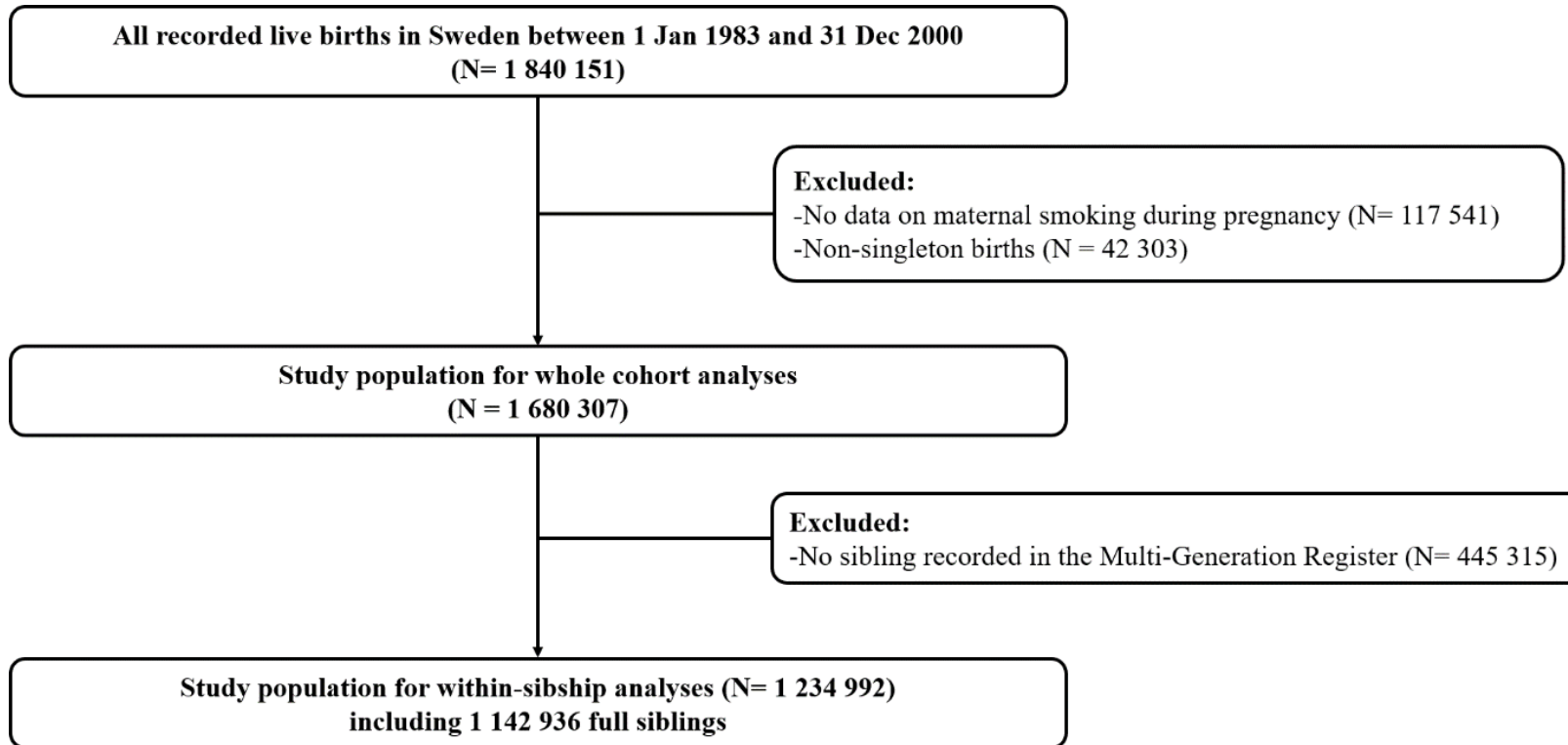
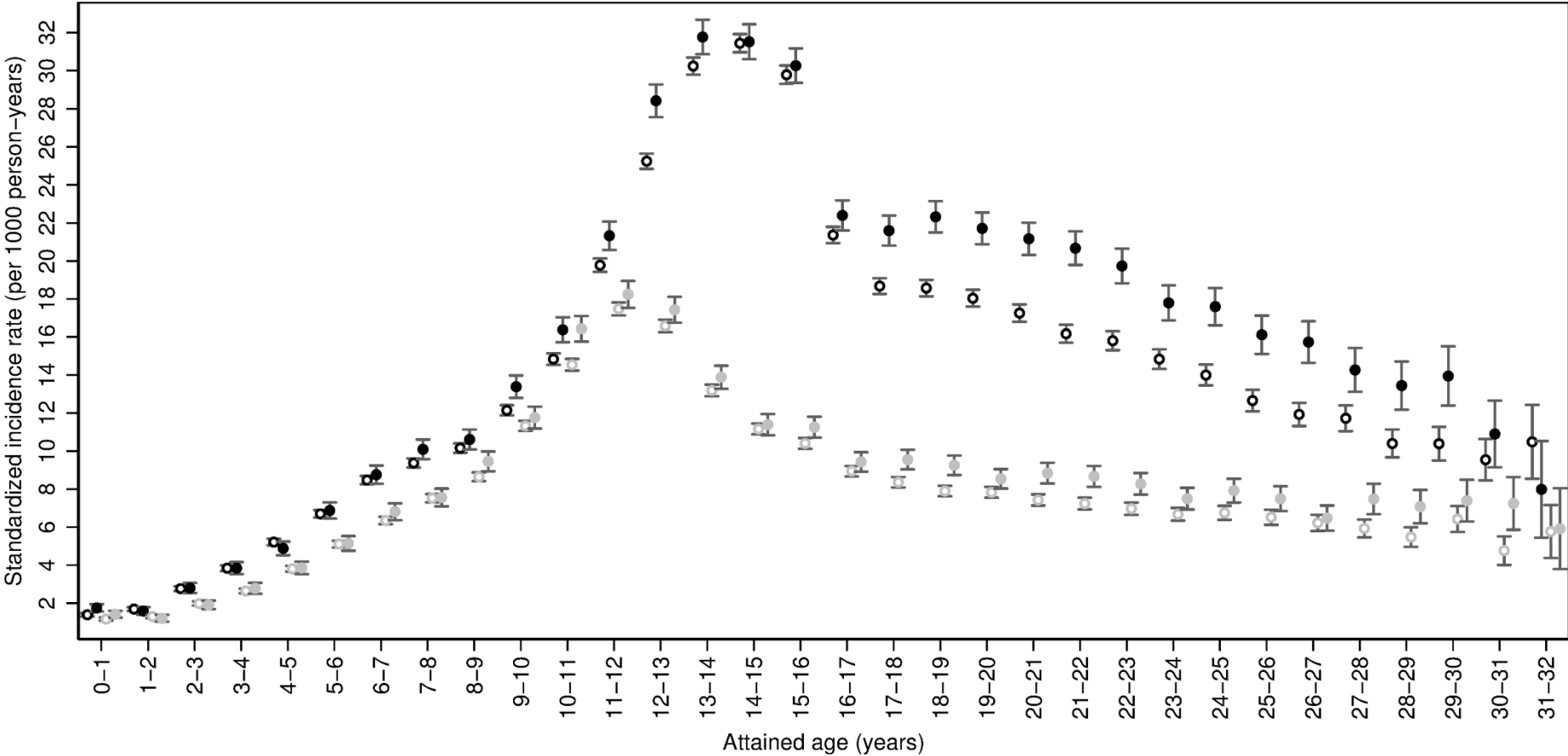


Supplementary Figure 1. Flow chart of the study population.



Supplementary Figure 2. Standardised incidence rates of bone fractures by attained age in male and female offspring exposed and unexposed to maternal smoking during pregnancy.



Incidence rates (per 1000 person-years) are standardised by calendar year of birth and stratified by attained age in males (black circles) and females (grey circles) separately. Incidence rates (95% confidence intervals) of fractures in offspring are for those whose mothers did smoke (filled circles) and did not smoke (open circles) during pregnancy.

Supplementary Methods

Description of Swedish registers used in this study

For this study, the data are from national Swedish registers. Each resident in Sweden is assigned a unique personal identification number which allows data linkage across the registers used here. The Medical Birth Register includes maternal, obstetric and neonatal data for > 98% of all births in Sweden since 1973.¹ The Multi-Generation Register includes information on familial relationships for all individuals born since 1932, such that siblings, parents and offspring can be identified.² The Total Population Register includes dates of birth, death, and migration since 1915.³ The Cause of Death Register is a virtually complete register of all deaths in Sweden since 1961.⁴ The National Patient Register was established in 1964 and has covered all inpatient hospital admissions since 1987 and outpatient physician visits since 2001.⁵ Diagnoses in the National Patient Register are coded according to Swedish versions of the International Classification of Diseases (ICD-8 from 1969 to 1986, ICD-9 from 1987 to 1996 and ICD-10 since 1997) and have been demonstrated to be of high validity with the reported positive predictive value for most diagnoses of 85-95%.⁵ Socioeconomic variables are registered in LISA (the Swedish acronym for the Longitudinal Integration Database for Health Insurance and Labour Market Studies),⁶ which is managed by Statistics Sweden. Using these data sources, we identified 1 680 307 singleton live births in Sweden between 1 January 1987 and 31 December 2000 with complete data on maternal smoking during pregnancy. For the sibling comparison analysis, we used a subset of the cohort comprising 1 234 992 individuals born to 531 884 mothers identified through the Multi-Generation Register. Follow-up in this cohort was up until 31 December 2014.

Analyses

The following variables were included as potential confounders in whole cohort analyses: year of birth (1983, 1984, 1985, 1986, 1987, 1988, 1989, 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000), sex, maternal age at birth (< 20, 20-24, 25-29, 30-34, ≥ 35 years), maternal height (< 155, 155-164, 165-174, ≥ 175 cm), maternal body mass index (< 18.5, 18.5-24.9, 25.0-29.9, ≥ 30.0 kg/m²), maternal parity (at the time of the index pregnancy, nulliparous, 1, 2, ≥ 3), maternal educational level (compulsory up to 9 years, secondary, post-secondary), maternal occupational classification (low, intermediate, high), parental marital status (unmarried, married, divorced/widow), paternal educational level (compulsory up to 9 years, secondary, post-secondary), paternal occupational classification (low, intermediate, high). We used stratified Cox models with a separate stratum for each family identifier to obtain within-sibship estimates. These within-sibship analyses were adjusted for the same covariates as the multivariable analysis in the whole cohort but excluding maternal height, a variable that is unlikely to vary among siblings in the same family.

To explore the extent to which associations were explained by small size at birth, models were additionally adjusted for gestational age at birth (in weeks) and birth weight for gestational age (in percentiles).

Handling of missing covariate data

In total, 569 526 offspring (34%) had missing data on one or more covariates, which was mainly due to missing information on early pregnancy maternal BMI and height (31%). This is because maternal weight and height were not routinely recorded in women who were pregnant before 1992. Primary analyses were based on complete case data, but we also conducted sensitivity analyses with multiple imputation of missing covariate data. Missing covariate data were imputed under the ‘missing at random assumption’ using multivariate multiple imputation with chained equations ⁷, and 10 imputed datasets were generated. The imputation model included the exposure (no daily smoking, < 10 cigarettes/day, ≥ 10 cigarettes/day), the outcome (i.e. Nelson-Aalen estimator of the baseline cumulative hazard and event indicator), all covariates included in the multivariable adjusted model (i.e. birth year, offspring sex, maternal age, parity,

height, body mass index, parental education, occupation and marital status) and other predictors that were not included in the main analysis model but were associated with some missing data (gestational age at birth and birth weight for gestational age).

References

- 1 National Board of Health and Welfare. The Swedish Medical Birth Register - A summary of Content and Quality. Stockholm: Centre for Epidemiology, 2003. <https://www.socialstyrelsen.se/en/statistics-and-data/registers/register-information/the-swedish-medical-birth-register/> accessed 29 November 2019.
- 2 Ekblom A. The Swedish Multi-generation Register. *Methods Mol Biol* 2011;675:215-20 doi:10.1007/978-1-59745-423-0_10 [doi].
- 3 Ludvigsson JF, Almqvist C, Bonamy AK, et al. Registers of the Swedish total population and their use in medical research. *Eur J Epidemiol* 2016;31:125-36 doi:10.1007/s10654-016-0117-y [doi].
- 4 Brooke HL, Talback M, Hornblad J, et al. The Swedish cause of death register. *Eur J Epidemiol* 2017;32:765-73 doi:10.1007/s10654-017-0316-1 [doi].
- 5 Ludvigsson JF, Andersson E, Ekblom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health* 2011;11:450,2458-11-450 doi:10.1186/1471-2458-11-450 [doi].
- 6 Ludvigsson JF, Svedberg P, Olen O, et al. The longitudinal integrated database for health insurance and labour market studies (LISA) and its use in medical research. *Eur J Epidemiol* 2019;34:423-37 doi:10.1007/s10654-019-00511-8 [doi].
- 7 White IR, Royston P. Imputing missing covariate values for the Cox model. *Stat Med* 2009;28:1982-98 doi:10.1002/sim.3618 [doi].

Supplementary Table 1. International classification of diseases (ICD) codes for bone fractures.

ICD-8 and 9	Description
800-804	Fracture of skull and facial bones
805-806	Fracture of vertebral column
807	Fracture of rib(s), sternum, larynx, and trachea
808	Fracture of pelvis
809	Ill-defined fractures of bones of trunk
810	Fracture of clavicle
811	Fracture of scapula
812	Fracture of humerus
813	Fracture of radius and ulna
814	Fracture of carpal bone(s)
815	Fracture of metacarpal bone(s)
816	Fracture of one or more phalanges of the hand
817	Multiple fractures of hand bones
818	Ill-defined fractures of upper limb
819	Multiple fractures involving both upper limbs, and upper limb with rib(s) and sternum
820-821	Fracture of femur
822	Fracture of patella
823	Fracture of tibia and fibula
824	Fracture of ankle
825	Fracture of one or more tarsal and metatarsal bones
826	Fracture of one or more phalanges of foot
827	Other, multiple, and ill-defined fractures of lower limb
828	Multiple fractures involving both lower limbs, lower with upper limb, and lower limb(s) with rib(s) and sternum
829	Fracture of unspecified bones
ICD-10	Description
S02	Fracture of skull and facial bones
S12	Fracture of neck
S22	Fracture of rib(s), sternum and thoracic spine
S32	Fracture of lumbar spine and pelvis
S42	Fracture of shoulder and upper arm including humerus
S52	Fracture of forearm including radius and ulna

S62	Fracture at wrist and hand level
S72	Fracture of femur
S82	Fracture of lower leg including ankle (including tibia and fibula)
S92	Fracture of foot, except ankle
T02	Fractures involving multiple body regions
T08	Fracture of spine, level unspecified
T10	Fracture of upper limb, level unspecified
T12	Fracture of lower limb, level unspecified

Supplementary Table 2. Diagnostic codes for bone fractures by anatomical site and mechanism of injury.

Fractures	ICD-8-9	ICD-10
Anatomical site		
Skull and face	800-804	S02
Neck and trunk	805-809	S12, S22, S32, T08
Upper extremity	810-818	S42, S52, S62, T10
-shoulder and upper arm	810-812	S42
-forearm	813	S52
-wrist and hand	814-817	S62
-unspecified	818	T10
Lower extremity	820-827	S72, S82, S92, T12
-femur	820-821	S72
-lower leg and ankle	822-824	S82
-foot	825-826	S92
-unspecified	827	T12
Other	819, 828, 829	T02
Mechanism of injury *		
Non-intentional	E80-E92	V01-V99, W00-X59
Assault	E96	X85-X99, Y00-Y09
Other	Any external cause code except those listed under non-intentional and assault	Any external cause code except those listed under non-intentional and assault

*External cause codes for defining the mechanism of injury are not available for fractures recorded in the Medical Birth Register.

Supplementary Table 3. Bone fractures by anatomical site and mechanism of injury in all offspring and those with and without siblings, overall and stratified by attained age.

	N (%)				
	Overall	0 to < 1 yr	1 to < 5 yrs	5 to < 15 yrs	≥ 15 yrs
Fractures – all offspring					
Anatomical site					
Skull and face	27480 (7.3)	1176 (52.2)	1308 (6.9)	7471 (3.5)	17525 (12.0)
Neck and trunk	12241 (3.2)	52 (2.3)	155 (0.8)	3132 (1.5)	8902 (6.1)
Upper extremity					
-shoulder and upper arm	47724 (12.6)	309 (13.7)	4978 (26.1)	29926 (14.2)	12511 (8.6)
-forearm	91049 (24.1)	30 (1.3)	3833 (20.1)	65906 (31.2)	21280 (14.6)
-wrist and hand	89678 (23.7)	34 (1.5)	1146 (6.0)	43726 (20.7)	44772 (30.8)
-unspecified	132 (0.0)	8 (0.4)	28 (0.1)	66 (0.0)	30 (0.0)
Lower extremity					
-femur	6997 (1.9)	468 (20.8)	2095 (11.0)	2955 (1.4)	1479 (1.0)
-lower leg and ankle	43495 (11.5)	92 (4.1)	3137 (16.4)	22367 (10.6)	17899 (12.3)
-foot	33316 (8.8)	3 (0.1)	892 (4.7)	16333 (7.7)	16088 (11.1)
-unspecified	66 (0.0)	3 (0.1)	18 (0.1)	31 (0.0)	14 (0.0)
Other	25792 (6.8)	78 (3.5)	1488 (7.8)	19148 (9.1)	5078 (3.5)
Mechanism of injury *					
Non-intentional	322246 (85.3)	1791 (79.5)	15831 (83.0)	177620 (84.2)	127004 (87.2)
Assault	6387 (1.7)	43 (1.9)	17 (0.1)	438 (0.2)	5889 (4.0)
Other	46993 (12.4)	76 (3.4)	2877 (15.1)	31638 (15.0)	12402 (8.5)
Unknown	2344 (0.6)	343 (15.2)	353 (1.9)	1365 (0.6)	283 (0.2)
Fractures – offspring with siblings					
Anatomical site					
Skull and face	20379 (7.2)	876 (52.2)	946 (7.2)	5614 (3.5)	12943 (11.8)
Neck and trunk	9019 (3.2)	34 (2.0)	115 (0.9)	2310 (1.4)	6560 (6.0)
Upper extremity					
-shoulder and upper arm	35756 (12.6)	227 (13.5)	3319 (25.2)	22528 (14.1)	9682 (8.8)
-forearm	68886 (24.2)	20 (1.2)	2587 (19.7)	49959 (31.2)	16320 (14.9)
-wrist and hand	68265 (24.0)	30 (1.8)	798 (6.1)	33793 (21.1)	33644 (30.7)
-unspecified	98 (0.0)	6 (0.4)	22 (0.2)	46 (0.0)	24 (0.0)
Lower extremity					
-femur	5222 (1.8)	356 (21.2)	1579 (12.0)	2155 (1.3)	1132 (1.0)
-lower leg and ankle	32473 (11.4)	72 (4.3)	2174 (16.5)	16753 (10.5)	13474 (12.3)
-foot	24838 (8.7)	2 (0.1)	567 (4.3)	12325 (7.7)	11944 (10.9)
-unspecified	47 (0.0)	3 (0.2)	11 (0.1)	24 (0.0)	9 (0.0)
Other	19550 (6.9)	51 (3.0)	1039 (7.9)	14668 (9.2)	3792 (3.5)
Mechanism of injury *					
Non-intentional	242927 (85.4)	1338 (79.8)	11180 (85.0)	134346 (83.9)	96063 (87.7)
Assault	4737 (1.7)	24 (1.4)	12 (0.1)	341 (0.2)	4360 (4.0)
Other	35131 (12.3)	54 (3.2)	1713 (13.0)	24455 (15.3)	8909 (8.1)
Unknown	1738 (0.6)	261 (15.6)	252 (1.9)	1033 (0.6)	192 (0.2)

Supplementary Table 3. Continued

	N (%)				
	Overall	0 to < 1 yr	1 to < 5 yrs	5 to < 15 yrs	≥ 15 yrs
Fractures – offspring without siblings					
Anatomical site					
Skull and face	7101 (7.6)	300 (52.1)	362 (6.1)	1857 (3.6)	4582 (12.7)
Neck and trunk	3222 (3.4)	18 (3.1)	40 (0.7)	822 (1.6)	2342 (6.5)
Upper extremity					
-shoulder and upper arm	11968 (12.8)	82 (14.2)	1659 (28.0)	7398 (14.5)	2829 (7.8)
-forearm	22163 (23.7)	10 (1.7)	1246 (21.0)	15947 (31.3)	4960 (13.8)
-wrist and hand	21413 (22.9)	4 (0.7)	348 (5.9)	9933 (19.5)	11128 (30.9)
-unspecified	34 (0.0)	2 (0.3)	6 (0.1)	20 (0.0)	6 (0.0)
Lower extremity					
-femur	1775 (1.9)	112 (19.4)	516 (8.7)	800 (1.6)	347 (1.0)
-lower leg and ankle	11022 (11.8)	20 (3.5)	963 (16.3)	5614 (11.0)	4425 (12.3)
-foot	8478 (9.1)	1 (0.2)	325 (5.5)	4008 (7.9)	4144 (11.5)
-unspecified	19 (0.0)	0 (0)	7 (0.1)	7 (0.0)	5 (0.0)
Other	6242 (6.7)	27 (4.7)	449 (7.6)	4480 (8.8)	1286 (3.6)
Mechanism of injury *					
Non-intentional	79319 (84.9)	453 (78.6)	4651 (78.6)	43274 (85.0)	30941 (85.8)
Assault	1650 (1.8)	19 (3.3)	5 (0.1)	97 (0.2)	1529 (4.2)
Other	11862 (12.7)	22 (3.8)	1164 (19.7)	7183 (14.1)	3493 (9.7)
Unknown	606 (0.6)	82 (14.2)	101 (1.7)	332 (0.7)	91 (0.3)

Values are numbers (percentages) unless stated otherwise.

*External cause codes for defining the mechanism of injury are not available for fractures recorded in the Medical Birth Register. The unknown category of mechanism of injury includes fractures without external cause code in the Medical Birth Register (i.e. all diagnoses recorded in this register) or the Patient Register.

Supplementary Table 4. Standardised incidence rates of bone fractures in offspring by attained age, overall and stratified by maternal smoking during pregnancy.

Attained age	IR per 1000 person-years (95% CI)			IRR (95% CI)
	All	No smoking	Smoking	
0 to <1 yr	1.35 (1.29 to 1.40)	1.28 (1.22 to 1.34)	1.59 (1.46 to 1.72)	1.24 (1.13 to 1.36)
1 to <2 yrs	1.48 (1.42 to 1.54)	1.50 (1.43 to 1.57)	1.40 (1.27 to 1.54)	0.94 (0.84 to 1.04)
2 to <3 yrs	2.38 (2.31 to 2.46)	2.39 (2.30 to 2.47)	2.37 (2.19 to 2.54)	0.99 (0.91 to 1.08)
3 to <4 yrs	3.27 (3.18 to 3.36)	3.26 (3.16 to 3.35)	3.33 (3.12 to 3.54)	1.02 (0.95 to 1.10)
4 to <5 yrs	4.50 (4.40 to 4.61)	4.53 (4.42 to 4.65)	4.38 (4.14 to 4.63)	0.97 (0.91 to 1.03)
5 to <6 yrs	5.94 (5.82 to 6.06)	5.92 (5.79 to 6.06)	6.03 (5.75 to 6.32)	1.02 (0.97 to 1.07)
6 to <7 yrs	7.50 (7.37 to 7.64)	7.44 (7.29 to 7.58)	7.81 (7.48 to 8.14)	1.05 (1.00 to 1.10)
7 to <8 yrs	8.54 (8.39 to 8.68)	8.47 (8.31 to 8.63)	8.86 (8.51 to 9.21)	1.05 (1.00 to 1.09)
8 to <9 yrs	9.53 (9.38 to 9.69)	9.42 (9.25 to 9.59)	10.05 (9.68 to 10.42)	1.07 (1.02 to 1.11)
9 to <10 yrs	11.90 (11.73 to 12.07)	11.74 (11.55 to 11.93)	12.59 (12.18 to 13.01)	1.07 (1.03 to 1.11)
10 to <11 yrs	15.02 (14.82 to 15.21)	14.69 (14.48 to 14.90)	16.40 (15.93 to 16.87)	1.12 (1.08 to 1.15)
11 to <12 yrs	18.88 (18.66 to 19.10)	18.65 (18.40 to 18.89)	19.82 (19.30 to 20.33)	1.06 (1.03 to 1.09)
12 to <13 yrs	21.40 (21.16 to 21.64)	20.99 (20.73 to 21.25)	23.03 (22.48 to 23.58)	1.10 (1.07 to 1.13)
13 to <14 yrs	22.04 (21.80 to 22.28)	21.81 (21.54 to 22.08)	22.92 (22.37 to 23.47)	1.05 (1.02 to 1.08)
14 to <15 yrs	21.35 (21.10 to 21.60)	21.32 (21.04 to 21.60)	21.46 (20.92 to 21.99)	1.01 (0.98 to 1.04)
15 to <16 yrs	20.17 (19.92 to 20.42)	20.02 (19.74 to 20.30)	20.67 (20.14 to 21.20)	1.03 (1.00 to 1.06)
16 to <17 yrs	15.23 (15.01 to 15.46)	15.06 (14.81 to 15.31)	15.80 (15.34 to 16.27)	1.05 (1.01 to 1.09)
17 to <18 yrs	13.91 (13.69 to 14.13)	13.42 (13.17 to 13.67)	15.44 (14.97 to 15.91)	1.15 (1.11 to 1.19)
18 to <19 yrs	13.73 (13.50 to 13.95)	13.11 (12.85 to 13.36)	15.61 (15.13 to 16.09)	1.19 (1.15 to 1.23)
19 to <20 yrs	13.34 (13.11 to 13.57)	12.79 (12.53 to 13.06)	14.92 (14.44 to 15.40)	1.17 (1.12 to 1.21)
20 to <21 yrs	12.86 (12.62 to 13.10)	12.19 (11.92 to 12.46)	14.78 (14.28 to 15.27)	1.21 (1.16 to 1.26)
21 to <22 yrs	12.32 (12.08 to 12.57)	11.56 (11.28 to 11.84)	14.43 (13.92 to 14.94)	1.25 (1.20 to 1.30)
22 to <23 yrs	11.92 (11.66 to 12.18)	11.24 (10.94 to 11.53)	13.75 (13.23 to 14.28)	1.22 (1.17 to 1.28)
23 to <24 yrs	11.10 (10.83 to 11.37)	10.61 (10.30 to 10.91)	12.40 (11.87 to 12.92)	1.17 (1.11 to 1.23)
24 to <25 yrs	10.88 (10.59 to 11.16)	10.24 (9.92 to 10.56)	12.51 (11.94 to 13.08)	1.22 (1.16 to 1.29)
25 to <26 yrs	10.07 (9.78 to 10.37)	9.47 (9.13 to 9.81)	11.58 (10.99 to 12.17)	1.22 (1.15 to 1.30)
26 to <27 yrs	9.52 (9.20 to 9.84)	8.97 (8.60 to 9.34)	10.86 (10.24 to 11.48)	1.21 (1.13 to 1.30)
27 to <28 yrs	9.30 (8.95 to 9.66)	8.72 (8.32 to 9.13)	10.69 (10.00 to 11.38)	1.23 (1.13 to 1.32)
28 to <29 yrs	8.53 (8.14 to 8.92)	7.86 (7.42 to 8.30)	10.11 (9.34 to 10.87)	1.29 (1.17 to 1.41)
29 to <30 yrs	8.99 (8.50 to 9.48)	8.34 (7.79 to 8.89)	10.52 (9.58 to 11.45)	1.26 (1.13 to 1.41)
30 to <31 yrs	7.66 (7.08 to 8.24)	7.08 (6.43 to 7.74)	8.99 (7.88 to 10.10)	1.27 (1.09 to 1.47)
31 to <32 yrs	7.71 (6.75 to 8.67)	8.06 (6.87 to 9.24)	6.92 (5.28 to 8.57)	0.86 (0.65 to 1.14)

All incidence rates are standardised by calendar year of birth year and presented stratified by attained age. Abbreviations: IR = incidence rate; IRR = incidence rate ratio; CI = confidence interval.

Supplementary Table 5. Standardised incidence rates of bone fractures in offspring before one year of age after excluding diagnoses recorded in the Medical Birth Register, overall and stratified by maternal smoking during pregnancy.

Attained age	IR per 1000 person-years (95% CI)			IRR (95% CI)
	All	No smoking	Smoking	
0 to <1 yr	1.22 (1.17 to 1.27)	1.15 (1.09 to 1.21)	1.47 (1.34 to 1.59)	1.28 (1.15 to 1.41)

All incidence rates are standardised by calendar year of birth year and presented for fractures before one year of age. Abbreviations: IR = incidence rate; IRR = incidence rate ratio; CI = confidence interval.

Supplementary Table 6. Standardised incidence rates of bone fractures in male and female offspring by attained age, overall and stratified by maternal smoking during pregnancy.

Attained age	IR per 1000 person-years (95% CI) – Males			IRR (95% CI)
	All	No smoking	Smoking	
0 to <1 yr	1.47 (1.39 to 1.55)	1.39 (1.30 to 1.48)	1.75 (1.56 to 1.94)	1.26 (1.11 to 1.43)
1 to <2 yrs	1.67 (1.59 to 1.76)	1.69 (1.59 to 1.79)	1.59 (1.39 to 1.79)	0.94 (0.82 to 1.08)
2 to <3 yrs	2.77 (2.66 to 2.88)	2.77 (2.64 to 2.89)	2.80 (2.53 to 3.06)	1.01 (0.91 to 1.12)
3 to <4 yrs	3.84 (3.71 to 3.97)	3.84 (3.69 to 3.99)	3.85 (3.53 to 4.16)	1.00 (0.91 to 1.10)
4 to <5 yrs	5.16 (5.00 to 5.31)	5.22 (5.04 to 5.39)	4.88 (4.53 to 5.24)	0.94 (0.86 to 1.01)
5 to <6 yrs	6.73 (6.55 to 6.91)	6.70 (6.50 to 6.90)	6.87 (6.45 to 7.30)	1.03 (0.96 to 1.10)
6 to <7 yrs	8.53 (8.32 to 8.73)	8.47 (8.25 to 8.69)	8.76 (8.28 to 9.24)	1.03 (0.97 to 1.10)
7 to <8 yrs	9.50 (9.29 to 9.72)	9.37 (9.14 to 9.61)	10.09 (9.58 to 10.61)	1.08 (1.02 to 1.14)
8 to <9 yrs	10.24 (10.02 to 10.46)	10.16 (9.91 to 10.40)	10.61 (10.08 to 11.14)	1.04 (0.99 to 1.10)
9 to <10 yrs	12.38 (12.13 to 12.62)	12.14 (11.87 to 12.41)	13.38 (12.79 to 13.98)	1.10 (1.05 to 1.16)
10 to <11 yrs	15.13 (14.86 to 15.40)	14.83 (14.53 to 15.14)	16.38 (15.72 to 17.03)	1.10 (1.06 to 1.15)
11 to <12 yrs	20.08 (19.76 to 20.40)	19.77 (19.42 to 20.13)	21.33 (20.58 to 22.07)	1.08 (1.04 to 1.12)
12 to <13 yrs	25.89 (25.52 to 26.25)	25.24 (24.84 to 25.65)	28.42 (27.56 to 29.28)	1.13 (1.09 to 1.17)
13 to <14 yrs	30.56 (30.16 to 30.97)	30.25 (29.79 to 30.70)	31.77 (30.87 to 32.68)	1.05 (1.02 to 1.09)
14 to <15 yrs	31.46 (31.04 to 31.89)	31.45 (30.97 to 31.93)	31.53 (30.61 to 32.44)	1.00 (0.97 to 1.04)
15 to <16 yrs	29.90 (29.47 to 30.33)	29.79 (29.31 to 30.28)	30.27 (29.36 to 31.18)	1.02 (0.98 to 1.05)
16 to <17 yrs	21.60 (21.22 to 21.98)	21.36 (20.93 to 21.79)	22.39 (21.60 to 23.19)	1.05 (1.01 to 1.09)
17 to <18 yrs	19.38 (19.01 to 19.75)	18.68 (18.26 to 19.09)	21.59 (20.80 to 22.38)	1.16 (1.11 to 1.21)
18 to <19 yrs	19.50 (19.12 to 19.89)	18.57 (18.14 to 19.00)	22.32 (21.50 to 23.14)	1.20 (1.15 to 1.26)
19 to <20 yrs	18.98 (18.58 to 19.37)	18.04 (17.59 to 18.49)	21.71 (20.88 to 22.55)	1.20 (1.15 to 1.26)
20 to <21 yrs	18.27 (17.87 to 18.68)	17.26 (16.80 to 17.71)	21.16 (20.31 to 22.02)	1.23 (1.17 to 1.29)
21 to <22 yrs	17.36 (16.94 to 17.78)	16.17 (15.70 to 16.64)	20.67 (19.79 to 21.55)	1.28 (1.21 to 1.35)
22 to <23 yrs	16.87 (16.42 to 17.31)	15.80 (15.30 to 16.30)	19.73 (18.83 to 20.64)	1.25 (1.18 to 1.32)
23 to <24 yrs	15.65 (15.19 to 16.10)	14.83 (14.32 to 15.35)	17.79 (16.88 to 18.71)	1.20 (1.13 to 1.28)
24 to <25 yrs	15.00 (14.51 to 15.48)	14.00 (13.45 to 14.55)	17.60 (16.61 to 18.58)	1.26 (1.18 to 1.34)
25 to <26 yrs	13.63 (13.13 to 14.14)	12.66 (12.09 to 13.22)	16.12 (15.11 to 17.13)	1.27 (1.18 to 1.37)
26 to <27 yrs	13.02 (12.48 to 13.56)	11.93 (11.32 to 12.54)	15.73 (14.64 to 16.83)	1.32 (1.21 to 1.44)
27 to <28 yrs	12.46 (11.87 to 13.06)	11.73 (11.05 to 12.40)	14.27 (13.11 to 15.42)	1.22 (1.10 to 1.34)
28 to <29 yrs	11.30 (10.65 to 11.95)	10.40 (9.67 to 11.13)	13.44 (12.17 to 14.72)	1.29 (1.15 to 1.45)
29 to <30 yrs	11.44 (10.65 to 12.23)	10.39 (9.51 to 11.27)	13.95 (12.39 to 15.50)	1.34 (1.17 to 1.54)
30 to <31 yrs	9.95 (9.00 to 10.90)	9.55 (8.46 to 10.64)	10.90 (9.15 to 12.65)	1.14 (0.94 to 1.38)
31 to <32 yrs	9.72 (8.17 to 11.27)	10.48 (8.55 to 12.42)	7.99 (5.45 to 10.53)	0.76 (0.53 to 1.10)

Supplementary Table 6. Continued

Attained age	IR per 1000 person-years (95% CI) – Females			IRR (95% CI)
	All	No smoking	Smoking	
0 to <1 yr	1.22 (1.14 to 1.29)	1.16 (1.08 to 1.25)	1.42 (1.24 to 1.59)	1.22 (1.05 to 1.41)
1 to <2 yrs	1.28 (1.20 to 1.36)	1.30 (1.21 to 1.38)	1.20 (1.03 to 1.38)	0.93 (0.79 to 1.09)
2 to <3 yrs	1.97 (1.87 to 2.07)	1.98 (1.88 to 2.09)	1.91 (1.68 to 2.14)	0.96 (0.84 to 1.10)
3 to <4 yrs	2.67 (2.55 to 2.78)	2.64 (2.52 to 2.77)	2.78 (2.50 to 3.06)	1.05 (0.94 to 1.18)
4 to <5 yrs	3.82 (3.68 to 3.95)	3.81 (3.66 to 3.96)	3.86 (3.53 to 4.19)	1.01 (0.92 to 1.11)
5 to <6 yrs	5.12 (4.96 to 5.27)	5.11 (4.94 to 5.28)	5.14 (4.76 to 5.53)	1.01 (0.93 to 1.09)
6 to <7 yrs	6.43 (6.25 to 6.61)	6.35 (6.15 to 6.54)	6.81 (6.37 to 7.25)	1.07 (1.00 to 1.15)
7 to <8 yrs	7.53 (7.33 to 7.72)	7.52 (7.31 to 7.74)	7.56 (7.10 to 8.02)	1.00 (0.94 to 1.08)
8 to <9 yrs	8.79 (8.58 to 9.00)	8.65 (8.42 to 8.88)	9.46 (8.94 to 9.98)	1.09 (1.03 to 1.16)
9 to <10 yrs	11.40 (11.16 to 11.64)	11.32 (11.06 to 11.59)	11.76 (11.19 to 12.33)	1.04 (0.98 to 1.10)
10 to <11 yrs	14.90 (14.62 to 15.17)	14.54 (14.24 to 14.85)	16.43 (15.76 to 17.11)	1.13 (1.08 to 1.18)
11 to <12 yrs	17.63 (17.32 to 17.93)	17.48 (17.14 to 17.82)	18.24 (17.53 to 18.95)	1.04 (1.00 to 1.09)
12 to <13 yrs	16.75 (16.45 to 17.05)	16.58 (16.25 to 16.92)	17.43 (16.74 to 18.11)	1.05 (1.01 to 1.10)
13 to <14 yrs	13.33 (13.06 to 13.60)	13.19 (12.89 to 13.49)	13.88 (13.28 to 14.49)	1.05 (1.00 to 1.11)
14 to <15 yrs	11.21 (10.96 to 11.47)	11.16 (10.88 to 11.45)	11.39 (10.84 to 11.94)	1.02 (0.97 to 1.08)
15 to <16 yrs	10.59 (10.34 to 10.85)	10.40 (10.12 to 10.69)	11.26 (10.70 to 11.81)	1.08 (1.02 to 1.14)
16 to <17 yrs	9.06 (8.82 to 9.30)	8.95 (8.67 to 9.22)	9.43 (8.92 to 9.94)	1.05 (0.99 to 1.12)
17 to <18 yrs	8.65 (8.41 to 8.89)	8.36 (8.09 to 8.64)	9.55 (9.04 to 10.07)	1.14 (1.07 to 1.22)
18 to <19 yrs	8.23 (7.99 to 8.48)	7.90 (7.63 to 8.18)	9.25 (8.74 to 9.77)	1.17 (1.10 to 1.25)
19 to <20 yrs	8.01 (7.76 to 8.26)	7.83 (7.55 to 8.12)	8.54 (8.03 to 9.05)	1.09 (1.02 to 1.17)
20 to <21 yrs	7.79 (7.53 to 8.05)	7.43 (7.14 to 7.72)	8.84 (8.30 to 9.38)	1.19 (1.11 to 1.28)
21 to <22 yrs	7.62 (7.35 to 7.89)	7.24 (6.93 to 7.55)	8.67 (8.12 to 9.22)	1.20 (1.11 to 1.29)
22 to <23 yrs	7.33 (7.05 to 7.61)	6.97 (6.65 to 7.29)	8.28 (7.71 to 8.85)	1.19 (1.09 to 1.29)
23 to <24 yrs	6.90 (6.61 to 7.19)	6.67 (6.34 to 7.01)	7.49 (6.92 to 8.06)	1.12 (1.03 to 1.23)
24 to <25 yrs	7.08 (6.76 to 7.40)	6.75 (6.39 to 7.12)	7.92 (7.29 to 8.54)	1.17 (1.07 to 1.29)
25 to <26 yrs	6.80 (6.46 to 7.14)	6.52 (6.13 to 6.91)	7.49 (6.84 to 8.15)	1.15 (1.03 to 1.28)
26 to <27 yrs	6.30 (5.93 to 6.66)	6.22 (5.80 to 6.65)	6.47 (5.81 to 7.14)	1.04 (0.92 to 1.17)
27 to <28 yrs	6.39 (5.98 to 6.80)	5.93 (5.46 to 6.40)	7.48 (6.68 to 8.28)	1.26 (1.11 to 1.44)
28 to <29 yrs	5.96 (5.51 to 6.42)	5.48 (4.96 to 5.99)	7.08 (6.20 to 7.96)	1.29 (1.11 to 1.51)
29 to <30 yrs	6.72 (6.12 to 7.31)	6.42 (5.74 to 7.11)	7.39 (6.30 to 8.49)	1.15 (0.96 to 1.38)
30 to <31 yrs	5.52 (4.83 to 6.21)	4.76 (4.01 to 5.52)	7.24 (5.86 to 8.63)	1.52 (1.19 to 1.94)
31 to <32 yrs	5.82 (4.65 to 6.98)	5.77 (4.37 to 7.16)	5.92 (3.80 to 8.04)	1.03 (0.67 to 1.58)

All incidence rates are standardised by calendar year of birth year and presented stratified by attained age in female and male offspring separately. Abbreviations: IR = incidence rate; IRR = incidence rate ratio; CI = confidence interval.

Supplementary Table 7. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age.

	Model 1		Model 2		Model 3	
Attained age	N all /fractures	HR (95% CI)	N all / fractures	HR (95% CI)	N all / fractures *	HR (95% CI)
0 to < 1 year						
Smoking						
No	1302940 / 1669	REF (1.00)	873913 / 1072	REF (1.00)	113 / 38	REF (1.00)
Yes	377367 / 584	1.24 (1.13 to 1.36)	236868 / 374	1.27 (1.12 to 1.45)	111 / 56	1.58 (1.01 to 2.46)
No. of cigarettes/day						
None	1302940 / 1669	REF (1.00)	873913 / 1072	REF (1.00)	113 / 38	REF (1.00)
1-9 cigarettes/day	236094 / 348	1.18 (1.05 to 1.32)	149855 / 221	1.20 (1.03 to 1.39)	74 / 38	1.55 (0.98 to 2.46)
≥ 10 cigarettes/day	141273 / 236	1.35 (1.17 to 1.54)	87013 / 153	1.41 (1.18 to 1.69)	37 / 18	1.63 (0.94 to 2.85)
<i>P</i> trend		< 0.001		< 0.001		0.08
1 to < 5 years						
Smoking						
No	1292632 / 15683	REF (1.00)	869657 / 12007	REF (1.00)	907 / 449	REF (1.00)
Yes	373599 / 3395	0.98 (0.95 to 1.02)	235430 / 2365	0.96 (0.92 to 1.01)	913 / 311	0.94 (0.80 to 1.12)
No. of cigarettes/day						
None	1292632 / 15683	REF (1.00)	869657 / 12007	REF (1.00)	907 / 449	REF (1.00)
1-9 cigarettes/day	233897 / 2150	0.97 (0.93 to 1.02)	149032 / 1502	0.94 (0.89 to 1.00)	696 / 236	0.89 (0.75 to 1.06)
≥ 10 cigarettes/day	139702 / 1245	1.01 (0.95 to 1.07)	86398 / 863	0.99 (0.92 to 1.07)	217 / 75	1.16 (0.92 to 1.46)
<i>P</i> trend		0.65		0.27		0.38
5 to < 15 years						
Smoking						
No	1258379 / 167585	REF (1.00)	850229 / 118356	REF (1.00)	8111 / 3901	REF (1.00)
Yes	365874 / 43476	1.06 (1.05 to 1.07)	231779 / 27724	1.07 (1.05 to 1.08)	8028 / 3263	1.01 (0.96 to 1.07)
No. of cigarettes/day						
None	1258379 / 167585	REF (1.00)	850229 / 118356	REF (1.00)	8111 / 3901	REF (1.00)
1-9 cigarettes/day	229015 / 27554	1.06 (1.05 to 1.07)	146706 / 17759	1.06 (1.05 to 1.08)	6145 / 2519	1.01 (0.96 to 1.07)
≥ 10 cigarettes/day	136859 / 15922	1.06 (1.05 to 1.08)	85073 / 9965	1.08 (1.06 to 1.10)	1883 / 744	1.02 (0.95 to 1.09)
<i>P</i> trend		< 0.001		< 0.001		0.63
≥ 15 years						
Smoking						
No	1015792 / 104435	REF (1.00)	675564 / 66001	REF (1.00)	5030 / 2119	REF (1.00)
Yes	310479 / 41143	1.15 (1.14 to 1.17)	195867 / 25423	1.11 (1.09 to 1.12)	4996 / 2337	0.96 (0.89 to 1.03)
No. of cigarettes/day						
No	1015792 / 104435	REF (1.00)	675564 / 66001	REF (1.00)	5030 / 2119	REF (1.00)
1-9 cigarettes/day	193498 / 25122	1.14 (1.12 to 1.15)	123344 / 15751	1.10 (1.08 to 1.12)	3758 / 1789	0.95 (0.88 to 1.02)
≥ 10 cigarettes/day	116981 / 16021	1.18 (1.16 to 1.20)	72523 / 9672	1.12 (1.09 to 1.14)	1238 / 548	0.97 (0.89 to 1.07)
<i>P</i> trend		< 0.001		< 0.001		0.51

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group). Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) and for the different analysis models: model 1: whole cohort analysis adjusted for birth year; model 2: whole cohort analysis with adjustment for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation and marital status; and model 3: within-sibship analysis including all covariates included in model 2 except for maternal height, a variable which is unlikely to vary among siblings in the same family. * The within-sibship analysis model includes all offspring with siblings, but only families who are discordant on both the exposure and outcome contribute to the estimation of the hazard ratio. The numbers presented in the table therefore refer to the total number of offspring with siblings discordant on bone fractures and maternal smoking during pregnancy. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 8. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age in months up to one year of age.

	Model 1		Model 2		Model 3	
Attained age	N all / fractures	HR (95% CI)	N all / fractures	HR (95% CI)	N all / fractures *	HR (95% CI)
0 to < 3 months						
Smoking						
No	1302940 / 514	REF (1.00)	873913 / 330	REF (1.00)	38 / 12	REF (1.00)
Yes	377367 / 181	1.25 (1.05 to 1.48)	236868 / 111	1.25 (0.99 to 1.58)	47 / 21	2.83 (1.18 to 6.76)
No. of cigarettes/day						
None	1302940 / 514	REF (1.00)	873913 / 330	REF (1.00)	38 / 12	REF (1.00)
1-9 cigarettes/day	236094 / 104	1.15 (0.93 to 1.42)	149855 / 60	1.08 (0.81 to 1.44)	24 / 11	2.39 (0.92 to 6.25)
≥ 10 cigarettes/day	141273 / 77	1.43 (1.12 to 1.82)	87013 / 51	1.56 (1.14 to 2.13)	23 / 10	3.36 (1.27 to 8.91)
<i>P</i> trend		0.003		0.01		0.02
3 months to < 1 year						
Smoking						
No	1297665 / 1155	REF (1.00)	871507 / 742	REF (1.00)	74 / 26	REF (1.00)
Yes	375332 / 403	1.24 (1.10 to 1.39)	236093 / 263	1.28 (1.10 to 1.49)	64 / 34	1.35 (0.78 to 2.36)
No. of cigarettes/day						
None	1297665 / 1155	REF (1.00)	871507 / 742	REF (1.00)	74 / 26	REF (1.00)
1-9 cigarettes/day	234903 / 244	1.19 (1.04 to 1.37)	149406 / 161	1.25 (1.04 to 1.49)	50 / 27	1.41 (0.80 to 2.48)
≥ 10 cigarettes/day	140429 / 159	1.31 (1.11 to 1.55)	86687 / 102	1.35 (1.09 to 1.68)	14 / 7	1.13 (0.54 to 2.36)
<i>P</i> trend		<0.001		0.001		0.70

Hazard ratios (with 95% confidence intervals) for infant bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group). Hazard ratios are presented by attained age (0 to < 3 months, 3 months to < 1 year) and for the different analysis models: model 1: whole cohort analysis adjusted for birth year; model 2: whole cohort analysis adjusted for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation and marital status; and model 3: within-sibship analysis including all covariates included in model 2 except for maternal height, a variable which is unlikely to vary among siblings in the same family. * The within-sibship analysis model includes all offspring with siblings, but only families who are discordant on both the exposure and outcome contribute to the estimation of the hazard ratio. The numbers presented in the table therefore refer to the total number of offspring with siblings discordant on bone fractures and maternal smoking during pregnancy. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 9. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – analyses with additional adjustment for gestational age at birth and birth weight for gestational age.

	Model 4		Model 5	
Attained age	N all / fractures	HR (95% CI)	N all / fractures	HR (95% CI)
0 to < 1 year				
Smoking				
No	870621 / 1069	REF (1.00)	113 / 38	REF (1.00)
Yes	235857 / 371	1.27 (1.11 to 1.44)	111 / 56	1.58 (1.01 to 2.48)
No. of cigarettes/day				
No	870621 / 1069	REF (1.00)	113 / 38	REF (1.00)
1-9 cigarettes/day	149206 / 220	1.19 (1.03 to 1.39)	74 / 38	1.56 (0.98 to 2.48)
≥ 10 cigarettes/day	86651 / 151	1.40 (1.16 to 1.67)	37 / 18	1.65 (0.94 to 2.90)
<i>P</i> trend		< 0.001		0.08
1 to < 5 years				
Smoking				
No	866540 / 11952	REF (1.00)	901 / 447	REF (1.00)
Yes	234467 / 2353	0.96 (0.92 to 1.01)	904 / 308	0.94 (0.79 to 1.11)
No. of cigarettes/day				
None	866540 / 11952	REF (1.00)	901 / 447	REF (1.00)
1-9 cigarettes/day	148409 / 1493	0.94 (0.89 to 1.00)	689 / 234	0.89 (0.74 to 1.05)
≥ 10 cigarettes/day	86058 / 860	0.99 (0.93 to 1.07)	215 / 74	1.14 (0.91 to 1.43)
<i>P</i> trend		0.28		0.47
5 to < 15 years				
Smoking				
No	847203 / 117989	REF (1.00)	8047 / 3872	REF (1.00)
Yes	230831 / 27628	1.07 (1.06 to 1.09)	7969 / 3239	1.01 (0.96 to 1.07)
No. of cigarettes/day				
None	847203 / 117989	REF (1.00)	8047 / 3872	REF (1.00)
1-9 cigarettes/day	146092 / 17695	1.07 (1.05 to 1.08)	6098 / 2499	1.01 (0.96 to 1.07)
≥ 10 cigarettes/day	84739 / 9933	1.08 (1.06 to 1.11)	1871 / 740	1.02 (0.95 to 1.09)
<i>P</i> trend		< 0.001		0.58
≥ 15 years				
Smoking				
No	673085 / 65762	REF (1.00)	5001 / 2105	REF (1.00)
Yes	195038 / 25309	1.11 (1.10 to 1.13)	4959 / 2322	0.96 (0.89 to 1.03)
No. of cigarettes/day				
None	673085 / 65762	REF (1.00)	5001 / 2105	REF (1.00)
1-9 cigarettes/day	122807 / 15682	1.11 (1.09 to 1.13)	3734 / 1782	0.95 (0.89 to 1.03)
≥ 10 cigarettes/day	72231 / 9627	1.13 (1.10 to 1.15)	1225 / 540	0.98 (0.89 to 1.08)
<i>P</i> trend		< 0.001		0.63

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes/day) to those unexposed (= reference group) – analyses with additional adjustment for gestational age at birth and birth weight for gestational age. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) and for the different analysis models: model 4: whole cohort analysis with adjustment for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation, marital status, gestational age at birth and birth weight for gestational age; and model 5: within-sibship analysis including all covariates included in model 4 except for maternal height, a variable which is unlikely to vary among siblings in the same family. * The within-sibship analysis model includes all offspring with siblings, but only families who are discordant on both the exposure and outcome contribute to the estimation of the hazard ratio. The numbers presented in the table therefore refer to the total number of offspring with siblings discordant on bone fractures and maternal smoking during pregnancy. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 10. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – whole cohort analyses stratified by offspring sex.

	Model 2 - males		Model 2 - females		
Attained age	N all / fractures	HR (95% CI)	N all / fractures	HR (95% CI)	P interaction
0 to < 1 year					
Smoking					
No	448853 / 588	REF (1.00)	425060 / 484	REF (1.00)	0.97
Yes	122065 / 206	1.29 (1.08 to 1.53)	114803 / 168	1.26 (1.04 to 1.52)	
No. of cigarettes/day					
None	448853 / 588	REF (1.00)	425060 / 484	REF (1.00)	0.98
1-9 cigarettes/day	77350 / 120	1.19 (0.97 to 1.46)	72505 / 101	1.21 (0.96 to 1.51)	
≥ 10 cigarettes/day	44715 / 86	1.46 (1.15 to 1.86)	42298 / 67	1.36 (1.04 to 1.77)	
<i>P</i> trend		0.001		0.01	
1 to < 5 years					
Smoking					
No	446527 / 7077	REF (1.00)	423130 / 4930	REF (1.00)	0.87
Yes	121255 / 1397	0.93 (0.87 to 0.99)	114175 / 968	1.01 (0.93 to 1.08)	
No. of cigarettes/day					
None	446527 / 7077	REF (1.00)	423130 / 4930	REF (1.00)	0.25
1-9 cigarettes/day	76879 / 891	0.92 (0.86 to 0.99)	72153 / 611	0.98 (0.90 to 1.07)	
≥ 10 cigarettes/day	44376 / 506	0.95 (0.87 to 1.04)	42022 / 357	1.06 (0.95 to 1.18)	
<i>P</i> trend		0.06		0.55	
5 to < 15 years					
Smoking					
No	435637 / 70609	REF (1.00)	414592 / 47747	REF (1.00)	< 0.001
Yes	119191 / 16912	1.07 (1.05 to 1.09)	112588 / 10812	1.07 (1.05 to 1.09)	
No. of cigarettes/day					
No	435637 / 70609	REF (1.00)	414592 / 47747	REF (1.00)	0.43
1-9 cigarettes/day	75571 / 10834	1.06 (1.04 to 1.09)	71135 / 6925	1.06 (1.04 to 1.09)	
≥ 10 cigarettes/day	43620 / 6078	1.08 (1.05 to 1.11)	41453 / 3887	1.08 (1.04 to 1.12)	
<i>P</i> trend		< 0.001		< 0.001	
≥ 15 years					
Smoking					
No	337045 / 45438	REF (1.00)	338519 / 20563	REF (1.00)	0.02
Yes	98048 / 17634	1.10 (1.08 to 1.12)	97819 / 7789	1.12 (1.09 to 1.15)	
No. of cigarettes/day					
No	337045 / 45438	REF (1.00)	338519 / 20563	REF (1.00)	0.19
1-9 cigarettes/day	61845 / 10977	1.10 (1.08 to 1.12)	61499 / 4774	1.10 (1.06 to 1.13)	
≥ 10 cigarettes/day	36203 / 6657	1.10 (1.07 to 1.13)	36320 / 3015	1.15 (1.10 to 1.20)	
<i>P</i> trend		< 0.001		< 0.001	

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group) – analyses stratified by offspring sex. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) for model 2: whole cohort analysis adjusted for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation and marital status. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 11. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – within-sibship analyses stratified by offspring sex.

	Model 3 - males		Model 3 - females		
Attained age	N all / fractures *	HR (95% CI)	N all / fractures *	HR (95% CI)	P interaction
0 to < 1 year					
Smoking					
No	38 / 13	REF (1.00)	18 / 6	REF (1.00)	0.22
Yes	38 / 19	1.48 (0.65 to 3.35)	15 / 7	0.99 (0.26 to 3.76)	
No. of cigarettes/day					
None	38 / 13	REF (1.00)	18 / 6	REF (1.00)	0.29
1-9 cigarettes/day	24 / 11	1.33 (0.56 to 3.14)	11 / 5	0.92 (0.24 to 3.54)	
≥ 10 cigarettes/day	14 / 8	1.96 (0.67 to 5.79)	4 / 2	2.12 (0.35;12.67)	
<i>P</i> trend		0.22		0.38	
1 to < 5 years					
Smoking					
No	273 / 146	REF (1.00)	168 / 90	REF (1.00)	0.77
Yes	270 / 97	0.87 (0.65 to 1.17)	158 / 57	0.89 (0.61 to 1.31)	
No. of cigarettes/day					
None	273 / 146	REF (1.00)	168 / 90	REF (1.00)	0.91
1-9 cigarettes/day	199 / 74	0.85 (0.63 to 1.15)	127 / 45	0.83 (0.56 to 1.23)	
≥ 10 cigarettes/day	71 / 23	0.95 (0.65 to 1.39)	31 / 12	1.22 (0.71 to 2.12)	
<i>P</i> trend		0.74		0.69	
5 to < 15 years					
Smoking					
No	2381 / 1209	REF (1.00)	1503 / 773	REF (1.00)	0.56
Yes	2356 / 1014	1.02 (0.93 to 1.12)	1519 / 635	1.03 (0.92 to 1.16)	
No. of cigarettes/day					
No	2381 / 1209	REF (1.00)	1503 / 773	REF (1.00)	0.39
1-9 cigarettes/day	1823 / 793	0.99 (0.90 to 1.09)	1155 / 485	1.04 (0.93 to 1.18)	
≥ 10 cigarettes/day	533 / 221	1.14 (1.01 to 1.29)	364 / 150	0.99 (0.85 to 1.16)	
<i>P</i> trend		0.07		0.97	
≥ 15 years					
Smoking					
No	1634 / 736	REF (1.00)	763 / 333	REF (1.00)	0.28
Yes	1620 / 797	0.94 (0.84 to 1.05)	773 / 374	0.91 (0.77 to 1.09)	
No. of cigarettes/day					
No	1634 / 736	REF (1.00)	763 / 333	REF (1.00)	0.33
1-9 cigarettes/day	1251 / 625	0.93 (0.82 to 1.04)	586 / 288	0.91 (0.76 to 1.08)	
≥ 10 cigarettes/day	369 / 172	0.98 (0.84 to 1.14)	187 / 86	0.94 (0.75 to 1.18)	
<i>P</i> trend		0.73		0.56	

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group) – analyses stratified by offspring sex. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) for model 3: within-sibship analysis adjusted for birth year, offspring sex, maternal age, parity, body mass index, parental education, occupation and marital status. * The within-sibship analysis model includes all offspring with siblings, but only families who are discordant on both the exposure and outcome contribute to the estimation of the hazard ratio. The numbers presented in the table therefore refer to the total number of offspring with siblings discordant on bone fractures and maternal smoking during pregnancy. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 12. Maternal smoking during pregnancy and risk of recurrent bone fractures in offspring.

	IRR (95% CI)		
	Model 1	Model 2	Model 3
Smoking			
No	REF (1.00)	REF (1.00)	REF (1.00)
Yes	1.12 (1.11 to 1.13)	1.10 (1.09 to 1.11)	0.98 (0.96 to 1.01)
No. of cigarettes/day			
None	1.11 (1.10 to 1.12)	REF (1.00)	REF (1.00)
1-9 cigarettes/day	1.14 (1.12 to 1.15)	1.09 (1.08 to 1.10)	0.98 (0.95 to 1.01)
≥ 10 cigarettes/day	1.11 (1.10 to 1.12)	1.11 (1.09 to 1.13)	0.98 (0.94 to 1.02)
<i>P</i> trend	< 0.001	< 0.001	0.27

Incidence rate ratios (with 95% confidence intervals) for recurrent bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group). Hazard ratios are presented for the different analysis models: model 1: whole cohort analysis adjusted for birth year; model 2: whole cohort analysis adjusted for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation and marital status; and model 3: within-sibship analysis including all covariates included in model 2 except for maternal height, a variable which is unlikely to vary among siblings in the same family. Abbreviations: IRR = incidence rate ratio; CI = confidence interval.

Supplementary Table 13. Parental and infant characteristics in offspring with and without siblings in the study population.

Parental characteristics	Offspring with siblings	
	No (N = 445385)	Yes (N = 1234922)
Maternal age (yrs)		
< 20	12579 (2.8)	31197 (2.5)
20-24	74221 (16.7)	276622 (22.4)
25-29	141956 (31.9)	480019 (38.9)
30-34	130725 (29.4)	323984 (26.2)
≥ 35	85904 (19.3)	123100 (10.0)
Maternal height (cm)		
< 155	12768 (3.4)	29254 (2.8)
155-164	140380 (37.3)	371588 (36.2)
165-174	192298 (51.1)	541068 (52.6)
≥175	30670 (8.2)	85836 (8.4)
Missing	69269 (15.6)	207176 (16.8)
Maternal body mass index (kg/m ²)		
< 18.5	16652 (5.1)	41888 (5.0)
18.5–24.9	232724 (71.7)	594693 (70.8)
25.0–29.9	57607 (17.8)	155425 (18.5)
≥30.0	17461 (5.4)	48219 (5.7)
Missing	120941 (27.2)	394697 (32.0)
Maternal parity		
Nulliparous	244771 (55.0)	449039 (36.4)
1	112101 (25.2)	495704 (40.1)
2	64656 (14.5)	201190 (16.3)
≥3	23857 (5.4)	88989 (7.2)
Maternal education		
Compulsory up to 9 years	81147 (19.1)	206266 (17.0)
Secondary	220847 (51.9)	672551 (55.5)
Post-secondary	123916 (29.1)	332752 (27.5)
Missing	19475 (4.4)	23353 (1.9)
Maternal occupational classification		
Low	244590 (54.9)	726565 (58.8)
Intermediate	89089 (20.0)	238929 (19.3)
High	85545 (19.2)	225532 (18.3)
Missing	26161 (5.9)	43896 (3.6)
Maternal marital status		
Unmarried	179007 (41.3)	472895 (38.6)
Married	230104 (53.1)	707752 (57.8)
Divorced/widow(er)	24635 (5.7)	43983 (3.6)
Missing	11639 (2.6)	10292 (0.8)
Paternal education		
Compulsory up to 9 years	93861 (22.3)	242406 (20.2)
Secondary	211880 (50.4)	640869 (53.3)
Post-secondary	114662 (27.3)	319564 (26.6)
Missing	24982 (5.6)	32083 (2.6)
Paternal occupational classification		
Low	259288 (58.2)	778326 (63.0)
Intermediate	53999 (12.1)	149005 (12.1)
High	104176 (23.4)	269050 (21.8)
Missing	27922 (6.3)	38541 (3.1)

Supplementary Table 13. Continued

Infant characteristics	Offspring with siblings	
	No (N = 445385)	Yes (N = 1234922)
Sex		
Male	228386 (51.3)	635252 (51.4)
Female	216999 (48.7)	599670 (48.6)
Birth weight (g)		
Mean, SD	3486 (572)	3556 (549)
Missing	0.5 (2221)	0.3 (3678)
Gestational age at birth (weeks)		
Mean, SD	39.3 (1.9)	39.4 (1.8)
Missing	0.1 (334)	0.1 (662)
Small for gestational age (< 10th percentile)		
No	391146 (88.3)	1117871 (90.8)
Yes	51693 (11.7)	112732 (9.2)
Missing	2546 (0.6)	4319 (0.3)

Abbreviation: SD = standard deviation. Occupational classification was defined using an approximation of the European Socio-economic Classification (ESeC) and grouped into lower, intermediate and higher level professions.

Supplementary Table 14. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – whole cohort analyses in offspring with and without siblings.

	Model 2 – offspring with siblings		Model 2 – offspring without siblings	
Attained age	N all /fractures	HR (95% CI)	N all / fractures	HR (95% CI)
0 to < 1 year				
Smoking				
No	645987 / 814	REF (1.00)	227926 / 258	REF (1.00)
Yes	164034 / 269	1.25 (1.08 to 1.45)	72834 / 105	1.32 (1.03 to 1.69)
No. of cigarettes/day				
None	645987 / 814	REF (1.00)	227926 / 258	REF (1.00)
1-9 cigarettes/day	103631 / 158	1.18 (0.99 to 1.41)	46224 / 63	1.23 (0.92 to 1.65)
≥ 10 cigarettes/day	60403 / 111	1.38 (1.12 to 1.70)	26610 / 42	1.49 (1.06 to 2.11)
<i>P</i> trend		0.001		0.01
1 to < 5 years				
Smoking				
No	642606 / 8163	REF (1.00)	227051 / 3844	REF (1.00)
Yes	162875 / 1625	0.99 (0.93 to 1.04)	72555 / 740	0.91 (0.84 to 0.99)
No. of cigarettes/day				
None	642606 / 8163	REF (1.00)	227051 / 3844	REF (1.00)
1-9 cigarettes/day	102970 / 999	0.96 (0.90 to 1.03)	46062 / 503	0.91 (0.82 to 1.00)
≥ 10 cigarettes/day	59905 / 626	1.03 (0.94 to 1.12)	26493 / 237	0.92 (0.80 to 1.05)
<i>P</i> trend		0.97		0.05
5 to < 15 years				
Smoking				
No	629581 / 89554	REF (1.00)	220648 / 28802	REF (1.00)
Yes	160443 / 20032	1.07 (1.05 to 1.09)	71336 / 7692	1.07 (1.04 to 1.10)
No. of cigarettes/day				
No	629581 / 89554	REF (1.00)	220648 / 28802	REF (1.00)
1-9 cigarettes/day	101465 / 12642	1.06 (1.04 to 1.08)	45241 / 5117	1.06 (1.03 to 1.10)
≥ 10 cigarettes/day	58978 / 7390	1.08 (1.05 to 1.10)	26095 / 2575	1.08 (1.03 to 1.13)
<i>P</i> trend		< 0.001		< 0.001
≥ 15 years				
Smoking				
No	508446 / 50404	REF (1.00)	167118 / 15597	REF (1.00)
Yes	135750 / 17431	1.09 (1.07 to 1.11)	60117 / 7992	1.14 (1.11 to 1.17)
No. of cigarettes/day				
No	508446 / 50404	REF (1.00)	167118 / 15597	REF (1.00)
1-9 cigarettes/day	85807 / 10903	1.08 (1.06 to 1.11)	37537 / 4848	1.14 (1.10 to 1.18)
≥ 10 cigarettes/day	49943 / 6528	1.11 (1.08 to 1.14)	22580 / 3144	1.14 (1.10 to 1.19)
<i>P</i> trend		< 0.001		< 0.001

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group) – analyses in offspring with and without siblings. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) for model 2: whole cohort analysis adjusted for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation and marital status. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 15. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – within-sibship analyses including full siblings only.

	Model 6	
Attained age	N all /fractures *	HR (95% CI)
0 to < 1 year		
Smoking		
No	90 / 31	REF (1.00)
Yes	86 / 44	1.49 (0.91 to 2.46)
No. of cigarettes/day		
None	90 / 31	REF (1.00)
1-9 cigarettes/day	62 / 33	1.43 (0.85 to 2.38)
≥ 10 cigarettes/day	24 / 11	1.75 (0.91 to 3.34)
<i>P</i> trend		0.09
1 to < 5 years		
Smoking		
No	716 / 350	REF (1.00)
Yes	702 / 254	1.01 (0.84 to 1.22)
No. of cigarettes/day		
None	716 / 350	REF (1.00)
1-9 cigarettes/day	546 / 198	0.97 (0.80 to 1.17)
≥ 10 cigarettes/day	156 / 56	1.20 (0.93 to 1.56)
<i>P</i> trend		0.26
5 to < 15 years		
Smoking		
No	6436 / 3109	REF (1.00)
Yes	6307 / 2621	1.03 (0.97 to 1.09)
No. of cigarettes/day		
No	6436 / 3109	REF (1.00)
1-9 cigarettes/day	4904 / 2069	1.03 (0.98 to 1.10)
≥ 10 cigarettes/day	1403 / 552	1.00 (0.92 to 1.08)
<i>P</i> trend		0.82
≥ 15 years		
Smoking		
No	4043 / 1739	REF (1.00)
Yes	3984 / 1859	0.95 (0.88 to 1.03)
No. of cigarettes/day		
No	4043 / 1739	REF (1.00)
1-9 cigarettes/day	3066 / 1447	0.94 (0.87 to 1.02)
≥ 10 cigarettes/day	918 / 412	0.98 (0.88 to 1.08)
<i>P</i> trend		0.58

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group) – analyses including full siblings only. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) for model 6: within-sibship analysis including full siblings only with adjustment for birth year, offspring sex, maternal age, parity, body mass index, parental education, occupation and marital status. * The within-sibship analysis model includes all offspring with full siblings, but only families who are discordant on both the exposure and outcome contribute to the estimation of the hazard ratio. The numbers presented in the table therefore refer to the total number of offspring with full siblings discordant on bone fractures and maternal smoking during pregnancy. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 16. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – whole cohort analyses stratified by calendar period of birth.

	Model 2 - 1983-1991 birth cohort		Model 2- 1992-2000 birth cohort		
Attained age	N all / fractures	HR (95% CI)	N all / fractures	HR (95% CI)	P interaction
0 to < 1 year					
Smoking					
No	322801 / 331	REF (1.00)	551112 / 741	REF (1.00)	0.27
Yes	128134 / 188	1.36 (1.13 to 1.65)	108734 / 186	1.20 (1.01 to 1.43)	
No. of cigarettes/day					
None	322801 / 331	REF (1.00)	551112 / 741	REF (1.00)	0.54
1-9 cigarettes/day	79478 / 110	1.30 (1.04 to 1.62)	70377 / 111	1.12 (0.91 to 1.38)	
≥ 10 cigarettes/day	48656 / 78	1.48 (1.14 to 1.92)	38357 / 75	1.36 (1.06 to 1.74)	
P trend		< 0.001		0.01	
1 to < 5 years					
Smoking					
No	321245 / 1881	REF (1.00)	548412 / 10126	REF (1.00)	0.01
Yes	127406 / 795	1.00 (0.91 to 1.09)	108024 / 1570	0.94 (0.89 to 0.99)	
No. of cigarettes/day					
None	321245 / 1881	REF (1.00)	548412 / 10126	REF (1.00)	0.05
1-9 cigarettes/day	79067 / 478	0.97 (0.88 to 1.08)	69965 / 1024	0.93 (0.87 to 0.99)	
≥ 10 cigarettes/day	48339 / 317	1.03 (0.91 to 1.17)	38059 / 546	0.96 (0.88 to 1.05)	
P trend		0.81		0.08	
5 to < 15 years					
Smoking					
No	317997 / 17491	REF (1.00)	532232 / 100865	REF (1.00)	0.12
Yes	126154 / 7169	1.08 (1.04 to 1.11)	105625 / 20555	1.07 (1.05 to 1.08)	
No. of cigarettes/day					
None	317997 / 17491	REF (1.00)	532232 / 100865	REF (1.00)	0.06
1-9 cigarettes/day	78326 / 4384	1.06 (1.02 to 1.09)	68380 / 13375	1.07 (1.05 to 1.09)	
≥ 10 cigarettes/day	47828 / 2785	1.11 (1.06 to 1.16)	37245 / 7180	1.07 (1.04 to 1.09)	
P trend		< 0.001		< 0.001	
≥ 15 years					
Smoking					
No	295521 / 41940	REF (1.00)	380043 / 24061	REF (1.00)	< 0.001
Yes	117654 / 19451	1.12 (1.10 to 1.14)	78213 / 5972	1.06 (1.03 to 1.10)	
No. of cigarettes/day					
None	295521 / 41940	REF (1.00)	380043 / 24061	REF (1.00)	< 0.001
1-9 cigarettes/day	73096 / 11955	1.11 (1.09 to 1.14)	50248 / 3796	1.07 (1.03 to 1.10)	
≥ 10 cigarettes/day	44558 / 7496	1.14 (1.11 to 1.17)	27965 / 2176	1.06 (1.01 to 1.11)	
P trend		< 0.001		< 0.001	

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group) – analyses stratified by calendar period of birth. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) for model 2: whole cohort analysis adjusted for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation and marital status. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 17. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – within-sibship analyses stratified by calendar period of birth.

	Model 3 - 1983-1991 birth cohort		Model 3 - 1992-2000 birth cohort		
Attained age	N all / fractures *	HR (95% CI)	N all / fractures *	HR (95% CI)	P interaction
0 to < 1 year					
Smoking					
No	23 / 10	REF (1.00)	46 / 18	REF (1.00)	0.68
Yes	25 / 13	1.30 (0.51 to 3.33)	42 / 22	1.29 (0.61 to 2.72)	
No. of cigarettes/day					
None	23 / 10	REF (1.00)	46 / 18	REF (1.00)	0.61
1-9 cigarettes/day	18 / 9	1.29 (0.49 to 3.41)	34 / 19	1.23 (0.58 to 2.62)	
≥ 10 cigarettes/day	7 / 4	1.32 (0.43 to 4.10)	8 / 3	1.82 (0.58 to 5.74)	
<i>P</i> trend		0.65		0.32	
1 to < 5 years					
Smoking					
No	121 / 55	REF (1.00)	486 / 271	REF (1.00)	0.33
Yes	125 / 60	1.11 (0.76 to 1.62)	476 / 167	0.97 (0.77 to 1.22)	
No. of cigarettes/day					
None	121 / 55	REF (1.00)	486 / 271	REF (1.00)	0.58
1-9 cigarettes/day	98 / 50	1.06 (0.72 to 1.57)	380 / 132	0.94 (0.74 to 1.19)	
≥ 10 cigarettes/day	27 / 10	1.30 (0.78 to 2.16)	96 / 35	1.11 (0.80 to 1.54)	
<i>P</i> trend		0.33		0.72	
5 to < 15 years					
Smoking					
No	944 / 474	REF (1.00)	3996 / 1995	REF (1.00)	0.37
Yes	925 / 407	1.07 (0.93 to 1.24)	3952 / 1774	0.99 (0.92 to 1.05)	
No. of cigarettes/day					
None	944 / 474	REF (1.00)	3996 / 1995	REF (1.00)	0.59
1-9 cigarettes/day	698 / 314	1.09 (0.94 to 1.27)	3128 / 1398	0.99 (0.92 to 1.06)	
≥ 10 cigarettes/day	227 / 93	1.02 (0.84 to 1.23)	824 / 376	0.98 (0.89 to 1.07)	
<i>P</i> trend		0.84		0.60	
≥ 15 years					
Smoking					
No	2008 / 989	REF (1.00)	885 / 357	REF (1.00)	0.89
Yes	1994 / 927	0.94 (0.86 to 1.04)	861 / 467	0.92 (0.77 to 1.10)	
No. of cigarettes/day					
None	2008 / 989	REF (1.00)	885 / 357	REF (1.00)	0.79
1-9 cigarettes/day	1528 / 709	0.94 (0.84 to 1.04)	689 / 376	0.92 (0.77 to 1.11)	
≥ 10 cigarettes/day	466 / 218	0.98 (0.86 to 1.11)	172 / 91	0.91 (0.72 to 1.15)	
<i>P</i> trend		0.68		0.42	

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group) – analyses stratified by calendar period of birth. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) for model 3: within-sibship analysis adjusted for birth year, offspring sex, maternal age, parity, body mass index, parental education, occupation and marital status.* The within-sibship analysis model includes all offspring with siblings, but only families who are discordant on both the exposure and outcome contribute to the estimation of the hazard ratio. The numbers presented in the table therefore refer to the total number of offspring with siblings discordant on bone fractures and maternal smoking during pregnancy. Abbreviations: HR = hazard ratio; CI = confidence interval.

Supplementary Table 18. Maternal smoking during pregnancy and risk of bone fractures in offspring by attained age – whole cohort and within-sibship analyses after imputation of missing covariate data.

	Model 2		Model 3	
Attained age	N all /fractures	HR (95% CI)	N all / fractures *	HR (95% CI)
0 to < 1 year				
Smoking				
No	1302940 / 1669	REF (1.00)	266 / 86	REF (1.00)
Yes	377367 / 584	1.19 (1.08 to 1.32)	260 / 105	1.44 (1.05 to 2.00)
No. of cigarettes/day				
None	1302940 / 1669	REF (1.00)	266 / 86	REF (1.00)
1-9 cigarettes/day	236094 / 348	1.14 (1.01 to 1.29)	186 / 75	1.48 (1.06 to 2.07)
≥ 10 cigarettes/day	141273 / 236	1.28 (1.11 to 1.48)	74 / 30	1.33 (0.89 to 2.00)
<i>P</i> trend		< 0.001		0.17
1 to < 5 years				
Smoking				
No	1292632 / 15683	REF (1.00)	1870 / 819	REF (1.00)
Yes	373599 / 3395	0.97 (0.93 to 1.00)	1830 / 575	0.95 (0.84 to 1.07)
No. of cigarettes/day				
None	1292632 / 15683	REF (1.00)	1870 / 819	REF (1.00)
1-9 cigarettes/day	233897 / 2150	0.96 (0.91 to 1.00)	1374 / 433	0.94 (0.83 to 1.06)
≥ 10 cigarettes/day	139702 / 1245	0.98 (0.92 to 1.04)	456 / 142	0.97 (0.82 to 1.14)
<i>P</i> trend		0.17		0.63
5 to < 15 years				
Smoking				
No	1258379 / 167585	REF (1.00)	18942 / 8481	REF (1.00)
Yes	365874 / 43476	1.08 (1.07 to 1.09)	18712 / 7221	1.02 (0.98 to 1.05)
No. of cigarettes/day				
None	1258379 / 167585	REF (1.00)	18942 / 8481	REF (1.00)
1-9 cigarettes/day	229015 / 27554	1.07 (1.06 to 1.09)	14091 / 5509	1.02 (0.98 to 1.05)
≥ 10 cigarettes/day	136859 / 15922	1.09 (1.07 to 1.10)	4621 / 1712	1.01 (0.96 to 1.06)
<i>P</i> trend		< 0.001		0.60
≥ 15 years				
Smoking				
No	1015792 / 104435	REF (1.00)	12700 / 5048	REF (1.00)
Yes	310479 / 41143	1.11 (1.09 to 1.12)	12617 / 5648	1.00 (0.95 to 1.04)
No. of cigarettes/day				
No	1015792 / 104435	REF (1.00)	12700 / 5048	REF (1.00)
1-9 cigarettes/day	193498 / 25122	1.10 (1.08 to 1.11)	9432 / 4275	0.99 (0.95 to 1.04)
≥ 10 cigarettes/day	116981 / 16021	1.13 (1.11 to 1.15)	3185 / 1373	1.01 (0.95 to 1.07)
<i>P</i> trend		< 0.001		0.84

Hazard ratios (with 95% confidence intervals) for bone fractures comparing offspring exposed to maternal smoking during pregnancy (any, 1-9 cigarettes/day, ≥ 10 cigarettes day) to those unexposed (= reference group) – analyses after multiple imputation of missing covariate data. Hazard ratios are presented by attained age (0 to < 1 year, 1 to < 5 years, 5 to < 15 years, ≥ 15 years) and for the different analysis models: model 2: whole cohort analysis adjusted for birth year, offspring sex, maternal age, parity, height, body mass index, parental education, occupation and marital status; and model 3: within-sibship analysis including all covariates included in model 2 except for maternal height, a variable which is unlikely to vary among siblings in the same family. * The within-sibship analysis model includes all offspring with siblings, but only families who are also discordant on both the exposure and outcome contribute to the estimation of the hazard ratio. The numbers presented in the table therefore refer to the total number of offspring with siblings discordant on bone fractures and maternal smoking during pregnancy. Abbreviations: HR = hazard ratio; CI = confidence interval.