483 (96)
Number of adults with CHD*	6,204	11,709	16,799	21,980	26,181	31,013

Values are n or n (%). *Age is measured at the beginning of each time period (e.g., on July 1, 1987, for the first restricted cohort).
CHD = congenital heart disease.

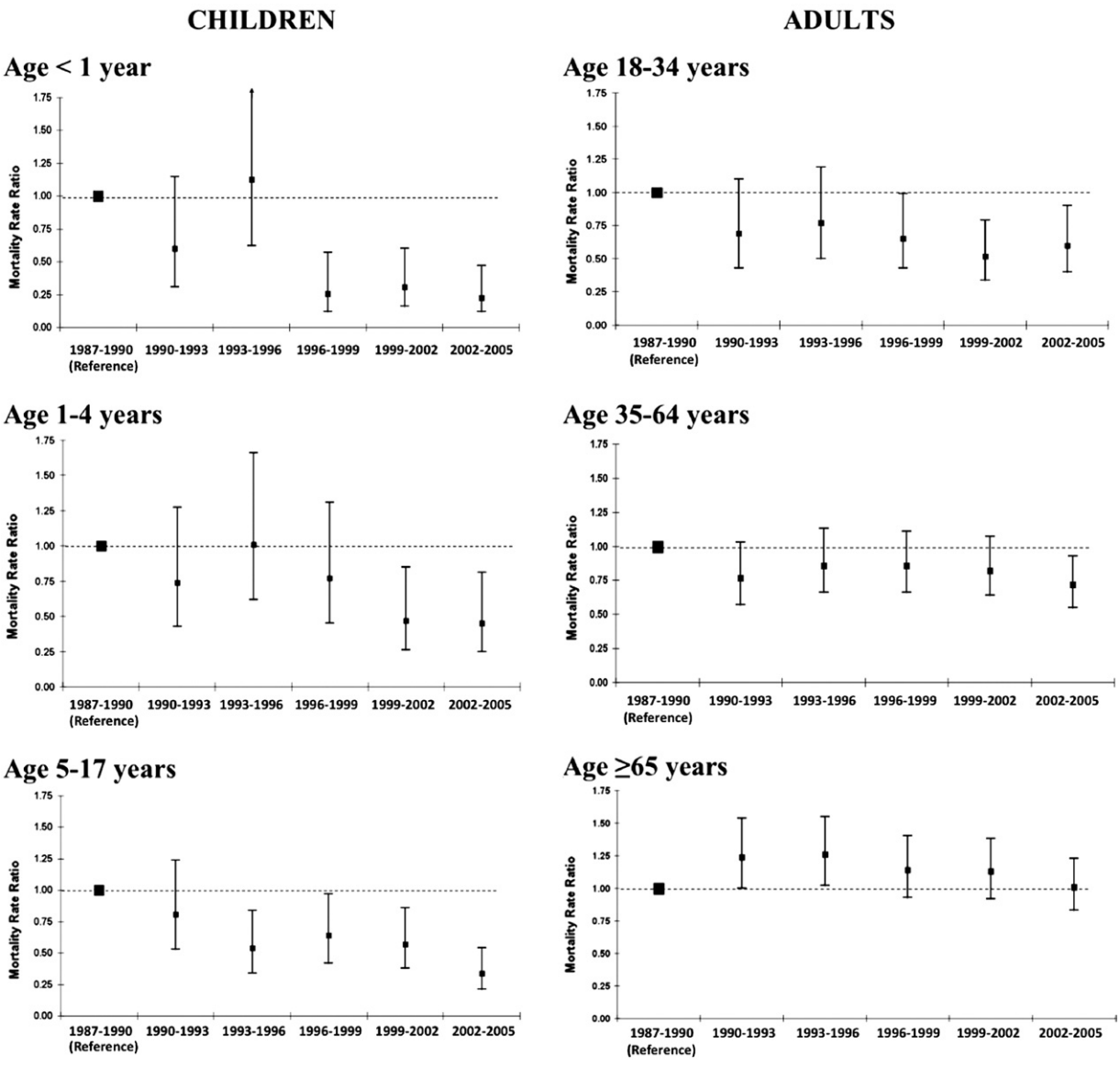

Figure 2 **Adjusted Age-Specific Changes in Mortality Over Time in Children and Adults With Congenital Heart Disease**

For each of the 6 age categories (6 panels), adjusted mortality rate ratios **(black squares)** and 95% confidence intervals **(vertical lines)** are plotted relative to the reference cohort (1987 to 1990). Mortality rates are based on restricted cohorts (see Statistical Analysis section) and were estimated by Poisson regression models that controlled for residual age differences, sex, and type of congenital heart disease. Sex was not available for infant deaths that were captured by a temporary administrative database prior to allocation of the permanent unique identifier. The difference in mortality is statistically significant at a 2-tailed alpha of 0.05, if the corresponding **vertical bar** for the 95% confidence interval does not cross the **horizontal dotted line** (corresponding to a mortality rate ratio of 1).

mortality in patients with CHD may include the impact of prenatal diagnosis and early detection (24); novel surgical procedures such as the arterial switch operation for transposition of the great arteries (25) and Norwood variants for single ventricles (26); interventional procedures such as balloon angioplasty for critical aortic stenosis and pulmonary stenosis (27); organization of care into intensive care units with coordinated efforts of specialized team members (28); and miniaturization of tools and techniques (29). In addition, a disproportionate termination of fetuses with the most severe forms of CHD may contribute to a less severe case-mix (30) that cannot be fully adjusted for in analyses.

Factors contributing to decreased mortality in older children and adolescents with CHD may include earlier detection, improvements in diagnostic techniques, refinement of selection criteria and risk assessment for surgical or percutaneous interventions, advances in surgical and perioperative care, and progress in outpatient management and follow-up (31,32). Importantly, the reduction in mortality observed in children was not accompanied by an increased

Table 4 Adjusted Mortality Rate Ratios in Subtypes of Congenital Heart Disease in 2002 to 2005 Relative to 1987 to 1990

	All Patients		Children (Age <18 yrs)		Adults (Age 18–64 yrs)	
Type of Congenital Heart Disease	Adjusted Mortality Ratio* (95% CI)	p Value	Adjusted Mortality Ratio* (95% CI)	p Value	Adjusted Mortality Ratio* (95% CI)	p Value
All types of congenital heart disease	0.69 (0.61–0.79)	<0.001	0.41 (0.29–0.56)	<0.001	0.84 (0.73–0.97)	0.02
Severe congenital heart disease	0.51 (0.37–0.72)	<0.001	0.33 (0.19–0.60)	<0.001	0.67 (0.39–1.14)	0.14
Endocardial cushion defect	0.52 (0.26–1.02)	0.06	0.37 (0.12–1.15)	0.09	1.02 (0.23–4.48)	0.98
Tetralogy of Fallot	0.54 (0.31–0.95)	0.03	0.45 (0.19–1.07)	0.07	0.58 (0.26–1.32)	0.20
Transposition of the great arteries	0.39 (0.17–0.89)	0.03	0.14 (0.03–0.67)	0.01	0.88 (0.19–4.03)	0.87
Univentricular hearts†	0.52 (0.22–1.25)	0.15	0.21 (0.04–1.02)	0.05	0.75 (0.17–3.38)	0.71
Other forms of congenital heart disease						
Atrial septal defect	0.79 (0.57–1.11)	0.17	1.14 (0.34–3.84)	0.84	0.77 (0.54–1.09)	0.14
Ventricular septal defect	0.40 (0.28–0.59)	<0.001	0.28 (0.13–0.60)	<0.001	0.54 (0.34–0.87)	0.01
Patent ductus arteriosus	0.90 (0.37–2.20)	0.82	NE		1.36 (0.47–3.94)	0.57

*Adjusted mortality rate ratios and 95% confidence intervals (CIs) for the final (2002 to 2005) relative to the first (1987 to 1990) period of observation were estimated from restricted cohorts (see Statistical Analysis section) with Poisson regression that controlled for age, sex, and type of congenital heart disease. †Includes hypoplastic left heart syndrome.
NE = nonestimable due to the limited number of deaths.

mortality rate in adults. In adults 18 to 64 years of age, the mortality rate declined by a comparable amount to the general population, suggesting that adults with CHD benefited from overall gains in population health. For reasons that remain speculative, mortality rates did not decrease in the oldest subgroup (age ≥65 years) with CHD, unlike the general population. Older age and comorbid conditions, such as chronic renal disease, heart failure, myocardial infarction, and malignant cancer, have been associated with mortality in adults with CHD ≥65 years of age (33). It may be hypothesized, therefore, that even within a given diagnostic category, patients who survived beyond 65 years in the earlier period had less severe disease and/or comorbid conditions when compared with "survivors" from later years. If so, for this age group, an improvement in population health may have been offset by residual confounding due to a "healthy survivor" effect.

Implications of decreasing mortality in CHD are considerable, particularly with regards to allocation of appropriate resources. It was once true that older patients had predominantly simple lesions compared with children. However, the absolute number of adults with CHD is now steadily increasing (1), with a spectrum of disease that is transitioning towards more complex forms, as even patients with severe subtypes survive beyond childhood. Neurocognitive impairment, which may range from subtle to overt, is well recognized in children with severe forms of CHD (34). Its impact on the aging and increasingly complex population with CHD is likely to be substantial, with implications for education, employability, insurability in the U.S., and more robust neurocognitive assessment and intervention. In addition, complications such as arrhythmias and heart failure often appear in later life (35), and health care needs and costs are generally highest in the year preceding death (36).

The burden of health in CHD is, therefore, shifting toward the adult. Further studies are required to determine the impact of changing mortality in CHD on a global scale. Whereas provision of care for children with CHD is well established in developed countries, clinical services for adults are comparatively scarce (37,38). Our findings lend further support to the urgent call for additional resources for education, training, research, and patient care in adults with CHD (39).

Study limitations. The targeted catchment population was the entire province of Quebec. However, subjects with CHD who had no contact with the health care system from January 1983 to June 2005 were not captured. This is more likely to affect those with mild forms of disease. Additionally, the open cohort design carries a higher risk for missing subjects with a shorter time frame to establish a diagnosis of CHD, either because they were born closer to the end of the study period or died shortly after the cohort inception. However, this potential bias should not have a sizeable impact on observed changes in ages at death since median values are quite robust with respect to the potential omission of a relatively small fraction of the total population. To avoid potential biases, our primary analyses of mortality rates were limited to restricted cohorts of subjects "at risk" at the beginning of each observation period (i.e., employed the same criteria to identify the population in the "denominator" and deaths in the "numerator"). Furthermore, since selection bias may result from a higher likelihood of detecting milder forms of CHD in more recent calendar years, we adjusted for CHD subtype. In addition, the proportion of patients who died, but were not included in restricted cohorts, were compared in an exploratory analysis. Since the proportion of excluded deaths stayed relatively constant over time, one could reasonably conclude that the selection effect had not changed substantially over time. To further address the potential for left-censoring bias, we conducted an analysis that restricted inclusion to patients diagnosed with CHD within 4 years of the start of each successive cohort. Despite the exclusion of 42% of deaths, this sensitivity analysis yielded congruent results (e.g., overall adjusted mortality rate ratio 0.69 [95% CI: 0.62 to 0.77] in comparison to 0.69 [95% CI: 0.61, 0.79]).

Our diagnostic classification system was limited by the ICD-9 codes. This coding system was previously used to quantify prevalence rates, births, and deaths in CHD (1,13,40). Given our reliance on administrative databases, diagnostic misclassification errors remain possible despite every effort to maximize data accuracy. However, misclassification errors are likely nondifferential such that any resulting potential bias would be towards the null (41) and could not, therefore, explain the observed statistically significant decreases in mortality. Finally, the impact of socioeconomic status was not assessed in the current analysis, and ethnic origin is not available in our concatenation of data resources. Nevertheless, racial variation, as reflected by the proportion of visible minorities in census bureau statistics, is substantially less in Quebec compared with the U.S. population.

Conclusions

In this large population-based study, we report a marked reduction over time in infant mortality, an increase in age at death, and decreasing mortality rates in children and adolescents with CHD. A consistent pattern is, therefore, emerging with regards to changing population trends. With decreasing mortality in the young, the CHD population is growing and aging (1). These changes are most notable for young patients with severe defects and exceed general population trends. The burden of health is, therefore, transitioning away from the child and towards the adult with CHD. The health community is challenged to meet these secular trends with appropriate allocation of resources.

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