

The Incidence of Congenital Heart Disease

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This study was designed to determine the reasons for the variability of the incidence of congenital heart disease (CHD), estimate its true value and provide data about the incidence of specific major forms of CHD. The incidence of CHD in different studies varies from about 4/1,000 to 50/1,000 live births. The relative frequency of different major forms of CHD also differs greatly from study to study. In addition, another 20/1,000 live births have bicuspid aortic valves, isolated anomalous lobar pulmonary veins or a silent patent ductus arteriosus. The incidences reported in 62 studies published after 1955 were examined. Attention was paid to the ways in which the studies were conducted, with special reference to the increased use of echocardiography in the neonatal nursery. The total incidence of CHD was related to the relative frequency of ventricular septal defects (VSDs), the most common type of CHD. The incidences of individual major forms of CHD were determined from 44 studies. The incidence of CHD depends primarily on the number of small VSDs included in the series, and this number in turn depends upon how early the diagnosis is made. If major forms of CHD are stratified into trivial, moderate and severe categories, the variation in incidence depends mainly on the number of trivial lesions included. The incidence of moderate and severe forms of CHD is about 6/1,000 live births (19/1,000 live births if the potentially serious bicuspid aortic valve is included), and of all forms increases to 75/1,000 live births if tiny muscular VSDs present at birth and other trivial lesions are included. Given the causes of variation, there is no evidence for differences in incidence in different countries or times. (J Am Coll Cardiol 2002;39:1890–900) © 2002 by the American College of Cardiology Foundation

The number of adults with some form of congenital heart disease (CHD) is growing rapidly as therapy becomes increasingly effective. Some of these patients have only mild disease with relatively little need for medical care, but others have complicated problems and require the services of an array of people with great expertise in the field. To assess the needs for care for these patients, we need first to determine the incidence of CHD as a group and of the individual major congenital heart lesions. This determination is usually incomplete, and there is substantial variation in the estimated incidence of CHD. The reasons for this variation will be examined and the current best estimates for incidence will be provided.

DEFINITIONS

Incidence refers to the number of new affected persons per unit of time or population; *prevalence* refers to the number present at any time and represents the difference between the incidence and those who die in the same period. The incidence of CHD is usually estimated by calculating the number of subjects with CHD per thousand or per million live births. Sometimes these numbers are collected in a region over one year, but at other times the data for several years may be combined. For some purposes it is useful to

calculate the incidence in a country per year. *Congenital heart disease*, in a definition proposed by Mitchell et al. (1), is “a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance.” This definition excludes functionless abnormalities of the great veins, such as persistent left superior cava (even though this might be important during surgery), or of the branches of the aortic arch such as a combined brachiocephalic-left carotid arterial trunk. It usually excludes congenital arrhythmias such as the long QT and the Wolf-Parkinson-White syndromes, even if the disorders are based on abnormalities present at birth. Lesions such as hypertrophic or dilated cardiomyopathy are usually not regarded as CHD. Even though the abnormal genes that cause these disorders are present at birth, the cardiomyopathy is rarely detected at this time but usually presents later in childhood or adolescence. Another genetically determined lesion, Marfan syndrome, is often included as CHD because the phenotype may be present at birth, although because the cardiac and aortic lesions may not appear for many years not all studies include this syndrome.

INCIDENCE

Studies of the incidence of CHD usually estimate the total incidence and the proportions of different CHDs, but occasionally one or the other result is reported alone. The medical equivalent of Heisenberg’s uncertainty principle is involved, inasmuch as very large studies of huge populations give sufficiently large numerators (live births) at the expense of not being able to detect all with CHD (denominator), whereas very intensive studies that find virtually all those

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Abbreviations and Acronyms

AS	= aortic stenosis
ASD	= atrial septal defect
AVSD	= atrioventricular septal defect
BAV	= bicuspid aortic valve
CHD	= congenital heart disease
Coarc	= coarctation of the aorta
DORV	= double outlet right ventricle
NERICP	= New England Regional Infant Cardiac Program
PDA	= patent ductus arteriosus
PS	= pulmonic stenosis
SV	= single ventricle
VSD	= ventricular septal defect

with CHD in a region cannot be done on very large populations. The former studies are usually passive, in that diagnosis is made in a large regional high-quality pediatric cardiology center but relies on referral of patients from local doctors. Thus, if a local physician is comfortable with the management of a tiny ventricular septal defect (VSD) or a mild pulmonic stenosis (PS), that patient might not be referred to a center and so not be counted. In addition, some lesions with subtle physical findings, such as atrial septal defects (ASDs), might not be detected until they appear in adult life (2,3). Finally, some neonates with severe critical heart disease may die in the first few days after birth, and without cardiologic or autopsy diagnosis would not be correctly identified (4,5). On the other hand, the more intensive studies, for example, of all neonates in a nursery, will detect all forms of CHD and allow for early deaths, but the incidence of uncommon forms of CHD will be inadequately assessed because of small numbers and stochastic variation.

Early studies of the incidence of CHD, as summarized by Hoffman (6) produced low incidences of about 4 to 5 per

1,000 live births, but this figure has been rising steadily until recently when incidences of 12 to 14/1,000 live births, or higher, have been reported in the literature (7) (Fig. 1) (1,8-67) as well as by P. Merlob (personal communication, June 2000).

Among the reasons for the early lower incidence rates of 4 to 5/1,000 live births is that only the most severely affected subjects were referred to a cardiac center, that there was relatively little interest in and knowledge of CHD by pediatricians and that cardiac surgery had not yet offered the spectacular results that now demand referral of these patients. Furthermore, before the availability of good echocardiography, diagnosis if not certain clinically had to be established by cardiac catheterization, and many doctors were reluctant to catheterize what was obviously a mild defect.

What accounts for the differences in incidence in the more recent studies? There are many reasons for a low incidence. A few studies were restricted to infancy (25) and so missed some patients who present later in life (68). Several of the later studies (51,54,67) based their data on the results of fetal echocardiography in unselected populations. These studies will not detect patients with a small ventricular or ASD, an abnormal patent ductus arteriosus (PDA) or many with coarctation of the aorta (Coarc). The increasing use of fetal echocardiography also leads in certain communities to therapeutic abortion for complex heart diseases, and can substantially reduce the incidence of specific lesions (69) or the total incidence (70). Some studies deliberately (15) excluded trivial lesions such as mild PS. Studies that cover a large region but rely on local physicians to refer patients will tend to underestimate the number of trivial lesions in the community (20,24,30,66). By contrast, high incidences were found in those studies that examined all or almost all newborn infants in a region, because they detected large numbers of small VSDs and other trivial

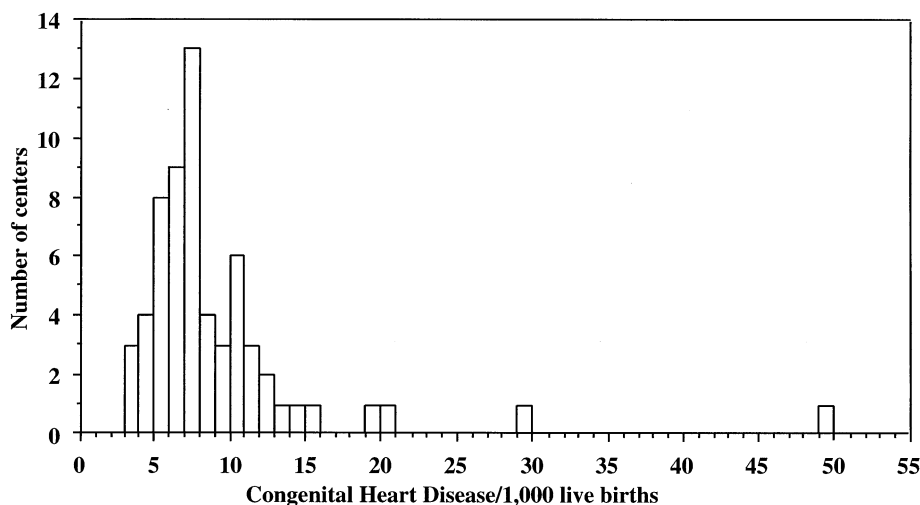


Figure 1. Histogram of the incidence of congenital heart disease per 1,000 live births in 62 reports. The six highest values all came from echocardiographic studies of infants in the newborn nursery.

lesions (37,40,48). Therefore, any assessment of the incidence of CHD must take into account the ages of the patients and the ways in which they entered the study. It is important to note that none of the studies analyzed included bicuspid aortic valves (BAVs), isolated lobar anomalous pulmonary venous connection or silent PDA, with respective incidences of about 13, 6 and 1 per 1,000 live births (to be described). If these are to be included, the incidences depicted in Figure 1 should be increased by 20/1,000 live births.

Today, clinical and echocardiographic diagnoses are so accurate that few misdiagnoses are made, but there remain important diagnostic problems of classification and, therefore, of inclusion as specific lesions. These problems vary by lesion and will be addressed briefly.

Isolated VSDs are by far the most common form of CHD. Some studies done by taking echocardiograms on every newborn infant in a nursery, including some with no murmurs, have found huge numbers of tiny muscular VSDs, the incidence of these varying from 2% to 5% (48,62). About 85% to 90% of these defects close spontaneously by one year of age (37,48,71-73). Therefore, the incidence of VSD will be much higher if all newborns are examined, lower if only those newborns with murmurs are examined and lower still if accession of these subjects is delayed until one year of age. Although these small defects that close spontaneously place little burden on the health care system, correct identification of their incidence has a possible bearing on studies of causation.

Patent ductus arteriosus is another common lesion, the incidence of which varies with the age at the time of study and the gestational age of the subject. Preterm infants have an increased incidence of PDA based on abnormal physiology rather than on a structural abnormality, so that any series that includes large numbers of preterm infants will inflate the incidence of PDA (74). In term infants the normal ductus may stay open for some time after birth. Scammon and Norris (75) found in autopsy studies that the ductus arteriosus was completely obliterated in 35% of subjects by one month, in 75% by three months and in virtually all by one year after birth. It is known, however, that functional closure precedes obliteration, often by a long time. Mitchell (76) observed in an autopsy study that no ductuses were widely patent after one week and that virtually all were closed by one month after birth. More recently, sensitive studies based on echocardiography (77-79) have shown that in the term infant the ductus arteriosus is almost always closed by four to seven days after birth. Therefore, studies done a few days after birth will record a larger number of subjects with a PDA than will studies done after three weeks (71). Recently some attention has been paid to the silent ductus arteriosus, a tiny ductus that is not detected by auscultation but found incidentally during echocardiography done for some other purpose. These may be common; estimates of 1 per 500 to 1,000 population have

been given (80). These silent ductuses are not included in any current incidence surveys.

Atrial septal defects of the fossa ovalis (secundum) type also give many problems of classification and diagnosis. Many infants have a patent foramen ovale with a tiny left-to-right shunt through it, and inclusion of these will inflate the incidence of ASD. Even if the patent foramen ovale is excluded, for example, by diagnosing ASD only when the defect is over 5 mm in diameter and the right atrium or ventricle are dilated (71), there appears to be a higher early spontaneous closure rate than has hitherto been appreciated (71,81-84). Once again, as for VSDs, the timing of the study and the population studied (all infants vs. those with murmurs or symptoms) influence the incidence attained. Furthermore, because an ASD is usually asymptomatic and has murmurs that are often soft, these defects frequently do not lead to early diagnosis or referral. This is why many of these subjects present in adult life (2,3), so the incidence in childhood usually underestimates the true incidence of the lesion.

Isolated partial anomalous pulmonary venous connection is a rare lesion clinically, and it resembles an ASD in producing a right ventricular volume overload. Some studies, however, have shown an incidence of 0.6% to 0.7% in routine autopsies (85,86), implying that most of these are small shunts of little clinical significance. This lesion is reported rarely in reports of the incidence of CHD and its apparent high incidence does not feature in incidence studies discussed here.

Atrioventricular septal defects (AVSDs) (endocardial cushion defects, common atrioventricular canal) have an incidence that varies with the age of the involved mothers. Trisomy 21 (Down syndrome) is much more common in mothers more than 34 years old, and AVSDs are much more frequent in those with trisomy 21 than with normal chromosomes. Thus, the proportion of older mothers in a series greatly increases the incidence of AVSDs. Because therapeutic abortions may be performed if trisomy 21 is discovered early in pregnancy, the incidence of AVSD at term is likely to decrease in future years.

Pulmonic stenosis if mild is often confused with an innocent pulmonic flow murmur. In fact, in our own incidence study (16), done before extensive use of echocardiography, this was our single greatest diagnostic difficulty. Various discriminatory standards have been used to diagnose this anomaly. Bound and Logan (15) diagnosed PS only if the systolic gradient across the valve at cardiac catheterization exceeded 25 mm Hg. More recently, using echocardiography, a flow velocity over 120 cm/s was used to decide if a newborn infant had PS (71). Pulmonic stenosis is another lesion in which the incidence changes with follow-up. Stenosis with thickened valves in the neonate can resolve with time and leave a normal valve, as described first by Johnson et al. (cited by Gielen et al. [87]); we have since observed several patients with this course. On the other hand, some subjects with very mild PS in the neonatal

period (who might not be included as PS in any series) might develop more severe PS with time (88–90).

Aortic stenosis (AS), if moderate or severe, is usually easy to diagnose, but when mild causes many problems. Many cardiologists distinguish between AS, in which there is a pressure gradient across the valve, and a bicuspid valve that is nonobstructive. Unfortunately, no accepted criteria for this distinction have been developed. Ooshima et al. (71) used the criterion of a flow velocity in the ascending aorta in newborns over 160 cm/s as indicating stenosis. Kitchiner et al. (91) diagnosed AS in children if the flow velocity in the ascending aorta exceeded 2 m/s or the peak systolic pressure gradient at cardiac catheterization exceeded 10 mm Hg. Because a nonstenotic BAV is thought to occur in about 1% of all live births (to be discussed), inclusion of a significant number of these as AS will inflate the incidence of this lesion.

Bicuspid aortic valves are important because of their frequency and their late complications. Most subjects with BAVs develop stenosis or incompetence after 40 years of age, and so they are not usually recorded in the other studies of incidence in pediatric populations cited in this article. Instead they have been studied as independent lesions. The standard for their detection is the postmortem examination done on unselected consecutive necropsies. There is some variation in incidence from about 0.4% to 2.25%. There are studies with incidences of 0.44% to 0.77% (92–97) that probably underestimate the true incidence, because these studies usually excluded subjects with other forms of heart disease or even with true stenosis or incompetence. Other studies give incidences of 0.9% to 2.25% (98–102). The high figure of 2.25% from Osler (98) might exaggerate the incidence because 8 of his 18 patients had infective endocarditis. The best single figure is 1.37% by Larson and Edwards (102) because of the large numbers seen (293 BAVs in 21,417 autopsies) and the expertise of the investigators in assessing abnormal aortic valves.

Coarctation of the aorta is an abnormality easily diagnosed by the combination of upper body hypertension and weak or absent femoral pulses. Nevertheless, studies in children's hospitals have shown that the diagnosis is often missed by the referring doctor (103–105), with little improvement over the past 20 years. If this is true for symptomatic children, it may be even more serious in asymptomatic subjects. As a consequence, many subjects with a Coarc are not detected until adult life, so that their incidence at birth is likely to be underestimated.

Mitral incompetence as an isolated congenital lesion is rare in children, and usually not recorded separately in most reported series. On the other hand, mitral valve prolapse, although rare in the newborn period, is common, occurring in perhaps 4% to 5% of the population (106–108). Inclusion of any of these as true congenital lesions inflates the incidence of CHD.

There is inconsistency in how multiple lesions are classified. For example, a VSD with a Coarc may be classified in

a separate category, it may be classified under the heading "Coarc" if the VSD is small, or as "VSD" if this seems to be the major lesion, and sometimes it is classified under the heading of *complex lesions* or just placed in a *miscellaneous* category. Some investigators use the miscellaneous category to include lesions too rare to deserve separate mention, for examples, anomalous origin of the coronary artery, partial anomalous pulmonary venous connection with an intact atrial septum, isolated cleft mitral valve, congenital endocardial fibroelastosis, l-transposition of the great arteries, cor triatriatum and so on. This category, however, sometimes includes slightly more common lesions such as truncus arteriosus, double outlet right ventricle (DORV) or single ventricle (SV) that in other series are separated out. Because of the varied composition of this category, it is not comparable from series to series.

CATEGORIES OF SEVERITY

If we consider which groups of patients with CHD use health care services, there will be obvious differences between the serious lesions like tetralogy of Fallot and AVSDs and those such as small VSDs. The same distinction by category also applies to studies of incidence, inasmuch as it is the least severe lesions that account for most of the differences between various studies. For example, two studies (30,66) documented that the increase in the incidence of CHD with time was due solely to the increase in the incidence of mild forms of heart disease. It is therefore useful to grade CHD into three groups of lesions and to consider their incidences separately. The following classification is similar in many ways to those published previously (109,110), except that late complications and the effects of surgery are not included here.

1. Severe CHD

This category includes the majority of the patients who present as severely ill in the newborn period or early infancy. Some of these patients who die very early might not be included in studies that do not track every infant born.

A. All those with cyanotic heart disease

1. d-transposition of the great arteries
2. Tetralogy of Fallot, including pulmonary atresia and absent pulmonary valve
3. Hypoplastic right heart
 - a. Tricuspid atresia
 - b. Pulmonary atresia with an intact ventricular septum
 - c. Ebstein anomaly
4. Hypoplastic left heart
 - a. Aortic atresia
 - b. Mitral atresia
5. SV
6. DORV
7. Truncus arteriosus
8. Total anomalous pulmonary venous connection

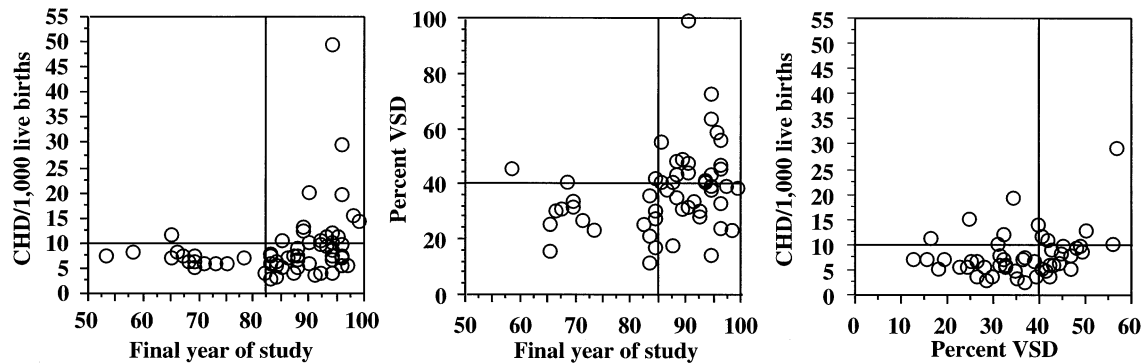


Figure 2. The incidence of congenital heart disease (CHD) per 1,000 live births is plotted against the final year of the study (left) and against the percentage of ventricular septal defects (VSDs) (right). In the center, the percentage of VSDs is plotted against the final year of the study. The horizontal lines are drawn arbitrarily at an incidence of 10/1,000 live births and 40% of all CHD, and the vertical lines are drawn arbitrarily at 1985 and 40%, respectively. An increasing proportion of the high incidences are beyond 1985 and for series that have over 40% VSDs.

- 9. Critical PS
- 10. Miscellaneous uncommon lesions like double outlet left ventricle, certain unusual malpositions and some forms of l-transposition of the great arteries.
- B. Acyanotic lesions
 - 1. AVSD
 - 2. Large VSD
 - 3. Large PDA
 - 4. Critical or severe AS
 - 5. Severe PS
 - 6. Critical Coarct
- 2. Moderate CHD

These require expert care, but less intensive than those listed above. Most of these are expected to be detected in a clinical study. They include:

 - A. Mild or moderate AS or aortic incompetence
 - B. Moderate PS or incompetence
 - C. Noncritical Coarct
 - D. Large ASD
 - E. Complex forms of VSD
- 3. Mild CHD

This is the most numerous group. Because these patients are asymptomatic, may not have significant murmurs and often undergo early spontaneous resolution of their lesions, inclusion of more or fewer of this group greatly influences the resulting observed incidence of CHD.

 - A. Small VSD
 - B. Small PDA
 - C. Mild PS
 - D. BAV without AS or aortic incompetence; these may move to moderate or severe categories if they deteriorate with age
 - E. Small or spontaneously closed ASD

It is probable that most of the patients in the severe and moderate groups will be detected in any good medical system, and that the lesions that are the major causes of variability appear in the mild group. Because VSDs have long been recognized as the most frequent isolated forms of CHD, their number will greatly influence the total inci-

dence of CHD. This is shown in Figure 2, where the incidence of CHD (excluding BAVs without AS or incompetence) and the percentage of VSDs reported in the more modern studies plotted against the final year of the study in the left and center panels, and the incidence of VSDs is plotted against the incidence of CHD in the right panel. The final year was chosen as an indication of the technology available for the study, and choosing the mid-year of the study did not affect the results. Studies were included if they ended in or after 1955 so as to include only studies done when cardiac catheterization was becoming a common diagnostic test. The horizontal lines are drawn arbitrarily at 10/1,000 live births (left and right panels) and 40% in the center panel. The vertical lines are drawn arbitrarily at 1985 in the left and center panels and at 40% in the right panel. It is clear from the left panel that after 1985 an increasing number of studies reported an incidence over 10/1,000 live births; this incidence was exceeded by only 1/24 studies ending before 1985, but by 17/38 studies ending at or after 1985 ($p = 0.0039$ by Fisher exact test). Because VSDs have always been the single most frequently reported lesion, their proportion of all CHD was examined in the center panel. In studies ending before 1985, only 3/20 studies had over 40% of VSDs, whereas this percentage was exceeded by 20/34 studies ending after 1985 ($p = 0.0016$ by Fisher exact test). This explains why in the right panel in which the percentage of VSDs is plotted against the incidence of CHD, incidences of over 10/1,000 live births were reported in only 5/30 studies with under 40% VSDs but in 11/24 studies with more than 40% of these defects ($p = 0.021$ by Fisher exact test). These differences still appear if the six studies of neonates with very high proportions of VSDs are excluded.

The principal reason for this increase in incidence of CHD and of VSDs after 1985 was the inclusion of more small VSDs with the increasing use of echocardiography. In fact, several investigators noted the increased incidence of small VSDs in the later years of their studies (11,30,33,40,42,49,111-113). The relationship between the incidence of VSD and the total incidence of CHD is shown more directly in the left panel of Figure 3. The slope of the

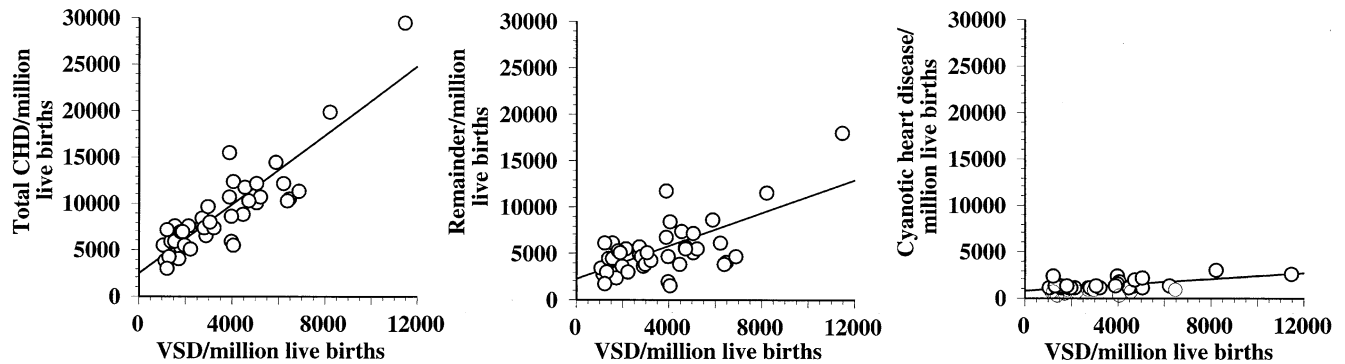


Figure 3. The incidence of ventricular septal defects (VSDs) on the horizontal axis is plotted against the total incidence of all congenital heart disease (CHD) in the **left panel**, against the incidence of the remainder of CHD (that is, all CHD except for VSD) in the **center panel**, and against the incidence of all cyanotic CHDs in the **right panel** (all incidences/million live births).

relationship of VSDs to total CHD is 1.9, showing that the total incidence rises faster than the incidence of VSDs. This is shown directly in the center panel of Figure 3, where the incidence of VSDs is plotted against the total incidence of all other forms of CHD. The significant positive slope of 0.9 shows clearly that as the incidence of ventricular defects increases, so does the total incidence of all forms of CHD. The likely mechanism of this positive relationship is that those studies that detect the small VSDs are intensive enough to detect more of the other mild forms of CHD. The right panel in Figure 3 provides data to support this contention by showing that the incidence of all cyanotic heart diseases, a surrogate for all serious CHD, rose little (slope 0.14) as the incidence of VSDs increased. These cyanotic diseases are always major and are usually detected even without intensive studies, so that adding universal neonatal echocardiography does little to increase their detection.

Another way of analyzing incidences is to examine the variability (expressed as median and interquartile distance) for total CHD, VSDs and the remainder when all VSDs are taken away from total CHD and cyanotic heart diseases taken as a group. The results are shown in Figure 4. Although there are more total patients in the remainder (that is, all CHD without the VSDs) than for VSDs or cyanotic heart disease, the remainder has a smaller variability than the total group or the VSDs, and the cyanotic group has the least variability.

Given the uncertainties of estimating incidence, there is no evidence that the true incidence of CHD has changed over the past 50 years, or that it varies in different countries. Several studies have shown, however, that the diagnosed incidence of CHD has increased over the years in a particular region because of longer follow-up (47) or because more subjects with mild lesions have been included (30,66). On the other hand, because parents (particularly mothers) with CHD have a higher incidence of children with CHD (114-116), there is reason to believe that the incidence of CHD will rise slowly in the years to come. Carter (117) has estimated that the incidence will double in seven generations. Finally, the availability of therapeutic abortion for

complex cardiac lesions will decrease their incidence to an unknown extent. In one population study (66), this factor had a negligible effect on total incidence, but some other studies suggest that therapeutic abortions substantially reduce the incidence of CHD in live births (118,119).

INCIDENCES OF SPECIFIC LESIONS

The data are presented in Table 1 and Figure 5; both of these emphasize the dominant role played by VSDs. They are taken from 44 published studies of the incidence of CHD in which there were at least 100 subjects with cardiac lesions and in which the lesions were not almost all tiny muscular VSDs found in the neonatal nursery (1,9,11-

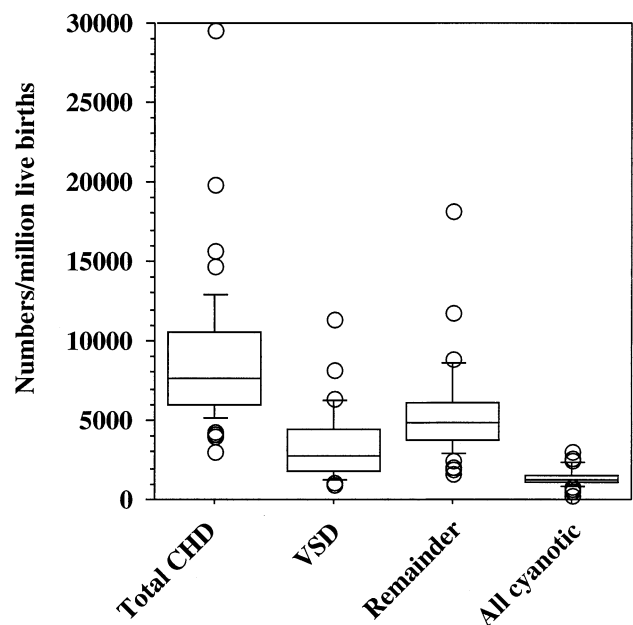


Figure 4. Modified box plots to show variability of the incidence per million live births of total congenital heart disease (CHD), ventricular septal defects (VSDs), the remainder of CHD (total minus VSD) and all cyanotic CHD. The plots were made with StatView 5 (SAS Institute Inc., Cary, North Carolina). In them, the **rectangle** shows the upper and lower quartiles and the **horizontal line** in the middle is the median. The **two short horizontal lines** connected to the rectangle by thin vertical lines indicate the 90th and 10th percentiles, and **data points** outside these limits are shown individually.

Table 1. Incidence per Million Live Births

Lesion	Number of Studies	Mean	SD	Lower Quartile	Median	Upper Quartile	NERICP 1975-1977
VSD	43	3,570	2,878	1,757	2,829	4,482	345
PDA	40	799	1,399	324	567	782	135
ASD	43	941	1,043	372	564	1,059	65
AVSD	40	348	165	242	340	396	110
PS	39	729	731	355	532	836	73
AS	37	401	543	161	256	388	41
Coarc	39	409	246	289	356	492	165
Tetralogy	41	421	188	291	356	577	196
d-TGA	41	315	115	231	303	388	218
HRH	32	222	199	105	160	224	—
Tricuspid atresia	11	79	52	24	92	118	56
Ebstein's anomaly	5	114	138	38	40	161	12
Pul Atresia	11	132	123	76	83	147	69
HLH	36	266	216	154	226	279	163
Truncus	30	107	71	61	94	136	30
DORV	16	157	103	82	127	245	32
SV	23	106	70	54	85	136	54
TAPVC	25	94	46	60	91	120	58
All cyanotic	37	1,391	590	1,078	1,270	1,533	888
All CHD*	43	9,596	7,484	6,020	7,669	10,567	2,033
BAV	10	13,556	13,049	5,336	9,244	13,817	—

*Excluding bicuspid nonstenotic aortic valves, isolated partial anomalous pulmonary venous connection and silent ductus arteriosus.

BAV = bicuspid aortic valve; CHD = congenital heart disease; Coarc = coarctation of the aorta; NERICP = New England Regional Infant Cardiac Program. Other abbreviations as in legend to Figure 5.

13,15-17,20-22,24-26,28-31,34-36,38-42,46,47,49,50, 53-55,57,58,62-67,84,120), as well as one personal communication (Merlob P, et al., June 2000).

If all the studies were unbiased and equally intensive, then the median value would give an excellent estimate of the incidence of that lesion at birth. However, some of these studies underestimated the incidence of a particular lesion by omitting mild disease or early spontaneous cure (such as PS, VSD), or by not having representatives of certain lesions with low frequencies in a small series, and others overemphasized the insignificant lesions by doing echocardiograms on every newborn infant. Because the value of the median is affected by the number of small or large outliers rather than by their magnitude, and because there are probably more studies that underestimated than overestimated incidence, we have included the lower and upper quartiles for readers to judge the variability. In our opinion, the upper quartile might be the best single figure to represent the incidence at birth of a particular congenital heart lesion. The mean and standard deviations are also given as another indication of the wide range and skewing of some of the data.

In 1980, Fyler et al. (121) reported the results of the New England Regional Infant Care Program (NERICP). This was based on a consortium of hospitals in New England that pooled their data concerning ill infants admitted with heart disease to one of the regional hospitals. For the period 1975 to 1977, the incidence of severe CHD was 2,033/million live births, 888 of these being one of the cyanotic lesions mentioned above, with another 200 to 300 possible cyanotic lesions (Table 8 in reference 126). If we include these latter

lesions (mostly heterotaxies, critical PS, l-transposition of the great arteries and miscellaneous lesions) the total of all cyanotic lesions (the lesions most likely to be detected in any series) in the NERICP data is between the lower quartile and the median values in Table 1. To these are added those with large VSDs, AVSD, the occasional ASD, critical Coarc and AS, and some miscellaneous lesions. Because most acyanotic lesions are relatively mild and thus not included in the NERICP series, the total incidence of CHD in their series refers only to the most severe disease.

Because of the inaccuracies in determining the incidence of CHD, it is difficult to know whether differences from study to study in the incidence of specific lesions are real or merely methodological. Some of the differences in the incidence of specific lesions, particularly the more common acyanotic lesions, are due to the problems described earlier. For the cyanotic lesions, their infrequency in any series leads to statistical uncertainty. For example, if there are only 2 patients with a truncus arteriosus out of 10,000 live births, for an apparent incidence rate of 200 per million live births, Poisson statistics suggest that the 95% confidence limits for this number are 0.242 to 7.22, equivalent to a range of 24 to 722/million live births. Failing to find a particular lesion in a series of 100 patients with CHD is compatible with a 3% incidence of that lesion, equivalent to an incidence of about 300/million live births!

Nevertheless, there are certain definite differences in the incidence of some types of CHD in different populations. The best documented of these is the excessively high proportion of subarterial VSDs in China and Japan (about

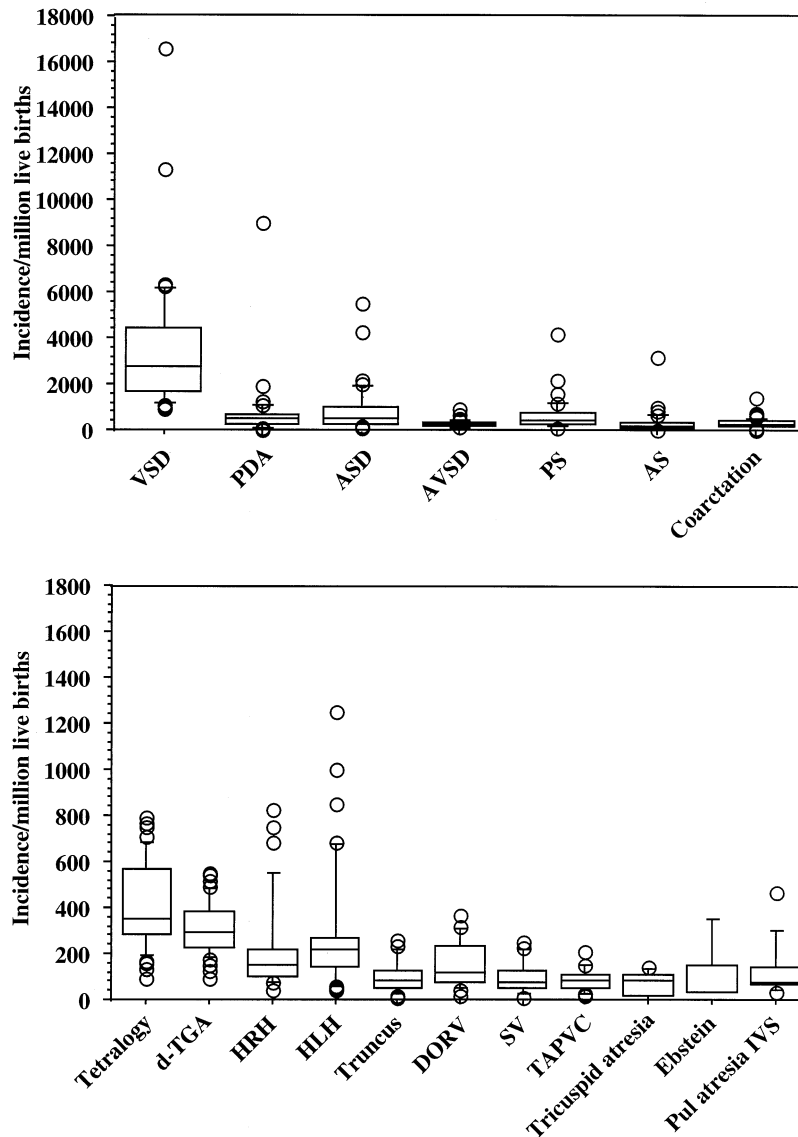


Figure 5. Modified box plots made in StatView 5; description as for Figure 4. Each panel has a different vertical scale, that on the top panel being 10 times larger than that on the bottom panel. **(Top)** The four major left-to-right shunts (ventricular septal defect [VSD]; patent ductus arteriosus [PDA]; atrial septal defect [ASD]; atrioventricular septal defect [AVSD]) and the three major obstructive lesions (pulmonic stenosis [PS]; aortic stenosis [AS]; coarctation of the aorta [Coarctation]). **(Bottom)** Tetralogy of Fallot (Tetralogy); complete transposition of the great arteries (d-TGA); hypoplastic right heart (HRH), which includes tricuspid atresia, Ebstein's anomaly, and pulmonary atresia with an intact ventricular septum (pul atresia IVS); hypoplastic left heart (HLH); truncus arteriosus (Truncus); double outlet right ventricle (DORV); single ventricle (SV); total anomalous pulmonary venous connection (TAPVC). The three components of the HRH syndrome do not add up to the total, because not all reports included all three.

35% vs. 5% in Caucasians (122,123). There are also indications of an excessive incidence of tetralogy of Fallot and other forms of right ventricular outflow tract obstruction in Malta (55,124), and Fixler et al. (30) observed that AS and Coarc were more common in Caucasians than in the black or Hispanic population.

CONCLUSIONS

The variations in the reported incidence of CHD are primarily due to variations in the ability to detect trivial lesions, notably small muscular VSDs that usually close in infancy. The incidence of severe CHD that will require expert cardiologic care is quite stable at about 2.5 to 3/1,000

live births. The moderately severe forms of CHD probably account for another 3 per 1,000 live births, although another 13/1,000 live births have BAVs that will also eventually need cardiologic care. The majority of minor forms of CHD do not need specialized cardiologic care, and indeed many of these, such as the tiny VSD or ASD and the small PDA, may either close spontaneously or never cause medical problems.

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