BMJ Open

Sibling rank and sibling number in relation to cardiovascular disease and mortality risk: a nationwide cohort study

Peter M Nilsson ,[1] Jan Sundquist,[2] Kristina Sundquist,[2] Xinjun Li[2]

To cite: Nilsson PM, Sundquist J, Sundquist K, *et al*. Sibling rank and sibling number in relation to cardiovascular disease and mortality risk: a nationwide cohort study. *BMJ Open* 2021;**11**:e042881. doi:10.1136/bmjopen-2020-042881

► Prepublication history and supplemental material for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-042881).

Received 28 July 2020
Revised 11 April 2021
Accepted 12 April 2021

Check for updates

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY. Published by BMJ.

[1]Clinical Sciences, Lund University, Malmö, Sweden
[2]Center for Primary Health Care Research, Lund University, Malmö, Sweden

Correspondence to
Professor Peter M Nilsson; Peter.Nilsson@med.lu.se

ABSTRACT

Background The number and rank order of siblings could be of importance for risk of cardiovascular disease and mortality. Previous studies have used only fatal events for risk prediction. We, therefore, aimed to use also non-fatal coronary and cardiovascular events in fully adjusted models.

Methods From the Multiple-Generation Register in Sweden, data were used from 1.36 million men and 1.32 million women (born 1932–1960), aged 30–58 years at baseline and with follow-up from 1990 to 2015. Mean age at follow-up was 67 years (range 55–83 years). Fatal and non-fatal events were retrieved from national registers.

Results Compared with men with no siblings, those with 1–2 siblings had a lower, and those with four or more siblings had a higher adjusted risk of cardiovascular events. Again, compared with men with no siblings, those with more than one sibling had a lower total mortality risk, and those with three or more siblings had an increased risk of coronary events.

Correspondingly, compared with women with no siblings those women with three siblings or more had an increased risk of cardiovascular events, and those with two siblings or more had an increased risk of coronary events. Women with one sibling or more were at lower total mortality risk, following full adjustment.

Conclusion Being first born is associated with a favourable effect on non-fatal cardiovascular and coronary events for both men and women. The underlying biological mechanisms for this should be studied in a sociocultural context.

Strengths and limitations of this study

- ► This national register linkage study across generations includes data on both fatal and, for the first time, non-fatal cardiovascular and coronary events, as well as total mortality in relation to sibling number and rank.
- ► Adjustment has been made for confounders including markers of social background (educational level, occupation) of the individual, but not for parental socioeconomic status. Competing risk analyses have been applied.
- ► Limitations of the study include the lack of data from primary healthcare visits and that the historical register data do not fully reflect the ethnical diversity of Sweden today.

INTRODUCTION

A positive family history of disease is a well-established variable to be used in risk algorithms for cardiovascular disease (CVD), even if it may be hard to quantify based on subjective recall only.[1 2] An alternative is to use register-based data for a more objective appraisal of the family burden of CVD.[3] One special feature of family structure is the number of siblings and sibling rank that can also be mapped by use of national registers such as the Multiple-Generation Register (MGR) of Sweden.[4] So far this register has been mostly used to describe the risk of some selected CVD manifestations of individuals in relation to the risk of their siblings, for example, for thromboembolic disease[5] or other diseases.[6–9]

In a previous report based on the MGR, it was shown that increased number of sibling reflecting family size was not associated with increased total and cause-specific mortality risk in ages 40–74 years, but no analyses were made for risk of non-fatal CVD or coronary disease.[10] However, another corresponding study based on MGR data could show that total and cause-specific mortality in ages 30–69 years increased with increasing birth order.[11]

The influence of sibling rank has been less well studied in relation to non-fatal cardiovascular and coronary risk. Previous studies have indicated a worse cardiovascular risk factor burden in first borns, for example, increased body mass index (BMI) and systolic blood pressure, but lower insulin sensitivity, than later born siblings.[12–16] On the other hand, first borns seem to have a better physical fitness at military conscript testing,[17] less

BMJ Open: first published as 10.1136/bmjopen-2020-042881 on 25 May 2021. Downloaded from http://bmjopen.bmj.com/ on March 13, 2024 by guest. Protected by copyright.

caries[18] and run a lower risk of leukaemia in adolescence[19] as well as lower suicide risk in a Finnish population.[20]

Against this background we aimed to analyse the influence of sibling number and rank on risk of non-fatal and fatal cardiovascular and coronary manifestations, as well as total mortality, in the MGR of Sweden, after extensive adjustment for background demographic factors and family social status.

SUBJECTS AND METHODS

Setting and participants

The dataset used in this study was constructed by linking several national Swedish registers. The Swedish government-owned Statistics Sweden provided the MGR, in which persons born in Sweden in or after 1932 (the present study population) are linked to their parents.[4] We included all births (multiple births, full and half siblings) in the analyses. Linkages were made to National Census data in order to ascertain individual-level socioeconomic status. The final link was made by adding data from the Swedish Cause of Death Register (1961–2015) and the Swedish Hospital Discharge Register, with recorded dates of hospitalisation and hospital diagnoses since 1964, but on a national level since 1987 and now until end of 2015. National Swedish registers are of high validity for medical research.[21 22] For analysing risk of CVD, coronary heart disease (CHD) and mortality in relation to number of siblings and birth order, we collected data from 1.36 million men and 1.32 million women (born 1932–1960), aged 30–58 years at baseline and with follow-up from 1990 to 2015. For the definition of study subjects based on the MGR (see online supplemental figure S1).

Patient and public involvement

No patient involved.

Follow-up of CVD events and total mortality

We used the following International Classification of Disease (ICD)-codes for fatal or non-fatal CVD (ICD-9, 390–459, ICD-10, I00-I99); and for CHD (ICD-9, 410–414, ICD-10, I20-I25). Non-fatal events were followed in the national Hospital Discharge Register, and fatal events and total mortality until 31 December 2015 in the national Mortality Register.

Definitions

Family income: family income was calculated at start of follow-up (1990) as annual family income divided by the number of members in the family, as previously reported.[23] The income calculation was weighted, taking the ages of the family members into account. For example, children were given lower consumption weights than adults. The calculation was performed as follows: 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 and classified as low, middle-low, middle-high and high.

Immigration status: born in Sweden or in other countries.

Marital status: individuals were classified as married/cohabitating or never married, widowed or divorced.

Socioeconomic status (SES): was divided into four categories: the self-employed/farmers/all others, blue collar workers, white collar workers or professionals, as previously reported.[24]

Education: was based on educational level, which was classified into three categories: ≤9 years, 10–11 years and ≥12 years.

Geographical region: was divided into large cities (cities with a population of more than 200 000 inhabitants), Southern Sweden and Northern Sweden.[24]

Comorbidity: was defined as the first hospitalisation during the follow-up period of: chronic obstructive pulmonary disease, Chronic Obstructive Pulmonary Disease (COPD) (both hospitalisation and mortality were included) (ICD-9 490–496 and ICD-10 J40-J49), obesity (ICD-9 278A and ICD-10 E65-E68), alcoholism-related liver disease (both hospitalisations and mortality were included) (ICD-9 291, 303, 571 and ICD-10 F10 and K70), hypertension (ICD-9 401–405 and ICD-10 I10–I15), and diabetes (both hospitalisations and mortality were included) (ICD-9 250 and ICD-10 E10-E14) and cancer (cancer were included both from cancer register and mortality, ICD-9 140–239 and ICD-10 C00-D48).

Statistical methods

Person-years at risk were calculated from the start of follow-up on 1 January 1990 until hospitalisation or death from CVD, death from other causes, emigration or the end of the follow-up, 31 December 2015. Age-adjusted incidence rates for first hospitalisation and mortality were calculated for the entire follow-up period. We used the Cox's proportional hazard model to calculate the HR with 95% CIs for total (fatal and non-fatal) CVD and CHD event risk, and for total mortality, for both men and women) in relation to number siblings and birth order. This was done after adjustment for age at start, individual characteristics (family income, marital status, immigrant background and educational level, region of residence, socioeconomic status) and finally for comorbidities in order to adjust for competing mortality risk. Individuals without sibling was used as the reference. The proportionality assumptions were checked by plotting the incidence rates over time and by calculating Schoenfeld (partial) residuals and these assumptions were fulfilled. We used SAS V.9.4 (SAS Institute) for all statistical analyses.

A further adjustment was made for total number of siblings in relation to birth order when the risk for different outcomes was calculated, using the category 'first birth' as reference. A competing risk model used for mortality as a competing risk for incident CVD. A $p<0.05$ was considered significant.

BMJ Open: first published as 10.1136/bmjopen-2020-042881 on 25 May 2021. Downloaded from http://bmjopen.bmj.com/ on March 13, 2024 by guest. Protected by copyright.

Table 1 Distribution of population, number of CVD, CHD and mortality events

	Population		CVD events		CHD events		Mortality events	
	No	(%)	No (% of population)	%	No (% of population)	%	No (% of population)	%
Men	1 358 647		592 863 (43.6)		131 533 (9.7)		240 371 (17.7)	
No of sibling								
Non-sibling	214 700	15.8	105 516 (49.1)	17.8	23 671 (11.0)	18	50 709 (23.6)	21.1
One sibling	443 877	32.7	189 839 (42.8)	32	39 729 (9.0)	30.2	73 140 (16.5)	30.4
Two siblings	338 812	24.9	140 361 (41.4)	23.7	30 184 (8.9)	22.9	52 790 (15.6)	22
Three siblings	183 067	13.5	77 378 (42.3)	13.1	17 663 (9.6)	13.4	30 266 (16.5)	12.6
Four or more siblings	178 191	13.1	79 769 (44.8)	13.5	20 286 (11.4)	15.4	33 466 (18.8)	13.9
Birth order								
First	684 765	50.4	318 341 (46.5)	53.7	70 238 (10.3)	53.4	140 857 (20.6)	58.6
Second	402 879	29.7	166 757 (41.4)	28.1	36 654 (9.1)	27.9	62 267 (15.5)	25.9
Third	164 540	12.1	65 853 (40.0)	11.1	14 736 (9.0)	11.2	23 081 (14.0)	9.6
Fourth	62 765	4.6	24 729 (39.4)	4.2	5737 (9.1)	4.4	8425 (13.4)	3.5
Fifth+	43 698	3.2	17 183 (39.3)	2.9	4168 (9.5)	3.2	5741 (13.1)	2.4
Women	1 315 037		486 147 (37.0)		55 933 (4.3)		160 269 (12.2)	
No of sibling								
Non-sibling	210 121	16	87 261 (41.5)	17.9	10 289 (4.9)	18.4	34 521 (16.4)	21.5
One sibling	430 315	32.7	154 154 (35.8)	31.7	16 280 (3.8)	29.1	49 132 (11.4)	30.7
Two siblings	324 379	24.7	113 739 (35.1)	23.4	12 500 (3.9)	22.3	34 843 (10.7)	21.7
Three siblings	176 631	13.4	63 871 (36.2)	13.1	7512 (4.3)	13.4	19 766 (11.2)	12.3
Four or more siblings	173 591	13.2	67 122 (38.7)	13.8	9352 (5.4)	16.7	22 007 (12.7)	13.7
Birth order								
First	664 459	50.5	262 015 (39.4)	53.9	30 342 (4.6)	54.2	94 779 (14.3)	59.1
Second	388 391	29.5	136 263 (35.1)	28	15 191 (3.9)	27.2	40 984 (10.6)	25.6
Third	159 311	12.1	53 711 (33.7)	11	6231 (3.9)	11.1	15 205 (9.5)	9.5
Fourth	60 676	4.6	20 264 (33.4)	4.2	2379 (3.9)	4.3	5558 (9.2)	3.5
Fifth+	42 200	3.2	13 894 (32.9)	2.9	1790 (4.2)	3.2	3743 (8.9)	2.3

CHD, coronary heart disease; CVD, cardiovascular disease.

RESULTS

With an average of 20 years (Q1–Q3 16–25 years) follow-up, in 1 358 647 men we used data on 592 863 CVD events, 131 533 coronary events and 240 371 total deaths. For 1 315 037 women, the corresponding numbers were 486 147 CVD events, 55 933 coronary events and 160 269 deaths, respectively. The mean age of the study population at the end of the follow-up was 67 years (range 55–83 years). The number of siblings and birth order of men and women are depicted in table 1.

Risk associated with number of siblings in men and women

Compared with men with no siblings, those with 1–2 siblings had a lower, and those with four or more siblings had a higher risk of cardiovascular events. Again, compared with men with no siblings, those with more than one sibling had a lower total mortality risk, and those with three or more siblings had an increased risk of coronary events, following full adjustment(table 2).

Correspondingly, compared with women with no siblings those women with three siblings or more had an increased risk of cardiovascular events, and those with two siblings or more had an increased risk of coronary events. Women with one sibling or more were at lower total mortality risk, following full adjustment, table 3.

Risk associated with sibling rank in men and women

According to sibling rank, first-born men had a lower risk of both cardiovascular and coronary events than their later-born siblings, but higher total mortality than second and third-born siblings, following full adjustment (table 2).

For first-born women the risks of cardiovascular and coronary events were also lower than in their later-born siblings. The mortality risk was higher than for second-born siblings, but equal to higher numbered siblings, following full adjustment (table 3).

BMJ Open: first published as 10.1136/bmjopen-2020-042881 on 25 May 2021. Downloaded from http://bmjopen.bmj.com/ on March 13, 2024 by guest. Protected by copyright.

Table 2 HR and 95% CI of CVD, CHD and mortality in men

	CVD		CHD		Mortality	
	HR*†	95% CI	HR*	95% CI	HR*	95% CI
No of siblings (ref. Non sibling)						
One sibling	0.98	0.97 to 0.99	0.99	0.97 to 1.01	0.93	0.92 to 0.94
Two siblings	0.97	0.97 to 0.98	1.01	0.99 to 1.03	0.91	0.9 to 0.92
Three siblings	0.98	0.97 to 0.99	1.04	1.02 to 1.07	0.93	0.92 to 0.94
Four or more siblings	1	0.99 to 1.01	1.1	1.07 to 1.12	0.96	0.94 to 0.97
Birth order (ref. first birth)						
Second	1	1 to 1.01	1.08	1.06 to 1.09	0.96	0.95 to 0.97
Third	1.02	1.02 to 1.03	1.13	1.11 to 1.15	0.98	0.96 to 0.99
Fourth	1.04	1.02 to 1.05	1.17	1.14 to 1.21	0.98	0.95 to 1
Fifth+	1.07	1.05 to 1.09	1.23	1.19 to 1.28	1.01	0.98 to 1.05

*Full adjusted model: Adjusted for age at start, individual characteristics of family income, marital status, educational attainment, immigrant status, socioeconomic status, region of residence, comorbidities, number of siblings and birth order.
†Multivariable competing risk survival analysis.
CHD, coronary heart disease; CVD, cardiovascular disease.

For HRs of CHD, CVD and total mortality by number of siblings and birth order in men and women, respectively (see figures 1–3).

Supplemental material

For detailed data on the distribution of the study population, number of CVD, CHD and mortality events in men and women (see online supplemental table S1). For detailed data on the risk associated with factors adjusted (see online supplemental tables S2–S4), for men and women, respectively.

DISCUSSION

In this very large observational study based on a national MGR, it was found that first-born men and women are at lower risk of both cardiovascular and coronary events than their later-born siblings, but had higher total mortality risk than second and third-born siblings (men). For women the mortality risk for first-born women was higher than for second-born siblings, following full adjustment for a number of background factors.

For total mortality in relation to sibling number our data are at odds with a previous study using the same register in Sweden, showing no increased mortality associated until 74 years with a higher number of siblings.[10] However, we used higher numbers, longer follow-up and more extensive adjustment.

For the influence of sibling rank, a previous study could show higher risk of total and cause-specific mortality with increasing sibling rank until 69 years.[11] This was similar in

Table 3 HR and 95% CI of CVD, CHD and mortality in women

	CVD		CHD		Mortality	
	HR*†	95% CI	HR*	95% CI	HR*	95% CI
No of siblings (ref. non-sibling)						
One sibling	0.98	0.98 to 0.99	0.99	0.97 to 1.02	0.94	0.93 to 0.95
Two siblings	0.99	0.98 to 1	1.03	1 to 1.06	0.92	0.91 to 0.94
Three siblings	1	0.99 to 1.01	1.07	1.04 to 1.11	0.93	0.91 to 0.95
Four or more siblings	1.01	1 to 1.03	1.17	1.13 to 1.21	0.95	0.93 to 0.96
Birth order (ref. first birth)						
Second	1.01	1 to 1.02	1.07	1.05 to 1.09	0.96	0.95 to 0.98
Third	1.02	1.01 to 1.03	1.14	1.11 to 1.18	0.98	0.96 to 1
Fourth	1.04	1.02 to 1.05	1.14	1.09 to 1.2	1	0.98 to 1.03
Fifth+	1.05	1.03 to 1.07	1.22	1.15 to 1.29	1.03	0.99 to 1.07

*Full adjusted model: Adjusted for age at start, individual characteristics of family income, marital status, educational attainment, immigrant status, socioeconomic status, region of residence, comorbidities, number of siblings, and birth order.
†Multivariable competing risk survival analysis.
CHD, coronary heart disease; CVD, cardiovascular disease.

BMJ Open: first published as 10.1136/bmjopen-2020-042881 on 25 May 2021. Downloaded from http://bmjopen.bmj.com/ on March 13, 2024 by guest. Protected by copyright.

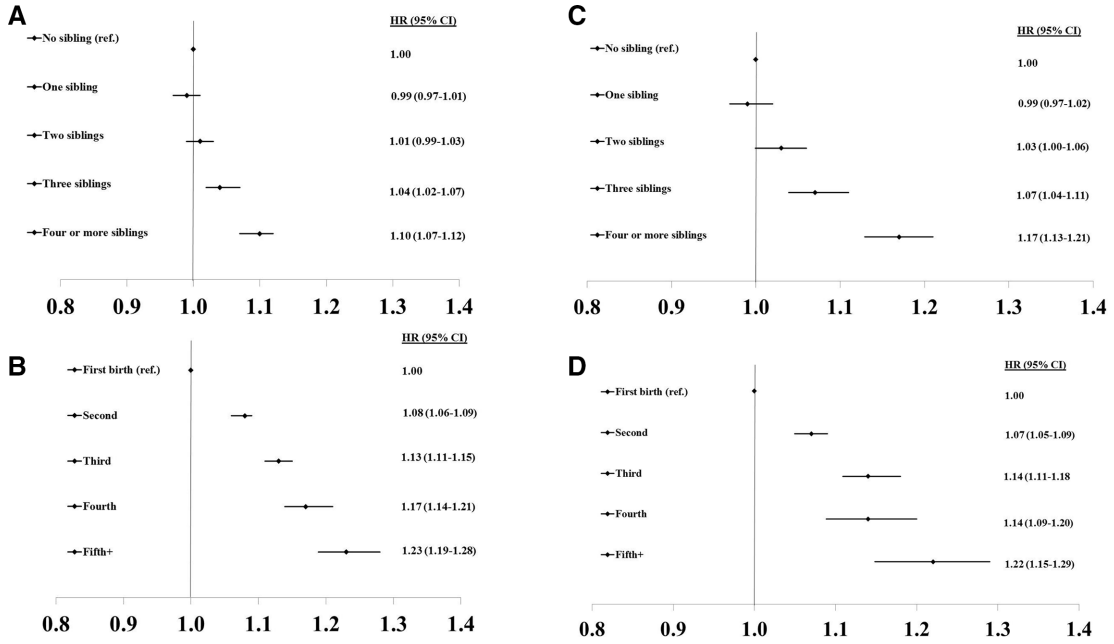


Figure 1 HRs of CHD by number of siblings and birth order in men (A, B) and women (C, D). CHD, coronary heart disease.

our study for risk of non-fatal cardiovascular and coronary events during longer follow-up and extensive adjustment.

These findings of lower cardiovascular risk in first borns are at contrast to previous reports of a higher level of cardiovascular risk factors in such individuals followed until adolescence or young adulthood.[12–16] The burden of risk factors might have been compensated for by a better physical fitness, as noticed in first-born men coming for military conscript testing at the age of around 18 years.[17] In contrast to these observations, our extensive data indicate a lower cardiovascular risk in first borns. Other unmeasured factors linked to being first born, such as cognition or bodily development, could have contributed to our findings of a relative protection, even if we adjusted for a long list of potential confounders such as educational level, socioeconomic status, marital status and comorbidities.

Besides filling a knowledge gap, this is of public health interest as different countries endorse different policies to support families and number of children. Our findings

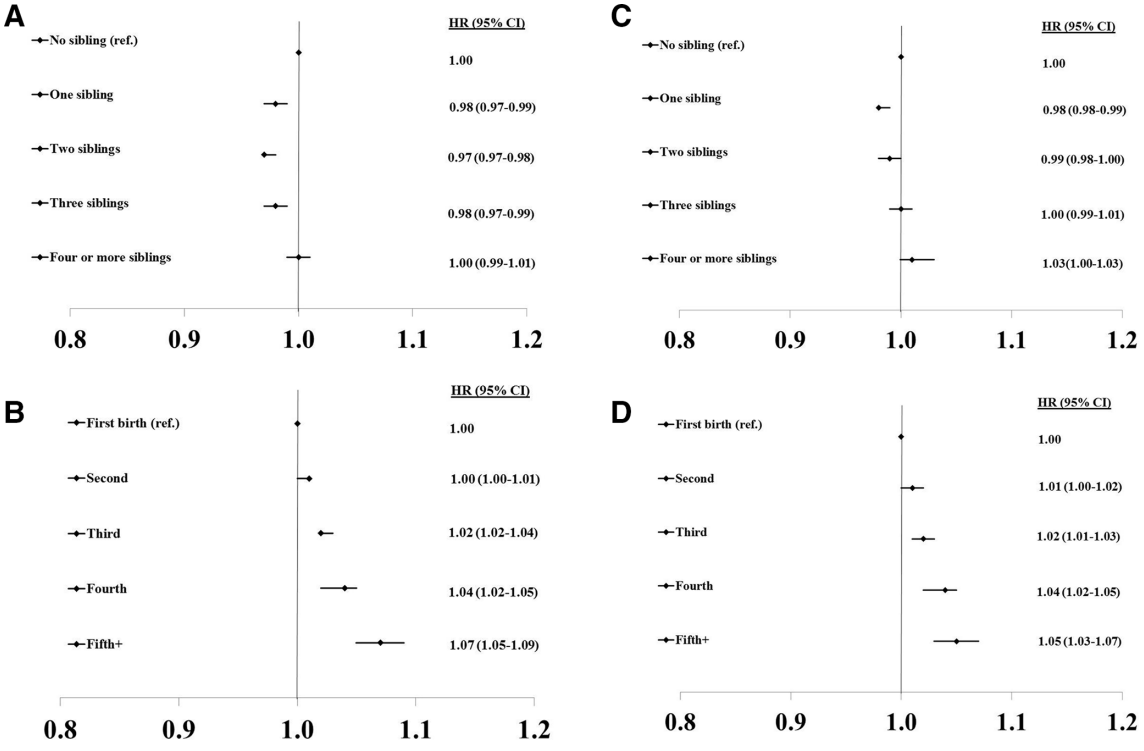


Figure 2 HRs of CVD by number of siblings and birth order in men (A, B) and women (C, D). CVD, cardiovascular disease.

BMJ Open: first published as 10.1136/bmjopen-2020-042881 on 25 May 2021. Downloaded from http://bmjopen.bmj.com/ on March 13, 2024 by guest. Protected by copyright.

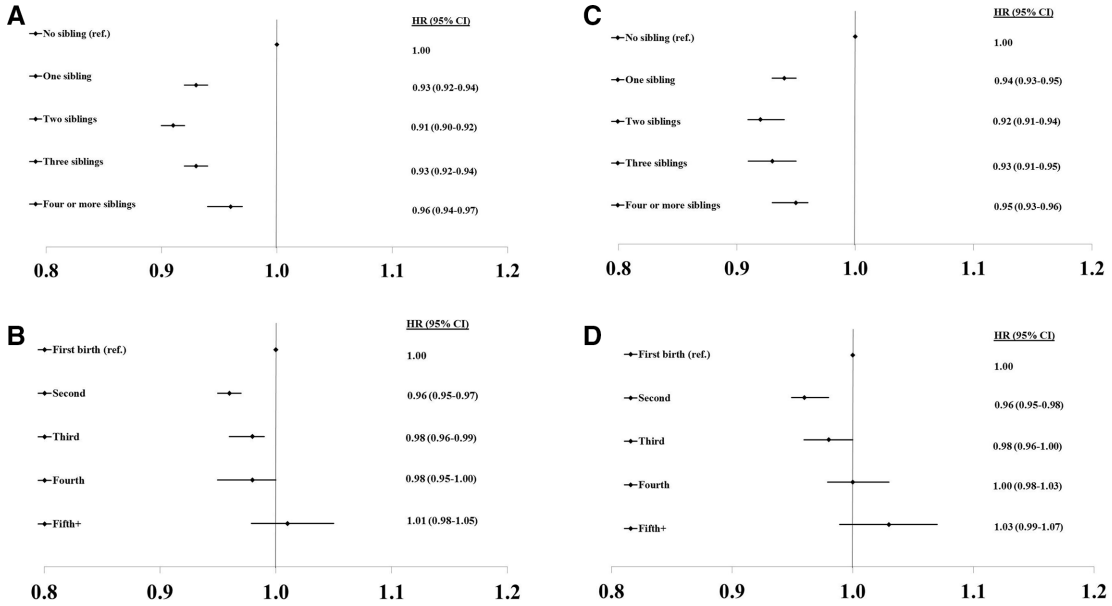


Figure 3 HRs of mortality by number of siblings and birth order in men (A, B) and women (C, D).

relate to family size and the biological as well as social roles related to sibling rank with its health implications.

More research is needed to understand the links between sibling number and rank with health outcomes. This could address, for example, the dilution of resources theory[25] of special relevance for disadvantaged girls; epigenetic factors influencing the metabolic syndrome in offspring[26] and maternal health during pregnancy, including the effects of multiple births/child rearing on maternal health and family resources, especially in deprived settings with large families.[27]

Limitations and strengths of the study

The Swedish hospital discharge register contains no information about diagnostic procedures, which is a limitation. Moreover, specialist doctors in hospital care made the diagnosis. Another limitation is that we had no data on life style-related factors such as BMI, smoking and diet, because it would be unrealistic to gather such data for an entire national population. However, we did adjust for socioeconomic status, obesity, diabetes, COPD and alcoholism and related liver disorders, which are associated with factors such as smoking and alcohol use. Given a focus on family size, knowing that siblings who died young, and therefore not contributed to resource dilution for a proportion of the index person's childhood, would be of interest and importance. It would also shed light (potentially) on family circumstances and health. Regretfully, we currently lack data on parental SES to adjust for.

Strengths of the study include complete nationwide coverage from 1990 in a country with high standards of diagnosis, and with diagnoses often being made by specialists during extended examinations in clinics. Another important strength of our study is that it was based on nationwide registers and was thus free of selection and recall bias. The Swedish MGR and the Swedish Hospital Discharge Register are validated data sources that have been proven to be reliable in the study of many diseases.[4 21 22] Data in our dataset are almost 100% complete.[4] Generalisability (external validity) should hold at least for countries and populations similar to Sweden.

Future research should be directed to find biological or social mechanisms linking the status of being first born to lower risk of CVD, as indicated by our observational findings. A previous Norwegian study in military conscripts indicated that the role of being first born is influenced by social factors, as a second-born son may achieve characteristics of a first-born brother who died young.[28]

In conclusion, our data indicate a favourable effect on non-fatal cardiovascular and coronary events by being first born, both for men and women.

Contributors PMN provided the original idea, and XL made the statistical analyses. PMN and XL drafted the first manuscript. All authors (PMN, XL, JS and KS) contributed to the final manuscript. PMN and XL made the revisions.

Funding This work was supported by the grants to Kristina Sundquist from The Swedish Research Council; ALF funding from Region Skåne and the Swedish Heart-Lung foundation.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study was approved by the Regional Ethics Review Board at the Lund University, Sweden (ID number 2012/795; approved 2013-02-06).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. Data will not be shared, but reasonable requests may be directed to Professor KS, the PI of the registers.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible

BMJ Open: first published as 10.1136/bmjopen-2020-042881 on 25 May 2021. Downloaded from http://bmjopen.bmj.com/ on March 13, 2024 by guest. Protected by copyright.

for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: https://creativecommons.org/licenses/by/4.0/.

ORCID iD

Peter M Nilsson http://orcid.org/0000-0002-5652-8459

REFERENCES

1 Banerjee A. A review of family history of cardiovascular disease: risk factor and research tool. *Int J Clin Pract* 2012;66:536–43.
2 Tada H, Melander O, Louie JZ, *et al*. Risk prediction by genetic risk scores for coronary heart disease is independent of self-reported family history. *Eur Heart J* 2016;37:561–7.
3 Nilsson PM, Nilsson J-A, Berglund G. Family burden of cardiovascular mortality: risk implications for offspring in a national register linkage study based upon the Malmo preventive project. *J Intern Med* 2004;255:229–35.
4 Ekbom A. The Swedish multi-generation register. *Methods Mol Biol* 2011;675:215–20.
5 Zöller B, Ji J, Sundquist J, *et al*. Body height and incident risk of venous thromboembolism: a Cosibling design. *Circ Cardiovasc Genet* 2017;10:e001651.
6 Kasiman K, Lundholm C, Sandin S, *et al*. Familial effects on ischemic stroke: the role of sibling kinship, sex, and age of onset. *Circ Cardiovasc Genet* 2012;5:226–33.
7 Martinsson A, Li X, Zöller B. Familial aggregation of aortic valvular stenosis: a nationwide study of sibling risk. *Circ Cardiovasc Genet* 2017;10:e001742.
8 Lindgren MP, Ji J, Smith JG, *et al*. Mortality risks associated with sibling heart failure. *Int J Cardiol* 2020;307:114–8.
9 Berntsson J, Li X, Zöller B, *et al*. Risk of stroke in patients with atrial fibrillation is associated with stroke in siblings: a nationwide study. *J Am Heart Assoc* 2020;9:e014132.
10 Baranowska-Rataj A, Barclay K, Kolk M. The effect of number of siblings on adult mortality: evidence from Swedish registers for cohorts born between 1938 and 1972. *Popul Stud* 2017;71:43–63.
11 Barclay K, Kolk M. Birth order and mortality: a population-based cohort study. *Demography* 2015;52:613–39.
12 Ayyavoo A, Derraik JGB, Hofman PL, *et al*. Is being first-born another risk factor for metabolic and cardiovascular diseases? *Future Cardiol* 2013;9:447–50.
13 Theodore RF, Broadbent J, Nagin D. Childhood to Early-Midlife systolic blood pressure trajectories: early-life predictors, effect modifiers, and adult cardiovascular outcomes. *Hypertension* 2015;66:1108–15.
14 Albert BB, de Bock M, Derraik JGB, *et al*. Among overweight middle-aged men, first-borns have lower insulin sensitivity than second-borns. *Sci Rep* 2015;4:3906.
15 Siervo M, Horta BL, Stephan BCM, *et al*. First-borns carry a higher metabolic risk in early adulthood: evidence from a prospective cohort study. *PLoS One* 2010;5:e13907.
16 Jelenkovic A, Silventoinen K, Tynelius P, *et al*. Association of birth order with cardiovascular disease risk factors in young adulthood: a study of one million Swedish men. *PLoS One* 2013;8:e63361.
17 Barclay K, Myrskylä M. Birth order and physical fitness in early adulthood: evidence from Swedish military conscription data. *Soc Sci Med* 2014;123:141–8.
18 Julihn A, Soares FC, Hammarfjord U, *et al*. Birth order is associated with caries development in young children: a register-based cohort study. *BMC Public Health* 2020;20:218.
19 Von Behren J, Spector LG, Mueller BA, *et al*. Birth order and risk of childhood cancer: a pooled analysis from five us states. *Int J Cancer* 2011;128:2709–16.
20 Saarela J, Cederström A, Rostila M. Birth order and mortality in two ethno-linguistic groups: register-based evidence from Finland. *Soc Sci Med* 2016;158:8–13.
21 Ludvigsson JF, Almqvist C, Bonamy A-KE, *et al*. Registers of the Swedish total population and their use in medical research. *Eur J Epidemiol* 2016;31:125–36.
22 Ludvigsson JF, Andersson E, Ekbom A, *et al*. External review and validation of the Swedish national inpatient register. *BMC Public Health* 2011;11:450.
23 Memarian E, Sundquist K, Calling S, *et al*. Socioeconomic factors, body mass index and bariatric surgery: a Swedish nationwide cohort study. *BMC Public Health* 2019;19:258.
24 Li X, Sundquist J, Zöller B, *et al*. Familial risks of glaucoma in the population of Sweden. *J Glaucoma* 2018;27:802–6.
25 Kalmijn M, van de Werfhorst HG. Sibship size and gendered resource dilution in different societal contexts. *PLoS One* 2016;11:e0160953.
26 Dunford AR, Sangster JM. Maternal and paternal periconceptional nutrition as an indicator of offspring metabolic syndrome risk in later life through epigenetic imprinting: a systematic review. *Diabetes Metab Syndr* 2017;11:S655–62.
27 Young MF, Ramakrishnan U. Maternal undernutrition before and during pregnancy and offspring health and development. *Ann Nutr Metab* 2021;1:1–13.
28 Kristensen P, Bjerkedal T. Explaining the relation between birth order and intelligence. *Science* 2007;316:1717.

BMJ Open: first published as 10.1136/bmjopen-2020-042881 on 25 May 2021. Downloaded from http://bmjopen.bmj.com/ on March 13, 2024 by guest. Protected by copyright.

Supplementary Table 1a. Distribution of population, number of CVD, CHD, and mortality events in *men*.

	Population		CVD events		CHD events		Mortality events	
	No.	(%)	No.	%	No.	%	No.	%
Total population (%)	1358647		592863		131533		240371	
Age (years)								
30-39	531559	39.1	152615	25.7	25327	19.3	39094	16.3
40-49	554137	40.8	265251	44.7	59088	44.9	96549	40.2
50-58	272951	20.1	174997	29.5	47118	35.8	104728	43.6
Family income								
Low income	334083	24.6	123575	20.8	26649	20.3	47582	19.8
Middle–low income	320284	23.6	135148	22.8	29613	22.5	51243	21.3
Middle–high income	321653	23.7	152589	25.7	35041	26.6	66400	27.6
High income	382627	28.2	181551	30.6	40230	30.6	75146	31.3
Marital status								
Married/cohabiting	809314	59.6	370633	62.5	85212	64.8	124039	51.6
Never married, Widowed, or divorced	549333	40.4	222230	37.5	46321	35.2	116332	48.4
Educational attainment								
≤ 9 years	281207	20.7	146179	24.7	38890	29.6	81428	33.9
10–11 years	173208	12.7	67512	11.4	13955	10.6	26218	10.9
≥ 12 years	904232	66.6	379172	64.0	78688	59.8	132725	55.2
Immigrant status								
Sweden	1322658	97.4	580707	97.9	128732	97.9	235464	98.0
Other countries	35989	2.6	12156	2.1	2801	2.1	4907	2.0
Socioeconomic status								
Farmers/self-employed/others	308729	22.7	129408	21.8	29064	22.1	71960	29.9
Blue collar workers	494090	36.4	217215	36.6	50626	38.5	89989	37.4
White collar workers	351621	25.9	157170	26.5	34594	26.3	52582	21.9
Professionals	204207	15.0	89070	15.0	17249	13.1	25840	10.8
Urban/rural status								
Large cities	495681	36.5	207593	35.0	41153	31.3	85765	35.7
Southern Sweden	618686	45.5	274100	46.2	61581	46.8	108663	45.2
Northern Sweden	244280	18.0	111170	18.8	28799	21.9	45943	19.1
Hospitalization of alcoholism and related liver disease								
No	1275305	93.9	548796	92.6	124051	94.3	202724	84.3
Yes	83342	6.1	44067	7.4	7482	5.7	37647	15.7
Hospitalization of diabetes								
No	1226642	90.3	494000	83.3	104716	79.6	200226	83.3
Yes	132005	9.7	988863	16.7	26817	20.4	40145	16.7

Hospitalization of hypertension								
No	1059935	78.0	294151	49.6	76609	58.2	183958	76.5
Yes	298712	22.0	298712	50.4	54924	41.8	56413	23.5
Hospitalization of obesity								
No	1338892	98.5	577543	97.4	128595	97.8	236644	98.4
Yes	19755	1.5	15320	2.6	2938	2.2	3727	1.6
Hospitalization of chronic lower respiratory disease								
No	1288108	94.8	546393	92.2	120575	91.7	216522	90.1
Yes	70539	5.2	46470	7.8	10958	8.3	23849	9.9
Cancer								
No	1109571	81.7	452446	76.3	103202	78.5	139486	58.0
Yes	249076	18.3	140417	23.7	28331	21.5	100885	42.0
Number of sibling								
Non sibling	214700	15.8	105516	17.8	23671	18.0	50709	21.1
One sibling	443877	32.7	189839	32.0	39729	30.2	73140	30.4
Two siblings	338812	24.9	140361	23.7	30184	22.9	52790	22.0
Three siblings	183067	13.5	77378	13.1	17663	13.4	30266	12.6
Four or more siblings	178191	13.1	79769	13.5	20286	15.4	33466	13.9
Birth order								
First	684765	50.4	318341	53.7	70238	53.4	140857	58.6
Second	402879	29.7	166757	28.1	36654	27.9	62267	25.9
Third	164540	12.1	65853	11.1	14736	11.2	23081	9.6
Fourth	62765	4.6	24729	4.2	5737	4.4	8425	3.5
Fifth+	43698	3.2	17183	2.9	4168	3.2	5741	2.4

Supplementary Table 1b. Distribution of population, number of CVD, CHD, and mortality events in *women.*

	Population		CVD events		CHD events		Mortality events	
	No.	(%)	No.	%	No.	%	No.	%
Total population (%)	1315037		486147		55933		160269	
Age (years)								
30-39	507872	38.6	125326	25.8	9681	17.3	24571	15.3
40-49	537035	40.8	210113	43.2	23738	42.4	64055	40.0
50+	270130	20.5	150708	31.0	22514	40.3	71643	44.7
Family income								
Low income	343296	26.1	100542	20.7	10467	18.7	29723	18.5
Middle–low income	340837	25.9	121716	25.0	13432	24.0	37773	23.6
Middle–high income	347955	26.5	142924	29.4	17579	31.4	50537	31.5
High income	282949	21.5	120965	24.9	14455	25.8	42236	26.4
Marital status								
Married/cohabiting	887258	67.5	331886	68.3	38106	68.1	96533	60.2
Never married, Widowed, or divorced	427779	32.5	154261	31.7	17827	31.9	63736	39.8
Educational attainment								
≤ 9 years	232824	17.7	102037	21.0	15415	27.6	48455	30.2
10–11 years	165367	12.6	60209	12.4	6867	12.3	20489	12.8
≥ 12 years	916846	69.7	323901	66.6	33651	60.2	91325	57.0
Immigrant status								
Sweden	1281472	97.4	476075	97.9	54756	97.9	157515	98.3
Other countries	33565	2.6	10072	2.1	1177	2.1	2754	1.7
Socioeconomic status								
Farmers/self-employed/others	272189	20.7	96279	19.8	12450	22.3	45553	28.4
Blue collar workers	437324	33.3	174549	35.9	21821	39.0	55960	34.9
White collar workers	496782	37.8	178249	36.7	18324	32.8	49169	30.7
Professionals	108742	8.3	37070	7.6	3338	6.0	9587	6.0
Urban/rural status								
Large cities	495097	37.6	173872	35.8	17499	31.3	57794	36.1
Southern Sweden	591636	45.0	223375	45.9	25965	46.4	72872	45.5
Northern Sweden	228304	17.4	88900	18.3	12469	22.3	29603	18.5
Hospitalization of alcoholism and related liver disease								
No	1283561	97.6	471088	96.9	54416	97.3	149212	93.1
Yes	31476	2.4	15059	3.1	1517	2.7	11057	6.9
Hospitalization of diabetes								
No	1234361	93.9	429522	88.4	45537	81.4	139644	87.1

Yes	80676	6.1	56625	11.6	10396	18.6	20625	12.9
Hospitalization of hypertension								
No	1067928	81.2	239038	49.2	31364	56.1	124898	77.9
Yes	247109	18.8	247109	50.8	24569	43.9	35371	22.1
Hospitalization of obesity								
No	1286838	97.9	468228	96.3	54003	96.5	156771	97.8
Yes	28199	2.1	17919	3.7	1930	3.5	3498	2.2
Hospitalization of chronic lower respiratory disease								
No	1226846	93.3	433906	89.3	48084	86.0	137028	85.5
Yes	88191	6.7	52241	10.7	7849	14.0	23241	14.5
Cancer								
No	1051617	80.0	364226	74.9	43617	78.0	70300	43.9
Yes	263420	20.0	121921	25.1	12316	22.0	89969	56.1
Number of sibling								
Non sibling	210121	16.0	87261	17.9	10289	18.4	34521	21.5
One sibling	430315	32.7	154154	31.7	16280	29.1	49132	30.7
Two siblings	324379	24.7	113739	23.4	12500	22.3	34843	21.7
Three siblings	176631	13.4	63871	13.1	7512	13.4	19766	12.3
Four or more siblings	173591	13.2	67122	13.8	9352	16.7	22007	13.7
Birth order								
First	664459	50.5	262015	53.9	30342	54.2	94779	59.1
Second	388391	29.5	136263	28.0	15191	27.2	40984	25.6
Third	159311	12.1	53711	11.0	6231	11.1	15205	9.5
Fourth	60676	4.6	20264	4.2	2379	4.3	5558	3.5
Fifth+	42200	3.2	13894	2.9	1790	3.2	3743	2.3

Supplementary Table 2a. Hazard ratio (HR) and 95% confidence interval of CVD in *men*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.97	0.97	0.98	0.98	0.97	0.98	0.98	0.97	0.99
Two siblings	0.97	0.96	0.98	0.97	0.96	0.97	0.97	0.97	0.98
Three siblings	0.99	0.98	1.00	0.98	0.97	0.99	0.98	0.97	0.99
Four or more children	1.04	1.03	1.05	1.00	0.99	1.01	1.00	0.99	1.01
Age (years)	1.07	1.07	1.07	1.08	1.07	1.08	1.06	1.06	1.06
Family income (ref. High)									
Low income				0.92	0.92	0.93	0.99	0.98	1.00
Middle–low income				1.02	1.01	1.03	1.05	1.04	1.06
Middle–high income				1.04	1.03	1.05	1.05	1.04	1.06
Educational level (ref. > 12 years)									
10–11 years				1.11	1.10	1.12	1.06	1.05	1.07
≥ 12 years				1.00	1.00	1.01	1.00	0.99	1.00
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.22	1.21	1.23	1.17	1.16	1.18
Blue collar workers				1.15	1.14	1.16	1.09	1.08	1.10
White collar workers				1.08	1.07	1.08	1.04	1.04	1.05
Region of residence (ref. Large cities)									
Southern Sweden				1.00	1.00	1.01	1.03	1.02	1.03
Northern Sweden				1.04	1.03	1.05	1.05	1.04	1.06
Immigrant status (ref. Born in Sweden)				0.95	0.93	0.97	0.96	0.95	0.98
Marital status (ref. Not married)				1.18	1.17	1.19	1.17	1.16	1.18
Birth order				1.01	1.01	1.01	1.01	1.01	1.02
Hospitalization of chronic lower respiratory disease (ref. Non)							1.26	1.25	1.28
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.74	1.73	1.76
Hospitalization of diabetes (ref. Non)							1.39	1.38	1.40
Hospitalization of obesity (ref. Non)							1.37	1.35	1.40
Hospitalization of hypertension (ref. Non)							3.72	3.70	3.74
Cancer (ref. Non)							1.36	1.35	1.36

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 2b. Hazard ratio (HR) and 95% confidence interval of CVD in *men*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Birth order (ref. First birth)									
Second	0.99	0.99	1.00	0.99	0.98	1.00	1.00	1.00	1.01
Third	1.02	1.01	1.03	1.01	1.00	1.02	1.02	1.02	1.03
Fourth	1.05	1.03	1.06	1.03	1.01	1.04	1.04	1.02	1.05
Fifth+	1.10	1.08	1.12	1.07	1.05	1.08	1.07	1.05	1.09
Age (years)	1.07	1.07	1.07	1.08	1.07	1.08	1.06	1.06	1.06
Family income (ref. High)									
Low income				0.92	0.92	0.93	0.99	0.98	1.00
Middle–low income				1.02	1.01	1.03	1.05	1.04	1.06
Middle–high income				1.04	1.03	1.05	1.05	1.04	1.06
Educational level (ref. > 12 years)									
10–11 years				1.11	1.10	1.12	1.06	1.05	1.07
≥ 12 years				1.00	1.00	1.01	1.00	0.99	1.00
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.22	1.21	1.23	1.17	1.16	1.18
Blue collar workers				1.15	1.14	1.16	1.09	1.08	1.10
White collar workers				1.08	1.07	1.08	1.04	1.04	1.05
Region of residence (ref. Large cities)									
Southern Sweden				1.00	1.00	1.01	1.03	1.02	1.03
Northern Sweden				1.04	1.03	1.05	1.05	1.04	1.06
Immigrant status (ref. Born in Sweden)				0.95	0.93	0.97	0.97	0.95	0.98
Marital status (ref. Not married)				1.18	1.17	1.19	1.17	1.16	1.18
Number of siblings				1.00	1.00	1.00	1.00	1.00	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.26	1.25	1.28
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.74	1.73	1.76
Hospitalization of diabetes (ref. Non)							1.39	1.38	1.40
Hospitalization of obesity (ref. Non)							1.37	1.35	1.40
Hospitalization of hypertension (ref. Non)							3.72	3.70	3.74
Cancer (ref. Non)							1.36	1.35	1.36

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 2c. Hazard ratio (HR) and 95% confidence interval of CVD in *women*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.98	0.97	0.98	0.98	0.97	0.98	0.98	0.98	0.99
Two siblings	0.99	0.98	0.99	0.98	0.97	0.99	0.99	0.98	1.00
Three siblings	1.01	1.00	1.02	1.00	0.99	1.01	1.00	0.99	1.01
Four or more children	1.06	1.05	1.07	1.03	1.02	1.04	1.01	1.00	1.03
Age (years)	1.06	1.06	1.07	1.06	1.06	1.06	1.04	1.04	1.04
Family income (ref. High)									
Low income				0.87	0.86	0.87	0.95	0.94	0.96
Middle–low income				1.01	1.00	1.02	1.04	1.03	1.05
Middle–high income				1.02	1.01	1.03	1.03	1.02	1.03
Educational level (ref. > 12 years)									
10–11 years				1.13	1.12	1.14	1.08	1.06	1.09
≥ 12 years				1.04	1.03	1.05	1.03	1.02	1.04
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.30	1.28	1.31	1.20	1.19	1.22
Blue collar workers				1.25	1.24	1.27	1.12	1.11	1.13
White collar workers				1.08	1.07	1.10	1.03	1.02	1.04
Region of residence (ref. Large cities)									
Southern Sweden				1.03	1.03	1.04	1.03	1.03	1.04
Northern Sweden				1.06	1.06	1.07	1.04	1.03	1.05
Immigrant status (ref. Born in Sweden)				0.97	0.96	0.99	0.98	0.96	1.00
Marital status (ref. Not married)				1.13	1.12	1.14	1.10	1.09	1.11
Birth order				1.00	1.00	1.01	1.01	1.01	1.01
Hospitalization of chronic lower respiratory disease (ref. Non)							1.38	1.36	1.39
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.67	1.65	1.69
Hospitalization of diabetes (ref. Non)							1.38	1.37	1.39
Hospitalization of obesity (ref. Non)							1.32	1.30	1.34
Hospitalization of hypertension (ref. Non)							4.86	4.83	4.89
Cancer (ref. Non)							1.62	1.61	1.63

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 2d. Hazard ratio (HR) and 95% confidence interval of CVD in *women*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Birth order (ref. First birth)									
Second	1.00	0.99	1.01	0.99	0.98	1.00	1.01	1.00	1.02
Third	1.03	1.02	1.04	1.00	0.99	1.01	1.02	1.01	1.03
Fourth	1.06	1.04	1.07	1.01	1.00	1.03	1.04	1.02	1.05
Fifth+	1.09	1.07	1.10	1.01	0.99	1.03	1.05	1.03	1.07
Age (years)	1.07	1.07	1.07	1.06	1.06	1.06	1.04	1.04	1.04
Family income (ref. High)									
Low income				0.87	0.86	0.87	0.95	0.94	0.96
Middle–low income				1.01	1.00	1.02	1.04	1.03	1.05
Middle–high income				1.02	1.01	1.03	1.03	1.02	1.03
Educational level (ref. > 12 years)									
10–11 years				1.13	1.12	1.14	1.08	1.06	1.09
≥ 12 years				1.04	1.03	1.05	1.03	1.02	1.04
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.30	1.28	1.31	1.21	1.19	1.22
Blue collar workers				1.26	1.24	1.27	1.12	1.11	1.13
White collar workers				1.09	1.07	1.10	1.03	1.02	1.05
Region of residence (ref. Large cities)									
Southern Sweden				1.03	1.03	1.04	1.03	1.03	1.04
Northern Sweden				1.06	1.06	1.07	1.04	1.03	1.05
Immigrant status (ref. Born in Sweden)				0.97	0.96	0.99	0.98	0.96	1.00
Marital status (ref. Not married)				1.13	1.13	1.14	1.10	1.09	1.11
Number of siblings				1.01	1.01	1.01	1.00	1.00	1.01
Hospitalization of chronic lower respiratory disease (ref. Non)							1.38	1.36	1.39
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.67	1.65	1.69
Hospitalization of diabetes (ref. Non)							1.38	1.37	1.39
Hospitalization of obesity (ref. Non)							1.32	1.30	1.34
Hospitalization of hypertension (ref. Non)							4.86	4.83	4.89
Cancer (ref. Non)							1.62	1.61	1.63

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 3a. Hazard ratio (HR) and 95% confidence interval of CHD in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	1.00	0.98	1.02	0.99	0.97	1.01	0.99	0.97	1.01
Two siblings	1.04	1.03	1.06	1.00	0.98	1.02	1.01	0.99	1.03
Three siblings	1.12	1.10	1.14	1.04	1.02	1.06	1.04	1.02	1.07
Four or more children	1.27	1.25	1.30	1.10	1.08	1.12	1.10	1.07	1.12
Age (years)	1.08	1.08	1.08	1.08	1.08	1.08	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.93	0.91	0.94	0.96	0.95	0.98
Middle–low income				1.00	0.98	1.01	1.02	1.00	1.03
Middle–high income				1.01	1.00	1.03	1.02	1.00	1.03
Educational level (ref. > 12 years)									
10–11 years				1.05	1.03	1.07	1.04	1.02	1.07
≥ 12 years				0.94	0.93	0.95	0.95	0.94	0.96
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.23	1.20	1.25	1.18	1.16	1.21
Blue collar workers				1.26	1.24	1.28	1.21	1.19	1.23
White collar workers				1.18	1.16	1.20	1.15	1.13	1.17
Region of residence (ref. Large cities)									
Southern Sweden				1.11	1.10	1.12	1.12	1.11	1.14
Northern Sweden				1.32	1.30	1.34	1.31	1.29	1.33
Immigrant status (ref. Born in Sweden)				1.09	1.05	1.13	1.10	1.06	1.14
Marital status (ref. Not married)				1.00	0.99	1.01	0.99	0.98	1.01
Birth order				1.05	1.04	1.05	1.05	1.05	1.06
Hospitalization of chronic lower respiratory disease (ref. Non)							1.29	1.26	1.31
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.01	0.99	1.04
Hospitalization of diabetes (ref. Non)							1.75	1.73	1.78
Hospitalization of obesity (ref. Non)							1.13	1.09	1.17
Hospitalization of hypertension (ref. Non)							1.86	1.84	1.88
Cancer (ref. Non)							0.91	0.89	0.92

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 3b. Hazard ratio (HR) and 95% confidence interval of CHD in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	1.09	1.08	1.10	1.06	1.05	1.07	1.08	1.06	1.09
Third	1.19	1.17	1.21	1.11	1.09	1.13	1.13	1.11	1.15
Fourth	1.28	1.25	1.32	1.15	1.12	1.19	1.17	1.14	1.21
Fifth+	1.44	1.39	1.48	1.22	1.17	1.26	1.23	1.19	1.28
Age (years)	1.08	1.08	1.09	1.08	1.08	1.08	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.93	0.91	0.94	0.96	0.95	0.98
Middle–low income				1.00	0.98	1.01	1.02	1.00	1.03
Middle–high income				1.01	1.00	1.02	1.02	1.00	1.03
Educational level (ref. > 12 years)									
10–11 years				1.05	1.03	1.08	1.05	1.03	1.07
≥ 12 years				0.94	0.93	0.95	0.95	0.94	0.97
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.23	1.20	1.25	1.18	1.16	1.21
Blue collar workers				1.26	1.24	1.28	1.21	1.19	1.23
White collar workers				1.18	1.16	1.20	1.15	1.13	1.17
Region of residence (ref. Large cities)									
Southern Sweden				1.11	1.10	1.13	1.12	1.11	1.14
Northern Sweden				1.32	1.30	1.34	1.31	1.29	1.33
Immigrant status (ref. Born in Sweden)				1.09	1.05	1.13	1.10	1.06	1.14
Marital status (ref. Not married)				1.00	0.99	1.01	0.99	0.98	1.01
Number of siblings				1.02	1.02	1.02	1.02	1.02	1.02
Hospitalization of chronic lower respiratory disease (ref. Non)							1.29	1.26	1.31
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.01	0.99	1.04
Hospitalization of diabetes (ref. Non)							1.75	1.73	1.78
Hospitalization of obesity (ref. Non)							1.13	1.09	1.17
Hospitalization of hypertension (ref. Non)							1.86	1.84	1.88
Cancer (ref. Non)							0.91	0.89	0.92

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 3c. Hazard ratio (HR) and 95% confidence interval of CHD in *women*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.99	0.97	1.02	0.98	0.96	1.01	0.99	0.97	1.02
Two siblings	1.07	1.04	1.10	1.03	1.00	1.05	1.03	1.00	1.06
Three siblings	1.17	1.13	1.20	1.08	1.04	1.11	1.07	1.04	1.11
Four or more children	1.40	1.36	1.44	1.20	1.16	1.24	1.17	1.13	1.21
Age (years)	1.09	1.09	1.09	1.09	1.08	1.09	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.85	0.83	0.88	0.91	0.88	0.93
Middle–low income				1.00	0.98	1.03	1.00	0.98	1.03
Middle–high income				1.02	1.00	1.05	1.02	0.99	1.04
Educational level (ref. > 12 years)									
10–11 years				1.07	1.04	1.10	1.06	1.03	1.09
≥ 12 years				0.92	0.90	0.94	0.94	0.92	0.96
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.52	1.46	1.59	1.37	1.31	1.42
Blue collar workers				1.47	1.42	1.53	1.33	1.28	1.38
White collar workers				1.19	1.14	1.23	1.14	1.10	1.18
Region of residence (ref. Large cities)									
Southern Sweden				1.14	1.12	1.16	1.15	1.13	1.17
Northern Sweden				1.40	1.37	1.44	1.38	1.34	1.41
Immigrant status (ref. Born in Sweden)				1.13	1.07	1.20	1.13	1.07	1.20
Marital status (ref. Not married)				1.12	1.10	1.14	1.08	1.06	1.10
Birth order				1.04	1.03	1.05	1.05	1.04	1.06
Hospitalization of chronic lower respiratory disease (ref. Non)							1.69	1.65	1.73
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.17	1.11	1.23
Hospitalization of diabetes (ref. Non)							2.20	2.15	2.25
Hospitalization of obesity (ref. Non)							1.11	1.06	1.17
Hospitalization of hypertension (ref. Non)							2.22	2.18	2.26
Cancer (ref. Non)							0.94	0.93	0.96

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 3d. Hazard ratio (HR) and 95% confidence interval of CHD in *women*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	1.10	1.07	1.12	1.05	1.02	1.07	1.07	1.05	1.09
Third	1.24	1.21	1.28	1.11	1.08	1.14	1.14	1.11	1.18
Fourth	1.33	1.27	1.38	1.11	1.06	1.16	1.14	1.09	1.20
Fifth+	1.56	1.48	1.63	1.17	1.11	1.24	1.22	1.15	1.29
Age (years)	1.09	1.09	1.09	1.09	1.08	1.09	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.85	0.83	0.88	0.91	0.88	0.93
Middle–low income				1.00	0.98	1.03	1.01	0.98	1.03
Middle–high income				1.02	1.00	1.05	1.02	0.99	1.04
Educational level (ref. > 12 years)									
10–11 years				1.07	1.04	1.10	1.06	1.03	1.09
≥ 12 years				0.92	0.90	0.94	0.94	0.92	0.96
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.52	1.46	1.59	1.37	1.31	1.42
Blue collar workers				1.47	1.42	1.53	1.33	1.28	1.38
White collar workers				1.19	1.14	1.23	1.14	1.10	1.18
Region of residence (ref. Large cities)									
Southern Sweden				1.14	1.12	1.17	1.15	1.13	1.17
Northern Sweden				1.40	1.37	1.44	1.38	1.34	1.41
Immigrant status (ref. Born in Sweden)				1.13	1.07	1.20	1.13	1.07	1.20
Marital status (ref. Not married)				1.12	1.10	1.14	1.08	1.06	1.10
Number of siblings				1.04	1.03	1.04	1.03	1.03	1.04
Hospitalization of chronic lower respiratory disease (ref. Non)							1.69	1.65	1.73
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.17	1.11	1.23
Hospitalization of diabetes (ref. Non)							2.20	2.15	2.25
Hospitalization of obesity (ref. Non)							1.11	1.06	1.17
Hospitalization of hypertension (ref. Non)							2.22	2.18	2.26
Cancer (ref. Non)							0.94	0.93	0.96

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4a. Hazard ratio (HR) and 95% confidence interval of mortality in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.91	0.90	0.92	0.92	0.91	0.93	0.93	0.92	0.94
Two siblings	0.92	0.91	0.93	0.91	0.90	0.92	0.91	0.90	0.92
Three siblings	0.96	0.94	0.97	0.93	0.92	0.94	0.93	0.92	0.94
Four or more children	1.03	1.01	1.04	0.96	0.94	0.97	0.96	0.94	0.97
Age (years)	1.10	1.10	1.10	1.11	1.11	1.11	1.10	1.10	1.10
Family income (ref. High)									
Low income				1.05	1.04	1.07	1.08	1.07	1.10
Middle–low income				1.17	1.15	1.18	1.14	1.13	1.15
Middle–high income				1.18	1.17	1.19	1.15	1.14	1.16
Educational level (ref. > 12 years)									
10–11 years				1.12	1.10	1.13	1.08	1.06	1.09
≥ 12 years				0.91	0.90	0.91	0.89	0.88	0.90
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.73	1.71	1.76	1.63	1.60	1.65
Blue collar workers				1.38	1.36	1.40	1.34	1.32	1.36
White collar workers				1.15	1.13	1.17	1.14	1.12	1.16
Region of residence (ref. Large cities)									
Southern Sweden				0.94	0.93	0.95	0.99	0.98	1.00
Northern Sweden				0.98	0.97	0.99	1.08	1.07	1.09
Immigrant status (ref. Born in Sweden)				1.04	1.01	1.07	1.06	1.03	1.09
Marital status (ref. Not married)				1.88	1.87	1.90	1.71	1.70	1.73
Birth order				1.00	1.00	1.01	0.99	0.99	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.28	1.26	1.30
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.02	2.98	3.05
Hospitalization of diabetes (ref. Non)							1.43	1.41	1.45
Hospitalization of obesity (ref. Non)							1.09	1.06	1.13
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							2.62	2.60	2.65

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4b. Hazard ratio (HR) and 95% confidence interval of mortality in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	0.98	0.97	0.99	0.97	0.96	0.98	0.96	0.95	0.97
Third	1.01	0.99	1.02	0.99	0.98	1.01	0.98	0.96	0.99
Fourth	1.04	1.01	1.06	1.00	0.98	1.03	0.98	0.95	1.00
Fifth+	1.11	1.08	1.14	1.06	1.02	1.09	1.01	0.98	1.05
Age (years)	1.10	1.10	1.10	1.11	1.11	1.11	1.10	1.10	1.10
Family income (ref. High)									
Low income				1.06	1.04	1.07	1.08	1.07	1.10
Middle–low income				1.17	1.15	1.18	1.14	1.13	1.16
Middle–high income				1.18	1.17	1.19	1.15	1.14	1.16
Educational level (ref. > 12 years)									
10–11 years				1.12	1.10	1.13	1.07	1.06	1.09
≥ 12 years				0.90	0.90	0.91	0.89	0.88	0.90
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.73	1.71	1.76	1.63	1.60	1.66
Blue collar workers				1.38	1.36	1.40	1.34	1.32	1.36
White collar workers				1.15	1.13	1.17	1.14	1.13	1.16
Region of residence (ref. Large cities)									
Southern Sweden				0.94	0.93	0.95	0.99	0.98	1.00
Northern Sweden				0.98	0.97	0.99	1.08	1.07	1.09
Immigrant status (ref. Born in Sweden)				1.05	1.02	1.08	1.06	1.03	1.09
Marital status (ref. Not married)				1.88	1.87	1.90	1.71	1.70	1.73
Number of siblings				1.00	0.99	1.00	1.00	0.99	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.28	1.26	1.30
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.02	2.98	3.05
Hospitalization of diabetes (ref. Non)							1.43	1.41	1.45
Hospitalization of obesity (ref. Non)							1.09	1.06	1.13
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							2.62	2.60	2.64

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4c. Hazard ratio (HR) and 95% confidence interval of mortality in *women*

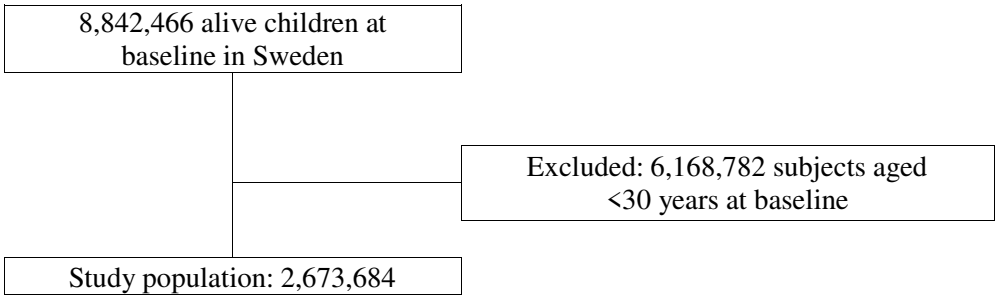
	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.92	0.91	0.94	0.93	0.92	0.95	0.94	0.93	0.95
Two siblings	0.92	0.91	0.94	0.91	0.90	0.93	0.92	0.91	0.94
Three siblings	0.95	0.93	0.96	0.92	0.90	0.93	0.93	0.91	0.95
Four or more children	1.01	0.99	1.03	0.94	0.92	0.95	0.95	0.93	0.96
Age (years)	1.10	1.10	1.10	1.10	1.10	1.10	1.09	1.08	1.09
Family income (ref. High)									
Low income				0.84	0.83	0.86	0.94	0.93	0.96
Middle–low income				1.03	1.01	1.05	1.06	1.04	1.07
Middle–high income				1.05	1.04	1.06	1.05	1.04	1.07
Educational level (ref. > 12 years)									
10–11 years				1.08	1.06	1.10	1.01	1.00	1.03
≥ 12 years				0.85	0.84	0.87	0.82	0.81	0.83
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.97	1.93	2.02	1.88	1.84	1.93
Blue collar workers				1.36	1.33	1.39	1.35	1.32	1.38
White collar workers				1.12	1.10	1.15	1.11	1.09	1.14
Region of residence (ref. Large cities)									
Southern Sweden				1.00	0.99	1.01	1.03	1.02	1.04
Northern Sweden				1.03	1.02	1.05	1.11	1.09	1.12
Immigrant status (ref. Born in Sweden)				0.89	0.86	0.92	0.95	0.92	0.99
Marital status (ref. Not married)				1.63	1.62	1.65	1.48	1.47	1.50
Birth order				1.01	1.00	1.01	1.00	0.99	1.01
Hospitalization of chronic lower respiratory disease (ref. Non)							1.61	1.58	1.63
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.26	3.20	3.32
Hospitalization of diabetes (ref. Non)							1.58	1.56	1.61
Hospitalization of obesity (ref. Non)							0.96	0.93	0.99
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							4.86	4.81	4.91

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4d. Hazard ratio (HR) and 95% confidence interval of mortality in *women*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	0.98	0.96	0.99	0.97	0.96	0.98	0.96	0.95	0.98
Third	1.01	1.00	1.03	1.00	0.98	1.02	0.98	0.96	1.00
Fourth	1.05	1.02	1.08	1.02	0.99	1.05	1.00	0.98	1.03
Fifth+	1.11	1.08	1.15	1.08	1.04	1.12	1.03	0.99	1.07
Age (years)	1.10	1.10	1.10	1.10	1.10	1.10	1.09	1.08	1.09
Family income (ref. High)									
Low income				0.84	0.83	0.86	0.94	0.93	0.96
Middle–low income				1.03	1.02	1.05	1.06	1.04	1.07
Middle–high income				1.05	1.04	1.07	1.05	1.04	1.07
Educational level (ref. > 12 years)									
10–11 years				1.08	1.06	1.10	1.01	0.99	1.03
≥ 12 years				0.85	0.84	0.86	0.82	0.81	0.83
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.98	1.93	2.02	1.88	1.84	1.93
Blue collar workers				1.36	1.33	1.39	1.35	1.32	1.38
White collar workers				1.12	1.10	1.15	1.11	1.09	1.14
Region of residence (ref. Large cities)									
Southern Sweden				1.00	0.99	1.01	1.03	1.02	1.04
Northern Sweden				1.03	1.02	1.05	1.11	1.09	1.12
Immigrant status (ref. Born in Sweden)				0.89	0.86	0.92	0.95	0.92	0.99
Marital status (ref. Not married)				1.63	1.62	1.65	1.48	1.47	1.50
Number of siblings				0.99	0.99	0.99	0.99	0.99	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.61	1.58	1.63
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.26	3.20	3.33
Hospitalization of diabetes (ref. Non)							1.58	1.56	1.61
Hospitalization of obesity (ref. Non)							0.96	0.93	0.99
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							4.86	4.81	4.91

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.


8,842,466 alive children at baseline in Sweden
Excluded: 6,168,782 subjects aged <30 years at baseline
Study population: 2,673,684

Supplementary Table 1a. Distribution of population, number of CVD, CHD, and mortality events in *men*.

	Population		CVD events		CHD events		Mortality events	
	No.	(%)	No.	%	No.	%	No.	%
Total population (%)	1358647		592863		131533		240371	
Age (years)								
30-39	531559	39.1	152615	25.7	25327	19.3	39094	16.3
40-49	554137	40.8	265251	44.7	59088	44.9	96549	40.2
50-58	272951	20.1	174997	29.5	47118	35.8	104728	43.6
Family income								
Low income	334083	24.6	123575	20.8	26649	20.3	47582	19.8
Middle–low income	320284	23.6	135148	22.8	29613	22.5	51243	21.3
Middle–high income	321653	23.7	152589	25.7	35041	26.6	66400	27.6
High income	382627	28.2	181551	30.6	40230	30.6	75146	31.3
Marital status								
Married/cohabiting	809314	59.6	370633	62.5	85212	64.8	124039	51.6
Never married, Widowed, or divorced	549333	40.4	222230	37.5	46321	35.2	116332	48.4
Educational attainment								
≤ 9 years	281207	20.7	146179	24.7	38890	29.6	81428	33.9
10–11 years	173208	12.7	67512	11.4	13955	10.6	26218	10.9
≥ 12 years	904232	66.6	379172	64.0	78688	59.8	132725	55.2
Immigrant status								
Sweden	1322658	97.4	580707	97.9	128732	97.9	235464	98.0
Other countries	35989	2.6	12156	2.1	2801	2.1	4907	2.0
Socioeconomic status								
Farmers/self-employed/others	308729	22.7	129408	21.8	29064	22.1	71960	29.9
Blue collar workers	494090	36.4	217215	36.6	50626	38.5	89989	37.4
White collar workers	351621	25.9	157170	26.5	34594	26.3	52582	21.9
Professionals	204207	15.0	89070	15.0	17249	13.1	25840	10.8
Urban/rural status								
Large cities	495681	36.5	207593	35.0	41153	31.3	85765	35.7
Southern Sweden	618686	45.5	274100	46.2	61581	46.8	108663	45.2
Northern Sweden	244280	18.0	111170	18.8	28799	21.9	45943	19.1
Hospitalization of alcoholism and related liver disease								
No	1275305	93.9	548796	92.6	124051	94.3	202724	84.3
Yes	83342	6.1	44067	7.4	7482	5.7	37647	15.7
Hospitalization of diabetes								
No	1226642	90.3	494000	83.3	104716	79.6	200226	83.3
Yes	132005	9.7	988863	16.7	26817	20.4	40145	16.7

Hospitalization of hypertension								
No	1059935	78.0	294151	49.6	76609	58.2	183958	76.5
Yes	298712	22.0	298712	50.4	54924	41.8	56413	23.5
Hospitalization of obesity								
No	1338892	98.5	577543	97.4	128595	97.8	236644	98.4
Yes	19755	1.5	15320	2.6	2938	2.2	3727	1.6
Hospitalization of chronic lower respiratory disease								
No	1288108	94.8	546393	92.2	120575	91.7	216522	90.1
Yes	70539	5.2	46470	7.8	10958	8.3	23849	9.9
Cancer								
No	1109571	81.7	452446	76.3	103202	78.5	139486	58.0
Yes	249076	18.3	140417	23.7	28331	21.5	100885	42.0
Number of sibling								
Non sibling	214700	15.8	105516	17.8	23671	18.0	50709	21.1
One sibling	443877	32.7	189839	32.0	39729	30.2	73140	30.4
Two siblings	338812	24.9	140361	23.7	30184	22.9	52790	22.0
Three siblings	183067	13.5	77378	13.1	17663	13.4	30266	12.6
Four or more siblings	178191	13.1	79769	13.5	20286	15.4	33466	13.9
Birth order								
First	684765	50.4	318341	53.7	70238	53.4	140857	58.6
Second	402879	29.7	166757	28.1	36654	27.9	62267	25.9
Third	164540	12.1	65853	11.1	14736	11.2	23081	9.6
Fourth	62765	4.6	24729	4.2	5737	4.4	8425	3.5
Fifth+	43698	3.2	17183	2.9	4168	3.2	5741	2.4

Supplementary Table 1b. Distribution of population, number of CVD, CHD, and mortality events in *women.*

	Population		CVD events		CHD events		Mortality events	
	No.	(%)	No.	%	No.	%	No.	%
Total population (%)	1315037		486147		55933		160269	
Age (years)								
30-39	507872	38.6	125326	25.8	9681	17.3	24571	15.3
40-49	537035	40.8	210113	43.2	23738	42.4	64055	40.0
50+	270130	20.5	150708	31.0	22514	40.3	71643	44.7
Family income								
Low income	343296	26.1	100542	20.7	10467	18.7	29723	18.5
Middle–low income	340837	25.9	121716	25.0	13432	24.0	37773	23.6
Middle–high income	347955	26.5	142924	29.4	17579	31.4	50537	31.5
High income	282949	21.5	120965	24.9	14455	25.8	42236	26.4
Marital status								
Married/cohabiting	887258	67.5	331886	68.3	38106	68.1	96533	60.2
Never married, Widowed, or divorced	427779	32.5	154261	31.7	17827	31.9	63736	39.8
Educational attainment								
≤ 9 years	232824	17.7	102037	21.0	15415	27.6	48455	30.2
10–11 years	165367	12.6	60209	12.4	6867	12.3	20489	12.8
≥ 12 years	916846	69.7	323901	66.6	33651	60.2	91325	57.0
Immigrant status								
Sweden	1281472	97.4	476075	97.9	54756	97.9	157515	98.3
Other countries	33565	2.6	10072	2.1	1177	2.1	2754	1.7
Socioeconomic status								
Farmers/self-employed/others	272189	20.7	96279	19.8	12450	22.3	45553	28.4
Blue collar workers	437324	33.3	174549	35.9	21821	39.0	55960	34.9
White collar workers	496782	37.8	178249	36.7	18324	32.8	49169	30.7
Professionals	108742	8.3	37070	7.6	3338	6.0	9587	6.0
Urban/rural status								
Large cities	495097	37.6	173872	35.8	17499	31.3	57794	36.1
Southern Sweden	591636	45.0	223375	45.9	25965	46.4	72872	45.5
Northern Sweden	228304	17.4	88900	18.3	12469	22.3	29603	18.5
Hospitalization of alcoholism and related liver disease								
No	1283561	97.6	471088	96.9	54416	97.3	149212	93.1
Yes	31476	2.4	15059	3.1	1517	2.7	11057	6.9
Hospitalization of diabetes								
No	1234361	93.9	429522	88.4	45537	81.4	139644	87.1

Yes	80676	6.1	56625	11.6	10396	18.6	20625	12.9
Hospitalization of hypertension								
No	1067928	81.2	239038	49.2	31364	56.1	124898	77.9
Yes	247109	18.8	247109	50.8	24569	43.9	35371	22.1
Hospitalization of obesity								
No	1286838	97.9	468228	96.3	54003	96.5	156771	97.8
Yes	28199	2.1	17919	3.7	1930	3.5	3498	2.2
Hospitalization of chronic lower respiratory disease								
No	1226846	93.3	433906	89.3	48084	86.0	137028	85.5
Yes	88191	6.7	52241	10.7	7849	14.0	23241	14.5
Cancer								
No	1051617	80.0	364226	74.9	43617	78.0	70300	43.9
Yes	263420	20.0	121921	25.1	12316	22.0	89969	56.1
Number of sibling								
Non sibling	210121	16.0	87261	17.9	10289	18.4	34521	21.5
One sibling	430315	32.7	154154	31.7	16280	29.1	49132	30.7
Two siblings	324379	24.7	113739	23.4	12500	22.3	34843	21.7
Three siblings	176631	13.4	63871	13.1	7512	13.4	19766	12.3
Four or more siblings	173591	13.2	67122	13.8	9352	16.7	22007	13.7
Birth order								
First	664459	50.5	262015	53.9	30342	54.2	94779	59.1
Second	388391	29.5	136263	28.0	15191	27.2	40984	25.6
Third	159311	12.1	53711	11.0	6231	11.1	15205	9.5
Fourth	60676	4.6	20264	4.2	2379	4.3	5558	3.5
Fifth+	42200	3.2	13894	2.9	1790	3.2	3743	2.3

Supplementary Table 2a. Hazard ratio (HR) and 95% confidence interval of CVD in *men*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.97	0.97	0.98	0.98	0.97	0.98	0.98	0.97	0.99
Two siblings	0.97	0.96	0.98	0.97	0.96	0.97	0.97	0.97	0.98
Three siblings	0.99	0.98	1.00	0.98	0.97	0.99	0.98	0.97	0.99
Four or more children	1.04	1.03	1.05	1.00	0.99	1.01	1.00	0.99	1.01
Age (years)	1.07	1.07	1.07	1.08	1.07	1.08	1.06	1.06	1.06
Family income (ref. High)									
Low income				0.92	0.92	0.93	0.99	0.98	1.00
Middle–low income				1.02	1.01	1.03	1.05	1.04	1.06
Middle–high income				1.04	1.03	1.05	1.05	1.04	1.06
Educational level (ref. > 12 years)									
10–11 years				1.11	1.10	1.12	1.06	1.05	1.07
≥ 12 years				1.00	1.00	1.01	1.00	0.99	1.00
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.22	1.21	1.23	1.17	1.16	1.18
Blue collar workers				1.15	1.14	1.16	1.09	1.08	1.10
White collar workers				1.08	1.07	1.08	1.04	1.04	1.05
Region of residence (ref. Large cities)									
Southern Sweden				1.00	1.00	1.01	1.03	1.02	1.03
Northern Sweden				1.04	1.03	1.05	1.05	1.04	1.06
Immigrant status (ref. Born in Sweden)				0.95	0.93	0.97	0.96	0.95	0.98
Marital status (ref. Not married)				1.18	1.17	1.19	1.17	1.16	1.18
Birth order				1.01	1.01	1.01	1.01	1.01	1.02
Hospitalization of chronic lower respiratory disease (ref. Non)							1.26	1.25	1.28
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.74	1.73	1.76
Hospitalization of diabetes (ref. Non)							1.39	1.38	1.40
Hospitalization of obesity (ref. Non)							1.37	1.35	1.40
Hospitalization of hypertension (ref. Non)							3.72	3.70	3.74
Cancer (ref. Non)							1.36	1.35	1.36

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 2b. Hazard ratio (HR) and 95% confidence interval of CVD in *men*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Birth order (ref. First birth)									
Second	0.99	0.99	1.00	0.99	0.98	1.00	1.00	1.00	1.01
Third	1.02	1.01	1.03	1.01	1.00	1.02	1.02	1.02	1.03
Fourth	1.05	1.03	1.06	1.03	1.01	1.04	1.04	1.02	1.05
Fifth+	1.10	1.08	1.12	1.07	1.05	1.08	1.07	1.05	1.09
Age (years)	1.07	1.07	1.07	1.08	1.07	1.08	1.06	1.06	1.06
Family income (ref. High)									
Low income				0.92	0.92	0.93	0.99	0.98	1.00
Middle–low income				1.02	1.01	1.03	1.05	1.04	1.06
Middle–high income				1.04	1.03	1.05	1.05	1.04	1.06
Educational level (ref. > 12 years)									
10–11 years				1.11	1.10	1.12	1.06	1.05	1.07
≥ 12 years				1.00	1.00	1.01	1.00	0.99	1.00
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.22	1.21	1.23	1.17	1.16	1.18
Blue collar workers				1.15	1.14	1.16	1.09	1.08	1.10
White collar workers				1.08	1.07	1.08	1.04	1.04	1.05
Region of residence (ref. Large cities)									
Southern Sweden				1.00	1.00	1.01	1.03	1.02	1.03
Northern Sweden				1.04	1.03	1.05	1.05	1.04	1.06
Immigrant status (ref. Born in Sweden)				0.95	0.93	0.97	0.97	0.95	0.98
Marital status (ref. Not married)				1.18	1.17	1.19	1.17	1.16	1.18
Number of siblings				1.00	1.00	1.00	1.00	1.00	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.26	1.25	1.28
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.74	1.73	1.76
Hospitalization of diabetes (ref. Non)							1.39	1.38	1.40
Hospitalization of obesity (ref. Non)							1.37	1.35	1.40
Hospitalization of hypertension (ref. Non)							3.72	3.70	3.74
Cancer (ref. Non)							1.36	1.35	1.36

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 2c. Hazard ratio (HR) and 95% confidence interval of CVD in *women*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.98	0.97	0.98	0.98	0.97	0.98	0.98	0.98	0.99
Two siblings	0.99	0.98	0.99	0.98	0.97	0.99	0.99	0.98	1.00
Three siblings	1.01	1.00	1.02	1.00	0.99	1.01	1.00	0.99	1.01
Four or more children	1.06	1.05	1.07	1.03	1.02	1.04	1.01	1.00	1.03
Age (years)	1.06	1.06	1.07	1.06	1.06	1.06	1.04	1.04	1.04
Family income (ref. High)									
Low income				0.87	0.86	0.87	0.95	0.94	0.96
Middle–low income				1.01	1.00	1.02	1.04	1.03	1.05
Middle–high income				1.02	1.01	1.03	1.03	1.02	1.03
Educational level (ref. > 12 years)									
10–11 years				1.13	1.12	1.14	1.08	1.06	1.09
≥ 12 years				1.04	1.03	1.05	1.03	1.02	1.04
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.30	1.28	1.31	1.20	1.19	1.22
Blue collar workers				1.25	1.24	1.27	1.12	1.11	1.13
White collar workers				1.08	1.07	1.10	1.03	1.02	1.04
Region of residence (ref. Large cities)									
Southern Sweden				1.03	1.03	1.04	1.03	1.03	1.04
Northern Sweden				1.06	1.06	1.07	1.04	1.03	1.05
Immigrant status (ref. Born in Sweden)				0.97	0.96	0.99	0.98	0.96	1.00
Marital status (ref. Not married)				1.13	1.12	1.14	1.10	1.09	1.11
Birth order				1.00	1.00	1.01	1.01	1.01	1.01
Hospitalization of chronic lower respiratory disease (ref. Non)							1.38	1.36	1.39
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.67	1.65	1.69
Hospitalization of diabetes (ref. Non)							1.38	1.37	1.39
Hospitalization of obesity (ref. Non)							1.32	1.30	1.34
Hospitalization of hypertension (ref. Non)							4.86	4.83	4.89
Cancer (ref. Non)							1.62	1.61	1.63

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 2d. Hazard ratio (HR) and 95% confidence interval of CVD in *women*, using multivariable competing risk survival analysis

	Model 1			Model 2			Model 3		
	HR*	95% CI		HR*	95% CI		HR*	95% CI	
Birth order (ref. First birth)									
Second	1.00	0.99	1.01	0.99	0.98	1.00	1.01	1.00	1.02
Third	1.03	1.02	1.04	1.00	0.99	1.01	1.02	1.01	1.03
Fourth	1.06	1.04	1.07	1.01	1.00	1.03	1.04	1.02	1.05
Fifth+	1.09	1.07	1.10	1.01	0.99	1.03	1.05	1.03	1.07
Age (years)	1.07	1.07	1.07	1.06	1.06	1.06	1.04	1.04	1.04
Family income (ref. High)									
Low income				0.87	0.86	0.87	0.95	0.94	0.96
Middle–low income				1.01	1.00	1.02	1.04	1.03	1.05
Middle–high income				1.02	1.01	1.03	1.03	1.02	1.03
Educational level (ref. > 12 years)									
10–11 years				1.13	1.12	1.14	1.08	1.06	1.09
≥ 12 years				1.04	1.03	1.05	1.03	1.02	1.04
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.30	1.28	1.31	1.21	1.19	1.22
Blue collar workers				1.26	1.24	1.27	1.12	1.11	1.13
White collar workers				1.09	1.07	1.10	1.03	1.02	1.05
Region of residence (ref. Large cities)									
Southern Sweden				1.03	1.03	1.04	1.03	1.03	1.04
Northern Sweden				1.06	1.06	1.07	1.04	1.03	1.05
Immigrant status (ref. Born in Sweden)				0.97	0.96	0.99	0.98	0.96	1.00
Marital status (ref. Not married)				1.13	1.13	1.14	1.10	1.09	1.11
Number of siblings				1.01	1.01	1.01	1.00	1.00	1.01
Hospitalization of chronic lower respiratory disease (ref. Non)							1.38	1.36	1.39
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.67	1.65	1.69
Hospitalization of diabetes (ref. Non)							1.38	1.37	1.39
Hospitalization of obesity (ref. Non)							1.32	1.30	1.34
Hospitalization of hypertension (ref. Non)							4.86	4.83	4.89
Cancer (ref. Non)							1.62	1.61	1.63

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.
*: Multivariable competing risk survival analysis

Supplementary Table 3a. Hazard ratio (HR) and 95% confidence interval of CHD in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	1.00	0.98	1.02	0.99	0.97	1.01	0.99	0.97	1.01
Two siblings	1.04	1.03	1.06	1.00	0.98	1.02	1.01	0.99	1.03
Three siblings	1.12	1.10	1.14	1.04	1.02	1.06	1.04	1.02	1.07
Four or more children	1.27	1.25	1.30	1.10	1.08	1.12	1.10	1.07	1.12
Age (years)	1.08	1.08	1.08	1.08	1.08	1.08	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.93	0.91	0.94	0.96	0.95	0.98
Middle–low income				1.00	0.98	1.01	1.02	1.00	1.03
Middle–high income				1.01	1.00	1.03	1.02	1.00	1.03
Educational level (ref. > 12 years)									
10–11 years				1.05	1.03	1.07	1.04	1.02	1.07
≥ 12 years				0.94	0.93	0.95	0.95	0.94	0.96
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.23	1.20	1.25	1.18	1.16	1.21
Blue collar workers				1.26	1.24	1.28	1.21	1.19	1.23
White collar workers				1.18	1.16	1.20	1.15	1.13	1.17
Region of residence (ref. Large cities)									
Southern Sweden				1.11	1.10	1.12	1.12	1.11	1.14
Northern Sweden				1.32	1.30	1.34	1.31	1.29	1.33
Immigrant status (ref. Born in Sweden)				1.09	1.05	1.13	1.10	1.06	1.14
Marital status (ref. Not married)				1.00	0.99	1.01	0.99	0.98	1.01
Birth order				1.05	1.04	1.05	1.05	1.05	1.06
Hospitalization of chronic lower respiratory disease (ref. Non)							1.29	1.26	1.31
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.01	0.99	1.04
Hospitalization of diabetes (ref. Non)							1.75	1.73	1.78
Hospitalization of obesity (ref. Non)							1.13	1.09	1.17
Hospitalization of hypertension (ref. Non)							1.86	1.84	1.88
Cancer (ref. Non)							0.91	0.89	0.92

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 3b. Hazard ratio (HR) and 95% confidence interval of CHD in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	1.09	1.08	1.10	1.06	1.05	1.07	1.08	1.06	1.09
Third	1.19	1.17	1.21	1.11	1.09	1.13	1.13	1.11	1.15
Fourth	1.28	1.25	1.32	1.15	1.12	1.19	1.17	1.14	1.21
Fifth+	1.44	1.39	1.48	1.22	1.17	1.26	1.23	1.19	1.28
Age (years)	1.08	1.08	1.09	1.08	1.08	1.08	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.93	0.91	0.94	0.96	0.95	0.98
Middle–low income				1.00	0.98	1.01	1.02	1.00	1.03
Middle–high income				1.01	1.00	1.02	1.02	1.00	1.03
Educational level (ref. > 12 years)									
10–11 years				1.05	1.03	1.08	1.05	1.03	1.07
≥ 12 years				0.94	0.93	0.95	0.95	0.94	0.97
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.23	1.20	1.25	1.18	1.16	1.21
Blue collar workers				1.26	1.24	1.28	1.21	1.19	1.23
White collar workers				1.18	1.16	1.20	1.15	1.13	1.17
Region of residence (ref. Large cities)									
Southern Sweden				1.11	1.10	1.13	1.12	1.11	1.14
Northern Sweden				1.32	1.30	1.34	1.31	1.29	1.33
Immigrant status (ref. Born in Sweden)				1.09	1.05	1.13	1.10	1.06	1.14
Marital status (ref. Not married)				1.00	0.99	1.01	0.99	0.98	1.01
Number of siblings				1.02	1.02	1.02	1.02	1.02	1.02
Hospitalization of chronic lower respiratory disease (ref. Non)							1.29	1.26	1.31
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.01	0.99	1.04
Hospitalization of diabetes (ref. Non)							1.75	1.73	1.78
Hospitalization of obesity (ref. Non)							1.13	1.09	1.17
Hospitalization of hypertension (ref. Non)							1.86	1.84	1.88
Cancer (ref. Non)							0.91	0.89	0.92

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 3c. Hazard ratio (HR) and 95% confidence interval of CHD in *women*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.99	0.97	1.02	0.98	0.96	1.01	0.99	0.97	1.02
Two siblings	1.07	1.04	1.10	1.03	1.00	1.05	1.03	1.00	1.06
Three siblings	1.17	1.13	1.20	1.08	1.04	1.11	1.07	1.04	1.11
Four or more children	1.40	1.36	1.44	1.20	1.16	1.24	1.17	1.13	1.21
Age (years)	1.09	1.09	1.09	1.09	1.08	1.09	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.85	0.83	0.88	0.91	0.88	0.93
Middle–low income				1.00	0.98	1.03	1.00	0.98	1.03
Middle–high income				1.02	1.00	1.05	1.02	0.99	1.04
Educational level (ref. > 12 years)									
10–11 years				1.07	1.04	1.10	1.06	1.03	1.09
≥ 12 years				0.92	0.90	0.94	0.94	0.92	0.96
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.52	1.46	1.59	1.37	1.31	1.42
Blue collar workers				1.47	1.42	1.53	1.33	1.28	1.38
White collar workers				1.19	1.14	1.23	1.14	1.10	1.18
Region of residence (ref. Large cities)									
Southern Sweden				1.14	1.12	1.16	1.15	1.13	1.17
Northern Sweden				1.40	1.37	1.44	1.38	1.34	1.41
Immigrant status (ref. Born in Sweden)				1.13	1.07	1.20	1.13	1.07	1.20
Marital status (ref. Not married)				1.12	1.10	1.14	1.08	1.06	1.10
Birth order				1.04	1.03	1.05	1.05	1.04	1.06
Hospitalization of chronic lower respiratory disease (ref. Non)							1.69	1.65	1.73
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.17	1.11	1.23
Hospitalization of diabetes (ref. Non)							2.20	2.15	2.25
Hospitalization of obesity (ref. Non)							1.11	1.06	1.17
Hospitalization of hypertension (ref. Non)							2.22	2.18	2.26
Cancer (ref. Non)							0.94	0.93	0.96

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 3d. Hazard ratio (HR) and 95% confidence interval of CHD in *women*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	1.10	1.07	1.12	1.05	1.02	1.07	1.07	1.05	1.09
Third	1.24	1.21	1.28	1.11	1.08	1.14	1.14	1.11	1.18
Fourth	1.33	1.27	1.38	1.11	1.06	1.16	1.14	1.09	1.20
Fifth+	1.56	1.48	1.63	1.17	1.11	1.24	1.22	1.15	1.29
Age (years)	1.09	1.09	1.09	1.09	1.08	1.09	1.07	1.07	1.07
Family income (ref. High)									
Low income				0.85	0.83	0.88	0.91	0.88	0.93
Middle–low income				1.00	0.98	1.03	1.01	0.98	1.03
Middle–high income				1.02	1.00	1.05	1.02	0.99	1.04
Educational level (ref. > 12 years)									
10–11 years				1.07	1.04	1.10	1.06	1.03	1.09
≥ 12 years				0.92	0.90	0.94	0.94	0.92	0.96
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.52	1.46	1.59	1.37	1.31	1.42
Blue collar workers				1.47	1.42	1.53	1.33	1.28	1.38
White collar workers				1.19	1.14	1.23	1.14	1.10	1.18
Region of residence (ref. Large cities)									
Southern Sweden				1.14	1.12	1.17	1.15	1.13	1.17
Northern Sweden				1.40	1.37	1.44	1.38	1.34	1.41
Immigrant status (ref. Born in Sweden)				1.13	1.07	1.20	1.13	1.07	1.20
Marital status (ref. Not married)				1.12	1.10	1.14	1.08	1.06	1.10
Number of siblings				1.04	1.03	1.04	1.03	1.03	1.04
Hospitalization of chronic lower respiratory disease (ref. Non)							1.69	1.65	1.73
Hospitalization of alcoholisms and related liver disease (ref. Non)							1.17	1.11	1.23
Hospitalization of diabetes (ref. Non)							2.20	2.15	2.25
Hospitalization of obesity (ref. Non)							1.11	1.06	1.17
Hospitalization of hypertension (ref. Non)							2.22	2.18	2.26
Cancer (ref. Non)							0.94	0.93	0.96

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4a. Hazard ratio (HR) and 95% confidence interval of mortality in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.91	0.90	0.92	0.92	0.91	0.93	0.93	0.92	0.94
Two siblings	0.92	0.91	0.93	0.91	0.90	0.92	0.91	0.90	0.92
Three siblings	0.96	0.94	0.97	0.93	0.92	0.94	0.93	0.92	0.94
Four or more children	1.03	1.01	1.04	0.96	0.94	0.97	0.96	0.94	0.97
Age (years)	1.10	1.10	1.10	1.11	1.11	1.11	1.10	1.10	1.10
Family income (ref. High)									
Low income				1.05	1.04	1.07	1.08	1.07	1.10
Middle–low income				1.17	1.15	1.18	1.14	1.13	1.15
Middle–high income				1.18	1.17	1.19	1.15	1.14	1.16
Educational level (ref. > 12 years)									
10–11 years				1.12	1.10	1.13	1.08	1.06	1.09
≥ 12 years				0.91	0.90	0.91	0.89	0.88	0.90
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.73	1.71	1.76	1.63	1.60	1.65
Blue collar workers				1.38	1.36	1.40	1.34	1.32	1.36
White collar workers				1.15	1.13	1.17	1.14	1.12	1.16
Region of residence (ref. Large cities)									
Southern Sweden				0.94	0.93	0.95	0.99	0.98	1.00
Northern Sweden				0.98	0.97	0.99	1.08	1.07	1.09
Immigrant status (ref. Born in Sweden)				1.04	1.01	1.07	1.06	1.03	1.09
Marital status (ref. Not married)				1.88	1.87	1.90	1.71	1.70	1.73
Birth order				1.00	1.00	1.01	0.99	0.99	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.28	1.26	1.30
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.02	2.98	3.05
Hospitalization of diabetes (ref. Non)							1.43	1.41	1.45
Hospitalization of obesity (ref. Non)							1.09	1.06	1.13
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							2.62	2.60	2.65

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4b. Hazard ratio (HR) and 95% confidence interval of mortality in *men*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	0.98	0.97	0.99	0.97	0.96	0.98	0.96	0.95	0.97
Third	1.01	0.99	1.02	0.99	0.98	1.01	0.98	0.96	0.99
Fourth	1.04	1.01	1.06	1.00	0.98	1.03	0.98	0.95	1.00
Fifth+	1.11	1.08	1.14	1.06	1.02	1.09	1.01	0.98	1.05
Age (years)	1.10	1.10	1.10	1.11	1.11	1.11	1.10	1.10	1.10
Family income (ref. High)									
Low income				1.06	1.04	1.07	1.08	1.07	1.10
Middle–low income				1.17	1.15	1.18	1.14	1.13	1.16
Middle–high income				1.18	1.17	1.19	1.15	1.14	1.16
Educational level (ref. > 12 years)									
10–11 years				1.12	1.10	1.13	1.07	1.06	1.09
≥ 12 years				0.90	0.90	0.91	0.89	0.88	0.90
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.73	1.71	1.76	1.63	1.60	1.66
Blue collar workers				1.38	1.36	1.40	1.34	1.32	1.36
White collar workers				1.15	1.13	1.17	1.14	1.13	1.16
Region of residence (ref. Large cities)									
Southern Sweden				0.94	0.93	0.95	0.99	0.98	1.00
Northern Sweden				0.98	0.97	0.99	1.08	1.07	1.09
Immigrant status (ref. Born in Sweden)				1.05	1.02	1.08	1.06	1.03	1.09
Marital status (ref. Not married)				1.88	1.87	1.90	1.71	1.70	1.73
Number of siblings				1.00	0.99	1.00	1.00	0.99	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.28	1.26	1.30
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.02	2.98	3.05
Hospitalization of diabetes (ref. Non)							1.43	1.41	1.45
Hospitalization of obesity (ref. Non)							1.09	1.06	1.13
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							2.62	2.60	2.64

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4c. Hazard ratio (HR) and 95% confidence interval of mortality in *women*

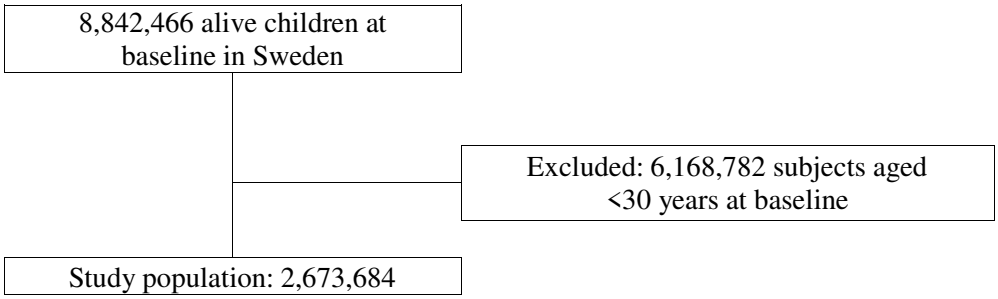
	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Number of siblings (ref. No sibling)									
One sibling	0.92	0.91	0.94	0.93	0.92	0.95	0.94	0.93	0.95
Two siblings	0.92	0.91	0.94	0.91	0.90	0.93	0.92	0.91	0.94
Three siblings	0.95	0.93	0.96	0.92	0.90	0.93	0.93	0.91	0.95
Four or more children	1.01	0.99	1.03	0.94	0.92	0.95	0.95	0.93	0.96
Age (years)	1.10	1.10	1.10	1.10	1.10	1.10	1.09	1.08	1.09
Family income (ref. High)									
Low income				0.84	0.83	0.86	0.94	0.93	0.96
Middle–low income				1.03	1.01	1.05	1.06	1.04	1.07
Middle–high income				1.05	1.04	1.06	1.05	1.04	1.07
Educational level (ref. > 12 years)									
10–11 years				1.08	1.06	1.10	1.01	1.00	1.03
≥ 12 years				0.85	0.84	0.87	0.82	0.81	0.83
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.97	1.93	2.02	1.88	1.84	1.93
Blue collar workers				1.36	1.33	1.39	1.35	1.32	1.38
White collar workers				1.12	1.10	1.15	1.11	1.09	1.14
Region of residence (ref. Large cities)									
Southern Sweden				1.00	0.99	1.01	1.03	1.02	1.04
Northern Sweden				1.03	1.02	1.05	1.11	1.09	1.12
Immigrant status (ref. Born in Sweden)				0.89	0.86	0.92	0.95	0.92	0.99
Marital status (ref. Not married)				1.63	1.62	1.65	1.48	1.47	1.50
Birth order				1.01	1.00	1.01	1.00	0.99	1.01
Hospitalization of chronic lower respiratory disease (ref. Non)							1.61	1.58	1.63
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.26	3.20	3.32
Hospitalization of diabetes (ref. Non)							1.58	1.56	1.61
Hospitalization of obesity (ref. Non)							0.96	0.93	0.99
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							4.86	4.81	4.91

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.

Supplementary Table 4d. Hazard ratio (HR) and 95% confidence interval of mortality in *women*

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Birth order (ref. First birth)									
Second	0.98	0.96	0.99	0.97	0.96	0.98	0.96	0.95	0.98
Third	1.01	1.00	1.03	1.00	0.98	1.02	0.98	0.96	1.00
Fourth	1.05	1.02	1.08	1.02	0.99	1.05	1.00	0.98	1.03
Fifth+	1.11	1.08	1.15	1.08	1.04	1.12	1.03	0.99	1.07
Age (years)	1.10	1.10	1.10	1.10	1.10	1.10	1.09	1.08	1.09
Family income (ref. High)									
Low income				0.84	0.83	0.86	0.94	0.93	0.96
Middle–low income				1.03	1.02	1.05	1.06	1.04	1.07
Middle–high income				1.05	1.04	1.07	1.05	1.04	1.07
Educational level (ref. > 12 years)									
10–11 years				1.08	1.06	1.10	1.01	0.99	1.03
≥ 12 years				0.85	0.84	0.86	0.82	0.81	0.83
Socioeconomic status (ref. professionals)									
Farmers/self-employed/others				1.98	1.93	2.02	1.88	1.84	1.93
Blue collar workers				1.36	1.33	1.39	1.35	1.32	1.38
White collar workers				1.12	1.10	1.15	1.11	1.09	1.14
Region of residence (ref. Large cities)									
Southern Sweden				1.00	0.99	1.01	1.03	1.02	1.04
Northern Sweden				1.03	1.02	1.05	1.11	1.09	1.12
Immigrant status (ref. Born in Sweden)				0.89	0.86	0.92	0.95	0.92	0.99
Marital status (ref. Not married)				1.63	1.62	1.65	1.48	1.47	1.50
Number of siblings				0.99	0.99	0.99	0.99	0.99	1.00
Hospitalization of chronic lower respiratory disease (ref. Non)							1.61	1.58	1.63
Hospitalization of alcoholisms and related liver disease (ref. Non)							3.26	3.20	3.33
Hospitalization of diabetes (ref. Non)							1.58	1.56	1.61
Hospitalization of obesity (ref. Non)							0.96	0.93	0.99
Hospitalization of hypertension (ref. Non)							0.66	0.65	0.67
Cancer (ref. Non)							4.86	4.81	4.91

Model 1. Adjusted for age at start; Model 2. Adjusted for age at start and individual characteristics; Model 3. Model 2 + comorbidities.


8,842,466 alive children at baseline in Sweden
Excluded: 6,168,782 subjects aged <30 years at baseline
Study population: 2,673,684

Number and relative age of siblings is linked to risk of cardiovascular events

First-born children have a lower risk of cardiovascular events, but having lots of siblings is associated with an increased risk

First-born children have a lower risk of cardiovascular events such as heart attacks and strokes than brothers and sisters born later, but people who are part of a large family with many siblings have an increased risk of these events, suggests the results of a large population study in Sweden, published in the online journal ***BMJ Open.***

It is well-known that family history – the health of parents and grandparents – has an impact on a person's health, including their risk of cardiovascular events, but now there is growing interest in what influence the make-up of a person's immediate family – the number and age of siblings – might have.

The authors accessed data on 1.36 million men and 1.32 million women born between 1932 and 1960 and aged 30–58 years in 1990 from the Multiple-Generation Register in Sweden. Data on fatal and non-fatal cardiovascular and coronary events over the next 25 years were retrieved from national registers.

Analysis of the data showed that first-borns had a lower risk of non-fatal cardiovascular and coronary events than siblings born later. First-born men had a higher risk of death than second and third-born siblings, while first-born women had a higher risk of death than second-born siblings, but equal to further siblings.

When family size was looked at, compared with men with no siblings, men with one or two siblings had a lower risk of cardiovascular events, while those with four or more siblings had a higher risk.

Similarly, compared with men with no siblings, men with more than one sibling had a lower risk of death, while those with three or more siblings had an increased risk of coronary events.

A similar pattern was seen in women. Compared with those with no siblings, women with three or more siblings had an increased risk of cardiovascular events, while those with two or more siblings had an increased risk of coronary events. Women with one or more siblings had a lower risk of death.

This is an observational study, and as such, can't establish cause. The authors also highlight some limitations, including that the Swedish registers included no information on diagnostic procedures and there were no data on lifestyle factors, such as body mass index, smoking and diet.

However, socioeconomic status, obesity, diabetes, chronic lung disease (COPD) and alcoholism and related liver disorders were taken into account. They also note that some of their findings conflict with those from previous studies.

The authors point out that, as policies to support families and the number of children currently vary widely between countries, their findings could have implications for public health.

“More research is needed to understand the links between sibling number and rank with health outcomes,” they say. “Future research should be directed to find biological or social mechanisms linking the status of being first born to lower risk of cardiovascular disease, as indicated by our observational findings.”