Recent Decrease in the Prevalence of Congenital Heart Defects in Europe

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Objectives To examine trends in the prevalence of congenital heart defects (CHDs) in Europe and to compare these trends with the recent decrease in the prevalence of CHDs in Canada (Quebec) that was attributed to the policy of mandatory folic acid fortification.

Study design We used data for the period 1990-2007 for 47 508 cases of CHD not associated with a chromosomal anomaly from 29 population-based European Surveillance of Congenital Anomalies registries in 16 countries covering 7.3 million births. We estimated trends for all CHDs combined and separately for 3 severity groups using random-effects Poisson regression models with splines.

Results We found that the total prevalence of CHDs increased during the 1990s and the early 2000s until 2004 and decreased thereafter. We found essentially no trend in total prevalence of the most severe group (group I), whereas the prevalence of severity group II increased until about 2000 and decreased thereafter. Trends for severity group III (the most prevalent group) paralleled those for all CHDs combined.

Conclusions The prevalence of CHDs decreased in recent years in Europe in the absence of a policy for mandatory folic acid fortification. One possible explanation for this decrease may be an as-yet-undocumented increase in folic acid intake of women in Europe following recommendations for folic acid supplementation and/or voluntary fortification. However, alternative hypotheses, including reductions in risk factors of CHDs (eg, maternal smoking) and improved management of maternal chronic health conditions (eg, diabetes), must also be considered for explaining the observed decrease in the prevalence of CHDs in Europe or elsewhere. *(J Pediatr 2013;162:108-13)*.

The prevalence of congenital heart defects (CHDs) is known to vary across populations and over time.[1,2] These variations are at least in part due to data issues such as completeness of the (prenatal and postnatal) diagnosis and/or registration of cases, whether pregnancy terminations are included, which (minor) anomalies are excluded, and the duration of ascertainment, among other issues.

Recently, 2 reports,[3,4] based on a study of trends in CHDs in Quebec, Canada, showed an increase in the live birth prevalence of severe CHDs in the early and middle 1990s, followed by a downward trend beginning in 1998. The authors attributed this downward trend to the implementation of folic acid fortification of food staples in Canada in 1998.

In Europe, although many countries have issued various recommendations regarding folic acid supplementation for women of reproductive age, or specifically for those who intend to become pregnant, mandatory fortification programs do

ASD	Atrial septal defect
CHD	Congenital heart defect
EUROCAT	European Surveillance of Congenital Anomalies
ICD	*International Classification of Diseases*
NTD	Neural tube defect
PR	Prevalence ratio

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not yet exist. Moreover, previous studies have shown that in the past, these recommendations have not had an appreciable effect on the prevalence of neural tube defects (NTDs) in European countries.[5] It is also worth noting that the currently available evidence is much stronger for the efficacy of folic acid for the prevention of NTDs than for the prevention of CHDs.[6,7]

In Europe, most population-based congenital anomaly registries are part of the European Surveillance of Congenital Anomalies (EUROCAT, http://www.eurocat-network.eu/), with a common database. Each year, EUROCAT performs statistical monitoring for trends and clusters in time.[8] In 2009, EUROCAT published a special report on CHDs,[9,10] partly in response to the World Health Organization Global Burden of Disease project. Based on some of the analyses for this report, a general decrease in CHDs was signaled and an additional pooled analysis of "severe" CHDs[11] provided preliminary evidence of a similar decrease to that in Quebec.

Given this background, and in particular given the difference between European countries and Canada in the policy for fortification of food staples with folic acid, we thought that it would be interesting to compare in more detail the trends in the prevalence of CHDs in Europe with those reported for Quebec. Hence, in this study, we examined trends in total and live birth prevalence of CHDs using data for >47 000 cases of CHD in EUROCAT registries. We estimated the trends for both all CHD combined and separately for 3 severity groupings of CHDs.

Methods

Since 1980, the EUROCAT central database has held individual anonymous records of cases of congenital anomaly occurring in the registry population, including live births, fetal deaths from 20 weeks' gestation, and terminations of pregnancy for fetal anomaly. Information on each of the registries, including their methods of case ascertainment and local procedures regarding ethics approval for the registries' activities and their collaborations with EUROCAT, are available elsewhere[12] and on the EUROCAT Web site (http://www.eurocat-network.eu/ABOUTUS/MemberRegistries/MembersAndRegistryDescriptions/AllMembers). All registries use the *International Classification of Diseases* (ICD)-*9* or -*10* with British Paediatric Association extension to code up to 9 syndrome or malformation codes for each case.

For the current study, all cases with a code for CHD were extracted from the EUROCAT database for the same 29 population-based registries in 16 countries that were included in the EUROCAT CHD Special Report[9] covering nearly 7.3 million births, 1990-2007 (**Table I**). Only registries with recent data (at least up to birth year 2004) and good ascertainment based on EUROCAT data quality indicators (>75% of EUROCAT average major congenital anomaly prevalence and more than half the EUROCAT average prevalence of selected severe CHDs [http://www.eurocat-network.eu/content/DQI-Introduction-May-2008.pdf]) were included. In practice, the participating registries had much higher thresholds for the EUROCAT data quality indicators than the a priori minimum values that had been set for participation in the study.

The ICD codes defining CHDs were Q20-26 (ICD-10) and 745, 746, 7470-7474 (ICD-9-British Paediatric Association). Minor cases of CHDs were excluded as per the EUROCAT list of minor anomalies for exclusion (http://www.eurocat-network.eu/content/EUROCAT-Guide-1.3.pdf), in particular patent ductus arteriosus among preterm babies. Cases of CHD and a chromosomal anomaly were also excluded from analysis.

We plotted the time trends, during the period 1990-2007, in the total and live birth prevalences of all nonchromosomal CHDs, as well as 3 severity groupings of nonchromosomal CHDs using the EUROCAT classification of the severity of CHDs,[9] which was based on relative perinatal mortality. These severity groupings were defined as follows: (1) severity group I: single ventricle, hypoplastic left heart syndrome, hypoplastic right heart syndrome, Ebstein anomaly, tricuspid atresia; (2) severity group II: pulmonary valve atresia, common arterial truncus, atrioventricular septal defects, aortic valve atresia/stenosis, transposition of great vessels, tetralogy of Fallot, total anomalous pulmonary venous return, coarctation of aorta; excluding cases with coexisting severity I CHD anomalies; and (3) severity group III: ventricular septal defect, atrial septal defect (ASD), pulmonary valve stenosis; excluding cases with coexisting severity I or severity II CHD anomalies.

Altogether, these 3 severity groups accounted for ~90% of all cases of CHD (**Table I**). Severity group I accounted for ~7%, severity group II for 20%, and severity group III for 60% of all cases. Of the cases, 10%, including those with patent ductus arteriosus in term infants and a few other CHDs, were not included in any of the 3 EUROCAT severity groups for CHDs.[9]

Total prevalence of CHD was defined as the total number of cases of CHD (live births plus fetal deaths after 20 weeks of gestation plus terminations of pregnancy for fetal anomaly) per 10 000 total births (live births plus fetal deaths). Live birth prevalence was defined as the number of live births with CHD per 10 000 live births.

We examined the plots of time trends in total and live birth prevalence of CHDs using restricted cubic splines,[13-15] which can provide a flexible, semiparametric, continuous model of the relation between prevalence of CHD and time.

Using the number of births as the "exposure" variable, we then used random-effects Poisson regression models to examine the annual trends in the prevalence of CHDs, for all CHDs combined and for the 3 severity groups of CHDs. Random-effects models were used to take into account heterogeneity that may exist across the registries[16] (http://www.eurocat-network.eu/content/DQI-Introduction-May-2008.pdf).

We excluded from our analyses of trends with Poisson models cases with isolated ASDs. This was done because the registration of the latter is likely to vary over time because