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

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5 TROBE Statement	-Chec Item	klist of items that should be included in reports of <i>cohort studies</i>
	No	Recommendation
Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term in the title or the <b>Page 1</b>
		(b) Provide in the abstract an informative and balanced summary of what wa and what was found Page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being re Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses Page 6
Methods		A
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 recru exposure, follow-up, and data collection <b>Page 7-10</b>
Participants	6	<ul> <li>(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</li> <li>Page 7-10</li> </ul>
		(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, an modifiers. Give diagnostic criteria, if applicable <b>Page 8-9</b>
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 in 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 <b>Page 8-9</b>
Statistical methods	12	( <i>a</i> ) Describe all statistical methods, including those used to control for confor Page 9-10
		<ul> <li>(b) Describe any methods used to examine subgroups and interactions</li> <li>Page 9-10</li> <li>(c) Explain how missing data were addressed</li> <li>N/A</li> </ul>
		(d) If applicable, explain how loss to follow-up was addressed

		N/A
		( <u>e</u> ) 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
I I I I I I I I I I I I I I I I I I I		information on exposures and potential confounders
		Page 23
		(b) Indicate number of participants with missing data for each variable of interest
		$\frac{N/A}{(a)}$
		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
		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
Conorolizabilit	21	Page 13 - 15
Generalisability	21	Discuss the generalisability (external validity) of the study results
		1 azı 15-10
Other information	22	Give the source of funding and the rale of the funders for the present study and if
rununig	22	applicable, for the original study on which the present article is based
		Page 18
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\*Give information separately for exposed and unexposed groups.

1	Childbirth, hospitalization, and sickness absence: a study of female twins
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26 27	Abstract Objective: To investigate associations of giving birth with morbidity in terms of
28	hospitalization and social consequences of morbidity in terms of sickness absence (SA), while
29	taking familial (genetics and shared environmental) factors into account.
30	Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA
31	were calculated as Hazard Ratios (HR) with 95% confidence intervals (CI).
32	Setting: All female twins, i.e. women with twin sister, born between 1959 and 1990 in
33	Sweden.
34	Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where
35	at least one in the twin pair had their first childbirth $(T_0)$ 1994-2009 and none gave birth
36	before 1994.
37	Main outcome measures: Hospitalization and SA during year 2-5 after first delivery or
38	equivalent.
39	Results: Preceding the first childbirth, the mean annual number of SA days increased for
40	mothers, and then decreased again. Hospitalization after $T_0$ was associated with higher HRs of
41	short-term and long-term SA. Hospitalization both before and after first childbirth was
42	associated with a higher risk of future SA. Familial factors influenced the association between
43	hospitalization and long-term SA, regardless of childbirth status.
44	Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth
45	and results indicate a positive health selection into giving birth. Mothers hospitalized before
46	and/or after giving birth had higher risks for future SA, that is, there was a strong association
47	between morbidity and future SA.
48	Keywords: sick leave, childbirth, inpatient care, hospitalization, cohort study, population
49	based, twins

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51 52	Articl Articl	e Summary e focus:
53	-	To investigate the associations of giving birth with subsequent morbidity in terms of
54		hospitalization and sickness absence
55	-	To study if hospitalization prior to (or after) childbirth increases the risk for future
56		hospitalization and sickness absence
57	Key n	nessages:
58	-	Women giving birth did not have a higher future SA risk than those not giving birth
59		and results indicate a positive health selection into giving birth
60	-	The high levels of inpatient care in women who did not give birth suggest that there is
61		a health selection in giving birth, where the women who give birth have a better health
62		initially
63	Streng	gths and limitations:
64	-	The strengths of the study include the population-based prospective design, using
65		national registers with high completeness and validity
66	-	With a twin study design, we were able to take familial influences into account
67	-	As inpatient care to a great extent has been replaced by outpatient treatment, some of
68		the decrease in hospitalization over the years is a result of a shift in the responsibility
69		for inpatient care from hospitals to outpatient care facilities
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72 73	Introduction In most countries with high labor force participation, women have higher levels of sickness
74	absence (SA) than men <sup>1-4</sup> . Many theories and mechanism regarding this have been suggested,
75	e.g., women having higher morbidity, higher workload (when combining paid and unpaid
76	work), tougher situation on the labor market, men being the norm for how the labor market is
77	organized, gender bias in healthcare and social insurance systems, discrimination and
78	domestic violence, etcetera <sup>5-9</sup> . Another hypothesis behind this gender difference in SA
79	focuses on SA during pregnancy and after childbirth <sup>6 10-13</sup> . Several studies show that women
80	have higher SA during pregnancy <sup>10 14</sup> and that pregnancy-related SA explains half of the
81	gender differences in SA in fertile ages <sup>15</sup> .
82	One of the changes in society that may affect health after childbirth is that the mean age for
83	having the first child has increased over the last years and that women with higher level of
84	morbidity now give birth. Further, nowadays, the proportion of caesarean sections has
85	increased as well as vacuum extraction deliveries, leading to risk of later health problems <sup>16 17</sup> .
86	In this study, focus is on childbirth, morbidity, and SA among women, to get a better
87	understanding of mechanisms behind SA among women in fertile ages. There are hardly any
88	studies on the associations between giving birth and morbidity and SA, and those conducted
89	have focused on a relatively short time period right after childbirth, most often within the first
90	year following the child delivery <sup>18 19</sup> , while prospective studies with longer follow-up of
91	mothers are rare <sup>6</sup> <sup>12</sup> <sup>20</sup> .
92	Pregnancy, delivery, and the postpartum period may imply large physical, mental, and
93	social changes during a short period of time, increasing the risk for disease and injury <sup>21 22</sup> .
94	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 95 hardly studied at all <sup>19</sup>. Giving birth may be associated with a higher risk of certain diseases 96

demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental 97

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98	disorders and different types of injuries <sup>23-26</sup> . For women with a disease present before the
99	childbirth, the disorder might deteriorate after childbirth <sup>23 24</sup> . Regarding symptoms related to
100	childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain,
101	fatigue, headache, and sleep disorders <sup>19 27</sup> . Most of these symptoms seem to remain up to one
102	year after childbirth <sup>17</sup> . Besides physical health effects, also depression and other mental
103	disorders have been linked to childbirth <sup>26 28</sup> , but again, prospective studies with longer
104	follow-up are lacking <sup>27</sup> . Even though having children has been shown to contribute to an
105	overall wellbeing, this is not the case for everybody and especially not among single mothers
106	whose economic situation and thereby possibilities for good health care might be worse <sup>29-31</sup> .
107	Morbidity can be measured in different ways, e.g., through self-reports and visits to
108	healthcare. Here we will use data on more severe morbidity and that involves assessments
109	from physicians, that is, morbidity that has led to hospitalization, a measure so far not used in
110	this type of studies. Sickness absence is not a good measure of morbidity- most people with
111	morbidity are not on SA <sup>4</sup> . Instead SA is considered a very good measure of social
112	consequences of morbidity, in terms of not being able to support yourself from work <sup>4</sup> . Yet,
113	there are surprisingly few studies on the association between morbidity and SA and in media
114	it sometimes even the level of morbidity among sickness absentees even is questioned.
115	Studies examining the role of familial factors (i.e. genetic and shared (mainly childhood)
116	environment) on morbidity have shown that genetics tends to explain a moderate to large
117	extent of the variability in most of the chronic diseases <sup>32 33</sup> . For example, heritability for
118	mental disorders varies between 30-90% <sup>34</sup> , whereas genetic factors have shown to explain
119	30-60% of the total variation in musculoskeletal disorders <sup>35 36</sup> . Taken together, familial
120	factors are important to account for when studying the association between morbidity (here in
121	terms of hospitalization) and SA as it could lead to erroneous conclusions otherwise. Twin

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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 ι and SA. hospitalization and SA. 

# 132 Methods133 Participants and data sources

134	We performed a prospective population-based cohort study of female twins. All female twins,
135	i.e., women with a twin sister, born in Sweden between 1959 and 1990 were selected from the
136	Swedish Twin Registry (STR) <sup>37</sup> . After excluding women who delivered their first child
137	before 1994 or whose twin sister had her first delivery before 1994, and twins where none in
138	the pair had their first delivery between 1994 and 2009 (n=7 304), the final cohort comprised
139	5 118 women. The Swedish Twin Registry (STR) is the largest population-based register of
140	twin births in the world, with information such as birth date, sex, zygosity, and pair
141	identification <sup>37 38</sup> . The selection of the study population is illustrated in Figure 1.
142	The unique personal identity number assigned to each Swedish resident <sup>39</sup> was used to link
143	information from several nationwide population-based registers at an individual level up
144	through 2009, as follows. The Causes of Death Register was used to obtain information on
145	date of death <sup>40</sup> . Information on all deliveries from the Medical Birth Register, which was
146	established in 1973 and includes information on almost all births in Sweden <sup>41</sup> . In order to
147	increase the coverage on delivery, we also used the National Patient Register (NPR) to obtain
148	information on all deliveries. This register was founded in 1964 and includes all individuals
149	admitted to any psychiatric or general hospital <sup>42</sup> . Information on hospitalization with a
150	principal diagnosis for delivery (as defined by the International Classification of Disease
151	(ICD): ICD-9: 650, 651.9, 652.2, 669.5-8; and ICD-10: O80-84) was obtained. The NPR was
152	also used to obtain annual information on other hospitalizations. Annual information on
153	educational level and on SA was obtained from Statistics Sweden.
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#### 158 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.

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### 163 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.

167 In order to examine if hospitalization prior to (or after) childbirth increases the risk for future 168 hospitalization, the first part of the regression analyses considered hospitalization as both 169 exposure and outcome. We created one dichotomous variable for hospitalization before  $T_0$ 170 (i.e., exposure), and two dichotomous outcome variables for hospitalization during year 2-5 171 after  $T_0$ : one for hospitalization with any diagnosis and one excluding hospitalization with 172 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).

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### 178 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<sub>0</sub>; and number of women with a new SA spell >90 sick-leave days during year 2-5 after T<sub>0</sub>.

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#### Sickness insurance in Sweden 183

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 185 186 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 187 188 not have data on most of the short sick-leave spells. In most of the years studied, there was no 189 limitation to duration of a sick-leave spell. Sickness benefits covered 80% of lost income, up 190 to a certain level. All were covered by a health care insurance covering the right to hospital 191 care when needed, at a much reduced cost, less than 10 Euros a day. Care during pregnancy and delivery was free. 192 193 **Potential confounding factor** 194 195 Educational level at  $T_0$  was classified into four categories; <9 years of compulsory school, 10-196 12 years of education (senior high school),  $\geq$ 13 years of education (college/university), missing. 197 198 199 **Statistical analysis** First, Cox proportional hazard models with constant time-at-risk <sup>44</sup> were applied to estimate 200 201 hazard ratios (HR) with 95% confidence intervals (CI) for having at least one hospitalization 202 after childbirth (T<sub>0</sub>). In a first model (model a), adjustments were made for age. Second 203 (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 204 outcomes, i.e., having at least one hospitalization after T<sub>0</sub>, and were analyzed. In the next step, 205 206 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

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208	model (model b), additional adjustments were made for delivery year and educational level at
209	time of T <sub>0</sub> . In the third model (model c), previous hospitalization was included. Thereafter,
210	twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e.,
211	having had a SA spell or long-term SA (>90 days) were analyzed.
212	Finally, in the step where we analyzed the association between hospitalization before and
213	after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-
214	b) from table 3. In a third model (model c), we fitted an additional model in which
215	adjustments were made for subsequent deliveries.
216	Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average 50%
217	for DZ pairs) and common environmental factors through childhood (100% for both MZ and
218	DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs).
219	An experimental design, which can control for familial influences, is to examine discordant
220	twin sisters, that is, where one twin sister has given birth and the other has not. If discordant
221	twin sisters show similar associations as the analyses of the whole cohort, this would indicate
222	that the childbirth may actually be a contributing cause of the future SA. If instead the
223	association found among the whole cohort cannot be replicated within discordant twin sisters,
224	then familial factors are of importance. Influence of familial factors (genetic and common
225	environment) is indicated if the association found in the analyses of the whole cohort
226	disappear or change considerably in the analyses of discordant twin pairs <sup>45</sup> .
227	All statistical analyses were performed with SAS 9.3 and STATA 12.1.
228	The project was approved by the Regional Ethical Review Board of Stockholm.
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#### Results

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231 Of the 5 118 women included in the study, 77% had given birth at least once between 1994 232 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 233 234 educational level distribution was rather similar when comparing those who gave birth to 235 those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were 236 excluded, 30% of the women who had given birth had at least one hospitalization during the 237 period six years prior to and six years after their first delivery (the delivery year excluded). 238 The corresponding rate for the women who had not given birth was 27%. Half of the women 239 who gave birth had at least one SA spell during the period six years prior to or the six years 240 after first delivery, when the year for childbirth was excluded. The majority of the women had 241 no SA spell at all in the six years following childbirth. 242 The average annual number of days with inpatient care and SA, respectively, is presented in 243 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 244

inpatient days increased rapidly during T<sub>0</sub> for women who gave birth, especially because of
hospitalization due to pregnancy and childbirth. After T<sub>0</sub>, the number of SA days decreased
quickly among these women. For women who gave birth, days with inpatient care and SA the

248 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).

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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<sub>0</sub>, 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<sub>0</sub> also was associated with long-term SA ( to beer texien only 

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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
- 282 have an influence on the studied association.

#### 283 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 <sup>10 20 46 47</sup>, 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 <sup>20</sup>. Several explanations have been suggested for such higher levels of SA, among others the double burden hypothesis <sup>20 48-50</sup>. 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 <sup>51-53</sup>. 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. 

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308	To our best knowledge, this is the first study to examine long-term associations between
309	childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not
310	have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to
311	subsequent pregnancy and childbirth) when compared to women who did not give birth.
312	Those who did not give birth had a more stable pattern of SA during the studied period,
313	however, with a slight increase in annual SA days over the years. This is in line with a
314	Swedish study examining whether family obligations influence the risk of SA in publicly
315	employed women and found a slight risk increase for SA among women without children <sup>54</sup> .
316	Further, a broad systematic literature review published in 2004 provided no evidence of an
317	association between having children in the household and an increased risk of SA <sup>55</sup> . It is
318	important to consider family situation when examining the association between having
319	children and morbidity, as single women with children have been shown to have worse health
320	$^{30\ 31\ 56}$ and higher levels of SA $^{6\ 54}$ .
321	Even though pregnancy, delivery, and the postpartum period may increase the risk for

disease and injury <sup>25 27</sup>, our findings do not suggest that women who gave birth are more 322 likely to be hospitalized after their first childbirth, except for hospitalizations related to 323 subsequent deliveries. We found no differences in risk for future hospitalization when 324 325 comparing those who gave birth to those who did not. Thus, giving birth does not have to be 326 associated with subsequent health problems. The fact that we found no differences in future 327 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 328 give birth may have worse health and choose not to have or cannot have a child. Also, giving 329 330 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 331 worldwide<sup>57</sup>. 332

2	333	Hospitalization prior to the first childbirth or equivalent $(T_0)$ was a risk factor for future SA
4 5	334	for all women regardless of childbirth status. In particular, women who had been hospitalized
6	004	for an women, regardless of emiddrial suitus. In particular, women who had been hospitalized
7 8	335	both before and after $T_0$ were at risk for future SA. Furthermore, we found an association
9 10	336	between hospitalization and future longer SA spells.
11 12	337	When comparing women who gave birth to those who did not, with respect to exposure to
13 14 15	338	hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had
16 17	339	slightly higher risk for future SA regardless of duration, whereas those who did not give birth
18 19	340	hospitalized after $T_0$ had higher risk for long-term SA.
20 21	341	Hospitalization both before and after the year T <sub>0</sub> seems to be the strongest indicator, i.e.,
22 23 24	342	these individuals had the highest risk for future SA. Consequently, the women who had been
24 25 26	343	hospitalized both before and after $T_0$ had the highest risk for future SA. Our analyses of
27 28	344	women who gave birth revealed a graded association between hospitalization and SA, where
29 30	345	those who only were hospitalized before or after their first childbirth had a higher risk of SA,
31 32	346	whereas those who were hospitalized both before and after the first childbirth had even higher
33 34 25	347	risks. Thus, we found a strong association between morbidity, here measured as
36 37	348	hospitalization, and future SA among women who have given birth- an association that often
38 39	349	has been question regarding women with children <sup>12</sup> .
40 41	350	Familial factors seemed to contribute to the association between hospitalization before and
42 43	351	after T <sub>0</sub> among those who did not give birth. The influence of familial factors may relate to
44 45 46	352	morbidity among women not giving birth – morbidity that might be more severe and
47 48	353	potentially also being relatively strongly influenced by genetics. Familial factors also played a
49 50	354	role in the associations between hospitalization and future long-term SA. This could be
51 52	355	related to the fact that the hospitalization usually is required for severe conditions that may
53 54 55	356	have a strong genetic component. However, since genetics have been shown to influence the
56 57 58	357	risk of DP $^{58}$ , and some indications exist that genetics also play a role in long-term SA and
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358	mortality, it can be suspected that the effects of familial factors on SA can be either direct or
359	through other influential factors.
360	
361	Strengths and limitations
362	The strengths of this study are the population-based prospective cohort study design,
363	including all in the study population, not a sample, using nationwide registers with high
364	completeness and validity <sup>40-42</sup> . Further, we used a large study cohort without loss to follow
365	up. With a twin study design, we were able to take familial influences into account. When
366	measuring both exposure and outcome with register-based data, we avoid problem with recall
367	bias.
368	This study has, however, some limitations. First of all, we do not know whether the women
369	who did not give birth were childless voluntarily or not. Differences in health between
370	voluntary and involuntary childlessness have been shown, where voluntarily childless women
371	showed higher levels of overall well-being <sup>57 59</sup> which might be related to hospitalization
372	and/or SA. Another limitation is that the terms for inpatient care have changed during the
373	studied period. In Sweden, inpatient care has to a great extent been replaced by outpatient
374	treatment. Therefore, some of the decrease in hospitalization over the years is a result of a
375	shift in the responsibility for inpatient care from hospitals to outpatient care facilities <sup>60</sup> ,
376	however, this affected all women equally, and is to some extent handled by adjusting for birth
377	year. The CIs are wider in the years far from $T_{0,}$ e.g., $T_{6,}$ due to fewer follow up year for some
378	– e.g., for those who gave birth late during the studied period.
379	It is important to be aware of that giving birth is in focus here, irrespective of whether the
380	child survived or not. Some of the women who did not give birth might be mothers, e.g., due
381	to adoption. Other studies in this area has 'being mother' or 'living with child' as exposure
382	term, rather than 'giving birth'.

383	
384	Conclusion
385	Women giving birth did not have a higher future SA risk than those not giving birth and
386	results indicate a positive health selection into giving birth. Mothers with different types of
387	morbidity, in terms of hospitalization before and/or after giving birth had higher risks for
388	future SA. Most women had no SA in the six years following childbirth and those who had
389	SA generally had that for shorter periods. Among the few women who had severe morbidity,
390	in terms of hospitalization, the future risk for SA was, as expected, higher. Hospitalization
391	prior to $T_0$ was strongly associated with later hospitalization and later SA. The high levels of
392	inpatient care in women who did not give birth suggest that there is a health selection in
393	giving birth, where the women who give birth have a better health initially. However, most
394	women had no hospitalization and no SA.

en had no hospitalization and no SA.

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

	Both dave	ly one in the pair gave birth			
Variables	birth	Twin 1 (gave birth)	Twin 2 (did not give birth)	Total	
Ν	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 T₀					
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 <sup>1</sup>					
≤ 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 <sup>2</sup>					
- At least one hospitalization during the period six years	0 404 (770()	700 (00%)	205 (200)	2 400 (00%)	
prior through six years after $I_0$ At least one herpitalization during the period six years prior	2 161 (77%)	703 (60%)	325 (28%)	3 189 (62%)	
through six years after $T_0$ (excluding hospitalizations with a					
diagnosis for pregnancy, childbirth, and the puerperium) - At least one hospitalization during the period six years	865 (31%)	315 (27%)	314 (27%)	1 494 (29%)	
prior through six years after $T_0$ (excluding hospitalizations	4 400 (400())		005 (000)		
- At least one hospitalization during the period six years	1 183 (42%)	407 (35%)	325 (28%)	1 915 (37%)	
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 after $T_{\scriptscriptstyle 0}$	483 (17%)	133 (11%)	60 (5%)	676 (13%)	
Sickness Absence (SA) <sup>3</sup>					
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 24 <u>5 (45</u> %)	382 (33%)	<u> </u>	<u>1 848 (36%</u> )	

<sup>1</sup> At time of T<sub>0</sub>

 $^2$  Excluding hospitalizations occurring during  $T_{\rm 0}$ 

<sup>3</sup> Excluding SA spells occurring during T<sub>0</sub>

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 <sup>1</sup>		
	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>2, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>3, 7</sup>
All women (n=5 118)						
No childbirth, no hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization before T <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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 T0 <sup>8</sup>	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 <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>4, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>5, 7</sup>
Women who had at least one childbirth (na	vho had at least one childbirth (n=2 792)		-			-
No hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Hospitalization before T <sub>0</sub> <sup>8</sup>	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)

<sup>1</sup> Diagnoses O00-O99

<sup>2</sup> Twin pairs where one had a hospitalization during the follow-up and the other not (n=1 016 pairs)

<sup>3</sup> Twin pairs where one had a hospitalization during the follow-up and the other not (n=456 pairs)

<sup>4</sup> Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)

<sup>5</sup> Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs) (n=2/1 pairs)

<sup>6</sup> Adjusted for birth year

<sup>7</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>8</sup> During the period 1-5 years prior to T<sub>0</sub>

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.

		SA (at lea	ast one day)			Long-term SA	\ (>90 days)	
Status childbirth and hospitalization	Model a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	Discordant twin pairs <sup>1, 7</sup>	Model a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	Discordant twin pairs <sup>2, 7</sup>
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 <sub>0</sub> <sup>8</sup>	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 a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	Discordant twin pairs <sup>3, 5</sup>	Model a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	Discordant twin pairs <sup>4, 7</sup>
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)
<ul> <li><sup>1</sup> Twin pairs where one had a SA spell during the follow-up and the other not (n=835 pairs)</li> <li><sup>2</sup> Twin pairs where one had a long-term SA spell during the follow-up and the other not (n=277 pairs)</li> <li><sup>3</sup> Twin pairs where one had a long-term SA spell during the follow-up and the other not (n=542 pairs)</li> <li><sup>4</sup> Twin pairs where one had a long-term SA spell during the follow-up and the other not (n=184 pairs)</li> <li><sup>5</sup> Adjusted for birth year</li> <li><sup>6</sup> Model a, and additional adjustments for delivery year, and educational level</li> <li><sup>7</sup> Model b, and additional adjustments for earlier hospitalization</li> </ul>								
<sup>8</sup> Diamana 000 000 and dad								

<sup>8</sup> 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)			) days)			
	Model a <sup>3</sup>	Model b⁴	Model c⁵	Discordant twin pairs <sup>1, 4</sup>	Model a <sup>3</sup>	Model b⁴	Model c⁵	Discordant twin pairs <sup>2, 4</sup>
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)

<sup>1</sup> Twin pairs where one had an SA spell during the follow-up and the other not (n=542)

<sup>2</sup> Twin pairs where one had a long-term SA spell during the follow-up and the other not (n=184)

<sup>3</sup> Adjusted for birth year

<sup>4</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>5</sup> Model b, and additional adjustments for subsequent deliveries

 $^{6}$  During the period 1-5 years prior to T<sub>0</sub>

<sup>7</sup> Diagnoses O00-O99 excluded

# **BMJ Open**

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

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25 26	Abstract Objective: To investigate associations of giving birth with morbidity in terms of
27	hospitalization and social consequences of morbidity in terms of sickness absence (SA), while
28	taking familial (genetics and shared environmental) factors into account.
29	Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA
30	were calculated as hazard ratios (HR) with 95% confidence intervals (CI).
31	Setting: All female twins, i.e., women with twin sister, born in Sweden.
32	Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where
33	at least one in the twin pair had their first childbirth ( $T_0$ ) 1994-2009 and none gave birth
34	before 1994.
35	Main outcome measures: Hospitalization and SA during year 3-5 after first delivery or
36	equivalent.
37	Results: Preceding the first childbirth, the mean annual number of SA days increased for
38	mothers, and then decreased again. Hospitalization after $T_0$ was associated with higher HRs of
39	short-term and long-term SA (HR for short-term SA: 3.0; 95% CI 2.5-3.6 and for long-term
40	SA: 2.3; 95% CI 1.6-3.2). Hospitalization both before and after first childbirth was associated
41	with a higher risk of future SA (HR for long-term SA: 4.2; 95% CI 2.7-6.4). Familial factors
42	influenced the association between hospitalization and long-term SA, regardless of childbirth
43	status.
44	Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth
45	and results indicate a positive health selection into giving birth. Mothers hospitalized before
46	and/or after giving birth had higher risks for future SA, that is, there was a strong association
47	between morbidity and future SA.
48	Keywords: sick leave, childbirth, inpatient care, hospitalization, cohort study, population
49	based, twins
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### 51 Article Summary

## 52 Article focus:

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

### 56 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
- 59 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

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# 62 Strengths and limitations:

- The strengths of the study include the population-based prospective design, using
   national registers with high completeness and validity
- 65 With a twin study design, we were able to take familial influences into account
- 66 As inpatient care to a great extent has been replaced by outpatient treatment, some of
- 67 the decrease in hospitalization over the years is a result of a shift in the responsibility
- 68 for inpatient care from hospitals to outpatient care facilities
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71 72	<b>Introduction</b> In most countries with high labor force participation, women have higher levels of sickness
73	absence (SA) than men <sup>1-4</sup> . Many theories and mechanism regarding this have been suggested,
74	e.g., women having higher morbidity, higher workload (when combining paid and unpaid
75	work), tougher situation on the labor market, men being the norm for how the labor market is
76	organized, gender bias in healthcare and social insurance systems, discrimination, and
77	domestic violence, etcetera <sup>5-9</sup> . Another hypothesis behind this gender difference in SA
78	focuses on SA during pregnancy and after childbirth <sup>6 10-13</sup> . Several studies show that women
79	have higher SA during pregnancy <sup>10 14</sup> and that pregnancy-related SA explains half of the
80	gender differences in SA in fertile ages <sup>15</sup> .
81	One of the changes in society that may affect health after childbirth is that the mean age for
82	having the first child has increased over the last years and that women with higher level of
83	morbidity now give birth. Further, nowadays, the proportion of caesarean sections has
84	increased as well as vacuum extraction deliveries, leading to risk of later health problems <sup>16 17</sup> .
85	In this study, focus is on childbirth, morbidity, and SA among women, to get a better
86	understanding of mechanisms behind SA among women in fertile ages. There are hardly any
87	studies on the associations between giving birth and morbidity and SA, and those conducted
88	have focused on a relatively short time period right after childbirth, most often within the first
89	year following the child delivery <sup>18 19</sup> , while prospective studies with longer follow-up of
90	mothers are rare <sup>6</sup> <sup>12</sup> <sup>20</sup> .
91	Pregnancy, delivery, and the postpartum period may imply large physical, mental, and
92	social changes during a short period of time, increasing the risk for disease and injury <sup>21 22</sup> .
93	Different types of physical and mental disorders are common during pregnancy and after

hardly studied at all <sup>19</sup>. Giving birth may be associated with a higher risk of certain diseases

childbirth - and can in some cases be longstanding or even permanent - however, this is

96 demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental

5

97	disorders, and different types of injuries <sup>23-26</sup> . For women with a disease present before the
98	childbirth, the disorder might deteriorate after childbirth <sup>23 24</sup> . Regarding symptoms related to
99	childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain,
100	fatigue, headache, and sleep disorders <sup>19 27</sup> . Most of these symptoms seem to remain up to one
101	year after childbirth <sup>17</sup> . Besides physical health effects, also depression and other mental
102	disorders have been linked to childbirth <sup>26 28</sup> , but again, prospective studies with longer
103	follow-up are lacking <sup>27</sup> . Even though having children has been shown to contribute to an
104	overall wellbeing, this is not the case for everybody and especially not among single mothers
105	whose economic situation and thereby possibilities for good health care might be worse <sup>29-31</sup> .
106	Morbidity can be measured in different ways, e.g., through self-reports and visits to
107	healthcare. Here we will use data on more severe morbidity that involves assessments from
108	physicians, that is, morbidity that has led to hospitalization, a measure so far not used in this
109	type of studies. Sickness absence is not a good measure of morbidity- most people with
110	morbidity are not on SA <sup>4</sup> . Instead SA is considered a very good measure of social
111	consequences of morbidity, in terms of not being able to support yourself from work <sup>4</sup> . Yet,
112	there are surprisingly few studies on the association between morbidity and SA and in media
113	sometimes even the level of morbidity among sickness absentees even is questioned.
114	Studies examining the role of familial factors (i.e. genetic and shared (mainly childhood)
115	environment) on morbidity have shown that genetics tends to explain a moderate to large
116	extent of the variability in most of the chronic diseases <sup>32 33</sup> . For example, heritability for
117	mental disorders varies between 30-90% <sup>34</sup> , whereas genetic factors have been shown to
118	explain 30-60% of the total variation in musculoskeletal disorders <sup>35 36</sup> . Taken together,
119	familial factors are important to account for when studying the association between morbidity
120	(here in terms of hospitalization) and SA as studies otherwise could lead to erroneous
121	conclusions. Twin settings provide a powerful tool for studies of these aspects in research of

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122	SA, a research area where different selection biases otherwise might have an impact on
123	results. Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average
124	50% for DZ pairs) and common environmental factors through childhood (100% for both MZ
125	and DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs).
126	An experimental design, which can control for these familial influences, is to examine
127	discordant twin sisters, that is, where one twin sister has given birth and the other has not. If
128	discordant twin sisters show similar associations as the analyses of the whole cohort, this
129	would indicate that the childbirth may actually be a contributing cause of the future SA. If
130	instead the association found among the whole cohort cannot be replicated within discordant
131	twin sisters, then familial factors are of importance. Influence of familial factors (genetic and
132	common environment) is indicated if the association found in the analyses of the whole cohort
133	disappear or change considerably in the analyses of discordant twin pairs <sup>37</sup> .
404	

135 The aim of the study was to investigate the associations of giving birth with subsequent

136 morbidity in terms of hospitalization and SA. Familial factors (genetics and shared/early

137 environmental) were taken into account in order to assess if familial factors explain a

138 potential association between childbirth and future hospitalization and SA.

# 140 Methods

# 141 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)<sup>38</sup>. 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 <sup>38 39</sup>. The selection of the study population is illustrated in Figure 1.

The unique personal identity number assigned to each Swedish resident <sup>40</sup> 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 <sup>41</sup>. 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 <sup>42</sup>. 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 <sup>43</sup>. 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., 

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	166	inpatient care. Annual information on educational level and on SA days was obtained from
	167	Statistics Sweden.
	168	
	169	Time in relation to childbirth
	170	The studied women were followed in relation to year of first childbirth, referred to as T <sub>0</sub> . In
	171	order to compare those who gave birth to those who did not, $T_0$ for the women who did not
	172	give birth was defined as year of her twin sister's first childbirth.
	173	
	174	Hospitalization
	175	Data on hospitalization covered the period six years prior to, and six years after year of first
	176	childbirth $(T_0)$ or equivalent. For descriptive purposes, the total and the average number of
	177	hospitalization days per year were calculated.
	178	In order to examine if hospitalization prior to (or after) childbirth increases the risk for future
	179	hospitalization, the first part of the regression analyses considered hospitalization as both
	180	exposure and outcome. We created one dichotomous variable for hospitalization before $T_0$
	181	(i.e., exposure), and two dichotomous outcome variables for hospitalization during year 3-5
	182	after T <sub>0</sub> : one for hospitalization with any diagnosis and one excluding hospitalization with
	183	diagnoses related to pregnancy, childbirth, and the postpartum period.
	184	In order to answer the research question "Does hospitalization prior to (or after) childbirth
	185	increase the risk for future SA?", we created two dichotomous hospitalization exposure
	186	variables: one for hospitalization before $T_0$ and one variable: hospitalization year 1-2 after $T_0$
	187	(excluding diagnoses related to pregnancy, childbirth, and the postpartum period).
	188	
	189	Sickness absence
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SA can be measured in several ways, related to duration and incidence <sup>44</sup>. 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  $T_0$ .

194 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 sickleave 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.

- 205 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)  $^{4546}$ , we adjusted for educational level at T<sub>0</sub>. Years of education was classified into four categories; <9 years of compulsory school, 10-12 years of education (senior high school),  $\geq$ 13years of education (college/university), missing.

- - 211 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<sub>0</sub>). In a first model (model a), adjustments were made for age. Second

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215	(model b), additional adjustments were made for delivery year and educational level at time of
216	T <sub>0</sub> . Thereafter, twin pairs who were discordant with respect to outcomes, i.e., having at least
217	one hospitalization after T <sub>0</sub> , were analyzed using Conditional Cox regression. In the next step,
218	we analyzed the associations between childbirth, hospitalization, and SA by fitting three Cox
219	regression models (table 3). The first (model a) was adjusted for birth year. In the second
220	model (model b), additional adjustments were made for delivery year and educational level at
221	time of T <sub>0</sub> . In the third model (model c), previous hospitalization was included. Thereafter,
222	twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e.,
223	having had SA or long-term SA (>90 days) were analyzed.
224	Finally, in the step where we analyzed the association between hospitalization before and
225	after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-
226	b) from table 3. In a third model (model c), we fitted an additional model in which
227	adjustments were made for subsequent deliveries.
228	The proportional hazards assumption was checked by including time-dependent versions of
229	all the covariates in the models. This did not indicate a violation of the proportionality
230	assumption.
231	All statistical analyses were performed with SAS 9.3 and STATA 12.1.
232	The STROBE checklist was used in designing and reporting the study.
233	The project was approved by the Regional Ethical Review Board of Stockholm.

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## Results

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235 Of the 5 118 women included in the study, 77% had given birth at least once between 1994 236 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 237 238 educational level distribution was rather similar when comparing those who gave birth to 239 those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were 240 excluded, 30% of the women, i.e., the 1 183 where both in a pair gave birth and the 407 twins 241 where only one in the pair gave birth had at least one hospitalization during the period six 242 years prior to and six years after their first delivery (the delivery year excluded). The 243 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 244 245 first delivery, when the year for childbirth was excluded. The majority of the women had no 246 SA at all in the six years following childbirth.

247 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 248 hospitalization days and SA days compared to those who gave birth. Women who gave birth 249 250 had approximately 0.3 hospitalization days per year whereas those who did not give birth had 251 around 0.5 hospitalization days per year. The average number of SA days for women giving 252 birth was 3.8 days/year and for those not giving birth 5.0 days/year. SA differences between 253 those giving birth and women not giving birth were statistically significant with the exception 254 of year (-4) and (-3). For inpatient care, the differences between those giving birth and women 255 not giving birth were not statistically significant. The average number of inpatient days 256 increased rapidly during  $T_0$  for women who gave birth, especially because of hospitalization 257 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 258 259 T<sub>0</sub> were to a large extent associated with subsequent childbirths.

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260	Table 2 presents HR for the association between childbirth and hospitalization, for all
261	diagnoses and for diagnoses where those related to pregnancy, childbirth, and the postpartum
262	period were excluded. When these diagnoses were removed, women who did not give birth
263	and who had been hospitalized at least once before $T_0$ had twice the risk of future
264	hospitalization compared to those not hospitalized prior to $T_0$ (HR: 2.3; 95% CI 1.6-3.3) after
265	adjustments for birth year, delivery year, and educational level. The association was explained
266	by familial factors in the analysis of discordant twin pairs (HR: 1.2; 0.8-1.9).
267	When restricting the analyses to women who gave birth, a total of 2 792 women were
268	studied, i.e., 1 396 complete pairs in which both twins had given birth. The reference group
269	constituted of mothers who had not been hospitalized prior to their first childbirth. Mothers
270	who had been hospitalized before their first childbirth had a slightly higher HR for future
271	hospitalization when diagnoses related to pregnancy and childbirth were excluded (HR 1.5;
272	1.2-2.0). This association disappeared in the analyses of discordant twin pairs, suggesting an
273	influence of familial factors (HR: 1.0; 0.8-1.3).
274	Regardless of childbirth status, hospitalization year 1-2 after $T_0$ was a predictor of having a
275	new SA in year 3-5 after $T_0$ (Table 3). Compared to women who did not give birth and who
276	were not hospitalized the first two years after T <sub>0</sub> , mothers hospitalized after first childbirth
277	had an HR of 2.4 (2.0-2.9) for a new SA after adjustments for birth year, delivery year, and
278	educational level. Hospitalization after $T_0$ was also associated with a new long-term SA (>90
279	days) in year 3-5 after $T_0$ (Table 3). Women who did not give birth had a nearly three-fold
280	risk of a new long-term SA year 3-5 after $T_0$ (HR 2.8; 1.5-5.1), whereas women who gave
281	birth had an HR of 1.8 (1.3-2.5). The analyses of twin pairs discordant for having a new long-
282	term SA year 3-5 after $T_0$ , showed attenuated point estimates, hence suggesting that familial
283	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<sub>0</sub> (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 <text> 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.

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#### Discussion 292

293 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 294 295 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 296 297 much for mothers, an increase that gradually decreased during the years after the delivery. We 298 found hospitalization prior to  $T_0$  to be a risk factor for future hospitalization, regardless of 299 childbirth status, also when excluding hospitalization due to childbirth. Furthermore, 300 hospitalization after the first childbirth was associated with a higher HR of both short-term 301 and long-term future SA. An additional analysis focusing solely on the women who gave birth 302 showed that hospitalization both before and after the first childbirth was associated with a 303 higher risk of future SA. Familial factors seemed to have an influence on the association 304 between hospitalization and long-term SA, regardless of childbirth status. In line with some previous studies <sup>10 20 48 49</sup>, we found that SA increased in women during 305 306 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 307 308 be due to subsequent pregnancies. A recent Norwegian study found that the increased SA risk 309 in women in the years after pregnancy disappeared when SA during subsequent pregnancies were accounted for <sup>20</sup>. Several explanations have been suggested for such higher levels of SA, 310 among others the double burden hypothesis <sup>20 50-52</sup>. This hypothesis has been questioned, as 311 312 research has indeed shown that women who occupy multiple roles tend to be healthier than those who enact fewer roles <sup>53-55</sup>. Thus, the combination of employment and parenthood does 313 314 not seem to imply worse health, on the contrary. In our study, the annual rates of SA 315 decreased steadily after the first childbirth, speaking in favor of this hypothesis. Further studies of this are warranted. 316

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317	To our best knowledge, this is the first study to examine long-term associations between
318	childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not
319	have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to
320	subsequent pregnancy and childbirth) when compared to women who did not give birth.
321	Those who did not give birth had a more stable pattern of SA during the studied period,
322	however, with a slight increase in annual SA days over the years. This is in line with a
323	Swedish study examining whether family obligations influence the risk of SA in publicly
324	employed women and found a slight risk increase for SA among women without children <sup>56</sup> .
325	Further, a broad systematic literature review published in 2004 provided no evidence of an
326	association between having children in the household and an increased risk of SA <sup>57</sup> . It is
327	important to consider family situation when examining the association between having
328	children and morbidity, as single women with children have been shown to have worse health
329	<sup>30 31 58</sup> and higher levels of SA <sup>6 56</sup> .
330	Even though pregnancy, delivery, and the postpartum period may increase the risk for
331	disease and injury <sup>25 27</sup> , our findings do not suggest that women who gave birth are more
332	likely to be hospitalized after their first childbirth, except for hospitalizations related to
333	subsequent deliveries. We found no differences in risk for future hospitalization when
334	comparing those who gave birth to those who did not. Thus, giving birth does not have to be
335	associated with subsequent health problems. The fact that we found no differences in future
336	hospitalization between those who gave birth and those who did not, may have different
337	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<sup>16 19 22</sup>. Further, during the
last decades, the number of women who voluntarily do not want to become parents has
increased worldwide<sup>59</sup>.

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2 3	342	Hospitalization prior to the first childbirth or equivalent $(T_0)$ was a risk factor for future SA
4 5 6	343	for all women, regardless of childbirth status. In particular, women who had been hospitalized
7 8	344	both before and after T <sub>0</sub> were at risk for future SA. Furthermore, we found an association
9 10	345	between hospitalization and future long-term SA.
11 12	346	When comparing women who gave birth to those who did not, with respect to exposure to
13 14 15	347	hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had
15 16 17	348	slightly higher risk for future SA regardless of duration, whereas those who did not give birth
18 19	349	hospitalized after $T_0$ had higher risk for long-term SA.
20 21	350	Hospitalization both before and after the year T <sub>0</sub> seems to be the strongest indicator, i.e.,
22 23	351	these individuals had the highest risk for future SA. Consequently, the women who had been
24 25 26	352	hospitalized both before and after $T_0$ had the highest risk for future SA. Our analyses of
27 28	353	women who gave birth revealed a graded association between hospitalization and SA, where
29 30	354	those who only were hospitalized before or after their first childbirth had a higher risk of SA,
31 32	355	whereas those who were hospitalized both before and after the first childbirth had even higher
33 34 35	356	risks. Thus, we found a strong association between morbidity, here measured as
36 37	357	hospitalization, and future SA among women who have given birth – an association that often
38 39	358	has been question regarding women with children <sup>12</sup> .
40 41	359	Familial factors seemed to contribute to the association between hospitalization before and
42 43	360	after T <sub>0</sub> among those who did not give birth. The influence of familial factors may relate to
44 45 46	361	morbidity among women not giving birth – morbidity that might be more severe and
47 48	362	potentially also being relatively strongly influenced by genetics. Familial factors also played a
49 50	363	role in the associations between hospitalization and future long-term SA. This could be
51 52	364	related to the fact that the hospitalization usually is required for severe conditions that may
53 54 55	365	have a strong genetic component. However, since genetics have been shown to influence the
55 56 57 58 59 60	366	risk of DP $^{60}$ , and some indications exist that genetics also play a role in long-term SA and 17

367 mortality, it can be suspected that the effects of familial factors on SA can be either direct or368 through other influential factors.

# 370 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 <sup>41-43</sup>. 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 <sup>59 61</sup> 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 <sup>62</sup>, 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<sub>0</sub>, e.g., T<sub>6</sub>, due to fewer follow up year for some – e.g., for those who gave birth late during the studied period. Also, 

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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'.

#### 401 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.

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413	Ethical approval
414	The study was approved by the Regional Ethical Review Board, Stockholm, Sweden
415	(2007/524-31).
416 417	Contributorship Statement
418	KA and PS originated the idea. EB analysed the data in consultation with KA, LK, JN, AR,
419	and PS. EB wrote the first and subsequent drafts of the manuscript, with important intellectual
420	input from all the co-authors. All authors contributed in designing the study and to the
421	interpretation of the results and to the writing and approval of the final article.
422	
423	Competing interest statement
424	We declare that no competing interests exist.
425	
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431	Registry is supported by the Swedish Research Council, the Ministry for Higher Education,
432	and AstraZeneca. Funding sources had no involvement in this study.
433	
434	Data sharing
435	No additional data available.
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	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2 3	440	Figure legends
4 5 6	441	Figure 1. Flow chart for the study population.
7	442	Figure 2 Average annual number of days on sickness absence (SA) and hospitalization
8	1/13	respectively (with 95% CI) six years prior through six year after T <sub>2</sub> for women who gave
9	440	high (did not size high (n=5.110)
10	444	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.

	Both dave	Twin pairs where or		
Variables	birth	Twin 1 (gave birth)	Twin 2 (did not give birth)	Total
Ν	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 T₀				
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 <sup>1</sup>				
≤ 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 <sup>2</sup> - 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 <sub>0</sub> (excluding hospitalizations with a diagnosis for pregnancy, childbirth, and the puerperium) - At least one hospitalization during the period six years after T <sub>0</sub> (available)	865 (31%)	315 (27%)	314 (27%)	1 494 (29%)
with a diagnosis for pregnancy, and childbirth) - At least one hospitalization during the period six years	1 183 (42%)	407 (35%)	325 (28%)	1 915 (37%)
- At least one hospitalization during the period six years	679 (24%)	251 (22%)	217 (19%)	1 147 (22%)
after $T_0$	1 965 (70%)	585 (50%)	168 (14%)	2 718 (53%)
- At least one hospitalization both before and after $T_{0}$	483 (17%)	133 (11%)	60 (5%)	676 (13%)
Sickness Absence (SA) <sup>3</sup> 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%)	<u>221 (19%)</u>	1 848 (36%)

<sup>1</sup> At time of T<sub>0</sub>

 $^2$  Excluding hospitalizations occurring during  $T_{\rm 0}$ 

<sup>3</sup> Excluding SA occurring during T<sub>0</sub>

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Table 2. Cox proportional hazard ratios (HR) with 95% CI for the association between childbirth, hospitalization before T<sub>0</sub>, and subsequent hospitalization (i.e., during year 3-5 after T<sub>0</sub>) 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	i	Diagnoses related to pregnancy, childbirth and the puerperium excluded <sup>1</sup>			
	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>2, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>3, 7</sup>	
All women (n=5 118)							
No childbirth, no hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
No childbirth, hospitalization before T <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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 <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>4, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>5, 7</sup>	
Women who had at least one childbirth (na	=2 792)						
No hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
Hospitalization before T <sub>0</sub> <sup>8</sup>	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)	

<sup>1</sup> Diagnoses O00-O99

 $^{2}$  Twin pairs where one had a hospitalization during the follow-up and the other not (n=1 016 pairs)

<sup>3</sup> Twin pairs where one had a hospitalization during the follow-up and the other not (n=456 pairs)

<sup>4</sup> Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)

<sup>5</sup> Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs)

<sup>6</sup> Adjusted for birth year

<sup>7</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>8</sup> During the period 1-5 years prior to T<sub>0</sub>

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<sub>0</sub>, 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.

	SA in year	3-5 after T <sub>0</sub> (re	gardless of nui	nber of days)	Long-ter	'm SA (>90 day	vs) in year 3-5	after T <sub>0</sub>
Status childbirth and hospitalization	Madal a <sup>5</sup>		Madal a <sup>7</sup>	Discordant twin	Madal a <sup>5</sup>		Madal a7	Discordant
	Model a	Model p	Model C	pairs	Model a*	Model b	Model C	twin pairs"
All women (n=5 118)								
No childbirth, no hospitalization year 1-2 after T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization year 1-2 after T <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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				Discordant twin				Discordant
(n=2 792)	Model a <sup>5</sup>	Model b <sup>6</sup>	Model c <sup>7</sup>	pairs <sup>3, 5</sup>	Model a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	twin pairs <sup>4, 7</sup>
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 <mark>-1.5)</mark>	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)
<sup>1</sup> Twin pairs where one had a SA during the follow-up and the o	other not (n=835 pai	rs)						
<sup>2</sup> Twin pairs where one had a long-term SA during the follow-u	p and the other not (	(n=277 pairs)						
<sup>3</sup> Twin pairs where one had a SA during the follow-up and the o	other not (n=542 pai	rs)						
<sup>4</sup> Twin pairs where one had a long-term SA during the follow-u	p and the other not (	(n=184 pairs)						
<sup>5</sup> Adjusted for birth year								
<sup>6</sup> Model a, and additional adjustments for delivery year, and edu	icational level							
<sup>4</sup> Model b, and additional adjustments for earlier hospitalization								
° Diagnoses O00-O99 excluded								
Table 4 Cox proportional HR with 95% CI for	the association	hetween hos	nitalization be	ore and after first	childbirth and	new sickness	absence (SA	) in vear
3-5 after T <sub>0</sub> , in twins who had their first childbird	th 1994-2009 (	n=2 792). Thre	e models for a	adjustments as we	ell as for discor	dant twin pairs	S.	in year
Status hospitalization before and after childbird	:h	SA	in year 3-5 af of numbe	ter T₀ (regardless r of days)		Long-term S	A (>90 days) i after T₀	n year 3-5

Status hospitalization before and after childbirth		of number of days)					after T <sub>0</sub>	
	Model a <sup>3</sup>	Model b <sup>4</sup>	Model c⁵	Discordant twin pairs <sup>1, 4</sup>	Model a <sup>3</sup>	Model b⁴	Model c⁵	Discordant twin pairs <sup>2, 4</sup>
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)

<sup>1</sup> Twin pairs where one had an SA during the follow-up and the other not (n=542)

<sup>2</sup> Twin pairs where one had a long-term SA during the follow-up and the other not (n=184)

<sup>3</sup> Adjusted for birth year

<sup>4</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>5</sup> Model b, and additional adjustments for subsequent deliveries

 $^{6}$  During the period 1-5 years prior to T<sub>0</sub>

<sup>7</sup> Diagnoses O00-O99 excluded









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STROBE Statement	—Chec	klist of items that should be included in reports of <i>cohort studies</i>
	Item	Decommondation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the
The and abstract	1	Page 1
		(b) Provide in the abstract an informative and balanced summary of what wa
		and what was found
		Page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being re
		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 recruit
		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
<b>X</b> 7 <sup>1</sup> 11	7	
Variables	1	Clearly define all outcomes, exposures, predictors, potential confounders, and
		modifiers. Give diagnostic criteria, il applicable
Data sources/	Q*	Fage 0-9
measurement	0	assessment (measurement). Describe comparability of assessment methods if
measurement		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 applicabl
		describe which groupings were chosen and why
		Page 8-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confo
		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
		( <u>e</u> ) 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
C		applicable, for the original study on which the present article is based
		Page 18
Limitations Interpretation Generalisability Other information Funding	19       20       21       22	Page 2 and page 13         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       Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence         Page 13 – 15       Discuss the generalisability (external validity) of the study results         Page 13-16       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.

# **BMJ Open**

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

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Secondary Subject Heading:	Epidemiology, Obstetrics and gynaecology
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, childbirth, sick leave, childbirth, hospitalization

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	BMJ Open
25 26	Abstract Objective: To investigate associations of giving birth with morbidity in terms of
27	hospitalization and social consequences of morbidity in terms of sickness absence (SA), while
28	taking familial (genetics and shared environmental) factors into account.
29	Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA
30	were calculated as hazard ratios (HR) with 95% confidence intervals (CI).
31	Setting: All female twins, i.e., women with twin sister, born in Sweden.
32	Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where
33	at least one in the twin pair had their first childbirth $(T_0)$ 1994-2009 and none gave birth
34	before 1994.
35	Main outcome measures: Hospitalization and SA during year 3-5 after first delivery or
36	equivalent.
37	Results: Preceding the first childbirth, the mean annual number of SA days increased for
38	mothers, and then decreased again. Hospitalization after T <sub>0</sub> was associated with higher HRs of
39	short-term and long-term SA (HR for short-term SA: 3.0; 95% CI 2.5-3.6 and for long-term
40	SA: 2.3; 95% CI 1.6-3.2). Hospitalization both before and after first childbirth was associated
41	with a higher risk of future SA (HR for long-term SA: 4.2; 95% CI 2.7-6.4). Familial factors
42	influenced the association between hospitalization and long-term SA, regardless of childbirth
43	status.
44	Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth
45	and results indicate a positive health selection into giving birth. Mothers hospitalized before
46	and/or after giving birth had higher risks for future SA, that is, there was a strong association
47	between morbidity and future SA.
48	Keywords: sick leave, childbirth, inpatient care, hospitalization, cohort study, population
49	based, twins
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# 51 Article Summary

# 52 Article focus:

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

# 56 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
- 59 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

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# 62 Strengths and limitations:

- The strengths of the study include the population-based prospective design, using
   national registers with high completeness and validity
- 65 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
- 67 the decrease in hospitalization over the years is a result of a shift in the responsibility
- 68 for inpatient care from hospitals to outpatient care facilities

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71	Introduction
72	In most countries with high labor force participation, women have higher levels of sickness
73	absence (SA) than men <sup>1-4</sup> . Many theories and mechanism regarding this have been suggested,
74	e.g., women having higher morbidity, higher workload (when combining paid and unpaid
75	work), tougher situation on the labor market, men being the norm for how the labor market is
76	organized, gender bias in healthcare and social insurance systems, discrimination, and
77	domestic violence, etcetera <sup>5-9</sup> . Another hypothesis behind this gender difference in SA
78	focuses on SA during pregnancy and after childbirth <sup>6 10-13</sup> . Several studies show that women
79	have higher SA during pregnancy <sup>10 14</sup> and that pregnancy-related SA explains half of the
80	gender differences in SA in fertile ages <sup>15</sup> .
81	One of the changes in society that may affect health after childbirth is that the mean age for
82	having the first child has increased over the last years and that women with higher level of
83	morbidity now give birth. Further, nowadays, the proportion of caesarean sections has
84	increased as well as vacuum extraction deliveries, leading to risk of later health problems <sup>16 17</sup> .
85	In this study, focus is on childbirth, morbidity, and SA among women, to get a better
86	understanding of mechanisms behind SA among women in fertile ages. There are hardly any
87	studies on the associations between giving birth and morbidity and SA, and those conducted
88	have focused on a relatively short time period right after childbirth, most often within the first
89	year following the child delivery <sup>18 19</sup> , while prospective studies with longer follow-up of
90	mothers are rare <sup>6</sup> <sup>12</sup> <sup>20</sup> .
01	Programmy delivery and the negther turn period may imply large physical mental and

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 <sup>21 22</sup>.
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 <sup>19</sup>. Giving birth may be associated with a higher risk of certain diseases
demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental

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97	disorders, and different types of injuries <sup>23-26</sup> . For women with a disease present before the
98	childbirth, the disorder might deteriorate after childbirth <sup>23 24</sup> . Regarding symptoms related to
99	childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain,
100	fatigue, headache, and sleep disorders <sup>19 27</sup> . Most of these symptoms seem to remain up to one
101	year after childbirth <sup>17</sup> . Besides physical health effects, also depression and other mental
102	disorders have been linked to childbirth <sup>26 28</sup> , but again, prospective studies with longer
103	follow-up are lacking <sup>27</sup> . Even though having children has been shown to contribute to an
104	overall wellbeing, this is not the case for everybody and especially not among single mothers
105	whose economic situation and thereby possibilities for good health care might be worse <sup>29-31</sup> .
106	Morbidity can be measured in different ways, e.g., through self-reports or visits to
107	healthcare. Here we will use data on more severe morbidity that involves assessments from
108	physicians, that is, morbidity that has led to hospitalization, a measure so far not used in this
109	type of studies. Sickness absence is not a good measure of morbidity- most people with
110	morbidity are not on SA <sup>4</sup> . Instead SA is considered a very good measure of social
111	consequences of morbidity, in terms of not being able to support yourself from work <sup>4</sup> . Yet,
112	there are surprisingly few studies on the association between morbidity and SA and in media
113	and among some researchers sometimes the level of morbidity among sickness absentees even
114	is questioned, especially for female sickness absentees – their sickness absence is rather
115	considered related to attitudes than to morbidity <sup>12 32 33</sup> .
116	Studies examining the role of familial factors (i.e., genetic and shared (mainly childhood)
117	environment) on morbidity have shown that genetics tends to explain a moderate to large
118	extent of the variability in most of the chronic diseases <sup>34 35</sup> . For example, heritability for
119	mental disorders varies between 30-90% <sup>36</sup> , whereas genetic factors have been shown to
120	explain 30-60% of the total variation in musculoskeletal disorders <sup>37 38</sup> . Taken together,
121	familial factors are important to account for when studying the association between morbidity

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122	(here in terms of hospitalization) and SA as studies otherwise could lead to erroneous
123	conclusions. Twin settings provide a powerful tool for studies of these aspects in research of
124	SA, a research area where different selection biases otherwise might have an impact on
125	results. Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average
126	50% for DZ pairs) and common environmental factors through childhood (100% for both MZ
127	and DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs).
128	An experimental design, which can control for these familial influences, is to examine
129	discordant twin sisters, that is, where one twin sister has given birth and the other has not. If
130	discordant twin sisters show similar associations as the analyses of the whole cohort, this
131	would indicate that the childbirth may actually be a contributing cause of the future SA. If
132	instead the association found among the whole cohort cannot be replicated within discordant
133	twin sisters, then familial factors are of importance. Influence of familial factors (genetic and
134	common environment) is indicated if the association found in the analyses of the whole cohort
135	disappear or change considerably in the analyses of discordant twin pairs <sup>39</sup> .
136	
137	The aim of the study was to investigate the associations of giving birth with subsequent
138	morbidity in terms of hospitalization and SA. Familial factors (genetics and shared/early

139 environmental) were taken into account in order to assess if familial factors explain a

140 potential association between childbirth and future hospitalization and SA.

# 142 Methods

# 143 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)<sup>40</sup>. 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 <sup>40 41</sup>. 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 <sup>43</sup>. 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<sup>44</sup>. 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 <sup>45</sup>. 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.,
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	168	inpatient care. Annual information on educational level and on SA days was obtained from
	169	Statistics Sweden.
	170	
	171	Time in relation to childbirth
	172	The studied women were followed in relation to year of first childbirth, referred to as $T_0$ . In
	173	order to compare those who gave birth to those who did not, $T_0$ for the women who did not
	174	give birth was defined as year of her twin sister's first childbirth.
	175	
	176	Hospitalization
	177	Data on hospitalization covered the period six years prior to, and six years after year of first
	178	childbirth $(T_0)$ or equivalent. For descriptive purposes, the total and the average number of
	179	hospitalization days per year were calculated.
	180	In order to examine if hospitalization prior to (or after) childbirth increases the risk for future
	181	hospitalization, the first part of the regression analyses considered hospitalization as both
	182	exposure and outcome. We created one dichotomous variable for hospitalization before $T_0$
	183	(i.e., exposure), and two dichotomous outcome variables for hospitalization during year 3-5
	184	after T <sub>0</sub> : one for hospitalization with any diagnosis and one excluding hospitalization with
	185	diagnoses related to pregnancy, childbirth, and the postpartum period.
	186	In order to answer the research question "Does hospitalization prior to (or after) childbirth
	187	increase the risk for future SA?", we created two dichotomous hospitalization exposure
	188	variables: one for hospitalization before $T_0$ and one variable: hospitalization year 1-2 after $T_0$
	189	(excluding diagnoses related to pregnancy, childbirth, and the postpartum period).
	190	
	191	Sickness absence

SA can be measured in several ways, related to duration and incidence <sup>46</sup>. 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  $T_0$ .

196 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.

- 207 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)  $^{4748}$ , we adjusted for educational level at T<sub>0</sub>. Years of education was classified into four categories; <9 years of compulsory school, 10-12 years of education (senior high school),  $\geq$ 13years of education (college/university), missing.

213 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<sub>0</sub>). In a first model (model a), adjustments were made for age. Second

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2	17	(model b), additional adjustments were made for delivery year and educational level at time of
2	18	T <sub>0</sub> . Thereafter, twin pairs who were discordant with respect to outcomes, i.e., having at least
2	19	one hospitalization after $T_0$ , were analyzed using Conditional Cox regression. In the next step,
2	20	we analyzed the associations between childbirth, hospitalization, and SA by fitting three Cox
2	21	regression models (table 3). The first (model a) was adjusted for birth year. In the second
2	22	model (model b), additional adjustments were made for delivery year and educational level at
2	23	time of T <sub>0</sub> . In the third model (model c), previous hospitalization was included. Thereafter,
2	24	twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e.,
2	25	having had SA or long-term SA (>90 days) were analyzed.
2	26	Finally, in the step where we analyzed the association between hospitalization before and
2	27	after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-
2	28	b) from table 3. In a third model (model c), we fitted an additional model in which
2	29	adjustments were made for subsequent deliveries.
2	30	The proportional hazards assumption was checked by including time-dependent versions of
2	31	all the covariates in the models. This did not indicate a violation of the proportionality
2	32	assumption.
2	33	All statistical analyses were performed with SAS 9.3 and STATA 12.1.
2	34	The STROBE checklist was used in designing and reporting the study.
2	35	The project was approved by the Regional Ethical Review Board of Stockholm.

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#### Results

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237 Of the 5 118 women included in the study, 77% had given birth at least once between 1994 238 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 239 240 educational level distribution was rather similar when comparing those who gave birth to 241 those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were 242 excluded, 30% of the women, i.e., the 1 183 where both in a pair gave birth and the 407 twins 243 where only one in the pair gave birth had at least one hospitalization during the period six 244 years prior to and six years after their first delivery (the delivery year excluded). The 245 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 246 247 first delivery, when the year for childbirth was excluded. The majority of the women had no 248 SA at all in the six years following childbirth.

249 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 250 251 hospitalization days and SA days compared to those who gave birth. Women who gave birth 252 had approximately 0.3 hospitalization days per year whereas those who did not give birth had 253 around 0.5 hospitalization days per year. The average number of SA days for women giving 254 birth was 3.8 days/year and for those not giving birth 5.0 days/year. SA differences between 255 those giving birth and women not giving birth were statistically significant with the exception 256 of year (-4) and (-3). For inpatient care, the differences between those giving birth and women 257 not giving birth were not statistically significant. The average number of inpatient days 258 increased rapidly during  $T_0$  for women who gave birth, especially because of hospitalization 259 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 260 261 T<sub>0</sub> were to a large extent associated with subsequent childbirths.

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262	Table 2 presents HR for the association between childbirth and hospitalization, for all
263	diagnoses and for diagnoses where those related to pregnancy, childbirth, and the postpartum
264	period were excluded. When these diagnoses were removed, women who did not give birth
265	and who had been hospitalized at least once before $T_0$ had twice the risk of future
266	hospitalization compared to those not hospitalized prior to $T_0$ (HR: 2.3; 95% CI 1.6-3.3) after
267	adjustments for birth year, delivery year, and educational level. The association was explained
268	by familial factors in the analysis of discordant twin pairs (HR: 1.2; 0.8-1.9).
269	When restricting the analyses to women who gave birth, a total of 2 792 women were
270	studied, i.e., 1 396 complete pairs in which both twins had given birth. The reference group
271	constituted of mothers who had not been hospitalized prior to their first childbirth. Mothers
272	who had been hospitalized before their first childbirth had a slightly higher HR for future
273	hospitalization when diagnoses related to pregnancy and childbirth were excluded (HR 1.5;
274	1.2-2.0). This association disappeared in the analyses of discordant twin pairs, suggesting an
275	influence of familial factors (HR: 1.0; 0.8-1.3).
276	Regardless of childbirth status, hospitalization year 1-2 after $T_0$ was a predictor of having a
277	new SA in year 3-5 after $T_0$ (Table 3). Compared to women who did not give birth and who
278	were not hospitalized the first two years after $T_0$ , mothers hospitalized after first childbirth
279	had an HR of 2.4 (2.0-2.9) for a new SA after adjustments for birth year, delivery year, and
280	educational level. Hospitalization after T <sub>0</sub> was also associated with a new long-term SA (>90
281	days) in year 3-5 after $T_0$ (Table 3). Women who did not give birth had a nearly three-fold
282	risk of a new long-term SA year 3-5 after $T_0$ (HR 2.8; 1.5-5.1), whereas women who gave
283	birth had an HR of 1.8 (1.3-2.5). The analyses of twin pairs discordant for having a new long-
284	term SA year 3-5 after $T_0$ , showed attenuated point estimates, hence suggesting that familial
285	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<sub>0</sub> (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 <text> 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.

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294	Discussion

295 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 296 297 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 298 299 much for mothers, an increase that gradually decreased during the years after the delivery. We 300 found hospitalization prior to  $T_0$  to be a risk factor for future hospitalization, regardless of 301 childbirth status, also when excluding hospitalization due to childbirth. Furthermore, 302 hospitalization after the first childbirth was associated with a higher HR of both short-term 303 and long-term future SA. An additional analysis focusing solely on the women who gave birth 304 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 305 between hospitalization and long-term SA, regardless of childbirth status. 306 In line with some previous studies <sup>10 20 50 51</sup>, we found that SA increased in women during 307 308 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 309 310 be due to subsequent pregnancies. A recent Norwegian study found that the increased SA risk 311 in women in the years after pregnancy disappeared when SA during subsequent pregnancies were accounted for <sup>20</sup>. Several explanations have been suggested for such higher levels of SA, 312 among others the double burden hypothesis <sup>20 52-54</sup>. This hypothesis has been questioned, as 313 314 research has indeed shown that women who occupy multiple roles tend to be healthier than those who enact fewer roles <sup>55-57</sup>. Thus, the combination of employment and parenthood does 315 not seem to imply worse health, on the contrary. In our study, the annual rates of SA 316 317 decreased steadily after the first childbirth, speaking in favor of this hypothesis. Further studies of this are warranted. 318

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319	To our best knowledge, this is the first study to examine long-term associations between
320	childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not
321	have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to
322	subsequent pregnancy and childbirth) when compared to women who did not give birth.
323	Those who did not give birth had a more stable pattern of SA during the studied period,
324	however, with a slight increase in annual SA days over the years. This is in line with a
325	Swedish study examining whether family obligations influence the risk of SA in publicly
326	employed women and found a slight risk increase for SA among women without children <sup>58</sup> .
327	Further, a broad systematic literature review published in 2004 provided no evidence of an
328	association between having children in the household and an increased risk of SA <sup>59</sup> . It is
329	important to consider family situation when examining the association between having
330	children and morbidity, as single women with children have been shown to have worse health
331	<sup>30 31 60</sup> and higher levels of SA <sup>6 58</sup> .
332	Even though pregnancy, delivery, and the postpartum period may increase the risk for
333	disease and injury <sup>25 27</sup> , our findings do not suggest that women who gave birth are more
334	likely to be hospitalized after their first childbirth, except for hospitalizations related to
335	subsequent deliveries. We found no differences in risk for future hospitalization when
336	comparing those who gave birth to those who did not. Thus, giving birth does not have to be
337	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

child. Also, giving birth is in itself a risk factor for future morbidity<sup>16 19 22</sup>. Further, during the
last decades, the number of women who voluntarily do not want to become parents has
increased worldwide<sup>61</sup>.

women who do not give birth may have worse health and choose not to have or cannot have a

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344	Hospitalization prior to the first childbirth or equivalent $(T_0)$ was a risk factor for future SA
345	for all women, regardless of childbirth status. In particular, women who had been hospitalized
346	both before and after $T_0$ were at risk for future SA. Furthermore, we found an association
347	between hospitalization and future long-term SA.
348	When comparing women who gave birth to those who did not, with respect to exposure to
349	hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had
350	slightly higher risk for future SA regardless of duration, whereas those who did not give birth
351	hospitalized after $T_0$ had higher risk for long-term SA.
352	Hospitalization both before and after the year T <sub>0</sub> seems to be the strongest indicator, i.e.,
353	these individuals had the highest risk for future SA. Consequently, the women who had been
354	hospitalized both before and after $T_0$ had the highest risk for future SA. Our analyses of
355	women who gave birth revealed a graded association between hospitalization and SA, where
356	those who only were hospitalized before or after their first childbirth had a higher risk of SA,
357	whereas those who were hospitalized both before and after the first childbirth had even higher
358	risks. Thus, we found a strong association between morbidity, here measured as
359	hospitalization, and future SA among women who have given birth – an association that often
360	has been question regarding women with children <sup>12</sup> .
361	Familial factors seemed to contribute to the association between hospitalization before and
362	after T <sub>0</sub> among those who did not give birth. The influence of familial factors may relate to
363	morbidity among women not giving birth – morbidity that might be more severe and
364	potentially also being relatively strongly influenced by genetics. Familial factors also played a
365	role in the associations between hospitalization and future long-term SA. This could be
366	related to the fact that the hospitalization usually is required for severe conditions that may
367	have a strong genetic component. However, since genetics have been shown to influence the
368	risk of DP <sup>62</sup> , and some indications exist that genetics also play a role in long-term SA and

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369 mortality, it can be suspected that the effects of familial factors on SA can be either direct or370 through other influential factors.

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# 372 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 <sup>43-45</sup>. 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.

379 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 380 381 voluntary and involuntary childlessness have been shown, where voluntarily childless women showed higher levels of overall well-being <sup>61 63</sup> which might be related to hospitalization 382 383 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 384 385 that does not include morbidity treated in outpatient care. Having had also other types of 386 morbidity data might have given another picture and hopefully future studies will have such 387 information. Another limitation is that the terms for inpatient care have changed during the 388 studied period. In Sweden, inpatient care has over the years to a great extent been replaced by 389 outpatient treatment. Therefore, some of the decrease in hospitalization over the years is a 390 result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities <sup>64</sup>, however, this affected all women equally, and is to some extent handled by 391 adjusting for birth year. The CIs are wider in the years far from T<sub>0</sub>, e.g., T<sub>6</sub>, due to fewer 392 follow up year for some – e.g., for those who gave birth late during the studied period. Also, 393

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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'.

#### 403 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.

414	
415	Ethical approval
416	The study was approved by the Regional Ethical Review Board, Stockholm, Sweden
417	(2007/524-31).
418 419 420 421	<b>Contributorship Statement</b> 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
422	input from all the co-authors. All authors contributed in designing the study and to the
423	interpretation of the results and to the writing and approval of the final article.
424	
425	Competing interest statement
426	We declare that no competing interests exist.
427	
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435	
436	Data sharing
437 438 439	No additional data available.
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2		Figure la sende
3	442	Figure legends
4 5 6	443	Figure 1. Flow chart for the study population.
7	444	Figure 2. Average annual number of days on sickness absence (SA) and hospitalization,
8	445	respectively. (with 95% CI), six years prior through six year after $T_0$ for women who gave
9	446	hirth/did not give hirth (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.

	Both dave	Twin pairs where or		
Variables	birth	Twin 1 (gave birth)	Twin 2 (did not give birth)	Total
N	2 792	1 163	1 163	5 118
Number of deliveries				
	711 (250/)	E01 (420/)		
Two or more delivering	711 (25%)	501 (43%)		
I wo or more deliveries	2 081 (75%)	662 (57%)		
Age at T₀				
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 vears	207 (7%)	109 (9%)		
>40 years	30 (1%)	15 (1%)		
Zvracity				
Monozygotic	1 726 (62%)	608 (52%)	608 (52%)	2 942 (57%)
	1 066 (38%)	555 ( <b>4</b> 8%)	555 (48%)	2 942 (37 %)
Dizygotte	1 000 (30 %)	555 (40%)	333 (4078)	2 170 (4370)
Highest attained education <sup>1</sup>				
≤ 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 <sup>2</sup>				
- 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				
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 (12%)	407 (35%)	325 (28%)	1 015 (37%)
- At least one hospitalization during the period six years	1 103 (42 /0)	407 (5578)	525 (2070)	1910 (5770)
prior to T <sub>0</sub>	679 (24%)	251 (22%)	217 (19%)	1 147 (22%)
- At least one hospitalization during the period six years	1 965 (70%)	585 (50%)	168 (14%)	2 718 (53%)
				2710(00%)
- At least one hospitalization both before and after $I_0$	483 (17%)	133 (11%)	60 (5%)	676 (13%)
Sickness Absence (SA) <sup>*</sup>				
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%)

<sup>1</sup> At time of T<sub>0</sub>

 $^2$  Excluding hospitalizations occurring during  $T_{\rm 0}$ 

<sup>3</sup> Excluding SA occurring during T<sub>0</sub>

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Table 2. Cox proportional hazard ratios (HR) with 95% CI for the association between childbirth, hospitalization before T<sub>0</sub>, and subsequent hospitalization (i.e., during year 3-5 after T<sub>0</sub>) 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 <sup>1</sup>			
	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>2, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>3, 7</sup>	
All women (n=5 118)							
No childbirth, no hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
No childbirth, hospitalization before T <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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 <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>4, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>5, 7</sup>	
Women who had at least one childbirth (n=	=2 792)						
No hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
Hospitalization before T <sub>0</sub> <sup>8</sup>	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)	

<sup>1</sup> Diagnoses O00-O99

<sup>2</sup> Twin pairs where one had a hospitalization during the follow-up and the other not (n=1 016 pairs) <sup>3</sup> Twin pairs where one had a hospitalization during the follow-up and the other not (n=456 pairs)

<sup>4</sup> Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)

.irs) <sup>5</sup> Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs)

<sup>6</sup> Adjusted for birth year

<sup>7</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>8</sup> During the period 1-5 years prior to T<sub>0</sub>

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<sub>0</sub>, 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.

	SA in year	3-5 after T <sub>0</sub> (re	Long-ter	Long-term SA (>90 days) in year 3-5 after T <sub>0</sub>				
Status childbirth and hospitalization	Madal a <sup>5</sup>	Madal h <sup>6</sup>	Madal a <sup>7</sup>	Discordant twin	Madal a <sup>5</sup>	Madal b <sup>6</sup>	Model e <sup>7</sup>	Discordant
	wouer a		woderc	pairs	wodera	Model b	Wodel C	twin pairs
All women (n=5 118)								
No childbirth, no hospitalization year 1-2 after $T_0^\circ$	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
No childbirth, hospitalization year 1-2 after T <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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				Discordant twin				Discordant
(n=2 792)	Model a <sup>5</sup>	Model b <sup>6</sup>	Model c <sup>7</sup>	pairs <sup>3, 5</sup>	Model a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	twin pairs <sup>4, 7</sup>
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)
<sup>1</sup> Twin pairs where one had a SA during the follow-up and the o	other not (n=835 pai	rs)						
<sup>2</sup> Twin pairs where one had a long-term SA during the follow-u	p and the other not (	(n=277 pairs)						
<sup>3</sup> Twin pairs where one had a SA during the follow-up and the o	other not (n=542 pai	rs)						
<sup>4</sup> Twin pairs where one had a long-term SA during the follow-u	p and the other not (	(n=184 pairs)						
<sup>5</sup> Adjusted for birth year								
<sup>o</sup> Model a, and additional adjustments for delivery year, and edu	ucational level							
<sup>7</sup> Model b, and additional adjustments for earlier hospitalization	1							
° Diagnoses O00-O99 excluded								
Table 4. Cov proportional HD with 05% Cl for	the encodetion	hotwoon hos	nitalization had	fore and offer first	obildbirth and	now oloknoop	abaanaa (C	) in year
3.5 after T in twins who had their first shidhid		Delween NOS	a models for a	ore and alter first	oniubirtin, and	new sickness		() iii year
	ui 1994-2009 (	$\frac{11-2}{2}$ $\frac{132}{2}$ . The		tor T (recordless			$\Delta \left( > 00 \text{ deve} \right)$	
Status hospitalization before and after childbird	th	54	of numbe	r of days)		Long-term S	after T <sub>0</sub>	n year 3-5
	M	odel a <sup>3</sup> Mo	del b <sup>4</sup> Mode	l c⁵ Discordant	Model a <sup>3</sup>	Model b <sup>₄</sup>	Model c⁵	Discordant

	Model a <sup>3</sup>	Model b⁴	Model c⁵	Discordant twin pairs <sup>1, 4</sup>	Model a <sup>3</sup>	Model b⁴	Model c⁵	Discordant twin pairs <sup>2, 4</sup>
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 ${\sf T_0}^6$ but not during year 1-2 after ${\sf T_0}^7$	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)

<sup>1</sup> Twin pairs where one had an SA during the follow-up and the other not (n=542)

<sup>2</sup> Twin pairs where one had a long-term SA during the follow-up and the other not (n=184)

<sup>3</sup> Adjusted for birth year

<sup>4</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>5</sup> Model b, and additional adjustments for subsequent deliveries

<sup>6</sup> During the period 1-5 years prior to T<sub>0</sub>

<sup>7</sup> Diagnoses O00-O99 excluded

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3	1	Childbirth, hospitalization, and sickness absence: a study of female twins
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25 26	Abstract Objective: To investigate associations of giving birth with morbidity in terms of
27	hospitalization and social consequences of morbidity in terms of sickness absence (SA), while
28	taking familial (genetics and shared environmental) factors into account.
29	Design: Prospective register-based cohort study. Estimates of risk of hospitalization and SA
30	were calculated as hazard ratios (HR) with 95% confidence intervals (CI).
31	Setting: All female twins, i.e., women with twin sister, born in Sweden.
32	Participants: 5118 Swedish female twins (women with twin sister), born 1959-1990, where
33	at least one in the twin pair had their first childbirth $(T_0)$ 1994-2009 and none gave birth
34	before 1994.
35	Main outcome measures: Hospitalization and SA during year 3-5 after first delivery or
36	equivalent.
37	Results: Preceding the first childbirth, the mean annual number of SA days increased for
38	mothers, and then decreased again. Hospitalization after $T_0$ was associated with higher HRs of
39	short-term and long-term SA (HR for short-term SA: 3.0; 95% CI 2.5-3.6 and for long-term
40	SA: 2.3; 95% CI 1.6-3.2). Hospitalization both before and after first childbirth was associated
41	with a higher risk of future SA (HR for long-term SA: 4.2; 95% CI 2.7-6.4). Familial factors
42	influenced the association between hospitalization and long-term SA, regardless of childbirth
43	status.
44	Conclusion: Women giving birth did not have a higher risk for SA than those not giving birth
45	and results indicate a positive health selection into giving birth. Mothers hospitalized before
46	and/or after giving birth had higher risks for future SA, that is, there was a strong association
47	between morbidity and future SA.

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

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# 51 Article Summary

52 Article focus:

53 To investigate associations of giving birth with morbidity in terms of hospitalization and

54 social consequences of morbidity in terms of sickness absence (SA), while taking familial

55 (genetics and shared environmental) factors into account.

# 56 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
- 59 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

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# 62 Strengths and limitations:

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

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1 Introduction	
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72 In most countries with high labor force participation, women have higher levels of sickness absence (SA) than men<sup>1-4</sup>. Many theories and mechanism regarding this have been suggested, 73 74 e.g., women having higher morbidity, higher workload (when combining paid and unpaid 75 work), tougher situation on the labor market, men being the norm for how the labor market is 76 organized, gender bias in healthcare and social insurance systems, discrimination, and domestic violence, etcetera <sup>5-9</sup>. Another hypothesis behind this gender difference in SA 77 focuses on SA during pregnancy and after childbirth <sup>6 10-13</sup>. Several studies show that women 78 have higher SA during pregnancy<sup>1014</sup> and that pregnancy-related SA explains half of the 79 gender differences in SA in fertile ages <sup>15</sup>. 80 81 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 82 83 morbidity now give birth. Further, nowadays, the proportion of caesarean sections has

84 increased as well as vacuum extraction deliveries, leading to risk of later health problems <sup>16 17</sup>.
85 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 <sup>18 19</sup>, while prospective studies with longer follow-up of
mothers are rare <sup>6 12 20</sup>.

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 <sup>21 22</sup>.
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 <sup>19</sup>. Giving birth may be associated with a higher risk of certain diseases
demanding hospitalization, such as cardiovascular diseases, musculoskeletal diseases, mental

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97	disorders, and different types of injuries <sup>23-26</sup> . For women with a disease present before the
98	childbirth, the disorder might deteriorate after childbirth <sup>23 24</sup> . Regarding symptoms related to
99	childbirth, high prevalence has been shown six months after childbirth for e.g., low back pain,
100	fatigue, headache, and sleep disorders <sup>19 27</sup> . Most of these symptoms seem to remain up to one
101	year after childbirth <sup>17</sup> . Besides physical health effects, also depression and other mental
102	disorders have been linked to childbirth <sup>26 28</sup> , but again, prospective studies with longer
103	follow-up are lacking <sup>27</sup> . Even though having children has been shown to contribute to an
104	overall wellbeing, this is not the case for everybody and especially not among single mothers
105	whose economic situation and thereby possibilities for good health care might be worse <sup>29-31</sup> .
106	Morbidity can be measured in different ways, e.g., through self-reports and or visits to
107	healthcare. Here we will use data on more severe morbidity that involves assessments from
108	physicians, that is, morbidity that has led to hospitalization, a measure so far not used in this
109	type of studies. Sickness absence is not a good measure of morbidity– most people with
110	morbidity are not on SA <sup>4</sup> . Instead SA is considered a very good measure of social
111	consequences of morbidity, in terms of not being able to support yourself from work <sup>4</sup> . Yet,
112	there are surprisingly few studies on the association between morbidity and SA and in media
113	and among some researchers sometimes even the level of morbidity among sickness absentees
114	even is questioned, especially for female sickness absentees – their sickness absence is rather
115	considered related to attitudes than to morbidity <sup>12 32 33</sup> .
116	Studies examining the role of familial factors (i.e., genetic and shared (mainly childhood)
117	environment) on morbidity have shown that genetics tends to explain a moderate to large
118	extent of the variability in most of the chronic diseases <sup>34 35</sup> . For example, heritability for
119	mental disorders varies between 30-90% $^{36}$ , whereas genetic factors have been shown to
120	explain 30-60% of the total variation in musculoskeletal disorders <sup>37 38</sup> . Taken together,
121	familial factors are important to account for when studying the association between morbidity

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122	(here in terms of hospitalization) and SA as studies otherwise could lead to erroneous
123	conclusions. Twin settings provide a powerful tool for studies of these aspects in research of
124	SA, a research area where different selection biases otherwise might have an impact on
125	results. Twins in a pair are optimally matched on genetic (100% for MZ pairs and on average
126	50% for DZ pairs) and common environmental factors through childhood (100% for both MZ
127	and DZ twin pairs when reared together) in addition to age and sex (for the same-sexed pairs).
128	An experimental design, which can control for these familial influences, is to examine
129	discordant twin sisters, that is, where one twin sister has given birth and the other has not. If
130	discordant twin sisters show similar associations as the analyses of the whole cohort, this
131	would indicate that the childbirth may actually be a contributing cause of the future SA. If
132	instead the association found among the whole cohort cannot be replicated within discordant
133	twin sisters, then familial factors are of importance. Influence of familial factors (genetic and
134	common environment) is indicated if the association found in the analyses of the whole cohort
135	disappear or change considerably in the analyses of discordant twin pairs <sup>39</sup> .
136	
137	The aim of the study was to investigate the associations of giving birth with subsequent
139	morbidity in terms of hospitalization and SA Familial factors (genetics and shared/early

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

140 potential association between childbirth and future hospitalization and SA.

# 142 Methods

# 143 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)<sup>40</sup>. 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 <sup>40 41</sup>. The selection of the study population is illustrated in Figure 1.

The unique personal identity number assigned to each Swedish resident <sup>42</sup> 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 <sup>43</sup>. 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<sup>44</sup>. 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 <sup>45</sup>. 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., 

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168	inpatient care. Annual information on educational level and on SA days was obtained from
169	Statistics Sweden.
170	
171	Time in relation to childbirth
172	The studied women were followed in relation to year of first childbirth, referred to as T <sub>0</sub> . In
173	order to compare those who gave birth to those who did not, $T_0$ for the women who did not
174	give birth was defined as year of her twin sister's first childbirth.
175	
176	Hospitalization
177	Data on hospitalization covered the period six years prior to, and six years after year of first
178	childbirth $(T_0)$ or equivalent. For descriptive purposes, the total and the average number of
179	hospitalization days per year were calculated.
180	In order to examine if hospitalization prior to (or after) childbirth increases the risk for future
181	hospitalization, the first part of the regression analyses considered hospitalization as both
182	exposure and outcome. We created one dichotomous variable for hospitalization before $T_0$
183	(i.e., exposure), and two dichotomous outcome variables for hospitalization during year 3-5
184	after T <sub>0</sub> : one for hospitalization with any diagnosis and one excluding hospitalization with
185	diagnoses related to pregnancy, childbirth, and the postpartum period.
186	In order to answer the research question "Does hospitalization prior to (or after) childbirth
187	increase the risk for future SA?", we created two dichotomous hospitalization exposure
188	variables: one for hospitalization before $T_0$ and one variable: hospitalization year 1-2 after $T_0$
189	(excluding diagnoses related to pregnancy, childbirth, and the postpartum period).
190	
191	Sickness absence

SA can be measured in several ways, related to duration and incidence <sup>46</sup>. 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  $T_0$ .

196 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.

- 207 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)  $^{4748}$ , we adjusted for educational level at T<sub>0</sub>. Years of education was classified into four categories; <9 years of compulsory school, 10-12 years of education (senior high school),  $\geq$ 13years of education (college/university), missing.

- - 213 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<sub>0</sub>). In a first model (model a), adjustments were made for age. Second

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2	17	(model b), additional adjustments were made for delivery year and educational level at time of
2	18	T <sub>0</sub> . Thereafter, twin pairs who were discordant with respect to outcomes, i.e., having at least
2	19	one hospitalization after $T_0$ , were analyzed using Conditional Cox regression. In the next step,
2	20	we analyzed the associations between childbirth, hospitalization, and SA by fitting three Cox
2	21	regression models (table 3). The first (model a) was adjusted for birth year. In the second
2	22	model (model b), additional adjustments were made for delivery year and educational level at
2	23	time of T <sub>0</sub> . In the third model (model c), previous hospitalization was included. Thereafter,
2	24	twin pairs who were discordant (Conditional Cox regression) with respect to outcomes i.e.,
2	25	having had SA or long-term SA (>90 days) were analyzed.
2	26	Finally, in the step where we analyzed the association between hospitalization before and
2	27	after first childbirth, and subsequent SA (table 4), we adopted the first two models (model a-
2	28	b) from table 3. In a third model (model c), we fitted an additional model in which
2	29	adjustments were made for subsequent deliveries.
2	30	The proportional hazards assumption was checked by including time-dependent versions of
2	31	all the covariates in the models. This did not indicate a violation of the proportionality
2	32	assumption.
2	33	All statistical analyses were performed with SAS 9.3 and STATA 12.1.
2	34	The STROBE checklist was used in designing and reporting the study.
2	35	The project was approved by the Regional Ethical Review Board of Stockholm.

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#### Results

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237 Of the 5 118 women included in the study, 77% had given birth at least once between 1994 238 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 239 240 educational level distribution was rather similar when comparing those who gave birth to 241 those who did not. When hospitalizations with diagnoses for pregnancy and childbirth were 242 excluded, 30% of the women, i.e., the 1 183 where both in a pair gave birth and the 407 twins 243 where only one in the pair gave birth had at least one hospitalization during the period six 244 years prior to and six years after their first delivery (the delivery year excluded). The 245 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 246 247 first delivery, when the year for childbirth was excluded. The majority of the women had no 248 SA at all in the six years following childbirth.

249 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 250 251 hospitalization days and SA days compared to those who gave birth. Women who gave birth 252 had approximately 0.3 hospitalization days per year whereas those who did not give birth had 253 around 0.5 hospitalization days per year. The average number of SA days for women giving 254 birth was 3.8 days/year and for those not giving birth 5.0 days/year. SA differences between 255 those giving birth and women not giving birth were statistically significant with the exception 256 of year (-4) and (-3). For inpatient care, the differences between those giving birth and women 257 not giving birth were not statistically significant. The average number of inpatient days 258 increased rapidly during  $T_0$  for women who gave birth, especially because of hospitalization 259 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 260 261 T<sub>0</sub> were to a large extent associated with subsequent childbirths.

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262	Table 2 presents HR for the association between childbirth and hospitalization, for all
263	diagnoses and for diagnoses where those related to pregnancy, childbirth, and the postpartum
264	period were excluded. When these diagnoses were removed, women who did not give birth
265	and who had been hospitalized at least once before $T_0$ had twice the risk of future
266	hospitalization compared to those not hospitalized prior to $T_0$ (HR: 2.3; 95% CI 1.6-3.3) after
267	adjustments for birth year, delivery year, and educational level. The association was explained
268	by familial factors in the analysis of discordant twin pairs (HR: 1.2; 0.8-1.9).
269	When restricting the analyses to women who gave birth, a total of 2 792 women were
270	studied, i.e., 1 396 complete pairs in which both twins had given birth. The reference group
271	constituted of mothers who had not been hospitalized prior to their first childbirth. Mothers
272	who had been hospitalized before their first childbirth had a slightly higher HR for future
273	hospitalization when diagnoses related to pregnancy and childbirth were excluded (HR 1.5;
274	1.2-2.0). This association disappeared in the analyses of discordant twin pairs, suggesting an
275	influence of familial factors (HR: 1.0; 0.8-1.3).
276	Regardless of childbirth status, hospitalization year 1-2 after $T_0$ was a predictor of having a
277	new SA in year 3-5 after $T_0$ (Table 3). Compared to women who did not give birth and who
278	were not hospitalized the first two years after $T_0$ , mothers hospitalized after first childbirth
279	had an HR of 2.4 (2.0-2.9) for a new SA after adjustments for birth year, delivery year, and
280	educational level. Hospitalization after T <sub>0</sub> was also associated with a new long-term SA (>90
281	days) in year 3-5 after $T_0$ (Table 3). Women who did not give birth had a nearly three-fold
282	risk of a new long-term SA year 3-5 after $T_0$ (HR 2.8; 1.5-5.1), whereas women who gave
283	birth had an HR of 1.8 (1.3-2.5). The analyses of twin pairs discordant for having a new long-
284	term SA year 3-5 after T <sub>0</sub> , showed attenuated point estimates, hence suggesting that familial
285	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<sub>0</sub> (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 <text> 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.

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# 294 Discussion

295 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 296 297 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 298 299 much for mothers, an increase that gradually decreased during the years after the delivery. We 300 found hospitalization prior to  $T_0$  to be a risk factor for future hospitalization, regardless of 301 childbirth status, also when excluding hospitalization due to childbirth. Furthermore, 302 hospitalization after the first childbirth was associated with a higher HR of both short-term 303 and long-term future SA. An additional analysis focusing solely on the women who gave birth 304 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 305 between hospitalization and long-term SA, regardless of childbirth status. 306 In line with some previous studies <sup>10 20 50 51</sup>, we found that SA increased in women during 307 308 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 309 310 be due to subsequent pregnancies. A recent Norwegian study found that the increased SA risk 311 in women in the years after pregnancy disappeared when SA during subsequent pregnancies were accounted for <sup>20</sup>. Several explanations have been suggested for such higher levels of SA, 312 among others the double burden hypothesis <sup>20 52-54</sup>. This hypothesis has been questioned, as 313 314 research has indeed shown that women who occupy multiple roles tend to be healthier than those who enact fewer roles <sup>55-57</sup>. Thus, the combination of employment and parenthood does 315 316 not seem to imply worse health, on the contrary. In our study, the annual rates of SA 317 decreased steadily after the first childbirth, speaking in favor of this hypothesis. Further studies of this are warranted. 318

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319	To our best knowledge, this is the first study to examine long-term associations between
320	childbirth, hospitalization and both short- and long-term SA. Women who gave birth did not
321	have a higher risk for long-term SA nor for hospitalization (besides hospitalization due to
322	subsequent pregnancy and childbirth) when compared to women who did not give birth.
323	Those who did not give birth had a more stable pattern of SA during the studied period,
324	however, with a slight increase in annual SA days over the years. This is in line with a
325	Swedish study examining whether family obligations influence the risk of SA in publicly
326	employed women and found a slight risk increase for SA among women without children <sup>58</sup> .
327	Further, a broad systematic literature review published in 2004 provided no evidence of an
328	association between having children in the household and an increased risk of SA $^{59}$ . It is
329	important to consider family situation when examining the association between having
330	children and morbidity, as single women with children have been shown to have worse health
331	<sup>30 31 60</sup> and higher levels of SA <sup>6 58</sup> .
332	Even though pregnancy, delivery, and the postpartum period may increase the risk for
333	disease and injury <sup>25 27</sup> , our findings do not suggest that women who gave birth are more
334	likely to be hospitalized after their first childbirth, except for hospitalizations related to
335	subsequent deliveries. We found no differences in risk for future hospitalization when
336	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

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<sup>16 19 22</sup>. Further, during the
last decades, the number of women who voluntarily do not want to become parents has

explanations. As mentioned above, one could expect that there is a health selection, where

343 increased worldwide<sup>61</sup>.

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344	Hospitalization prior to the first childbirth or equivalent $(T_0)$ was a risk factor for future SA
345	for all women, regardless of childbirth status. In particular, women who had been hospitalized
346	both before and after $T_0$ were at risk for future SA. Furthermore, we found an association
347	between hospitalization and future long-term SA.
348	When comparing women who gave birth to those who did not, with respect to exposure to
349	hospitalization and risk of SA, mothers hospitalized at least once after the first childbirth had
350	slightly higher risk for future SA regardless of duration, whereas those who did not give birth
351	hospitalized after $T_0$ had higher risk for long-term SA.
352	Hospitalization both before and after the year T <sub>0</sub> seems to be the strongest indicator, i.e.,
353	these individuals had the highest risk for future SA. Consequently, the women who had been
354	hospitalized both before and after $T_0$ had the highest risk for future SA. Our analyses of
355	women who gave birth revealed a graded association between hospitalization and SA, where
356	those who only were hospitalized before or after their first childbirth had a higher risk of SA,
357	whereas those who were hospitalized both before and after the first childbirth had even higher
358	risks. Thus, we found a strong association between morbidity, here measured as
359	hospitalization, and future SA among women who have given birth – an association that often
360	has been question regarding women with children <sup>12</sup> .
361	Familial factors seemed to contribute to the association between hospitalization before and
362	after $T_0$ among those who did not give birth. The influence of familial factors may relate to
363	morbidity among women not giving birth – morbidity that might be more severe and
364	potentially also being relatively strongly influenced by genetics. Familial factors also played a
365	role in the associations between hospitalization and future long-term SA. This could be
366	related to the fact that the hospitalization usually is required for severe conditions that may
367	have a strong genetic component. However, since genetics have been shown to influence the
368	risk of DP <sup>62</sup> , and some indications exist that genetics also play a role in long-term SA and

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

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# 372 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 <sup>43-45</sup>. 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.

379 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 380 381 voluntary and involuntary childlessness have been shown, where voluntarily childless women showed higher levels of overall well-being <sup>61 63</sup> which might be related to hospitalization 382 383 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 384 385 that does not include morbidity treated in outpatient care. Having had also other types of 386 morbidity data might have given another picture and hopefully future studies will have such 387 information. Another limitation is that the terms for inpatient care have changed during the 388 studied period. In Sweden, inpatient care has over the years to a great extent been replaced by 389 outpatient treatment. Therefore, some of the decrease in hospitalization over the years is a 390 result of a shift in the responsibility for inpatient care from hospitals to outpatient care facilities <sup>64</sup>, however, this affected all women equally, and is to some extent handled by 391 adjusting for birth year. The CIs are wider in the years far from T<sub>0</sub>, e.g., T<sub>6</sub>, due to fewer 392 follow up year for some – e.g., for those who gave birth late during the studied period. Also, 393
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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'.

### 403 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.

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415	Ethical approval
416	The study was approved by the Regional Ethical Review Board, Stockholm, Sweden
417	(2007/524-31).
418 419 420 421	<b>Contributorship Statement</b> 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
422	input from all the co-authors. All authors contributed in designing the study and to the
423	interpretation of the results and to the writing and approval of the final article.
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425	Competing interest statement
426	We declare that no competing interests exist.
427	
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434	and AstraZeneca. Funding sources had no involvement in this study.
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436	Data sharing
437 438 439	No additional data available.
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2	440	Figure legende
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5 6	443	Figure 1. Flow chart for the study population.
7	444	Figure 2. Average annual number of days on sickness absence (SA) and hospitalization,
8	445	respectively, (with 95% CI), six years prior through six year after $T_0$ for women who gave
9	446	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.

	Both gave	Twin pairs where or		
Variables	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 To				
16-19 vears	47 (2%)	33 (2%)		
20-24 vears	511 (18%)	239 (21%)		
25-29 vears	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%)		
Zuracity				
Monozyractic	1 726 (62%)	609 (52%)	609 (52%)	2 042 (57%)
Diargetie	1 720 (02 %)	606 (52 %)	608 (52 %)	2 942 (37 %)
Dizygolic	1 000 (30%)	555 (46%)	555 (46%)	2 170 (43%)
Highest attained education <sup>1</sup>				
≤ 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 <sup>2</sup>				
- 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				
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%)	1 015 (37%)
- At least one hospitalization during the period six years	1 103 (42 /0)	407 (35%)	525 (2676)	1915 (37 %)
prior to T <sub>0</sub>	679 (24%)	251 (22%)	217 (19%)	1 147 (22%)
- At least one hospitalization during the period six years	1 965 (70%)	585 (50%)	168 (14%)	2 718 (53%)
	1 303 (1070)	303 (30%)		2710 (00%)
- At least one hospitalization both before and after I $_0$	483 (17%)	133 (11%)	60 (5%)	676 (13%)
Sickness Absence (SA) <sup>3</sup>				
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%)

<sup>1</sup> At time of T<sub>0</sub>

 $^2$  Excluding hospitalizations occurring during  $T_{\rm 0}$ 

<sup>3</sup> Excluding SA occurring during T<sub>0</sub>

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Table 2. Cox proportional hazard ratios (HR) with 95% CI for the association between childbirth, hospitalization before T<sub>0</sub>, and subsequent hospitalization (i.e., during year 3-5 after T<sub>0</sub>) 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 <sup>1</sup>			
	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>2, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>3, 7</sup>	
All women (n=5 118)							
No childbirth, no hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
No childbirth, hospitalization before T <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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 <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>4, 7</sup>	Model a <sup>6</sup>	Model b <sup>7</sup>	Discordant twin pairs <sup>5, 7</sup>	
Women who had at least one childbirth (na	=2 792)						
No hospitalization before T <sub>0</sub> <sup>8</sup>	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
Hospitalization before T <sub>0</sub> <sup>8</sup>	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)	

<sup>1</sup> 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)

<sup>4</sup> Twin pairs (both giving birth) where one having had a hospitalization during the follow-up and the other not (n=508 pairs)

<sup>5</sup> Twin pairs (both giving birth) with one had a hospitalization during the follow-up and the other not (n=271 pairs)

<sup>6</sup> Adjusted for birth year

<sup>7</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>8</sup> During the period 1-5 years prior to T<sub>0</sub>

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<sub>0</sub>, 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.

	SA in year	3-5 after T <sub>0</sub> (re	gardless of nur	nber of days)	Long-ter	Long-term SA (>90 days) in year 3-5 after T <sub>0</sub>			
Status childbirth and hospitalization	Madal a <sup>5</sup>	Madal h <sup>6</sup>	Model e <sup>7</sup>	Discordant twin	Madal a <sup>5</sup>	Madal h <sup>6</sup>	Medel o <sup>7</sup>	Discordant	
	Model a	Niodel D	Model c	pairs '	Model a	MODELD	wodel c	twin pairs '	
All women (n=5 118)									
No childbirth, no hospitalization year 1-2 after T <sub>0</sub> *	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
No childbirth, hospitalization year 1-2 after T <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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 <sub>0</sub> <sup>8</sup>	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				Discordant twin				Discordant	
(n=2 792)	Model a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	pairs <sup>3, 5</sup>	Model a⁵	Model b <sup>6</sup>	Model c <sup>7</sup>	twin pairs <sup>4, 7</sup>	
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 <mark>-1.5</mark> )	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)	
<sup>1</sup> Twin pairs where one had a SA during the follow-up and the o	other not (n=835 pai	rs)							
<sup>2</sup> Twin pairs where one had a long-term SA during the follow-up	p and the other not (	(n=277 pairs)							
<sup>3</sup> Twin pairs where one had a SA during the follow-up and the o	other not (n=542 pai	rs)							
<sup>4</sup> Twin pairs where one had a long-term SA during the follow-up	p and the other not (	(n=184 pairs)							
<sup>3</sup> Adjusted for birth year									
<sup>o</sup> Model a, and additional adjustments for delivery year, and edu	icational level								
<sup>8</sup> Discusses 000 000 methods	l								
Diagnoses 000-099 excluded									
Table 4 Cov proportional HD with 05% CL for t	the ecoepiction	hotwoon hoo	nitalization haf	are and ofter first	childhirth and	now sicknoss	abaanaa (SA	) in voor	
Table 4. Cox proportional RR with 95% CI for $2.5$ after T in twine who had their first shildhirt		1 Delween 1105	pitalization bei	divermente ac w		dept twin pair		() IT year	
	11 1994-2009 (1	<u>11–2 792). TINE</u>					$\Delta $ (>00 days) :		
Status hospitalization before and after childbirt	:h	54	of number	r of days)		Long-term 5	after T₀	n year o-o	
	M	odel a <sup>3</sup> Mo	del b <sup>4</sup> Mode	l c <sup>5</sup> Discordant	Model a <sup>3</sup>	Model b <sup>4</sup>	Model c <sup>5</sup>	Discordant	

		-							
	Model a <sup>3</sup>	Model b⁴	Model c⁵	Discordant twin pairs <sup>1, 4</sup>	Model a <sup>3</sup>	Model b⁴	Model c⁵	Discordant twin pairs <sup>2, 4</sup>	
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 ${\sf T_0}^6$ but not during year 1-2 after ${\sf T_0}^7$	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)	

<sup>1</sup> Twin pairs where one had an SA during the follow-up and the other not (n=542)

<sup>2</sup> Twin pairs where one had a long-term SA during the follow-up and the other not (n=184)

<sup>3</sup> Adjusted for birth year

<sup>4</sup> Model a, and additional adjustments for delivery year, and educational level

<sup>5</sup> Model b, and additional adjustments for subsequent deliveries

<sup>6</sup> During the period 1-5 years prior to T<sub>0</sub>

<sup>7</sup> Diagnoses O00-O99 excluded

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STRODE Statement	—Chec	is the statist of items that should be included in reports of <i>conort studies</i>
	Item No	Decommondation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the a
The and abstract	1	Page 1
		(b) Provide in the abstract an informative and balanced summary of what was
		and what was found
		Page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being rep
		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 recruit
		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	1	Clearly define all outcomes, exposures, predictors, potential confounders, and
		modifiers. Give diagnostic criteria, if applicable
Data sources/	Q*	Fage 9-10
measurement	0	assessment (measurement). Describe comparability of assessment methods if
measurement		more than one group
		Page 8-11
Bias	9	Describe any efforts to address potential sources of bias
2100	-	N/A
Study size	10	Explain how the study size was arrived at
5		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 confou
		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

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		N/A
		( <u>e</u> ) 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)
		NA
Outcome data	15*	Report numbers of outcome events or summary measures over time
	16	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their meeting (applicable, confidence interval). Make clear which confounder-adjusted estimates and
		adjusted for and why they were included
		Bage 24.25
		(b) Papart astagary boundaries when continuous variables were estagarized
		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
Disaussian		
Key results	18	Summarise key results with reference to study objectives
Key results	10	Page 2. 4 and nage 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,
1		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.