

# BMJ Open Does tobacco use influence bone mineral density levels in a Norwegian youth cohort followed from adolescence to young adulthood? The Fit Futures Study (2010–2022)

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## ABSTRACT

**Objectives** To investigate the longitudinal associations between tobacco use (smoking and snuff) and bone mineral density (BMD) at femoral sites and in the total body in a Norwegian adolescent cohort, aged 16–27 years.

**Design** Prospective longitudinal cohort study.

**Setting** A population-based study in Norwegian adolescents from the general population.

**Participants** In total, 722 adolescents (385 females and 337 males) with a mean age of 16 years (SD: 0.5) from the Fit Futures Study (FF) were included at FF1 (2010–2011), with follow-up measures at age 18 years (FF2 (2012–2013)) and 27 years (FF3 (2021–2022)). Inclusion criteria were completed dual-energy X-ray absorptiometry (DXA) scans, serum vitamin D blood samples and information on smoking, snuff use, physical activity, height, alcohol intake, hormonal contraceptive use and puberty status, all at baseline (FF1).

## Primary and secondary outcome measures

Associations between self-reported smoking and snuff use (categorised as never, sometimes or daily) and changes in BMD (g/cm<sup>2</sup>) at the total hip, femoral neck and total body, measured using DXA.

**Results** Total hip BMD (mean (g/cm<sup>2</sup>), 95% CI) slightly increased from FF1 (females: 1.066, 95% CI 1.054 to 1.079; males: 1.121, 95% CI 1.105 to 1.136) to FF2 (females: 1.076, 95% CI 1.063 to 1.089; males: 1.141, 95% CI 1.126 to 1.157;  $p < 0.001$ ), but thereafter decreased to FF3 (females: 1.050, 95% CI 1.036 to 1.063; males: 1.091, 95% CI 1.074 to 1.107; females and males, both  $p < 0.001$ ). Similar patterns were observed for the femoral neck, while total body BMD increased from FF1 through FF3 ( $p < 0.001$ ). We observed interactions between time and smoking and between time and snuff use in all models (all  $p < 0.001$ ). However, we generally observed no statistically significant differences in BMD levels across smoking and snuff use groups at different time points (all  $p > 0.07$ ), except in females at 18 years (FF2), where those who never smoked had higher total hip BMD than those who sometimes and never smoked ( $p < 0.001$ ).

**Conclusions** We found no statistically significant associations between smoking or snuff use and BMD

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study used a population-based cohort design, allowing control for a wide range of potential confounders and ensuring a balanced sample of both sexes, with a long follow-up period from adolescence to young adulthood, enhancing generalisability to Western populations.
- ⇒ The use of dual-energy X-ray absorptiometry for bone mineral density measurements, performed by trained personnel, minimised measurement errors and improved data reliability.
- ⇒ Participant dropout over time may have introduced bias, though linear mixed models were used to mitigate missing data effects.
- ⇒ Self-reported smoking data may be subject to desirability bias and under-reporting, leading to misclassification and reduced statistical power, particularly given the low prevalence of smoking in this cohort.

levels in Norwegian adolescents from a median age of 16 to 27 years. Notably, only 2.6% of females and 3.9% of males reported smoking daily. However, in this study, moderate tobacco use did not appear to negatively influence bone growth from adolescence to young adulthood.

## INTRODUCTION

Osteoporotic fractures in later life are associated with loss of function, increased mortality<sup>1</sup> and high societal costs.<sup>2</sup> Although hip fracture incidence has declined in the past decades, the number of fractures is expected to increase due to a growing elderly population.<sup>3</sup> Indeed, the lower incidence of hip fractures appears to also coincide with increases in other types of fractures in elderly people, such as forearm, shoulder and leg fractures.<sup>4,5</sup>

Even though osteoporotic fractures occur at an older age, preventive measures at an

early age should also be considered.<sup>6–8</sup> Although age and sex are important predictors of osteoporosis,<sup>9–10</sup> peak bone mass in adolescence and during the transition to adulthood is also an important predictor of future fracture risk.<sup>11</sup> Consequently, this highlights the need for preventive measures to lower fracture incidence at all body sites, including a life course approach to optimising bone health across the lifespan.

About 20–40% of peak bone mass can be attributed to body composition and lifestyle behaviours, such as physical activity levels and drug and tobacco use.<sup>12–14</sup> Although the negative associations between tobacco use and bone mineral density (BMD) mainly include smoking,<sup>12</sup> snuff use is highly prevalent in the Nordic countries.<sup>15</sup> Snuff is a non-smoking tobacco substance used orally and has become increasingly popular in Norway in the past three decades, especially among adolescents and young adults.<sup>15</sup> Even though snuff is mainly sold and used in Norway and Sweden and banned in many other developed countries, snuff use is also increasing in Finland.<sup>16</sup>

Although smoking is associated with low BMD in older adults,<sup>17</sup> studies on the association between smoking and BMD at a younger age are conflicting and potentially influenced by methodological challenges, including low follow-up duration in prospective studies.<sup>12</sup> In one study, the negative effect on bones was higher among older adolescent females than younger ones.<sup>13</sup> Studies examining snuff use and BMD are limited. In one Norwegian study, snuff use was associated with lower BMD from 16 to 18 years in males but not in females.<sup>18</sup> To our knowledge,

despite studies on smoking and BMD,<sup>12</sup> no study has examined snuff use and BMD over longer time periods.

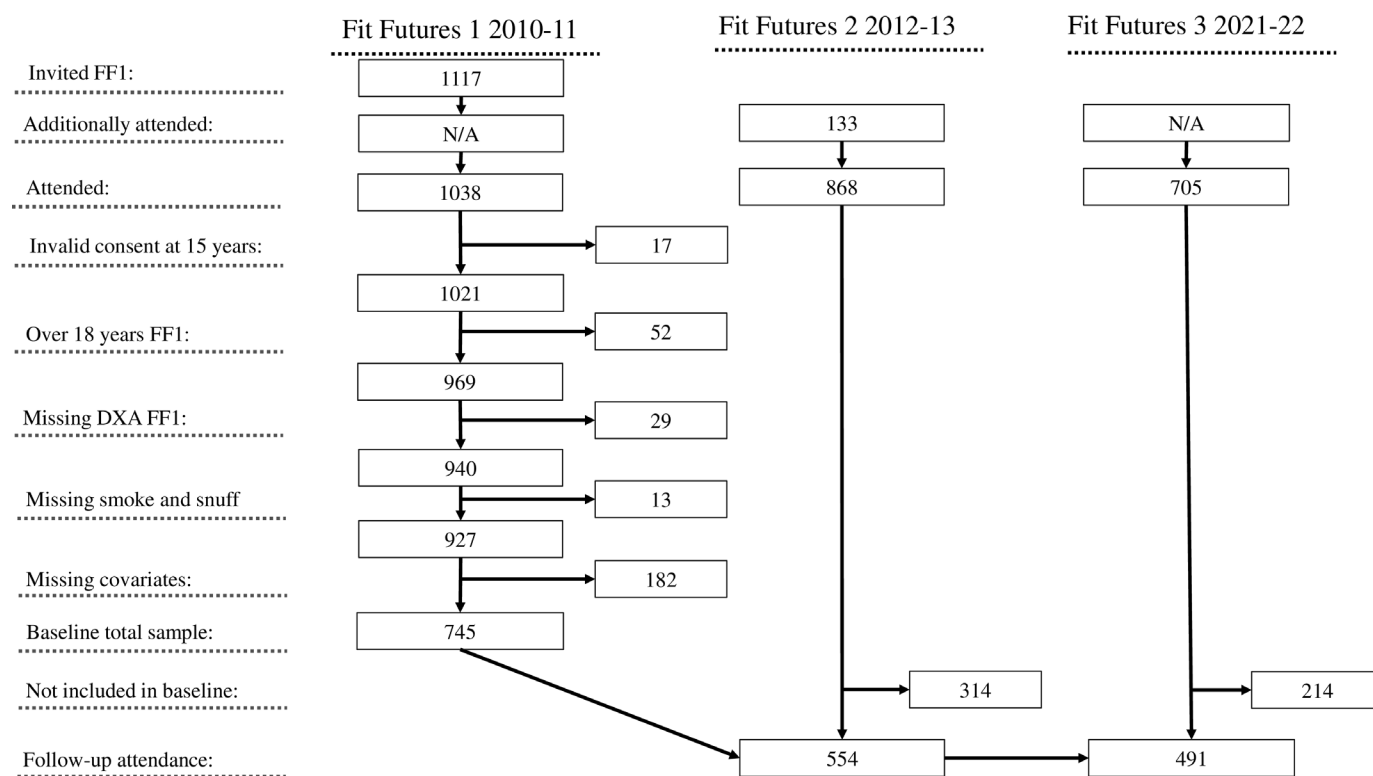
The aim of the present study was, therefore, to examine longitudinal associations between tobacco use (smoking and snuff) and BMD (g/cm<sup>2</sup>) at the total hip, femoral neck and total body in a cohort of Norwegian adolescents followed from the age of 16 years into young adulthood at 27 years.

## MATERIALS AND METHODS

### Study population

This is a prospective cohort study of participants attending the Fit Futures Study (FF),<sup>19</sup> which includes three waves of data collection: FF1 (2010–2011), FF2 (2012–2013) and FF3 (2021–2022). At baseline, all first-year students (n=1117) from all upper-secondary schools in the neighbouring municipalities of Tromsø and Balsfjord were invited to participate, and 1038 students (92.9%) attended.<sup>20</sup> All FF1 attendants were invited to FF2, where 738 participated. Additionally, 133 new participants who attended the same high schools were invited, resulting in a total sample of 868 participants in FF2. All who attended FF1 or FF2 were invited to FF3, where altogether 705 participants attended. Data for 17 were not available for this study due to unconfirmed consent, thus leaving 1021, 846 and 705 participants for inclusion at FF1, FF2 and FF3, respectively (figure 1).

We excluded those who were aged over 18 years (52 participants) in FF1 and those who did not attend FF1



**Figure 1** Flowchart of included participants in the FF (2010–2022). DXA, dual-energy X-ray absorptiometry and FF, Fit Futures Study.

in the follow-up surveys. Inclusion criteria included those who had valid dual-energy X-ray absorptiometry (DXA) scans and vitamin D blood samples, and those who provided information on smoking and snuff use, physical activity, height, alcohol intake, hormonal contraceptive use (females only) and puberty indicators at baseline (FF1). Consequently, we ended up with a total sample size of 745, of which 390 were females and 355 were males. Of these, 554 attended FF2 and 491 attended FF3 (figure 1).

### Patient and public involvement

There was no public involvement in the design of this study. Participating schools were included in the design of the data collection for the FF.

### Measurements of BMD

BMD was measured with DXA (GE Lunar Prodigy, Lunar Corporation, USA), the gold standard for BMD measurements.<sup>21</sup> We used total hip, femoral neck and total body BMD measurements, expressed as g/cm<sup>2</sup>. We chose the mean total hip BMD as our primary outcome and mean femoral neck and total body BMD as secondary outcomes. Trained technicians performed DXA scans, and quality assessment procedures were performed according to protocol on a daily basis. The DXA device used in the FF has previously been validated, with a coefficient of variation of 1.17% for the total hip and 1.72% for femoral neck measurements.<sup>22</sup> The coefficient of variation for total body scans has not been estimated for the DXA device used in this study.

### Smoking and snuff information

Participants self-reported their smoking and snuff use by answering the following question: 'do you smoke/use snuff?' Answer options were 'never', 'sometimes' and 'daily' in FF1, and 'never', 'previous', 'sometimes' and 'daily' in FF2 and FF3. To harmonise all surveys, we collapsed 'sometimes' and 'previous' into one group, resulting in three exposure groups at each survey.

### Covariates

We chose age, ethnicity, serum vitamin D, fat mass, lean mass, height, alcohol intake, physical activity, puberty status and hormonal contraceptive use as covariates, as these are known covariates likely to influence bone formation.<sup>12</sup> Additionally, we included reported educational level (primary school, high school vocational training, high school general studies, university<4 years, university≥4 years) at FF3. All participants were recorded as having completed primary school in FF1 and FF2, as this is a prerequisite for attending high school. Finally, we also included breastfeeding data in FF3, as all females were recorded as not breastfeeding in FF1 and FF2.

Age and sex (strata variable) were self-reported by the participants. Serum vitamin D levels were obtained from blood samples only at FF1. Fat and lean mass in kg were retrieved from total body DXA scans. Ethnicity was recorded by technicians when measuring DXA. Alcohol intake (frequency of drinking), leisure time physical

activity (Saltin-Grimby Physical Activity Scale<sup>23</sup>) and educational level were obtained from questionnaires. Height was measured to the nearest 0.1 cm with participants wearing no shoes. For females, puberty status was self-reported as age at menarche, and males were rated according to the puberty development scale, ranging from 1 to 4, as described by Petersen *et al.*<sup>24</sup> All males were considered to have a puberty score of 4 at FF3 (median age 26 years). Hormonal contraceptive use (yes/no) and breastfeeding (yes/no) were self-reported.

For descriptive purposes, we also used weight and Body Mass Index (BMI). Weight was measured to the nearest 0.1 kg using an automatic electronic scale (Jenix DS 102 stadiometer, Dong Sahn Jenix, Seoul, Korea), with participants wearing light clothing and no shoes. We calculated BMI as weight divided by height squared (kg/m<sup>2</sup>), and used iso-BMI to classify participants as normal weight (corresponding to <25 kg/m<sup>2</sup> for adults), overweight (25–29 kg/m<sup>2</sup> for adults) and obese (≥30 kg/m<sup>2</sup> for adults), according to Cole and Lobstein.<sup>25</sup>

### Statistical analyses

All analyses were stratified by sex. For all analyses, we used linear mixed models with maximum likelihood and random intercept at the individual level. We included surveys (1, 2 and 3) as a categorical variable and tested the main effect of time on mean total hip, mean femoral neck and total body BMD from FF1 through FF3. We, therefore, modelled categorical 'time×smoking groups' and 'time×snuff use groups' interactions in separate models to test for time by tobacco use interactions. From these models, we also tested between-subjects effects to examine differences in BMD levels by smoking and snuff groups at different time points, using Bonferroni-corrected post hoc tests between different groups if a between-subjects effect was observed. We performed both crude models and models adjusted for age (survey), height, ethnicity, fat mass, lean mass, alcohol intake, physical activity, puberty status, serum vitamin D (at FF1), educational level (at FF3), hormonal contraceptive use (females only) and mutual adjustment for smoking and snuff use (in models using smoking as the exposure, snuff acted as a covariate and *vice versa*). We used a first-order autoregressive model, with homogeneous variance as the covariance structure in all models. For sensitivity analyses, we also categorised 'sometimes' smokers and snuff users into 'daily' smokers to evaluate whether 'sometimes' smokers and snuff users masked a potential effect of quitting smoking or using snuff. Alpha was set to 0.05. Data are shown as mean with 95% CI and as mean±SD and frequency (%) for descriptive values. All statistical analyses were performed using Stata V.17 (StataCorp, Texas, USA).

### RESULTS

Approximately 80% of the study population was aged 16 years (mean age females: 16.2 years, SD: 0.5 years; males: 16.2 years, SD: 0.5 years) and of normal weight at baseline



**Table 1** Descriptive characteristics of the participants at baseline in the FF (2010–2022)

|                                         | Females     | Males      |
|-----------------------------------------|-------------|------------|
| Total, n                                | 390         | 355        |
| Age (years), mean±SD                    | 16.2±0.5    | 16.2±0.5   |
| 15 years, n (%)                         | 7 (1.8)     | 8 (2.3)    |
| 16 years, n (%)                         | 316 (81.0)  | 288 (81.1) |
| 17 years, n (%)                         | 61 (15.6)   | 51 (14.4)  |
| 18 years, n (%)                         | 6 (1.5)     | 8 (2.3)    |
| Ethnicity                               |             |            |
| Caucasian, n (%)                        | 380 (97.4)  | 344 (96.9) |
| Other, n (%)                            | 10 (1.3)    | 11 (3.1)   |
| Anthropometric                          |             |            |
| Height (m), mean±SD                     | 1.65±0.06   | 1.77±0.07  |
| Weight (kg), mean±SD                    | 60.8±11.5   | 70.0±13.2  |
| BMI (kg/m <sup>2</sup> ), mean±SD       | 22.3±4.0    | 22.2±3.8   |
| Normal weight (<25 kg/m <sup>2</sup> )* | 309 (79.2)  | 274 (77.2) |
| Overweight (25–29 kg/m <sup>2</sup> )*  | 57 (14.6)   | 58 (16.3)  |
| Obese (≥30 kg/m <sup>2</sup> )*         | 24 (6.2)    | 23 (6.5)   |
| Fat mass (kg), mean±SD                  | 20.1±8.8    | 14.1±10.1  |
| Lean mass (kg), mean±SD                 | 38.6±4.6    | 54.0±6.5   |
| High school main programme              |             |            |
| General studies, n (%)                  | 210 (53.9)  | 133 (37.5) |
| Sports high school, n (%)               | 36 (9.2)    | 59 (16.6)  |
| Vocational training, n (%)              | 144 (36.9)  | 163 (45.9) |
| Puberty                                 |             |            |
| Menarche females, n (%)                 | 385 (100.0) | N/A        |
| Age at menarche, mean±SD                | 12.7±1.2    | N/A        |
| Hormonal contraceptives, n (%)          | 144 (36.9)  | N/A        |
| Breastfeeding FF3, n (%)†               | 23 (8.3)    | N/A        |
| PDS males, mean±SD                      | N/A         | 3.3±0.4    |
| Alcohol intake                          |             |            |
| Never, n (%)                            | 98 (25.1)   | 116 (32.7) |
| Once per month, n (%)                   | 175 (44.9)  | 132 (37.2) |
| 2–4 times per month, n (%)              | 112 (28.7)  | 103 (29.0) |
| 2–3 times per week, n (%)               | 5 (1.3)     | 2 (0.6)    |
| ≥4 times per week, n (%)                | 0 (0)       | 2 (0.6)    |
| Leisure time physical activity          |             |            |
| Inactive, n (%)                         | 49 (12.6)   | 97 (27.3)  |
| Moderate, n (%)                         | 154 (39.5)  | 82 (23.1)  |
| Vigorous, n (%)                         | 117 (30.0)  | 82 (23.1)  |
| Very vigorous, n (%)                    | 70 (18.0)   | 94 (26.5)  |
| Serum vitamin D                         |             |            |
| nmol/L, mean±SD                         | 55.1±23.3   | 41.0±21.1  |

Continued

**Table 1** Continued

|                                                                                                                                                                                                                                                                                                                                                                                                                            | Females | Males |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|-------|
| Characteristics mainly at FF1.<br>PDS as described by Petersen <i>et al.</i> <sup>24</sup><br>n=number of participants<br>*Iso-BMI derived from Cole and Lobstein. <sup>25</sup><br>†Not all attending FF1 reported on breastfeeding at FF3 (n=266, 23 breastfeeding), all females were not computed to not breastfeeding at FF1 and FF2.<br>BMI, Body Mass Index; FF, Fit Futures Study; PDS, Pubertal Development Score. |         |       |

(table 1). About 50% attended general studies, and 88% of females and 73% of males were at least moderately physically active in leisure time (table 1). At baseline, 81% of females and 78% of males reported never smoking, while 16% and 18% of females and males reported smoking sometimes, and 2.6% and 3.9% smoked daily (online supplemental table S1). Over 60% of participants reported never using snuff at baseline, while approximately 15% reported sometimes using snuff and about 20% reported daily use (online supplemental table S1). Throughout the surveys, fewer participants reported smoking daily, and more participants reported using snuff daily (online supplemental table S1).

### Smoking and BMD levels

In crude models, we observed a time (ie, survey) by smoking interaction in the association with mean total hip BMD for females ( $p<0.001$ ) (table 2). We also observed differences in BMD levels across smoking groups (main effect of smoking:  $p=0.008$ ) (table 2). For males, we observed a time by smoking interaction ( $p<0.001$ ); however, there were no statistically significant differences in mean total hip BMD levels between smoking groups ( $p=0.11$ ) (table 2).

In the adjusted models, we observed a time by smoking interaction in the association with mean total hip BMD levels in females ( $p<0.001$ ). We also observed differences in BMD levels by smoking status (between-subjects effect:  $p=0.006$ ), where females who smoked daily at FF2 had higher total hip BMD than those who sometimes and never smoked at FF2 (both  $p<0.001$ ) (table 2, figure 2). In males, there was a time by smoking status interaction ( $p<0.001$ ); however, we observed no statistically significant differences in mean total hip BMD across smoking status at different time points ( $p=0.09$ ) (table 2, figure 2).

In crude models of mean femoral neck BMD levels, there were time by smoking status interactions for both females and males (both  $p<0.001$ ), but differences in BMD levels between smoking status were observed only in females ( $p=0.049$ ) and not in males ( $p=0.17$ ) (table 2). In the adjusted models, there were still time by smoking interactions in both sexes (both  $p<0.001$ ) and differences in mean femoral neck BMD between smoking status categories in females ( $p=0.049$ ), with females who never smoked at FF1 having higher femoral neck BMD than

**Table 2** Association between smoking and BMD (g/cm<sup>2</sup>) in the FF (2010–2022), n=390 females and 355 males

|                  |        | FF1 (2010–2011)     | FF2 (2012–2013) | FF3 (2021–2022) |
|------------------|--------|---------------------|-----------------|-----------------|
|                  |        | <b>Total hip</b>    |                 |                 |
| Females          |        |                     |                 |                 |
| <i>Never</i>     |        |                     |                 |                 |
| Crude            | Mean   | 1.068               | 1.082           | 1.052           |
|                  | 95% CI | 1.056 to 1.081      | 1.069 to 1.095  | 1.038 to 1.065  |
| Adjusted         | Mean   | 1.080               | 1.073           | 1.086           |
|                  | 95% CI | 1.068 to 1.092      | 1.058 to 1.087  | 1.058 to 1.113  |
| <i>Sometimes</i> |        |                     |                 |                 |
| Crude            | Mean   | 1.058               | 1.061           | 1.042           |
|                  | 95% CI | 1.042 to 1.073      | 1.046 to 1.075  | 1.022 to 1.061  |
| Adjusted         | Mean   | 1.089               | 1.070           | 1.074           |
|                  | 95% CI | 1.077 to 1.101      | 1.056 to 1.084  | 1.047 to 1.102  |
| <i>Daily</i>     |        |                     |                 |                 |
| Crude            | Mean   | 1.065               | 1.069           | 1.027           |
|                  | 95% CI | 1.035 to 1.095      | 1.039 to 1.099  | 0.927 to 1.127  |
| Adjusted         | Mean   | 1.026               | 1.012           | 0.992           |
|                  | 95% CI | 1.008 to 1.043      | 0.992 to 1.033  | 0.901 to 1.083  |
| Males            |        |                     |                 |                 |
| <i>Never</i>     |        |                     |                 |                 |
| Crude            | Mean   | 1.119               | 1.147           | 1.096           |
|                  | 95% CI | 1.104 to 1.135      | 1.131 to 1.164  | 1.079 to 1.114  |
| Adjusted         | Mean   | 1.135               | 1.138           | 1.130           |
|                  | 95% CI | 1.121 to 1.150      | 1.119 to 1.156  | 1.099 to 1.161  |
| <i>Sometimes</i> |        |                     |                 |                 |
| Crude            | Mean   | 1.126               | 1.135           | 1.096           |
|                  | 95% CI | 1.106 to 1.147      | 1.117 to 1.152  | 1.075 to 1.117  |
| Adjusted         | Mean   | 1.139               | 1.130           | 1.100           |
|                  | 95% CI | 1.125 to 1.154      | 1.114 to 1.146  | 1.069 to 1.131  |
| <i>Daily</i>     |        |                     |                 |                 |
| Crude            | Mean   | 1.118               | 1.105           | 1.040           |
|                  | 95% CI | 1.083 to 1.153      | 1.070 to 1.140  | 0.971 to 1.110  |
| Adjusted         | Mean   | 1.076               | 1.083           | 1.032           |
|                  | 95% CI | 1.055 to 1.097      | 1.061 to 1.105  | 0.971 to 1.094  |
|                  |        | <b>Femoral neck</b> |                 |                 |
| Females          |        |                     |                 |                 |
| <i>Never</i>     |        |                     |                 |                 |
| Crude            | Mean   | 1.075               | 1.085           | 1.042           |
|                  | 95% CI | 1.062 to 1.088      | 1.072 to 1.098  | 1.028 to 1.055  |
| Adjusted         | Mean   | 1.085               | 1.082           | 1.096           |
|                  | 95% CI | 1.073 to 1.098      | 1.067 to 1.097  | 1.066 to 1.126  |
| <i>Sometimes</i> |        |                     |                 |                 |
| Crude            | Mean   | 1.069               | 1.066           | 1.034           |
|                  | 95% CI | 1.052 to 1.085      | 1.051 to 1.081  | 1.014 to 1.054  |
| Adjusted         | Mean   | 1.090               | 1.073           | 1.077           |
|                  | 95% CI | 1.078 to 1.103      | 1.059 to 1.087  | 1.047 to 1.107  |
| <i>Daily</i>     |        |                     |                 |                 |
| Crude            | Mean   | 1.077               | 1.074           | 0.977           |
|                  | 95% CI | 1.046 to 1.109      | 1.043 to 1.106  | 0.871 to 1.083  |
| Adjusted         | Mean   | 1.022               | 1.010           | 0.952           |
|                  | 95% CI | 1.004 to 1.040      | 0.989 to 1.032  | 0.853 to 1.051  |
| Males            |        |                     |                 |                 |
| <i>Never</i>     |        |                     |                 |                 |

Continued

**Table 2** Continued

|                   |        | FF1 (2010–2011) | FF2 (2012–2013) | FF3 (2021–2022) |
|-------------------|--------|-----------------|-----------------|-----------------|
| Crude             | Mean   | 1.112           | 1.147           | 1.074           |
|                   | 95% CI | 1.097 to 1.127  | 1.131 to 1.164  | 1.056 to 1.092  |
| Adjusted          | Mean   | 1.134           | 1.129           | 1.129           |
|                   | 95% CI | 1.120 to 1.148  | 1.110 to 1.149  | 1.095 to 1.163  |
| <i>Sometimes</i>  |        |                 |                 |                 |
| Crude             | Mean   | 1.113           | 1.136           | 1.075           |
|                   | 95% CI | 1.091 to 1.135  | 1.118 to 1.154  | 1.053 to 1.097  |
| Adjusted          | Mean   | 1.138           | 1.130           | 1.086           |
|                   | 95% CI | 1.123 to 1.152  | 1.114 to 1.146  | 1.086 to 1.120  |
| <i>Daily</i>      |        |                 |                 |                 |
| Crude             | Mean   | 1.110           | 1.092           | 1.034           |
|                   | 95% CI | 1.072 to 1.147  | 1.054 to 1.130  | 0.958 to 1.110  |
| Adjusted          | Mean   | 1.043           | 1.053           | 1.019           |
|                   | 95% CI | 1.021 to 1.066  | 1.030 to 1.076  | 0.953 to 1.086  |
| <b>Total body</b> |        |                 |                 |                 |
| Females           |        |                 |                 |                 |
| <i>Never</i>      |        |                 |                 |                 |
| Crude             | Mean   | 1.182           | 1.228           | 1.316           |
|                   | 95% CI | 1.172 to 1.193  | 1.217 to 1.240  | 1.304 to 1.329  |
| Adjusted          | Mean   | 1.155           | 1.154           | 1.152           |
|                   | 95% CI | 1.148 to 1.163  | 1.144 to 1.163  | 1.132 to 1.171  |
| <i>Sometimes</i>  |        |                 |                 |                 |
| Crude             | Mean   | 1.191           | 1.222           | 1.304           |
|                   | 95% CI | 1.176 to 1.206  | 1.210 to 1.235  | 1.289 to 1.319  |
| Adjusted          | Mean   | 1.168           | 1.163           | 1.169           |
|                   | 95% CI | 1.160 to 1.176  | 1.154 to 1.172  | 1.149 to 1.188  |
| <i>Daily</i>      |        |                 |                 |                 |
| Crude             | Mean   | 1.190           | 1.223           | 1.275           |
|                   | 95% CI | 1.165 to 1.215  | 1.197 to 1.248  | 1.230 to 1.321  |
| Adjusted          | Mean   | 1.186           | 1.170           | 1.160           |
|                   | 95% CI | 1.174 to 1.197  | 1.157 to 1.184  | 1.094 to 1.225  |
| Males             |        |                 |                 |                 |
| <i>Never</i>      |        |                 |                 |                 |
| Crude             | Mean   | 1.182           | 1.228           | 1.316           |
|                   | 95% CI | 1.172 to 1.193  | 1.217 to 1.240  | 1.304 to 1.329  |
| Adjusted          | Mean   | 1.208           | 1.210           | 1.211           |
|                   | 95% CI | 1.199 to 1.218  | 1.198 to 1.223  | 1.190 to 1.232  |
| <i>Sometimes</i>  |        |                 |                 |                 |
| Crude             | Mean   | 1.191           | 1.222           | 1.304           |
|                   | 95% CI | 1.176 to 1.206  | 1.210 to 1.235  | 1.289 to 1.319  |
| Adjusted          | Mean   | 1.230           | 1.226           | 1.223           |
|                   | 95% CI | 1.221 to 1.239  | 1.215 to 1.236  | 1.202 to 1.244  |
| <i>Daily</i>      |        |                 |                 |                 |
| Crude             | Mean   | 1.190           | 1.223           | 1.275           |
|                   | 95% CI | 1.165 to 1.215  | 1.197 to 1.248  | 1.230 to 1.321  |
| Adjusted          | Mean   | 1.269           | 1.271           | 1.244           |
|                   | 95% CI | 1.255 to 1.283  | 1.256 to 1.285  | 1.207 to 1.281  |

Linear mixed models of smoking and BMD.<sup>24</sup>

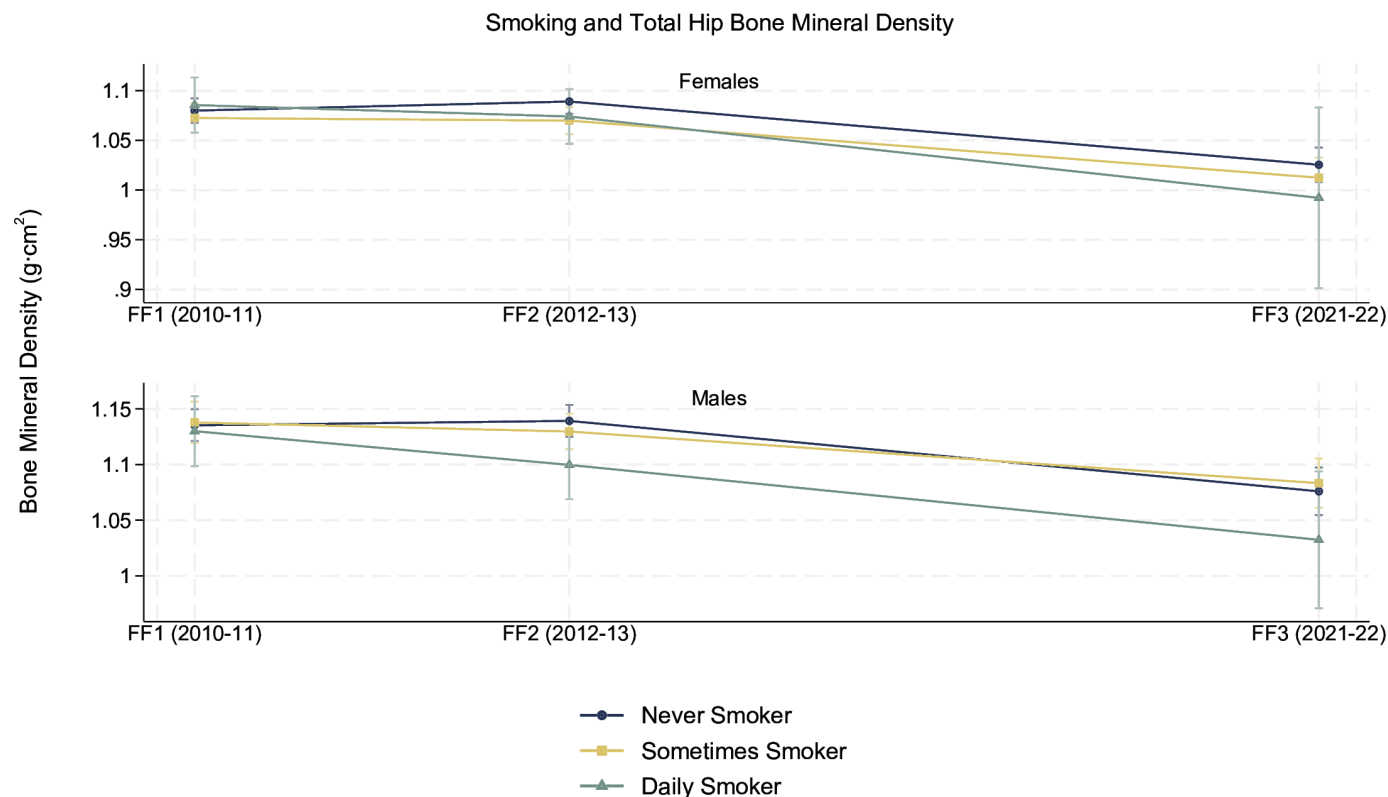
Data are shown as mean with 95% CI, both crude and adjusted models for snuff use, physical activity, fat mass, lean mass, height, ethnicity, serum vitamin D at baseline, alcohol intake, hormonal contraceptive use, puberty, education at FF3 and breastfeeding at FF3.

All participants had completed primary school at FF1 and FF2.

Contraceptives and breastfeeding were recorded only for females. All females were recorded as not breastfeeding at FF1 and FF2.

Puberty refers to the age at menarche for females, and the puberty score for males was recorded as described by Petersen *et al.*<sup>24</sup>

BMD, bone mineral density; FF, Fit Futures Study.



**Figure 2** Associations between smoking and total hip bone mineral density in females and males. The Fit Futures Study (FF) (2010–2022). Data are shown as mean with 95% CI, adjusted for age, ethnicity, fat mass, lean mass, alcohol intake, physical activity, puberty status and vitamin D (at FF1), attained education (at FF3), hormonal contraceptive use (females only) and snuff use.

those who sometimes smoked ( $p<0.001$ ) (table 2). For males, there were no differences in femoral neck BMD across smoking status categories ( $p=0.21$ ) (table 2).

In crude models for total body BMD levels, we observed time by smoking interactions (both  $p<0.001$ ), but not statistically significant differences between smoking status and total body BMD levels in either females ( $p=0.09$ ) or males ( $p=0.47$ ) (table 2). In the adjusted models, there were time by smoking interactions in both sexes (both  $p<0.001$ ), and we observed differences in total body BMD between smoking status categories in females ( $p=0.037$ ); however, Bonferroni-corrected post hoc tests revealed no differences between the specific groups at different time points (all  $p=1.00$ ) (table 2). There were no differences in BMD levels between smoking status categories in males ( $p=0.54$ ) (table 2).

### Snuff use and BMD levels

In the crude models, there were time by snuff use interactions in the association with mean total hip BMD for both females and males (both  $p<0.001$ ), but no differences between snuff use status were observed for either females ( $p=0.71$ ) or males ( $p=0.89$ ) (table 3). Similar results were observed in the adjusted models; although we observed an interaction of time by snuff use (both  $p<0.001$ ), there were no differences in mean total hip BMD and snuff use status in both sexes (females:  $p=0.37$ ; males:  $p=0.63$ ) (table 3, figure 3).

For mean femoral neck BMD, in both crude and adjusted models, we observed time by snuff use interactions (all  $p<0.001$ ), but no statistically significant differences in mean femoral neck BMD between snuff use status (crude: females,  $p=0.68$ ; males,  $p=0.98$ ; adjusted: females,  $p=0.83$ ; males,  $p=0.46$ ) (table 3).

Similarly, for total body BMD, we observed time by snuff use interactions in both crude and adjusted models (all  $p<0.001$ ), but no differences in total body BMD levels between snuff use groups (crude: females,  $p=0.56$ ; males,  $p=0.59$ ; adjusted: females,  $p=0.81$ ; males,  $p=0.51$ ) (table 3).

### Sensitivity analyses

In the sensitivity analyses where we categorised ‘sometimes’ smokers and snuff users into ‘daily’ smokers and snuff users at FF2 and FF3, the results generally remained unchanged (online supplemental tables S2 and S3). However, we observed statistically significant differences in total body BMD and smoking status in females at FF3 ( $p=0.004$ ), where females who never smoked had higher total body BMD than those who were ‘previous’ and ‘daily’ smokers ( $p<0.001$ ) (online supplemental table S2).

### DISCUSSION

Few studies have examined longitudinal associations of tobacco use and BMD changes from adolescence into

**Table 3** Association between snuff use and BMD (g/cm<sup>2</sup>) in the FF (2010–2022), n=390 females and 355 males

|              |                | FF1 (2010–2011)         | FF2 (2012–2013)         | FF3 (2021–2022)         |
|--------------|----------------|-------------------------|-------------------------|-------------------------|
| Total hip    |                |                         |                         |                         |
| Females      |                |                         |                         |                         |
| Never        |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.067<br>1.054 to 1.080 | 1.081<br>1.067 to 1.094 | 1.050<br>1.035 to 1.065 |
| Adjusted     | Mean<br>95% CI | 1.078<br>1.066 to 1.091 | 1.072<br>1.057 to 1.087 | 1.087<br>1.072 to 1.103 |
| Sometimes    |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.062<br>1.046 to 1.078 | 1.073<br>1.057 to 1.088 | 1.051<br>1.032 to 1.069 |
| Adjusted     | Mean<br>95% CI | 1.086<br>1.074 to 1.100 | 1.082<br>1.067 to 1.096 | 1.084<br>1.070 to 1.098 |
| Daily        |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.069<br>1.052 to 1.085 | 1.069<br>1.054 to 1.084 | 1.049<br>1.032 to 1.067 |
| Adjusted     | Mean<br>95% CI | 1.022<br>1.003 to 1.040 | 1.022<br>1.001 to 1.042 | 1.023<br>1.005 to 1.042 |
| Males        |                |                         |                         |                         |
| Never        |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.115<br>1.098 to 1.131 | 1.144<br>1.127 to 1.161 | 1.106<br>1.085 to 1.126 |
| Adjusted     | Mean<br>95% CI | 1.127<br>1.111 to 1.143 | 1.144<br>1.124 to 1.165 | 1.142<br>1.125 to 1.160 |
| Sometimes    |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.134<br>1.111 to 1.156 | 1.149<br>1.126 to 1.172 | 1.078<br>1.051 to 1.104 |
| Adjusted     | Mean<br>95% CI | 1.133<br>1.118 to 1.149 | 1.140<br>1.120 to 1.161 | 1.134<br>1.118 to 1.151 |
| Daily        |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.127<br>1.108 to 1.147 | 1.135<br>1.117 to 1.154 | 1.090<br>1.070 to 1.110 |
| Adjusted     | Mean<br>95% CI | 1.083<br>1.060 to 1.106 | 1.079<br>1.052 to 1.105 | 1.079<br>1.057 to 1.101 |
| Femoral neck |                |                         |                         |                         |
| Females      |                |                         |                         |                         |
| Never        |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.074<br>1.061 to 1.087 | 1.084<br>1.070 to 1.097 | 1.041<br>1.026 to 1.057 |
| Adjusted     | Mean<br>95% CI | 1.084<br>1.071 to 1.097 | 1.078<br>1.062 to 1.093 | 1.092<br>1.075 to 1.108 |
| Sometimes    |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.071<br>1.054 to 1.087 | 1.079<br>1.063 to 1.095 | 1.044<br>1.025 to 1.062 |
| Adjusted     | Mean<br>95% CI | 1.087<br>1.074 to 1.100 | 1.085<br>1.070 to 1.100 | 1.085<br>1.070 to 1.099 |
| Daily        |                |                         |                         |                         |
| Crude        | Mean<br>95% CI | 1.075<br>1.058 to 1.092 | 1.073<br>1.058 to 1.088 | 1.035<br>1.018 to 1.053 |

Continued

Table 3 Continued

|            |                | FF1 (2010–2011)         | FF2 (2012–2013)         | FF3 (2021–2022)         |
|------------|----------------|-------------------------|-------------------------|-------------------------|
| Adjusted   | Mean<br>95% CI | 1.021<br>1.001 to 1.040 | 1.021<br>1.000 to 1.042 | 1.014<br>0.994 to 1.034 |
| Males      |                |                         |                         |                         |
| Never      |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.104<br>1.088 to 1.121 | 1.141<br>1.124 to 1.158 | 1.081<br>1.060 to 1.102 |
| Adjusted   | Mean<br>95% CI | 1.123<br>1.107 to 1.139 | 1.144<br>1.123 to 1.165 | 1.140<br>1.122 to 1.158 |
| Sometimes  |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.129<br>1.105 to 1.152 | 1.143<br>1.119 to 1.167 | 1.056<br>1.028 to 1.085 |
| Adjusted   | Mean<br>95% CI | 1.130<br>1.115 to 1.145 | 1.133<br>1.112 to 1.155 | 1.136<br>1.119 to 1.153 |
| Daily      |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.121<br>1.101 to 1.141 | 1.139<br>1.121 to 1.158 | 1.071<br>1.050 to 1.091 |
| Adjusted   | Mean<br>95% CI | 1.050<br>1.026 to 1.074 | 1.050<br>1.022 to 1.078 | 1.052<br>1.030 to 1.075 |
| Total body |                |                         |                         |                         |
| Females    |                |                         |                         |                         |
| Never      |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.144<br>1.135 to 1.153 | 1.162<br>1.153 to 1.171 | 1.209<br>1.199 to 1.219 |
| Adjusted   | Mean<br>95% CI | 1.156<br>1.148 to 1.164 | 1.153<br>1.143 to 1.163 | 1.157<br>1.146 to 1.167 |
| Sometimes  |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.144<br>1.132 to 1.155 | 1.162<br>1.151 to 1.173 | 1.204<br>1.192 to 1.217 |
| Adjusted   | Mean<br>95% CI | 1.167<br>1.159 to 1.175 | 1.170<br>1.160 to 1.179 | 1.167<br>1.158 to 1.176 |
| Daily      |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.141<br>1.130 to 1.153 | 1.156<br>1.146 to 1.166 | 1.205<br>1.193 to 1.217 |
| Adjusted   | Mean<br>95% CI | 1.183<br>1.170 to 1.195 | 1.177<br>1.163 to 1.191 | 1.182<br>1.169 to 1.194 |
| Males      |                |                         |                         |                         |
| Never      |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.179<br>1.168 to 1.191 | 1.227<br>1.215 to 1.239 | 1.326<br>1.312 to 1.341 |
| Adjusted   | Mean<br>95% CI | 1.204<br>1.194 to 1.214 | 1.211<br>1.198 to 1.225 | 1.214<br>1.203 to 1.225 |
| Sometimes  |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.189<br>1.173 to 1.205 | 1.230<br>1.214 to 1.246 | 1.304<br>1.285 to 1.323 |
| Adjusted   | Mean<br>95% CI | 1.227<br>1.217 to 1.237 | 1.232<br>1.219 to 1.246 | 1.228<br>1.217 to 1.238 |
| Daily      |                |                         |                         |                         |
| Crude      | Mean<br>95% CI | 1.193<br>1.179 to 1.207 | 1.224<br>1.211 to 1.237 | 1.299<br>1.285 to 1.314 |

Continued

**Table 3** Continued

|          |        | FF1 (2010–2011) | FF2 (2012–2013) | FF3 (2021–2022) |
|----------|--------|-----------------|-----------------|-----------------|
| Adjusted | Mean   | 1.277           | 1.276           | 1.262           |
|          | 95% CI | 1.262 to 1.292  | 1.258 to 1.293  | 1.248 to 1.277  |

Linear models of snuff use and BMD. I

Data are shown as mean with 95% CI, both crude and adjusted models for smoking, physical activity, fat mass, lean mass, height, ethnicity, serum vitamin D at baseline, alcohol intake, hormonal contraceptive use, puberty, education at FF3 and breastfeeding at FF3.

All participants had completed primary school at FF1 and FF2.

Contraceptives and breastfeeding were recorded only for females. All females were recorded as not breastfeeding at FF1 and FF2.

Puberty refers to the age at menarche for females, and the puberty score for males was recorded as described by Petersen *et al.*<sup>24</sup>

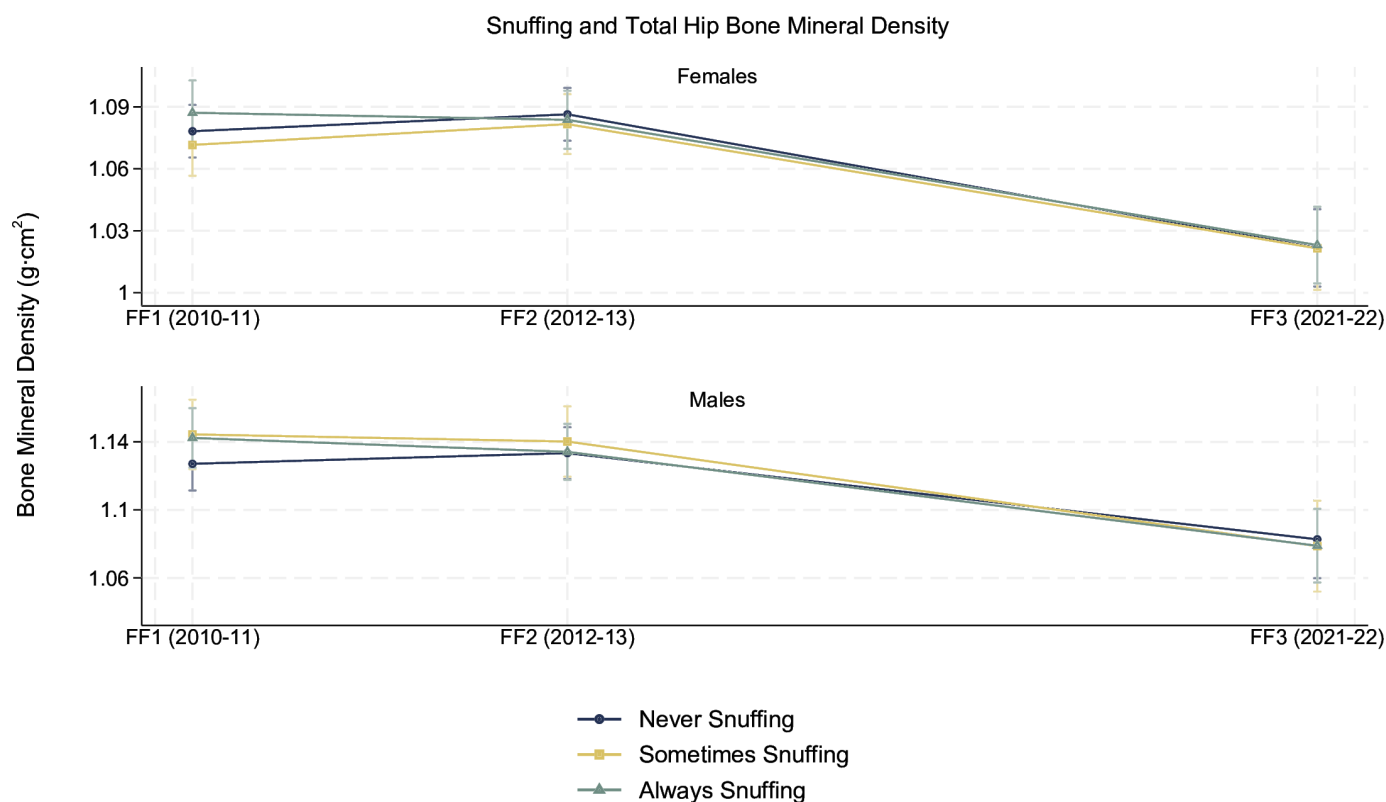
BMD, bone mineral density; FF, Fit Futures Study.

adulthood. In this longitudinal cohort study of Norwegian adolescents from a median age of 16 to 27 years, we examined associations between tobacco use (smoking and snuff) and BMD at the total hip, femoral neck and total body. While we found no overall associations between tobacco use and BMD levels, site-specific associations were observed between total hip and femoral neck BMD in females.

Previous studies on associations between smoking and BMD in young adults are conflicting.<sup>12</sup> In a recent systematic review,<sup>12</sup> most prospective studies found negative associations between smoking and BMD, indicating that smoking has a negative impact on bone health,<sup>13 26–29</sup> except for one study.<sup>30</sup> However, these prospective studies were limited, especially in sample size, given the prevalence

of smokers at a young age.<sup>12</sup> In a recent study by Nilsen *et al.*<sup>18</sup> using data from the FF, which is the same cohort as our study, there were no associations between smoking and changes in BMD in females, but smoking appeared to result in lower total body BMD in males between 16 and 18 years of age. Our study, now extending the work by Nilsen *et al.*<sup>18</sup> following the same sample from 16 years to 27 years of age, mainly confirms the findings, except that in males, there also appears to be a limited effect of smoking on BMD in the transition to young adulthood.

To our knowledge, only the study by Nilsen *et al.*<sup>18</sup> has previously examined prospective associations between snuff use and BMD levels in adolescents. They reported no association in females, but male snuff users had a lower increase in BMD compared with non-snuff users from 16



**Figure 3** Associations between snuff use and total hip bone mineral density in females and males in the Fit Futures Study (FF) (2010–2022). Data are shown as mean with 95% CI, adjusted for age, ethnicity, fat mass, lean mass, alcohol intake, physical activity, puberty status and vitamin D (at FF1), attained education (at FF3), hormonal contraceptive use (females only) and smoking.

to 18 years of age.<sup>18</sup> Following the same cohort from 16 to 27 years of age, we found no differences in BMD levels between snuff users and non-snuff users at any measurement site and time point. Although these conflicting findings are surprising, they are likely explained by our study having more measurement time points than Nilsen *et al.*<sup>18</sup> These additional measuring points allowed us to overcome the challenge of using only baseline-to-follow-up measures,<sup>31</sup> as in Nilsen *et al.*<sup>18</sup> which allowed us to apply more robust analyses, such as linear mixed models. Furthermore, maturation influences bone growth, and it has been previously shown that bone accretion is more dependent on biological rather than chronological age.<sup>32</sup> Thus, although speculative, it may be that snuff use is more influential at earlier maturation levels than in mid-20s, where our measurement at 27 years is too late to detect any influence from snuff use. Nevertheless, based on our study with a longer duration of follow-up, it appears that neither smoking nor snuff use exerts any severe influence on BMD levels in adolescence and in the transition to young adulthood under current levels of exposure.

Given that smoking has been thought to lead to lower bone mass levels in adults,<sup>33</sup> our observed lack of association between smoking and BMD in this cohort is surprising. It may be that the number of smokers in our study was of insufficient sample size to detect any associations, as only 2.6% of females and 3.9% of males in the study sample reported smoking at baseline, as also observed in previous studies on smoking and bone health in young adults.<sup>12</sup> It was previously found that females reach peak BMD levels earlier than males,<sup>34</sup> and we observed that females who never smoked had a greater increase in BMD from 16 to 18 years than those who previously smoked. As males typically reach peak BMD levels later than females, it is difficult in a biological way to explain why no such association could be observed in males in this study.

There were more snuff users than smokers in our study. It has been suggested that snuff use may have different effects on bones than smoking, as snuff does not involve combustion.<sup>19</sup> In adults, it was previously reported that use of smokeless tobacco products (chewing tobacco or non-combustible tobacco) prevents proper healing of fractures, resulting in non-union of bones.<sup>35 36</sup> It has also been shown that a change in BMD levels is accelerated in females using smokeless tobacco products compared with non-users.<sup>37</sup> However, it has also been suggested that snuff includes lower levels of harmful chemical products than other smokeless tobacco types and is thus not directly comparable.<sup>38</sup> Consequently, snuff use may have some deleterious effects on bone health, and since these are mostly observed in adults and females using other types of smokeless tobacco, more research on type-specific smokeless tobacco products is needed.

Further, the latency of tobacco use may also influence BMD levels in adolescence;<sup>39</sup> however, due to the few transitions in our sample, we were unable to examine the latency effects of tobacco use on BMD levels. It has

also previously been suggested that individuals who use tobacco products may also engage in other behaviours that negatively impact bone health, such as lower physical activity and poorer diet quality.<sup>12 40</sup> However, a recent systematic review reported that young snuff users were more likely to engage in physical activity or sports.<sup>41</sup> Thus, even though we adjusted our analysis for physical activity, it may be that the negative effects of snuff and BMD were confounded by physical activity levels in our study, which are associated with greater BMD levels.<sup>12</sup> Indeed, self-reported physical activity is subject to measurement bias,<sup>42</sup> and adjustment in observational studies cannot rule out residual confounding.

## Strengths

The strengths of this study include a multipurpose population-based cohort design that allowed us to control for a rich set of possible confounders, a balanced sample of both sexes and the long follow-up duration from adolescence to young adulthood. This may increase the generalisability of our results, at least towards Western populations. Another strength includes our use of DXA measurements, which were performed by trained personnel, potentially reducing measurement errors.

## Limitations

We only used a crude classification of tobacco use in this study. Due to the limited sample size and, especially, the limited number of participants reporting smoking, any tobacco use intensity and duration as an outcome could not be examined. Therefore, we cannot rule out any dose-response association,<sup>43</sup> and future research warrants further examination of a dose-response association between tobacco use and BMD in adolescents.

Although we invited all adolescents from two municipalities and most adolescents attended, our study may suffer from limited statistical power, especially since there were relatively few who reported smoking daily. Additionally, self-reported smoking suffers from self-desirability bias and thus under-reporting of smoking.<sup>44</sup> This may have hindered proper analysis of the exposures, as also observed previously.<sup>12</sup>

Furthermore, although we had a high attendance rate (93% at baseline) and acceptable follow-up attendance (75% at FF2 and 66% at FF3 of the included sample), we cannot rule out the possibility that dropout may have influenced our results. Given that the tendency towards differences was most pronounced at FF2, while all groups appeared to converge at FF3, there may be imprecision in the estimates despite the use of linear mixed models, which are theoretically robust in handling missing data. Finally, as we only had two-dimensional DXA measurements, which are a proxy for bone strength,<sup>45</sup> we could not examine the possible associations with cancellous and cortical bone dimensions. Therefore, BMD levels may not detect the complete bone mass growth, as bone growth during maturation includes both an increase in volume and mass.<sup>46</sup>

## CONCLUSIONS

In this longitudinal cohort study of Norwegian adolescents from a median age of 16 to 27 years, we could not detect statistically significant associations between smoking or snuff use and BMD levels. Based on this study, in which only 2.6% of females and 3.9% of males reported smoking daily, moderate tobacco use appeared not to negatively influence bone growth from adolescence to young adulthood.

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**Contributors** AW, NE and OAN designed the study. EHS performed the statistical analyses and is the guarantor for the study's results. EHS wrote the initial draft of the manuscript. All authors contributed to revisions and approved the final version of this study.

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**Patient consent for publication** Consent obtained directly from patient(s)

**Ethics approval** This study involved human participants, and all participants gave written informed consent at all three waves before taking part. Participants under 16 years of age in FF1 provided written consent from their legal guardians. The present study was approved by the Regional Committee of Medical Research Ethics (Ref. 2013/1459/ REK nord).

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

**Data availability statement** Data are available upon reasonable request. Data may be obtained from a third party and are not publicly available. The data supporting the findings of this study are provided by the Fit Futures study (Third-party). However, access to these data is restricted due to local and national ethical and security policies. Information about the Fit Futures study and metadata is available on the website. Data are available from the Fit Futures study on reasonable request, following the steps presented on their website: [https://uit.no/research/fitfutures\\_en#region\\_837245](https://uit.no/research/fitfutures_en#region_837245). Requests for data access should be directed to the Fit Futures study at UiT The Arctic University of Norway, Department of Community Medicine. Please contact via email at [fitfutures@uit.no](mailto:fitfutures@uit.no).

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