Cardiovascular disease in individuals with a history of out-of-home care: a Swedish national cohort study

Anders Hjern,[1,2] Lars Brännström,[3] Bo Vinnerljung,[3] Philipp Frank,[4] G. David Batty[4]

[1]Centre for Health Equity Studies, Karolinska Institutet/Stockholm University, Stockholm, Sweden
[2]Clinical Epidemiology/Department of Medicine, Karolinska Institutet, Stockholm, Sweden
[3]Department of Social Work, Stockholm University, S 106 91 Stockholm, Sweden
[4]Department of Epidemiology and Public Health, University College London, London, UK

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Corresponding author: Anders Hjern, Centre for Health Equity Studies, Karolinska Institute/Stockholm University, 106 91 Stockholm, Sweden. E-mail: anders.hjern@ki.se

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Abstract

Background: Individuals with a history of out-of-home care in childhood experience elevated rates of mortality from all-causes and suicide in adulthood but the relationship with chronic disease is unknown. We examined the association between out-of-home care and cardiovascular disease (CVD) in a large cohort study and, in the women, explored how care is embodied to give rise to CVD.

Methods: This is a cohort study generated from linkage of a range of Swedish national registers. Born 1972-1981, 447,516 men (12711 with a care background) and 415,910 women (11926 with a care background) were followed between care graduation at age 18 and up to age 48 years for hospitalisations and death. A subgroup of 377,500 women (87% of the birth cohort) were linked to a maternity database which yielded data on adult cigarette smoking and metabolic risk factors.

Results: A maximum of 30 years of health surveillance gave rise to 5519 CVD events (2049 in women). After adjusting for the confounding factors of year of birth and maternal education, men (hazard ratio 1.95 [95% CI 1.68-2.25]) and women (1.80 [1.48-2.18]) with a history of out-of-home care in childhood had around a doubling of CVD risk in adulthood compared with general population controls. Separate presentations of CVD, such as myocardial infarction and stroke, revealed similar magnitudes of association with care. In women who had given birth, adjustment for the mediating variables of adult smoking status (1.41 [1.12-1.78]) and educational performance (1.57 [1.25-1.98]), but not metabolic risk factors (1.98 [1.24-3.15]), led to marked attenuation in CVD risk.

Conclusion: In the present study, men and women separated from their family of origin in early life experienced an increased burden of CVD as adults. Results for women suggest that targeting health behaviours, teenage pregnancy, and educational performance in these groups may potentially mitigate risk. These findings add to the array of adverse adult health outcomes seemingly experienced following care graduation.

Results in Context

Evidence before this study

It is becoming increasingly well established that people who experience periods of state (out-of-home) care in childhood have an elevated risk of unfavourable social, economic, and psychological outcomes in adult life, some of which are themselves known risk factors for CVD. Moreover, higher rates of mortality from all-causes relative to general population controls have also been reported, so raising the suggestion that care is linked to later chronic disease. A search of PubMed and Embase using a variety of terms for out-of-home care (e.g., state care, public care, looked-after) and chronic disease (cardiovascular disease, heart disease, stroke, cancer) did not identify any relevant studies.

Added value of the study

For the first time to our knowledge, we examined the association between a history of out-of-home care in early life and adult CVD. In a large cohort of men and women generated from a series of linkages to administrative datasets, after taking into account confounding factors, we found that those with a history of childhood out-of-home care experienced a doubling of the risk of adult CVD. For women for whom we had mediating data from adulthood, there was a suggestion that this effect was explained by low maternal age at birth of offspring, cigarette smoking, and socioeconomic disadvantage in later life.

Implications of all the available evidence

Interventions designed to target the prevention of smoking, teenage pregnancy, and sub-optimal educational achievement might have potential for CVD risk reduction in women with a pre-adult record of out-of-home care.

Introduction

The prevalence of out-of-home care, also known as state care, public care, being looked after, or substitute care, has increased in several countries in recent years with as many as 13% of children having such a history.[1] While the fundamental purpose of out-of-home care is to improve the quality of life of individuals separated from their family of origin, as adults, relative to their unexposed counterparts, this group in fact has a higher burden of negative health outcomes. A recent meta-analysis of prospective cohort studies, for instance, found that people with a history of childhood care experienced a doubling in the rate of total mortality compared with same-aged, unexposed peers, while there was tripling in the occurrence of completed suicide.[1]

In that meta-analysis there were too few studies to examine the impact of out-of-home care on other health outcomes, including chronic conditions such as cardiovascular disease (CVD). Owing to the tendency for people with a care history to have a higher prevalence of health-related outcomes in later life that are also CVD risk factors in their own right, there is a reasonable prima facie case to anticipate such a relationship. These include engaging in unfavourable health behaviours such as smoking, heavy alcohol intake, and illicit drug use; [2,3] experiencing greater socioeconomic disadvantage, as evidenced by unemployment and lower occupational prestige alongside the chronic psychosocial stress that may result;[4] having more basic educational qualifications;[5] and showing less beneficial levels of metabolic, immune, neuroendocrine, and autonomic functioning. [6]

The present analyses of data from a cohort study of 850,000 Swedish men and women have two purposes. First, for the first time to our knowledge, to test if individuals with a record of care in childhood have a higher risk of later CVD relative to unexposed population controls, and explore any sex-differentials. Second, if higher rates of adult CVD are apparent in people with a care history, to examine if these are embodied by adverse health behaviours, metabolic factors, early pregnancy, or educational performance.

Methods

We used a series of linked population-based, national Swedish registers to generate a cohort study. The linkage process is based on the unique personal identity number assigned to all Swedish residents at birth (or time of immigration) which ensures that the linkage has complete coverage. The study was approved by the Swedish Ethical Review Authority in 2020 (#2020–00250).

Assessment of exposure and confounding factors

The study population comprised 447,516 men and 415,910 women born in Sweden between 1972 and 1981 who were alive and resident in the country on their 18th birthday and had no record of emigration according to the Register of the Total Population.[7] The study population was linked to records of out-of-home care via the Swedish Child Welfare Register.[8] Any care record, regardless of length of stay, denoted exposure to care; the remainder represented the group of general population controls. The Multi-Generation Register[9] provided data on the birth mother for whom information on country of birth was retrieved from the Register of the Total Population. Her educational attainment, our proxy for the socioeconomic background of the birth family, was obtained from the Longitudinal Integration Database for Health Insurance and Labour Market Studies for 1990.[10] Missing data for this variable denoted school placement in an institute for people with intellectual disability and was therefore recoded as the lowest category (≤9 years).

Assessment of mediator variables

Women with a minimum of one live birth between 1986 and 2017, were linked to the Swedish Medical Birth Register national maternity database.[11] In this dataset a live birth is denoted the birth of a live child, or a miscarriage after at least 28 weeks of pregnancy. This registry also captured data on cigarette smoking habits and metabolic risk for 377,500 (87%) of women in the present birth cohort. Smoking habits were reported to midwives during the first visit to the maternity clinic in early pregnancy. During the pregnancy and after the delivery, midwives and physicians recorded any medical complications on the Swedish Medical Birth register. Based on these diagnoses, we created the following metabolic indices: obesity (ICD-

9 278 and ICD-10 E66), gestational hypertension (ICD 9 642D, 642X and ICD-10 O13, 014, 016), pregestational hypertension (ICD 9 642C and ICD-10 O10), gestational diabetes (ICD-9 648W and ICD-10 O244) and pregestational diabetes (ICD-9 648A and ICD-10 O240, O241, O242, O243). Lastly, school performance of the index mothers from the final compulsory school year in Sweden (age 16) was also extracted from The National School Register for the study population.[10] The average grade point was categorized into quintiles (quintile 1 denotes lowest scoring group).

Ascertainment of cardiovascular disease

Cardiovascular disease (CVD) events were identified using registers for hospitalisations and deaths.[12,13] CVD was coded according to the International Classification of Diseases (ICD) as myocardial infarction (ICD-9 410-412[14] or ICD-10 I21-I23[15]), other coronary disease (ICD-9 413-414, or ICD-10 I20, I24-I25) and stroke (ICD-9 430-439, ICD-10 I60-I69) as a main or contributory diagnosis in the inpatient section of the Patient register, or as an underlying cause of death in the Cause of death register.[16] The study population was followed using these two registers from their 18th birthday until December 31 2020 when they were aged 39-48 years.

Statistical analysis

With there being no violation of the proportional hazards assumption apparent using Kaplan-Meier curves, hazard ratios with accompanying 95% confidence intervals for out-of-home care were estimated using Cox proportional hazards regression.[17] In these analyses, CVD in aggregate and its various presentations were the outcomes of interest. Follow-up time was calculated from the 18th birthday until the first hospital admission for a CVD event, date of death, or December 2020 – whichever came first. In the only subgroup analyses, we examined the relationship of characteristics of care (direction and age at entry) with CVD risk. In doing so, our cohort for analyses was study members with a history of care. All statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS Statistics version 27.0, [SPSS, Inc., IBM Corp., Armonk, NY, USA]).

Role of the funding source

This report had no direct funding. All authors had final responsibility for the decision to submit for publication.

Results

Of the 447,516 men, 12711 had a history of out-of-home care, and in the 415,910 women there were 11926 so exposed. The socio-demographic characteristics of study members with a care history relative to general population controls is presented in Table 1. While year and maternal country of birth were essentially the same in individuals with and without a record of out-of-home care, between-group differences in socioeconomic characteristics were stark. Thus, mothers of male and female care recipients were twice as likely to have belonged to the lowest educational attainment category relative to the general population. Similarly, the proportion of women from care background who had the lowest school grades in the final year of mandatory education was three times higher than the general population and, for men, it was more than double.

A maximum of 30 years of mortality and hospital surveillance gave rise to 5519 CVD events (2049 in women). In figure 1 and supplemental table 1, we show the relationship of a history of out-of-home care in childhood with CVD and its different presentations in adulthood. After adjusting for the confounding factors of year of birth and maternal education, men (hazard ratio 1.95 [95% CI 1.68-2.25]) and women (1.80 [1.48-2.18]) with a history of out-of-home care in childhood had around a doubling of CVD risk in adulthood compared with general population controls. This pattern of association across the sexes was essentially the same irrespective of separate presentations of CVD. Thus, for the two major presentations of cardiovascular disease of stroke (1.83 [1.48-2.26] in men; 1.68 [1.32-2.15] in women – p-value for interaction by sex = 0.43) and myocardial infarction (1.98 [1.56-2.51] in men; 1.61 [1.06-2.45] in women – p-value = 0.46), relationships with early life care were similar. An exception was the care–cardiovascular death gradient which, while directionally consist, was stronger in women (p-value 0.024); these analyses

were, however, based on a very low number of cases. Similar effects of care were also evident for total mortality in men (4.18 [3.89-4.48]) and women (3.69 [3.29-4.13]), although the magnitude of these effects was higher than those apparent for the analyses of CVD and its subtypes.

Next, in the subgroup of 377,500 women with a record of birth, we were able to use maternity data to explore the mediating role of metabolic factors and cigarette smoking on these relationships between care and cardiovascular disease. The pregnancy characteristics of these women are depicted in table 2. Women gave birth between the ages of 12 and 45 years, with those with a background in care being five times more likely to have birth early in the life course (12 and 19 years) than the general population. While the care group was also more than four times more likely to have smoked cigarettes during pregnancy (35.3 versus 7.9%), their metabolic characteristics were very similar to the general population controls. That is, there was no clear group differences in pre-pregnancy or pregnancy diabetes, hypertension, or obesity, and their aggregation.

In table 3 we show results from survival analyses in women for each of the four potential mediating variables and out-of-home care in relation to later CVD in which basic adjustment was for year of birth and maternal education. As anticipated, the mediating variables of lower maternal age; cigarette smoking; having at least one of the metabolic risk factors of obesity, and gestational hypertension or diabetes; and being in the lowest category of school grades were associated with around a doubling in the risk of future CVD. As we show in figure 2, taking these mediating factors into account when examining the relationship between out-of-home care and CVD had variable impact. Relative to the hazard ratio for out-of-home care in the most basic model containing the cofounding factors (1.91 [1.53-2.39]), controlling for metabolic indices had no influence (1.98 [1.24-3.15]). Marked attenuation in the strength of the out-of-home care–CVD gradient was, however, apparent after control for maternal age at first birth (1.63 [1.30-2.05]) and educational performance (1.57 [1.25-1.98]), with the most pronounced mediation seen after cigarette smoking was added to the multivariable model (1.41 [1.12-1.78]). Simultaneous control for the four

mediating factors eliminated the care–CVD association (1.07 [0.66-1.72]). There were too few events to robustly explore the relationship of care with separate presentations of CVD.

In secondary analyses, we examined the association of duration and timing of care with cardiovascular disease in the cohort of people with a care history (supplemental table 2). Owing to the low number of cases in this subgroup, we only examined relationships for CVD in a pooled analyses of men and women. The mean duration of care was 3.9 years (SD 5.0) for men and women, with the age at care entry being 9.1 years (SD 6.2). There was a suggestion that study members who entered care after age 11 experienced higher risk than those doing so earlier in childhood (1.27]1.01-1.59]), while for care duration there was no convincing evidence of a relationship with CVD.

Discussion

The main findings of the present study of a Swedish national cohort of around 850,000 individuals were that, relative to general population controls, both men and women exposed to childhood out-of-home care experienced around a doubling in the risk of adult CVD and also its separate presentations such as stroke and myocardial infarction; and that, for women in whom we were able to investigate how this elevated risk of CVD attributed to care was embodied, there was marked mediation by cigarette smoking, educational achievement, and age at first birth but not metabolic factors. The lack of impact of controlling for metabolic factors is unsurprising given the lack of association with pre-adult care in other studies.[6,18]

In secondary analyses, we found support for the observation that men and women with a care history had markedly elevated risk of total mortality in adulthood.[1] Similarly, we were able to recapitulate known associations for our mediating variables in relation to later CVD, such as cigarette smoking,[19,20] low educational achievement,[21,22] and early age at first birth.[23] These findings therefore give us a degree of confidence in our the new results for care and later CVD.

Comparison with existing evidence

To the best of our knowledge, this is the first study to have investigated the occurrence of cardiovascular disease in adults exposed to out-of-home care in early life. In the only partially-related comparator study we could locate, children who were evacuated from Finland to ostensibly safer countries during World War II did not subsequently develop different rates of CVD relative to those remaining with their family of origin.[24,25] Relative to the present cohort, however, the circumstances of removal from family of origin into care were very different whereby Finnish parents volunteered their children for migration because of an abundance of concern for their welfare.

Study strengths and limitations

This cohort study was generated using multiple Swedish national registers to create the large cohort necessary to study a low frequency outcome like CVD in people who are under 48 years of age at censoring. A particular strength of register-based design relative to field-based studies is the minimal and unselected attrition. Additionally, much of what is known about early life adversity, including experience of childhood care, has been gleaned from studies where participants responded to enquiries about childhood adversity when they were middle- or older-aged.[26] Based on a systematic review of 20 studies which have explored agreement between childhood prospective assessment (gold standard) and distant recall in adulthood,[27] there is evidence that this approach to exposure assessment leads to very low agreement. That we have prospectively gathered data that are not self-reported but are drawn from long-standing care records is a distinct advantage of our work. The use of registry data on state care is particularly important relative to the alternative of asking study members to respond to enquiries on issue as sensitive as childhood separation from one's biological family that could have occurred many decades earlier.[1 28]

Our study is not of course without its limitations. First, while we were able to explore the association of childhood care with adult CVD in men and women after taking into account adjustment for a modest array of confounding factors, we only had data potentially mediating factors for women who had given birth. In

representing the large majority (87%) of women in the birth cohorts from which they are derived, it is likely, however, that these findings are generalisable. While it is also plausible that the same mediators would have produced similar results in men, this requires empirical testing. Of the mediating data, the prevalence of metabolic factors, particularly obesity was seemingly very low at 1.3%. Comparably, in a report sampling around half of the present population of women where body mass index (BMI) was computed from the direct measurement of height and weight, around 15% of women had a BMI of ≥30kg/m^2.[29] This clear differential may be at least partially explained by the ascertainment of obesity in our study being based on a health professionals' observation resulting in a diagnosis, rather than actual measurement. Importantly, in that study,[29] as in the present one, the prevalence of gestational obesity, diabetes, and hypertension were the same in the out-of-home care group and the general population controls. Relatedly, in being related to elevated CVD risk in the expected directions (table 3), the metabolic indices of gestational obesity, diabetes, and hypertension have predictive validity.

Second, the present data are observational and, as such, our results do not imply cause and effect. An alternative approach to addressing the present question is a randomised controlled trial in which only half of children requiring transfer to a safer environment would be allocated to state care. With such a trial being unethical, a further option is a natural experiment whereby the impact of changes in care policy on mortality, such as legislation to reduce the number of children being placed out of the home, are explored. Third, there are marked variations in state care child policies across countries and this may mean the present results are not readily transportable to other environments. In a systematic review with meta-analysis, we found that the relationship between childhood care and adult mortality was essentially the same across the UK, USA, Australia, and Sweden.[1] Whether this is also the case for when CVD is the outcome of interest is of course an empirical question. Fourth, the comparison group in the present analyses was represented by the general population. This is not a truly unexposed group because it includes people from disadvantaged background (care, adoptees, and other adversities). Based on the findings herein and elsewhere, these adversities will elevate the rate of CVD and, as such, narrow the differential between the care and general population group in our analyses. This would therefore result in

the current hazard ratios being an underestimate of the true effect of care on CVD. Fifth, while we were able to explore the association of duration of care and age at care entry with CVD, we do not have data on other characteristics, including type, cause, quality, and disruption in care placement. Sixth, our cohort is predominantly ethnically white so testing our results in minority groups would be informative. Lastly, in exploring the prospective association of a history of state care with later CVD, we captured only one of several childhood adversities.[28] We specifically selected care for focus here because it represents one of the more severe experiences and, as such, if an association with adult health is to be seen, it is more likely for this component of early adversity. Additional studies are required to examine if prospectively gathered data on other adversities such as physical (including sexual) and psychological abuse have similar relationships with CVD.

Potential policy implications

Although evidence from a single observational study cannot be used to steer policy,[30] the explanatory power of adult cigarette smoking, educational achievement, and age at first birth in the relationship between out-of-home care in early life and adult CVD raises the potential utility of intervention in these areas, specifically at the intersection of experience of care in women who have given birth. Smoking habit is often developed during the later school years[31] when the prevalence of care also tends to peak in Sweden.[32] Primary care-based behaviour-based interventions in adolescents appear to have an impact on smoking prevention though not cessation,[33] while psychosocial interventions which include counselling, feedback, and incentives during pregnancy appear to be effective in the process of quitting.[34] Educational and contraceptive-promoting interventions to address unintended teenage pregnancy show some success,[35] but definitive conclusions about the most effective approach are not currently possible, while programs directed at elevating the academic performance of children in care[36] – and indeed education more broadly[37] – are typically insufficiently rigorous to draw recommendations.

Conclusions

In the present study, people with a history of out-of-home care experienced an elevated risk of early cardiovascular disease events and, in women, this was at least partially generated by unfavourable health behaviours in later life, young age at birth of offspring, and low educational achievement. These findings add to the array of adverse health outcomes seemingly experienced following care graduation.

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Table 1. Socio-demographic characteristics of study members according to out-of-home care in childhood

	Women		Men	
	Out-of-home care	General population	Out-of-home care	General population
	N (%)	N (%)	N (%)	N (%)
Year of birth				
1972-74	3895 (32.7)	133,032 (32.7)	4303 (33.9)	143,372 (33.0)
1975-77	3393 (28.5)	119,431 (29.6)	3562 (28.0)	128,538 (29.6)
1978-81	4638 (38.9)	151,521 (37.5)	4846 (38.1)	162,895 (37.5)
Maternal country of birth				
Sweden	10,985 (92.2)	372,601 (92.1)	11,789 (92.7)	401,260 (92.3)
Other Western	748 (6.0)	24,181 (6.0)	704 (5.5)	25,940 (6.0)
Non-Western	193 (1.8)	7202 (1.6)	218 (1.7)	7605 (1.7)
Maternal education (9-18 years)				
≤ 9 years	3772 (31.6)	63,365 (15.7)	4030 (31.7)	67,864 (15.6)
10-12 years	7160 (60.0)	240,090 (59.4)	7644 (60.1)	257,932 (59.3)
≥13 years	994 (8.3)	100,529 (24.9)	1037 (8.2)	109,009 (25.1)

Owing to the large numbers of observations, even with small group differences, the p-value for heterogeneity for each socio-demographic characteristic is <0.001

Table 2. Characteristics of women who had given birth according to out-of-home care in childhood

	Out-of-home care (N=10,673)	General population (N=366,827)
	N (%)	N (%)
Age of index mother at first birth (years)		
12-19	1602 (15.0)	10,085 (2.9)
20-24	3844 (36.0)	63,430 (17.3)
25-29	2698 (25.3)	127,737 (34.8)
30-34	1834 (17.2)	124,555 (34.0)
≥35	695 (6.5)	41,020 (11.2)
Own educational performance (15-16 years)		
First quintile (lowest)	5881 (55.1)	54,810 (14.9)
Second	1844 (17.2)	51,102 (13.9)
Third	1344 (12.5)	70,431 (19.2)
Fourth	1106 (10.4)	100,869 (27.5)
Fifth	508 (4.8)	89,615 (24.4)
Cigarette smoking in early pregnancy		
None	6336 (59.4)	318,827 (86.9)
1-9 cigarettes/day	2553 (23.9)	22,400 (6.1)
10+ cigarettes/day	1213 (11.4)	6588 (1.8)
Missing data	571 (5.3)	19012 (5.2)
Metabolic factors		
Obesity	139 (1.3)	4682 (1.3)
Pre-pregnancy hypertension	23 (0.2)	1280 (0.3)
Pregnancy hypertension	511 (4.8)	21,956 (6.0)
Pre-Gestational diabetes	61 (0.6)	2050 (0.6)
Gestational diabetes	84 (0.8)	2159 (0.6)
Number of metabolic factors		
None	9938 (93.1)	337,008 (91.9)
1	663 (6.2)	27,679 (7.6)
2	69 (0.6)	1969 (0.5)
≥3	3 (0.0)	153 (0.0)

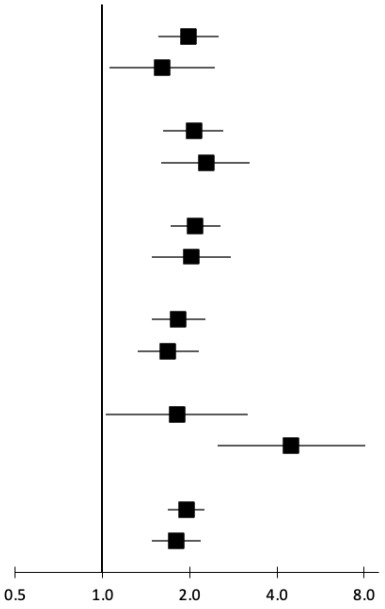
Table 3. Association of out-of-home care in childhood and mediating factors in adulthood with cardiovascular disease in adulthood in 357 917 women who had given birth

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
General population	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Out-of-home care	1.91 (1.53-2.39)	1.63 (1.30-2.05)	1.41 (1.12-1.78)	1.98 (1.24-3.15)	1.57 (1.25-1.98)	1.07 (0.66-1.72)
Maternal age at first birth (13-24 years vs. ≥25 years)		1.76 (1.58-1.86)				1.71 (1.35-2.16)
Cigarette smoking (yes versus no)			2.51 (2.21-2.85)			2.03 (1.55-2.67)
Metabolic factors (any versus none)				2.47 (1.88-3.23)		2.70 (2.06-3.54)
Own educational performance at age 16 years (1 quintile [lowest] versus 2-5)					1.81 (1.61-2.05)	1.80 (1.41-2.30)

Results are hazard ratios (95% confidence interval) adjusted for year of birth and maternal education.
Analyses are based on 10102 women in the OHC study group (82 CVD events) and 347815 (1412 CVD events) in the general population.

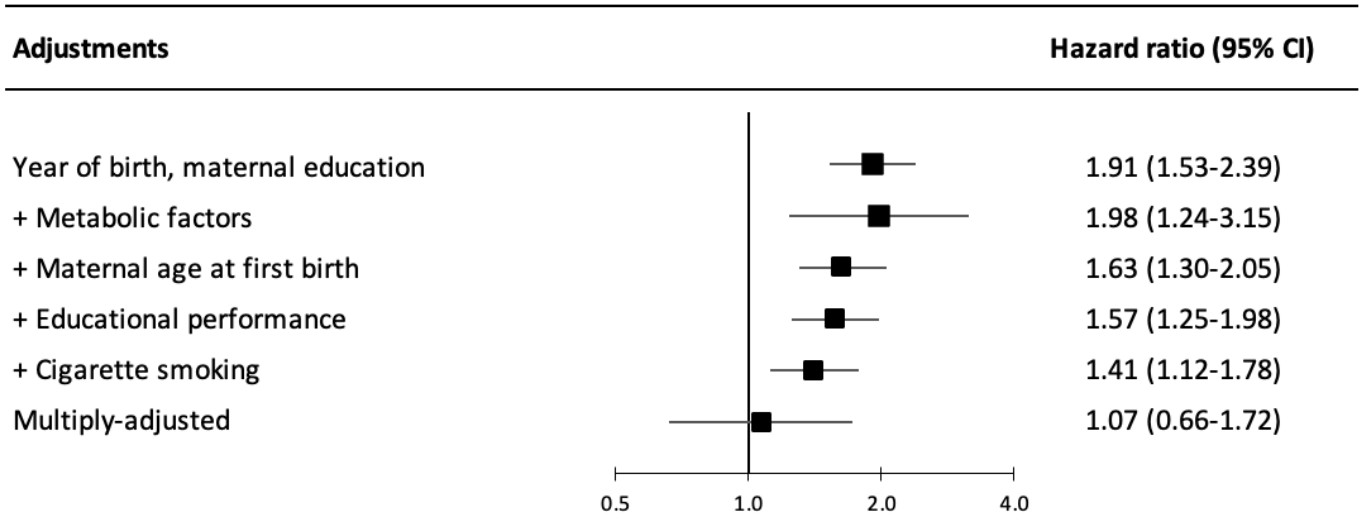
Figure 1. Association of out-of-home care in childhood with different presentations of cardiovascular disease in adulthood in the full cohort

		n/N Out-of-home care	n/N General population	Hazard ratio (95% CI)	P-value for interaction
Myocardial infarction	Men	73/12,711	1178/434,805	1.98 (1.56-2.51)	
	Women	23/11,926	435/403,984	1.61 (1.06-2.45)	0.46
Other coronary disease	Men	73/12,711	1126/434,805	2.07 (1.62-2.62)	
	Women	34/11,926	468/403,984	2.28 (1.60-3.23)	0.80
Any coronary disease	Men	107/12,711	1640/434,805	2.09 (1.72-2.55)	
	Women	42/11,926	647/403,984	2.02 (1.48-2.77)	0.70
Stroke	Men	92/12,711	1696/434,805	1.83 (1.48-2.26)	
	Women	68/11,926	1325/403,984	1.68 (1.32-2.15)	0.43
Cardiovascular death	Men	10/12,711	160/434,805	1.81 (1.03-3.17)	
	Women	7/11,926	46/403,984	4.48 (2.49-8.07)	0.02
Any cardiovascular disease	Men	194/12,711	3276/434,805	1.95 (1.68-2.25)	
	Women	108/11,926	1941/403,984	1.80 (1.48-2.18)	0.47



Some CVD presentations are not mutually exclusive; for instance, 'any coronary disease' includes 'myocardial infarction', while 'other coronary disease' and includes 'cardiovascular death'.

Figure 2. Association of out-of-home care in childhood with cardiovascular disease after adjustment for adult mediating factors in 357 917 women who had given birth



Analyses are based on 10102 women in the OHC study group (82 CVD events) and 347815 (1412 CVD events) in the general population.