Published in final edited form as:

Int J Behav Med. 2016 February ; 23(1): 112–120. doi:10.1007/s12529-015-9488-9.

Neighbourhood Deprivation, Individual-Level and Familial-Level Socio-demographic Factors and Risk of Congenital Heart Disease: A Nationwide Study from Sweden

Xinjun Li¹, Jan Sundquist^{1,2}, Tsuyoshi Hamano³, Bengt Zöller¹, and Kristina Sundquist^{1,2}

Xinjun Li: xinjun.li@med.lu.se

1

2

3

Abstract

Objectives—The purpose of the study is to examine whether there is an association between neighbourhood deprivation and incidence of congenital heart disease (CHD), after accounting for family- and individual-level potential confounders.

Methods—All children aged 0 to 11 years and living in Sweden ($n=748,951$) were followed between January 1, 2000 and December 31, 2010. Data were analysed by multilevel logistic regression, with family- and individual-level characteristics at the first level and level of neighbourhood deprivation at the second level.

Results—During the study period, among a total of 748,951 children, 1499 (0.2 %) were hospitalised with CHD. Age-adjusted cumulative hospitalisation rates for CHD increased with increasing level of neighbourhood deprivation. In the study population, 1.8 per 1000 and 2.2 per 1000 children in the least and most deprived neighbourhoods, respectively, were hospitalised with CHD. The incidence of hospitalisation for CHD increased with increasing neighbourhood-level deprivation across all family and individual-level socio-demographic categories. The odds ratio (OR) for hospitalisation for CHD for those living in high-deprivation neighbourhoods versus those living in low-deprivation neighbourhoods was 1.23 (95 % confidence interval (CI)=1.04–1.46). In the full model, which took account for age, paternal and maternal individual-level socio-economic characteristics, comorbidities (e.g. maternal type 2 diabetes, OR=3.03; maternal hypertension, OR=2.01), and family history of CHD (OR=3.27), the odds of CHD were slightly attenuated but did not remain significant in the most deprived neighbourhoods (OR=1.20, 95 % CI=0.99–1.45, $p=0.057$).

Conclusions—This study is the largest so far on neighbourhood influences on CHD, and the results suggest that deprived neighbourhoods have higher rates of CHD, which represents

Correspondence to: Xinjun Li, xinjun.li@med.lu.se.

Electronic supplementary material The online version of this article (doi:10.1007/s12529-015-9488-9) contains supplementary material, which is available to authorized users.

Conflict of Interest Xinjun Li, Jan Sundquist, Tsuyoshi Hamano, Bengt Zöller, and Kristina Sundquist declare that they have no conflict of interest.

important clinical knowledge. However, the association does not seem to be independent of individual- and family-level characteristics.

Keywords

Congenital heart disease; Neighbourhood-level deprivation; Incidence; Socio-demographic factors; Multilevel modelling

Introduction

Congenital heart disease (CHD) is a major health risk in childhood [1–4], affecting 1 % of children. The prognosis varies depending on type and severity of the CHD. Although the specific mechanisms behind CHD are largely unknown, some of the known risk factors include familial history of CHD [5, 6], ethnicity and migration [7], maternal obesity [8], smoking [9, 10], diabetes [11, 12], hypertension [12], rubella infection and influenza during pregnancy [13], phenylketonuria (PKU) [14], and maternal occupational exposure [15]. There is also a growing body of evidence that suggests that individual-level socio-economic status (SES) is a risk factor for CHD [10, 16–20]. Low SES may influence the risk of CHD in multiple ways. For example, exposure to harmful agents may result from residential, lifestyle or occupational factors, all of which may be related to SES. These individual-level socio-demographic characteristics do not, however, fully explain the disparities of SES in CHD risk that exist between different population groups [19]. Efforts have therefore been made to study whether the socioeconomic environment (e.g. deprivation and social capital) is associated with the risk of CHD. Neighbourhood environments have been shown to be an important independent risk factor for many congenital health problems [21–28]. However, no previous studies have investigated whether neighbourhood deprivation is associated with CHD after accounting for family- and individual-level factors.

The present study had the following two aims: (1) to determine whether the relationship between neighbourhood deprivation and risk of hospitalisation for CHD remains significant after adjusting for family- and individual-level factors and (2) to examine possible cross-level interactions between individual-level factors and neighbourhood-level deprivation to determine whether neighbourhood-level deprivation has a differential effect on risk of CHD across subgroups of families and individuals (effect modification).

Methods

Data used in this study were retrieved from a national database that contains information on the entire population of Sweden for a period of 40 years. The dataset that we used contains nationwide information on parents and their offspring at the individual and neighbourhood levels, including comprehensive demographic and socio-economic data. The information comes from several Swedish national registers. The registers used in the present study were the Total Population Register, the Multi-Generation Register, the Hospital Discharge Register, and the Out-Patient Register. The Swedish nationwide population and health care registers have exceptionally high completeness and validity [29]. Individuals (children and their parents) were tracked using the personal identification numbers, which are assigned to each resident of Sweden. These identification numbers were replaced with serial numbers to

provide anonymity. The follow-up period ran from January 1, 2000 until hospitalisation/out-patient treatment for CHD, death, emigration or the end of the study period on December 31, 2010. In the study period, there were 1213 (0.16 %) children who died and 16006 (2.1 %) children who emigrated before the age of 11.

Outcome Variable: CHD

The outcome variable in this study was a hospital or outpatient diagnosis of CHD (age at diagnosis 0 to 11 years) during the study period. Data on in-patient and out-patient diagnoses of CHD were retrieved from the Hospital Discharge Register and Out-Patient Register, which include information on all hospital visits, including diagnoses. We searched these two registers for the International Classification of Diseases (ICD)-10 codes Q20–Q26, denoting CHD as the main diagnosis during the study period. The serial numbers were used to ensure that each individual appeared only once in the dataset, for his or her first diagnosis of CHD during the study period.

Neighbourhood-Level Deprivation

The home addresses of all Swedish individuals have been geocoded to small geographic units with boundaries defined by homogeneous types of buildings. These neighbourhood areas, called small-area market statistics or SAMS, each contain an average of 1000 residents and were created by the Swedish Government-owned statistics bureau Statistics Sweden. SAMS were used as proxies for neighbourhoods, as they were in previous research [30, 31]. Neighbourhood of residence is determined annually using the National Land Survey of Sweden register.

A summary index was calculated to characterise neighbourhood-level deprivation. The neighbourhood index was based on information about female and male residents aged 20 to 64 because this age group represents those who are among the most socio-economically active in the population (i.e. a population group that has a stronger impact on the socio-economic structure in the neighbourhood than children, younger women and men, and retirees do). The neighbourhood index was based on four items: low education level (<10 years of formal education), low income (income from all sources, including interest and dividends, that is <50 % of the median individual income), unemployment (excluding full-time students, those completing military service, and early retirees), and receipt of social welfare. The index of the year 2000 was used to categorise neighbourhood deprivation as low (more than one SD below the mean), moderate (within one SD of the mean), and high (more than one SD above the mean) [32].

Individual-Level Socio-demographic Variables

Sex of child: male or female.

Age ranged from 0 to 11 years and was divided into three categories: 0–4, 5–8, and 9–11 years.

Maternal marital status was categorised as (1) married/cohabitating or (2) never married, widowed, or divorced.

Family income was calculated as annual family income divided by the number of people in the family. The family income measure took into consideration the ages of the family members and used a weighted system whereby small children were given lower weights than adolescents and adults. The sum of all family members' incomes was multiplied by the individual's consumption weight divided by the family members' total consumption weight. The final variable was calculated as empirical quartiles from the distribution.

Maternal and paternal education levels were categorised as completion of compulsory school or less (< 9 years), practical high school or some theoretical high school (10–12 years) and completion of theoretical high school and/or college (>12 years).

Maternal and paternal country of birth was categorised as Sweden, European countries, and others.

Maternal urban/rural status: this variable was included because access to preventive antenatal care may vary according to urban/rural status. Mothers were classified as living in a large city, a middle-sized town, or a small town/rural area. Large cities were those with a population of >200,000 (Stockholm, Gothenburg and Malmö), middle-sized towns were towns with a population of >90,000 but <200,000, small towns were towns with a population of >27,000 and <90,000, and rural areas were areas with populations smaller than those of small towns. This classification yielded three equally sized groups.

Mobility: children were classified as length of time lived in neighbourhood, i.e. <5 years (moved) or ≥5 years (not moved).

Maternal age at childbirth was classified as <20, 20–24, 25–29, 30–34, 35–39, 40–44, and ≥45 years, and *paternal age at childbirth* was classified as <20, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, and ≥50 years.

Maternal and paternal hospitalisations were defined separately as the first diagnosis of the diseases in question from the Swedish Hospital Register during the follow-up period of as follows: (1) maternal type 2 diabetes (ICD-10 E11–E14), (2) maternal hypertension (ICD-10 I10–I15), (3) paternal chronic obstructive pulmonary disease (COPD) (ICD-10 J40–J49), and (4) maternal alcoholism and alcohol-related liver disease (ICD-10 F10 and K70).

Maternal smoking history was based on the mother's smoking history during pregnancy and divided into three groups: yes, no, and unknown.

Maternal body mass index (BMI) was calculated as $\text{weight(kg)}/\text{height}^2(\text{m}^2)$ and was defined as BMI<18.5, 18.5–24.9, 25.0–29.9, BMI ≥30, and unknown.

Parental occupation was divided into six categories: (1) farmers, (2) self-employed, (3) professionals, (4) white collar workers, (5) unskilled/skilled workers, and (6) others.

Because CHD is known to cluster in families, children were classified according to whether or not they had a *family history (parents or siblings) of CHD*.

During the study period, there were 141 mothers diagnosed with influenza and no mothers diagnosed with rubella during the pregnancy. There were seven cases of PKU during the study period. However, there were no associations between these factors and CHD, and they were therefore not included as covariates.

Statistical Analysis

The rate of hospitalisation for CHD was calculated for the total study population and for each subgroup after assessment of neighbourhood of residence for children. Multilevel (hierarchical) logistic regression models were used to estimate odds ratios (ORs) and 95 % confidence intervals (CIs). The analyses were performed using MLwiN version 2.27. First, a null model was calculated to determine the variance among neighbourhoods. Then, to determine the crude odds of CHD by level of neighbourhood deprivation, a neighbourhood model that included only neighbourhood-level deprivation was calculated. Next, a full model that included neighbourhood-level deprivation and sex, age and the family and individual-level variables, added simultaneously to the model, was calculated (Aim 1). Finally, a full model tested for cross-level interactions between the family- and individual-level socio-demographic variables and neighbourhood-level deprivation to determine whether the effects of neighbourhood-level deprivation on congenital incidence differed across the socio-demographic variables (Aim 2).

Random effects: the between-neighbourhood variance was estimated both with and without a random intercept. It was regarded to be significant if it was more than 1.96 times the size of the standard error, in accordance with the precedent set in previous studies [33–35].

For comparison, we also calculated Cox regression models and logistic regression models using the SAS statistical package (version 9.3; SAS Institute, Cary, NC, USA).

Ethical Considerations

This study was approved by the Ethics Committee at Lund University.

Results

In the total study population (748,951 children), 20, 62, and 18 % of children aged 0 to 11 years lived in low-, moderate- and high-deprivation neighbourhoods, respectively. During the follow-up period (January 1, 2000 to December 31, 2010), 1499 children (0.2 %) were diagnosed with CHD (Table 1). CHD cumulative rates increased from 1.8 per 1000 in neighbourhoods with low deprivation to 2.0 per 1000 in neighbourhoods with moderate deprivation and 2.2 per 1000 in neighbourhoods with high deprivation. A similar pattern of higher hospitalisation rates with increasing neighbourhood deprivation was observed across all family- and individual-level socio-demographic categories and comorbidities.

The OR for CHD for children living in high- versus low-deprivation neighbourhoods in the crude neighbourhood-level model was 1.23 (95 % CI = 1.04–1.46) (Table 2). Neighbourhood-level deprivation did not remain significantly associated with CHD odds after adjustment for age, sex, and the family- and individual-level socio-demographic variables (OR = 1.20, 95 % CI = 0.99–1.45, $p = 0.057$) for high-deprivation versus low-

deprivation neighbourhoods but for moderate-deprivation versus low-deprivation neighbourhoods (OR=1.17, 95 % CI=1.01–1.35). The OR of CHD was highest in children whose mothers had high BMI, mothers were hospitalised for type 2 diabetes or hypertension, those with advanced maternal age at childbirth, and those with a family history of CHD.

A test for cross-level interactions between the individual-level socio-demographic variables and neighbourhood-level deprivation in the context of odds of CHD showed no meaningful cross-level interactions or effect modification.

The between-neighbourhood variance (i.e. the random intercept) was more than 1.96 times the size of the standard error in all models, indicating that there were significant differences in CHD incidence between neighbourhoods after accounting for neighbourhood deprivation and the individual-level variables. Neighbourhood deprivation explained 7 % of the between-neighbourhood variance in the null model (see Table 2). After inclusion of the family- and individual-level variables, the explained variance was 31 %.

We performed an additional analysis using logistic regression models and the results were almost identical. In the full model, the OR for CHD was 1.20 (95 % CI=1.00–1.45) for children living in the most deprived neighbourhoods compared with those living in low-deprivation neighbourhoods (Supplementary Table 1). We also performed an analysis using Cox regression models. In the full model, the hazard ratio (HR) for CHD was 1.21 (95 % CI=1.00–1.46) among children living in the most deprived neighbourhoods compared with those living in low-deprivation neighbourhoods (Supplementary Table 2).

Discussion

We found that living in a high-deprivation neighbourhood increased the odds of CHD by 23 %. It is noteworthy that we found these results in a country with a comparatively strong system of universal health care and social welfare. Our finding that neighbourhood deprivation is associated with higher rates of CHD is consistent with the findings of a small number of previous studies [19]. However, few previous neighbourhood researchers have had access to data enabling them to use CHD as a specific outcome variable and the possibility to adjust for several family- and individual-level covariates. For example, the strongest associations with CHD were found for maternal diabetes type 2 and family history of CHD. Some of the family- and individual-level covariates may have acted as confounders or mediators in the associations between neighbourhood deprivation and CHD.

Level of neighbourhood deprivation may influence risk of CHD through a number of general mechanisms, including unfavourable health-related behaviours of women during pregnancy [36–38], neighbourhood social disintegration (i.e. criminality, high mobility or unemployment) [33], low social capital [31, 39, 40], and neighbourhood stress mediated by factors that can influence immunological and/or hormonal stress reactions [41–43]. Consistent with this hypothesis are the results of a US study, which found that neighbourhood socio-economic disparities were associated with adult CHD [44].

Living in deprived neighbourhoods can cause isolation from health-promoting milieus (e.g. safe places to exercise and decent housing) and services. In comparisons of wealthy nations, associations between neighbourhood characteristics and different health outcomes were inconsistent [45]. This implies that neighbourhood determinants of health are complex. Such determinants may include access to health care, education, and social services. Access to these services is uneven in the USA, where the effects of income inequalities on health are more pronounced [46]. For example, low income is associated with high risk of CHD [18, 19].

Neighbourhood-level inequities include unequal access to and quality of primary and secondary health care services [47]. In Sweden, medical care is provided to all permanent residents, and primary health care clinics and hospitals are equally distributed and located centrally in all types of neighbourhoods [47]. However, the actual number of health care professionals working in primary health care clinics can vary considerably by neighbourhood type. This is due to difficulties in recruiting and retaining health care personnel in high-deprivation neighbourhoods. The uneven distribution of medical personnel across neighbourhoods has also been documented in Canada, another country with universal health care [19].

It is possible that infections are more easily spread in high-deprivation neighbourhoods. In addition, rubella infection and influenza during pregnancy [13] have been reported to be associated with CHD. In Sweden, however, rubella is very uncommon and no child with rubella has been registered since 1985 [48].

The present study has several limitations. These include the possibility that some selective factors operate in the process of hospitalisation to favour certain children being hospitalised. Neither affordability of health care is a selective factor in Sweden nor is the likelihood of seeking medical advice important because of equal access to primary and hospital care [47]. It is, however, possible that residual confounding exists because socio-economic status cannot be fully measured by family income and education level. The Swedish Hospital Discharge Register contains no information about diagnostic procedures, which is a limitation, but any bias that this caused would be non-differential. However, with respect to CHD, the overall diagnostic validity of the Hospital Discharge Register is close to 90 % [49, 50].

The limitations of the study are countered by its strengths, which include as follows: (1) the ability to analyse data on a large national cohort of children aged 0 to 11 years, (2) the prospective design, (3) the completeness of the data (for example, only 1 % of the data on maternal education level and family income were missing), (4) the use of small, well-defined neighbourhoods with an average of 1000 residents, and (5) the ability to adjust for a set of family- and individual-level socio-demographic factors (e.g. age, sex, family income, maternal marital status, parental country of birth, parental education level, urban/rural status, mobility, parental age, maternal and paternal hospitalisation, and family history of CHD). Accounting for family income is particularly important as it is a major confounder that can affect an individual's choice of neighbourhood. Another strength is the possibility to

generalise our results to other populations (external validity), particularly to populations in industrialised societies.

Conclusions

This prospective nationwide study is the largest so far on neighbourhood influences on CHD, and the results suggest that deprived neighbourhoods have higher rates of CHD, which represents important clinical knowledge. However, the association does not seem to be independent of individual- and family-level characteristics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors wish to thank Science Editor Stephen Gilliver for his useful comments on the text. This work was supported by ALF funding from Region Skåne awarded to Jan Sundquist, Bengt Zöller and Kristina Sundquist; the Swedish Research Council (awarded to Kristina Sundquist); grants to Dr Bengt Zöller from the Swedish Heart-Lung Foundation and the Swedish Research Council. Research reported in this publication was also supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Number R01HL116381 to Kristina Sundquist. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The registers used in the present study are maintained by Statistics Sweden and the National Board of Health and Welfare.

References

1. Blue GM, Kirk EP, Sholler GF, Harvey RP, Winlaw DS. Congenital heart disease: current knowledge about causes and inheritance. *Med J Aust.* 2012; 197:155–9. [PubMed: 22860792]
2. Hoffman JI. Congenital heart disease: incidence and inheritance. *Pediatr Clin N Am.* 1990; 37:25–43.
3. Marino BS, Lipkin PH, Newburger JW, et al. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. *Circulation.* 2012; 126:1143–72. [PubMed: 22851541]
4. Rodan L, McCrindle BW, Manlhiot C, et al. Stroke recurrence in children with congenital heart disease. *Ann Neurol.* 2012; 72:103–11. [PubMed: 22829272]
5. Oyen N, Poulsen G, Wohlfahrt J, et al. Recurrence of discordant congenital heart defects in families. *Circ Cardiovasc Genet.* 2010; 3:122–8. [PubMed: 20173214]
6. Romano-Zelekha O, Hirsh R, Blieden L, Green M, Shohat T. The risk for congenital heart defects in offspring of individuals with congenital heart defects. *Clin Genet.* 2001; 59:325–9. [PubMed: 11359463]
7. Mangones T, Manhas A, Visintainer P, Hunter-Grant C, Brumberg HL. Prevalence of congenital cardiovascular malformations varies by race and ethnicity. *Int J Cardiol.* 2010; 143:317–22. [PubMed: 19345430]
8. Mills JL, Troendle J, Conley MR, Carter T, Druschel CM. Maternal obesity and congenital heart defects: a population-based study. *Am J Clin Nutr.* 2010; 91:1543–9. [PubMed: 20375192]
9. Alverson CJ, Strickland MJ, Gilboa SM, Correa A. Maternal smoking and congenital heart defects in the Baltimore-Washington Infant Study. *Pediatrics.* 2011; 127:e647–53. [PubMed: 21357347]
10. Hackshaw A, Rodeck C, Boniface S. Maternal smoking in pregnancy and birth defects: a systematic review based on 173 687 malformed cases and 11.7 million controls. *Hum Reprod Update.* 2011; 17:589–604. [PubMed: 21747128]

11. Macintosh MC, Fleming KM, Bailey JA, et al. Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study. *BMJ*. 2006; 333:177. [PubMed: 16782722]
12. Ul Haq F, Jalil F, Hashmi S, et al. Risk factors predisposing to congenital heart defects. *Ann Pediatr Cardiol*. 2011; 4:117–21. [PubMed: 21976868]
13. Levy HL, Guldberg P, Guttler F, et al. Congenital heart disease in maternal phenylketonuria: report from the Maternal PKU Collaborative Study. *Pediatr Res*. 2001; 49:636–42. [PubMed: 11328945]
14. Luteijn JM, Brown MJ, Dolk H. Influenza and congenital anomalies: a systematic review and meta-analysis. *Hum Reprod*. 2014; 29:809–23. [PubMed: 24365800]
15. Thulstrup AM, Bonde JP. Maternal occupational exposure and risk of specific birth defects. *Occup Med*. 2006; 56:532–43.
16. Gilboa SM, Desrosiers TA, Lawson C, et al. Association between maternal occupational exposure to organic solvents and congenital heart defects, National Birth Defects Prevention Study, 1997–2002. *Occup Environ Med*. 2012; 69:628–35. [PubMed: 22811060]
17. Langlois PH, Brender JD, Suarez L, et al. Maternal residential proximity to waste sites and industrial facilities and conotruncal heart defects in offspring. *Paediatr Perinat Epidemiol*. 2009; 23:321–31. [PubMed: 19523079]
18. Limbers CA, Emery K, Uzark K. Factors associated with perceived cognitive problems in children and adolescents with congenital heart disease. *J Clin Psychol Med Settings*. 2012; 10:1007/s10880-012-9326-z
19. Agha MM, Glazier RH, Moineddin R, Moore AM, Guttman A. Socioeconomic status and prevalence of congenital heart defects: does universal access to health care system eliminate the gap? *Birth Defects Res A Clin Mol Teratol*. 2011; 91:1011–8. [PubMed: 22002854]
20. Gorini F, Chiappa E, Gargani L, Picano E. Potential effects of environmental chemical contamination in congenital heart disease. *Pediatr Cardiol*. 2014; 35:559–568. [PubMed: 24452958]
21. Hart D, Atkins R, Matsuba MK. The association of neighborhood poverty with personality change in childhood. *J Pers Soc Psychol*. 2008; 94:1048–61. [PubMed: 18505317]
22. Singh GK, Kogan MD, van Dyck PC. A multilevel analysis of state and regional disparities in childhood and adolescent obesity in the United States. *J Community Health*. 2008; 33:90–102. [PubMed: 18049885]
23. Navalpotro L, Regidor E, Ortega P, et al. Area-based socioeconomic environment, obesity risk behaviours, area facilities and childhood overweight and obesity: socioeconomic environment and childhood overweight. *Prev Med*. 2012; 55:102–7. [PubMed: 22634427]
24. Kroll ME, Stiller CA, Murphy MF, Carpenter LM. Childhood leukaemia and socioeconomic status in England and Wales 1976–2005: evidence of higher incidence in relatively affluent communities persists over time. *Br J Cancer*. 2011; 105:1783–7. [PubMed: 22027710]
25. Shih M, Dumke K, Goran MI, Simon P. The association between community-level economic hardship and childhood obesity prevalence in Los Angeles. *Pediatr Obes*. 2012; 8:411–7. [PubMed: 23239616]
26. Bammann K, Gwozdz W, Lanfer A, et al. Socioeconomic factors and childhood overweight in Europe: results from the multi-centre IDEFICS study. *Pediatr Obes*. 2013; 8:1–12. [PubMed: 22888012]
27. El-Sayed AM, Scarborough P, Galea S. Socioeconomic inequalities in childhood obesity in the United Kingdom: a systematic review of the literature. *Obes Facts*. 2012; 5:671–92. [PubMed: 23108336]
28. Grigsby-Toussaint DS, Lipton R, Chavez N, et al. Neighborhood socioeconomic change and diabetes risk: findings from the Chicago childhood diabetes registry. *Diabetes Care*. 2010; 33:1065–8. [PubMed: 20150301]
29. Rosen, M.; Hakulinen, T. Use of disease registers. In: Ahrens, W.; Pigeot, I., editors. *Handbook of epidemiology*. Berlin: Springer-Verlag; 2005. p. 232–51.
30. Cubbin C, Sundquist K, Ahlen H, et al. Neighborhood deprivation and cardiovascular disease risk factors: protective and harmful effects. *Scand J Public Health*. 2006; 34:228–37. [PubMed: 16754580]

31. Sundquist J, Johansson SE, Yang M, Sundquist K. Low linking social capital as a predictor of coronary heart disease in Sweden: a cohort study of 2.8 million people. *Soc Sci Med.* 2006; 62:954–63. [PubMed: 16081195]
32. Winkleby M, Sundquist K, Cubbin C. Inequities in CHD incidence and case fatality by neighborhood deprivation. *Am J Prev Med.* 2007; 32:97–106. [PubMed: 17234484]
33. Sundquist K, Theobald H, Yang M, et al. Neighborhood violent crime and unemployment increase the risk of coronary heart disease: a multilevel study in an urban setting. *Soc Sci Med.* 2006; 62:2061–71. [PubMed: 16203075]
34. Johnell K, Lindstrom M, Melander A, et al. Anxiolytic-hypnotic drug use associated with trust, social participation, and the miniaturization of community: a multilevel analysis. *Soc Sci Med.* 2006; 62:1205–14. [PubMed: 16115711]
35. Johnell K, Lindstrom M, Sundquist J, Eriksson C, Merlo J. Individual characteristics, area social participation, and primary non-concordance with medication: a multilevel analysis. *BMC Public Health.* 2006; 6:52. [PubMed: 16512907]
36. Lee LJ, Lupo PJ. Maternal smoking during pregnancy and the risk of congenital heart defects in offspring: a systematic review and metaanalysis. *Pediatr Cardiol.* 2012; 34:398–407. [PubMed: 22886364]
37. Lupo PJ, Symanski E, Langlois PH, et al. Maternal occupational exposure to polycyclic aromatic hydrocarbons and congenital heart defects among offspring in the national birth defects prevention study. *Birth Defects Res A Clin Mol Teratol.* 2012; 94:875–81. [PubMed: 22945317]
38. Franklin WJ, Gandhi M. Congenital heart disease in pregnancy. *Cardiol Clin.* 2012; 30:383–94. [PubMed: 22813364]
39. Lofors J, Sundquist K. Low-linking social capital as a predictor of mental disorders: a cohort study of 4.5 million Swedes. *Soc Sci Med.* 2007; 64:21–34. [PubMed: 17011689]
40. Sundquist K, Yang M. Linking social capital and self-rated health: a multilevel analysis of 11,175 men and women in Sweden. *Health Place.* 2007; 13:324–34. [PubMed: 16584907]
41. Daniel M, Moore S, Kestens Y. Framing the biosocial pathways underlying associations between place and cardiometabolic disease. *Health Place.* 2008; 14:117–32. [PubMed: 17590377]
42. Brosschot JF, Benschop RJ, Godaert GL, et al. Influence of life stress on immunological reactivity to mild psychological stress. *Psychosom Med.* 1994; 56:216–24. [PubMed: 8084967]
43. McEwen BS, Biron CA, Brunson KW, et al. The role of adrenocorticoids as modulators of immune function in health and disease: neural, endocrine and immune interactions. *Brain Res Brain Res Rev.* 1997; 23:79–133. [PubMed: 9063588]
44. Diller GP, Inuzuka R, Kempny A, et al. Detrimental impact of socioeconomic status on exercise capacity in adults with congenital heart disease. *Int J Cardiol.* 2011; 165:80–6. [PubMed: 21868115]
45. Lynch J, Smith GD, Hillemeier M, et al. Income inequality, the psychosocial environment, and health: comparisons of wealthy nations. *Lancet.* 2001; 358:194–200. [PubMed: 11476836]
46. Lochner K, Pamuk E, Makuc D, Kennedy BP, Kawachi I. State-level income inequality and individual mortality risk: a prospective, multilevel study. *Am J Public Health.* 2001; 91:385–91. [PubMed: 11236402]
47. van Doorslaer E, Wagstaff A, Bleichrodt H, et al. Income-related inequalities in health: some international comparisons. *J Health Econ.* 1997; 16:93–112. [PubMed: 10167346]
48. Bottiger M, Forsgren M. Twenty years' experience of rubella vaccination in Sweden: 10 years of selective vaccination (of 12-year-old girls and of women postpartum) and 13 years of a general two-dose vaccination. *Vaccine.* 1997; 15:1538–44. [PubMed: 9330465]
49. Ludvigsson JF, Andersson E, Ekblom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health.* 2011; 11:450. [PubMed: 21658213]
50. Centre for Epidemiology. Validity of the diagnoses from the Swedish In-Care Register 1987 and 1995 Swedish. Stockholm: The National Board of Health and Welfare; 2000.

Distribution of population, number of congenital heart disease (CHD) events, and age-standardised incidence (per 1000) by neighbourhood-level deprivation

Table 1

	Population distribution		CHD events		Neighbourhood deprivation		
	No.	%	No.	%	Low	Moderate	High
Total population (%)	748,951				148,871 (20 %)	464,075 (62 %)	136,005 (18 %)
Total number of CHD events			1499		1.8	2.0	2.2
Gender							
Males	384,376	51.3	807	53.8	1.8	2.4	2.4
Females	364,575	48.7	692	46.2	1.8	2.0	2.0
Age (years)							
0–4	261,589	34.9	805	53.7	2.8	3.2	3.1
5–8	265,903	35.5	404	27.0	1.2	1.5	1.9
9–11	221,459	29.6	290	19.3	1.2	1.3	1.4
Family income							
Low income	188,108	25.1	375	25.0	1.8	1.9	2.1
Middle–low income	187,488	25.0	382	25.5	1.7	2.2	2.2
Middle–high income	186,308	24.9	330	22.0	1.8	1.7	2.1
High income	187,047	25.0	412	27.5	1.8	2.3	2.7
Marital status							
Married/Cohabiting	422,188	56.4	808	53.9	1.7	2.0	2.2
Never married, widowed, or divorced	326,763	43.6	691	46.1	1.9	2.0	2.2
Maternal country of birth							
Sweden	645,287	86.2	1283	85.6	1.8	2.0	2.3
European countries	45,240	6.0	90	6.0	2.1	2.2	1.7
Other countries	58,424	7.8	126	8.4	1.6	1.8	2.3
Paternal country of birth							
Sweden	644,169	86.0	1268	84.6	1.7	2.0	2.2
European countries	49,170	6.6	98	6.5	2.0	2.3	1.7
Other countries	55,612	7.4	133	8.9	2.4	2.0	2.5
Maternal educational attainment							

	Population distribution		CHD events		Neighbourhood deprivation		
	No.	%	No.	%	Low	Moderate	High
9 years	242,702	32.4	564	37.6	2.0	2.1	2.2
10–12 years	278,492	37.2	494	33.0	1.6	1.9	2.2
>12 years	227,757	30.4	441	29.4	1.8	2.0	2.4
Paternal educational attainment							
9 years	246,843	33.0	547	36.5	2.0	2.2	2.2
10–12 years	288,912	38.6	541	36.1	1.7	1.9	2.3
>12 years	213,196	28.5	411	27.4	1.7	2.0	2.4
Urban/Rural status							
Large cities	225,046	30.0	481	32.1	1.8	2.2	2.3
Middle-sized towns	299,847	40.0	576	38.4	1.8	1.9	2.0
Small towns/rural areas	224,058	29.9	442	29.5	1.6	2.0	2.3
Mobility							
Not moved	429,024	57.3	733	48.9	1.8	1.8	2.1
Moved	319,927	42.7	766	51.1	1.6	2.3	2.3
Maternal age at child birth							
<30	421,981	56.3	802	53.5	1.6	2.0	2.0
30–39	308,621	41.2	643	42.9	1.8	1.9	2.5
40	18,349	2.4	54	3.6	3.4	2.6	2.8
Paternal age at child birth							
<30	282,860	37.8	520	34.7	1.5	1.9	2.1
30–39	386,357	51.6	803	53.6	1.8	2.1	2.1
40	79,734	10.6	176	11.7	2.2	1.9	2.6
Maternal occupation							
Farmers	1249	0.2	3	0.2	0.0	1.6	4.7
Self-employed	7260	1.0	8	0.5	1.6	0.8	3.4
Professionals	28,769	3.8	66	4.4	2.0	2.6	6.7
White collar workers	177,987	23.8	311	20.7	1.7	1.9	2.1
Unskilled/Skilled workers	270,017	36.1	497	33.2	1.8	1.9	2.1
Others	263,669	35.2	614	41.0	1.7	2.2	2.3
Paternal occupation							

	Population distribution		CHD events		Neighbourhood deprivation		
	No.	%	No.	%	Low	Moderate	High
Farmers	7168	1.0	13	0.9	2.6	1.8	1.6
Self-employed	22,336	3.0	31	2.1	2.2	1.2	1.9
Professionals	52,296	7.0	94	6.3	2.1	1.9	1.7
White collar workers	131,952	17.6	221	14.7	1.5	1.8	2.9
Unskilled/Skilled workers	338,277	45.2	654	43.6	1.6	2.0	2.0
Others	196,922	26.3	486	32.4	2.0	2.3	2.3
Maternal smoking history							
Yes	138,922	18.5	239	15.9	1.4	1.9	1.9
No	545,998	72.9	1089	72.6	1.7	1.9	2.3
Unknown	64,031	8.5	171	11.4	2.8	3.1	2.2
Maternal BMI							
<18.5	11,594	1.5	20	1.3	1.8	1.0	1.4
18.5–24.9	270,731	36.1	548	36.6	1.3	1.4	1.6
25.0–29.9	93,812	12.5	218	14.5	1.0	1.6	2.1
30	42,805	5.7	133	8.9	2.3	2.8	2.4
Unknown	330,009	44.1	580	38.7	2.3	2.5	2.1
Maternal hospitalisation for alcoholism and alcohol-related diseases							
No	742,097	99.1	1489	99.3	1.8	2.0	2.2
Yes	6854	0.9	10	0.7	1.6	1.8	1.2
Maternal hospitalisation for type 2 diabetes							
No	745,039	99.5	1472	98.2	1.8	2.0	2.1
Yes	3912	0.5	27	1.8	8.7	5.3	9.3
Maternal hospitalisation for hypertension							
No	741,488	99.0	1470	98.1	1.7	2.0	2.2
Yes	7463	1.0	29	1.9	4.9	4.3	5.7
Paternal hospitalisation for chronic lower respiratory disease							
No	743,902	99.3	1490	99.4	1.8	2.0	2.2
Yes	5049	0.7	9	0.6	1.3	2.4	1.0
Family history of congenital heart disease							
No	745,262	99.5	1471	98.1	1.7	2.0	2.1

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Yes	Population distribution		CHD events		Neighbourhood deprivation		
	No.	%	No.	%	Low	Moderate	High
	3689	0.5	28	1.9	8.8	4.7	11.0

Table 2

Odds ratios (OR) and 95 % confidence intervals (CI) for congenital heart disease

	Model 1		Model 2		Model 3		p value			
	OR	95 % CI	OR	95 % CI	OR	95 % CI				
Neighbourhood-level variable (ref. low)										
Moderate	1.13	0.98	1.30	1.13	0.98	1.30	1.17	1.01	1.35	0.036
High	1.23	1.04	1.46	1.19	1.00	1.41	1.20	0.99	1.45	0.057
Age				0.88	0.86	0.89	0.87	0.85	0.88	<0.001
Gender to males (ref. females)				1.11	1.00	1.22	1.11	1.00	1.22	0.057
Family income (ref. high income)										
Middle-high income							0.82	0.71	0.96	0.012
Middle-low income							0.95	0.82	1.10	0.484
Low income							0.83	0.71	0.98	0.021
Marital status (ref. married/cohabiting)										
Never married, widowed, or divorced							1.01	0.91	1.13	0.842
Maternal country of birth (ref. born in Sweden)										
European countries							0.96	0.75	1.24	0.764
Others							0.79	0.61	1.03	0.089
Paternal country of birth (ref. born in Sweden)										
European countries							0.93	0.73	1.18	0.549
Others							1.17	0.91	1.51	0.230
Maternal education attainment (ref. >12 years)										
9 years							0.99	0.83	1.17	0.889
10–12 years							0.96	0.83	1.12	0.617
Paternal education attainment (ref. >12 years)										
9 years							1.01	0.85	1.18	0.920
10–12 years							0.97	0.83	1.13	0.689
Urban/Rural status (ref. large cities)										
Middle-sized towns							0.91	0.81	1.04	0.162
Small towns/rural areas							0.90	0.79	1.03	0.134
Mobility (ref. not moved)							1.06	0.95	1.19	0.271

	Model 1		Model 2		Model 3		p value
	OR	95 % CI	OR	95 % CI	OR	95 % CI	
Maternal age at child birth (ref. <30 years)							
30–39					0.98	0.86 1.11	0.764
40					1.31	0.96 1.78	0.089
Paternal age at child birth (ref. <30 years)							
30–39					1.07	0.94 1.22	0.317
40					1.06	0.86 1.30	0.549
Maternal socio-economic status (ref. professionals)							
Farmers					1.26	0.37 4.25	0.689
Self-employed					0.53	0.25 1.12	0.089
White collar workers					0.76	0.58 1.00	0.057
Blue collar workers					0.78	0.58 1.04	0.089
Others					0.80	0.59 1.07	0.134
Paternal socio-economic status (ref. professionals)							
Farmers					1.06	0.57 1.96	0.842
Self-employed					0.88	0.57 1.34	0.549
White collar workers					0.95	0.74 1.22	0.689
Blue collar workers					1.09	0.84 1.40	0.549
Others					1.10	0.85 1.43	0.484
Maternal smoking history (ref. no)							
Yes					0.95	0.82 1.10	0.484
Unknown					1.23	1.03 1.47	0.021
Maternal BMI (ref. 18.5–24.9)							
Unknown					1.40	1.21 1.60	<0.001
<18.5					0.88	0.56 1.38	0.617
25.0–29.9					1.08	0.92 1.27	0.317
30					1.38	1.14 1.67	0.003
Maternal hospitalisation for alcoholism and alcohol-related diseases (ref. no)					0.74	0.39 1.38	0.368
Maternal hospitalisation for type 2 diabetes (ref. no)					3.03	2.05 4.47	<0.001
Maternal hospitalisation for hypertension (ref. no)					2.01	1.38 2.93	<0.001
Paternal hospitalisation for chronic lower respiratory disease (ref. no)					0.91	0.47 1.76	0.764

	Model 1		Model 2		Model 3		p value
	OR	95 % CI	OR	95 % CI	OR	95 % CI	
Family history of congenital heart disease (ref. without family history)					3.27	2.23 4.80	<0.001
Variance (S.E.)	0.103 (0.054)		0.097(0.054)		0.077 (0.053)		
Explained variance (%)	7		13		31		

Model 1, crude model; model 2, adjusted for age and gender; model 3, full model