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Oral tobacco (snus) use and sperm quality in men attending fertility treatment: a cross-sectional study

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Abstract

Background

Snus, a moist oral tobacco product, is widely used in Norway and Sweden, but its association with semen quality is uncertain. This study aimed to determine if the use of oral tobacco (snus) is associated with sperm quality in men undergoing fertility treatment.

Methods

This was a single-center cross-sectional study using data from 1805 men with a mean age of 34.5 years who were undergoing their first fertility treatment at St. Olavs Hospital in Norway from January 2017 to March 2022. Using linear and logistic regression, we compared sperm parameters between men with and without snus use, adjusting for age, body mass index, and smoking status.

Results

Of the 1583 men with known snus status, 461 used snus. Snus users had lower sperm concentration (-12.1%, 95% CI -19.5 to -8.1), lower total progressive motile sperm count (-20.5%, 95% CI -25.9 to -15.3), and lower total sperm count (-16.2%, 95% CI -25.6 to -12.0) than those who did not use snus. Furthermore, snus users had higher odds of having a total sperm count below the World Health Organization cutoff of 39 x 10^6/sample (odds ratio 1.26, 95% confidence interval 1.01–1.60). The results were consistent in sensitivity analyses.

Conclusions

Men undergoing fertility treatment who used snus had lower sperm concentration, total number of progressive motile sperm cells, and total sperm count, but similar semen volume and progressive motility percentage compared to men who did not use snus. These findings highlight the importance of considering snus use as a potential risk factor in male fertility assessment.

Background

Recent publications consistently indicate a global decline in sperm counts over the past four decades [1–3]. Various environmental and lifestyle factors have been hypothesized to contribute to this trend, including exposure to microplastics [4], tobacco smoke [5], air pollution [6], and more recently the use of oral tobacco products [7–9]. Smokeless tobacco is consumed in over 115 countries and is estimated to contribute to approximately 652,000 deaths worldwide annually, including over 266,000 deaths from ischemic heart disease and cancers of the mouth, pharynx, and esophagus [10, 11].

In Northern Europe, the most common type of smokeless tobacco is Swedish snus, a moist oral snuff made from ground dry tobacco to which water, sodium chloride, sodium carbonate, aromatic compounds and moisture preserving agents are added [12]. Despite a European Union ban on snus sales since 1992 [13], its

use has increased in several countries over the last decade [14–16]. The highest consumption is reported in Sweden and Norway, where snus sale is legal, with about 15% daily snus users in the total population [17–19]. The World Health Organization (WHO) estimates that approximately 8.1 million people used smokeless tobacco products in the European population in 2010–2020 [20], with similar results presented in a European study from 2016 [21]. In the US, 2.1% of the adult population uses smokeless tobacco, translating to around 5 million individuals [22].

It is well established that cigarette exposure in men has a detrimental effect on sperm concentration [5, 23], sperm motility [23], and DNA damage [23–26]. Additionally, both male and female smoking have been associated with longer time-to-pregnancy (TTP), while smokeless tobacco users appear to have a shorter TTP compared to smokers, though further research is warranted [27]. Cigarette exposure in men is associated with congenital malformations in the child [28], and is associated with an increased risk of early miscarriage and increased time to pregnancy [29, 30]. Furthermore, males exposed to maternal smoking in utero have lower sperm concentration and total sperm count [31], raising the question of how smokeless tobacco might affect the next generations.

Like cigarettes, snus contains nicotine and heavy metals like cadmium, both known to affect sperm quality [32–34]. However, empirical findings on the impact of snus on male sperm parameters have been inconsistent. Studies in Denmark and Sweden comparing snus users (ranging from 17 to 112 individuals) with non-users (ranging from 45 to 922 individuals) showed either no clear associations of snus use on sperm quality [8, 35], or reduced sperm quality among snus users [7, 9].

A broader understanding of the potential reproductive consequences of snus use is important not only for couples experiencing male infertility, but also from a population perspective. The aim of this study was to investigate the impact of snus use on male sperm quality, using data from male patients attending a fertility clinic.

Methods

Study design, study population and data sources

This single-center cross-sectional study used routinely collected data from all male-female couples undergoing their first fertility treatment using assisted reproductive technology (ART) at the Department of Fertility at St. Olavs Hospital in Norway, from January 2017 to March 2022 (n = 1983 couples). The study excluded couples where testicular aspiration was performed (n = 85) since azoospermia in those men was most likely due to a genetic factor or an obstruction rather than snus use. Furthermore, we excluded couples where cryopreserved sperm was used in the treatment (n = 60) due to the negative effect of cryopreservation on sperm motility, and couples where donor sperm was used (n = 3) or where the information on sperm concentration was missing (n = 30). The final sample included 1805 couples, all of whom underwent their first oocyte retrieval within the defined study-period. All eligible couples during the study period were included, and no formal sample size calculation was performed.

During routine fertility work-up, all participants underwent a consultation wherein the fertility specialist records age, height, weight, medical history, smoking status, and snus use. Information was also collected on whether

the male partner had children prior to the start of fertility treatment. Data on smoking and snus use were self-reported and recorded just before the couple started their first ovarian stimulation cycle. Snus use was recorded as yes or no, without information on product type, amount or duration of use. Causes of infertility were registered according to the International Classification of Diseases, version 10, and the main cause of infertility was used to classify as female factor, male factor or other.

Semen samples and parameters

We collected data from semen samples analyzed on the day of oocyte retrieval. Only semen samples from the first ART cycle were included in the study. Semen samples were obtained through masturbation after a recommended abstinence period of 24–72 hours. All samples were analyzed within an hour post-ejaculation, adhering to the WHO criteria [36]. The evaluated semen parameters included volume (mL), concentration (10^6/mL), total progressive motility (10^6/sample), total ejaculated sperm cells (10^6/sample), and progressive motility percentage. An automated Sperm Class Analyzer SCA® CASA System (Microptic, Barcelona, Spain) was utilized for semen sample analysis. Low sperm quality was defined as semen parameters below the WHO 2021 5th percentile, for volume (< 1.4 mL), sperm concentration (< 16 x 10^6/mL), total sperm count (< 39 x 10^6 per ejaculate), total motility (< 42%), and progressive motility (< 30%).

Statistical methods

The main analyses included all men with known snus status (n = 1583; 1122 non-users and 461 users), and men with missing information on snus use (n = 222) were excluded. We applied linear regression to estimate the association between snus use and various sperm quality parameters, estimating mean differences between users and non-users. These analyses were conducted with and without adjustment for potential confounders, specifically age (grouped as 18–29, 30–39, 40 + years), body mass index (BMI) categories (< 25, 25–29, 30 + kg/m²) and smoking status (smoking vs non-smoking). Precision was estimated by 95% confidence intervals (CIs).

The normality of sperm parameter distributions was examined using the Shapiro-Wilk test. Several parameters (sperm concentration, total progressive motility, and total ejaculated sperm count) were not normally distributed and were transformed using a square root function before statistical analysis. After regression analysis, the transformed means for sperm concentration, total progressive motility, and total ejaculated sperm count were converted back to their original scales for interpretation. Semen volume and progressive motility percentage were normally distributed and required no transformation.

We performed logistic regression to estimate the association between snus use and the odds of falling below the WHO-defined 5th percentile sperm quality values [36]. The adjustments made in these analyses were the same as those applied for the linear regression.

Additionally, to visualize any potential distributional differences between snus users and non-users, we plotted unadjusted Kernel density plots for the semen parameters.

We examined the consistency of our results in sensitivity analyses, where we restricted the analyses to 1) Known non-smokers (1500 patients), 2) Men without diseases known to affect fertility such as cystic fibrosis, primary ciliary dyskinesia, testis cancer, colon cancer and diabetes type 1 and 2 (1783 patients), and 3) Men whose female partner was considered the main cause of infertility (753 patients). We assumed that the fertility of men in this latter group is closer to the fertility in the background male population.

Statistical analyses were performed using Stata/SE 18.5 (StataCorp, College Station, TX, USA). The study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Additional file 1).

Results

Basic characteristics

The study included males with a mean age of 34.5 years (SD 5.9). Approximately 62% (n=1122) of the participants did not use snus, 26% were snus users (n=461), and for 12% (n=222) we had no information on snus use. The mean age was comparable between the two groups (34.6 vs 34.1 years for non-users vs users), and so was the mean BMI (26.4 vs 27.1 kg/m^2 for non-users vs users) and the proportion of smokers (6.1 and 5.9% for non-users vs users). Furthermore, the proportions of men whose partner was diagnosed with female causes of infertility were comparable between the groups (Table 1), and accounted for 40.6% and 41.2% in the non-snus group and snus group respectively. We found a slightly higher proportion of male infertility among men who used snus (24.7%) versus those who did not (21.1%).

Semen parameters and use of snus

The distributions of unadjusted semen parameters (Figure 1) among snus users were slightly shifted towards lower sperm concentration, total sperm count, progressive motile sperm cell counts and volume in snus users compared to non-users.

In Figure 2 we show adjusted differences in sperm quality parameters between snus users and non-users. Snus users had lower sperm concentration, total progressive motile sperm count, and total sperm count, with decrements of 12.1% (95% CI 8.1 to 19.5), 20.5% (95% CI 15.3 to 25.9), and 16.2% (95% CI 12.0 to 25.6), respectively, when compared to non-users.

Sensitivity analyses excluding smokers, men with diseases affecting fertility, and men whose female partner was considered infertile, showed results consistent with the main analysis. Across all subgroups, the direction and magnitude of effect estimates remained similar, particularly for sperm concentration, progressive motile count, total sperm count, and semen volume. Confidence intervals overlapped with those of the main analyses, indicating robustness of the findings across these restricted samples.

Consistent with these results, the odds of having a total sperm count below the WHO threshold, was higher among men using snus compared to those who did not (OR 1.26, 95% CI 1.01-1.60, Table 2). For the remaining sperm parameters, the odds of falling below the WHO threshold was also higher for snus users, but precision was low and confidence interval were also compatible with no association or lower odds.

Discussion

This study of men undergoing fertility treatment includes, to our knowledge, more snus users than any previous study of snus and semen quality. Snus use was associated with lower sperm quality, including a 12% lower sperm concentration, 20% lower number of progressive motile sperm, and a 16% lower total sperm count. Notably, we found no clear association between snus use and semen volume or progressive motility percentage. This analysis indicates that the impact of snus is more pronounced on sperm production rather than its functional quality, with motility and semen volume showing no clear differences between the groups. Sensitivity analysis showed similar results and added robustness to our findings.

Four previous studies have analyzed the association between snus use and semen parameters. In a study of 242 Swedish men aged 18 to 21 years recruited at military service examinations, of whom 51 used snus, Richthoff et al. found no association between snus use and semen quality [35]. A study by Pärn showed a negative association between snus use and sperm concentration, total number of sperm, motile sperm concentration, total motile sperm and total motility percentage [9]. The study was conducted on patients attending fertility treatment, and was limited by its relatively small sample size with a total of 62 participants, only 17 of whom used snus. Similar to Richthoff et al., a study by Holmboe [8] showed no association between snus use and semen parameters. The study included 1221 presumably healthy young men with a median age of 19 years, of whom 68 used snus daily and 231 occasionally. The most recent study by Kimblad [7] included 613 young men from the general population in Sweden, of whom 109 used snus. They found that men who used snus had 24% lower total sperm count after adjustment for smoking and abstinence time. While no statistically significant association was observed between snus use and sperm concentration, semen volume, or progressive motility percentage, there was a trend toward lower sperm concentration.

Kimblad et al. also measured reproductive hormones and found 14% higher serum testosterone and higher follicle-stimulating hormone (FSH) levels among snus users, and cotinine levels in urine were positively associated with testosterone and estradiol [7]. In contrast, Richthoff et al. and Holmboe et al. found no association between snus use and reproductive hormones [8, 35]. Reproductive hormones were not available in our data, so we could not examine whether the lower sperm counts we observed were associated with hormonal changes.

The main strengths of our study are the large number of snus users, the clinically relevant study population attending fertility treatment, semen analysis performed in one laboratory with the same computer-assisted system according to WHO criteria, and consistent results across several sensitivity analyses.

Our study has several limitations. The cross-sectional design combined with a study population drawn from couples with subfertility limits our ability to infer causation from the observed associations. Specifically, restricting the study population to individuals undergoing fertility treatment, could introduce collider bias, where selection into the study based on subfertility could induce or distort associations between snus use and sperm quality. However, in sensitivity analyses of men in couples where a female infertility had been diagnosed, the negative associations persisted. These men might be expected to have a fertility more similar to the background population, indicating that the associations might not be fully explained by selection bias. The reliance on self-reported data for snus use and smoking habits, without additional information on product type, quantity and duration of use, could introduce non-differential misclassification and residual confounding,

respectively, as there is a possibility that participants may underreport or inaccurately recall their usage as have been shown in studies using self-reported smoking data [37, 38]. Still, exclusion of smokers from the analyses had limited impact on the associations. We did not have information about sexual abstinence time. In the study by Kimblad et al., snus users reported shorter abstinence than non-users (mean 63 versus 75 hours), but the lower total sperm count among snus users persisted after adjustment for abstinence time [7]. We cannot exclude that differences in abstinence time contributed to our findings. Lastly, residual confounding from unmeasured factors, such as other lifestyle factors, cannot be ruled out. These limitations underscore the need for prospective studies in unselected populations to validate our findings and explore the mechanisms underlying the association of snus use with male fertility. Such studies should also distinguish tobacco-containing snus from tobacco-free nicotine pouches, which would help clarify whether nicotine itself is involved [7].

Conclusions

Our study adds to this growing body of evidence on sperm quality and snus users, by providing a more comprehensive evaluation of the impact of snus on sperm quality in a large cohort of men undergoing fertility treatment. Our findings demonstrate consistent negative associations with key measures of sperm production, including sperm concentration, progressive motile sperm count, and total sperm count, while showing no clear effect on motility percentage or semen volume. These associations remained robust across multiple sensitivity analyses, adding to a growing body of evidence from a large and clinically relevant cohort. With a worldwide reduction in sperm count reported over recent decades, it is plausible that snus use could be one of many factors contributing to this decline [1, 3, 39, 40].

Abbreviations

ART: assisted reproductive technology; BMI: body mass index; CASA: computer-assisted sperm analysis; CI: confidence interval; FSH: follicle-stimulating hormone; OR: odds ratio; REK: Regional Committee for Medical and Health Research Ethics; SD: standard deviation; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology; TTP: time to pregnancy; WHO: World Health Organization

Declarations

Ethics approval and consent to participate

The ethical approval for this study was granted by the Regional Committee for Medical and Health Research Ethics in Central Norway (REK Midt, reference 2020 – 68788), adhering to the ethical standards laid out in the Declaration of Helsinki. REK Midt granted a waiver of the requirement to obtain informed consent and approved a dispensation from confidentiality, in accordance with the Norwegian Health Personnel Act, due to the minimal intrusion of the data collection and the significant expected benefit of the research. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The data supporting the findings of this study are not publicly available because they contain patient record information that is subject to restrictions under Norwegian health research legislation and the terms of the ethics approval. De-identified data may be obtained from the corresponding author upon reasonable request, subject to approval by REK and St. Olavs Hospital.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ALS and FBS designed the study. ALS obtained ethical approval, retrieved and analyzed the data, and wrote the first draft of the manuscript. KWJ and SO advised in the analyses. All authors were involved in the interpretation of the results. All authors were involved in revision and improvements of the manuscript. The corresponding author confirms that all the listed authors meet the authorship criteria. ALS and FBS had full access to all the data in the study. All authors read and approved the final manuscript.

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Tables

Table 1 Baseline characteristics of the study participants according to snus use

	No snus use		Snus use		Missing snus status		Total	
Participants, n (%, columns)	1122	(62.2)	461	(25.5)	222	(12.3)	1805	(100)
Age								
Mean (SD) in years	34.6	(6.0)	34.1	(5.8)	34.8	(5.9)	34.5	(5.9)
18-29 years, n (%)	230	(20.5)	91	(19.7)	40	(18.0)	361	(20.0)
30-39	679	(60.5)	291	(63.1)	138	(62.2)	1108	(61.4)
40 +	213	(19.0)	79	(17.1)	44	(19.8)	336	(18.6)
BMI								
Mean (SD) in Kg/m^2	26.4	(3.8)	27.1	(4.0)	26.6	(4.0)	26.6	(3.8)
< 25	429	(38.2)	142	(30.8)	63	(28.4)	634	(35.1)
25-29	490	(43.7)	218	(47.3)	69	(31.1)	777	(43.0)
30 +	170	(15.2)	89	(19.3)	29	(13.1)	288	(16.0)
Missing	33	(2.9)	12	(2.6)	61	(27.5)	106	(5.9)
Causes of infertility								
Female infertility	455	(40.6)	190	(41.2)	108	(48.6)	753	(41.7)
Male infertility	237	(21.1)	114	(24.7)	46	(20.7)	397	(22.0)
Other	430	(38.3)	157	(34.1)	68	(30.6)	655	(36.3)
Smoking status								
Smoking, n (%)	68	(6.1)	27	(5.9)	30	(13.5)	125	(6.9)
Not smoking, n (%)	1052	(93.8)	384	(83.3)	64	(28.8)	1500	(83.1)
Missing, n (%)	2	(0.2)	50	(10.8)	128	(57.7)	180	(10.0)
Previous children								
Yes, n (%)	89	(7.9)	64	(13.9)	19	(8.6)	172	(9.5)
No, n (%)	796	(70.9)	290	(62.9)	107	(48.2)	1193	(66.1)
Missing, n (%)	237	(21.1)	107	(23.2)	96	(43.2)	440	(24.4)

Participants: number of men providing a semen sample at the time of first oocyte retrieval.
BMI: body mass index (weight (kg)/height² (m^2)).

Missing: information not available in the medical record or not reported by the participant.
Previous children: biological children fathered by the male participant prior to the start of fertility treatment.

Table 2 Comparison of semen parameters between snus users and non-users

		n	Mean	<WHO threshold OR	95% CI
Volume (mL)	No snus	1122	3.52	1	ref
	Snus	461	3.42	1.59	0.99-2.58
Concentration (10^6/mL)	No snus	1122	47.8	1	ref
	Snus	461	42.7	1.08	0.85-1.38
Total sperm count (10^6/sample)	No snus	1122	160.3	1	ref
	Snus	461	137.4	1.26	1.01-1.60
Progressive motility (%)	No snus	1117	41.8	1	ref
	Snus	461	42.4	1.12	0.88-1.42

n = number of participants.

OR = odds ratio; CI = confidence interval.

"WHO threshold" refers to semen quality cut-offs based on the WHO 2021 5th percentile values.

Adjusted for age group (18–29, 30–39, ≥40 years), body mass index (BMI <25, 25–29, ≥30 kg/m²), and smoking status (current smoker vs. non-smoker).

Odds ratios estimate the odds of semen parameters below the WHO lower reference limits (5th percentile).

Figures

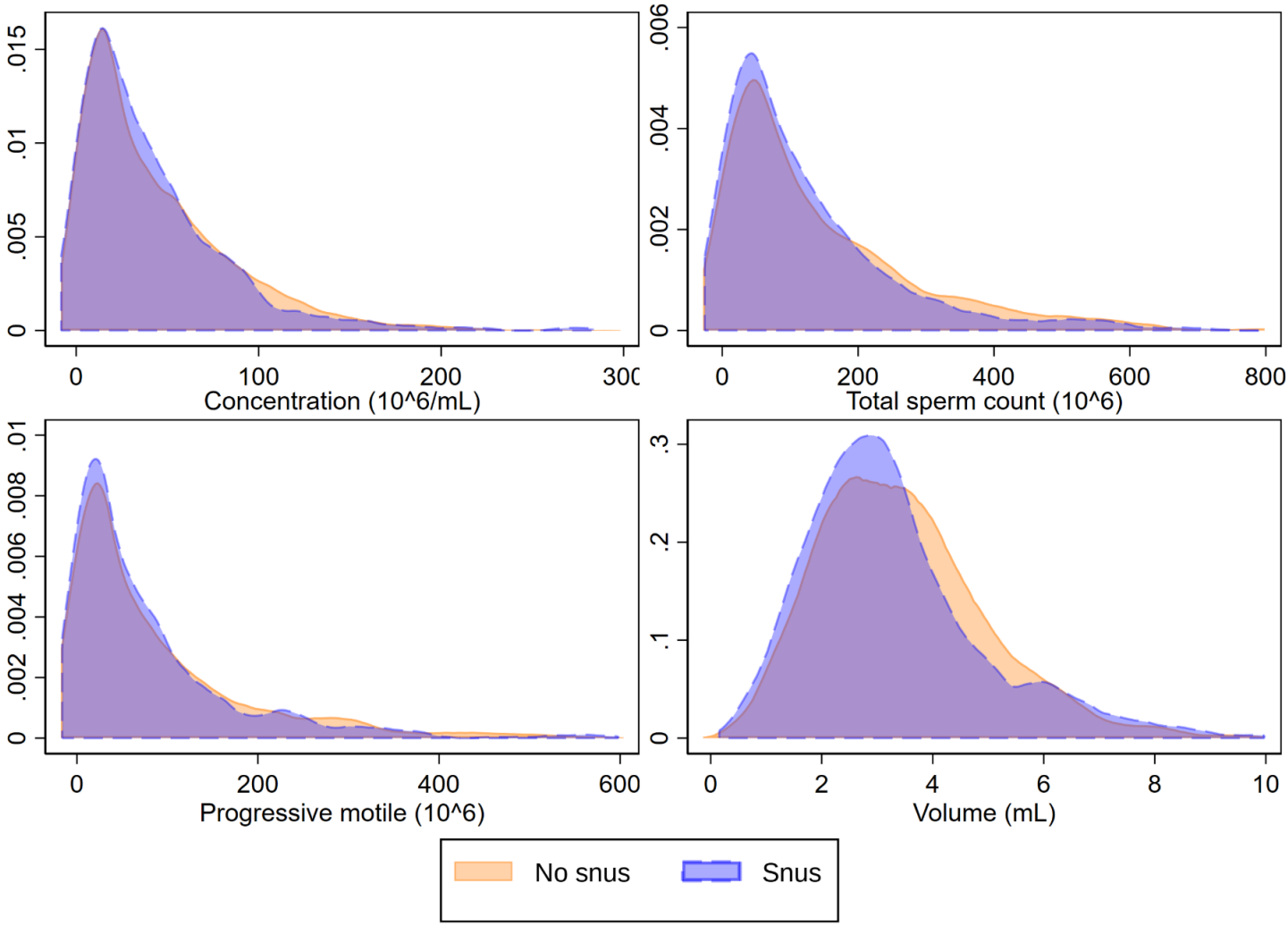


Figure 1

Unadjusted distributions of semen parameters in snus users and non-users. Kernel density plots for snus users (purple) and non-users (orange).

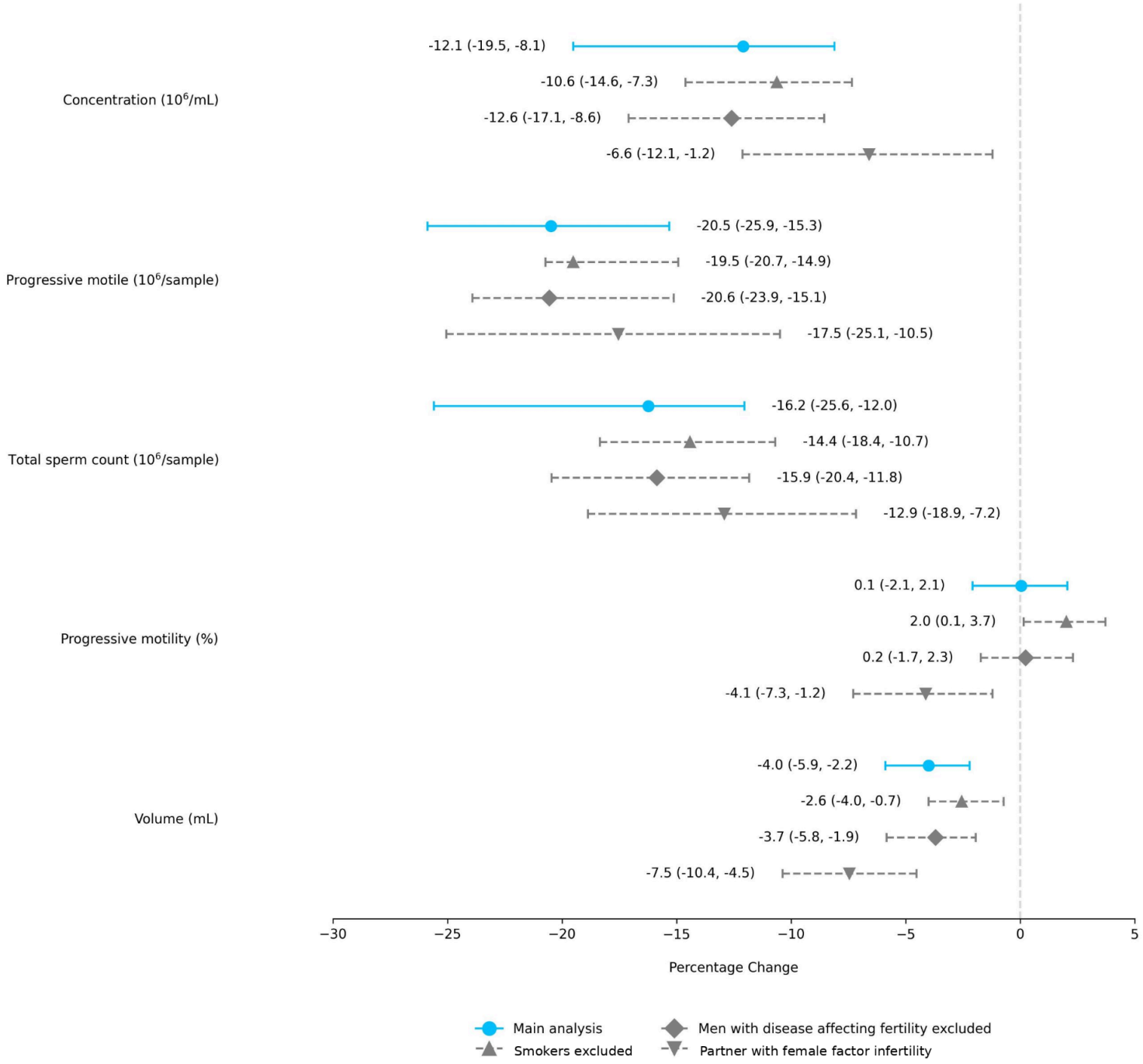


Figure 2

Adjusted differences (%) in semen parameters between snus users and non-users. Estimates with 95% confidence intervals, adjusted for age group, body mass index category and smoking status. Main analysis in blue solid lines and sensitivity analyses in gray dashed lines.