Earnings during adulthood in patients with childhood-onset inflammatory bowel disease: a nationwide population-based cohort study

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Summary

Background: IBD with onset during childhood seems to represent a severe disease phenotype with increased morbidity. We have previously demonstrated that children with IBD have significantly lower final grades in compulsory school compared to healthy peers.

Aim: To evaluate the association of childhood-onset IBD with a later professional career and subsequent earnings

Methods: We identified 5404 individuals diagnosed with childhood-onset (<18 years) IBD between 1990 and 2014 (2818 with ulcerative colitis and 2328 with Crohn's disease) in the Swedish National Patient Register. Patients were matched with 10 general population reference individuals by sex, birth year, and place of residence (n = 51,295). Data on earnings during 1992–2017 were obtained through the longitudinal integration database for health insurance and labour market studies. Earnings were converted into Euros (inflation-adjusted to 2019). The differences in earnings between patients and general population reference individuals were calculated through quantile regression.

Results: Patients with childhood-onset IBD had significantly lower annual taxable earnings from ages 20 to 30 (adjusted median annual income difference (AMAID) at age 30: −5.4\% [95\% CI −9.1\% to −1.8\%]). In particular, annual taxable earnings through early adult age were lower in patients who, during childhood, had had surgery or long-term inpatient treatment for IBD (AMAID at age 30: −16.3\% [95\% CI −24.7\% to −7.9\%]).

Conclusions: Overall, the negative influence of disease on earnings in early adult age was modest for patients with childhood-onset IBD. The markedly larger negative income gap from ages 20 to 30 in patients with more severe IBD during childhood should be recognised.
1 | INTRODUCTION

IBD with onset in childhood seems to represent a severe disease phenotype and is associated with increased morbidity and mortality.1–6 Compared to healthy peers and siblings, children with IBD have significantly lower taxable earnings up to 10 years after diagnosis than IBD-free siblings.11 Several studies have also shown that adult-onset IBD has a negative impact on work ability and professional career as patients are reported to have more sick leave,12–15 disability pension12–17 and unemployment12,18 than the general population.

It seems plausible that childhood-onset IBD can have profound negative consequences for later educational and professional career, but very few studies have addressed this association19–21 (Table S1). The interpretations of these somewhat contradictory studies are restricted by small numbers,19–21 low response rate (questionnaire study)20 and the non-contemporary study periods.19,20

If childhood-onset IBD has a significant negative impact on earnings in adult age, this should be recognised by the health care and educational and social security systems and be used as a foundation for discussions on what the society could do to support these chronically diseased young patients to reach their full professional career potential.

The aim of this study was to examine if childhood-onset IBD patients have lower earnings in adult age than general population reference individuals. A secondary aim was to study whether some subsets of children with IBD, characterised by sex, IBD subtype and disease severity, are at higher risk of low earnings as adults.

2 | METHODS

2.1 | Study design

In a cohort study design, we compared earnings in adult age between individuals with childhood-onset IBD and matched general population reference individuals.

2.2 | Setting and data sources

In Sweden, all patients with childhood-onset IBD are treated by paediatricians until the age of 18 years and they are then referred for follow-up by adult gastroenterologists.22 Sweden is a high-income country with publicly funded healthcare including both inpatient and outpatient care as well as medications for all residents.23 We used the personal identity number, assigned to all Swedish residents, to link data from national administrative and clinical registers.24–28 (Table S2).

2.3 | Study population

2.3.1 | IBD patients

We identified all individuals diagnosed with IBD before their 18th birthday in the Swedish National Patient Register (NPR) from 1990 until 2014.20 The study period was chosen to estimate the impact of childhood-onset IBD during the modern immunomodulatory era (azathioprine was widely introduced in Swedish paediatric IBD care during the first years of the 1990s).1

To increase sensitivity for IBD and to better define the first date of diagnosis, we also used colorectal histopathology data from the ESPRESSO cohort (Table S3). The ESPRESSO database is a nationwide initiative to strengthen the validity of Swedish health register data through histopathology.27 To be classified as childhood-onset IBD patients had to have ≥2 hits (either two IBD listings in NPR or one IBD listing in NPR and one in the ESPRESSO register) before their 18th birthday. This combination of 1 listing in each of the two registers has been shown to have a positive predictive value of 93% (95% confidence interval [CI], 89%–96%) when using patient chart data-based diagnosis of childhood-onset IBD as gold standard.29

Identified childhood-onset IBD patients were followed from ≥20 to 30 years of age, until emigration, death or end of study period (2017).

2.3.2 | General population reference individuals

For each IBD patient, we randomly selected up to 10 individuals from the Total Population Register. The patients with IBD and the general population reference individuals were matched on sex, birth year, age and place of residence. The reference individuals had to be free of IBD at date of diagnosis of the index patient and stopped contributing person-time if later diagnosed with IBD.

2.3.3 | Patient characteristics during childhood

To categorise childhood-onset IBD patients and their disease phenotype (subtype and proxies for disease severity) we used all information available from the date of the first IBD diagnosis until the date when the patients turned 18 years.

The IBD subtype definition was based on the first two diagnostic listings (or when combined with a colorectal biopsy, on the first IBD ICD diagnosis). Patients with listings of both ulcerative colitis and Crohn’s disease, or a listing of IBD unclassified (IBD-U) were defined as IBD-U (Table S3). Patients who before 18 years of age had a diagnostic or procedure code typical of CD (Table S4) were classified as CD.30

The patients were further categorised according to year of diagnosis, age at IBD diagnosis, exposure to IBD-related surgery or
The difference between patients and general population reference individuals was calculated through quantile regression (median regression using the QUANTREG procedure) and 95% CIs were obtained using resampling. Adjusted median proportional difference in percent of annual taxable earnings and annual personalised disposable household incomes comparing IBD patients and reference individuals were calculated by using the point estimate (of adjusted median difference from the quantile regression) divided by the median (annual taxable earnings, respectively, annual personalised disposable household incomes) in patients with IBD.

Chi-squared analysis was used to compare distributions of dichotomous outcome variables at age 30.

All statistical tests were two-sided and \( p < 0.05 \) was considered statistically significant. We used statistical software from SAS (version 9.2; SAS Institute Inc.).

3 | RESULTS

3.1 | Background data

We identified 7436 patients who were diagnosed with IBD during childhood (<18 years). Of these, 2019 did not reach 20 years of age during the study period and 13 patients were excluded as no matched comparator could be found (Figure S1).

From the remaining 5404 IBD patients, 2818 (52%) were classified as UC, 2328 (43%) as CD and 258 (5%) as IBD-U. The majority of the IBD patients were boys (\( n = 3038 \) [56%]). Almost half of the patients were diagnosed with IBD before 15 years of age (\( n = 2538 \) [47%]) and the majority were diagnosed with IBD after 2001 (\( n = 2538 \) [59%]). However, as the study window opened in 1990 relatively few of the childhood-onset IBD patients that reached age 30 during the study period were diagnosed after 2001 (\( n = 216 \) [12%]) and only a small minority of them were below 10 years of age when diagnosed with IBD (\( n = 91 \) [5%]) (Table 1). A smaller fraction of the IBD patients had been exposed to IBD-related surgery or inpatient treatment for more than 30 days with IBD as main diagnosis before 18 years of age (\( n = 923 \) [17%]), IBD-related surgery \( n = 634 \) [12%), long-term inpatient treatment \( n = 458 \) [9%]) (Table 2).

We identified 54,170 matched (by sex, birth year and place of residence) potential general population reference individuals. As the reference individuals were matched on birth year some of these (\( n = 1979 \)) had already seen their 18th birthday at index date (date of diagnosis for the patient) and some (\( n = 762 \)) had not turned 20
(in contrast to their index patient) during the study period. These reference individuals were excluded and also those 134 reference individuals that were diagnosed with IBD between ages 18 and 20 (Figure S1). For the analyses, the 5404 childhood-onset IBD patients were compared to the remaining 51,295 matched IBD-free general population reference individuals (Table 1).

### 3.2 | Socioeconomic status at age 30

The 1809 patients with childhood-onset IBD that reached age 30 during the study period had similar educational level (>12 years of education: 47.4% vs 47.1%, p = 0.86), marital status (married: 20.8% vs 22.5%, p = 0.10) and unemployment status (unemployed: 6.8% vs 7.2%, p = 0.51) as general population reference individuals. A larger proportion of childhood-onset IBD patients had disability pension (5.0% vs. 2.8%, p < 0.00001) and were on sick leave (16.6% vs 10.3%, p < 0.00001) compared to the general population reference individuals at age 30 (Table 2).

Out of the 403 IBD patients that were exposed to IBD-related surgery or long-term inpatient treatment during childhood, fewer attained >12 years of education (41.9% vs 47.2%, p = 0.05) but the patients within the subset had similar marital status (married: 20.3% vs 23.7%, p = 0.14)

| Variable | IBD | UC | CD | Reference individuals |
|----------|-----|----|----|-----------------------|
| N (%)    | 5404| 2818| 2328| 51,295 (100%)         |
| Sex, n (%) |
| Women | 2366 (43.8) | 1255 (44.5) | 992 (42.6) | 22,308 (43.5) |
| Men   | 3038 (56.2) | 1563 (55.5) | 1336 (57.4) | 28,978 (56.5) |
| Age at diagnosis, n (%) |
| <10 years | 448 (8.3%) | 280 (9.9%) | 156 (6.7%) | 4314 (8.4%) |
| 10 to <15 years | 2090 (38.7%) | 1042 (37.0%) | 971 (41.7%) | 20,661 (40.3%) |
| 15 to <18 years | 2866 (53.0%) | 1496 (53.1%) | 1201 (51.6%) | 26,320 (51.3%) |
| Year of diagnosis, n (%) |
| 1990–1995 | 795 (14.7) | 442 (15.7) | 328 (14.1) | 7638 (14.9) |
| 1996–2001 | 1402 (25.9) | 817 (29.0) | 549 (23.6) | 13,408 (26.1) |
| 2002–2007 | 1954 (36.2) | 964 (34.2) | 919 (39.5) | 18,734 (36.5) |
| 2008–2014 | 1253 (23.2) | 595 (21.1) | 532 (22.9) | 11,515 (22.4) |
| Start year of follow-up, n (%) |
| 1992–1997 | 269 (5.0) | 129 (4.6) | 132 (5.7) | 2502 (4.9) |
| 1998–2001 | 497 (9.2) | 280 (9.9) | 199 (8.5) | 4712 (9.2) |
| 2002–2007 | 1463 (27.1) | 846 (30.0) | 577 (24.8) | 13,954 (27.2) |
| 2008–2012 | 1764 (32.6) | 894 (31.7) | 800 (34.4) | 16,764 (32.7) |
| 2013–2017 | 1411 (26.1) | 669 (23.7) | 620 (26.6) | 13,363 (26.1) |
| IBD subtype, n (%) |
| Ulcerative colitis | 2818 (52.1) | 2818 (100) | 0 |
| Crohn’s disease | 2328 (43.1) | 0 | 2328 (100) |
| IBD-unclassified | 258 (4.8) | 0 | 0 |
| IBD surgery and hospitalisation during childhood, n (%) |
| IBD-related surgery | 634 (11.7) | 113 (4.0) | 497 (21.3) |
| Hospitalisation >30days | 458 (8.5) | 240 (8.5) | 195 (8.4) |
| IBD-related surgery or hospitalisation >30days | 923 (17.1) | 289 (10.3) | 597 (25.6) |
| Age at end of follow-up |
| Median (range) | 27.1 (20.0–44.7) | 27.8 (20.0–44.5) | 26.8 (20.0–44.7) | 27.1 (20.0–44.9) |

*Inpatient treatment during childhood (<18 years) with IBD as the main diagnosis.

**TABLE 1** Characteristics of patients diagnosed with childhood-onset inflammatory bowel disease (IBD) between 1990 and 2014 that during the study period (1990–2017) reached adult age (≥20 years) and general population reference individuals.
and unemployment status (unemployed: 7.7% vs 8.1%, \( p = 0.77 \)), compared to general population reference individuals. More patients with severe disease during childhood had disability pension (8.7% vs 2.5%, \( p < 0.00001 \)) and were on sick leave (22.1% vs 10.5%, \( p < 0.00001 \)) at age 30 (Table S7).

### 3.3 Annual taxable earnings

Patients with childhood-onset IBD had statistically significantly lower median annual taxable earnings from ages 20 to 30 years of age (Figure 1). As demonstrated by the trajectory in Figure 1, there

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**Table 2** Characteristics at age 30 of patients diagnosed with childhood-onset inflammatory bowel disease (IBD) between 1990 and 2004\(^a\) and general population reference individuals

| Variable                              | IBD       | UC        | CD        | Reference individuals |
|---------------------------------------|-----------|-----------|-----------|-----------------------|
| N                                     | 1809      | 1006      | 750       | 17,157                |
| Sex, n (%)                            |           |           |           |                       |
| Women                                 | 808 (44.7)| 450 (44.7)| 331 (44.1)| 7569 (44.1)           |
| Men                                   | 1001 (55.3)| 556 (55.3)| 419 (55.9)| 9588 (55.9)           |
| Age at diagnosis, n (%)               |           |           |           |                       |
| <10 years                             | 93 (5.1)  | 57 (5.7)  | 35 (4.7)  | 859 (5.0)             |
| 10 to <15 years                       | 614 (33.9)| 352 (35.0)| 242 (32.3)| 6287 (36.6)           |
| 15 to <18 years                       | 1102 (60.9)| 597 (59.3)| 473 (63.1)| 10,011 (58.3)         |
| Year of diagnosis, n (%)              |           |           |           |                       |
| 1990–1995                             | 690 (38.1)| 381 (37.9)| 287 (38.3)| 6678 (38.9)           |
| 1996–2001                             | 903 (49.9)| 518 (51.5)| 358 (47.7)| 8550 (49.8)           |
| 2002–2004                             | 216 (11.9)| 107 (10.6)| 105 (14.0)| 1929 (11.2)           |
| Education, n (%)                      |           |           |           |                       |
| ≤9 years                              | 158 (8.7) | 99 (9.8)  | 53 (7.1)  | 1472 (8.6)            |
| 10–12 years                           | 786 (43.4)| 425 (42.2)| 337 (44.9)| 7494 (43.7)           |
| >12 years                             | 858 (47.4)| 477 (47.4)| 358 (47.7)| 8076 (47.1)           |
| Missing                                | 7 (0.4)   | 5 (0.5)   | 2 (0.3)   | 115 (0.7)             |
| Married, n (%)                        |           |           |           |                       |
| Yes                                   | 376 (20.8)| 207 (20.6)| 158 (21.1)| 3860 (22.5)           |
| No                                    | 1433 (79.2)| 799 (79.4)| 592 (78.9)| 13,297 (77.5)         |
| Unemployed, n (%)                     |           |           |           |                       |
| Yes                                   | 123 (6.8) | 75 (7.5)  | 44 (5.9)  | 1238 (7.2)            |
| No                                    | 1686 (93.2)| 931 (92.5)| 706 (94.1)| 15,919 (92.8)         |
| Sick leave and disability pension, n (%)|       |           |           |                       |
| Sick leave                            | 301 (16.6)| 163 (16.2)| 131 (17.5)| 1773 (10.3)           |
| Disability pension                    | 90 (5.0)  | 47 (4.7)  | 41 (5.5)  | 484 (2.8)             |
| Annual taxable earnings (k€, inflation adjusted to 2019) |           |           |           |                       |
| Median (IQR)                          | 24.2 (9.4–34.2) | 24.0 (9.9–34.0) | 24.6 (7.1–34.6) | 26.4 (11.1–35.2) |
| Adjusted median earnings difference (k€, 95 CI) | -1.3 (-2.2; -0.4) | -1.1 (-2.2; 0.0) | -1.4 (-3.0; 0.1) | Reference |
| Adjusted median earnings difference (%, 95 CI) | -5.4 (-9.1; -1.8) | -4.5 (-9.0; 0.1) | -5.8 (-12.1; 0.5) | Reference |
| N (%) with no taxable earnings         | 209 (11.6)| 110 (10.9)| 96 (12.8) | 1800 (10.5) |
| Annual personalised disposable household income (k€, inflation adjusted to 2019) |           |           |           |                       |
| Median (IQR)                          | 17.6 (11.6–24.7) | 17.5 (11.5–24.9) | 17.8 (11.8–24.6) | 18.1 (11.5–25.1) |
| Adjusted median income difference (k€, 95 CI) | -0.3 (-0.8; 0.2) | -0.3 (-1.0; 0.4) | -0.3 (-1.1; 0.5) | Reference |
| Adjusted median income difference (%, 95 CI) | -1.3 (-3.4; 0.9) | -1.1 (-4.0; 1.8) | -1.3 (-4.7; 2.1) | Reference |
| N (%) with no disposable income       | 23 (1.3)  | 13 (1.3)  | 9 (1.2)   | 174 (1.0)             |

\( a\)To reach age 30, the childhood-onset IBD patients had to be diagnosed no later than 2004.
was no trend of growing annual difference (nor absolute nor relative) in taxable earnings between childhood-onset IBD patients and reference individuals with increasing age. The median annual taxable earnings at age 30 in patients diagnosed with childhood-onset IBD was 24,200 € compared to 26,400 € in matched general population reference individuals (Table 2). After adjustment, the annual median difference in taxable earnings at age 30 between childhood-onset IBD patients and reference individuals was estimated to −1300 € (95% CI −2200 € to −400 €), equivalent to −5.4% (95% CI −9.1% to −1.8%) lower annual taxable earnings.

Similar trajectory patterns with lower median annual taxable earnings from ages 20 to 30 years, but with no trend for growing annual earning differences by age, were seen in both female and male patients with childhood-onset IBD (Figure 2).

Separate analyses of patients with childhood-onset UC and CD also demonstrated similar trajectories for annual taxable earnings, although the statistically significant associations with lower adjusted annual median taxable earnings differences were lost in both strata with increasing age (as the confidence interval gradually widened following the shrinking number of older study subjects) (Figures S2 and S3; Table 2).

Larger, and by age increasing, absolute differences in taxable earnings were seen in patients with surgery or long-term inpatient IBD treatment during childhood (Figure 3). In this subset of patients
with more severe disease during childhood, the adjusted median annual difference in taxable earnings at age 30 was −3600 € (95% CI −5500 € to −1800 €) equivalent to −16.3% (95% CI −24.7% to −7.9%) lower earnings (Table S7).

3.4 | Annual personalised disposable household income

Patients with childhood-onset IBD had almost similar annual median personalised disposable household income as general population reference individuals in early adult age (Figure S4). The Swedish social security system seemed to compensate also for the substantially lower earnings in patients with more severe disease during childhood, as no statistically significant difference in personalised disposable household income was seen in this subset throughout early adult age (Figure S5).

4 | DISCUSSION

4.1 | Main findings

In this nationwide cohort study, from a high-income country with a comprehensive social insurance system covering all residents, we found that childhood-onset IBD patients overall had significantly lower earnings in early adult age compared to matched general
population reference individuals. Although childhood-onset IBD patients overall had significantly lower earnings already from age 20, the differences in median annual earnings were relatively modest at age 30 (~5%). However, our study also demonstrated that patients with more severe disease during childhood (exposed to IBD-related surgery or long-term inpatient treatment) had markedly lower earnings throughout early adult age (~16% at age 30).

### 4.2 Findings compared to earlier studies

To our knowledge, this is the first population-based study that has explored the association of childhood-onset IBD with earnings in adult age. However, there are some earlier studies that have tried to estimate the impact of childhood onset of IBD for later educational level and socioeconomic status. In 2017, El Matary published a questionnaire-based single-centre study of 112 adult patients with childhood-onset IBD versus 565 sex- and age-matched healthy controls recruited from the 2012 Canadian Community Health Survey.\textsuperscript{21} The results of that study were reassuring as these patients seemed to achieve higher education levels and receive higher earnings than individuals without IBD. These findings contrasted with a 2006 paper from the Netherlands where 274 adolescents (15–24 years) with IBD, compared to 248 age-matched controls without gastrointestinal disease randomly selected from general practitioners, more often were unemployed or employed with a part-time job.\textsuperscript{20}
However, both these studies suffer from small numbers and incomplete response rates.

In a recently published study, we demonstrated that the median annual earnings were lower in women with IBD compared to their healthy sisters from the year of diagnosis and at least 5 years onwards. This contrasted to the findings in men diagnosed with IBD in adult age that had similar annual taxable earnings as their brothers throughout the first years after diagnosis. However, in this childhood-onset IBD cohort study, the risk of lower earnings was similar in male and female patients. Neither did we find any difference in the pattern of lower earnings in young adult age between patients with UC or CD. This is somewhat noteworthy as follow-up studies on both childhood-onset IBD and adult-onset IBD cohorts have demonstrated that patients with CD more often seem to be burdened by disease than patients with UC.

### 4.3 | Mechanistic explanations

There are probably several factors why patients with childhood-onset IBD had lower earnings in adult age compared to general population reference individuals. We have recently shown that patients with childhood-onset IBD have poorer achievements in school and speculated that this underperformance to a large extent could be explained by lower school attendance (following disabling symptom and frequent hospital visits) but also to some extent might be explained by disease-associated fatigue. Lower grades from compulsory and high school constitute a major obstacle for patients to qualify for highly ranked educations and highly paid professional careers. Being diagnosed with IBD in childhood will also foreclose some career paths and some patients will be forced to give up their professional dreams due to an incapacitating disease. Young patients may also experience disappointment and loss of career drive when they realise that their professional plans are no longer in line with their health needs. It is also possible that facing a chronic disease in early age will redirect career dreams to more caring occupations that might be more personally satisfying but less financially rewarding. The lower earnings could also in part be explained by lower labour market involvement in patients with childhood-onset IBD. Although at age 30, an equal proportion of childhood-onset IBD patients were employed, sick leave and disability pension were somewhat more common in patients than among general population reference individuals (Table 2).

### 4.4 | Strengths and limitations

The major strength of our study is the population-based design and the identification of a large number of childhood-onset IBD patients that were diagnosed and treated during the modern era of immunomodulatory therapy. Through the personal identity number, we were able to link nationwide prospectively collected IBD data from routine clinical practice in virtually complete health registers to compulsory nationwide administrative population registers.

There are several limitations to our study. The results of our study might not be generalisable to other countries as social security systems and job security regulations differ from among nations. However, by presenting estimates both for taxable earnings and disposable income the results of our study should be relevant to at least other high-income countries in the world. The social security system in Sweden is more extensive than in many other countries and childhood-onset IBD might thus have a stronger negative effect on disposable income in countries with less comprehensive social security systems and job security.

Another limitation is the lack of high-resolution data on professional career which might have provided us with information that could further explain why patients with childhood-onset IBD had lower taxable earnings in early adult age; that is how much of the earnings gap could be explained by personal choice of labour market sector and working hours and how much could be considered a consequence of poorer career development and lower wages?

The study period was tailored to estimate the impact of childhood-onset IBD in the modern immunomodulatory era. Following the narrow time window, few of the study patients that reached age 30 during the study period were diagnosed after 2001 (in the anti-TNF era) and only a small minority of them were below 10 years of age when diagnosed with IBD. The small number of patients in these stratas precluded meaningful comparisons why we could not provide valid estimates on the associations of earnings at age 30 stratified by date or age at diagnosis.

### 4.5 | Clinical implications

Our findings should be reassuring to most children with IBD and their parents, as most young patients can expect a disease course with minor impact on later professional, educational and social career in early adult age. Nevertheless, our study also showed that lower earnings in early adult age were more common in patients with more severe IBD during childhood and that this absolute earnings gap seemed to increase by age.

Our study suggests that a dialogue between healthcare and schools should be established early for children with more severe IBD, to minimise the negative impact of chronic disease on educational achievements. Young patients with more disabling disease should preferably be followed at IBD centres with a special interest in transitional (from childhood to adulthood) medicine. These patients at risk should be informed of their expected forthcoming disease burden so that they timely can adapt to a professional career in line with their health needs.

### 5 | Conclusions

Although most patients with childhood-onset IBD had almost comparable earnings in early adult age as their healthy peers, the markedly larger earnings gaps from age 20 to age 30 in patients with more
severe IBD during childhood calls for strengthened educational and labour market support for this subset.

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AUTHOR CONTRIBUTIONS

Petter Malmborg: Conceptualization (equal); investigation (equal); methodology (equal); project administration (equal); writing - original draft (lead); writing - review and editing (equal). Åsa Everhov: Investigation (equal); methodology (equal); writing - review and editing (equal). Jonas K Söderling: Formal analysis (equal); software (lead); visualization (lead); writing - review and editing (equal). Jonas F Ludvigsson: Data curation (equal); investigation (equal); methodology (equal); writing - review and editing (equal). Gustaf Bruze: Conceptualization (equal); investigation (equal); methodology (equal); supervision (equal); writing - review and editing (equal). Ola Olén: Conceptualization (equal); data curation (lead); formal analysis (equal); funding acquisition (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing - review and editing (equal).

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AUTHORSHIP

Guarantor of the article: Olén.

STUDY REPORT GUIDELINE

The study is presented according to the recommendation in the STROBE statement on how to report observational studies in epidemiology.39

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