Osteoporosis International
https://doi.org/10.1007/s00198-024-07361-5

ORIGINAL ARTICLE

Is there an association between birth characteristics and fractures in young adults? The HUNT Study, Norway

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Received: 19 June 2024 / Accepted: 17 December 2024

Abstract

Summary This population study investigated the association between birth characteristics and fracture risk in 11,099 young adults (aged 19–54 years). Our findings indicate that birth weight, gestational age, and birth weight for gestational age were not associated with fractures in the wrist, humerus, hip, and spine in this population.

Purpose Skeletal development starts during fetal life, and it is estimated that most bone formation occurs in the 3rd trimester. This study examined the association between birth characteristics and fractures of the wrist, humerus, hip, and spine, in young adults (19–54 years).

Methods 11.099 participants in the 3rd survey of the HUNT Study (2006–2008) were linked with the Medical Birth Registry of Norway and hospital records. Fractures of the wrist, humerus, hip, and spine were identified using ICD9/10 codes between 1988 and 2021. Follow-up was from date of participation in HUNT until a first fracture, emigration, death, or end of study. Cox regression was used to estimate hazard ratios (HR) of fracture associated with birth characteristics (95% CI), adjusted for birth year, sex, maternal age, and maternal morbidity. In a secondary analysis, follow-up started in 1988.

Results During a median follow-up of 14.0 years (153,657 person-years), 290 fractures occurred. Mean age at first fracture was 41.4 years (SD 7.4). Overall, there were no clear associations between birth characteristics and fractures in these data. HR for fracture was 0.43 (0.15–1.24) for those with a birth weight < 2.5 kg (reference birth weight 3.5 – 3.9 kg); 1.04 (0.74 – 1.46) for those born small for gestational age (< 10th percentile, reference 10 – 90th percentile); and 0.63 (0.33 – 1.23) for those born preterm (reference term births). The secondary analysis from 1988, including 539 fractures, gave similar results as the main analysis.

Conclusion Birth weight, gestational age, or birth weight for gestational age was not associated with an increased risk of fractures of the wrist, humerus, hip, and spine in young adults.

Keywords Birth weight · Fracture · Premature · Young adults

Introduction

Fractures are a global health challenge. Although the age-standardized fracture incidence rate decreased slightly worldwide between 1990 and 2019, the number of new fractures increased by 30% during this period due to population growth and aging [1]. An individual's risk of developing osteoporosis accumulates throughout life, starting during fetal development [1]. Skeletal development begins early in pregnancy, with rapid growth in the last trimester, when it is estimated that 80% of the bone mass formation in the newborn is attained [1, 2]. During this period, placental transfer of important nutrients for the fetal skeleton takes place and it is a crucial period for bone mineralization. Notably, infants born preterm may face an increased risk of poor bone health [1, 2]. During childhood and adolescence, skeletal development continues until the maximum bone gained in young adulthood, peak bone mass, is reached [3, 4]. Women typically attain peak bone mass in their early twenties, while men tend to reach it in their later twenties [3].

Several studies have found an association between birth weight and bone mineral density (BMD), with lower BMD among children and adults who had been born preterm [2, 4–7]. Limited data currently exists regarding the relationship between birth weight and fracture risk in young adults.

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Published online: 08 January 2025

Most of the studies have focused primarily on children up to adolescents or older adults, with conflicting results.

Four studies found no association between birth characteristics and fractures in children [8–11]. One study reported an increased risk of childhood fractures in those born before 37 weeks of gestation [11], while another study showed a reduced risk of childhood fractures in children born very preterm or with a very low birth weight (VLBW < 1.5 kg) [12]. Three Finnish studies [13–15] and one Swedish study [16] did not find any relationship between birth weight and fracture in older age [17].

However, Mendelian randomization analyses of birth weight and the risk of osteoporosis based on the UK Biobank [18] found that higher birth weight was associated with an increased risk of fractures in adults aged 40–69.

The impact of birth characteristics on fracture risk in young adults remains unclear. As most of the bone mass formation in infants occurs during the last trimester [1, 2], we hypothesized that the risk of fractures in the wrist, humerus, hip, and spine may occur earlier among those born with low birth weight. We aimed to investigate whether specific birth characteristics, including birth weight, gestational age, and birth weight for gestational age, are associated with fractures in young adults 20–54 years.

Material and methods

Study population and data sources

We used data from the Trøndelag Health Study (HUNT), the Medical Birth Registry of Norway (MBRN), and hospital records in the catchment area to identify fractures. Data were linked via their unique national 11-digit personal identification number.

HUNT

Data were collected from the third survey of the Trøndelag Health study, HUNT 3 (2006–2008), a large longitudinal population-based health study in central Norway. The geographic, demographic, and occupational structure of this region are considered representative of the country as a whole [19, 20]. All individuals aged 20 years or older in that year were invited to participate, and 50,821 (54.1%) responded. The participants completed comprehensive questionnaires and underwent a short clinical examination at the screening station. We included 11,099 participants (64,314 women and 4665 men) born 1967–1988 with available information on their own birth in the MBRN, see flowchart (Fig. 1).

Medical Birth Registry of Norway

Information on birth characteristics was collected from the Medical Birth Registry of Norway (MBRN). The MBRN is a national health register established in 1967 that collects information on all births reported by Norwegian maternity units as well as home births and births during transportation [21]. In addition to the name and personal identification number of both the child and the parents, the register contains information about the mother's health before and during pregnancy and any complications in connection with the birth. Furthermore, it documents the newborn's health information, such as birth length, birth weight, head circumference, and Apgar (Activity, Pulse, Grimace, Appearance, Respiration) score, among others.

Exposures: birth characteristics

Birth weight was categorized as follows:

< 2.5 kg (low birth weight, LBW) [22]; 2.5–2.9 kg; 3.0–3.4 kg; 3.5–3.9 kg (reference group, representing the average weight of both boys and girls in Norway) [23]; 4.0–4.4 kg; ≥ 4.5 kg (high birthweight, HBW).

Additionally, birth weight was included as a continuous variable.

Gestational age at delivery was defined as the duration of a pregnancy, measured from the first day of the woman's last menstrual period:

- Preterm (< 37 weeks) [24]
- Term (37–41 weeks, reference group) and
- Post-term birth (≥ 42 weeks)

Birth weight for gestational age was defined as the infant's weight relative to their gestational age, categorized by standardized birth weight (z-score) [25] into the following groups:

- Small for gestational age (SGA): Birth weight below the 10th percentile (z-score < − 1.28).
- Appropriate for gestational age (AGA): Birth weight between the 10th and 90th percentile (z-score between − 1.28 and 1.28 SD) (reference group).
- Large for gestational age (LGA): Birth weight above the 90th percentile (z-score > 1.28 SD).

Outcome: fractures

Fractures were identified from the only two hospitals in the catchment area by using the International Classification of Disease (ICD) codes: version 9 (for fractures obtained

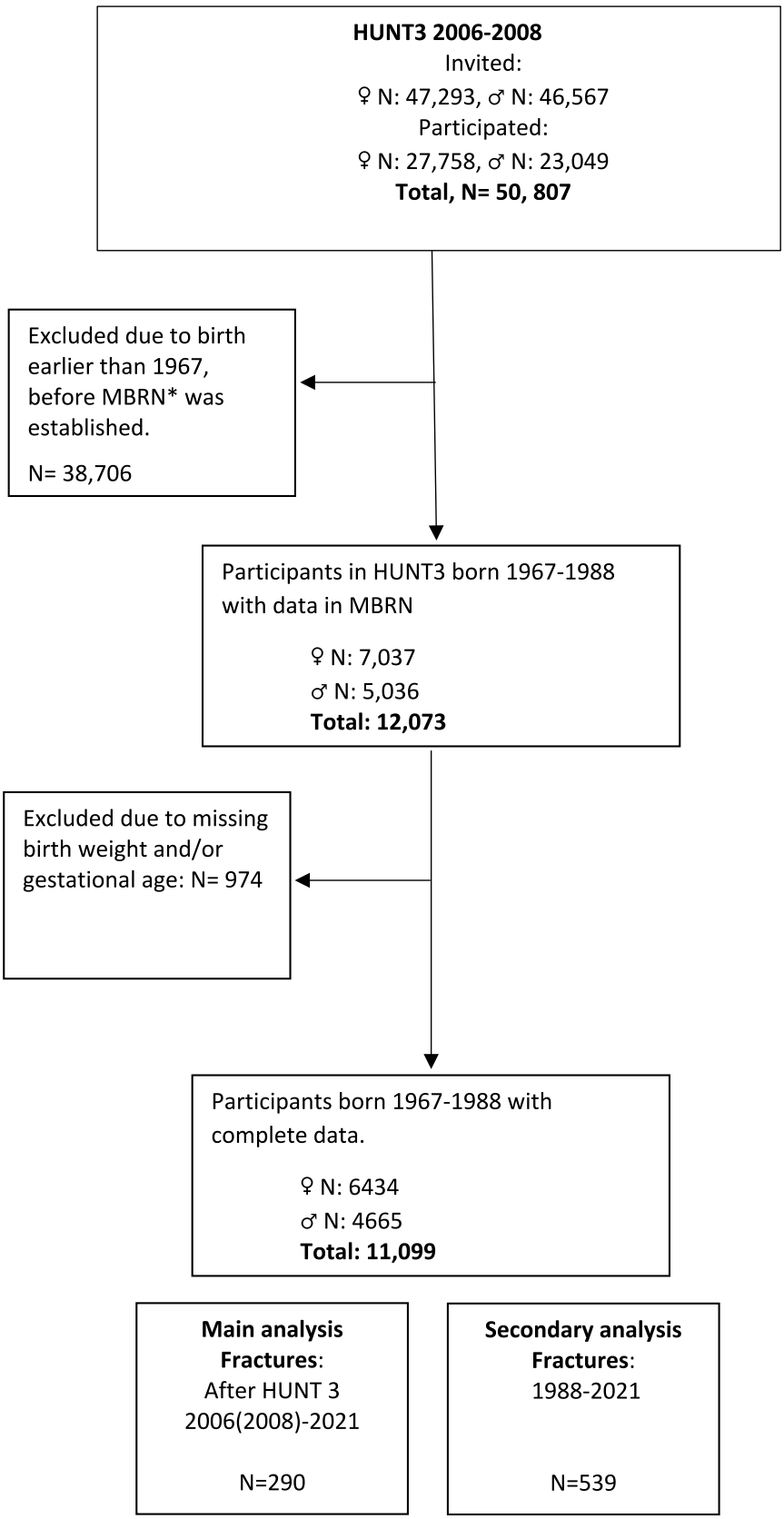

Fig. 1 Flowchart of the included participants in the present study. *MBRN, Medical Birth Registry of Norway

before 2000 in the secondary analysis) or version 10. None of these fractures is treated in primary care or private hospitals. The fracture types we aimed to study, and those we had access to, included proximal humerus (812.0–812.3; S42.2–S42.31); distal forearm (813.4, 813.5; S52.5–S52.61); hip (820.0–820.3; S72.0–S72.21); and spine (805.2–805.5; 806.0–806.5; S12.0–S12.21; S22.0– S22.1; S32.0– S32.01; T08, T08.90). Where available, we also used the NOMESCO Classification of Surgical Procedures codes (NCPS) for surgery, cast, or splint.

To ensure accuracy and avoid misclassification of suspected fractures, a non-vertebral fracture was defined as one of the following: (1) two identical ICD codes within 3 months; (2) one ICD code and one relevant NCSP code registered within 2 months before and 3 months after the ICD code. For fractures of the spine, only one ICD diagnosis code was required. Fracture diagnosis codes that occurred less than a year after a defined fracture were considered to represent new registrations of the same fracture [26]. The fractures were recorded from 1988 (the beginning of electronic recording at regional hospitals) until October 21, 2021.

Covariates

Potential confounders were selected based on a Directed Acyclic Graph (Fig. 2) and included sex, birth year, maternal age, and maternal morbidity. Maternal morbidity comprised conditions recorded before or during pregnancy that may potentially affect the offspring [27], including chronic inflammatory joint disease, diabetes, and preeclampsia/eclampsia.

Statistical analysis

Descriptive data are presented as means with standard deviations (SD) for continuous data and numbers and percentages for categorical data. All birth characteristics were analyzed

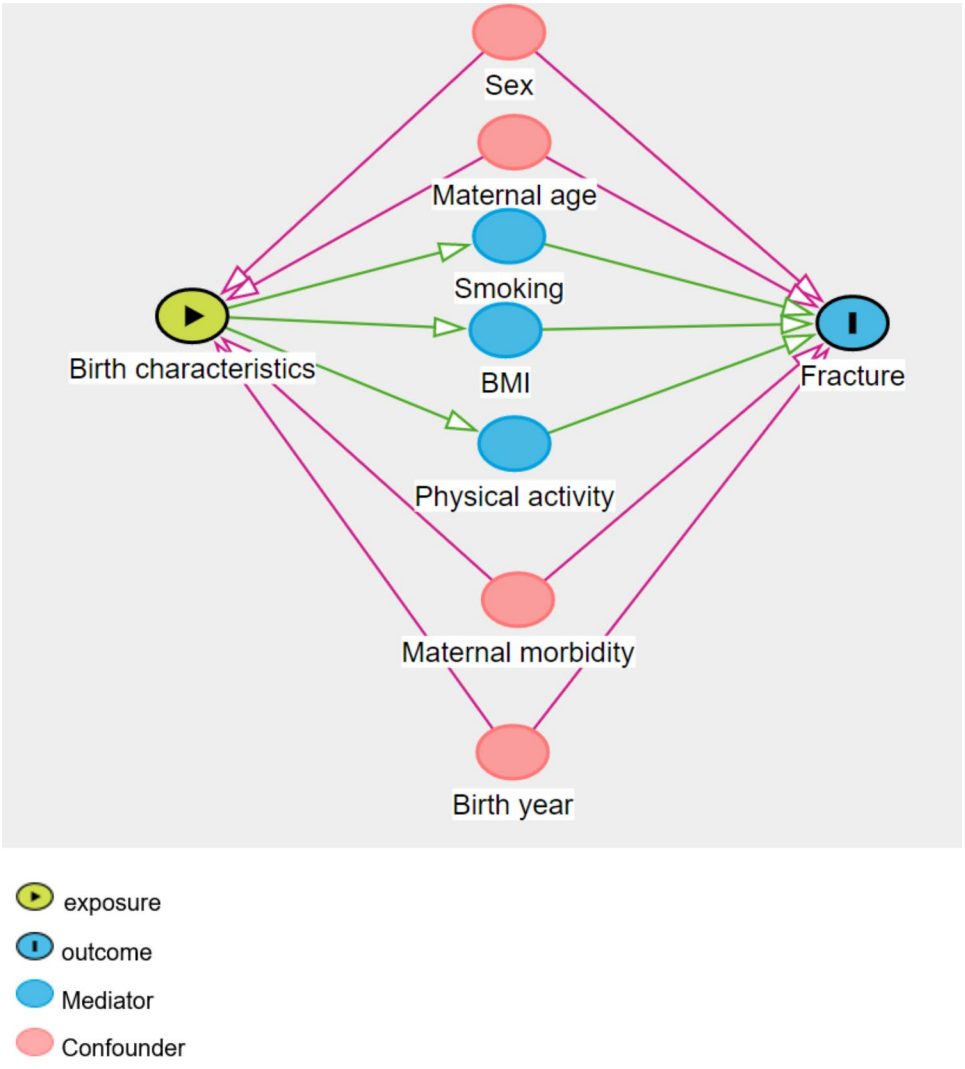

Fig. 2 Directed Acyclic Graph with confounders and mediators

as categorical variables, and birth weight was additionally analyzed as a continuous variable using either standard deviation scores or per 100 g increase in birth weight. Crude and adjusted hazard ratios (HRs) of fracture associated with the various birth characteristics were estimated using Cox regression. The precision of all estimated associations is given by a 95% confidence interval (CI). Sex and maternal morbidity were included as categorical variables, while maternal age and birth year were continuous. In analyses of birth weight, we also adjusted for gestational age, to isolate the specific impact of birth weight on the outcome variable. While we focus on young adults, the time at risk in the main analysis started on the date of participation in HUNT 3 when the participants were 19–41 years old, and ended on the date of first fracture, emigration, death, or end of follow-up (October 21, 2021). This approach helps address potential selection bias that could arise if we started from birth. We also present a secondary analysis, where the time at risk started on January 1, 1988, and ended on the same events as in the main analysis.

We also conducted a test for linear trend across categories of birth characteristics adjusting for relevant confounders, treating the categories as an ordinal variable in the regression model.

In the main analysis, several sensitivity analyses were conducted: excluding participants with birth weights < 2.5 kg to address potential non-linear relationships, assessing the impact of cesarean section on birth weight categories and gestational groups in relation to fracture risk, and analyzing outcomes for distal forearm fractures and excluding spine fractures to evaluate their impact on results.

The proportional hazards assumption was evaluated using Schoenfeld residuals and graphical methods, including visual inspection of log-minus-log plots. All statistical analyses were performed using Stata 18.0 (StataCorp LCC, College Station, TX, USA).

Ethics

Participants in HUNT 3 gave written, informed consent for the data to be used for research, including a linkage with other registers. The study was approved by the Regional Committee for Medical Research Ethics, Central Norway (application number 246732) [21].

Results

Characteristics of the participants, both at birth (1967–1988) and at baseline in HUNT 3 (2006–2008), along with maternal information, are summarized in Table 1.

A total of 11,099 participants aged 19–54 years were included from HUNT 3 with a mean (SD) age of 31.8 (6.3) years. Of these, 58% were women. Among the participants, a total of 389 (3.5%) were born with a LBW, of which 30 were born with a VLBW. Further, 1362 (12.3%) were born SGA, 8719 (78.6%) AGA, and 1018 (9.2%) were born LGA. In total, 517 (4.7%) were born preterm, 8777 (79.1%) at term, and 1801 (16.2%) post-term.

The mothers' mean age at delivery was 26.3 years. Preeclampsia affected 2.2% of all pregnancies, whereas diabetes (both pre-pregnancy and gestational diabetes) and chronic inflammatory joint disease each affected 0.1% (Table 1).

At HUNT 3, participants had a mean BMI of 26.2 kg/m^2. There were minor differences in adult BMI, physical activity, and smoking across different birth weight categories (Table 1).

In total, we had 290 fractures registered, with 176 among women and 114 among men. The forearm was the most common fracture site, accounting for 168 cases (58%). This was followed by fractures of the humerus (54 cases, 19%), spine (53 cases, 18%), and hips (15 cases, 5%). None of those with VLBW experienced a fracture, and among the participants with LBW only four fractures occurred in the main analysis and 15 fractures during the follow-up period starting from 1988.

Main analysis

In the main analysis with follow-up from HUNT 3, a total of 153,657 person-years were included, during which 290 fractures were recorded. The mean age at the time of fracture was 41.4 years (SD 7.4). Participants were followed up to a mean age of 45.2 years, and the mean follow-up duration was 13.8 years (SD 1.47) (Table 2).

Overall, birth weight was not associated with fractures. For fractures recorded after enrolment in HUNT 3 (Table 2), participants with LBW had an HR of 0.43 (95% CI, 0.15–1.24) compared to those with normal birth weight (3.5–3.9 kg) after adjustment for maternal morbidity, maternal age, year of birth, and sex. Conversely, those born with a birth weight greater than 4.5 kg had an adjusted HR of 1.23 (0.71–2.12). When assessing the trend between birth weight and fracture risk, the adjusted HR in the main analysis was 0.97 (0.88–1.08).

For birth weight standardized for gestational age, the adjusted HR was 1.04 (0.74–1.46) for participants born SGA, and 0.99 (0.66–1.51) for those born LGA, when compared to those born AGA. In the trend analysis, the adjusted HR was 0.99 (0.83–1.19).

There was no significant association between gestational age and the occurrence of fractures, with an adjusted HR of 0.63 (0.33–1.23) for those born preterm and 0.86 (0.62–1.19) for those born post-term, compared with term births. The trends for gestational age and fracture risk were 1.01 (0.78–1.31).

Table 1 Characteristics of the study population

	Total	Birth weight, kg					
Characteristics at birth		< 2.5 kg	2.5–2.9 kg	3.0–3.4 kg	3.5–3.9 kg	4.0–4.4 kg	≥ 4.5 kg
No. of participants (%)	11,099 (100.0)	389 (3.5)	842 (7.6)	3157 (28.4)	4227 (38.1)	1968 (17.7)	516 (4.7)
Female, *n* (%)	6434 (58.0)	240 (61.7)	566 (67.2)	2055 (65.1)	2418 (57.2)	952 (48.4)	203 (39.3)
Small for gestational age, *n* (%) [a]	1362 (12.3)	267 (19.6)	605 (44.4)	490 (35.4)	0	0	0
Appropriate for gestational age, *n* (%) [b]	8719 (78.6)	117 (1.3)	235 (2.7)	2646 (30.3)	4169 (47.8)	1538 (17.7)	14 (0.2)
Large for gestational age, *n* (%) [c]	1018 (9.2)	5 (0.5)	2 (0.2)	21 (2.1)	58 (5.7)	430 (42.2)	502(49.4)
Cesarean, *n* (%)	508 (4.6)	63 (16.2)	61 (7.2)	140 (4.4)	146 (3.5)	77 (3.9)	21 (4.1)
Maternal characteristics							
Primiparous, *n* (%)	4235 (56.8)	183 (57.5)	380 (64.2)	1390 (63.5)	1582 (56.9)	599 (47.2)	101 (30.1)
Multiparous (≥ 2), *n* (%)	3218 (43.2)	135 (42.5)	212 (35.8)	798 (36.5)	1200 (43.1)	669 (52.8)	234 (69.9)
Married/registered partner, *n* (%)	9628 (86.8)	307 (78.9)	714 (84.8)	2681 (85.0)	3675 (87.0)	1774 (90.2)	477 (92.4)
Maternal age at delivery, years, *n* (%)							
- ≤ 19	781 (7.0)	35 (9.0)	71 (8.4)	259 (8.2)	286 (6.8)	111 (5.6)	19 (3.7)
- 20–34	9583 (86.3)	325 (83.6)	712 (84.6)	2730 (86.5)	3670 (86.8)	1716 (87.2)	430 (83.3)
- ≥ 35	735 (6.6)	29 (7.5)	59 (7.0)	168 (5.3)	271 (6.4)	141 (7.2)	67 (13.0)
Preeclampsia/eclampsia, *n* (%)	241 (2.2)	37 (9.5)	33 (3.9)	51 (1.6)	62 (1.5)	48 (2.4)	10 (1.9)
Diabetes, *n* (%) *	14 (0.1)	0 (0)	1 (0.1)	3 (0.1)	4 (0.1)	5 (0.3)	1 (0.2)
Chronic inflammatory joint disease, *n* (%)	15 (0.1)	0 (0)	2 (0.2)	4 (0.1)	5 (0.1)	4 (0.2)	0 (0)
Characteristics at HUNT 3							
Age, mean (SD) years	31.8 (6.3)	31.8 (6.3)	32.4 (6.1)	31.8 (6.3)	32.0 (6.4)	31.4 (6.4)	31.5 (6.2)
BMI, mean (SD) kg/m^2	26.2 (4.7)	26.6 (5.1)	26.1 (4.8)	25.9 (4.8)	26.2 (4.6)	26.6 (4.8)	27.0 (4.4)
Height, mean (SD) cm	172.5 (8.9)	168.8 (8.8)	168.3 (8.5)	170.4 (8.4)	172.9 (8.6)	175.8 (8.6)	178.4 (8.5)
Current smokers, *n* (%)	2882 (26.0)	105 (27.0)	232 (27.6)	826 (26.2)	1083 (25.6)	514 (26.1)	122 (23.6)
Physical activity, %							
≥ 2–3/week	5802 (52.8)	203 (52.7)	414 (49.6)	1670 (53.6)	2258 (53.9)	994 (51.2)	263 (51.3)
≤ 1/week	5181 (47.2)	182 (47.3)	421 (50.4)	1447 (46.4)	1932 (46.1)	949 (48.8)	250 (48.7)

[a]($p < 10$), [b](p 10–90), [c]($p > 90$). *Both pre-pregnancy and gestational diabetes

Sensitivity analyses

Excluding participants with a birth weight of less than 2.5 kg, assessing the effect of cesarean section, and conducting separate analyses for distal forearm and vertebral fracture removal did not significantly change the results.

Secondary analysis

For the secondary analysis starting in 1988, we included data from 367,148 person-years of follow-up, resulting in 539 recorded fractures. The mean follow-up during this period was 33.1 years (SD 0.03), and the mean age at fracture was 32.1 years (SD 12.6). There was no association between birth weight and fractures, birth weight standardized for gestational age and fractures, or gestational age and fractures (Table 3). The same adjustments were made as in the main analysis.

Discussion

In this population-based cohort study, we found no association between birth characteristics and fracture risk in young adults born between 1967 and 1988 (aged 19–54 years during follow-up). Our findings do not support that people who are born prematurely or with LBW, and thus theoretically with reduced mineralization of the skeleton, suffer more fractures than the general population in early adulthood. To our knowledge, this is the first study examining birth characteristics and fracture risk in this age group.

Studies have shown that most children born SGA and/or with LBW tend to catch up during the first 2–3 years of life [28, 29]. In addition, other studies examining childhood growth and its association with later hip fracture risk show that children with low growth rates during childhood and adolescence are at higher risk [13–15]. In our study, the number of hip fractures was rather low. Interestingly, our study found no differences in BMI by birth weight

Table 2 Risk of fractures between participation in HUNT 3 (2006/08) through October 2021 according to birth characteristics (main analysis)

Variable	Number (%)	Person-year	Fractures (n)	HR, crude	HR Adjusted** (95% CI)	HR (95% CI), Trend test***
Birth weight, kg						
Continuous (per 100 g increase)	11,099(100)	153, 657	290	1.00	0.99 (0.97–1.01)	0.99 (0.98–1.01)
Continuous (per SD increase) *	11,099 (100)	153, 657	290	0.99	0.94 (0.86–1.03)	0.98 (0.90–1.07)
< 2.5 kg	389 (3.5)	5, 429	4	0.39	0.43 (0.15–1.24)	0.97 (0.88–1.08)
2.5–2.9 kg	842 (7.6)	11, 673	30	1.38	1.36 (0.90–2.05)	
3.0–3.4 kg	3157 (28.4)	43, 665	89	1.09	1.09 (0.82–1.44)	
3.5–3.9 kg	4227 (38.1)	58, 436	109	1 (ref)	1 (ref)	
4.0–4.4 kg	1968 (17.7)	27, 343	43	0.84	0.89 (0.62–1.27)	
≥ 4.5 kg	516 (4.7)	7, 110	15	1.31	1.23 (0.71–2.12)	
Birth weight for gestational age						
Small for gestational age (SGA)	1362 (12.3)	18, 937	38	1.07	1.04 (0.74–1.46)	0.99 (0.83–1.19)
Appropriate for gestational age (AGA)	8719 (78.6)	120, 663	227	1 (ref)	1 (ref)	
Large for gestational age (LGA)	1018 (9.2)	14, 057	25	0.95	0.99 (0.66–1.51)	
Gestational age						
< 37 weeks (preterm)	518 (4.7)	7, 159	9	0.64	0.63 (0.33–1.23)	1.01 (0.78–1.31)
37–41 weeks (term)	8777 (79.1)	121, 526	238	1 (ref)	1 (ref)	
≥ 42 weeks (post-term)	1802 (16.2)	24, 972	43	0.88	0.86 (0.62–1.19)	

*SD = 546 g for birthweight across all gestational weeks

**Models are adjusted for birth year, sex, maternal age, and maternal morbidity. For birth weight, we also adjusted for gestational length

***A trend test was conducted to assess the association between birth weight and fracture risk, with birth weight as a continuous variable

categories among the study participants in adulthood. In fact, we observed a relatively high average BMI (mean 26.2 kg/m^2) across all birth weight categories, including those born SGA and with LBW, when compared to what is considered a normal BMI (18.5–24.9 kg/m^2). These results may indicate that factors after birth play a more crucial role than birth size in determining fracture risk later in life. Furthermore, it is important to note that a low BMI in adulthood is associated with a significant increase in fracture risk, whereas a higher BMI appears to be protective against fractures [30]. This relationship may offer a plausible explanation for the findings presented in our article. Although our analysis did not find group-level differences in BMI by birth weight categories, further investigation using interaction measures could provide insights. However, the low fracture rate in our study may limit statistical power to demonstrate this interaction.

Another potential explanation for our findings is that the cohort was too young to manifest any effects of birth characteristics on fracture risk. A systematic review of studies investigating LBW and adult bone mass found that people with LBW tend to have lower bone mass in adulthood [31]. Thus, birth weight may serve as a risk marker for future osteoporosis, a condition characterized by reduced bone mineral density. We did not find any increase in fractures at sites of osteoporotic fractures among those with LBW.

Studies have shown that the incidence of fractures in young adults under the age of 50 is highest in men, with high-energy injuries being the most common cause [32]. In contrast, older individuals experience low-energy fractures primarily due to osteoporosis, a condition more prevalent among women [32]. However, even high-trauma fractures have been shown to be associated with low bone mineral density [33, 34]. Further, studies indicate that preterm children have lower rates of risk-taking behavior [35] and are less likely to participate in sports [36] compared to full-term children. In this study, none of the 30 participants born with VLBW underwent a fracture after the age of 20. Studies have demonstrated that adults born with VLBW have inferior general, fine, and gross motor skills compared to adults born at term [37]. It is plausible that this difference contributes to reduced participation in situations with a risk of fracture, persisting through young adulthood.

The major strength of this study is the use of a large population-based cohort with a long follow-up time and registers with high quality and attendance. Fracture information was extracted from medical records through careful review and the utilization of ICD and NCSP codes following official

Table 3 Risk of fractures according to birth characteristics including all fractures from 1988 through October 2021 (secondary analysis)

Variable	Number (%)	Person-year	Fractures (n)	HR, crude	HR Adjusted** (95% CI)	Trend test***
Birth weight, kg						
Continuous (per 100 g increase)	11,099 (100)	367, 148	539	1.00	0.99 (0.97–1.01)	1.00 (0.98–1.01)
Continuous (per SD increase) *	11,099 (100)	367, 148	539	0.99	0.94 (0.86–1.03)	0.98 (0.90–1.07)
< 2.5	389 (3.50)	12, 869	15	0.82	0.97 (0.55–1.71)	0.99 (0.92–1.07)
2.5–2.9	842 (7.59)	27, 953	44	1.10	1.16 (0.83–1.61)	
3.0–3.4	3157 (28.44)	104, 279	162	1.09	1.11 (0.90–1.36)	
3.5–3.9	4227 (38.08)	139, 919	200	1 (ref)	1 (ref)	
4.0–4.4	1968 (17.73)	65, 059	93	1.00	0.98 (0.77–1.26)	
≥ 4.5	516 (4.65)	17, 069	25	1.03	1.00 (0.65–1.51)	
Birth weight for gestational age						
Small for gestational age (SGA)	1362 (12.27)	45, 071	67	1.00	1.01 (0.78–1.31)	0.95 (0.83–1.09)
Appropriate for gestational age (AGA)	8719 (78.56)	288, 461	428	1 (ref)	1 (ref)	
Large for gestational age (LGA)	1018 (9.17)	33, 752	44	0.88	0.88 (0.64–1.20)	
Gestational age						
< 37 weeks (preterm)	517 (4.7)	17, 147	20	0.78	0.77 (0.49–1.20)	1.03 (0.85–1.24)
37–41 weeks (term)	8777 (79.1)	290, 432	434	1 (ref)	1 (ref)	
≥ 42 weeks (post-term)	1801 (16.2)	59, 568	85	0.96	0.95 (0.76–1.21)	

*SD = 546 g for birthweight across all gestational weeks

**Models are adjusted for birth year, sex, maternal age, and maternal morbidity. For birth weight we also adjusted for gestational length

***A trend test was conducted to assess the association between birth weight and fracture risk, with birth weight as a continuous variable

coding standards for the healthcare services, ensuring precise numerical data. Birth characteristics were accurately measured in Norwegian maternity units [38]. Our participants, born in 1967 and later, allowed us to assess fracture risk in individuals living in a prosperous country (by today's standards).

However, the study has limitations. Firstly, few fractures occurred due to the inclusion of young participants, and we chose to focus on fractures associated with osteoporotic sites: spine, hip, proximal humerus, and distal forearm. Secondly, our data lack information on fractures occurring before 1988, so we could not explore fractures in children. While selection bias may contribute to the low number of LBW individuals in our study, information was not available on whether individuals born with LBW were less likely to participate in the HUNT survey. However, notably, the LBW prevalence in the Norwegian capital during the same time period is comparable in magnitude [39]. Furthermore, the MBRN did not record maternal smoking habits during pregnancy before 1999, and it is known that pregnant women in Norway had one of the highest smoking prevalences globally in the mid-1980s [40]. Another limitation is the lack of complete follow-up, which may affect the generalizability and robustness of our findings.

Lastly, the effect of birth characteristics may have changed over time due to improved prenatal care, potentially diminishing the impact of LBW. However, due to the limited number of fractures, we did not explore this further.

To mitigate confounding effects, we adjusted for birth weight by gestational age; however, it should be recognized that this adjustment may inadvertently introduce collider bias [41].

Conclusions

In this population-based cohort study evaluating the association between birth characteristics and fracture risk in adults aged 19–54 years, we conclude that neither birth weight, birth weight for gestational age, nor gestational age was associated with subsequent fractures.

Funding Open access funding provided by NTNU Norwegian University of Science and Technology (incl St. Olavs Hospital - Trondheim University Hospital). Hilde Thomasli Holltrø has received a doctoral scholarship from the Norwegian Women's Health Association (Norske kvinners sanitetsforening, N.K.S., grant number: 40027) in collaboration with the Norwegian University of Science and Technology, NTNU. The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between HUNT Research Center (Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU)), Trøndelag County Council, Central Norway Regional Health Authority, and the Norwegian Institute of Public Health.

Declarations

Conflicts of interest None.

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