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Review

The Future of ACHD Care Symposium: Changing demographics of congenital heart disease

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ABSTRACT

In this article, we demonstrate that congenital heart disease (CHD) has now become a life-long condition spanning from birth to old age. We begin by understanding the determinants of demographics in terms of the changing epidemiology of CHD: incidence, survival and prevalence of CHD across the lifespan.
The reported birth prevalence of CHD most commonly clusters around 8/1000 live births. Advances in medical and surgical therapy have led to an increase in the survival of CHD patients with an increase in the median age at death in those with severe CHD of 20 years since 1987. The prevalence of CHD increased by 22% in children and 85% in adults with severe CHD from 1985 to 2000 such that in the year 2000, CHD prevalence in Quebec was 4/1000 adults and 12/1000 children. Thus, the median age of those alive with severe CHD has also increase from 11 to 17 years as observed from 1985 to 2000 and is expected to further increase between 2000 and 2020. There are data suggesting a female predominance in the ACHD population which may impact birth rates of CHD in the future. The estimated number of adults with CHD who have severe or complex disease is likely to be 10–25% when population data are considered.
The impact of changing demographics on clinical outcomes and disease burden on the adult CHD population has become considerable. Our commitment to patient care necessitates that we continue to improve the quality of care based on the needs of this population as illustrated by trends in medical complications and health services utilization.

1. Introduction

The adult congenital heart disease population (ACHD) is one of the fastest growing populations in cardiology. Strides in diagnosis and management of children born with congenital heart lesions (CHD) have changed the demographic landscape of those born with congenital lesions [1]. CHD is now a life-long condition spanning from birth to old age. On a population level, it therefore now becomes relevant to discuss CHD from newborns to geriatric populations. Previously almost exclusively in the domain of pediatric cardiology, a hybridization of knowledge needs to occur. Adult cardiologists need to become familiar with common CHD lesions and pediatric cardiologists need to become versatile with acquired complications associated with prolonged survival.

Fig. 1 provides a conceptual model bridging epidemiology and clinical care both of which determine demographics and prevalence of lesions carried from birth. This figure illustrates the demographic *characteristics and determinants* of the CHD population as well as the *primary and intervening pathways* impacting them. The demographics of the CHD population are characterized by the distribution of age, sex, and CHD disease severity. These are in turn determined by the *incidence* and *survival* of patients with CHD resulting in the *prevalence* of disease in adults as we observe it. The *modifying factors* of incidence and survival of CHD are both *primary* or biological affecting birth rates and *intervening* including surgical and medical care as well as health care behavior.

This chapter will be divided in two parts. In part I, we review the cornerstone notions of the epidemiology of CHD. The aim is to familiarize the reader with the principles of population science that provide the basis for understanding the changing demographics of CHD. This should facilitate critical thinking and understanding of the publications aimed at estimating the size of the CHD population. In part II, we review the impact of the epidemiology on the demographics of the CHD population in terms of age, sex, and severity of disease distribution.

It is important to highlight that the purpose of this paper is not to provide a systematic review of data available for each of the topics below. The emphasis in what follows is on the data used in the lecture presented from which this paper originates. The data sources drew predominantly from population based administrative and surveillance data sources that have been published in industrialized countries. Specifically data was presented from the Quebec CHD database in Canada, from the Center for Disease Control (CDC) in the US and from the European Congenital Anomalies Surveillance of Congenital Anomalies (EUROCAT) in Europe.

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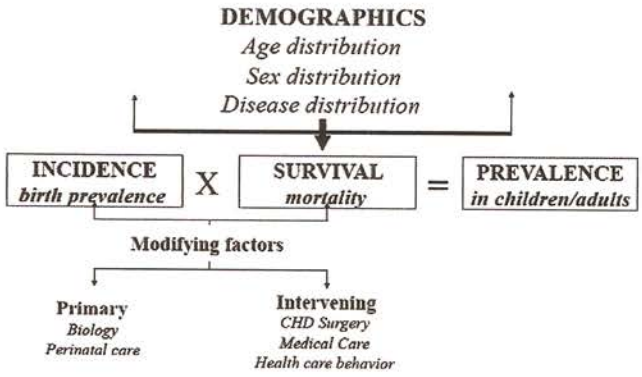

Fig. 1. The demographic characteristics of the CHD population (age, sex, and disease distribution) and their epidemiologic determinants (incidence, survival and prevalence) and associated modifying factors (primary and intervening) are schematically illustrated.

2. Part I. The epidemiology of CHD (Fig. 2: panels A, B; Fig. 3)

Fig. 2 uses a beaker to visually illustrate how the size of a population during any given observation period can be quantified. The size of the population (prevalent cases) results from the difference between the number of cases entering (new or incident cases) and those exiting (surviving cases) during the duration of the observation. During the observation period in panel A when mortality of CHD is high, the long vertical arrow indicates that majority of cases entering the cohort die. Thus the number of surviving cases is small. During the observation period in panel B, the mortality is reduced and the number of survivors has thus increased.

Fig. 3 models the elements contributing to the observed changes in the prevalence of ACHD showing the interplay between incidence and mortality over time. What we have observed in the last several

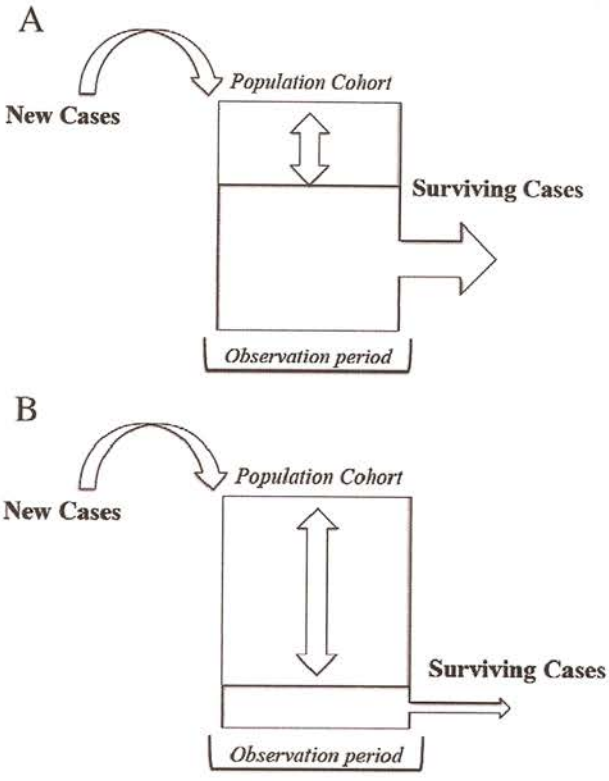

Fig. 2. Visual representation of the size of the CHD population based on new cases entering and surviving cases exiting the population cohort over an observation period when the number of surviving cases is small (panel A) and when the number of surviving cases is large (panel B).

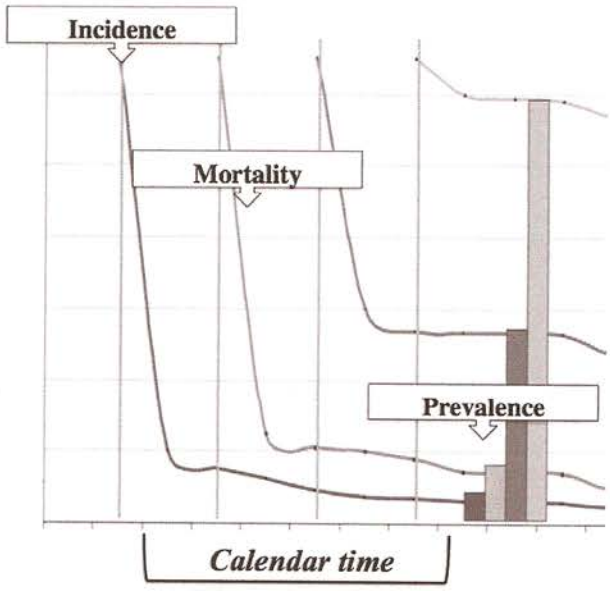

Fig. 3. Conceptual model illustrating the contribution of changing incidence and mortality to the growing prevalence of the congenital heart disease population over calendar time. Assuming that the prevalence of CHD at birth remains constant, as mortality decreases over time, the number of surviving patients increases and the observed prevalence of CHD increases.

decades is a rise in the prevalence of adults with CHD that has been directly influenced by the incidence and mortality of CHD (Fig. 3). Prevalence is thus the product of incidence and survival (Fig. 1). What then amongst these elements have we been able to accurately measure and what does this tell us about future trends?

2.1. Birth prevalence of CHD — the most accurate proxy for incidence of CHD

The incidence of CHD cannot be accurately measured because we would need to track the number of new cases of CHD in utero. Since this measurement cannot be systematically obtained, what has been reported is the measurement and report of the number of observed *cases at birth* following, in-utero attrition due to spontaneous or planned pregnancy termination. What we are really reporting then, is prevalence at birth as the best possible proxy for incidence of CHD.

The reported birth prevalence of CHD varies widely depending on the lesions included, the surveillance method used and the geographical area of source and accounts for the large variation in published rates. Most commonly the reported rates of birth prevalence cluster around 8/1000 live births but vary between 4/1000 and 50/1000 [2]. In the US the most recent report using data from the CDC has reported birth prevalence rates between 8 and 10/1000 live births [3]. Variations in birth prevalence have also been analyzed using the EUROCAT registry that assembles data from 16 European countries. In 26,598 cases observed from 2000 to 2005, the prevalence of CHD at birth was reported to be up to 13/1000 live births [4].

Using birth prevalence rates of CHD to estimate the number of ACHD patients is further limited by the assumption that birth rates have remained constant over time. Fig. 1 draws attention to some of the modifying factors impacting birth prevalence of CHD. Primary modifiers may be biologically determined or may act through prenatal care including pregnancy termination and prevention. Biological determinants of birth prevalence are related to the proportion of infants born with chromosomal abnormalities associated with a higher frequency of CHD [5,6]. The EUROCAT registry is one of the only data sources that examine the impact of perinatal mortality and pregnancy termination rates on birth rates of CHD in the same population [4]. In this registry perinatal mortality due to CHD in the fetus is most

commonly reported from .2 to .4/1000 births. Not surprisingly, pregnancy termination rates susceptible to cultural trends varied more widely occurring in up to 1–1.3/1000 births depending on the country [4]. Using the Quebec CHD database, we examined the impact of policy aimed at reducing birth defect rates at a population level. In a time-series analysis of 2050 births with severe CHD of 1,247,623 infants born in Quebec from 1990 to 2004, we observed a significant decrease in birth prevalence of severe CHD from 1.68 to 1.57/1000 before and after the introduction of mandatory folic acid supplementation in grain products [7].

Thus, prevalence at birth is the best proxy available to estimate incident or new cases of CHD born each year. As modeled in Fig. 3, even if we assume constant rates of birth prevalence of CHD, the next challenge is estimating the sequential variations in death rates of CHD patients over the last several decades (cohort effect). Looking back at Fig. 1 we have therefore reviewed the measurements and pitfalls of the first part of the prevalence equation. What about survival, and what do we know of the change in survival over time?

2.1.1. Mortality — a shift away from the young and towards adulthood

The reciprocal of survival is mortality. Although estimating survival itself over time with a uniform methodology is difficult, mortality of CHD patients has been measured. Using CDC data in the US, the age adjusted yearly infant mortality decreased by 40% from nearly 2.6 to 1.8/100,000 live births between 1979 and 1993 [8]. Although death from CHD remains the most common cause of infant mortality from birth defect in the US, CDC data from 1979 to 1997 indicated that mortality due to CHD decreased most dramatically in children and infants 0–10 years of age from a rate of 100/100,000 to <1/100,000 population during the observation period [8]. Also using CDC registry data, all age mortality rates in cyanotic and cyanotic CHD decreased by 40% in patients with tetralogy of Fallot and 60% in those with VSD as observed between 1980 and 2005 [9]. Using the Quebec CHD database, in 8123 patients followed Q3 for 1,008,835 years, we showed that the median age of death in the CHD patients increased from 2 years of age in 1997–98 to 23 years of age in 2004–05 [10]. Thus mortality from CHD changed from a bimodal distribution of death to a distribution skewed towards older age, resembling that of the normal population (Fig. 4) [10].

As illustrated in Fig. 1, mortality is likely to be the element where we have observed the largest number of modifying factors manifested by way of intervening pathways. Surgical and percutaneous interventions, medical care pertinent to diagnosis and complications of CHD and health care behavior as determined by insurance, access and psycho-social determinants have all made significant contributions to the change in mortality of CHD over time [11].

Thus going back to Fig. 3, the chronological decrease in mortality is expected to result in a sequential increase in survival rates contributing to an increasing pool of prevalent CHD patients. From an epidemiologic perspective, as illustrated in Fig. 1, the product of incidence and survival is prevalence. What then have we observed on the changing prevalence of CHD on a population level? Specifically we turn our attention to the prevalence of the CHD population across the life-span.

2.1.2. Prevalence of CHD throughout the lifespan

The challenge in measuring prevalence beyond birth into childhood and adulthood is obtaining a meaningful denominator. The number of CHD patients can be counted in various jurisdictions, but a prevalence rate requires the judicious choice of denominators. To our knowledge the Québec CHD database is the only data source Q4 that attempts a prevalence estimate of CHD in the general population [1]. Where health insurance is universal and health services are tracked using a single unique identifier throughout an individual's life, we measured the prevalence of CHD in children, adults and overall in the same population (Fig. 5). In a population of 7,357,029 in Québec in the year 2000 the prevalence of CHD in patients 0–18 years of age was 11.89/1000 children and 4.09/1000 adults with an overall prevalence of CHD across the lifespan of 5.78/1000 in the general population [1]. The estimated prevalence in children is higher than published estimates of prevalence at birth but this is not surprising if one considers the number of cases of CHD that can be detected after birth, over an observation period of up to 18 years and particularly with the advent of cardiac ultrasound since the mid-1980s. Although the prevalence rates are higher in children than adults, since there are more adults than children in most industrialized nations, the absolute number of adults with CHD is now at least equal to the number of children with CHD. In the same study, we showed that the prevalence of severe CHD increased by 22% in children and 85% in adults from 1985 to 2000 [1]. This differential rise in children and adults over the same observation period is less likely to be influenced by ascertainment bias using cardiac ultrasound as there is no reason to suspect that adults had more access to ultrasound diagnosis than children in the same jurisdiction. When we stratified the increase in prevalence by age group, as shown in Fig. 6, we see that the largest increase in prevalence ratios over time occurred in those 13–18 followed by those 18–25 years of age [1]. We can therefore expect that a further increase occurred in the number of CHD patients entering adult cohorts in the last decade.

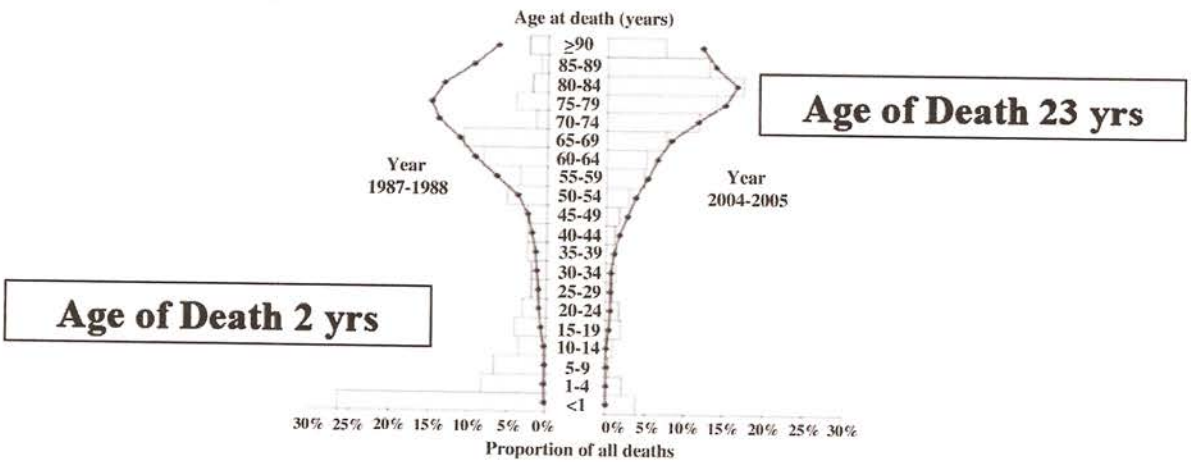

Fig. 4. In 1987–88 the pattern of death in the CHD population was bimodal with a predominant peak in childhood during which time the median age of death for patients with severe CHD was 2 years. By 2004–05, the peak in childhood had disappeared and the shape of the age distribution of death espouses that of the normal population (dotted black line). During this latter observation period, the median age of death in those with severe CHD increased to 23 years.

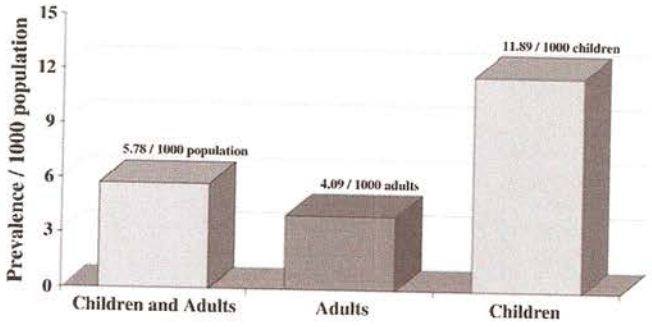

Fig. 5. Prevalence rates of CHD are reported overall, in adults and in children measured in the same population in the same year.

In the US then what are the numbers? In 2000, the total number of adults living with CHD in the US was estimated to be 800,000 with the estimated number of children living with CHD being 600,000 [11]. There are no population-based longitudinal CHD data on children, adolescents, and adults living with CHD. Based on Canadian data from 1990 to 2000 [12] extrapolated to US Census data in 2010, it is estimated that 2–3 million people of all ages may potentially be living with CHD in the US in 2010 [13]. The estimated number of children living with CHD is between 975,000 and 1.4 million, while the estimated number of adults is between 959,000 and 1.5 million [13].

Thus, where exact survival estimates are unavailable, a direct *calculation* of the product of incidence and survival (Fig. 1) cannot be obtained. Nonetheless it is possible to *observe* the changing prevalence of CHD (Fig. 3) in different age groups where population based denominators are available.

3. Part II. The demographics of CHD — the impact of epidemiology

3.1. The aging of the CHD population

As mortality shifts away from the young and towards adults (Fig. 4), the median age of those alive with CHD has increased. Fig. 7 illustrates the increase in the median age of patients who are alive with severe CHD. In 1985 the median age was 11 years (IQR 4,22) while in 2000, the median age was 17 years (IQR 10,28). At the other end of the spectrum, we analyzed 3239 geriatric ACHD patients from 1990 to 2005 [1]. In 2005, the prevalence of ACHD was 3.7 per 1000 in the elderly adults [14]. Using 1990 as a reference, the prevalence remained constant in the elderly whereas it increased in nonelderly adults [14]. As the population ages, what is known about the gender distribution of ACHD adults?

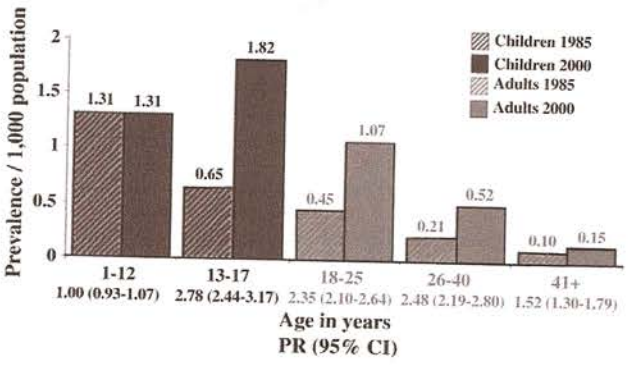

Fig. 6. On the Y axis the prevalence rate is expressed per 1000 population. On the X axis, the age strata are shown with the change in prevalence ratios (PR) and 95% confidence intervals between 1985 and 2000. The increase in PR is significant in all age groups above age 12 but the greatest increase occurs in those 13 to 25 years of age.

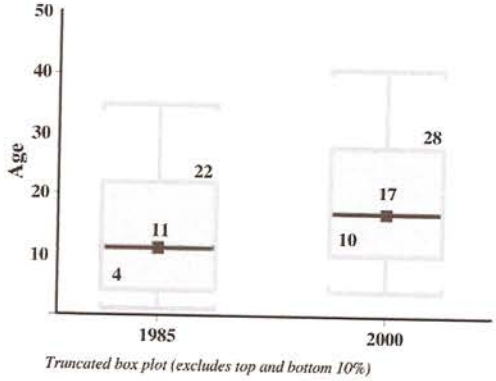

Fig. 7. The increase in median age of those alive with severe CHD increasing from 11 to 17 years from 1985 to 2000.

3.2. A predominance of females in adults with CHD?

Sex distribution in the CHD population has received relatively little attention. In Canada in over 45,000 adults with CHD, females accounted for 57% of patients, a proportion which was significantly higher than the predominance of females observed in the general population [1]. The prevalence was 4.55 per 1000 for females compared to 3.61 per 1000 in males (Fig. 8). Consistent with these findings, using death registry data in 11,040 adults the US, the CDC demonstrated lower mortality rates in females with CHD compared to males [15]. Potential causes of a shift in demographics towards a predominance of females in the ACHD population include milder lesions in females born with CHD, differences in mortality related to CHD surgery or sentinel effects related to a decrease in the proportion of males in the general population of industrialized nations [16]. Using Healthcare Cost & Utilization Project (HCUP) data in the US, we analyzed the KIDs' Inpatient Database in 2000, 2003 and 2006 which samples pediatric discharges, up to 20 years of age in 38 US states and showed that 55% of all children having surgery were males and males were more likely to have high risk procedures [16]. This is consistent with the observation that the most common CHD lesion, atrial septal defect, has a higher frequency in females while conotruncal anomalies such as transposition of the great arteries are more common in males [17].

The interplay between factors impacting the sex distribution of the CHD population at birth and during adulthood is illustrated in Fig. 9. A predominantly female ACHD population is likely to result in increased transmission rates of CHD to offspring. The effect will be

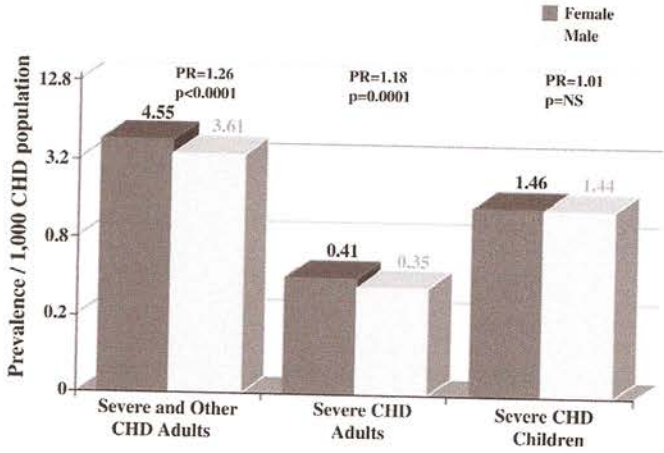

Fig. 8. Difference in prevalence between females and males with CHD per 1000 population in adults and children. Although there is no significant difference in the prevalence ratio (PR) between females and males in children, there is a predominance of females amongst adults with severe and other forms of CHD.

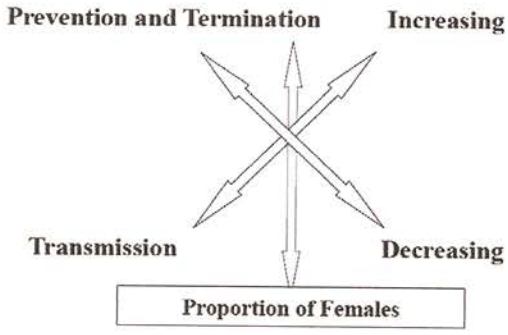

Fig. 9. This diagram is illustrating the interplay of the factors that can result in increasing or decreasing birth prevalence of CHD in future generations. With a higher proportion of females, the increasing transmission rates may result in increasing prevalence while prevention and pregnancy termination may have the opposite effect thereby decreasing the prevalence of CHD.

further magnified if surviving adult females are less likely to have severe disease both because of biologically-driven distribution of lesions at birth and potential differences in mortality during adult years. Thus the proportion of females and the disease distribution of CHD amongst them may result in *increasing* numbers of patients with CHD in the future. On the other hand, these trends may be offset by CHD prevention and pregnancy termination as discussed above in the context of prevalence of CHD. We have seen that grain fortification may decrease the birth prevalence of severe defects [7]. Voluntary or involuntary pregnancy termination may also result in decreasing rates of infants with severe CHD at birth. It is interesting to speculate then, that a larger proportion of surviving healthy females with less severe lesions, in addition to prevention and pregnancy termination of fetuses with severe lesions will conspire to decrease the number of patients with severe CHD from one generation to the next. From an evolutionary point of view, this would be consistent with biology's natural intelligence. What then do we know about the distribution of disease severity in the ACHD population at the current time?

3.3. Distribution of disease severity in ACHD patients

There is a continuing debate about what proportion of the ACHD population has severe or complex CHD. As we have seen above, this number is subject to change over time due to factors outlined in Fig. 1 and in all probability it is likely to evolve in the coming decades. The nature of the debate results at least in part from the inter-dependence between *advocacy* and *data*. There is a need for the numbers required for our advocacy platforms to move us forward in order to overcome the existing limitations of the data currently available. One cannot occur without the other. In addition, the language of this debate suffers from *definitional* and *methodological* uncertainty.

The definition of disease severity and the question of who should be followed in ACHD centers, are related but are different and often used interchangeably. The first is traditionally based on anatomy and physiology, the second is based on health services requirements. The definition of the *severity of CHD* has undergone several modifications over the last 70 years [18,17]. In children severe or complex CHD has been linked with cyanosis. We have previously defined "severe" CHD as that which has the highest probability of being associated with cyanosis at birth. For adults, during the 32nd Bethesda conference, lesions were classified as "complex", "moderate" or "simple" based on a combination of anatomy and surgical interventions [11]. Although it is generally agreed that ACHD with lesions of great complexity should receive specialized services [11], making recommendations for those with mild and moderate disease is thus more problematic. For example when looking at surgical trends in ACHD patients between 1990 and 2000, the fastest growing segment of patients requiring interventions was that classified as having "moderate" disease as defined at the 32nd Bethesda conference [19]. Not surprisingly, with evolving percutaneous procedures paralleling a growing need to *prevent* rather than to treat complications, specialized ACHD care, may need to be delivered to a wider range of ACHD patients.

Despite these limitations, the proportion of ACHD patients having complex or severe disease is one of several important metrics of disease burden. The proportion of ACHD patients with complex or severe lesions has been *estimated* and *measured* [2,20,1,11] and are summarized in Table 1. Estimates are based on prevalence at birth rates with assumptions about survival. The range of reported estimates of adults with CHD of great complexity varies from 5 to 14% depending on if the assumption is made that no patients with severe CHD at birth are treated or if all are treated. Using estimates of survival by cohort and the Bethesda disease severity classification an approximate 15% of adults are expected to have lesions of great complexity while those with moderate lesions were estimated to account for approximately one third of patients. Using the general population as the denominator we measured a proportion of 9% of ACHD patients with severe disease as defined with administrative data sources.

Using *birth prevalence* rates of CHD requiring referral for specialized care, the NERCP determined that in 1976 there were 2.4 NERICP infants per 1000 live births identifiable in the New England states referred for definitive treatment [17]. It is reasonable to suppose that these infants represent the sickest children from that era. Using 2000–2005 as a measurement period, the EUROCAT registry identified between 2 and 3/1000 infants who had severe and moderately severe CHD lesions at birth [4]. If we accept that the birth prevalence of CHD is 8–10/1000, this suggests that up to 25% of infants born with CHD require early attention.

It would therefore be reasonable to suppose that the proportion of adults with advanced forms of heart disease is between 10 and 25% depending on the method of estimation, measurement and jurisdiction. The limitations of this statement underscore the need for more uniform disease severity definitions, based on anatomy *and* health services utilization across the life-span as well as measurement based studies in the US.

4. Summary and future directions

Prevalence at birth rates are the best proxy available to estimate incident or new cases of CHD born each year. Available population data from industrialized nations suggest that birth rates of CHD are between 8 and 10/1000 live births with CHD patients requiring intervention at an early age accounting for up to 25% of these. Ultimately, disease distribution in adults is determined by disease distribution at birth and survival. The proportion of adults with severe or complex CHD is probably between 10 and 25%.

The sex distribution of the CHD population at birth and during adulthood will impact future trends in the total number of patients with CHD as well as the sex and disease distribution of CHD in

Table 1
Estimated and measured proportion of patients with complex or severe CHD in the ACHD population.

	Complex or severe CHD
Estimated (assuming all treated) *Hoffman IE et al. Am Heart J 2004; 147:425*	14%
Estimated (assuming none treated) *Hoffman IE et al. Am Heart J 2004; 147:425*	5%
Estimated *Warnes CA et al. JACC 2001; 37:116*	15%
Measured in the general population *Marelli AJ et al. Circulation 2007; 115:163*	9%

generations to come. This is likely to be influenced by preventive measures aimed at decreasing congenital malformations in the fetus and variations in laws governing pregnancy termination.

Where exact survival estimates are not available the closest approximation remains to be mortality. Using CDC data in the US, infant mortality due to CHD, death from CHD and death from specific cyanotic and acyanotic lesions have been shown to consistently decrease between 1979 and 2005. Using Canadian data we observed a shift in mortality away from the young and towards older adults. Thus the pediatric CHD population is aging with the median age of those with severe disease on the cusp of adulthood. At the other end of the spectrum, there are sufficient numbers to turn our attention to geriatric ACHD patients, perhaps with more simple forms of CHD but with a growing burden of acquired disease.

Measuring the prevalence of CHD across the life-span remains a challenge. We observed a significant rise in the prevalence of severe CHD in adults compared to children consistent with the notion of increased survival and observed decrease in mortality of the CHD population. Extrapolating Canadian data to the US, it is estimated that 2–3 million people are living with CHD in the US of which adults constitute at least half.

The unique needs of this population center around life-long co-morbidities. Using the Quebec CHD database we have documented the impact of ongoing disease burden including atrial arrhythmias [21], pulmonary hypertension [22] and repeated need for interventions [23] resulting in significant increases in health services utilization during childhood [24], transition years [25] and adulthood [26] extending into the geriatric populations [14] which are at the crossroads between congenital and acquired lesions. The demographics of this population will continue to evolve requiring a growing need for CHD expertise that crosses age groups and spans general and sub-specialty care. The trends in long-term outcomes and health services utilization are an important departure point for studies measuring and improving the quality of care for these patients.

Acknowledgments

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