

# Socio-demographic characteristics of women sustaining injuries during pregnancy: a study from the Danish National Birth Cohort

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## ABSTRACT

**Objectives:** To describe adverse birth outcomes associated with hospital-treated injuries that took place among women in the Danish National Birth Cohort.

**Design:** Longitudinal cohort study.

**Setting:** Denmark.

**Participants:** 90 452 women and their offspring selected from the Danish National Birth Cohort.

**Primary and secondary outcome measures:** To determine if injured women were more likely to deliver an infant preterm, with low birth weight, stillborn or have a spontaneous abortion, the authors estimated HRs. ORs were generated to assess APGAR scores and infants born small for gestational age (SGA). Models were adjusted for maternal smoking and drinking during pregnancy, household socioeconomic status, eclampsia/pre-eclampsia or gestational diabetes status during pregnancy and maternal age at birth; estimates for preterm birth were also adjusted for prior history of preterm birth.

**Results:** In the cohort of 90 452 pregnant women, 3561 (3.9%) received medical treatment for an injury during pregnancy. Injured pregnant women were more likely to deliver infants that were stillborn or have pregnancies terminated by spontaneous abortion. The authors did not detect an adverse effect between injuries sustained during pregnancy and delivery of preterm, low birth weight or SGA infants, or infants with an APGAR score of <7.

**Conclusions:** The study shows that injuries occurring among women from an unselected population may not have an adverse effect on birth weight, gestational age, APGAR score or SGA status but may adversely affect the risk of stillbirth and spontaneous abortions in some situations.

## INTRODUCTION

During pregnancy, up to 7% of women sustain unintentional injuries,<sup>1</sup> and traumatic injuries are a major cause of maternal and neonatal morbidity and mortality.<sup>2-3</sup> The association of complications arising from blunt trauma in the presence of bleeding and contractions are evident, but less is known

## ARTICLE SUMMARY

### Article focus

- We describe adverse birth outcomes associated with injuries that took place among pregnant women in the Danish National Birth Cohort and include in our assessment injury severity, cause and mechanism.

### Key messages

- Injured pregnant women were more likely to deliver infants that were stillborn or have pregnancies that were terminated by spontaneous abortion. We did not detect an adverse effect between injuries sustained during pregnancy and delivery of preterm, low birth weight or SGA infants, or infants with an APGAR score of <7.
- Women sustaining head or neck injuries were more likely to deliver an infant SGA and have a stillbirth, though these results were not statistically significant.

### Strengths and limitations of this study

- Previous studies have selected pregnant trauma patients or emergency room patients; our study, however, presents injuries among pregnant women from a general population.
- We only have data on late spontaneous abortions, and if injured fetuses are aborted early, we would not detect an association.

about adverse birth outcomes linked to minor injuries. It is possible that minor trauma during pregnancy may lead to subclinical chronic placental disruption that persists during pregnancy, which may cause an increase in the risk for acute placental abruption, preterm labour, preterm premature rupture of the membranes and placental insufficiency that restricts fetal growth.<sup>4</sup> But we know less about the occurrence of minor injuries as they are not captured the same way as severe injuries, and the impact they have on the fetus is expected to be small or not harmful. Not much is known about the

context in which these injuries take place and the socio-demographic characteristics of women sustaining these injuries, and furthermore, there are limited data on long-term consequences of these injuries for the offspring. In this paper, we describe adverse birth outcomes associated with hospital-treated injuries that took place among women in the Danish National Birth Cohort (DNBC) and we include in our assessment injury severity, cause and mechanism.

## METHODS

We used data collected from the DNBC, which is a longitudinal population-based cohort of pregnant women and their offspring established during 1996–2002. During these years, women were contacted to take part in the study by physicians providing their primary care during pregnancy. Approximately half of all general practitioners in Denmark participated in the study, and approximately 60% of women who were invited participated. Additional information on study design and data collection methods for the DNBC are described elsewhere.<sup>5</sup> Information was collected twice during pregnancy using computer-assisted telephone interviews, at gestational age 12 and 30 weeks, and again when the children reached 6 and 18 months of age. All Regional Ethics Committee in Denmark approved the establishment of the cohort, and this study was further approved by the Danish Data Protection Agency and UCLA Office for Protection of Research Subjects.

To obtain information regarding birth outcomes, data for each woman were linked through her personal civil registration number to the Danish National Birth Registry and the Danish National Patient Registry for the entire pregnancy period. The Danish National Birth Registry has collected data since 1968 for the primary purpose of monitoring the health of newborns and the quality of antenatal care and has been increasingly used for research.<sup>6</sup> The gestational age at birth and birth weight was obtained from the Birth Register. Small for gestational age (SGA) was defined as a weight below the 10th percentile for gestational age, grouped by week, among children born in the DNBC.

Information regarding injuries sustained during pregnancy was obtained from the Danish National Patient Registry, which contains data on all hospital stays and outpatient visits for the duration of each woman's pregnancy. For each admission or visit, the patient registry collects information on the primary discharge diagnosis (the discharge diagnosis that best describes the condition leading to the admission or outpatient visit and that is the primary reason for the prescribed and completed course of tests and treatments) and up to 20 subsidiary diagnoses. It also collects information on external cause of injury, including the mode, location and mechanism causing the injury. Data were extracted for the entire study period (1996–2002) with the use of *International Classification of Diseases, 10th Revision (ICD Website, 2007)*<sup>7</sup> and the second edition of the Nordic

Medico-Statistical Committee's (NOMESCO) Classification of External Causes of Injuries (NCECI).<sup>8</sup>

We identified 90 452 women who completed the first interview. All injuries were classified by the body location and mechanism causing the injury; transportation injuries were further described by mode of transportation. Women were categorised as injured if they sustained an injury at any point during pregnancy, regardless of mode, body region and mechanism causing the injury, and uninjured otherwise.

To determine if injured women were more likely to deliver preterm (<34 weeks, 34–36 weeks, ≥37 weeks), low birth weight (<1500, 1500–2499, ≥2500 g), stillbirth or have a spontaneous abortion, we estimated Cox proportional HRs, using PROC PHREG in SAS Statistical Software (version 9.2), to allow for a time-to-event analysis. These models were adjusted for maternal smoking and drinking during pregnancy, household socioeconomic status, eclampsia/pre-eclampsia or gestational diabetes status during pregnancy and maternal age at birth; estimates for preterm birth were also adjusted for prior history of preterm birth. To determine if injured women were more likely to deliver SGA infants or infants with an APGAR score of <3 or between 4–6 using ≥7 as a baseline, we generated ORs using PROC GENMOD in SAS statistical software. Approximately 8% of women in the study participated more than once. Repeated subject statement was entered into each statistical model. To assess severity of injuries sustained, we compared women who sustained head and head and neck injuries with uninjured women.

## RESULTS

In our cohort of 90 452 pregnant women, 3561 (3.9%) received medical treatment for an injury during their pregnancy. Socio-demographic characteristics of all women in the cohort are presented in [table 1](#). Results have been stratified by presence/absence of injury. Injured women were younger, smoked cigarettes more often and had lower household socioeconomic status. Maternal age, parity, smoking status, alcohol consumption, household socioeconomic status and partner cohabitation status were statistically different in the injured versus non-injured groups (p values <0.05 were calculated by  $\chi^2$  test). Injury characteristics such as mode of injury, activity engaged in while sustaining injury, mechanism causing injury and body region of injury are presented in [table 2](#). Approximately one-third of the injuries were due to falls and took place during a leisure activity. Less than one-fifth of the injuries were related to transportation. HR and OR are presented in [table 3](#). We found that injured pregnant women were slightly more likely to deliver infants that were stillborn or have pregnancies that were terminated by spontaneous abortion. We did not detect an adverse effect between injuries sustained during pregnancy and delivery of preterm, low birth weight or SGA infants, or infants with an APGAR score of <7.

**Table 1** Demographic statistics on study population stratified by injury status and department of hospital admittance

Characteristics	Total cohort			
	All (N=90 452), n (%)	Non-injured (n=86 891), n (%)	Injured* ‡ (n=3561), n (%)	Head or neck injuries (n=534), n (%)
Maternal age at delivery (years)				
<25	8695 (9.6)	8142 (9.4)	553 (15.5)	86 (16.1)
25–29	34 726 (38.4)	33 341 (38.4)	1385 (38.9)	194 (36.3)
30–34	33 537 (37.1)	32 392 (37.3)	1145 (32.2)	180 (33.7)
35–39	12 006 (13.3)	11 594 (13.3)	412 (11.6)	63 (11.8)
≥40	1488 (1.6)	1422 (1.6)	66 (1.9)	11 (2.1)
Gestational age at delivery (weeks)				
<34	1227 (1.5)	1177 (1.4)	50 (1.5)	9 (1.8)
34–36	2756 (3.2)	2629 (3.2)	127 (3.8)	20 (4.0)
≥37	82 642 (95.3)	79 454 (95.4)	3188 (94.7)	475 (94.2)
Birth weight (g)				
<1500	538 (0.6)	538 (0.6)	18 (0.5)	4 (0.8)
1500–2499	2074 (2.5)	2074 (2.5)	101 (3.0)	15 (3.0)
≥2500	80 451 (96.9)	80 451 (96.9)	3238 (96.5)	484 (96.2)
Sex of child				
Female	42 284 (48.8)	40 696 (48.8)	1588 (47.2)	236 (46.8)
Male	44 435 (51.2)	42 656 (51.2)	1779 (52.8)	268 (53.2)
Parity				
1	39 224 (46.3)	37 569 (47.2)	1655 (50.7)	238 (48.1)
2	31 604 (37.3)	30 463 (38.3)	1141 (35.0)	192 (38.8)
3+	13 859 (16.4)	11 593 (14.6)	466 (14.3)	65 (13.1)
Smoking status				
None	64 589 (73.4)	62 299 (73.7)	2290 (66.7)	344 (67.3)
Stopped during pregnancy	12 530 (14.2)	11 923 (14.1)	607 (17.7)	91 (17.8)
1–10	10 725 (12.2)	10 193 (12.1)	532 (15.5)	76 (14.9)
≥10	120 (0.1)	117 (0.1)	3 (0.1)	0 (0)
Average alcohol consumption (drinks/week)				
None	41 325 (64.9)	39 642 (64.7)	1683 (68.8)	270 (34.3)
1	10 480 (16.5)	10 124 (16.5)	356 (14.5)	466 (59.2)
2	6872 (10.8)	6649 (10.9)	223 (9.1)	29 (3.7)
3	2554 (4.0)	2462 (4.0)	92 (3.8)	7 (0.9)
4+	2442 (3.8)	2351 (3.8)	91 (3.7)	15 (1.977)
≥5 at one time	26 779 (30.8)	25 663 (29.5)	1116 (31.3)	167 (31.2)
Household socioeconomic status				
Higher grade professionals	20 713 (23.5)	19 989 (23.6)	724 (21.1)	126 (24.7)
Middle-grade professionals	27 304 (31.0)	26 326 (31.1)	978 (28.5)	135 (26.4)
Skilled work	24 577 (27.9)	23 587 (27.9)	990 (28.8)	143 (28.0)
Unskilled work	12 408 (14.1)	11 804 (14.0)	604 (17.6)	83 (16.2)
Student	2075 (2.4)	1991 (2.4)	84 (2.4)	11 (2.2)
Unemployed >1 year	683 (0.8)	641 (0.8)	42 (1.2)	9 (1.8)
Unclassified	204 (0.2)	194 (0.2)	10 (0.3)	4 (0.8)
Partner cohabitation status				
Cohabits	66 859 (99.0)	64 359 (98.1)	2500 (98.1)	353 (98.1)
Does not cohabit	687 (1.0)	639 (1.9)	48 (1.95)	7 (1.95)
Place of delivery				
Urban†	48 570 (53.7)	46 681 (53.0)	1889 (53.0)	274 (51.3)
Rural	41 882 (46.3)	40 210 (47.0)	1672 (47.0)	260 (48.7)
Outcome				
Low birth weight (<2500 g)	2731 (3.0)	2612 (3.0)	119 (3.8)	19 (3.6)
Preterm birth (<37 weeks)	3886 (4.3)	3715 (4.3)	171 (4.8)	29 (5.4)
Small for gestational age	8528 (9.4)	8162 (9.4)	336 (9.4)	59 (11.0)
Spontaneous abortion	33 55 (3.7)	3181 (3.7)	174 (4.9)	27 (5.1)
Stillbirth	288 (0.3)	271 (0.3)	17 (0.5)	3 (0.6)
APGAR score <7	605 (0.7)	586 (0.7)	19 (0.5)	1 (0.2)

\*p Values <0.05 stratified by injury status and calculated by  $\chi^2$  test: maternal age, parity, maternal smoking, alcohol consumption, household socioeconomic status and partner cohabitation status.

†Urban residence includes Aarhus, Gentofte, Fredericksburg, Odense, Aalborg.

‡Missing values: gestational age =184, birth weight =389, sex of child =90, parity =5765, smoking =1155, cohabitation status =22920.

**Table 2** Description of injuries

	n (%)
Mode of injury	
Knock, blow due to bodily contact with object/animal/person	975 (27)
Crushing/cut/sting	621 (17)
Knock, blow caused by fall on the same level	519 (15)
Knock, blow caused by fall on stairway/lower level	381 (11)
Acute overload of the whole or part of the body	331 (9)
Foreign object	115 (3)
Thermal/electrical impact or radiation	55 (2)
Chemical influence	28 (1)
Other/unspecified cause of injury	74 (2)
Activity during injury	
Play, hobby and other leisure activity	913 (26)
Work	545 (15)
Vital activity*	300 (8)
Sport, exercise	185 (5)
Unpaid work	161 (5)
Other activity/unspecified	765 (21)
Description of transportation injuries	
Car	351 (66)
Bicycle	131 (25)
Moped/motorbike/scooter	21 (4)
On foot	12 (2)
Delivery van/truck/bus or other	10 (2)
Other/unspecified transportation	7 (1)

\*Includes sleep, rest, taking meals and personal hygiene.

**DISCUSSION**

Our study shows that injuries occurring in an unselected Danish population of pregnant women do not adversely

affect birth weight, gestational age, APGAR scores or SGA status but are adversely associated with stillbirth and spontaneous abortion. Adverse pregnancy outcomes resulting from maternal injury have been documented in other studies.<sup>9–25</sup> Severely injured pregnant women are more likely to have preterm labour, placental abruption, cesarean section, uterine rupture, low birth weight and their infants are more likely to result in preterm delivery and suffer from fetal distress, asphyxia, respiratory distress syndrome and circum to fetal, neonatal and infant death compared with their uninjured counterparts.<sup>14</sup> Minor trauma has also been recognised as contributor to poor fetal outcomes. Fischer *et al*<sup>26</sup> found that minor injuries were associated with fetal demise, preterm birth and low birth weight. We were not able to corroborate these findings, possibly due to the nature of the healthcare system in Denmark, where the first point of medical intervention is often with a primary care physician. It is possible that we missed detection of injuries seen by midwives or the primary care physician, which restrict our effect estimates to more severe outcomes.

Our results may not apply to other healthcare settings. This study is based on a Danish population, which has low fertility and where most women take part in the work force. Furthermore, duration of pregnancy leave is generous, compensated and accesses to healthcare services are covered at no cost to patients. In this study, we were able to assess socio-demographic characteristics of this population, and our data show that injured women were slightly younger than their non-injured counterparts. Trends in household socioeconomic status also seemed to differ slightly; there were fewer injured women with higher grade professional household status

**Table 3** OR and HR and 95% confidence limits for adverse birth outcomes following maternal exposure to injuries during pregnancy\*

Outcome	Non-injured women (N=86 891)	Injured women (N=3561)	Women with head or neck injuries (N=534)	Women with head injuries (N=312)
Small for gestational age†	Reference	1.06 (0.95 to 1.18)	1.15 (0.88 to 1.52)	1.18 (0.84 to 1.64)
Spontaneous abortion‡	Reference	1.18 (0.99 to 1.40)	1.02 (0.68 to 1.53)	0.93 (0.60 to 1.44)
Stillbirth‡	Reference	1.67 (1.01 to 2.77)	2.08 (0.67 to 6.50)	3.17 (1.02 to 9.88)
Low birth weight (g)†				
<1500	–	0.76 (0.48 to 1.24)	0.89 (0.22 to 3.57)	0.83 (0.12 to 5.95)
1500–2499	–	1.05 (0.90 to 1.23)	1.12 (0.67 to 1.89)	1.09 (0.70 to 1.71)
≥2500	–	Reference	Reference	Reference
Preterm birth‡				
<34 weeks	–	0.77 (0.39 to 1.48)	0.89 (0.22 to 3.57)	0.92 (0.13 to 6.60)
34–36 weeks	–	1.05 (0.90 to 1.23)	0.99 (0.68 to 1.45)	1.35 (0.86 to 2.12)
≥37 weeks	–	Reference	Reference	Reference
APGAR score†				
≤3	–	1.15 (0.93 to 1.40)	Not enough data	Not enough data
4–6	–	0.78 (0.47 to 1.31)	Not enough data	Not enough data
7–10	–	Reference	Reference	Reference

\*All models were adjusted for eclampsia/pre-eclampsia and gestational diabetes status during pregnancy, maternal smoking and drinking during pregnancy, household socioeconomic status, and maternal age at birth, preterm birth model includes all aforementioned variables and history of preterm birth; non-injured women were used as the comparison group.

†ORs.  
‡HRs.

and more injured women with unskilled work status compared with their non-injured counterparts. Injured women were also slightly more likely to smoke cigarettes and consume three or more alcoholic drinks per week. The high prevalence of binge drinking in the DNBC occurred often at very early stage of pregnancy, when pregnancy status may be uncertain or unknown to the mother. Nine of 10 traumatic injuries during pregnancy are minor; however, 60%–70% of fetal losses during pregnancy have been reported as a result of minor injuries.<sup>17</sup> In this study, we only have data on late spontaneous abortions, and if injured fetuses are aborted early, it may explain why we detect limited associations among newborns.

Future studies should focus on long-term infant outcomes that extend beyond the perinatal period to fully assess the effects of maternal injury. Additional research evaluating maternal characteristics that may influence injury severity and proneness may aid in maternal injury prevention. At present, it is reassuring that even women hospitalised for an injury during pregnancy will in only a few cases have an excess risk of having an adverse pregnancy outcome.

**Contributors** JV, JO and PH contributed to conception and design of the paper. JO contributed to acquisition of data. JV and PH contributed to analysis of the data. JV, JO and PH contributed to interpretation of data. JV wrote the original paper draft; JO and PH contributed to revisions of the paper. JV, JO and PH approved the final version of the paper to be published.

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**Competing interests** None.

**Ethics approval** Ethics approval was provided by the Danish Data Protection Agency and the UCLA Office for Protection of Research Subjects.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** Data from the Danish National Birth Cohort are available to research institutions. Additional information can be found at: <http://www.ssi.dk/English/RandD/Epidemiology/DNBC/>

## REFERENCES

- Chames MC, Pearlman MD. Trauma during pregnancy: outcomes and clinical management. *Clin Obstet Gynecol* 2008;51:398–408.
- Oxford CM, Ludmir J. Trauma in pregnancy. *Clin Obstet Gynecol* 2009;52:611–29.
- Mirza FG, Devine PC, Gaddipati S. Trauma in pregnancy: a systematic approach. *Am J Perinatol* 2010;27:579–86.
- Melamed N, Aviram A, Silver M, *et al.* Pregnancy course and outcome following blunt trauma. *J Matern Fetal Neonatal Med*. Published Online First: 1 February 2012. doi:10.3109/14767058.2011.648243
- Olsen J, Melbye M, Olsen SF, *et al.* The Danish National Birth Cohort—its background, structure and aim. *Scand J Public Health* 2001;29:300–7.
- Virk J, Zhang J, Olsen J. Medical abortion and the risk of subsequent adverse pregnancy outcomes. *N Engl J Med* 2007;357:648–53.
- International Classification of Diseases (ICD) Online*. Geneva: World Health Organization. <http://www.who.int/classifications/icd/en/> (accessed 20 Jul 2007).
- Nordic Medico-Statistical Committee's (NOMESCO) Classification of External Causes of Injuries (NCECI)*. Nordic Medico-Statistical Committee. Copenhagen, 1990.
- Schiff MA, Holt VL, Daling JR. Maternal and infant outcomes after injury during pregnancy in Washington State from 1989 to 1997. *J Trauma* 2002;53:939–45.
- Ikossi DG, Lazar AA, Morabito D, *et al.* Profile of mothers at risk: an analysis of injury and pregnancy loss in 1,195 trauma patients. *J Am Coll Surg* 2005;200:49–56. Erratum in: *J Am Coll Surg* 2005;200:482.
- Weiss HB, Lawrence B, Miller T. Prevalence and risk of hospitalized pregnant occupants in car crashes. *Annu Proc Assoc Adv Automot Med* 2002;46:355–66.
- Weiss HB, Strotmeyer S. Characteristics of pregnant women in motor vehicle crashes. *Inj Prev* 2002;8:207–10.
- Schiff MA, Holt VL. Pregnancy outcomes following hospitalization for motor vehicle crashes in Washington State from 1989 To 2001. *Am J Epidemiol* 2005;161:503–10.
- El-Kady D, Gilbert WM, Anderson J, *et al.* Trauma during pregnancy: an analysis of maternal and fetal outcomes in a large population. *Am J Obstet Gynecol* 2004;190:1661–8.
- Hitosugi M, Motozawa Y, Kido M, *et al.* Traffic injuries of the pregnant women and fetal or neonatal outcomes. *Forensic Sci Int* 2006;159:51–4.
- Hyde LK, Cook LJ, Olson LM, *et al.* Effect of motor vehicle crashes on adverse fetal outcomes. *Obstet Gynecol* 2003;102:279–86.
- El Kady D. Perinatal outcomes of traumatic injuries during pregnancy. *Clin Obstet Gynecol* 2007;50:582–91.
- El Kady D, Gilbert WM, Xing G, *et al.* Maternal and neonatal outcomes of assaults during pregnancy. *Obstet Gynecol* 2005;105:357–63.
- El Kady D, Gilbert WM, Xing G, *et al.* Association of maternal fractures with adverse perinatal outcomes. *Am J Obstet Gynecol* 2006;195:711–16.
- Gandhi SG, Gilbert WM, McElvy SS, *et al.* Maternal and neonatal outcomes after attempted suicide. *Obstet Gynecol* 2006;107:984–90.
- Lipsky S, Holt VL, Easterling TR, *et al.* Police-reported intimate partner violence during pregnancy and the risk of antenatal hospitalization. *Matern Child Health J* 2004;8:55–63.
- Patterson RM. Trauma in pregnancy. *Clin Obstet Gynecol* 1984;27:32–8.
- Shah KH, Simons RK, Holbrook T, *et al.* Trauma in pregnancy: maternal and fetal outcomes. *J Trauma* 1998;45:83–6.
- Weiss HB, Songer TJ, Fabio A. Fetal deaths related to maternal injury. *JAMA* 2001;286:1863–8.
- Weiss HB, Sauber-Schatz EK, Cook LJ. The epidemiology of pregnancy-associated emergency department injury visits and their impact on birth outcomes. *Accid Anal Prev* 2008;40:1088–95.
- Fischer PE, Zarzaur BL, Fabian TC, *et al.* Minor trauma is an unrecognized contributor to poor fetal outcomes: a population-based study of 78,552 pregnancies. *J Trauma* 2011;71:90–3.

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

	<b>Item No</b>	<b>Recommendation</b>
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses
<b>Results</b>		
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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
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 (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
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

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.