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Childbirth, hospitalization, and sickness absence: a study of female twins

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Page 1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Page 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Page 4**
Objectives	3	State specific objectives, including any prespecified hypotheses **Page 6**
Methods		
Study design	4	Present key elements of study design early in the paper **Page 7**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Page 7-10**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **Page 7-10**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed **N/A**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Page 8-9**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Page 7-10**
Bias	9	Describe any efforts to address potential sources of bias **N/A**
Study size	10	Explain how the study size was arrived at **Page 7**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Page 8-9**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **Page 9-10**
		(*b*) Describe any methods used to examine subgroups and interactions **Page 9-10**
		(*c*) Explain how missing data were addressed **N/A**
		(*d*) If applicable, explain how loss to follow-up was addressed

		N/A
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **Page 7, and page 22**
		(b) Give reasons for non-participation at each stage **N/A**
		(c) Consider use of a flow diagram **Page 22**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Page 23**
		(b) Indicate number of participants with missing data for each variable of interest **N/A**
		(c) Summarise follow-up time (eg, average and total amount) **N/A**
Outcome data	15*	Report numbers of outcome events or summary measures over time **Page 23**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Page 24-25**
		(*b*) Report category boundaries when continuous variables were categorized **Page 23**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **N/A**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Page 24-25**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Page 2 and page 13**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Page 16**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Page 13 – 15**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Page 13-16**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Page 18**

*Give information separately for exposed and unexposed groups.

Childbirth, hospitalization, and sickness absence: a study of female twins

Authors

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Abstract

Objective: To investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account.

Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA were calculated as Hazard Ratios (HR) with 95% confidence intervals (CI).

Setting: All female twins, i.e. women with twin sister, born between 1959 and 1990 in Sweden.

Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where at least one in the twin pair had their first childbirth (T_0) 1994-2009 and none gave birth before 1994.

Main outcome measures: Hospitalization and SA during year 2-5 after first delivery or equivalent.

Results: Preceding the first childbirth, the mean annual number of SA days increased for mothers, and then decreased again. Hospitalization after T_0 was associated with higher HRs of short-term and long-term SA. Hospitalization both before and after first childbirth was associated with a higher risk of future SA. Familial factors influenced the association between hospitalization and long-term SA, regardless of childbirth status.

Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth and results indicate a positive health selection into giving birth. Mothers hospitalized before and/or after giving birth had higher risks for future SA, that is, there was a strong association between morbidity and future SA.

Keywords: sick leave, childbirth, inpatient care, hospitalization, cohort study, population based, twins

Article Summary

Article focus:

- To investigate the associations of giving birth with subsequent morbidity in terms of hospitalization and sickness absence
- To study if hospitalization prior to (or after) childbirth increases the risk for future hospitalization and sickness absence

Key messages:

- Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth
- The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially

Strengths and limitations:

- The strengths of the study include the population-based prospective design, using national registers with high completeness and validity
- With a twin study design, we were able to take familial influences into account
- As inpatient care to a great extent has been replaced by outpatient treatment, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities

Introduction

In most countries with high labor force participation, women have higher levels of sickness absence (SA) than men [1-4]. Many theories and mechanism regarding this have been suggested, e.g., women having higher morbidity, higher workload (when combining paid and unpaid work), tougher situation on the labor market, men being the norm for how the labor market is organized, gender bias in healthcare and social insurance systems, discrimination and domestic violence, etcetera [5-9]. Another hypothesis behind this gender difference in SA focuses on SA during pregnancy and after childbirth [6 10-13]. Several studies show that women have higher SA during pregnancy [10 14] and that pregnancy-related SA explains half of the gender differences in SA in fertile ages [15].

One of the changes in society that may affect health after childbirth is that the mean age for having the first child has increased over the last years and that women with higher level of morbidity now give birth. Further, nowadays, the proportion of caesarean sections has increased as well as vacuum extraction deliveries, leading to risk of later health problems [16 17].

In this study, focus is on childbirth, morbidity, and SA among women, to get a better understanding of mechanisms behind SA among women in fertile ages. There are hardly any studies on the associations between giving birth and morbidity and SA, and those conducted have focused on a relatively short time period right after childbirth, most often within the first year following the child delivery [18 19], while prospective studies with longer follow-up of mothers are rare [6 12 20].

Pregnancy, delivery, and the postpartum period may imply large physical, mental, and social changes during a short period of time, increasing the risk for disease and injury [21 22]. Different types of physical and mental disorders are common during pregnancy and after childbirth – and can in some cases be longstanding or even permanent – however, this is hardly studied at all [19]. Giving birth may be associated with a higher risk of certain diseases demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental

disorders and different types of injuries [23-26]. For women with a disease present before the childbirth, the disorder might deteriorate after childbirth [23 24]. Regarding symptoms related to childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain, fatigue, headache, and sleep disorders [19 27]. Most of these symptoms seem to remain up to one year after childbirth [17]. Besides physical health effects, also depression and other mental disorders have been linked to childbirth [26 28], but again, prospective studies with longer follow-up are lacking [27]. Even though having children has been shown to contribute to an overall wellbeing, this is not the case for everybody and especially not among single mothers whose economic situation and thereby possibilities for good health care might be worse [29-31].

Morbidity can be measured in different ways, e.g., through self-reports and visits to healthcare. Here we will use data on more severe morbidity and that involves assessments from physicians, that is, morbidity that has led to hospitalization, a measure so far not used in this type of studies. Sickness absence is not a good measure of morbidity– most people with morbidity are not on SA [4]. Instead SA is considered a very good measure of social consequences of morbidity, in terms of not being able to support yourself from work [4]. Yet, there are surprisingly few studies on the association between morbidity and SA and in media it sometimes even the level of morbidity among sickness absentees even is questioned.

Studies examining the role of familial factors (i.e. genetic and shared (mainly childhood) environment) on morbidity have shown that genetics tends to explain a moderate to large extent of the variability in most of the chronic diseases [32 33]. For example, heritability for mental disorders varies between 30-90% [34], whereas genetic factors have shown to explain 30-60% of the total variation in musculoskeletal disorders [35 36]. Taken together, familial factors are important to account for when studying the association between morbidity (here in terms of hospitalization) and SA as it could lead to erroneous conclusions otherwise. Twin

settings provide a powerful tool for studies of these aspects in research of SA, a research area where selection, e.g., regarding type of work, otherwise might have a great impact on results.

The aims of the study were twofold. First we set out to investigate the associations of giving birth with subsequent morbidity in terms of hospitalization and SA. Second, we aimed to study if hospitalization prior to (or after) childbirth increases the risk for future hospitalization and SA. Familiar factors (genetics and shared/early environmental) were taken into account in order to assess if familial factors explain a potential association between childbirth and future hospitalization and SA.

Methods

Participants and data sources

We performed a prospective population-based cohort study of female twins. All female twins, i.e., women with a twin sister, born in Sweden between 1959 and 1990 were selected from the Swedish Twin Registry (STR) [37]. After excluding women who delivered their first child before 1994 or whose twin sister had her first delivery before 1994, and twins where none in the pair had their first delivery between 1994 and 2009 (n=7 304), the final cohort comprised 5 118 women. The Swedish Twin Registry (STR) is the largest population-based register of twin births in the world, with information such as birth date, sex, zygosity, and pair identification [37 38]. The selection of the study population is illustrated in Figure 1.

The unique personal identity number assigned to each Swedish resident [39] was used to link information from several nationwide population-based registers at an individual level up through 2009, as follows. The Causes of Death Register was used to obtain information on date of death [40]. Information on all deliveries from the Medical Birth Register, which was established in 1973 and includes information on almost all births in Sweden [41]. In order to increase the coverage on delivery, we also used the National Patient Register (NPR) to obtain information on all deliveries. This register was founded in 1964 and includes all individuals admitted to any psychiatric or general hospital [42]. Information on hospitalization with a principal diagnosis for delivery (as defined by the International Classification of Disease (ICD): ICD-9: 650, 651.9, 652.2, 669.5-8; and ICD-10: O80-84) was obtained. The NPR was also used to obtain annual information on other hospitalizations. Annual information on educational level and on SA was obtained from Statistics Sweden.

Time in relation to childbirth

The studied women were followed in relation to year of first childbirth, referred to as T_0. In order to compare those who gave birth to those who did not, T_0 for the women who did not give birth was defined as year of her twin sister's first childbirth.

Hospitalization

Data on hospitalization covered the period six years prior to, and six years after year of first childbirth (T_0) or equivalent. For descriptive purposes, the total and the average number of hospitalization days per year were calculated.

In order to examine if hospitalization prior to (or after) childbirth increases the risk for future hospitalization, the first part of the regression analyses considered hospitalization as both exposure and outcome. We created one dichotomous variable for hospitalization before T_0 (i.e., exposure), and two dichotomous outcome variables for hospitalization during year 2-5 after T_0: one for hospitalization with any diagnosis and one excluding hospitalization with diagnoses related to pregnancy, childbirth, and the postpartum period.

In order to answer the research question "Does hospitalization prior to (or after) childbirth increase the risk for future SA?", we created two dichotomous hospitalization exposure variables: one for hospitalization before T_0, and one variable: hospitalization year 1-2 after T_0 (excluding diagnoses related to pregnancy, childbirth, and the postpartum period).

Sickness absence

SA can be measured in several ways, related to duration and incidence [43]. Here we used the following four measures: total and average number of SA days per year; number of women with a new SA spell during year 2-5 after T_0; and number of women with a new SA spell >90 sick-leave days during year 2-5 after T_0.

Sickness insurance in Sweden

In Sweden, all residents aged 16-65 years who have income from work or unemployment benefits are entitled to sickness benefits from the Swedish Social Insurance Agency, if unable to work due to disease or injury. Among employed individuals, sick pay was in most cases paid by the employer during the first 14 days of a sick-leave spell, which means that we do not have data on most of the short sick-leave spells. In most of the years studied, there was no limitation to duration of a sick-leave spell. Sickness benefits covered 80% of lost income, up to a certain level. All were covered by a health care insurance covering the right to hospital care when needed, at a much reduced cost, less than 10 Euros a day. Care during pregnancy and delivery was free.

Potential confounding factor

Educational level at T_0 was classified into four categories; <9 years of compulsory school, 10-12 years of education (senior high school), ≥13years of education (college/university), missing.

Statistical analysis

First, Cox proportional hazard models with constant time-at-risk [44] were applied to estimate hazard ratios (HR) with 95% confidence intervals (CI) for having at least one hospitalization after childbirth (T_0). In a first model (model a), adjustments were made for age. Second (model b), additional adjustments were made for delivery year and educational level at time of T_0. Thereafter, twin pairs who were discordant (Conditional Cox regression) with respect to outcomes, i.e., having at least one hospitalization after T_0, and were analyzed. In the next step, we analyzed the associations between childbirth, hospitalization, and SA by fitting three Cox regression models (table 3). The first (model a) was adjusted for birth year. In the second

model (model b), additional adjustments were made for delivery year and educational level at time of T_0. In the third model (model c), previous hospitalization was included. Thereafter, twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e., having had a SA spell or long-term SA (>90 days) were analyzed.

Finally, in the step where we analyzed the association between hospitalization before and after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-b) from table 3. In a third model (model c), we fitted an additional model in which adjustments were made for subsequent deliveries.

Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average 50% for DZ pairs) and common environmental factors through childhood (100% for both MZ and DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs). An experimental design, which can control for familial influences, is to examine discordant twin sisters, that is, where one twin sister has given birth and the other has not. If discordant twin sisters show similar associations as the analyses of the whole cohort, this would indicate that the childbirth may actually be a contributing cause of the future SA. If instead the association found among the whole cohort cannot be replicated within discordant twin sisters, then familial factors are of importance. Influence of familial factors (genetic and common environment) is indicated if the association found in the analyses of the whole cohort disappear or change considerably in the analyses of discordant twin pairs [45].

All statistical analyses were performed with SAS 9.3 and STATA 12.1.

The project was approved by the Regional Ethical Review Board of Stockholm.

Results

Of the 5 118 women included in the study, 77% had given birth at least once between 1994 and 2009 (Table 1). Of these women, nearly 70% also had given birth later, at least once. A majority of the women who gave birth had their first delivery before the age of 30 (61%). The educational level distribution was rather similar when comparing those who gave birth to those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were excluded, 30% of the women who had given birth had at least one hospitalization during the period six years prior to and six years after their first delivery (the delivery year excluded). The corresponding rate for the women who had not given birth was 27%. Half of the women who gave birth had at least one SA spell during the period six years prior to or the six years after first delivery, when the year for childbirth was excluded. The majority of the women had no SA spell at all in the six years following childbirth.

The average annual number of days with inpatient care and SA, respectively, is presented in Figure 2. Up to year T_0, women who did not give birth had a higher average number of hospitalization days and SA days compared to those who gave birth. The average number of inpatient days increased rapidly during T_0 for women who gave birth, especially because of hospitalization due to pregnancy and childbirth. After T_0, the number of SA days decreased quickly among these women. For women who gave birth, days with inpatient care and SA the years following T_0 were to a large extent associated with subsequent childbirths.

Table 2 presents HR for the association between childbirth and hospitalization, for all diagnoses and for diagnoses where those related to pregnancy, childbirth, and the postpartum period were excluded. When these diagnoses were removed, women who did not give birth and who had been hospitalized at least once before T_0 had twice the risk of future hospitalization compared to those not hospitalized prior to T_0 (HR: 2.3; 95% CI 1.6-3.3) after adjustments for birth year, delivery year, and educational level. The association was explained by familial factors in the analysis of discordant twin pairs (HR: 1.2; 0.8-1.9).

When restricting the analyses to women who gave birth, a total of 2 792 women were studied, i.e., 1 396 complete pairs in which both twins had given birth. The reference group constituted of mothers who had not been hospitalized prior to their first childbirth. Mothers who had been hospitalized before their first childbirth had a slightly higher HR for future hospitalization when diagnoses related to pregnancy and childbirth were excluded (HR 1.5; 1.2-2.0). This association disappeared in the analyses of discordant twin pairs, suggesting an influence of familial factors (HR: 1.0; 0.8-1.3).

Regardless of childbirth status, hospitalization year 1-2 after T_0 was a predictor of having a new SA spell (

Table 3). Compared to women who did not give birth and who were not hospitalized the first two years after T_0, mothers hospitalized after first childbirth had an HR of 2.4 (2.0-2.9) after adjustments for birth year, delivery year, and educational level. Hospitalization after T_0 also was associated with long-term SA (

Table 3). Women who did not give birth had a nearly three-fold risk of long-term SA (HR 2.8; 1.5-5.1), whereas women who gave birth had an HR of 1.8 (1.3-2.5). The analyses of twin pairs discordant for having a new long-term SA spell year 2-5 after T_0, show attenuated point estimates, hence suggesting that familial effects may play a role.

The analyses, in which we considered hospitalization before and after first childbirth as exposure, and outcome was future SA (Table 4) show that mothers who had been hospitalized at least once both before and after their first child birth had a higher risk of future SA (HR 1.8; 1.4-2.2). These women also had a higher risk of long-term SA; however, these risk estimates were not statistically significant. After controlling for familial confounding, the estimated risk for long-term SA (>90 days) for those who had been hospitalized before T_0 was in the same direction but the HR was reduced, which suggest that also familial factors may have an influence on the studied association.

Discussion

In this register study of a population-based Swedish cohort of female twins born between 1959 and 1990, the associations of delivery with hospitalization and SA were examined as well as whether familial (i.e. genetic and shared, mainly childhood, environmental) factors were contributing to these associations. Just before the first childbirth, the SA days increased much for mothers, an increase that gradually decreased during the years after the delivery. We found hospitalization prior to T_0 to be a risk factor for future hospitalization, regardless of childbirth status, also when excluding hospitalization due to childbirth. Furthermore, hospitalization after the first childbirth was associated with a higher HR of both short-term and long-term future SA. An additional analysis focusing solely on the women who gave birth showed that hospitalization both before and after the first childbirth was associated with a higher risk of future SA. Familial factors seemed to have an influence on the association between hospitalization and long-term SA, regardless of childbirth status.

In line with some previous studies [10 20 46 47], we found that SA increased in women during the time before the first childbirth. Giving birth was also associated with a future somewhat higher risk for SA, in line with that of those not giving birth. However, this higher risk could be due to subsequent pregnancies. A recent Norwegian study found that the increased SA risk in women in the years after pregnancy disappeared when SA during subsequent pregnancies were accounted for [20]. Several explanations have been suggested for such higher levels of SA, among others the double burden hypothesis [20 48-50]. This hypothesis has been questioned, as research has indeed shown that women who occupy multiple roles tend to be healthier than those who enact fewer roles [51-53]. Thus, the combination of employment and parenthood does not seem to imply worse health, on the contrary. In our study, the annual rates of SA decreased steadily after the first childbirth, speaking in favor of this hypothesis. Further studies of this are warranted.

To our best knowledge, this is the first study to examine long-term associations between childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to subsequent pregnancy and childbirth) when compared to women who did not give birth.

Those who did not give birth had a more stable pattern of SA during the studied period, however, with a slight increase in annual SA days over the years. This is in line with a Swedish study examining whether family obligations influence the risk of SA in publicly employed women and found a slight risk increase for SA among women without children [54]. Further, a broad systematic literature review published in 2004 provided no evidence of an association between having children in the household and an increased risk of SA [55]. It is important to consider family situation when examining the association between having children and morbidity, as single women with children have been shown to have worse health [30 31 56] and higher levels of SA [6 54].

Even though pregnancy, delivery, and the postpartum period may increase the risk for disease and injury [25 27], our findings do not suggest that women who gave birth are more likely to be hospitalized after their first childbirth, except for hospitalizations related to subsequent deliveries. We found no differences in risk for future hospitalization when comparing those who gave birth to those who did not. Thus, giving birth does not have to be associated with subsequent health problems. The fact that we found no differences in future hospitalization between those who gave birth and not, may have different explanations. As mentioned above, one could expect that there is a health selection, where women who do not give birth may have worse health and choose not to have or cannot have a child. Also, giving birth is in itself a risk factor for future morbidity. Further, we know that, during the last decades, the number of women who voluntarily do not want to become parents has increased worldwide[57].

Hospitalization prior to the first childbirth or equivalent (T_0) was a risk factor for future SA for all women, regardless of childbirth status. In particular, women who had been hospitalized both before and after T_0 were at risk for future SA. Furthermore, we found an association between hospitalization and future longer SA spells.

When comparing women who gave birth to those who did not, with respect to exposure to hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had slightly higher risk for future SA regardless of duration, whereas those who did not give birth hospitalized after T_0 had higher risk for long-term SA.

Hospitalization both before and after the year T_0 seems to be the strongest indicator, i.e., these individuals had the highest risk for future SA. Consequently, the women who had been hospitalized both before and after T_0 had the highest risk for future SA. Our analyses of women who gave birth revealed a graded association between hospitalization and SA, where those who only were hospitalized before *or* after their first childbirth had a higher risk of SA, whereas those who were hospitalized both before and after the first childbirth had even higher risks. Thus, we found a strong association between morbidity, here measured as hospitalization, and future SA among women who have given birth– an association that often has been question regarding women with children[12].

Familial factors seemed to contribute to the association between hospitalization before and after T_0 among those who did not give birth. The influence of familial factors may relate to morbidity among women not giving birth – morbidity that might be more severe and potentially also being relatively strongly influenced by genetics. Familial factors also played a role in the associations between hospitalization and future long-term SA. This could be related to the fact that the hospitalization usually is required for severe conditions that may have a strong genetic component. However, since genetics have been shown to influence the risk of DP [58], and some indications exist that genetics also play a role in long-term SA and

mortality, it can be suspected that the effects of familial factors on SA can be either direct or through other influential factors.

Strengths and limitations

The strengths of this study are the population-based prospective cohort study design, including all in the study population, not a sample, using nationwide registers with high completeness and validity [40-42]. Further, we used a large study cohort without loss to follow up. With a twin study design, we were able to take familial influences into account. When measuring both exposure and outcome with register-based data, we avoid problem with recall bias.

This study has, however, some limitations. First of all, we do not know whether the women who did not give birth were childless voluntarily or not. Differences in health between voluntary and involuntary childlessness have been shown, where voluntarily childless women showed higher levels of overall well-being [57 59] which might be related to hospitalization and/or SA. Another limitation is that the terms for inpatient care have changed during the studied period. In Sweden, inpatient care has to a great extent been replaced by outpatient treatment. Therefore, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities [60], however, this affected all women equally, and is to some extent handled by adjusting for birth year. The CIs are wider in the years far from $T_{0,}$ e.g., $T_{6,}$ due to fewer follow up year for some – e.g., for those who gave birth late during the studied period.

It is important to be aware of that giving birth is in focus here, irrespective of whether the child survived or not. Some of the women who did not give birth might be mothers, e.g., due to adoption. Other studies in this area has 'being mother' or 'living with child' as exposure term, rather than 'giving birth'.

Conclusion

Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth. Mothers with different types of morbidity, in terms of hospitalization before and/or after giving birth had higher risks for future SA. Most women had no SA in the six years following childbirth and those who had SA generally had that for shorter periods. Among the few women who had severe morbidity, in terms of hospitalization, the future risk for SA was, as expected, higher. Hospitalization prior to T_0 was strongly associated with later hospitalization and later SA. The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially. However, most women had no hospitalization and no SA.

Ethical approval

The study was approved by the Regional Ethical Review Board, Stockholm, Sweden (2007/524-31).

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Competing interest statement

We declare that no competing interests exist.

Author's contributions

KA and PS originated the idea. EB analysed the data in consultation with KA, LK, JN, AR and PS. EB wrote the first and subsequent drafts of the manuscript, with important intellectual input from all the co-authors. All authors contributed in designing the study and to the interpretation of the results and to the writing and approval of the final article.

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Suggested figures and tables

Figure 1. Flow chart for the study population

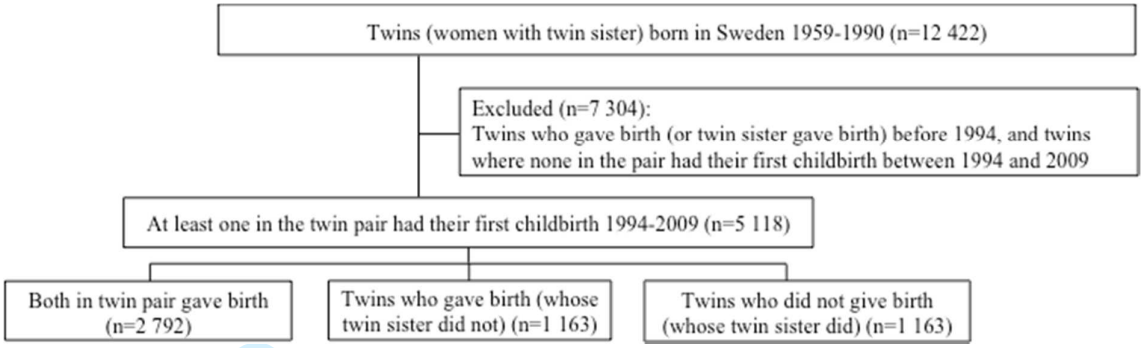

Figure 2. Average annual number of days on sickness absence (SA) and hospitalization, respectively, (with 95% CI), six years prior through six year after T_0 for women who gave birth/did not give birth (n=5 118).

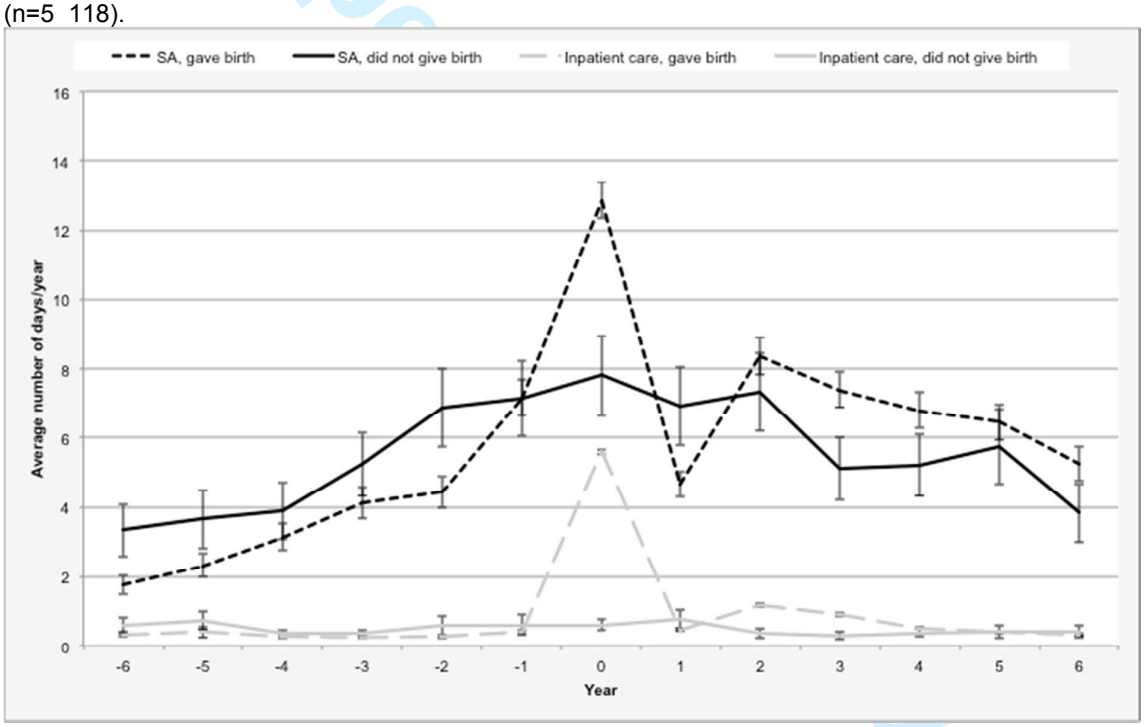

Table 1. Cohort characteristics for twins (women with twin sister) born in Sweden 1959-1990 (excluding those who gave birth before age 16 and those who died before age 16), where at least one in the pair had their first childbirth 1994-2009 and none before 1994. T_0 is defined as year for first childbirth for women who gave birth, and year of twin sister's childbirth for those who did not give birth.

		Twin pairs where only one in the pair gave birth		
Variables	**Both gave birth**	**Twin 1 (gave birth)**	**Twin 2 (did not give birth)**	**Total**
N	2 792	1 163	1 163	5 118
Number of deliveries				
One delivery	711 (25%)	501 (43%)		
Two or more deliveries	2 081 (75%)	662 (57%)		
Age at T_0				
16-19 years	47 (2%)	33 (21%)		
20-24 years	511 (18%)	239 (21%)		
25-29 years	1 150 (41%)	444 (38%)		
30-34 years	847 (30%)	323 (28%)		
35-39 years	207 (7%)	109 (9%)		
<40 years	30 (1%)	15 (1%)		
Zygosity				
Monozygotic	1 726 (62%)	608 (52%)	608 (52%)	2 942 (57%)
Dizygotic	1 066 (38%)	555 (48%)	555 (48%)	2 176 (43%)
Highest attained education[1]				
≤ 9 year	179 (6%)	74 (6%)	55 (5%)	308 (6%)
10-12 year	1 434 (51%)	608 (52%)	621 (53%)	2 663 (52%)
≥ 13 year	1 173 (42%)	474 (41%)	422 (36%)	2 069 (40%)
Information on education missing	6 (0%)	7 (1%)	65 (6%)	78 (2%)
Hospitalization[2]				
- At least one hospitalization during the period six years prior through six years after T_0	2 161 (77%)	703 (60%)	325 (28%)	3 189 (62%)
-At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, childbirth, and the puerperium)	865 (31%)	315 (27%)	314 (27%)	1 494 (29%)
- At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, and childbirth)	1 183 (42%)	407 (35%)	325 (28%)	1 915 (37%)
- At least one hospitalization during the period six years prior to T_0	679 (24%)	251 (22%)	217 (19%)	1 147 (22%)
- At least one hospitalization during the period six years after T_0	1 965 (70%)	585 (50%)	168 (14%)	2 718 (53%)
- At least one hospitalization both before and afterT_0	483 (17%)	133 (11%)	60 (5%)	676 (13%)
Sickness Absence (SA)[3]				
At least one SA spell during the period six years prior through six years after T_0	1 526 (55%)	530 (46%)	365 (31%)	2 420 (47%)
At least one SA spell during the period six years prior to T_0	690 (25%)	274 (24%)	224 (19%)	1 188 (23%)
At least one SA spell during the period six years after T_0	1 245 (45%)	382 (33%)	221 (19%)	1 848 (36%)

[1] At time of T_0

[2] Excluding hospitalizations occurring during T_0

[3] Excluding SA spells occurring during T_0

Table 2. Cox proportional hazard ratios (HR) with 95% CI for the association between childbirth and hospitalization in twins where at least one in the pair had her first childbirth 1994-2009 and none before 1994.

Status childbirth and hospitalization	All diagnoses			Diagnoses related to pregnancy, childbirth and the puerperium excluded[1]		
	Model a[6]	Model b[7]	Discordant twin pairs[2, 7]	Model a[6]	Model b[7]	Discordant twin pairs[3, 7]
All women (n=5 118)						
No childbirth, no hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization before T_0[8]	2.5 (1.7-3.6)	2.3 (1.6-3.3)	2.4 (1.3-4.5)	2.7 (1.8-3.9)	2.3 (1.6-3.4)	1.2 (0.8-1.9)
Childbirth, no hospitalization before T_0[8]	6.1(5.0-7.5)	5.5 (4.5-6.8)	8.3 (5.8-11.8)	1.1 (0.8-1.3)	0.9 (0.7-1.2)	0.9 (0.7-1.1)
Childbirth, hospitalization before T_0[8]	6.5 (5.2-8.1)	5.6 (4.4-7.1)	7.9 (5.4-11.5)	1.9 (1.4-2.5)	1.4 (1.1-1.9)	0.9 (0.7-1.2)
	Model a[6]	**Model b[7]**	**Discordant twin pairs[4, 7]**	**Model a[6]**	**Model b[7]**	**Discordant twin pairs[5, 7]**
Women who had at least one childbirth (n=2 792)						
No hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[8]	1.0 (0.9-1.2)	1.0 (0.9-1.1)	1.0 (0.8-1.2)	1.7 (1.3-2.3)	1.5 (1.2-2.0)	1.0 (0.8-1.3)

[1] Diagnoses O00-O99
[2] Twin pairs where one had a hospitalization during the follow-up and the other not (n=1 016 pairs)
[3] Twin pairs where one had a hospitalization during the follow-up and the other not (n=456 pairs)
[4] Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)
[5] Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs)
[6] Adjusted for birth year
[7] Model a, and additional adjustments for delivery year, and educational level
[8] During the period 1-5 years prior to T_0

Table 3. Cox proportional HR with 95% CI for the association between childbirth, hospitalization and sickness absence (SA), in twins where at least one in the pair had their first childbirth 1994-2009.

Status childbirth and hospitalization	SA (at least one day)				Long-term SA (>90 days)			
	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[1, 7]	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[2, 7]
All women (n=5 118)								
No childbirth, no hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization year 1-2 after T_0[8]	2.7 (1.8-4.1)	2.2 (1.5-3.4)	2.1 (1.4-3.2)	1.5 (0.8-2.9)	4.5 (2.5-8.2)	3.5 (1.9-6.2)	2.8 (1.5-5.1)	1.1 (0.5-2.3)
Childbirth, no hospitalization year 1-2 after T_0[8]	2.1 (1.8-2.5)	1.8 (1.5-2.2)	1.8 (1.5-2.2)	1.7 (1.3-2.2)	1.1 (0.8-1.6)	1.0 (0.7-1.4)	1.0 (0.7-1.3)	0.8 (0.6-1.2)
Childbirth, hospitalization year 1-2 after T_0[8]	3.0 (2.5-3.6)	2.4 (2.0-2.9)	2.4 (2.0-2.9)	2.0 (1.5-2.6)	2.3 (1.6-3.2)	1.8 (1.3-2.5)	1.8 (1.3-2.5)	1.0 (0.7-1.5)
Women who had at least one childbirth (n=2 792)	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[3, 5]**	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[4, 7]**
No hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization year 1-2 after T_0[8]	1.3 (1.2-1.5)	1.3 (1.1-1.4)	1.2 (1.1-1.4)	1.2 (1.0-1.5)	2.0 (1.5-2.6)	1.9 (1.4-2.5)	1.8 (1.4-2.4)	1.4 (1.0-1.9)

[1] Twin pairs where one had a SA spell during the follow-up and the other not (n=835 pairs)
[2] Twin pairs where one had a long-term SA spell during the follow-up and the other not (n=277 pairs)
[3] Twin pairs where one had a SA spell during the follow-up and the other not (n=542 pairs)
[4] Twin pairs where one had a long-term SA spell during the follow-up and the other not (n=184 pairs)
[5] Adjusted for birth year
[6] Model a, and additional adjustments for delivery year, and educational level
[7] Model b, and additional adjustments for earlier hospitalization
[8] Diagnoses O00-O99 excluded

Table 4. Cox proportional HR with 95% CI for the association between hospitalization before and after first childbirth, and sickness absence (SA), in twins who had their first childbirth 1994-2009 (n=2 792).

Status hospitalization before and after childbirth	SA (at least one day)				Long-term SA (>90 days)			
	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[1, 4]	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[2, 4]
No hospitalization either before T_0[6] or during year 1-2 after T_0[7]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[6] but not during year 1-2 after T_0[7]	1.2 (1.0-1.5)	1.2 (1.0-1.4)	1.2 (1.0-1.4)	1.0 (0.8-1.3)	2.3 (1.6-3.4)	2.1 (1.5-3.1)	2.2 (1.5-3.1)	1.2 (0.8-1.7)
No hospitalization before T_0[6] but during year 1-2 after T_0[7]	1.2 (1.1-1.4)	1.2 (1.0-1.4)	1.1 (0.9-1.2)	1.1 (0.9-1.4)	2.0 (1.5-2.8)	1.9 (1.4-2.7)	1.9 (1.4-2.7)	1.4 (1.0-2.1)
Hospitalization before T_0[6] and during year 1-2 after T_0[7]	2.0 (1.6-2.5)	1.8 (1.4-2.2)	1.6 (1.3-2.1)	1.6 (1.1-2.2)	4.2 (2.7-6.4)	3.5 (2.3-5.3)	3.5 (2.3-5.4)	1.5 (0.9-2.4)

[1] Twin pairs where one had an SA spell during the follow-up and the other not (n=542)
[2] Twin pairs where one had a long-term SA spell during the follow-up and the other not (n=184)
[3] Adjusted for birth year
[4] Model a, and additional adjustments for delivery year, and educational level
[5] Model b, and additional adjustments for subsequent deliveries
[6] During the period 1-5 years prior to T_0
[7] Diagnoses O00-O99 excluded

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Childbirth, hospitalization, and sickness absence: a study of female twins

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Abstract

Objective: To investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account.

Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA were calculated as hazard ratios (HR) with 95% confidence intervals (CI).

Setting: All female twins, i.e., women with twin sister, born in Sweden.

Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where at least one in the twin pair had their first childbirth (T_0) 1994-2009 and none gave birth before 1994.

Main outcome measures: Hospitalization and SA during year 3-5 after first delivery or equivalent.

Results: Preceding the first childbirth, the mean annual number of SA days increased for mothers, and then decreased again. Hospitalization after T_0 was associated with higher HRs of short-term and long-term SA (HR for short-term SA: 3.0; 95% CI 2.5-3.6 and for long-term SA: 2.3; 95% CI 1.6-3.2). Hospitalization both before and after first childbirth was associated with a higher risk of future SA (HR for long-term SA: 4.2; 95% CI 2.7-6.4). Familial factors influenced the association between hospitalization and long-term SA, regardless of childbirth status.

Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth and results indicate a positive health selection into giving birth. Mothers hospitalized before and/or after giving birth had higher risks for future SA, that is, there was a strong association between morbidity and future SA.

Keywords: sick leave, childbirth, inpatient care, hospitalization, cohort study, population based, twins

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Article Summary

Article focus:

To investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account.

Key messages:

- Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth
- The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially

Strengths and limitations:

- The strengths of the study include the population-based prospective design, using national registers with high completeness and validity
- With a twin study design, we were able to take familial influences into account
- As inpatient care to a great extent has been replaced by outpatient treatment, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities

Introduction

In most countries with high labor force participation, women have higher levels of sickness absence (SA) than men [1-4]. Many theories and mechanism regarding this have been suggested, e.g., women having higher morbidity, higher workload (when combining paid and unpaid work), tougher situation on the labor market, men being the norm for how the labor market is organized, gender bias in healthcare and social insurance systems, discrimination, and domestic violence, etcetera [5-9]. Another hypothesis behind this gender difference in SA focuses on SA during pregnancy and after childbirth [6 10-13]. Several studies show that women have higher SA during pregnancy [10 14] and that pregnancy-related SA explains half of the gender differences in SA in fertile ages [15].

One of the changes in society that may affect health after childbirth is that the mean age for having the first child has increased over the last years and that women with higher level of morbidity now give birth. Further, nowadays, the proportion of caesarean sections has increased as well as vacuum extraction deliveries, leading to risk of later health problems [16 17].

In this study, focus is on childbirth, morbidity, and SA among women, to get a better understanding of mechanisms behind SA among women in fertile ages. There are hardly any studies on the associations between giving birth and morbidity and SA, and those conducted have focused on a relatively short time period right after childbirth, most often within the first year following the child delivery [18 19], while prospective studies with longer follow-up of mothers are rare [6 12 20].

Pregnancy, delivery, and the postpartum period may imply large physical, mental, and social changes during a short period of time, increasing the risk for disease and injury [21 22]. Different types of physical and mental disorders are common during pregnancy and after childbirth – and can in some cases be longstanding or even permanent – however, this is hardly studied at all [19]. Giving birth may be associated with a higher risk of certain diseases demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental

disorders, and different types of injuries [23-26]. For women with a disease present before the childbirth, the disorder might deteriorate after childbirth [23 24]. Regarding symptoms related to childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain, fatigue, headache, and sleep disorders [19 27]. Most of these symptoms seem to remain up to one year after childbirth [17]. Besides physical health effects, also depression and other mental disorders have been linked to childbirth [26 28], but again, prospective studies with longer follow-up are lacking [27]. Even though having children has been shown to contribute to an overall wellbeing, this is not the case for everybody and especially not among single mothers whose economic situation and thereby possibilities for good health care might be worse [29-31].

Morbidity can be measured in different ways, e.g., through self-reports and visits to healthcare. Here we will use data on more severe morbidity that involves assessments from physicians, that is, morbidity that has led to hospitalization, a measure so far not used in this type of studies. Sickness absence is not a good measure of morbidity– most people with morbidity are not on SA [4]. Instead SA is considered a very good measure of social consequences of morbidity, in terms of not being able to support yourself from work [4]. Yet, there are surprisingly few studies on the association between morbidity and SA and in media sometimes even the level of morbidity among sickness absentees even is questioned.

Studies examining the role of familial factors (i.e. genetic and shared (mainly childhood) environment) on morbidity have shown that genetics tends to explain a moderate to large extent of the variability in most of the chronic diseases [32 33]. For example, heritability for mental disorders varies between 30-90% [34], whereas genetic factors have been shown to explain 30-60% of the total variation in musculoskeletal disorders [35 36]. Taken together, familial factors are important to account for when studying the association between morbidity (here in terms of hospitalization) and SA as studies otherwise could lead to erroneous conclusions. Twin settings provide a powerful tool for studies of these aspects in research of

SA, a research area where different selection biases otherwise might have an impact on results. Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average 50% for DZ pairs) and common environmental factors through childhood (100% for both MZ and DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs). An experimental design, which can control for these familial influences, is to examine discordant twin sisters, that is, where one twin sister has given birth and the other has not. If discordant twin sisters show similar associations as the analyses of the whole cohort, this would indicate that the childbirth may actually be a contributing cause of the future SA. If instead the association found among the whole cohort cannot be replicated within discordant twin sisters, then familial factors are of importance. Influence of familial factors (genetic and common environment) is indicated if the association found in the analyses of the whole cohort disappear or change considerably in the analyses of discordant twin pairs [37].

The aim of the study was to investigate the associations of giving birth with subsequent morbidity in terms of hospitalization and SA. Familial factors (genetics and shared/early environmental) were taken into account in order to assess if familial factors explain a potential association between childbirth and future hospitalization and SA.

Methods

Participants and data sources

We performed a prospective population-based cohort study of female twins. All female twins, i.e., women with a twin sister, born in Sweden between 1959 and 1990 were selected from the Swedish Twin Registry (STR) [38]. After excluding women who delivered their first child before 1994 or whose twin sister had her first delivery before 1994, and twins where none in the pair had their first delivery between 1994 and 2009 (n=7 304), the final cohort comprised 5 118 women of which 95% had income from work, the others had income from parental benefits, unemployment benefits, student benefits, different types of sickness benefits, or a mixture of those (in the year prior to the birth year, i.e., T(-1). All had some of those types of income, all granting rights to SA benefits. The Swedish Twin Registry (STR) is the largest population-based register of twin births in the world, with information such as birth date, sex, zygosity, and pair identification [38 39]. The selection of the study population is illustrated in Figure 1.

The unique personal identity number assigned to each Swedish resident [40] was used to link information from several nationwide population-based registers at an individual level up through 2009, as follows. The Causes of Death Register was used to obtain information on date of death [41]. This register contains information on all deceased Swedish residents since 1952. Information on all deliveries (including still births) was derived from the Medical Birth Register, which was established in 1973 and includes information on almost all births in Sweden [42]. In order to increase the coverage on delivery, we also used the National Patient Register (NPR) to obtain information on all deliveries. This register was founded in 1964 and includes all individuals admitted to any psychiatric or general hospital [43]. Information on hospitalization with a principal diagnosis for delivery (as defined by the International Classification of Disease (ICD): ICD-9: 650, 651.9, 652.2, 669.5-8; and ICD-10: O80-84) was obtained. The NPR was also used to obtain annual information on other hospitalizations, i.e.,

inpatient care. Annual information on educational level and on SA days was obtained from Statistics Sweden.

Time in relation to childbirth

The studied women were followed in relation to year of first childbirth, referred to as T_0. In order to compare those who gave birth to those who did not, T_0 for the women who did not give birth was defined as year of her twin sister's first childbirth.

Hospitalization

Data on hospitalization covered the period six years prior to, and six years after year of first childbirth (T_0) or equivalent. For descriptive purposes, the total and the average number of hospitalization days per year were calculated.

In order to examine if hospitalization prior to (or after) childbirth increases the risk for future hospitalization, the first part of the regression analyses considered hospitalization as both exposure and outcome. We created one dichotomous variable for hospitalization before T_0 (i.e., exposure), and two dichotomous outcome variables for hospitalization during year 3-5 after T_0: one for hospitalization with any diagnosis and one excluding hospitalization with diagnoses related to pregnancy, childbirth, and the postpartum period.

In order to answer the research question "Does hospitalization prior to (or after) childbirth increase the risk for future SA?", we created two dichotomous hospitalization exposure variables: one for hospitalization before T_0 and one variable: hospitalization year 1-2 after T_0 (excluding diagnoses related to pregnancy, childbirth, and the postpartum period).

Sickness absence

SA can be measured in several ways, related to duration and incidence [44]. Here we used the following four measures: total and average number of SA days per year; number of SA days during year 3-5 after T_0; and number of SA days >90 sick-leave days during year 3-5 after T_0.

Sickness insurance in Sweden

In Sweden, all residents aged 16-65 years who have income from work, unemployment benefits, parental benefits, or student benefits are entitled to sickness benefits from the Swedish Social Insurance Agency, if unable to work due to disease or injury. Among employed individuals, sick pay was in most cases paid by the employer during the first 14 days of a sick-leave spell, which means that we do not have data on most of the short sick-leave spells. In most of the years studied, there was no limitation to duration of a sick-leave spell. Sickness benefits covered 80% of lost income, up to a certain level. All were covered by a health care insurance covering the right to hospital care when needed, at a much reduced cost, less than 10 Euros a day. Care during pregnancy and delivery was free.

Potential confounding factor

As research has shown socioeconomic disparities in age at first birth (e.g., the higher the education, the later the first birth) [45 46], we adjusted for educational level at T_0. Years of education was classified into four categories; <9 years of compulsory school, 10-12 years of education (senior high school), ≥13years of education (college/university), missing.

Statistical analysis

First, Cox proportional hazard models with constant time-at-risk [47] were applied to estimate hazard ratios (HR) with 95% confidence intervals (CI) for having at least one hospitalization after childbirth (T_0). In a first model (model a), adjustments were made for age. Second

(model b), additional adjustments were made for delivery year and educational level at time of T_0. Thereafter, twin pairs who were discordant with respect to outcomes, i.e., having at least one hospitalization after T_0, were analyzed using Conditional Cox regression. In the next step, we analyzed the associations between childbirth, hospitalization, and SA by fitting three Cox regression models (table 3). The first (model a) was adjusted for birth year. In the second model (model b), additional adjustments were made for delivery year and educational level at time of T_0. In the third model (model c), previous hospitalization was included. Thereafter, twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e., having had SA or long-term SA (>90 days) were analyzed.

Finally, in the step where we analyzed the association between hospitalization before and after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-b) from table 3. In a third model (model c), we fitted an additional model in which adjustments were made for subsequent deliveries.

The proportional hazards assumption was checked by including time-dependent versions of all the covariates in the models. This did not indicate a violation of the proportionality assumption.

All statistical analyses were performed with SAS 9.3 and STATA 12.1.

The STROBE checklist was used in designing and reporting the study.

The project was approved by the Regional Ethical Review Board of Stockholm.

Results

Of the 5 118 women included in the study, 77% had given birth at least once between 1994 and 2009 (Table 1). Of these women, nearly 70% also had given birth later, at least once. A majority of the women who gave birth had their first delivery before the age of 30 (61%). The educational level distribution was rather similar when comparing those who gave birth to those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were excluded, 30% of the women, i.e., the 1 183 where both in a pair gave birth and the 407 twins where only one in the pair gave birth had at least one hospitalization during the period six years prior to and six years after their first delivery (the delivery year excluded). The corresponding rate for the women who had not given birth was 27%. Half of the women who gave birth had at least one day of SA during the period six years prior to or the six years after first delivery, when the year for childbirth was excluded. The majority of the women had no SA at all in the six years following childbirth.

The average annual number of days with inpatient care and SA, respectively, is presented in Figure 2. Up to year T_0, women who did not give birth had a higher average number of hospitalization days and SA days compared to those who gave birth. Women who gave birth had approximately 0.3 hospitalization days per year whereas those who did not give birth had around 0.5 hospitalization days per year. The average number of SA days for women giving birth was 3.8 days/year and for those not giving birth 5.0 days/year. SA differences between those giving birth and women not giving birth were statistically significant with the exception of year (-4) and (-3). For inpatient care, the differences between those giving birth and women not giving birth were not statistically significant. The average number of inpatient days increased rapidly during T_0 for women who gave birth, especially because of hospitalization due to pregnancy and childbirth. After T_0, the number of SA days decreased quickly among these women. For women who gave birth, days with inpatient care and SA the years following T_0 were to a large extent associated with subsequent childbirths.

Table 2 presents HR for the association between childbirth and hospitalization, for all diagnoses and for diagnoses where those related to pregnancy, childbirth, and the postpartum period were excluded. When these diagnoses were removed, women who did not give birth and who had been hospitalized at least once before T_0 had twice the risk of future hospitalization compared to those not hospitalized prior to T_0 (HR: 2.3; 95% CI 1.6-3.3) after adjustments for birth year, delivery year, and educational level. The association was explained by familial factors in the analysis of discordant twin pairs (HR: 1.2; 0.8-1.9).

When restricting the analyses to women who gave birth, a total of 2 792 women were studied, i.e., 1 396 complete pairs in which both twins had given birth. The reference group constituted of mothers who had not been hospitalized prior to their first childbirth. Mothers who had been hospitalized before their first childbirth had a slightly higher HR for future hospitalization when diagnoses related to pregnancy and childbirth were excluded (HR 1.5; 1.2-2.0). This association disappeared in the analyses of discordant twin pairs, suggesting an influence of familial factors (HR: 1.0; 0.8-1.3).

Regardless of childbirth status, hospitalization year 1-2 after T_0 was a predictor of having a new SA in year 3-5 after T_0 (Table 3). Compared to women who did not give birth and who were not hospitalized the first two years after T_0, mothers hospitalized after first childbirth had an HR of 2.4 (2.0-2.9) for a new SA after adjustments for birth year, delivery year, and educational level. Hospitalization after T_0 was also associated with a new long-term SA (>90 days) in year 3-5 after T_0 (Table 3). Women who did not give birth had a nearly three-fold risk of a new long-term SA year 3-5 after T_0 (HR 2.8; 1.5-5.1), whereas women who gave birth had an HR of 1.8 (1.3-2.5). The analyses of twin pairs discordant for having a new long-term SA year 3-5 after T_0, showed attenuated point estimates, hence suggesting that familial effects may play a role.

The analyses, in which we considered hospitalization before and after first childbirth as exposure, and outcome was a new SA year 3-5 after T_0 (Table 4) show that mothers who had been hospitalized at least once both before and after their first child birth had a higher risk of future SA (HR 1.8; 1.4-2.2). These women also had a higher risk of long-term SA; however, these risk estimates were not statistically significant. After controlling for familial confounding, the estimated risk for long-term SA for those who had been hospitalized before T_0 was in the same direction but the HR was reduced, which suggest that also familial factors may have an influence on the studied association.

Discussion

In this register study of a population-based Swedish cohort of female twins born between 1959 and 1990, the associations of delivery with hospitalization and SA were examined as well as whether familial (i.e., genetic and shared, mainly childhood, environmental) factors were contributing to these associations. Just before the first childbirth, the SA days increased much for mothers, an increase that gradually decreased during the years after the delivery. We found hospitalization prior to T_0 to be a risk factor for future hospitalization, regardless of childbirth status, also when excluding hospitalization due to childbirth. Furthermore, hospitalization after the first childbirth was associated with a higher HR of both short-term and long-term future SA. An additional analysis focusing solely on the women who gave birth showed that hospitalization both before and after the first childbirth was associated with a higher risk of future SA. Familial factors seemed to have an influence on the association between hospitalization and long-term SA, regardless of childbirth status.

In line with some previous studies [10 20 48 49], we found that SA increased in women during the time before the first childbirth. Giving birth was also associated with a future somewhat higher risk for SA, in line with that of those not giving birth. However, this higher risk could be due to subsequent pregnancies. A recent Norwegian study found that the increased SA risk in women in the years after pregnancy disappeared when SA during subsequent pregnancies were accounted for [20]. Several explanations have been suggested for such higher levels of SA, among others the double burden hypothesis [20 50-52]. This hypothesis has been questioned, as research has indeed shown that women who occupy multiple roles tend to be healthier than those who enact fewer roles [53-55]. Thus, the combination of employment and parenthood does not seem to imply worse health, on the contrary. In our study, the annual rates of SA decreased steadily after the first childbirth, speaking in favor of this hypothesis. Further studies of this are warranted.

To our best knowledge, this is the first study to examine long-term associations between childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to subsequent pregnancy and childbirth) when compared to women who did not give birth.

Those who did not give birth had a more stable pattern of SA during the studied period, however, with a slight increase in annual SA days over the years. This is in line with a Swedish study examining whether family obligations influence the risk of SA in publicly employed women and found a slight risk increase for SA among women without children [56]. Further, a broad systematic literature review published in 2004 provided no evidence of an association between having children in the household and an increased risk of SA [57]. It is important to consider family situation when examining the association between having children and morbidity, as single women with children have been shown to have worse health [30 31 58] and higher levels of SA [6 56].

Even though pregnancy, delivery, and the postpartum period may increase the risk for disease and injury [25 27], our findings do not suggest that women who gave birth are more likely to be hospitalized after their first childbirth, except for hospitalizations related to subsequent deliveries. We found no differences in risk for future hospitalization when comparing those who gave birth to those who did not. Thus, giving birth does not have to be associated with subsequent health problems. The fact that we found no differences in future hospitalization between those who gave birth and those who did not, may have different explanations. As mentioned above, one could expect that there is a health selection, where women who do not give birth may have worse health and choose not to have or cannot have a child. Also, giving birth is in itself a risk factor for future morbidity[16 19 22]. Further, during the last decades, the number of women who voluntarily do not want to become parents has increased worldwide[59].

Hospitalization prior to the first childbirth or equivalent (T_0) was a risk factor for future SA for all women, regardless of childbirth status. In particular, women who had been hospitalized both before and after T_0 were at risk for future SA. Furthermore, we found an association between hospitalization and future long-term SA.

When comparing women who gave birth to those who did not, with respect to exposure to hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had slightly higher risk for future SA regardless of duration, whereas those who did not give birth hospitalized after T_0 had higher risk for long-term SA.

Hospitalization both before and after the year T_0 seems to be the strongest indicator, i.e., these individuals had the highest risk for future SA. Consequently, the women who had been hospitalized both before and after T_0 had the highest risk for future SA. Our analyses of women who gave birth revealed a graded association between hospitalization and SA, where those who only were hospitalized before *or* after their first childbirth had a higher risk of SA, whereas those who were hospitalized both before and after the first childbirth had even higher risks. Thus, we found a strong association between morbidity, here measured as hospitalization, and future SA among women who have given birth – an association that often has been question regarding women with children [12].

Familial factors seemed to contribute to the association between hospitalization before and after T_0 among those who did not give birth. The influence of familial factors may relate to morbidity among women not giving birth – morbidity that might be more severe and potentially also being relatively strongly influenced by genetics. Familial factors also played a role in the associations between hospitalization and future long-term SA. This could be related to the fact that the hospitalization usually is required for severe conditions that may have a strong genetic component. However, since genetics have been shown to influence the risk of DP [60], and some indications exist that genetics also play a role in long-term SA and

mortality, it can be suspected that the effects of familial factors on SA can be either direct or through other influential factors.

Strengths and limitations

The strengths of this study are the population-based prospective cohort study design, including all in the study population, not a sample, using nationwide registers with high completeness and validity [41-43]. Further, we used a large study cohort without loss to follow up. With a twin study design, we were able to take familial influences into account. When measuring both exposure and outcome with register-based data, we avoid problem with recall bias.

This study has, however, some limitations. First of all, we do not know whether the women who did not give birth were childless voluntarily or not. Differences in health between voluntary and involuntary childlessness have been shown, where voluntarily childless women showed higher levels of overall well-being [59 61] which might be related to hospitalization and/or SA. Using inpatient care as a measure of morbidity has both its strengths and limitations. One limitation is that we thus selected more severe types of morbidity, and hence that does not include morbidity treated in outpatient care. Having had also other types of morbidity data might have given another picture and hopefully future studies will have such information. Another limitation is that the terms for inpatient care have changed during the studied period. In Sweden, inpatient care has over the years to a great extent been replaced by outpatient treatment. Therefore, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities [62], however, this affected all women equally, and is to some extent handled by adjusting for birth year. The CIs are wider in the years far from T_0, e.g., T_6, due to fewer follow up year for some – e.g., for those who gave birth late during the studied period. Also,

we lack information on the shorter SA spells among those employed. Further, the Swedish Twin Registry (STR) contains all twin births in Sweden; hence, immigrants are not included in this study and as a consequence the external validity might be lower to women born outside of Sweden.

It is important to be aware of that giving birth is in focus here, irrespective of whether the child survived or not. Some of the women who did not give birth might be mothers, e.g., due to adoption. Other studies in this area has 'being mother' or 'living with child' as exposure term, rather than 'giving birth'.

Conclusion

Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth. Mothers with different types of morbidity, in terms of hospitalization before and/or after giving birth had higher risks for future SA. Most women had no SA in the six years following childbirth and those who had SA generally had that for shorter periods. Among the few women who had severe morbidity, in terms of hospitalization, the future risk for SA was, as expected, higher. Hospitalization prior to T_0 was strongly associated with later hospitalization and later SA. The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially. However, most women had no hospitalization and no SA.

Ethical approval

The study was approved by the Regional Ethical Review Board, Stockholm, Sweden (2007/524-31).

Contributorship Statement

KA and PS originated the idea. EB analysed the data in consultation with KA, LK, JN, AR, and PS. EB wrote the first and subsequent drafts of the manuscript, with important intellectual input from all the co-authors. All authors contributed in designing the study and to the interpretation of the results and to the writing and approval of the final article.

Competing interest statement

We declare that no competing interests exist.

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Data sharing

No additional data available.

Figure legends

Figure 1. Flow chart for the study population.

Figure 2. Average annual number of days on sickness absence (SA) and hospitalization, respectively, (with 95% CI), six years prior through six year after T_0 for women who gave birth/did not give birth (n=5 118).

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Table 1. Cohort characteristics for twins (women with twin sister) born in Sweden 1959-1990 (excluding those who gave birth before age 16 and those who died before age 16), where at least one in the pair had their first childbirth 1994-2009 and none before 1994. T_0 is defined as year for first childbirth for women who gave birth, and year of twin sister's childbirth for those who did not give birth.

		Twin pairs where only one in the pair gave birth		
Variables	**Both gave birth**	**Twin 1 (gave birth)**	**Twin 2 (did not give birth)**	**Total**
N	2 792	1 163	1 163	5 118
Number of deliveries				
One delivery	711 (25%)	501 (43%)		
Two or more deliveries	2 081 (75%)	662 (57%)		
Age at T_0				
16-19 years	47 (2%)	33 (2%)		
20-24 years	511 (18%)	239 (21%)		
25-29 years	1 150 (41%)	444 (38%)		
30-34 years	847 (30%)	323 (28%)		
35-39 years	207 (7%)	109 (9%)		
>40 years	30 (1%)	15 (1%)		
Zygosity				
Monozygotic	1 726 (62%)	608 (52%)	608 (52%)	2 942 (57%)
Dizygotic	1 066 (38%)	555 (48%)	555 (48%)	2 176 (43%)
Highest attained education[1]				
≤ 9 year	179 (6%)	74 (6%)	55 (5%)	308 (6%)
10-12 year	1 434 (51%)	608 (52%)	621 (53%)	2 663 (52%)
≥ 13 year	1 173 (42%)	474 (41%)	422 (36%)	2 069 (40%)
Information on education missing	6 (0%)	7 (1%)	65 (6%)	78 (2%)
Hospitalization[2]				
- At least one hospitalization during the period six years prior through six years after T_0	2 161 (77%)	703 (60%)	325 (28%)	3 189 (62%)
-At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, childbirth, and the puerperium)	865 (31%)	315 (27%)	314 (27%)	1 494 (29%)
- At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, and childbirth)	1 183 (42%)	407 (35%)	325 (28%)	1 915 (37%)
- At least one hospitalization during the period six years prior to T_0	679 (24%)	251 (22%)	217 (19%)	1 147 (22%)
- At least one hospitalization during the period six years after T_0	1 965 (70%)	585 (50%)	168 (14%)	2 718 (53%)
- At least one hospitalization both before and afterT_0	483 (17%)	133 (11%)	60 (5%)	676 (13%)
Sickness Absence (SA)[3]				
At least one SA during the period six years prior through six years after T_0	1 526 (55%)	530 (46%)	365 (31%)	2 420 (47%)
At least one SA during the period six years prior to T_0	690 (25%)	274 (24%)	224 (19%)	1 188 (23%)
At least one SA during the period six years after T_0	1 245 (45%)	382 (33%)	221 (19%)	1 848 (36%)

[1] At time of T_0

[2] Excluding hospitalizations occurring during T_0

[3] Excluding SA occurring during T_0

Table 2. Cox proportional hazard ratios (HR) with 95% CI for the association between childbirth, hospitalization before T_0, and subsequent hospitalization (i.e., during year 3-5 after T_0) in twins where at least one in the pair had her first childbirth in 1994-2009 and none before 1994, both including and excluding hospitalization related to pregnancy, childbirth, and the puerperium. Two models for adjustments as well as for discordant twin pairs.

Status childbirth and hospitalization	All diagnoses			Diagnoses related to pregnancy, childbirth and the puerperium excluded[1]		
	Model a[6]	Model b[7]	Discordant twin pairs[2, 7]	Model a[6]	Model b[7]	Discordant twin pairs[3, 7]
All women (n=5 118)						
No childbirth, no hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization before T_0[8]	2.5 (1.7-3.6)	2.3 (1.6-3.3)	2.4 (1.3-4.5)	2.7 (1.8-3.9)	2.3 (1.6-3.4)	1.2 (0.8-1.9)
Childbirth, no hospitalization before T_0[8]	6.1(5.0-7.5)	5.5 (4.5-6.8)	8.3 (5.8-11.8)	1.1 (0.8-1.3)	0.9 (0.7-1.2)	0.9 (0.7-1.1)
Childbirth, hospitalization before T_0[8]	6.5 (5.2-8.1)	5.6 (4.4-7.1)	7.9 (5.4-11.5)	1.9 (1.4-2.5)	1.4 (1.1-1.9)	0.9 (0.7-1.2)
	Model a[6]	Model b[7]	Discordant twin pairs[4, 7]	Model a[6]	Model b[7]	Discordant twin pairs[5, 7]
Women who had at least one childbirth (n=2 792)						
No hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[8]	1.0 (0.9-1.2)	1.0 (0.9-1.1)	1.0 (0.8-1.2)	1.7 (1.3-2.3)	1.5 (1.2-2.0)	1.0 (0.8-1.3)

[1] Diagnoses O00-O99
[2] Twin pairs where one had a hospitalization during the follow-up and the other not (n=1 016 pairs)
[3] Twin pairs where one had a hospitalization during the follow-up and the other not (n=456 pairs)
[4] Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)
[5] Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs)
[6] Adjusted for birth year
[7] Model a, and additional adjustments for delivery year, and educational level
[8] During the period 1-5 years prior to T_0

Table 3. Cox proportional HR with 95% CI for the association between childbirth, hospitalization, and new sickness absence (SA) in year 3-5 after T_0, in twins where at least one in the pair had their first childbirth 1994-2009. Three models for adjustments as well as for discordant twin pairs.

Status childbirth and hospitalization	SA in year 3-5 after T_0 (regardless of number of days)				Long-term SA (>90 days) in year 3-5 after T_0			
	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[1, 7]	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[2, 7]
All women (n=5 118)								
No childbirth, no hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization year 1-2 after T_0[8]	2.7 (1.8-4.1)	2.2 (1.5-3.4)	2.1 (1.4-3.2)	1.5 (0.8-2.9)	4.5 (2.5-8.2)	3.5 (1.9-6.2)	2.8 (1.5-5.1)	1.1 (0.5-2.3)
Childbirth, no hospitalization year 1-2 after T_0[8]	2.1 (1.8-2.5)	1.8 (1.5-2.2)	1.8 (1.5-2.2)	1.7 (1.3-2.2)	1.1 (0.8-1.6)	1.0 (0.7-1.4)	1.0 (0.7-1.3)	0.8 (0.6-1.2)
Childbirth, hospitalization year 1-2 after T_0[8]	3.0 (2.5-3.6)	2.4 (2.0-2.9)	2.4 (2.0-2.9)	2.0 (1.5-2.6)	2.3 (1.6-3.2)	1.8 (1.3-2.5)	1.8 (1.3-2.5)	1.0 (0.7-1.5)
Women who had at least one childbirth (n=2 792)	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[3, 5]**	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[4, 7]**
No hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization year 1-2 after T_0[8]	1.3 (1.2-1.5)	1.3 (1.1-1.4)	1.2 (1.1-1.4)	1.2 (1.0-1.5)	2.0 (1.5-2.6)	1.9 (1.4-2.5)	1.8 (1.4-2.4)	1.4 (1.0-1.9)

[1] Twin pairs where one had a SA during the follow-up and the other not (n=835 pairs)
[2] Twin pairs where one had a long-term SA during the follow-up and the other not (n=277 pairs)
[3] Twin pairs where one had a SA during the follow-up and the other not (n=542 pairs)
[4] Twin pairs where one had a long-term SA during the follow-up and the other not (n=184 pairs)
[5] Adjusted for birth year
[6] Model a, and additional adjustments for delivery year, and educational level
[7] Model b, and additional adjustments for earlier hospitalization
[8] Diagnoses O00-O99 excluded

Table 4. Cox proportional HR with 95% CI for the association between hospitalization before and after first childbirth, and new sickness absence (SA) in year 3-5 after T_0, in twins who had their first childbirth 1994-2009 (n=2 792). Three models for adjustments as well as for discordant twin pairs.

Status hospitalization before and after childbirth	SA in year 3-5 after T_0 (regardless of number of days)				Long-term SA (>90 days) in year 3-5 after T_0			
	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[1, 4]	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[2, 4]
No hospitalization either before T_0[6] or during year 1-2 after T_0[7]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[6] but not during year 1-2 after T_0[7]	1.2 (1.0-1.5)	1.2 (1.0-1.4)	1.2 (1.0-1.4)	1.0 (0.8-1.3)	2.3 (1.6-3.4)	2.1 (1.5-3.1)	2.2 (1.5-3.1)	1.2 (0.8-1.7)
No hospitalization before T_0[6] but during year 1-2 after T_0[7]	1.2 (1.1-1.4)	1.2 (1.0-1.4)	1.1 (0.9-1.2)	1.1 (0.9-1.4)	2.0 (1.5-2.8)	1.9 (1.4-2.7)	1.9 (1.4-2.7)	1.4 (1.0-2.1)
Hospitalization before T_0[6] and during year 1-2 after T_0[7]	2.0 (1.6-2.5)	1.8 (1.4-2.2)	1.6 (1.3-2.1)	1.6 (1.1-2.2)	4.2 (2.7-6.4)	3.5 (2.3-5.3)	3.5 (2.3-5.4)	1.5 (0.9-2.4)

[1] Twin pairs where one had an SA during the follow-up and the other not (n=542)
[2] Twin pairs where one had a long-term SA during the follow-up and the other not (n=184)
[3] Adjusted for birth year
[4] Model a, and additional adjustments for delivery year, and educational level
[5] Model b, and additional adjustments for subsequent deliveries
[6] During the period 1-5 years prior to T_0
[7] Diagnoses O00-O99 excluded

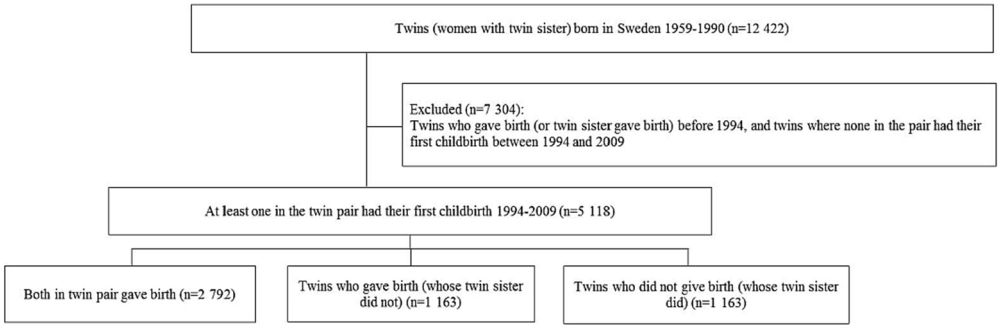

Figure 1
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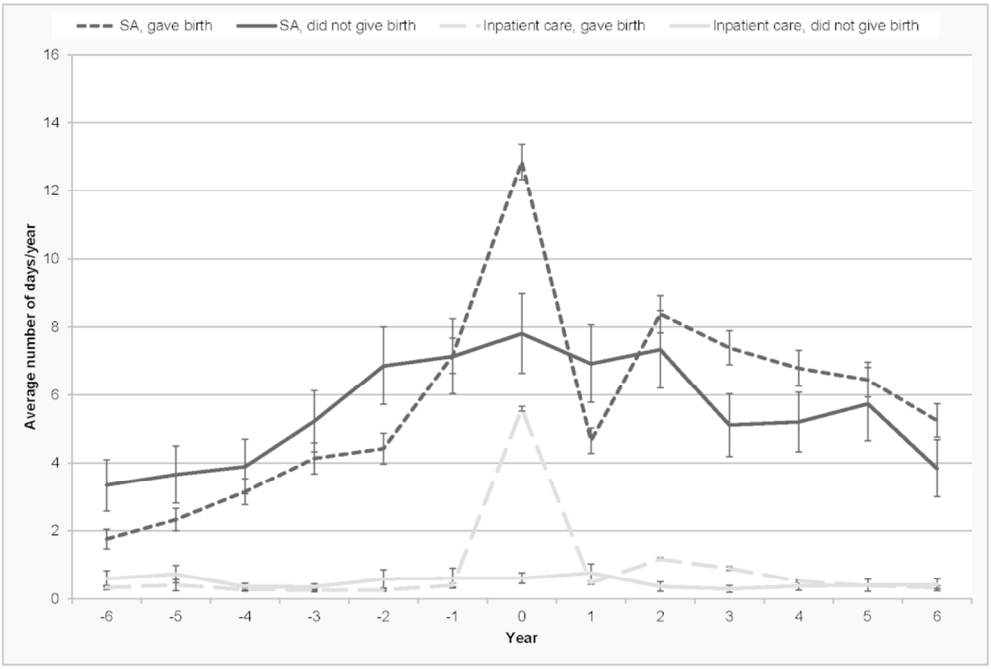

Figure 2
90x60mm (300 x 300 DPI)

BMJ Open - Childbirth, hospitalization, and sickness absence: a study of female twins

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Page 1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Page 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Page 4**
Objectives	3	State specific objectives, including any prespecified hypotheses **Page 6**
Methods		
Study design	4	Present key elements of study design early in the paper **Page 7**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Page 7-10**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **Page 7-10**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed **N/A**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Page 8-9**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Page 7-10**
Bias	9	Describe any efforts to address potential sources of bias **N/A**
Study size	10	Explain how the study size was arrived at **Page 7**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Page 8-9**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **Page 9-10**
		(*b*) Describe any methods used to examine subgroups and interactions **Page 9-10**
		(*c*) Explain how missing data were addressed **N/A**
		(*d*) If applicable, explain how loss to follow-up was addressed

		N/A
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **Page 7, and page 22**
		(b) Give reasons for non-participation at each stage **N/A**
		(c) Consider use of a flow diagram **Page 22**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Page 23**
		(b) Indicate number of participants with missing data for each variable of interest **N/A**
		(c) Summarise follow-up time (eg, average and total amount) **N/A**
Outcome data	15*	Report numbers of outcome events or summary measures over time **Page 23**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Page 24-25**
		(*b*) Report category boundaries when continuous variables were categorized **Page 23**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **N/A**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Page 24-25**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Page 2 and page 13**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Page 16**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Page 13 – 15**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Page 13-16**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Page 18**

*Give information separately for exposed and unexposed groups.

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Childbirth, hospitalization, and sickness absence: a study of female twins

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Childbirth, hospitalization, and sickness absence: a study of female twins

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Abstract

Objective: To investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account.

Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA were calculated as hazard ratios (HR) with 95% confidence intervals (CI).

Setting: All female twins, i.e., women with twin sister, born in Sweden.

Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where at least one in the twin pair had their first childbirth (T_0) 1994-2009 and none gave birth before 1994.

Main outcome measures: Hospitalization and SA during year 3-5 after first delivery or equivalent.

Results: Preceding the first childbirth, the mean annual number of SA days increased for mothers, and then decreased again. Hospitalization after T_0 was associated with higher HRs of short-term and long-term SA (HR for short-term SA: 3.0; 95% CI 2.5-3.6 and for long-term SA: 2.3; 95% CI 1.6-3.2). Hospitalization both before and after first childbirth was associated with a higher risk of future SA (HR for long-term SA: 4.2; 95% CI 2.7-6.4). Familial factors influenced the association between hospitalization and long-term SA, regardless of childbirth status.

Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth and results indicate a positive health selection into giving birth. Mothers hospitalized before and/or after giving birth had higher risks for future SA, that is, there was a strong association between morbidity and future SA.

Keywords: sick leave, childbirth, inpatient care, hospitalization, cohort study, population based, twins

50

Article Summary

Article focus:

To investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account.

Key messages:

- Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth
- The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially

Strengths and limitations:

- The strengths of the study include the population-based prospective design, using national registers with high completeness and validity
- With a twin study design, we were able to take familial influences into account
- As inpatient care to a great extent has been replaced by outpatient treatment, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities

Introduction

In most countries with high labor force participation, women have higher levels of sickness absence (SA) than men [1-4]. Many theories and mechanism regarding this have been suggested, e.g., women having higher morbidity, higher workload (when combining paid and unpaid work), tougher situation on the labor market, men being the norm for how the labor market is organized, gender bias in healthcare and social insurance systems, discrimination, and domestic violence, etcetera [5-9]. Another hypothesis behind this gender difference in SA focuses on SA during pregnancy and after childbirth [6 10-13]. Several studies show that women have higher SA during pregnancy [10 14] and that pregnancy-related SA explains half of the gender differences in SA in fertile ages [15].

One of the changes in society that may affect health after childbirth is that the mean age for having the first child has increased over the last years and that women with higher level of morbidity now give birth. Further, nowadays, the proportion of caesarean sections has increased as well as vacuum extraction deliveries, leading to risk of later health problems [16 17].

In this study, focus is on childbirth, morbidity, and SA among women, to get a better understanding of mechanisms behind SA among women in fertile ages. There are hardly any studies on the associations between giving birth and morbidity and SA, and those conducted have focused on a relatively short time period right after childbirth, most often within the first year following the child delivery [18 19], while prospective studies with longer follow-up of mothers are rare [6 12 20].

Pregnancy, delivery, and the postpartum period may imply large physical, mental, and social changes during a short period of time, increasing the risk for disease and injury [21 22]. Different types of physical and mental disorders are common during pregnancy and after childbirth – and can in some cases be longstanding or even permanent – however, this is hardly studied at all [19]. Giving birth may be associated with a higher risk of certain diseases demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental

disorders, and different types of injuries [23-26]. For women with a disease present before the childbirth, the disorder might deteriorate after childbirth [23 24]. Regarding symptoms related to childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain, fatigue, headache, and sleep disorders [19 27]. Most of these symptoms seem to remain up to one year after childbirth [17]. Besides physical health effects, also depression and other mental disorders have been linked to childbirth [26 28], but again, prospective studies with longer follow-up are lacking [27]. Even though having children has been shown to contribute to an overall wellbeing, this is not the case for everybody and especially not among single mothers whose economic situation and thereby possibilities for good health care might be worse [29-31].

Morbidity can be measured in different ways, e.g., through self-reports or visits to healthcare. Here we will use data on more severe morbidity that involves assessments from physicians, that is, morbidity that has led to hospitalization, a measure so far not used in this type of studies. Sickness absence is not a good measure of morbidity– most people with morbidity are not on SA [4]. Instead SA is considered a very good measure of social consequences of morbidity, in terms of not being able to support yourself from work [4]. Yet, there are surprisingly few studies on the association between morbidity and SA and in media and among some researchers sometimes the level of morbidity among sickness absentees even is questioned, especially for female sickness absentees – their sickness absence is rather considered related to attitudes than to morbidity [12 32 33].

Studies examining the role of familial factors (i.e., genetic and shared (mainly childhood) environment) on morbidity have shown that genetics tends to explain a moderate to large extent of the variability in most of the chronic diseases [34 35]. For example, heritability for mental disorders varies between 30-90% [36], whereas genetic factors have been shown to explain 30-60% of the total variation in musculoskeletal disorders [37 38]. Taken together, familial factors are important to account for when studying the association between morbidity

(here in terms of hospitalization) and SA as studies otherwise could lead to erroneous conclusions. Twin settings provide a powerful tool for studies of these aspects in research of SA, a research area where different selection biases otherwise might have an impact on results. Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average 50% for DZ pairs) and common environmental factors through childhood (100% for both MZ and DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs). An experimental design, which can control for these familial influences, is to examine discordant twin sisters, that is, where one twin sister has given birth and the other has not. If discordant twin sisters show similar associations as the analyses of the whole cohort, this would indicate that the childbirth may actually be a contributing cause of the future SA. If instead the association found among the whole cohort cannot be replicated within discordant twin sisters, then familial factors are of importance. Influence of familial factors (genetic and common environment) is indicated if the association found in the analyses of the whole cohort disappear or change considerably in the analyses of discordant twin pairs [39].

The aim of the study was to investigate the associations of giving birth with subsequent morbidity in terms of hospitalization and SA. Familial factors (genetics and shared/early environmental) were taken into account in order to assess if familial factors explain a potential association between childbirth and future hospitalization and SA.

Methods

Participants and data sources

We performed a prospective population-based cohort study of female twins. All female twins, i.e., women with a twin sister, born in Sweden between 1959 and 1990 were selected from the Swedish Twin Registry (STR) [40]. After excluding women who delivered their first child before 1994 or whose twin sister had her first delivery before 1994, and twins where none in the pair had their first delivery between 1994 and 2009 (n=7 304), the final cohort comprised 5 118 women of which 95% had income from work, the others had income from parental benefits, unemployment benefits, student benefits, different types of sickness benefits, or a mixture of those (in the year prior to the birth year, i.e., T(-1). All had some of those types of income, all granting rights to SA benefits. The Swedish Twin Registry (STR) is the largest population-based register of twin births in the world, with information such as birth date, sex, zygosity, and pair identification [40 41]. The selection of the study population is illustrated in Figure 1.

The unique personal identity number assigned to each Swedish resident [42] was used to link information from several nationwide population-based registers at an individual level up through 2009, as follows. The Causes of Death Register was used to obtain information on date of death [43]. This register contains information on all deceased Swedish residents since 1952. Information on all deliveries (including still births) was derived from the Medical Birth Register, which was established in 1973 and includes information on almost all births in Sweden [44]. In order to increase the coverage on delivery, we also used the National Patient Register (NPR) to obtain information on all deliveries. This register was founded in 1964 and includes all individuals admitted to any psychiatric or general hospital [45]. Information on hospitalization with a principal diagnosis for delivery (as defined by the International Classification of Disease (ICD): ICD-9: 650, 651.9, 652.2, 669.5-8; and ICD-10: O80-84) was obtained. The NPR was also used to obtain annual information on other hospitalizations, i.e.,

inpatient care. Annual information on educational level and on SA days was obtained from Statistics Sweden.

Time in relation to childbirth

The studied women were followed in relation to year of first childbirth, referred to as T_0. In order to compare those who gave birth to those who did not, T_0 for the women who did not give birth was defined as year of her twin sister's first childbirth.

Hospitalization

Data on hospitalization covered the period six years prior to, and six years after year of first childbirth (T_0) or equivalent. For descriptive purposes, the total and the average number of hospitalization days per year were calculated.

In order to examine if hospitalization prior to (or after) childbirth increases the risk for future hospitalization, the first part of the regression analyses considered hospitalization as both exposure and outcome. We created one dichotomous variable for hospitalization before T_0 (i.e., exposure), and two dichotomous outcome variables for hospitalization during year 3-5 after T_0: one for hospitalization with any diagnosis and one excluding hospitalization with diagnoses related to pregnancy, childbirth, and the postpartum period.

In order to answer the research question "Does hospitalization prior to (or after) childbirth increase the risk for future SA?", we created two dichotomous hospitalization exposure variables: one for hospitalization before T_0 and one variable: hospitalization year 1-2 after T_0 (excluding diagnoses related to pregnancy, childbirth, and the postpartum period).

Sickness absence

SA can be measured in several ways, related to duration and incidence [46]. Here we used the following four measures: total and average number of SA days per year; number of SA days during year 3-5 after T_0; and number of SA days >90 sick-leave days during year 3-5 after T_0.

Sickness insurance in Sweden

In Sweden, all residents aged 16-65 years who have income from work, unemployment benefits, parental benefits, or student benefits are entitled to sickness benefits from the Swedish Social Insurance Agency, if unable to work due to disease or injury. Among employed individuals, sick pay was in most cases paid by the employer during the first 14 days of a sick-leave spell, which means that we do not have data on most of the short sick-leave spells. In most of the years studied, there was no limitation to duration of a sick-leave spell. Sickness benefits covered 80% of lost income, up to a certain level. All were covered by a health care insurance covering the right to hospital care when needed, at a much reduced cost, less than 10 Euros a day. Care during pregnancy and delivery was free.

Potential confounding factor

As research has shown socioeconomic disparities in age at first birth (e.g., the higher the education, the later the first birth) [47 48], we adjusted for educational level at T_0. Years of education was classified into four categories; <9 years of compulsory school, 10-12 years of education (senior high school), ≥13years of education (college/university), missing.

Statistical analysis

First, Cox proportional hazard models with constant time-at-risk [49] were applied to estimate hazard ratios (HR) with 95% confidence intervals (CI) for having at least one hospitalization after childbirth (T_0). In a first model (model a), adjustments were made for age. Second

(model b), additional adjustments were made for delivery year and educational level at time of T_0. Thereafter, twin pairs who were discordant with respect to outcomes, i.e., having at least one hospitalization after T_0, were analyzed using Conditional Cox regression. In the next step, we analyzed the associations between childbirth, hospitalization, and SA by fitting three Cox regression models (table 3). The first (model a) was adjusted for birth year. In the second model (model b), additional adjustments were made for delivery year and educational level at time of T_0. In the third model (model c), previous hospitalization was included. Thereafter, twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e., having had SA or long-term SA (>90 days) were analyzed.

Finally, in the step where we analyzed the association between hospitalization before and after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-b) from table 3. In a third model (model c), we fitted an additional model in which adjustments were made for subsequent deliveries.

The proportional hazards assumption was checked by including time-dependent versions of all the covariates in the models. This did not indicate a violation of the proportionality assumption.

All statistical analyses were performed with SAS 9.3 and STATA 12.1.

The STROBE checklist was used in designing and reporting the study.

The project was approved by the Regional Ethical Review Board of Stockholm.

Results

Of the 5 118 women included in the study, 77% had given birth at least once between 1994 and 2009 (Table 1). Of these women, nearly 70% also had given birth later, at least once. A majority of the women who gave birth had their first delivery before the age of 30 (61%). The educational level distribution was rather similar when comparing those who gave birth to those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were excluded, 30% of the women, i.e., the 1 183 where both in a pair gave birth and the 407 twins where only one in the pair gave birth had at least one hospitalization during the period six years prior to and six years after their first delivery (the delivery year excluded). The corresponding rate for the women who had not given birth was 27%. Half of the women who gave birth had at least one day of SA during the period six years prior to or the six years after first delivery, when the year for childbirth was excluded. The majority of the women had no SA at all in the six years following childbirth.

The average annual number of days with inpatient care and SA, respectively, is presented in Figure 2. Up to year T_0, women who did not give birth had a higher average number of hospitalization days and SA days compared to those who gave birth. Women who gave birth had approximately 0.3 hospitalization days per year whereas those who did not give birth had around 0.5 hospitalization days per year. The average number of SA days for women giving birth was 3.8 days/year and for those not giving birth 5.0 days/year. SA differences between those giving birth and women not giving birth were statistically significant with the exception of year (-4) and (-3). For inpatient care, the differences between those giving birth and women not giving birth were not statistically significant. The average number of inpatient days increased rapidly during T_0 for women who gave birth, especially because of hospitalization due to pregnancy and childbirth. After T_0, the number of SA days decreased quickly among these women. For women who gave birth, days with inpatient care and SA the years following T_0 were to a large extent associated with subsequent childbirths.

Table 2 presents HR for the association between childbirth and hospitalization, for all diagnoses and for diagnoses where those related to pregnancy, childbirth, and the postpartum period were excluded. When these diagnoses were removed, women who did not give birth and who had been hospitalized at least once before T_0 had twice the risk of future hospitalization compared to those not hospitalized prior to T_0 (HR: 2.3; 95% CI 1.6-3.3) after adjustments for birth year, delivery year, and educational level. The association was explained by familial factors in the analysis of discordant twin pairs (HR: 1.2; 0.8-1.9).

When restricting the analyses to women who gave birth, a total of 2 792 women were studied, i.e., 1 396 complete pairs in which both twins had given birth. The reference group constituted of mothers who had not been hospitalized prior to their first childbirth. Mothers who had been hospitalized before their first childbirth had a slightly higher HR for future hospitalization when diagnoses related to pregnancy and childbirth were excluded (HR 1.5; 1.2-2.0). This association disappeared in the analyses of discordant twin pairs, suggesting an influence of familial factors (HR: 1.0; 0.8-1.3).

Regardless of childbirth status, hospitalization year 1-2 after T_0 was a predictor of having a new SA in year 3-5 after T_0 (Table 3). Compared to women who did not give birth and who were not hospitalized the first two years after T_0, mothers hospitalized after first childbirth had an HR of 2.4 (2.0-2.9) for a new SA after adjustments for birth year, delivery year, and educational level. Hospitalization after T_0 was also associated with a new long-term SA (>90 days) in year 3-5 after T_0 (Table 3). Women who did not give birth had a nearly three-fold risk of a new long-term SA year 3-5 after T_0 (HR 2.8; 1.5-5.1), whereas women who gave birth had an HR of 1.8 (1.3-2.5). The analyses of twin pairs discordant for having a new long-term SA year 3-5 after T_0, showed attenuated point estimates, hence suggesting that familial effects may play a role.

The analyses, in which we considered hospitalization before and after first childbirth as exposure, and outcome was a new SA year 3-5 after T_0 (Table 4) show that mothers who had been hospitalized at least once both before and after their first child birth had a higher risk of future SA (HR 1.8; 1.4-2.2). These women also had a higher risk of long-term SA; however, these risk estimates were not statistically significant. After controlling for familial confounding, the estimated risk for long-term SA for those who had been hospitalized before T_0 was in the same direction but the HR was reduced, which suggest that also familial factors may have an influence on the studied association.

Discussion

In this register study of a population-based Swedish cohort of female twins born between 1959 and 1990, the associations of delivery with hospitalization and SA were examined as well as whether familial (i.e., genetic and shared, mainly childhood, environmental) factors were contributing to these associations. Just before the first childbirth, the SA days increased much for mothers, an increase that gradually decreased during the years after the delivery. We found hospitalization prior to T_0 to be a risk factor for future hospitalization, regardless of childbirth status, also when excluding hospitalization due to childbirth. Furthermore, hospitalization after the first childbirth was associated with a higher HR of both short-term and long-term future SA. An additional analysis focusing solely on the women who gave birth showed that hospitalization both before and after the first childbirth was associated with a higher risk of future SA. Familial factors seemed to have an influence on the association between hospitalization and long-term SA, regardless of childbirth status.

In line with some previous studies [10 20 50 51], we found that SA increased in women during the time before the first childbirth. Giving birth was also associated with a future somewhat higher risk for SA, in line with that of those not giving birth. However, this higher risk could be due to subsequent pregnancies. A recent Norwegian study found that the increased SA risk in women in the years after pregnancy disappeared when SA during subsequent pregnancies were accounted for [20]. Several explanations have been suggested for such higher levels of SA, among others the double burden hypothesis [20 52-54]. This hypothesis has been questioned, as research has indeed shown that women who occupy multiple roles tend to be healthier than those who enact fewer roles [55-57]. Thus, the combination of employment and parenthood does not seem to imply worse health, on the contrary. In our study, the annual rates of SA decreased steadily after the first childbirth, speaking in favor of this hypothesis. Further studies of this are warranted.

To our best knowledge, this is the first study to examine long-term associations between childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to subsequent pregnancy and childbirth) when compared to women who did not give birth.

Those who did not give birth had a more stable pattern of SA during the studied period, however, with a slight increase in annual SA days over the years. This is in line with a Swedish study examining whether family obligations influence the risk of SA in publicly employed women and found a slight risk increase for SA among women without children [58]. Further, a broad systematic literature review published in 2004 provided no evidence of an association between having children in the household and an increased risk of SA [59]. It is important to consider family situation when examining the association between having children and morbidity, as single women with children have been shown to have worse health [30 31 60] and higher levels of SA [6 58].

Even though pregnancy, delivery, and the postpartum period may increase the risk for disease and injury [25 27], our findings do not suggest that women who gave birth are more likely to be hospitalized after their first childbirth, except for hospitalizations related to subsequent deliveries. We found no differences in risk for future hospitalization when comparing those who gave birth to those who did not. Thus, giving birth does not have to be associated with subsequent health problems. The fact that we found no differences in future hospitalization between those who gave birth and those who did not, may have different explanations. As mentioned above, one could expect that there is a health selection, where women who do not give birth may have worse health and choose not to have or cannot have a child. Also, giving birth is in itself a risk factor for future morbidity[16 19 22]. Further, during the last decades, the number of women who voluntarily do not want to become parents has increased worldwide[61].

Hospitalization prior to the first childbirth or equivalent (T_0) was a risk factor for future SA for all women, regardless of childbirth status. In particular, women who had been hospitalized both before and after T_0 were at risk for future SA. Furthermore, we found an association between hospitalization and future long-term SA.

When comparing women who gave birth to those who did not, with respect to exposure to hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had slightly higher risk for future SA regardless of duration, whereas those who did not give birth hospitalized after T_0 had higher risk for long-term SA.

Hospitalization both before and after the year T_0 seems to be the strongest indicator, i.e., these individuals had the highest risk for future SA. Consequently, the women who had been hospitalized both before and after T_0 had the highest risk for future SA. Our analyses of women who gave birth revealed a graded association between hospitalization and SA, where those who only were hospitalized before *or* after their first childbirth had a higher risk of SA, whereas those who were hospitalized both before and after the first childbirth had even higher risks. Thus, we found a strong association between morbidity, here measured as hospitalization, and future SA among women who have given birth – an association that often has been question regarding women with children [12].

Familial factors seemed to contribute to the association between hospitalization before and after T_0 among those who did not give birth. The influence of familial factors may relate to morbidity among women not giving birth – morbidity that might be more severe and potentially also being relatively strongly influenced by genetics. Familial factors also played a role in the associations between hospitalization and future long-term SA. This could be related to the fact that the hospitalization usually is required for severe conditions that may have a strong genetic component. However, since genetics have been shown to influence the risk of DP [62], and some indications exist that genetics also play a role in long-term SA and

mortality, it can be suspected that the effects of familial factors on SA can be either direct or through other influential factors.

Strengths and limitations

The strengths of this study are the population-based prospective cohort study design, including all in the study population, not a sample, using nationwide registers with high completeness and validity [43-45]. Further, we used a large study cohort without loss to follow up. With a twin study design, we were able to take familial influences into account. When measuring both exposure and outcome with register-based data, we avoid problem with recall bias.

This study has, however, some limitations. First of all, we do not know whether the women who did not give birth were childless voluntarily or not. Differences in health between voluntary and involuntary childlessness have been shown, where voluntarily childless women showed higher levels of overall well-being [61 63] which might be related to hospitalization and/or SA. Using inpatient care as a measure of morbidity has both its strengths and limitations. One limitation is that we thus selected more severe types of morbidity, and hence that does not include morbidity treated in outpatient care. Having had also other types of morbidity data might have given another picture and hopefully future studies will have such information. Another limitation is that the terms for inpatient care have changed during the studied period. In Sweden, inpatient care has over the years to a great extent been replaced by outpatient treatment. Therefore, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities [64], however, this affected all women equally, and is to some extent handled by adjusting for birth year. The CIs are wider in the years far from T_0, e.g., T_6, due to fewer follow up year for some – e.g., for those who gave birth late during the studied period. Also,

we lack information on the shorter SA spells among those employed. Further, the Swedish Twin Registry (STR) contains all twin births in Sweden; hence, immigrants are not included in this study and as a consequence the external validity might be lower to women born outside of Sweden.

It is important to be aware of that giving birth is in focus here, irrespective of whether the child survived or not. Some of the women who did not give birth might be mothers, e.g., due to adoption. Other studies in this area has 'being mother' or 'living with child' as exposure term, rather than 'giving birth'.

Conclusion

Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth. Mothers with different types of morbidity, in terms of hospitalization before and/or after giving birth had higher risks for future SA. Most women had no SA in the six years following childbirth and those who had SA generally had that for shorter periods. Among the few women who had severe morbidity, in terms of hospitalization, the future risk for SA was, as expected, higher. Hospitalization prior to T_0 was strongly associated with later hospitalization and later SA. The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially. However, most women had no hospitalization and no SA.

Ethical approval

The study was approved by the Regional Ethical Review Board, Stockholm, Sweden (2007/524-31).

Contributorship Statement

KA and PS originated the idea. EB analysed the data in consultation with KA, LK, JN, AR, and PS. EB wrote the first and subsequent drafts of the manuscript, with important intellectual input from all the co-authors. All authors contributed in designing the study and to the interpretation of the results and to the writing and approval of the final article.

Competing interest statement

We declare that no competing interests exist.

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Data sharing

No additional data available.

Figure legends

Figure 1. Flow chart for the study population.

Figure 2. Average annual number of days on sickness absence (SA) and hospitalization, respectively, (with 95% CI), six years prior through six year after T_0 for women who gave birth/did not give birth (n=5 118).

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Table 1. Cohort characteristics for twins (women with twin sister) born in Sweden 1959-1990 (excluding those who gave birth before age 16 and those who died before age 16), where at least one in the pair had their first childbirth 1994-2009 and none before 1994. T_0 is defined as year for first childbirth for women who gave birth, and year of twin sister's childbirth for those who did not give birth.

		Twin pairs where only one in the pair gave birth		
Variables	**Both gave birth**	**Twin 1 (gave birth)**	**Twin 2 (did not give birth)**	**Total**
N	2 792	1 163	1 163	5 118
Number of deliveries				
One delivery	711 (25%)	501 (43%)		
Two or more deliveries	2 081 (75%)	662 (57%)		
Age at T_0				
16-19 years	47 (2%)	33 (2%)		
20-24 years	511 (18%)	239 (21%)		
25-29 years	1 150 (41%)	444 (38%)		
30-34 years	847 (30%)	323 (28%)		
35-39 years	207 (7%)	109 (9%)		
>40 years	30 (1%)	15 (1%)		
Zygosity				
Monozygotic	1 726 (62%)	608 (52%)	608 (52%)	2 942 (57%)
Dizygotic	1 066 (38%)	555 (48%)	555 (48%)	2 176 (43%)
Highest attained education[1]				
≤ 9 year	179 (6%)	74 (6%)	55 (5%)	308 (6%)
10-12 year	1 434 (51%)	608 (52%)	621 (53%)	2 663 (52%)
≥ 13 year	1 173 (42%)	474 (41%)	422 (36%)	2 069 (40%)
Information on education missing	6 (0%)	7 (1%)	65 (6%)	78 (2%)
Hospitalization[2]				
- At least one hospitalization during the period six years prior through six years after T_0	2 161 (77%)	703 (60%)	325 (28%)	3 189 (62%)
-At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, childbirth, and the puerperium)	865 (31%)	315 (27%)	314 (27%)	1 494 (29%)
- At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, and childbirth)	1 183 (42%)	407 (35%)	325 (28%)	1 915 (37%)
- At least one hospitalization during the period six years prior to T_0	679 (24%)	251 (22%)	217 (19%)	1 147 (22%)
- At least one hospitalization during the period six years after T_0	1 965 (70%)	585 (50%)	168 (14%)	2 718 (53%)
- At least one hospitalization both before and afterT_0	483 (17%)	133 (11%)	60 (5%)	676 (13%)
Sickness Absence (SA)[3]				
At least one SA during the period six years prior through six years after T_0	1 526 (55%)	530 (46%)	365 (31%)	2 420 (47%)
At least one SA during the period six years prior to T_0	690 (25%)	274 (24%)	224 (19%)	1 188 (23%)
At least one SA during the period six years after T_0	1 245 (45%)	382 (33%)	221 (19%)	1 848 (36%)

[1] At time of T_0

[2] Excluding hospitalizations occurring during T_0

[3] Excluding SA occurring during T_0

Table 2. Cox proportional hazard ratios (HR) with 95% CI for the association between childbirth, hospitalization before T_0, and subsequent hospitalization (i.e., during year 3-5 after T_0) in twins where at least one in the pair had her first childbirth in 1994-2009 and none before 1994, both including and excluding hospitalization related to pregnancy, childbirth, and the puerperium. Two models for adjustments as well as for discordant twin pairs.

Status childbirth and hospitalization	All diagnoses			Diagnoses related to pregnancy, childbirth and the puerperium excluded[1]		
	Model a[6]	Model b[7]	Discordant twin pairs[2, 7]	Model a[6]	Model b[7]	Discordant twin pairs[3, 7]
All women (n=5 118)						
No childbirth, no hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization before T_0[8]	2.5 (1.7-3.6)	2.3 (1.6-3.3)	2.4 (1.3-4.5)	2.7 (1.8-3.9)	2.3 (1.6-3.4)	1.2 (0.8-1.9)
Childbirth, no hospitalization before T_0[8]	6.1(5.0-7.5)	5.5 (4.5-6.8)	8.3 (5.8-11.8)	1.1 (0.8-1.3)	0.9 (0.7-1.2)	0.9 (0.7-1.1)
Childbirth, hospitalization before T_0[8]	6.5 (5.2-8.1)	5.6 (4.4-7.1)	7.9 (5.4-11.5)	1.9 (1.4-2.5)	1.4 (1.1-1.9)	0.9 (0.7-1.2)
	Model a[6]	**Model b[7]**	**Discordant twin pairs[4, 7]**	**Model a[6]**	**Model b[7]**	**Discordant twin pairs[5, 7]**
Women who had at least one childbirth (n=2 792)						
No hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[8]	1.0 (0.9-1.2)	1.0 (0.9-1.1)	1.0 (0.8-1.2)	1.7 (1.3-2.3)	1.5 (1.2-2.0)	1.0 (0.8-1.3)

[1] Diagnoses O00-O99
[2] Twin pairs where one had a hospitalization during the follow-up and the other not (n=1 016 pairs)
[3] Twin pairs where one had a hospitalization during the follow-up and the other not (n=456 pairs)
[4] Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)
[5] Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs)
[6] Adjusted for birth year
[7] Model a, and additional adjustments for delivery year, and educational level
[8] During the period 1-5 years prior to T_0

Table 3. Cox proportional HR with 95% CI for the association between childbirth, hospitalization, and new sickness absence (SA) in year 3-5 after T_0, in twins where at least one in the pair had their first childbirth 1994-2009. Three models for adjustments as well as for discordant twin pairs.

Status childbirth and hospitalization	SA in year 3-5 after T_0 (regardless of number of days)				Long-term SA (>90 days) in year 3-5 after T_0			
	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[1, 7]	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[2, 7]
All women (n=5 118)								
No childbirth, no hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization year 1-2 after T_0[8]	2.7 (1.8-4.1)	2.2 (1.5-3.4)	2.1 (1.4-3.2)	1.5 (0.8-2.9)	4.5 (2.5-8.2)	3.5 (1.9-6.2)	2.8 (1.5-5.1)	1.1 (0.5-2.3)
Childbirth, no hospitalization year 1-2 after T_0[8]	2.1 (1.8-2.5)	1.8 (1.5-2.2)	1.8 (1.5-2.2)	1.7 (1.3-2.2)	1.1 (0.8-1.6)	1.0 (0.7-1.4)	1.0 (0.7-1.3)	0.8 (0.6-1.2)
Childbirth, hospitalization year 1-2 after T_0[8]	3.0 (2.5-3.6)	2.4 (2.0-2.9)	2.4 (2.0-2.9)	2.0 (1.5-2.6)	2.3 (1.6-3.2)	1.8 (1.3-2.5)	1.8 (1.3-2.5)	1.0 (0.7-1.5)
Women who had at least one childbirth (n=2 792)	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[3, 5]**	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[4, 7]**
No hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization year 1-2 after T_0[8]	1.3 (1.2-1.5)	1.3 (1.1-1.4)	1.2 (1.1-1.4)	1.2 (1.0-1.5)	2.0 (1.5-2.6)	1.9 (1.4-2.5)	1.8 (1.4-2.4)	1.4 (1.0-1.9)

[1] Twin pairs where one had a SA during the follow-up and the other not (n=835 pairs)
[2] Twin pairs where one had a long-term SA during the follow-up and the other not (n=277 pairs)
[3] Twin pairs where one had a SA during the follow-up and the other not (n=542 pairs)
[4] Twin pairs where one had a long-term SA during the follow-up and the other not (n=184 pairs)
[5] Adjusted for birth year
[6] Model a, and additional adjustments for delivery year, and educational level
[7] Model b, and additional adjustments for earlier hospitalization
[8] Diagnoses O00-O99 excluded

Table 4. Cox proportional HR with 95% CI for the association between hospitalization before and after first childbirth, and new sickness absence (SA) in year 3-5 after T_0, in twins who had their first childbirth 1994-2009 (n=2 792). Three models for adjustments as well as for discordant twin pairs.

Status hospitalization before and after childbirth	SA in year 3-5 after T_0 (regardless of number of days)				Long-term SA (>90 days) in year 3-5 after T_0			
	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[1, 4]	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[2, 4]
No hospitalization either before T_0[6] or during year 1-2 after T_0[7]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[6] but not during year 1-2 after T_0[7]	1.2 (1.0-1.5)	1.2 (1.0-1.4)	1.2 (1.0-1.4)	1.0 (0.8-1.3)	2.3 (1.6-3.4)	2.1 (1.5-3.1)	2.2 (1.5-3.1)	1.2 (0.8-1.7)
No hospitalization before T_0[6] but during year 1-2 after T_0[7]	1.2 (1.1-1.4)	1.2 (1.0-1.4)	1.1 (0.9-1.2)	1.1 (0.9-1.4)	2.0 (1.5-2.8)	1.9 (1.4-2.7)	1.9 (1.4-2.7)	1.4 (1.0-2.1)
Hospitalization before T_0[6] and during year 1-2 after T_0[7]	2.0 (1.6-2.5)	1.8 (1.4-2.2)	1.6 (1.3-2.1)	1.6 (1.1-2.2)	4.2 (2.7-6.4)	3.5 (2.3-5.3)	3.5 (2.3-5.4)	1.5 (0.9-2.4)

[1] Twin pairs where one had an SA during the follow-up and the other not (n=542)
[2] Twin pairs where one had a long-term SA during the follow-up and the other not (n=184)
[3] Adjusted for birth year
[4] Model a, and additional adjustments for delivery year, and educational level
[5] Model b, and additional adjustments for subsequent deliveries
[6] During the period 1-5 years prior to T_0
[7] Diagnoses O00-O99 excluded

Childbirth, hospitalization, and sickness absence: a study of female twins

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Abstract

Objective: To investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account.

Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA were calculated as hazard ratios (HR) with 95% confidence intervals (CI).

Setting: All female twins, i.e., women with twin sister, born in Sweden.

Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where at least one in the twin pair had their first childbirth (T_0) 1994-2009 and none gave birth before 1994.

Main outcome measures: Hospitalization and SA during year 3-5 after first delivery or equivalent.

Results: Preceding the first childbirth, the mean annual number of SA days increased for mothers, and then decreased again. Hospitalization after T_0 was associated with higher HRs of short-term and long-term SA (HR for short-term SA: 3.0; 95% CI 2.5-3.6 and for long-term SA: 2.3; 95% CI 1.6-3.2). Hospitalization both before and after first childbirth was associated with a higher risk of future SA (HR for long-term SA: 4.2; 95% CI 2.7-6.4). Familial factors influenced the association between hospitalization and long-term SA, regardless of childbirth status.

Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth and results indicate a positive health selection into giving birth. Mothers hospitalized before and/or after giving birth had higher risks for future SA, that is, there was a strong association between morbidity and future SA.

Keywords: sick leave, childbirth, inpatient care, hospitalization, cohort study, population based, twins

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Article Summary

Article focus:

To investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account.

Key messages:

- Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth
- The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially

Strengths and limitations:

- The strengths of the study include the population-based prospective design, using national registers with high completeness and validity
- With a twin study design, we were able to take familial influences into account
- As inpatient care to a great extent has been replaced by outpatient treatment, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities

Introduction

In most countries with high labor force participation, women have higher levels of sickness absence (SA) than men [1-4]. Many theories and mechanism regarding this have been suggested, e.g., women having higher morbidity, higher workload (when combining paid and unpaid work), tougher situation on the labor market, men being the norm for how the labor market is organized, gender bias in healthcare and social insurance systems, discrimination, and domestic violence, etcetera [5-9]. Another hypothesis behind this gender difference in SA focuses on SA during pregnancy and after childbirth [6 10-13]. Several studies show that women have higher SA during pregnancy [10 14] and that pregnancy-related SA explains half of the gender differences in SA in fertile ages [15].

One of the changes in society that may affect health after childbirth is that the mean age for having the first child has increased over the last years and that women with higher level of morbidity now give birth. Further, nowadays, the proportion of caesarean sections has increased as well as vacuum extraction deliveries, leading to risk of later health problems [16 17].

In this study, focus is on childbirth, morbidity, and SA among women, to get a better understanding of mechanisms behind SA among women in fertile ages. There are hardly any studies on the associations between giving birth and morbidity and SA, and those conducted have focused on a relatively short time period right after childbirth, most often within the first year following the child delivery [18 19], while prospective studies with longer follow-up of mothers are rare [6 12 20].

Pregnancy, delivery, and the postpartum period may imply large physical, mental, and social changes during a short period of time, increasing the risk for disease and injury [21 22]. Different types of physical and mental disorders are common during pregnancy and after childbirth – and can in some cases be longstanding or even permanent – however, this is hardly studied at all [19]. Giving birth may be associated with a higher risk of certain diseases demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental

disorders, and different types of injuries [23-26]. For women with a disease present before the childbirth, the disorder might deteriorate after childbirth [23 24]. Regarding symptoms related to childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain, fatigue, headache, and sleep disorders [19 27]. Most of these symptoms seem to remain up to one year after childbirth [17]. Besides physical health effects, also depression and other mental disorders have been linked to childbirth [26 28], but again, prospective studies with longer follow-up are lacking [27]. Even though having children has been shown to contribute to an overall wellbeing, this is not the case for everybody and especially not among single mothers whose economic situation and thereby possibilities for good health care might be worse [29-31].

Morbidity can be measured in different ways, e.g., through self-reports ~~and~~ or visits to healthcare. Here we will use data on more severe morbidity that involves assessments from physicians, that is, morbidity that has led to hospitalization, a measure so far not used in this type of studies. Sickness absence is not a good measure of morbidity– most people with morbidity are not on SA [4]. Instead SA is considered a very good measure of social consequences of morbidity, in terms of not being able to support yourself from work [4]. Yet, there are surprisingly few studies on the association between morbidity and SA and in media and among some researchers sometimes ~~even~~ the level of morbidity among sickness absentees even is questioned, especially for female sickness absentees – their sickness absence is rather considered related to attitudes than to morbidity [12 32 33].

Studies examining the role of familial factors (i.e., genetic and shared (mainly childhood) environment) on morbidity have shown that genetics tends to explain a moderate to large extent of the variability in most of the chronic diseases [34 35]. For example, heritability for mental disorders varies between 30-90% [36], whereas genetic factors have been shown to explain 30-60% of the total variation in musculoskeletal disorders [37 38]. Taken together, familial factors are important to account for when studying the association between morbidity

(here in terms of hospitalization) and SA as studies otherwise could lead to erroneous conclusions. Twin settings provide a powerful tool for studies of these aspects in research of SA, a research area where different selection biases otherwise might have an impact on results. Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average 50% for DZ pairs) and common environmental factors through childhood (100% for both MZ and DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs). An experimental design, which can control for these familial influences, is to examine discordant twin sisters, that is, where one twin sister has given birth and the other has not. If discordant twin sisters show similar associations as the analyses of the whole cohort, this would indicate that the childbirth may actually be a contributing cause of the future SA. If instead the association found among the whole cohort cannot be replicated within discordant twin sisters, then familial factors are of importance. Influence of familial factors (genetic and common environment) is indicated if the association found in the analyses of the whole cohort disappear or change considerably in the analyses of discordant twin pairs [39].

The aim of the study was to investigate the associations of giving birth with subsequent morbidity in terms of hospitalization and SA. Familial factors (genetics and shared/early environmental) were taken into account in order to assess if familial factors explain a potential association between childbirth and future hospitalization and SA.

Methods

Participants and data sources

We performed a prospective population-based cohort study of female twins. All female twins, i.e., women with a twin sister, born in Sweden between 1959 and 1990 were selected from the Swedish Twin Registry (STR) [40]. After excluding women who delivered their first child before 1994 or whose twin sister had her first delivery before 1994, and twins where none in the pair had their first delivery between 1994 and 2009 (n=7 304), the final cohort comprised 5 118 women of which 95% had income from work, the others had income from parental benefits, unemployment benefits, student benefits, different types of sickness benefits, or a mixture of those (in the year prior to the birth year, i.e., T(-1). All had some of those types of income, all granting rights to SA benefits. The Swedish Twin Registry (STR) is the largest population-based register of twin births in the world, with information such as birth date, sex, zygosity, and pair identification [40 41]. The selection of the study population is illustrated in Figure 1.

The unique personal identity number assigned to each Swedish resident [42] was used to link information from several nationwide population-based registers at an individual level up through 2009, as follows. The Causes of Death Register was used to obtain information on date of death [43]. This register contains information on all deceased Swedish residents since 1952. Information on all deliveries (including still births) was derived from the Medical Birth Register, which was established in 1973 and includes information on almost all births in Sweden [44]. In order to increase the coverage on delivery, we also used the National Patient Register (NPR) to obtain information on all deliveries. This register was founded in 1964 and includes all individuals admitted to any psychiatric or general hospital [45]. Information on hospitalization with a principal diagnosis for delivery (as defined by the International Classification of Disease (ICD): ICD-9: 650, 651.9, 652.2, 669.5-8; and ICD-10: O80-84) was obtained. The NPR was also used to obtain annual information on other hospitalizations, i.e.,

inpatient care. Annual information on educational level and on SA days was obtained from Statistics Sweden.

Time in relation to childbirth

The studied women were followed in relation to year of first childbirth, referred to as T_0. In order to compare those who gave birth to those who did not, T_0 for the women who did not give birth was defined as year of her twin sister's first childbirth.

Hospitalization

Data on hospitalization covered the period six years prior to, and six years after year of first childbirth (T_0) or equivalent. For descriptive purposes, the total and the average number of hospitalization days per year were calculated.

In order to examine if hospitalization prior to (or after) childbirth increases the risk for future hospitalization, the first part of the regression analyses considered hospitalization as both exposure and outcome. We created one dichotomous variable for hospitalization before T_0 (i.e., exposure), and two dichotomous outcome variables for hospitalization during year 3-5 after T_0: one for hospitalization with any diagnosis and one excluding hospitalization with diagnoses related to pregnancy, childbirth, and the postpartum period.

In order to answer the research question "Does hospitalization prior to (or after) childbirth increase the risk for future SA?", we created two dichotomous hospitalization exposure variables: one for hospitalization before T_0 and one variable: hospitalization year 1-2 after T_0 (excluding diagnoses related to pregnancy, childbirth, and the postpartum period).

Sickness absence

SA can be measured in several ways, related to duration and incidence [46]. Here we used the following four measures: total and average number of SA days per year; number of SA days during year 3-5 after T_0; and number of SA days >90 sick-leave days during year 3-5 after T_0.

Sickness insurance in Sweden

In Sweden, all residents aged 16-65 years who have income from work, unemployment benefits, parental benefits, or student benefits are entitled to sickness benefits from the Swedish Social Insurance Agency, if unable to work due to disease or injury. Among employed individuals, sick pay was in most cases paid by the employer during the first 14 days of a sick-leave spell, which means that we do not have data on most of the short sick-leave spells. In most of the years studied, there was no limitation to duration of a sick-leave spell. Sickness benefits covered 80% of lost income, up to a certain level. All were covered by a health care insurance covering the right to hospital care when needed, at a much reduced cost, less than 10 Euros a day. Care during pregnancy and delivery was free.

Potential confounding factor

As research has shown socioeconomic disparities in age at first birth (e.g., the higher the education, the later the first birth) [47 48], we adjusted for educational level at T_0. Years of education was classified into four categories; <9 years of compulsory school, 10-12 years of education (senior high school), ≥13years of education (college/university), missing.

Statistical analysis

First, Cox proportional hazard models with constant time-at-risk [49] were applied to estimate hazard ratios (HR) with 95% confidence intervals (CI) for having at least one hospitalization after childbirth (T_0). In a first model (model a), adjustments were made for age. Second

(model b), additional adjustments were made for delivery year and educational level at time of T_0. Thereafter, twin pairs who were discordant with respect to outcomes, i.e., having at least one hospitalization after T_0, were analyzed using Conditional Cox regression. In the next step, we analyzed the associations between childbirth, hospitalization, and SA by fitting three Cox regression models (table 3). The first (model a) was adjusted for birth year. In the second model (model b), additional adjustments were made for delivery year and educational level at time of T_0. In the third model (model c), previous hospitalization was included. Thereafter, twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e., having had SA or long-term SA (>90 days) were analyzed.

Finally, in the step where we analyzed the association between hospitalization before and after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-b) from table 3. In a third model (model c), we fitted an additional model in which adjustments were made for subsequent deliveries.

The proportional hazards assumption was checked by including time-dependent versions of all the covariates in the models. This did not indicate a violation of the proportionality assumption.

All statistical analyses were performed with SAS 9.3 and STATA 12.1.

The STROBE checklist was used in designing and reporting the study.

The project was approved by the Regional Ethical Review Board of Stockholm.

Results

Of the 5 118 women included in the study, 77% had given birth at least once between 1994 and 2009 (Table 1). Of these women, nearly 70% also had given birth later, at least once. A majority of the women who gave birth had their first delivery before the age of 30 (61%). The educational level distribution was rather similar when comparing those who gave birth to those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were excluded, 30% of the women, i.e., the 1 183 where both in a pair gave birth and the 407 twins where only one in the pair gave birth had at least one hospitalization during the period six years prior to and six years after their first delivery (the delivery year excluded). The corresponding rate for the women who had not given birth was 27%. Half of the women who gave birth had at least one day of SA during the period six years prior to or the six years after first delivery, when the year for childbirth was excluded. The majority of the women had no SA at all in the six years following childbirth.

The average annual number of days with inpatient care and SA, respectively, is presented in Figure 2. Up to year T_0, women who did not give birth had a higher average number of hospitalization days and SA days compared to those who gave birth. Women who gave birth had approximately 0.3 hospitalization days per year whereas those who did not give birth had around 0.5 hospitalization days per year. The average number of SA days for women giving birth was 3.8 days/year and for those not giving birth 5.0 days/year. SA differences between those giving birth and women not giving birth were statistically significant with the exception of year (-4) and (-3). For inpatient care, the differences between those giving birth and women not giving birth were not statistically significant. The average number of inpatient days increased rapidly during T_0 for women who gave birth, especially because of hospitalization due to pregnancy and childbirth. After T_0, the number of SA days decreased quickly among these women. For women who gave birth, days with inpatient care and SA the years following T_0 were to a large extent associated with subsequent childbirths.

Table 2 presents HR for the association between childbirth and hospitalization, for all diagnoses and for diagnoses where those related to pregnancy, childbirth, and the postpartum period were excluded. When these diagnoses were removed, women who did not give birth and who had been hospitalized at least once before T_0 had twice the risk of future hospitalization compared to those not hospitalized prior to T_0 (HR: 2.3; 95% CI 1.6-3.3) after adjustments for birth year, delivery year, and educational level. The association was explained by familial factors in the analysis of discordant twin pairs (HR: 1.2; 0.8-1.9).

When restricting the analyses to women who gave birth, a total of 2 792 women were studied, i.e., 1 396 complete pairs in which both twins had given birth. The reference group constituted of mothers who had not been hospitalized prior to their first childbirth. Mothers who had been hospitalized before their first childbirth had a slightly higher HR for future hospitalization when diagnoses related to pregnancy and childbirth were excluded (HR 1.5; 1.2-2.0). This association disappeared in the analyses of discordant twin pairs, suggesting an influence of familial factors (HR: 1.0; 0.8-1.3).

Regardless of childbirth status, hospitalization year 1-2 after T_0 was a predictor of having a new SA in year 3-5 after T_0 (Table 3). Compared to women who did not give birth and who were not hospitalized the first two years after T_0, mothers hospitalized after first childbirth had an HR of 2.4 (2.0-2.9) for a new SA after adjustments for birth year, delivery year, and educational level. Hospitalization after T_0 was also associated with a new long-term SA (>90 days) in year 3-5 after T_0 (Table 3). Women who did not give birth had a nearly three-fold risk of a new long-term SA year 3-5 after T_0 (HR 2.8; 1.5-5.1), whereas women who gave birth had an HR of 1.8 (1.3-2.5). The analyses of twin pairs discordant for having a new long-term SA year 3-5 after T_0, showed attenuated point estimates, hence suggesting that familial effects may play a role.

The analyses, in which we considered hospitalization before and after first childbirth as exposure, and outcome was a new SA year 3-5 after T_0 (Table 4) show that mothers who had been hospitalized at least once both before and after their first child birth had a higher risk of future SA (HR 1.8; 1.4-2.2). These women also had a higher risk of long-term SA; however, these risk estimates were not statistically significant. After controlling for familial confounding, the estimated risk for long-term SA for those who had been hospitalized before T_0 was in the same direction but the HR was reduced, which suggest that also familial factors may have an influence on the studied association.

Discussion

In this register study of a population-based Swedish cohort of female twins born between 1959 and 1990, the associations of delivery with hospitalization and SA were examined as well as whether familial (i.e., genetic and shared, mainly childhood, environmental) factors were contributing to these associations. Just before the first childbirth, the SA days increased much for mothers, an increase that gradually decreased during the years after the delivery. We found hospitalization prior to T_0 to be a risk factor for future hospitalization, regardless of childbirth status, also when excluding hospitalization due to childbirth. Furthermore, hospitalization after the first childbirth was associated with a higher HR of both short-term and long-term future SA. An additional analysis focusing solely on the women who gave birth showed that hospitalization both before and after the first childbirth was associated with a higher risk of future SA. Familial factors seemed to have an influence on the association between hospitalization and long-term SA, regardless of childbirth status.

In line with some previous studies [10 20 50 51], we found that SA increased in women during the time before the first childbirth. Giving birth was also associated with a future somewhat higher risk for SA, in line with that of those not giving birth. However, this higher risk could be due to subsequent pregnancies. A recent Norwegian study found that the increased SA risk in women in the years after pregnancy disappeared when SA during subsequent pregnancies were accounted for [20]. Several explanations have been suggested for such higher levels of SA, among others the double burden hypothesis [20 52-54]. This hypothesis has been questioned, as research has indeed shown that women who occupy multiple roles tend to be healthier than those who enact fewer roles [55-57]. Thus, the combination of employment and parenthood does not seem to imply worse health, on the contrary. In our study, the annual rates of SA decreased steadily after the first childbirth, speaking in favor of this hypothesis. Further studies of this are warranted.

To our best knowledge, this is the first study to examine long-term associations between childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to subsequent pregnancy and childbirth) when compared to women who did not give birth.

Those who did not give birth had a more stable pattern of SA during the studied period, however, with a slight increase in annual SA days over the years. This is in line with a Swedish study examining whether family obligations influence the risk of SA in publicly employed women and found a slight risk increase for SA among women without children [58]. Further, a broad systematic literature review published in 2004 provided no evidence of an association between having children in the household and an increased risk of SA [59]. It is important to consider family situation when examining the association between having children and morbidity, as single women with children have been shown to have worse health [30 31 60] and higher levels of SA [6 58].

Even though pregnancy, delivery, and the postpartum period may increase the risk for disease and injury [25 27], our findings do not suggest that women who gave birth are more likely to be hospitalized after their first childbirth, except for hospitalizations related to subsequent deliveries. We found no differences in risk for future hospitalization when comparing those who gave birth to those who did not. Thus, giving birth does not have to be associated with subsequent health problems. The fact that we found no differences in future hospitalization between those who gave birth and those who did not, may have different explanations. As mentioned above, one could expect that there is a health selection, where women who do not give birth may have worse health and choose not to have or cannot have a child. Also, giving birth is in itself a risk factor for future morbidity[16 19 22]. Further, during the last decades, the number of women who voluntarily do not want to become parents has increased worldwide[61].

Hospitalization prior to the first childbirth or equivalent (T_0) was a risk factor for future SA for all women, regardless of childbirth status. In particular, women who had been hospitalized both before and after T_0 were at risk for future SA. Furthermore, we found an association between hospitalization and future long-term SA.

When comparing women who gave birth to those who did not, with respect to exposure to hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had slightly higher risk for future SA regardless of duration, whereas those who did not give birth hospitalized after T_0 had higher risk for long-term SA.

Hospitalization both before and after the year T_0 seems to be the strongest indicator, i.e., these individuals had the highest risk for future SA. Consequently, the women who had been hospitalized both before and after T_0 had the highest risk for future SA. Our analyses of women who gave birth revealed a graded association between hospitalization and SA, where those who only were hospitalized before *or* after their first childbirth had a higher risk of SA, whereas those who were hospitalized both before and after the first childbirth had even higher risks. Thus, we found a strong association between morbidity, here measured as hospitalization, and future SA among women who have given birth – an association that often has been question regarding women with children [12].

Familial factors seemed to contribute to the association between hospitalization before and after T_0 among those who did not give birth. The influence of familial factors may relate to morbidity among women not giving birth – morbidity that might be more severe and potentially also being relatively strongly influenced by genetics. Familial factors also played a role in the associations between hospitalization and future long-term SA. This could be related to the fact that the hospitalization usually is required for severe conditions that may have a strong genetic component. However, since genetics have been shown to influence the risk of DP [62], and some indications exist that genetics also play a role in long-term SA and

mortality, it can be suspected that the effects of familial factors on SA can be either direct or through other influential factors.

Strengths and limitations

The strengths of this study are the population-based prospective cohort study design, including all in the study population, not a sample, using nationwide registers with high completeness and validity [43-45]. Further, we used a large study cohort without loss to follow up. With a twin study design, we were able to take familial influences into account. When measuring both exposure and outcome with register-based data, we avoid problem with recall bias.

This study has, however, some limitations. First of all, we do not know whether the women who did not give birth were childless voluntarily or not. Differences in health between voluntary and involuntary childlessness have been shown, where voluntarily childless women showed higher levels of overall well-being [61 63] which might be related to hospitalization and/or SA. Using inpatient care as a measure of morbidity has both its strengths and limitations. One limitation is that we thus selected more severe types of morbidity, and hence that does not include morbidity treated in outpatient care. Having had also other types of morbidity data might have given another picture and hopefully future studies will have such information. Another limitation is that the terms for inpatient care have changed during the studied period. In Sweden, inpatient care has over the years to a great extent been replaced by outpatient treatment. Therefore, some of the decrease in hospitalization over the years is a result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities [64], however, this affected all women equally, and is to some extent handled by adjusting for birth year. The CIs are wider in the years far from T_0, e.g., T_6, due to fewer follow up year for some – e.g., for those who gave birth late during the studied period. Also,

we lack information on the shorter SA spells among those employed. Further, the Swedish Twin Registry (STR) contains all twin births in Sweden; hence, immigrants are not included in this study and as a consequence the external validity might be lower to women born outside of Sweden.

It is important to be aware of that giving birth is in focus here, irrespective of whether the child survived or not. Some of the women who did not give birth might be mothers, e.g., due to adoption. Other studies in this area has 'being mother' or 'living with child' as exposure term, rather than 'giving birth'.

Conclusion

Women giving birth did not have a higher future SA risk than those not giving birth and results indicate a positive health selection into giving birth. Mothers with different types of morbidity, in terms of hospitalization before and/or after giving birth had higher risks for future SA. Most women had no SA in the six years following childbirth and those who had SA generally had that for shorter periods. Among the few women who had severe morbidity, in terms of hospitalization, the future risk for SA was, as expected, higher. Hospitalization prior to T_0 was strongly associated with later hospitalization and later SA. The high levels of inpatient care in women who did not give birth suggest that there is a health selection in giving birth, where the women who give birth have a better health initially. However, most women had no hospitalization and no SA.

Ethical approval

The study was approved by the Regional Ethical Review Board, Stockholm, Sweden (2007/524-31).

Contributorship Statement

KA and PS originated the idea. EB analysed the data in consultation with KA, LK, JN, AR, and PS. EB wrote the first and subsequent drafts of the manuscript, with important intellectual input from all the co-authors. All authors contributed in designing the study and to the interpretation of the results and to the writing and approval of the final article.

Competing interest statement

We declare that no competing interests exist.

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Data sharing

No additional data available.

Figure legends

Figure 1. Flow chart for the study population.

Figure 2. Average annual number of days on sickness absence (SA) and hospitalization, respectively, (with 95% CI), six years prior through six year after T_0 for women who gave birth/did not give birth (n=5 118).

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Table 1. Cohort characteristics for twins (women with twin sister) born in Sweden 1959-1990 (excluding those who gave birth before age 16 and those who died before age 16), where at least one in the pair had their first childbirth 1994-2009 and none before 1994. T_0 is defined as year for first childbirth for women who gave birth, and year of twin sister's childbirth for those who did not give birth.

		Twin pairs where only one in the pair gave birth		
Variables	**Both gave birth**	**Twin 1 (gave birth)**	**Twin 2 (did not give birth)**	**Total**
N	2 792	1 163	1 163	5 118
Number of deliveries				
One delivery	711 (25%)	501 (43%)		
Two or more deliveries	2 081 (75%)	662 (57%)		
Age at T_0				
16-19 years	47 (2%)	33 (2%)		
20-24 years	511 (18%)	239 (21%)		
25-29 years	1 150 (41%)	444 (38%)		
30-34 years	847 (30%)	323 (28%)		
35-39 years	207 (7%)	109 (9%)		
>40 years	30 (1%)	15 (1%)		
Zygosity				
Monozygotic	1 726 (62%)	608 (52%)	608 (52%)	2 942 (57%)
Dizygotic	1 066 (38%)	555 (48%)	555 (48%)	2 176 (43%)
Highest attained education[1]				
≤ 9 year	179 (6%)	74 (6%)	55 (5%)	308 (6%)
10-12 year	1 434 (51%)	608 (52%)	621 (53%)	2 663 (52%)
≥ 13 year	1 173 (42%)	474 (41%)	422 (36%)	2 069 (40%)
Information on education missing	6 (0%)	7 (1%)	65 (6%)	78 (2%)
Hospitalization[2]				
- At least one hospitalization during the period six years prior through six years after T_0	2 161 (77%)	703 (60%)	325 (28%)	3 189 (62%)
-At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, childbirth, and the puerperium)	865 (31%)	315 (27%)	314 (27%)	1 494 (29%)
- At least one hospitalization during the period six years prior through six years after T_0 (excluding hospitalizations with a diagnosis for pregnancy, and childbirth)	1 183 (42%)	407 (35%)	325 (28%)	1 915 (37%)
- At least one hospitalization during the period six years prior to T_0	679 (24%)	251 (22%)	217 (19%)	1 147 (22%)
- At least one hospitalization during the period six years after T_0	1 965 (70%)	585 (50%)	168 (14%)	2 718 (53%)
- At least one hospitalization both before and afterT_0	483 (17%)	133 (11%)	60 (5%)	676 (13%)
Sickness Absence (SA)[3]				
At least one SA during the period six years prior through six years after T_0	1 526 (55%)	530 (46%)	365 (31%)	2 420 (47%)
At least one SA during the period six years prior to T_0	690 (25%)	274 (24%)	224 (19%)	1 188 (23%)
At least one SA during the period six years after T_0	1 245 (45%)	382 (33%)	221 (19%)	1 848 (36%)

[1] At time of T_0

[2] Excluding hospitalizations occurring during T_0

[3] Excluding SA occurring during T_0

Table 2. Cox proportional hazard ratios (HR) with 95% CI for the association between childbirth, hospitalization before T_0, and subsequent hospitalization (i.e., during year 3-5 after T_0) in twins where at least one in the pair had her first childbirth in 1994-2009 and none before 1994, both including and excluding hospitalization related to pregnancy, childbirth, and the puerperium. Two models for adjustments as well as for discordant twin pairs.

Status childbirth and hospitalization	All diagnoses			Diagnoses related to pregnancy, childbirth and the puerperium excluded[1]		
	Model a[6]	Model b[7]	Discordant twin pairs[2, 7]	Model a[6]	Model b[7]	Discordant twin pairs[3, 7]
All women (n=5 118)						
No childbirth, no hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization before T_0[8]	2.5 (1.7-3.6)	2.3 (1.6-3.3)	2.4 (1.3-4.5)	2.7 (1.8-3.9)	2.3 (1.6-3.4)	1.2 (0.8-1.9)
Childbirth, no hospitalization before T_0[8]	6.1(5.0-7.5)	5.5 (4.5-6.8)	8.3 (5.8-11.8)	1.1 (0.8-1.3)	0.9 (0.7-1.2)	0.9 (0.7-1.1)
Childbirth, hospitalization before T_0[8]	6.5 (5.2-8.1)	5.6 (4.4-7.1)	7.9 (5.4-11.5)	1.9 (1.4-2.5)	1.4 (1.1-1.9)	0.9 (0.7-1.2)
	Model a[6]	Model b[7]	Discordant twin pairs[4, 7]	Model a[6]	Model b[7]	Discordant twin pairs[5, 7]
Women who had at least one childbirth (n=2 792)						
No hospitalization before T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[8]	1.0 (0.9-1.2)	1.0 (0.9-1.1)	1.0 (0.8-1.2)	1.7 (1.3-2.3)	1.5 (1.2-2.0)	1.0 (0.8-1.3)

[1] Diagnoses O00-O99
[2] Twin pairs where one had a hospitalization during the follow-up and the other not (n=1 016 pairs)
[3] Twin pairs where one had a hospitalization during the follow-up and the other not (n=456 pairs)
[4] Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)
[5] Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs)
[6] Adjusted for birth year
[7] Model a, and additional adjustments for delivery year, and educational level
[8] During the period 1-5 years prior to T_0

Table 3. Cox proportional HR with 95% CI for the association between childbirth, hospitalization, and new sickness absence (SA) in year 3-5 after T_0, in twins where at least one in the pair had their first childbirth 1994-2009. Three models for adjustments as well as for discordant twin pairs.

Status childbirth and hospitalization	SA in year 3-5 after T_0 (regardless of number of days)				Long-term SA (>90 days) in year 3-5 after T_0			
	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[1, 7]	Model a[5]	Model b[6]	Model c[7]	Discordant twin pairs[2, 7]
All women (n=5 118)								
No childbirth, no hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization year 1-2 after T_0[8]	2.7 (1.8-4.1)	2.2 (1.5-3.4)	2.1 (1.4-3.2)	1.5 (0.8-2.9)	4.5 (2.5-8.2)	3.5 (1.9-6.2)	2.8 (1.5-5.1)	1.1 (0.5-2.3)
Childbirth, no hospitalization year 1-2 after T_0[8]	2.1 (1.8-2.5)	1.8 (1.5-2.2)	1.8 (1.5-2.2)	1.7 (1.3-2.2)	1.1 (0.8-1.6)	1.0 (0.7-1.4)	1.0 (0.7-1.3)	0.8 (0.6-1.2)
Childbirth, hospitalization year 1-2 after T_0[8]	3.0 (2.5-3.6)	2.4 (2.0-2.9)	2.4 (2.0-2.9)	2.0 (1.5-2.6)	2.3 (1.6-3.2)	1.8 (1.3-2.5)	1.8 (1.3-2.5)	1.0 (0.7-1.5)
Women who had at least one childbirth (n=2 792)	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[3, 5]**	**Model a[5]**	**Model b[6]**	**Model c[7]**	**Discordant twin pairs[4, 7]**
No hospitalization year 1-2 after T_0[8]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization year 1-2 after T_0[8]	1.3 (1.2-1.5)	1.3 (1.1-1.4)	1.2 (1.1-1.4)	1.2 (1.0-1.5)	2.0 (1.5-2.6)	1.9 (1.4-2.5)	1.8 (1.4-2.4)	1.4 (1.0-1.9)

[1] Twin pairs where one had a SA during the follow-up and the other not (n=835 pairs)
[2] Twin pairs where one had a long-term SA during the follow-up and the other not (n=277 pairs)
[3] Twin pairs where one had a SA during the follow-up and the other not (n=542 pairs)
[4] Twin pairs where one had a long-term SA during the follow-up and the other not (n=184 pairs)
[5] Adjusted for birth year
[6] Model a, and additional adjustments for delivery year, and educational level
[7] Model b, and additional adjustments for earlier hospitalization
[8] Diagnoses O00-O99 excluded

Table 4. Cox proportional HR with 95% CI for the association between hospitalization before and after first childbirth, and new sickness absence (SA) in year 3-5 after T_0, in twins who had their first childbirth 1994-2009 (n=2 792). Three models for adjustments as well as for discordant twin pairs.

Status hospitalization before and after childbirth	SA in year 3-5 after T_0 (regardless of number of days)				Long-term SA (>90 days) in year 3-5 after T_0			
	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[1, 4]	Model a[3]	Model b[4]	Model c[5]	Discordant twin pairs[2, 4]
No hospitalization either before T_0[6] or during year 1-2 after T_0[7]	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T_0[6] but not during year 1-2 after T_0[7]	1.2 (1.0-1.5)	1.2 (1.0-1.4)	1.2 (1.0-1.4)	1.0 (0.8-1.3)	2.3 (1.6-3.4)	2.1 (1.5-3.1)	2.2 (1.5-3.1)	1.2 (0.8-1.7)
No hospitalization before T_0[6] but during year 1-2 after T_0[7]	1.2 (1.1-1.4)	1.2 (1.0-1.4)	1.1 (0.9-1.2)	1.1 (0.9-1.4)	2.0 (1.5-2.8)	1.9 (1.4-2.7)	1.9 (1.4-2.7)	1.4 (1.0-2.1)
Hospitalization before T_0[6] and during year 1-2 after T_0[7]	2.0 (1.6-2.5)	1.8 (1.4-2.2)	1.6 (1.3-2.1)	1.6 (1.1-2.2)	4.2 (2.7-6.4)	3.5 (2.3-5.3)	3.5 (2.3-5.4)	1.5 (0.9-2.4)

[1] Twin pairs where one had an SA during the follow-up and the other not (n=542)
[2] Twin pairs where one had a long-term SA during the follow-up and the other not (n=184)
[3] Adjusted for birth year
[4] Model a, and additional adjustments for delivery year, and educational level
[5] Model b, and additional adjustments for subsequent deliveries
[6] During the period 1-5 years prior to T_0
[7] Diagnoses O00-O99 excluded

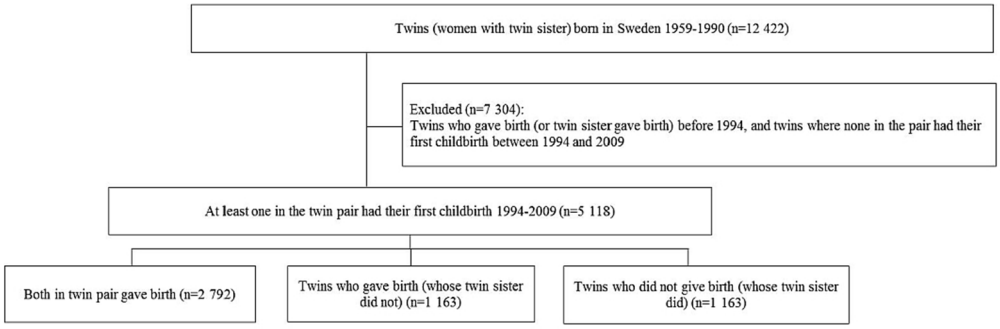

Figure 1
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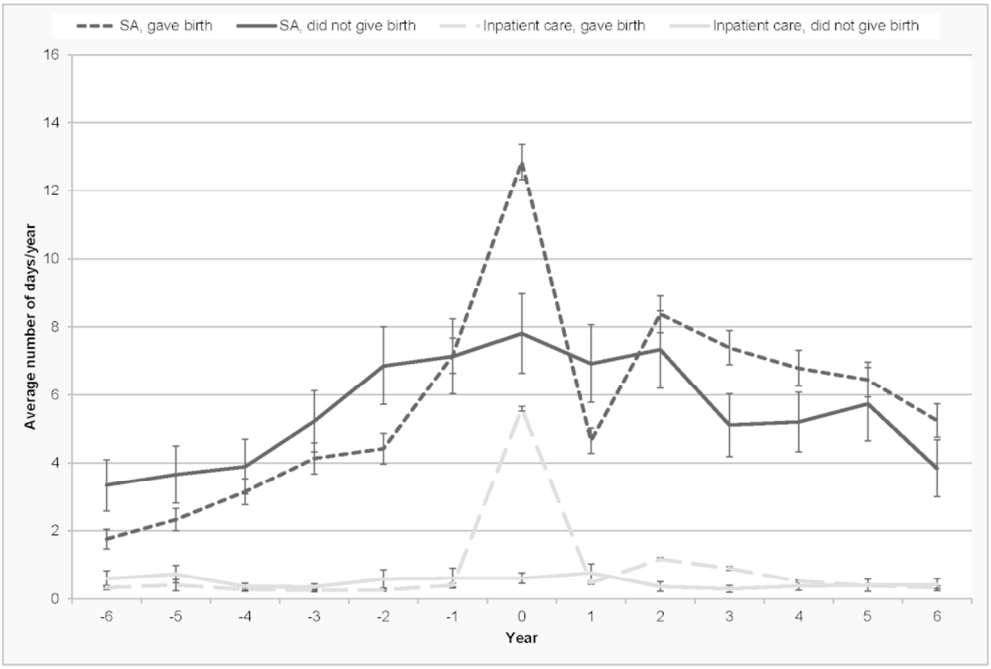

Figure 2
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BMJ Open - Childbirth, hospitalization, and sickness absence: a study of female twins

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Page 1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Page 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Page 5**
Objectives	3	State specific objectives, including any prespecified hypotheses **Page 7**
Methods		
Study design	4	Present key elements of study design early in the paper **Page 8**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Page 8-11**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up **Page 8-11**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed **N/A**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Page 9-10**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Page 8-11**
Bias	9	Describe any efforts to address potential sources of bias **N/A**
Study size	10	Explain how the study size was arrived at **Page 8**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Page 9-10**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **Page 10-11**
		(*b*) Describe any methods used to examine subgroups and interactions **Page 10-11**
		(*c*) Explain how missing data were addressed **N/A**
		(*d*) If applicable, explain how loss to follow-up was addressed

		N/A
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **Page 8, and page 24**
		(b) Give reasons for non-participation at each stage **N/A**
		(c) Consider use of a flow diagram **Page 21**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Page 24**
		(b) Indicate number of participants with missing data for each variable of interest **N/A**
		(c) Summarise follow-up time (eg, average and total amount) **N/A**
Outcome data	15*	Report numbers of outcome events or summary measures over time **Page 24**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Page 24-25**
		(*b*) Report category boundaries when continuous variables were categorized **Page 23**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **N/A**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Page 25-26**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Page 2, 4 and page 15**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Page 18**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Page 15-17**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Page 15-17**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Page 20**

*Give information separately for exposed and unexposed groups.