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Smokeless Tobacco and Carriage of *Staphylococcus aureus*

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5th year assignment in Medicine (MED-3950)

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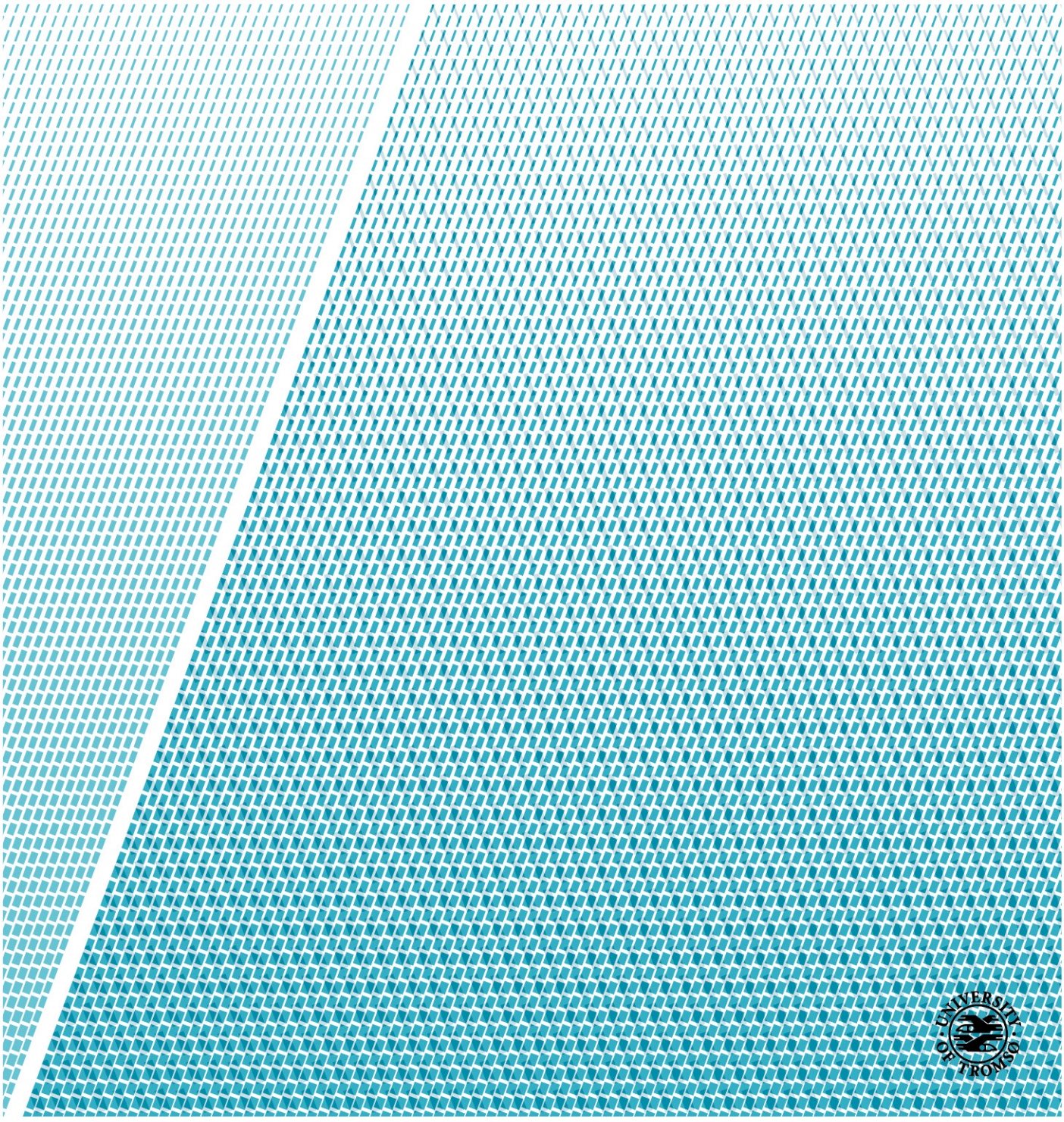

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Preface

In the autumn of 2017 I contacted Gunnar Skov Simonsen to ask him for help to choose a topic for my thesis. He connected me with Anne-Sofie Furberg, who ended up being my main supervisor, in collaboration with Skov Simonsen. We agreed that my thesis should focus on *S. aureus* carriage and whether we could find a correlation between use of smokeless tobacco products and carriage of *S. aureus* in adolescents.

The purpose of this thesis is to expand the knowledge of risk factors for nasal and throat carriage of *Staphylococcus aureus* (*S. aureus*), focusing on smokeless tobacco products which are highly prevalent in the Norwegian population, but understudied in relation to human health.

I would like to thank my supervisors Anne-Sofie Furberg and Gunnar Skov Simonsen for brilliant help and guidance in the process of writing the thesis. I would also like to thank the participants in the Tromsø Study Fit Futures 1.

Summary

Staphylococcus aureus (*S. aureus*) is one of the most potent human bacterial pathogens, yet 20-30% of us carry this bacterium in our nose as part of our habitual microbiota. Due to its infection potential, and the development of multi-resistant strains (MRSA), there has been a growing interest in this bacterium in the research environment. If we can identify which factors affect carrier status, we may be able to prevent some of the serious infections caused by *S. aureus*. Studies have found association between smoking and *S. aureus* nasal carriage, while data on smokeless tobacco (SLT) have been largely lacking.

As use of SLT is increasing among adolescents in Norway, it would be interesting to see if the use of SLTs influences *S. aureus* carriage.

Method

The study population includes the participants in the Tromsø Study – Fit Futures 1 (TFF1). In 2010-2011 TFF1 invited all first-year upper-secondary school students in Tromsø and Balsfjord to an examination of health and lifestyle. There were 1038 participants (93% attendance). A total of 457 boys and 445 girls had complete data on smokeless tobacco use and two nasal and throat swab cultures with one week interval for the assessment of *S. aureus* carriage. The association between smokeless tobacco use and nasal and throat carriage was examined with logistic regression analysis, and odds ratio (OR) for nasal and throat carriage was adjusted for known risk factors.

Results

Girls who used snuff sometimes or daily, had adjusted OR for *S. aureus* throat carriage of 1.59 (95% CI = 1.01-2.50; carriage defined as two positive throat cultures) compared with non-users. In analysis of the total study population of girls and boys, snuff use sometimes or daily was associated with adjusted OR for *S. aureus* nasal carriage of 1.48 (95% CI = 1.09-1.99; carriage defined as one or two positive nasal cultures). In analysis stratified by sex, the association was found in girls only, with an adjusted OR of 1.86 (95% CI = 1.18-2.94; carriage defined as one or two positive nasal cultures) for *S. aureus* nasal carriage among those who used snuff sometimer or daily. There was no association between snuff use and *S. aureus* throat or nasal carriage among boys.

Conclusion

We found an association between snuff use and *S. aureus* nasal and throat carriage among adolescents girls. Girls who use snuff sometimes or daily have higher odds for *S. aureus* carriage (59% for throat, 86% for nasal) compared with girls who do not use snuff.

1 Background

1.1 Staphylococcus aureus

Staphylococcus aureus (*S. aureus*) is a gram-positive coccal bacterium arranged in clusters. The word aureus means yellow, and it is named so because of the yellow colour it presents when grown on media.

20-30% of the human population are colonized with *S. aureus*. The most frequent site of colonization is the anterior of the nose – the vestibulum nasi. Other known sites of colonization are the throat, the axilla and the perineum. *S. aureus* will not normally cause disease in healthy individuals, but it is known to cause opportunistic infections in individuals with particular vulnerability, i.e. weakened immune system.

S. aureus is one of the most potent human bacterial pathogens and can lead to a series of skin and soft tissue infections, but also more invasive and life-threatening infections such as endocarditis, pneumonitis and sepsis.(1, 2) Carriers of *S. aureus* have a higher infection rate than those who are not carriers of the bacteria, and the infections are predominantly found to be by the same strain of bacteria that colonizes the nose of the infected individual.(2) This suggests autoinfection - that one is infected by ones' own microbiota. For this reason, many hospitals have chosen to eradicate nasal colonization with antibiotics or antiseptics prior to surgeries and invasive procedures, to prevent postoperative infections.(3) Interestingly enough, research show that in the case of bacteremia, nasal carriers of *S. aureus* have better treatment outcome and lower mortality than non-carriers.(4)

Fighting *S. aureus* infections is a major clinical challenge, especially with the bacteria strains that have developed resistance – commonly known as MRSA (methicillin-resistant *S. aureus*). This has led to a growing interest in *S. aureus* research – aimed at identifying risk factors that affect carrier status.

Carrier status, naturally, depends both on the ability of the bacteria to colonize humans, as well as the hosts ability to eradicate them. Several studies have attempted to map the different determinants of human carriage. Well documented factors that affect carriage, are age, sex, smoking, BMI, circulating vitamin D level and diabetes mellitus.(5-7)

1.1.1 Carriage

S. aureus carriage status has traditionally been divided into three groups: non-carriers, intermittent carriers and persistent carriers(8). The culture rule proposed by Nouwen et al

states that two qualitative and quantitative nasal swabs taken with a one-week interval is sufficient for defining persistent nasal carriage. This combination predicted the persistent *S. aureus* carriage state with a reliability of 93.6% in their validation study.(9) As for intermittent carriage, seven or more swab cultures are needed to distinguish intermittent carriers from non-carriers.(9)

This division into non-, intermittent and persistent carriage was challenged in 2009 by a study which showed that intermittent and non-carriers share similar *S. aureus* nasal elimination kinetics and anti-staphylococcal antibody profiles.(10) This suggests that a reclassification into two carrier groups might be more correct: persistent carriers and others (non- or intermittent carriers).

Most studies of *S. aureus*, have focused on nasal carriage. Vestibulum nasi is the primary niche for *S. aureus* growth and endogenous inter-individual transmission(8, 11) Nevertheless, several more recent studies show a higher prevalence of colonization in the oropharynx compared to the nose.(12-14) This suggests that the oropharynx is an important reservoir for *S. aureus* and that the oropharynx might be a more frequent site of colonization than the nares.

This is an important discovery, as many of the topical treatments used to eradicate nasal colonization prior to surgery and invasive procedures are unlikely to affect oropharyngeal colonization. Colonization of the throat is also associated with more long-term carriage than other sites of colonization.(15) The oropharynx seems to be a more protected reservoir for *S. aureus*. Successful decolonization is more difficult to achieve with throat colonization, and studies have shown a negative correlation with outcome of treatment when colonized with the MRSA in the oropharynx.(16, 17)

A study from 2009 shows that age is a significant risk factor for oropharyngeal colonization. After the age of 30, oropharyngeal colonization decreases, while nasal colonization remains stable.(18) This variation by age might explain why the major *S. aureus* colonization site varies between studies. The oropharynx may be the most frequent site of colonization in younger individuals, while nasal colonization may be more frequent among older individuals. However, several studies that have shown a higher prevalence of oropharyngeal carriage compared to nasal carriage were conducted on adults, which supports that oropharynx is the most frequent site of colonization.(12-14, 19)

1.2 Smokeless tobacco

1.2.1 Types of smokeless tobacco

Smokeless tobacco is tobacco that you do not inhale and absorb through the lungs, but rather through the oral mucosa of the mouth. There are different kinds of smokeless tobacco. A study from 2016 (20) splits smokeless tobacco products into four different groups: A) Loose moist snuff, B) Moist snuff in pouches, C) Snus and D) Chewing tobacco (Figure 1).

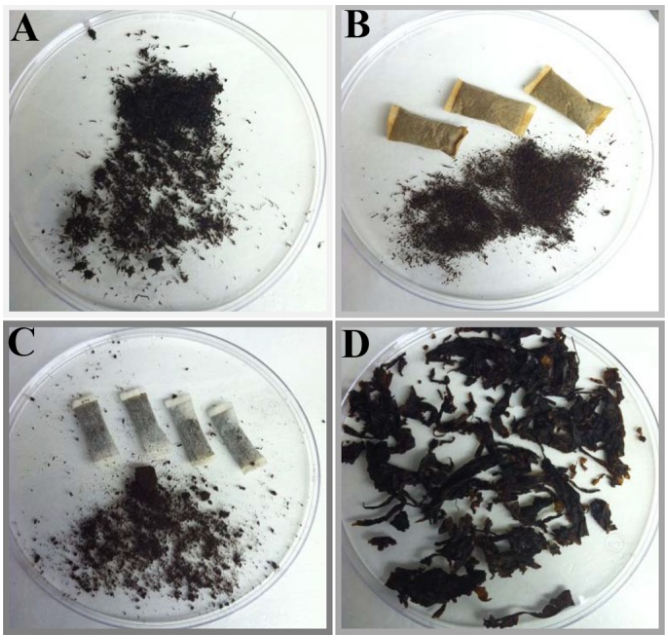

Figure 1 - Different types of smokeless tobacco (20)

In this study we will focus on snuff, which includes loose moist snuff, moist snuff in pouches and snus (A-C).

Snuff is a finely ground tobacco product that is sold loose or packaged in pouches. The tobacco sold in pouches can be either moist or dry. The snuff is used by putting the snuff between the lip and the gum, where the product is absorbed through the oral mucosa.

1.2.2 Use of smokeless tobacco in Norway

The use of smokeless tobacco products (SLTs) has been increasing in Norway over the past 10 years.(21) Data from Statistics Norway show that in the age-group 16-24 years there has been an increase in daily users of snuff from 11% in 2008 to 19% in 2018 (Figure 2).(22) Lack of knowledge about possible adverse health effects of SLTs may contribute to the increasing use among adolescents in Norway. Many may choose SLTs as a “healthier” alternative to smoking.

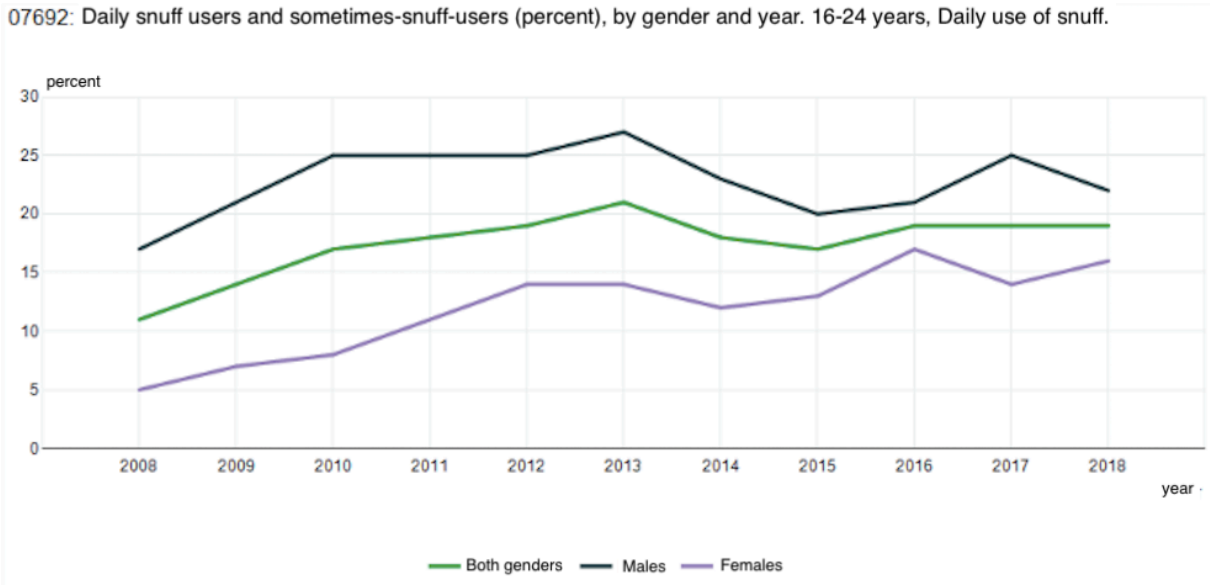

Figure 2 - Chart of daily snuff use in age group 16-24 (22)

1.2.3 Known health effects of smokeless tobacco

Use of smokeless tobacco has been viewed by many as a "safer" alternative to smoking.(23) Health effects of cigarette smoking have been studied for years, and have well documented associated health risks. Assuming that smokeless tobacco might share some of the health effects of smoke, one can assume a hypothesis based on the research done on smoking and *S. aureus* carriage. Research has shown a higher prevalence of *S. aureus* nasal carriage among smokers compared to non-smokers.(7) Cessation from smoking improves the innate host defense and reduces the incidence of *S. aureus* nasal colonization.(7) However, some studies have reported no association (24) or a lower prevalence of *S. aureus* nasal carriage in smokers as in the Tromsø Staph and Skin Study.(25)

Research on SLT health effects is scarce compared to the research on smoking. Thus, there may be significant negative health effects of SLT use that we are not yet aware of. Still, some health effects of SLT use have been documented. Studies show that there is an association between use of SLTs and oral, esophageal and pancreatic cancers.(26-30) SLT use is also associated with cancers of the respiratory and digestive tract, stomach and cervix, as well as ischemic heart disease and stroke.(31, 32)

In regard to *S. aureus*, a study from 2016 shows that *S. aureus* can be found in some of the smokeless tobacco products.(20) This suggests that one might actually be colonized with the bacteria from using smokeless tobacco products, or at least that smokeless tobacco products do not prevent the growth of this bacterium.

2 Objective

The aim of this study was to determine whether there is an association between the use of smokeless tobacco products (moist loose snuff, moist snuff in pouches and snus) and nasal and throat carriage of *S. aureus* in adolescents attending upper-secondary school in the Tromsø region.

3 Material and methods

3.1 Study population

The study population includes participants in The Tromsø Study – Fit Futures 1 (TFF1). In 2010-2011, TFF1 invited all first-year upper-secondary school students in Tromsø and Balsfjord to an examination of health and lifestyle. A total of 1038 boys and girls participated (93% attendance).

The TFF1 participants came to the Clinical Research Unit, University Hospital of North Norway, for a half-day visit.(33) Information about family, lifestyle and health was collected by a self-administered electronic questionnaire. Trained nurses performed an interview about diseases and use of medicine, and a general physical examination. The interview included detailed registration of any use of antibiotics the last 24 hours. The examination included nasal and throat swab samples, and measurements of blood pressure, heart rate, height, weight, percent of body fat, waist and hip circumference and blood analyses such as HbA1c and vitamin D. Repeated nasal and throat swab samples and interview about use of antibiotics were taken within approx. one week at school.

In the present study, 36 participants were excluded due to age > 19 years, according to the World Health Organization's definition of adolescents as individuals in the 10-19 years age group(34). Furthermore, we excluded 17 participants who had taken antibiotics the last 24 hours prior to nasal and throat swabbing. As the study aims to test whether smokeless tobacco use is associated with *S.aureus* carriage, we excluded 83 participants with missing values for smokeless tobacco use and/or nasal and throat samples.

Figure 3 show the selection of the study population based on the participants in TFF1.

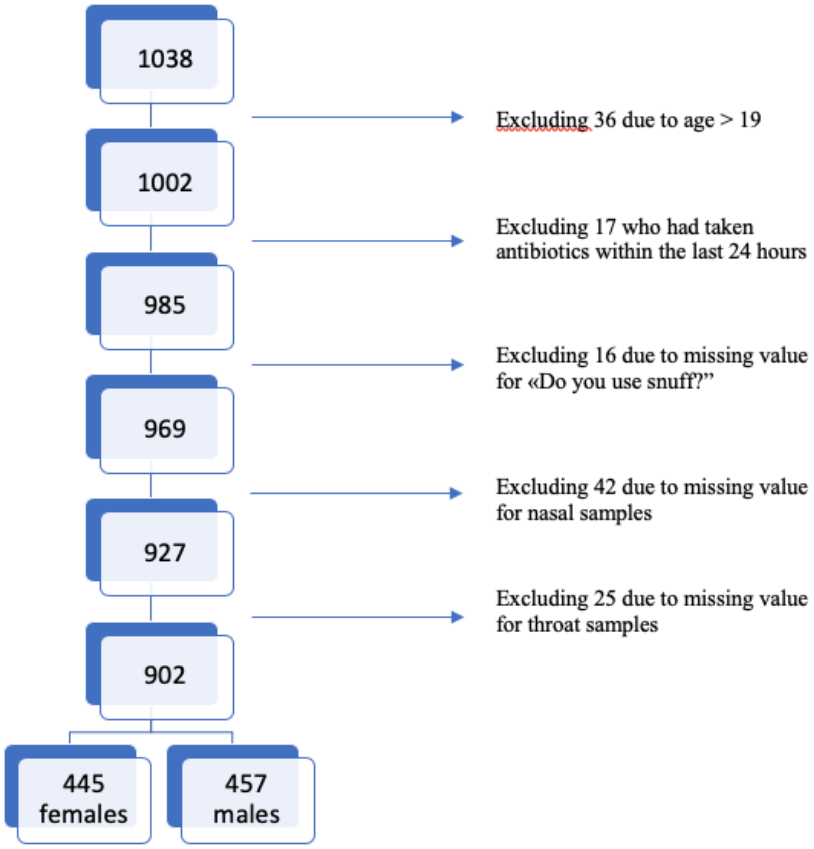

Figure 3 - Selection of Study Population

3.2 *S. aureus* carriage

To detect *S. aureus* carriage repeated swabs from the anterior nares and tonsils were taken; the first set of swabs at the screening site and the second set at school one week after. The swabs were taken from the anterior nares and the surface of both tonsils with a moist sterile brush. The brushes were placed in Amies charcoal transport medium (Copan, Brescia, Italy) and analysed by the microbiology laboratory at the University hospital of North Norway (UNN) within 24 hours. Selective agar plates and standard laboratory methods were used to detect *S. aureus* and MRSA. All *S. aureus* isolates were frozen at -70 degrees Celsius. Based on the culturing results, the *S. aureus* phenotype was categorized into three groups: Non-carriers (two negative swabs), Intermittent carriers (one positive swab), and Persistent carriers (two positive swab). In the logistic regression models, we used a dichotomous *S. aureus* variable; "Non- or intermittent carriers" versus "Persistent carriers" in line with the reclassification of *S. aureus* carriage types suggested by van Belkum et al.(10) We also used an alternative dichotomization of the *S. aureus* variable; "Carriers" and "Non-carriers", where carriers were defined as at least one positive swab, and non-carrier as two consecutive negative swabs.

3.3 Smokeless tobacco use

The participants filled in an electronic questionnaire on lifestyle and health. Smokeless tobacco use was mapped with the question "Do you use snuff?" and alternatives "No, never", "Yes, sometimes", "Yes, daily". It is important to emphasize that in Norway the word "snuff" or "snus" is used about both packaged and loose SLTs. Snuff use was recoded into a dichotomous variable in the analysis, with categories "Never" and "Sometimes or daily".

3.4 Ethics

The data collection in TFF1 was approved by REK North and the Norwegian Data Inspectorate. The present study was approved by REK North.

All participants signed a declaration when arriving at the study site, and participants younger than 16 years had to bring written permission from their guardians.

3.5 Statistical analysis

In order to examine whether snuff use is associated with nasal and throat carriage of *S. aureus*, we used descriptive analysis and logistic regression models. Differences in *S. aureus* carriage rates between users (sometimes or daily) and non-users of snuff were tested by chi-square test. We used logistic regression analysis to estimate odds ratio for *S. aureus* nasal and throat carriage in users of snuff compared to non-users in an age-adjusted model and in multivariate model including age and serum vitamin D which is known risk factors for *S. aureus* colonization. In analysis of throat carriage, tonsillectomy was also included in the model, while in analysis of nasal carriage, BMI was included. The pattern of *S. aureus* carriage by snuff use differed between girls and boys, and we therefore chose to stratify the analysis by sex, even though test for interaction was not statistically significant. All statistical analyses were done in SPSS version 25, and the level of statistical significance was set to $P<0.05$.

4 Results

The study population in TFF1 consisted of 445 girls and 457 boys. 33.0% of the girls and 39.4% of the boys used snuff sometimes or daily. The mean age was 16.17 (see Table 1).

4.1 Snuff use and *S. aureus* throat carriage

4.1.1 *S. aureus* carriage defined as two positive throat cultures

The prevalence of *S. aureus* throat carriage for the total study population was 51.2% (carriage defined as two positive swabs). Among girls who never use snuff, the prevalence of *S. aureus* throat carriage was 38.6%, while the prevalence among girls who use snuff sometimes or

daily was 49.7%. The difference in prevalence was statistically significant (P=0.032, see table 3). There was no statistically significant difference in prevalence of *S. aureus* throat carriage between boys who never use snuff and boys who use snuff sometimes or daily.

Logistic regression analysis was used to determine whether there was an association between snuff use sometimes or daily and *S. aureus* oropharyngeal carriage. Girls who used snuff sometimes or daily, had an age-adjusted OR for *S. aureus* throat carriage of 1.57 (95% CI = 1.05-2.33, see table 5) compared to non-users. The estimate was almost unchanged when including tonsillectomy and serum vitamin D in the model, OR=1.59 (95% CI = 1.01-2.50, see table 5). There was no significant association between snuff use and *S. aureus* throat carriage among boys. In age-adjusted analysis, the OR for *S. aureus* throat carriage was significantly lower for those who had had a tonsillectomy and significantly higher for those with alcohol use once per month or less, both for the total study population and for the girls.

When stratifying by tonsillectomy, girls without tonsillectomy who used snuff sometimes or daily had an OR of 1.82 (95% CI = 1.18-2.84; age-adjusted) compared to non-users. Among boys without tonsillectomy who used snuff sometimes or daily OR was 0.88 (95% CI = 0.57-1.34; age-adjusted).

4.1.2 *S. aureus* carriage defined as one or two positive throat cultures

We repeated the analysis using the alternative definition of *S. aureus* carriage, where all participants with at least one positive culture were included in the carrier group. There was no statistically significant association between snuff use sometimes or daily and *S. aureus* throat carriage. The OR for *S. aureus* throat carriage was significantly higher for boys than for girls, and significantly lower for those who had had a tonsillectomy.

4.2 Snuff use and *S. aureus* nasal carriage

4.2.1 *S. aureus* carriage defined as two positive nasal cultures

Prevalence rates of persistent *S. aureus* nasal carriage in the total study population were 43.3% for non-users of snuff and 50.2% for users, P = 0.047 (Table 7). In sex-specific analysis, there were no statistically significant differences in *S. aureus* rates using the two positive cultures critera.

Logistic regression analysis was used to determine whether there was an association between snuff use sometimes or daily and *S. aureus* nasal carriage. In the total study population, snuff use sometimes or daily was associated with an OR for *S. aureus* nasal carriage of 1.32 (95% CI = 1.00-1.73; age-adjusted) compared to non-use, although the risk estimate was not

statistically significant in the multivariable logistic regression model. Among girls, there was a statistically significantly lower OR for *S. aureus* nasal carriage associated with BMI.

4.2.2 *S. aureus* carriage defined as one or two positive nasal cultures

The prevalence of *S. aureus* nasal carriage for the total study population was 59.1% (carriage defined as one or two positive swabs). Among those who never used snuff, the prevalence of *S. aureus* nasal carriage was 55.3%, while the prevalence among those who used snuff sometimes or daily was 65.7%. The difference in prevalence was statistically significant (P=0.002, see table 4). Among girls who never used snuff, the prevalence of *S. aureus* nasal carriage was 49.3%, while the prevalence among girls who used snuff sometimes or daily was 63.3%. The difference in prevalence was statistically significant (P=0.006, see table 4).

For snuff use sometimes or daily in the total study population there was an age-adjusted OR for *S. aureus* nasal carriage of 1.55 (95% CI = 1.17-2.05, see table 8). When adjusting for serum vitamin D and BMI the OR was 1.48 (95% CI = 1.09-1.99). We found an association between snuff use sometimes or daily and *S. aureus* nasal carriage among girls, with an age-adjusted OR of 1.76 (95% CI = 1.17-2.65, see table 8) compared to non-use. The estimate was almost unchanged when adjusting for serum vitamin D and BMI in the model, OR=1.86 (95% CI = 1.18-2.94). Among boys, there was no association between snuff use and risk of *S. aureus* nasal carriage.

For the total study population, OR of *S. aureus* nasal carriage was significantly higher for boys than girls. Among girls, the OR of *S. aureus* nasal carriage was significantly higher with higher age, and with alcohol use. The OR of *S. aureus* nasal carriage among girls was significantly lower with higher BMI and with higher circulating vitamin D-levels.

5 Discussion

In this population-based cross-sectional study, we identified an association between snuff use and *S. aureus* carriage among adolescent girls. Our data show that girls using snuff sometimes or daily, have higher risk of both nasal and throat carriage of *S. aureus* (59% for throat, 86% for nasal, see table 5 and 8). When filtering out the girls who have had a tonsillectomy, there is 82% higher odds for *S. aureus* throat carriage among girls who use snuff compared with girls who do not use snuff.

As far as we know, there are no former studies on snuff use and *S. aureus* nasal or throat carriage. However, assuming that smoking and SLTs may share some of the same health effects, there is some available research. A study from 2018 showed that smoking cessation is

associated with enhanced expression of *S. aureus*-associated interleukin 1β (IL-1β) and granulocyte colony-stimulating factor (G-CSF) in nasal fluids.(7) This suggest that smoking is associated with depression of the expression of IL-1β and G-CSF, and therefore has an immune-suppressive effect. Smokeless tobacco having similar effects on the immune response is contradicted by a study that shows that smokeless tobacco extract (STE) at low concentrations enhanced the production of both TNF-α and IL-1β.(35) However, Hasseus et. al. showed that water soluble extract from Swedish moist snuff significantly inhibited con A-stimulated T-cell proliferation induced by accessory cells from rat oral epithelium.(36) This suggests that snuff use inhibits immune response. The research is not completely unambiguously, and it is hard to come to a definite conclusion regarding the effects of smokeless tobacco on the immune response. As our study shows an association between the use of smokeless tobacco and higher prevalence of *S. aureus* colonization, one might assume that SLTs in some way inhibits the innate immune response or stimulate adherence and growth of the microbe.

In our study, the association between snuff use and *S. aureus* carriage was only observed among girls. We may only speculate why the same association was not seen among boys. Test for statistical interaction was not significant. Male sex is a well-established risk factor for *S. aureus* nasal carriage.(37) It has been hypothesised that sex-steroid hormones play a role in regulating the immune response against *S. aureus*. Interestingly, smoking and smoke exposure have been associated with levels of circulating sex-steroids and their binding proteins in both women and men.(38) Whether the same association can be found between SLTs and circulating sex-steroids is currently unknown.

It remains unclear whether snuff use or factors associated with snuff use, are the cause of the higher prevalence of *S. aureus* nasal and throat carriage associated with snuff use. However, a study from 2016 found that *S. aureus* could be found in some of the smokeless tobacco products.(20) This supports our theory that snuff use may be a risk factor for *S. aureus* carriage. Nevertheless, further research, including prospective data, needs to be done in order to establish this as a cause-effect relationship. In the present study, girls who used snuff sometimes or regularly had higher mean circulating vitamin D levels, higher prevalence of smoking, higher alcohol consume, were less physical active and had higher use of hormonal contraceptives (results not presented in tables). These aspects may be included in more detailed analysis in the future.

Strengths of the study include the high response rate (93% attendance), which may contribute to reduce selection bias. We had a large data set with a wide range of information about each of the participants, and this made it possible for us to adjust for known risk factors associated with *S. aureus* nasal and throat carriage. The study is population-based and therefore to a large degree representative for the general population. It is however conducted on a limited age-group, and the results cannot be transferred to other age groups without further research.

A weakness with this study is that the data on snuff use was self-reported. As it is illegal to sell snuff and tobacco products to individuals under the age of 18 in Norway, there may be under-reported snuff use. We did not include data on average number of snuff portions per week among users of snuff, as we believe these data are afflicted with a lot of uncertainty (e.g. broad categories for reporting frequency of snuff use). Thus, we were not able to test for dose-response relationship.

There is always a risk of error when sampling nasal and throat swabs. To eliminate sources of error, repeated swabs were taken from both nose and oropharynx by trained personnel. The logistic regression analysis was adjusted for known confounding variables (i.e. sex, age, tonsillectomy, vitamin D, BMI). However, we cannot rule out that our results are partly due to unmeasured confounders. We also chose not to adjust for covariates that were strongly correlated with snuff use and not reported as a risk factor for *S. aureus* carriage; i.e. alcohol intake.

Our findings show a higher risk of colonization by a bacteria capable of causing serious and possibly life-threatening infections, among girls who use snuff. This supports the theory that there are negative health effects associated with use of SLTs that we may not yet be aware of. Our findings is important in relation to educating people on the possible health effects associated with using SLTs, and expanding the knowledge of these effects. Studies show that SLTs are often used as a "safer" alternative to smoking.(23) As more negative health effects of SLT use are discovered, the importance of preventing the use of these products increases.

Our findings contribute to map the possible determinants of human *S. aureus* carriage. This is useful, as *S. aureus* infections is a major clinical challenge, and many of the infected individuals are autoinfected with their own strain of bacteria. Our findings may offer new perspectives for the control of the *S. aureus* reservoir and prevention of *S. aureus* disease in the population. However, future studies should examine whether there is a cause-effect relationship between smokeless tobacco products and *S. aureus* carriage, including larger population-based prospective studies.

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Tables

Table 1 - Characteristics of Study Population. The Tromsø Study Fit Futures 1. Figures are means (standard deviation) and numbers (percent)			
	Total, N=902	Girls, N=445	Boys, N=457
Age at screening, years	16.2 (0.6)	16.2 (0.6)	16.2 (0.6)
BMI, kg/m²	22.5 (4.2)	22.5 (4.1)	22.5 (4.3)
Glycated haemoglobin (%) EDTA whole blood	5.3 (0.3)	5.3 (0.3)	5.3 (0.3)
25-hydroxyvitamin D (nmol/L) serum	47.2 (22.9)	54.4 (23.3)	40.6 (20.6)
Diabetes			
Yes	3 (0.3%)	2 (0.4%)	1 (0.2%)
No	896 (99.7%)	443 (99.6%)	453 (99.8%)
Skin rash on predilection sites for atopic eczema			
Yes	256 (28.5%)	143 (32.2%)	113 (24.8%)
No	643 (71.5%)	301 (67.8%)	342 (75.2%)
Tonsillectomy			
Yes	113 (13.0%)	57 (13.1%)	56 (12.8%)
No	759 (87.0%)	377 (86.9%)	382 (87.2%)
How do you rate your own oral health?			
Good	501 (56.7%)	279 (63.6%)	222 (49.9%)
Neither good nor bad	298 (33.7%)	126 (28.7%)	172 (38.7)
Bad	85 (9.6%)	34 (7.7%)	51 (11.5%)
Girls: Have you started menstruating?			
Yes		441 (99.1%)	
No		4 (0.9%)	
Use of hormonal contraceptives			
Combined contraceptive		128 (29.0%)	
Progesterone contraceptive		13 (2.9%)	
No hormonal contraceptive		301 (68.1%)	
Do you smoke?			
No, never	706 (78.4%)	353 (79.5%)	353 (77.2%)
Sometimes	162 (18.0%)	74 (16.7%)	88 (19.3%)
Daily	33 (3.7%)	17 (3.8%)	16 (3.5%)
Do you use snuff?			
No, never	575 (63.7%)	298 (67.0%)	277 (60.6%)
Sometimes	121 (13.4%)	65 (14.6%)	56 (12.3%)
Daily	206 (22.8%)	82 (18.4%)	124 (27.1%)
How often do you drink alcohol?			
Never	253 (28.1%)	105 (23.6%)	148 (32.5%)
Once per month or less	371 (41.2%)	202 (45.4%)	169 (37.1%)
2-4 times per month	261 (29.0%)	130 (29.2%)	131 (28.8%)
2-3 times per week	12 (1.3%)	8 (1.8%)	4 (0.9%)
4 or more times per week	3 (0.3%)	0 (0.0%)	3 (0.7%)
How many alcohol units do you usually drink when you drink alcohol?			
1-2	114 (17.6%)	70 (20.6%)	44 (14.3%)
3-4	188 (29.1%)	127 (37.4%)	61 (19.9%)
5-6	202 (31.2%)	104 (30.6%)	98 (31.9%)
7-9	82 (12.7%)	29 (8.5%)	53 (17.3%)
10 or more	61 (9.4%)	10 (2.9%)	51 (16.6%)
Are you actively doing sports or physical activity outside school hours?			
Yes	601 (66.7%)	301 (67.8%)	300 (65.6%)
No	300 (33.3%)	143 (32.2%)	157 (34.4%)

If you are actively doing sports or physical activity outside school, how many hours a week are you active?			
None	1 (0.2%)	1 (0.3%)	0 (0.0%)
About half an hour	17 (2.8%)	8 (2.7%)	9 (3.0%)
About 1-1.5 hours	64 (10.7%)	30 (10.0%)	34 (11.4%)
About 2-3 hours	157 (26.2%)	87 (28.9%)	70 (23.4%)
About 4-6 hours	209 (34.8%)	115 (38.2%)	94 (31.4%)
7 hours or more	152 (25.3%)	60 (19.9%)	92 (30.8%)
Main high school program			
Program for Specialization in General Studies	369 (40.9%)	230 (51.7%)	139 (30.4%)
Program for Sports and Physical Education	99 (11.0%)	37 (8.3%)	62 (13.6%)
Vocational Program	434 (48.1%)	178 (40.0%)	256 (56.0%)

Table 2 - Throat carriage by snuff use

Table 3. *S. aureus* throat carriage by snuff use (N and percent in brackets). The Tromsø Study Fit Futures 1, N = 902

	Total				Girls				Boys			
	Non-carrier[a]	Interm. carrier[b]	Persistent[c]	P-value	Non-carrier[a]	Interm. carrier[b]	Persistent[c]	P-value	Non-carrier[a]	Interm. carrier[b]	Persistent[c]	P-value
Never	124 (21.6)	165 (28.7)	286 (49.7)	.383	81 (27.2)	102 (34.2)	115 (38.6)	.213	43 (15.5)	63 (22.7)	171 (61.7)	.310
Sometimes	29 (24.0)	33 (27.3)	59 48.8)		14 (21.5)	21 (32.3)	30 (46.2)		15 (26.8)	12 (21.4)	29 (51.8)	
Daily	35 (17.0)	54 (26.2)	117 (56.8)		16 (19.5)	23 (28.0)	43 (52.4)		19 (15.3)	31 (25.0)	74 (59.7)	
Never	124 (21.6)	165 (28.7)	286 (49.7)	.496	81 (27.2)	102 (34.2)	115 (38.6)	.074	43 (15.5)	63 (22.7)	171 (61.7)	.558
Sometimes or Daily	64 (19.6)	87 (26.6)	176 (53.8)		30 (20.4)	44 (29.9)	73 (49.7)		34 (18.9)	43 (23.9)	103 (57.2)	
		Non- or interm.[a,b]	Persistent[c]	P-value		Non- or interm.[a,b]	Persistent[c]	P-value		Non- or interm.[a,b]	Persistent[c]	P-value
Never		289 (50.3)	286 (49.7)	.186		183 (61.4)	115 (38.6)	.063		106 (38.3)	171 (61.7)	.382
Sometimes		62 (51.2)	59 (48.8)			35 (53.8)	30 (46.2)			27 (48.2)	29 (51.8)	
Daily		89 (43.2)	117 (56.8)			39 (47.6)	43 (52.4)			50 (40.3)	74 (59.7)	
Never		289 (50.3)	286 (49.7)	.240		183 (61.4)	115 (38.6)	**.032**		106 (38.3)	171 (61.7)	.379
Sometimes or Daily		151 (46.2)	176 (53.8)			74 (50.3)	73 (49.7)			77 (42.8)	103 (57.2)	
	Non-carrier[a]	Carrier[d]		P-value	Non-carrier[a]	Carrier[d]		P-value	Non-carrier[a]	Carrier[d]		P-value
Never	124 (21.6)	451 (78.4)		.253	81 (27.2)	217 (72.8)		.288	43 (15.5)	234 (84.5)		.105
Sometimes	29 (24.0)	92 (76.0)			14 (21.5)	51 (78.5)			15 (26.8)	41 (73.2)		
Daily	35 (17.0)	171 (83.0)			16 (19.5)	66 (80.5)			19 (15.3)	105 (84.7)		
Never	124 (21.6)	451 (78.4)		.496	81 (27.2)	217 (72.8)		.131	43 (15.5)	234 (84.5)		.372
Sometimes or Daily	64 (19.6)	263 (80.4)			30 (20.4)	17 (79.6)			34 (18.9)	146 (81.1)		

[a]Non-carrier: no growth of *S.aureus* in the two throat swab cultures
[b]Intermittent carrier: growth of *S.aureus* in one of the two throat swab cultures
[c]Persistent carrier: growth of *S.aureus* in both throat swab cultures
[d]Carrier: growth of *S.aureus* in at least one of the throa swab cultures

Table 3 - Nasal carriage by snuff use

Table 4. *S. aureus* nasal carriage by snuff use (N and percent in brackets). The Tromsø Study Fit Futures 1, N = 902												
	Total				Girls				Boys			
	Non-carrier[a]	Interm.[b]	Persistent[c]	P-value	Non-carrier[a]	Interm.[b]	Persistent[c]	P-value	Non-carrier[a]	Interm.[b]	Persistent[c]	P-value
Never	257 (44.7)	69 (12.0)	249 (43.3)	**.037**	151 (50.7)	39 (13.1)	108 (36.2)	.082	106 (38.3)	30 (10.8)	141 (50.9)	.542
Sometimes	41 (33.9)	17 (14.0)	63 (52.1)		23 (35.4)	12 (18.5)	30 (46.2)		18 (32.1)	5 (8.9)	33 (58.9)	
Daily	71 (34.5)	34 (16.5)	101 (49.0)		31 (37.8)	16 (19.5)	35 (42.7)		40 (32.3)	18 (14.5)	66 (53.2)	
Never	257 (44.7)	69 (12.0)	249 (43.3)	**0.008**	151 (50.7)	39 (13.1)	108 (36.2)	**.018**	106 (38.3)	30 (10.8)	141 (50.9)	.400
Sometimes or Daily	112 (34.3)	51 (15.6)	164 (50.2)		54 (36.7)	28 (19.0)	65 (44.2)		58 (32.2)	23 (12.8)	99 (55.0)	
		Non- or Interm[a,b]	Persistent[c]	P-value		Non- or Interm[a,b]	Persistent[c]	P-value		Non- or Interm[a,b]	Persistent[c]	P-value
Never		326 (56.7)	249 (43.3)	0.12		190 (63.8)	108 (36.2)	0.24		136 (49.1)	141 (50.9)	0.54
Sometimes		58 (47.9)	63 (52.1)			35 (53.8)	30 (46.2)			23 (41.1)	33 (58.9)	
Daily		105 (51.0)	101 (49.0)			47 (57.3)	35 (42.7)			58 (46.8)	66 (53.2)	
Never		326 (56.7)	249 (43.3)	**0.047**		190 (63.8)	108 (36.2)	0.10		136 (49.1)	141 (50.9)	0.39
Sometimes or Daily		163 (49.8)	164 (50.2)			82 (55.8)	65 (44.2)			81 (45.0)	99 (55.0)	
	Non-carrier[a]	Carrier[d]		P-value	Non-carrier[a]	Carrier[d]		P-value	Non-carrier[a]	Carrier[d]		P-value
Never	257 (44.7)	318 (55.3)		**0.009**	151 (50.7)	147 (49.3)		**0.020**	106 (38.3)	171 (61.7)		0.42
Sometimes	41 (33.9)	80 (66.1)			23 (35.4)	42 (64.6)			18 (32.1)	38 (67.9)		
Daily	71 (34.5)	135 (65.5)			31 (37.8)	51 (62.2)			40 (32.3)	84 (67.7)		
Never	257 (44.7)	318 (55.3)		**0.002**	151 (50.7)	147 (49.3)		**0.006**	106 (38.3)	171 (61.7)		0.19
Sometimes or Daily	112 (34.3)	215 (65.7)			54 (36.7)	93 (63.3)			58 (32.2)	122 (67.8)		

[a]Non-carrier: no growth of S. aureus in the two nasal swab cultures
[b]Intermittent carrier: growth of S. aureus in one of the two nasal swab cultures
[c]Persistent carrier: growth of S. aureus in both nasal swab cultures
[d]Carrier: growth of S. aureus in at least one of the nasal swab cultures

Table 4 - Associations between snuff use and S. aureus throat carriage – two positive throat cultures defined as carriers (ref. Van Belkum et. al)

Table 5. Associations between snuff use and *S. aureus* throat carriage. Odds ratios (OR) and 95% confidence intervals (95% CI) from multivariable logistic regression analysis. Observations with two *S. aureus* positive throat cultures defined as carriers (ref. Van Belkum et. al) The Tromsø Study Fit Futures 1.

		Total (N=902)		**Girls (N=445)**		**Boys (N=457)**	
		OR* (95% CI)	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**
Snuff use	Non-user	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	Sometimes or daily	1.18 (0.90-1.55)	1.10 (0.81-1.49)	**1.57 (1.05-2.33)**	**1.59 (1.01-2.50)**	0.83 (0.57-1.22)	0.79 (0.53-1.20)
Sex	Girls	1.0 (ref)	1.0 (ref)				
	Boys	**2.05 (1.57-2.68)**	**2.33 (1.73-3.15)**				
Age	years	1.03 (0.83-1.29)	1.14 (0.89-1.47)	1.18 (0.86-1.64)	1.15 (0.811.62)	0.96 (0.71-1.30)	1.13 (0.78-1.64)
BMI	kg/m^2	1.01 (0.98-1.04)		1.00 (0.95-1.04)		1.02 (0.98-1.07)	
HbA1c	% glycated	1.16 (0.75-1.81)		0.95 (0.49-1.84)		1.36 (0.70-2.63)	
25-hydroxyvitamin D	nmol/l	1.00 (0.99-1.00)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Tonsillectomy	No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	Yes	**0.54 (0.36-0.81)**	**0.55 (0.36-0.85)**	**0.48 (0.26-0.89)**	**0.48 (0.25-0.92)**	0.57 (0.32-1.00)	0.62 (0.35-1.12)
Atopic eczema	No	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Yes	1.19 (0.82-1.74)		1.22 (0.75-2.00)		1.54 (0.81-2.93)	
Hormonal contraceptive	No			1.0 (ref)			
	Yes			1.23 (0.83-1.83)			
Smoking	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Sometimes or daily	1.18 (0.86-1.62)		1.23 (0.77-1.95)		1.09 (0.79-1.71)	
Alcohol use	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Once per month or less	**1.49 (1.08-2.05)**		**1.99 (1.21-3.28)**		1.47 (0.94-2.31)	
	Two or more times/ month	1.29 (0.91-1.82)		1.62 (0.95-2.76)		1.26 (0.78-2.02)	
Recreational physical activity	Less than 2 hours/week	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	2-3 hours/week	0.87 (0.60-1.25)		0.98 (0.58-1.65)		0.85 (0.49-1.47)	
	4-6 hours/week	1.01 (0.72-1.42)		1.11 (0.69-1.79)		1.04 (0.63-1.71)	
	7 hours or more/week	1.08 (0.74-1.57)		0.85 (0.47-1.54)		1.15 (0.69-1.92)	

BMI = body mass index; HbA1c, glycated haemoglobin.
*Age-adjusted logistic regression model, **Multivariable logistic regression model: Snuff use, Age, Sex, Vitamin D, and Tonsillectomy
Test for interaction between snuff use and sex, age-adjusted: P=0.11. Test for interaction between snuff use and tonsillectomy, age-adjusted: P=0.22 among girls and P=0.57 among boys.

Table 5 - Association between snuff use and S. aureus throat carriage – one or two S. aureus positive throat cultures defined as carriers

Table 6. Association between snuff use and *S. aureus* throat carriage. Odds ratios (OR) and 95% confidence intervals (95% CI) from multivariable logistic regression analysis. Observations with one or two *S. aureus* positive throat cultures defined as carriers. The Tromsø Study Fit Futures 1.

		Total (N=902)		**Girls (N=445)**		**Boys (N=457)**	
		OR* (95% CI)	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**
Snuff use	Non-user	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	Sometimes or daily	1.13 (0.81-1.58)	1.13 (0.78-1.64)	1.45 (0.90-2.33)	1.55 (0.91-2.65)	0.79 (0.48-1.30)	0.81 (0.47-1.40)
Sex	Girls	1.0 (ref)	1.0 (ref)				
	Boys	**1.64 (1.19-2.28)**	**1.80 (1.24-2.60)**				
Age	years	1.03 (0.78-1.35)	1.20 (0.87-1.66)	1.30 (0.86-1.96)	1.41 (0.91-2.20)	0.84 (0.57-1.22)	0.97 (0.60-1.57)
BMI	kg/m^2	0.99 (0.95-1.02)		0.97 (0.92-1.01)		1.01 (0.95-1.07)	
HbA1c	% glycated	1.57 (0.87-2.82)		1.20 (0.57-2.52)		2.24 (0.85-5.92)	
25-hydroxyvitamin D	nmol/l	1.00 (0.99-1.00)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.991.01)
Tonsillectomy	No	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	Yes	**0.53 (0.34-0.82)**	**0.54 (0.34-0.87)**	**0.50 (0.28-0.91)**	**0.50 (0.27-0.93)**	0.55 (0.28-1.08)	0.59 (0.29-1.20)
Atopic eczema	No	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Yes	1.38 (0.84-2.27)		1.36 (0.75-2.47)		1.82 (0.70-4.75)	
Hormonal contraceptive	No			1.0 (ref)			
	Yes			1.33 (0.84-2.12)			
Smoking	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Sometimes or daily	1.07 (0.72-1.59)		1.34 (0.76-2.34)		0.82 (0.47-1.44)	
Alcohol use	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Once per month or less	1.22 (0.83-1.80)		1.26 (0.74-2.15)		1.43 (0.80-2.59)	
	Two or more times/ month	1.22 (0.81-1.85)		1.31 (0.74-2.35)		1.26 (0.68-2.31)	
Recreational physical activity	Less than 2 hours/week	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	2-3 hours/week	0.98 (0.63-1.53)		1.31 (0.71-2.41)		0.74 (0.38-1.43)	
	4-6 hours/week	1.12 (0.74-1.70)		1.00 (0.59-1.70)		1.63 (0.79-3.38)	
	7 hours or more/week	1.30 (0.80-2.11)		1.29 (0.64-2.59)		1.22 (0.62-2.39)	

BMI = body mass index; HbA1c, glycated haemoglobin.
*Age-adjusted logistic regression model
**Multivariable logistic regression model: Snuff use, Age, Sex, Vitamin D, and Tonsillectomy

Table 6 - Associations between snuff use and S. aureus nasal carriage - two S. aureus positive nasal cultures defined as carriers (ref. Van -Belkum et al.)

Table 7. Associations between snuff use and *S. aureus* nasal carriage. Odds ratios (OR) and 95% confidence intervals (95% CI) from multivariable logistic regression analysis. Observations with two *S. aureus* positive nasal cultures defined as carriers (ref. Van Belkum et al.) The Tromsø Study Fit Futures 1.

		Total (N=902)		**Girls (N=445)**		**Boys (N=457)**	
		OR* (95% CI)	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**
Snuff use	Non-user	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	Sometimes or daily	**1.55 (1.17-2.05)**	**1.48 (1.09-1.99)**	**1.76 (1.17-2.65)**	**1.86 (1.18-2.94)**	1.31 (0.88-1.94)	1.35 (0.89-2.05)
Sex	Girls	1.0 (ref)	1.0 (ref)				
	Boys	**1.54 (1.18-2.02)**	**1.52 (1.13-2.04)**				
Age	years	1.20 (0.95-1.50)	1.05 (0.83-1.34)	**1.71 (1.19-2.47)**	1.19 (0.84-1.69)	0.91 (0.67-1.25)	0.97 (0.70-1.34)
BMI	kg/m^2	0.98 (0.95-1.01)	0.97 (0.94-1.00)	**0.94 (0.90-0.99)**	**0.93 (0.88-0.98)**	1.01 (0.96-1.05)	1.01 (0.96-1.06)
HbA1c	% glycated	0.90 (0.58-1.41)		0.69 (0.35-1.34)		1.08 (0.58-2.02)	
25-hydroxyvitamin D	nmol/l	1.00 (0.99-1.00)	1.00 (0.99-1.01)	1.00 (0.99-1.00)	**0.99 (0.98-1.00)**	1.01 (1.00-1.02)	1.01 (1.00-1.02)
Tonsillectomy	No	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Yes	1.00 (0.67-1.50)		1.06 (0.60-1.87)		0.95 (0.53-1.70)	
Atopic eczema	No	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Yes	1.25 (0.85-1.85)		1.46 (0.88-2.42)		1.13 (0.60-2.14)	
Hormonal contraceptive	No			1.0 (ref)			
	Yes			1.29 (0.86-1.92)			
Smoking	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Sometimes or daily	1.13 (0.82-1.57)		1.12 (0.70-1.79)		1.14 (0.72-1.81)	
Alcohol use	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Once per month or less	1.29 (0.93-1.78)		**1.77 (1.10-2.87)**		1.15 (0.73-1.82)	
	Two or more times/ month	**1.56 (1.10-2.22)**		**2.15 (1.27-3.62)**		1.35 (0.83-2.20)	
Recreational physical activity	Less than 2 hours/week	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	2-3 hours/week	0.75 (0.52-1.09)		0.71 (0.42-1.19)		0.86 (0.49-1.50)	
	4-6 hours/week	0.89 (0.63-1.25)		0.73 (0.46-1.18)		1.23 (0.74-2.06)	
	7 hours or more/week	1.28 (0.86-1.90)		1.09 (0.60-1.98)		1.39 (0.82-2.36)	

BMI = body mass index; HbA1c, glycated haemoglobin.
*Age-adjusted logistic regression model
**Multivariable logistic regression model: Snuff use, Age, Sex, Vitamin D, and BMI

Table 7 - Associations between snuff use and S. aureus nasal carriage - one or two S. aureus positive throat cultures defined as carriers

Table 7. Associations between snuff use and *S. aureus* nasal carriage. Odds ratios (OR) and 95% confidence intervals (95% CI) from multivariable logistic regression analysis. Observations with one or two *S. aureus* positive nasal cultures defined as carriers. The Tromsø Study Fit Futures 1.

		Total (N=902)		**Girls (N=445)**		**Boys (N=457)**	
		OR* (95% CI)	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**	**OR* (95% CI)**	**OR** (95% CI)**
Snuff use	Non-user	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	Sometimes or daily	**1.55 (1.17-2.05)**	**1.48 (1.09-1.99)**	**1.76 (1.17-2.65)**	**1.86 (1.18-2.94)**	1.31 (0.88-1.94)	1.35 (0.89-2.05)
Sex	Girls	1.0 (ref)	1.0 (ref)				
	Boys	**1.54 (1.18-2.02)**	**1.52 (1.13-2.04)**				
Age	years	1.20 (0.95-1.50)	**1.29 (1.01-1.66)**	**1.71 (1.19-2.47)**	**1.73 (1.17-2.54)**	0.91 (0.67-1.25)	1.03 (0.73-1.45)
BMI	kg/m^2	0.98 (0.95-1.01)	0.97 (0.94-1.00)	**0.94 (0.90-0.99)**	**0.93 (0.88-0.98)**	1.01 (0.96-1.05)	1.01 (0.96-1.06)
HbA1c	% glycated	0.90 (0.58-1.41)		0.69 (0.35-1.34)		1.08 (0.58-2.02)	
25-hydroxyvitamin D	nmol/l	1.00 (0.99-1.00)	1.00 (0.99-1.01)	1.00 (0.99-1.00)	**0.99 (0.98-1.00)**	1.01 (1.00-1.02)	1.01 (1.00-1.02)
Tonsillectomy	No	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Yes	1.00 (0.67-1.50)		1.06 (0.60-1.87)		0.95 (0.53-1.70)	
Atopic eczema	No	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Yes	1.25 (0.85-1.85)		1.46 (0.88-2.42)		1.13 (0.60-2.14)	
Hormonal contraceptive	No			1.0 (ref)			
	Yes			1.29 (0.86-1.92)			
Smoking	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Sometimes or daily	1.13 (0.82-1.57)		1.12 (0.70-1.79)		1.14 (0.72-1.81)	
Alcohol use	Never	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	Once per month or less	1.29 (0.93-1.78)		**1.77 (1.10-2.87)**		1.15 (0.73-1.82)	
	Two or more times/ month	**1.56 (1.10-2.22)**		**2.15 (1.27-3.62)**		1.35 (0.83-2.20)	
Recreational physical activity	Less than 2 hours/week	1.0 (ref)		1.0 (ref)		1.0 (ref)	
	2-3 hours/week	0.75 (0.52-1.09)		0.71 (0.42-1.19)		0.86 (0.49-1.50)	
	4-6 hours/week	0.89 (0.63-1.25)		0.73 (0.46-1.18)		1.23 (0.74-2.06)	
	7 hours or more/week	1.28 (0.86-1.90)		1.09 (0.60-1.98)		1.39 (0.82-2.36)	

BMI = body mass index; HbA1c, glycated haemoglobin.
*Age-adjusted logistic regression model
**Multivariable logistic regression model: Snuff use, Age, Sex, Vitamin D, and BMI

Grade

Referanse: Lund KE. Association Between Willingness to Use Snus to Quit Smoking and Perception of Relative Risk Between Snus and Cigarettes. Oxford Journals. 2012.

Design: Cross-sectional study	
Dokumentasjonsnivå	IV
GRADE	⊕⊕

Formål

To see how perception of risks from snus use compared with cigarette smoking was associated with the willingness of trying snus as a quit-smoking method.

Konklusjon

Devising a way to inform smokers about the risk continuum of tobacco products could be an important research priority in countries where snus is allowed to compete with cigarettes for market share.

Land

Norway

År data innsamling

April-May 2007

Materiale og metode

Rekruttering deltakere:
The data were gathered by online interviews with a sample drawn from a web panel comprising more than 62 000 Norwegians. People were recruited to this web panel when they had participated in previous nationally representative population surveys, carried out by telephone, post, or personal interview, and had agreed to receive further invitations to participate in surveys by e-mail. Of the 14 744 men who were invited to participate, 7 170 (48.6%) responded.

Inklusjonskriterier
- Men aged 20-50 years.

Datagrunnlaget
Former daily smokers were asked to report method for quitting smoking and current daily smokers were asked to state their willingness to try different methods for quitting smoking. They were also asked to assess the relative risk between daily use of snus and cigarettes.

Statistiske metoder
The ORs for reporting having used snus when quitting smoking (former smokers) and for reporting a "very likely og likely" intention to use snus in a future quit attempt (current smokers) were calculated using logistic regression controlling for these independent variables: perception of relative risk snus/cigarettes, age, highest completed education, and number of previous attempts to quit smoking. For current smokers, we also controlled for action plans to quit smoking and history of snus use.

Resultater

Adjusted odd ratio (AOR) for reporting willingness to try snus in future quit attempts was significantly higher (AOR=4.82, p<0.001) for the 22.9% of the current smokers who, consistent with scientific evidence, believed that the health risks were "far lower" for snus than for cigarettes compared with the 39.8% who incorrectly perceived the health risks to be "equal or higher" for snus (reference AOR=1). About 37.2% of the daily smokers believed that the risk was "somewhat lower" for snus than for cigarettes and had a significantly higher AOR of reporting willingness to try snus (AOR=2.31, p<0.001) compared with the reference group.

Percentage of Former and Current Daily Smokers Who Used Different Methods to Quit Smoking at Last Quit Attempt, and Willingness Among Current Smokers to Retry the Same Method in a Future Attempt

	I. Former daily smokers (N=1.155)	II. Current daily smokers (N=1.132)	% of II who will retry same method		
				n/N	95% CI
Nicotine chewing gum	13.9 (n=160)	31.3 (n=354)	57.4	187/326	52.0-62.8
Nicotine patch	7.0 (n=81)	18.9 (n=214)	51.3	100/195	44.3-58.3
Snus	31.6 (n=365)	30.4 (n=344)	70.0	217/310	64.9-75.1
Inhaler	1.4 (n=16)	3.5 (n=40)	-	-	
Zyban	4.1 (n=47)	9.5 (n=107)	32.1	31/97	22.7-41.3
Champix	1.0 (n=12)	1.8 (n=20)	-	-	
Telephone helpline	0.8 (n=9)	2.4 (n=27)	-	-	
Consult health care personnel	3.1 (n=36)	6.6 (n=75)	38.9	28/72	27.6-50.2
Self-help material	10.4 (n=120)	20.4 (n=231)	63.7	137/215	57.3-70.1

Diskusjon/kommentarer

Is the topic question of the study formulated clearly? **Yes.**
Is a prevalence study a suitable method for answering the topic question? **Yes.**
Is the population from which the sample is taken clearly defined? **Yes.**
Was the sample included in the study in a satisfactory way? **Yes.**
Has is been explained whether the respondents differ from those who have not responded? **Yes.**
Is the response rate high enough? **No, the response rate was 48.6%.**
Does the study use measurement methods that are reliable (valid) for what you want to measure? **Yes.**
Is the data collection standardized? **Yes.**
Is the data analysis standardized? **Yes.**
What is the result of this study? **The participants that believed the risk of snus was lower than that of smoking reported higher willingness to try snus as a method for quitting smoking.**
Can the results be due to chance? **No.**
Can the results be transferred to practice? **Yes.**
Does the results of this study coincide with the results of other available studies? **Yes.**

Strengths:
- Coincides with the results of other studies
- Large study population (n=7170)
- Significant results
- Sample and study population generally very similar on key variables

Weaknesses:
- Low overall response rate (48.6%)
- Underrepresentation of respondents with short education
- Women not included

Referanse: Lund I, Scheffels J. Adolescent tobacco use practices and user profiles in a mature Swedish moist snuff (snus) market: Results from a school-based cross-sectional study. Scandinavian Journal of Public Health. 2016;44(7):646-53.	**Design:** Qualitative study
	Dokumentasjonsnivå VI
	GRADE ☺

Formål	**Materiale og metode**	**Resultater**	**Diskusjon/kommentarer**
The aim was to study the diversity of tobacco use among Norwegian adolescent tobacco users and to investigate how different user groups compared with each other in terms of lifestyle and risk correlates. **Konklusjon** Fragmented use patterns in adolescence undermine the dichotomy often applied between smokers and snus users. For associations with lifestyle and risk correlates, use frequency and high-frequency dual use seem to be more important than the choice of product. **Land** Norway **År data innsamling** 2016	**Recruitment:** Data was obtained from a cross-sectional school-based survey among Norwegian tenth grade adolescents as part of a larger European study. In total 3196 adolescents participated. **Criteria for exclusion:** - All current non-users of tobacco were excluded from the analysis. **Data:** In addition to information on tobacco use, this study made use of variables on leisure time activities, various problem behaviours or experiences and alcohol use. **Statistical methods:** Principal components analyses were applied to seven leisure time activities items and 10 risk experience items. The principal axis method was used to extract the components and this was followed by a varimax (orthogonal) rotation. Components with eigenvalues>1 were retained for rotation. The bivariate analyses included a description of the frequencies of the various tobacco use practices and a calculation of the mean leisure time and risk experience component scores and mean alcohol consumption episodes within different tobacco user groups. Analysis of variance was applied to test for differences in the group means. The multivariate analysis consisted of a logistic regression on a dummy variable for using both cigarettes and snus daily, with leisure time acitivites, problem experiences and risk behaviours, last-month alcohol consumption episodes, and sex as explanatory variables.	The study sample consisted of 736 tobacco users, implying a tobacco user proportion of 23% in the original sample. Principal components analysis on seven leisure time activities resulted in the three components social orientation, cultural orientation and gambling. The ten original last-year problem experiences and risk behavior items were reduced to two risk behavior components, legal risk and relational risk. **Use patterns** In total, 41.5% of the tobacco users were dual users, but with large variations in the frequency of dual use. Focusing only on daily smokers, the occurrence of dual use was 78%, whereas among the daily snus users, 59% also smoked cigarettes. **Lifestyle and risk profiles for smokers, snus users and dual users** For snus users, the only significant difference in leisure time orientation between groups was found for gambling ($p<0.001$). Regarding risk-taking and problem experiences, positive associations was found between snus use frequency and last-month drinking episodes ($p<0.001$). Smoking frequency was positively associated with the leisure time components social orientation ($p<0.001$) and gambling ($p<0.001$) and the risk behavior components legal risk ($p<0.001$). A positive association was found between smoking frequency and last-month drinking episodes ($p<0.001$), with the highest occurrence found for daily smokers. Occasional snus users, occasional smokers and occasional dual users had low scores on all components. A distinction between daily snus users and daily smokers was that daily snus users scored higher on cultural orientation, and daily smokers scored higher on relational risk. For legal risk, exclusive daily smokers scored low, whereas daily smokers who used snus occasionally scored high. Unlike all other daily users, exclusive daily snus users scored low on social orientation and gambling. Daily dual users had much higher leisure time and risk component scores and also reported more last-month drinking episodes than what was seen in the separate snus user and smoker analyses. Statistical testing showed that the differences between these pooled tobacco user groups were significant ($p<0.001$) for all components expect cultural leisure time orientation.	**Study design:** Qualitative study Is the purpose of the study well formulated? **Yes.** Is the qualitative method appropriate to answer the topic question? **Yes.** Is the study design appropriate to answer the topic question? **Yes.** Is the study population appropriate to answer the topic question? **Yes, although it is missing a population characteristics table.** Was the data collected in such a way that the topic question was answered? **Yes.** Is it clear how the analysis was carried out? Is the interpretation of data understandable, clear and reasonable? **Yes.** Were background conditions explained that may have affected the interpretation of data? **Yes.** Have attempts been made to substantiate the findings? **Yes.** Are ethical matters considered? **No**. Is it clear what the main findings of the study are? **Yes.** How useful are the findings in this study? **I do not find the findings to be particularly useful. High frequency use is the factor that correlates with lifestyle and risk correlates, more than use in itself. The medical goal would be prevention of use either way.** **Strengths:** - This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. **Weaknesses**: - Limited sample size means that separation into eight different tobacco user categories gave relatively small groups. - Measurement problems in the data because cigarette smoking and snus were asked about in two different ways. - Information on the amount of snus per day or week was not available.

Referanse: Olsen K, Danielsen K, Wilsgaard T, Sangvik M, Sollid JUE, Thune I, et al. Obesity and Staphylococcus aureus Nasal Colonization among Women and Men in a General Population. PLoS ONE. 2013.

Design: Cross-sectional study

Dokumentasjonsnivå	IIb
GRADE	☺☺☺

Formål

To see if body mass index (BMI) and waist circumference (WC) could be associated with *S.aureus* colonization independent of diabetes mellitus (DM).

Konklusjon

The results support that obesity is a possible determinant for *S.aureus* nasal colonization independent of diabetes mellitus, in particular for premenopausal women. The role of obesity at different ages and by sex should be addressed in future prospective studies of *S.aureus* colonization.

Land

Norway

År data innsamling

October 2007-December 2008

Materiale og metode

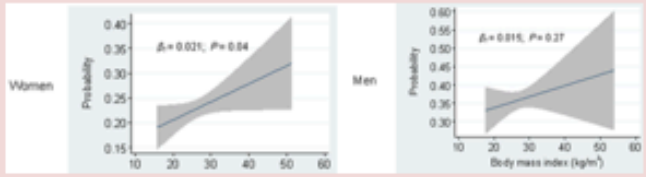
Recruitment:
The participants in the Tromsø Stap and Skin Study (TSSS) were recruited from a population-based study, the sixth Tromsø Study. There were 12 984 participants and an attendance rate of 65.7%.

Data:
Nasal swab cultures were collected in a random sample of 4 026 participants aged 30-87 years, during October 2007 to June 2008, estimated to give sufficient power for subgroup analysis of host-microbe relationships in the TSSS.

Statistical methods:
The interrelationships between BMI and WC and *S.aureus* nasal colonization were evaluated in logistic regression models stratified by sex.
Selected characteristics of women and men were compared using age-adjusted regression analysis with linear *Ptrend* across all BMI categories.
On the basis of biological plausibility and model fit, the variables age (continuous), DM, current daily smoking, education level and total household income were included as covariates in the multivariable regression model.
To control for possible confounding by pre-diabetes and undiagnosed diabetes, sensitivity analysis restricted to those with HbA1c<6.0% was performed. To control for possible confounding by hormonal contraceptives, additional restriction analysis, including only non-users of hormonal contraceptives, was performed among young and premenopausal women.
Tests of model fit were performed by the Hosmer-Lemeshow goodness-of-fit test.

Resultater

In the female population, each 2.5 kg/m^2 increase in BMI was associated with a 7% higher odds of *S.aureus* nasal colonization (p=0.01). When comparing obese and lean women aged 30-43 years, we observed that BMI≥32.5 versus <22.5 kg/m^2 and WC≥101 versus <80 cm was associated with a 2.60 and 2.12 times higher odds of *S.aureus* colonization, respectively (95% confidence intervals 1.35-4.98 nd 1.17-3.85). Among men, high WC was also associated with *S.aureus* nasal colonization. The associations did not change significantly when the analysis was restricted to participants without signs of pre-diabetes (HbA1c<6.0%) among women and men, and to non-users of hormonal contraceptives among women.



BMI (kg/m²)	Total n	Colonized n	(%)	Crude OR	Crude OR*	OR*(95% CI)
Women (n=2 162)						
<22.5	442	91	(20.6)	Ref.	Ref.	Ref.
22.5-<25.0	470	113	(24.0)	1.22 (0.89-1.67)	1.22 (0.87-1.70)	1.20 (0.85-1.68)
25.0-<27.5	462	102	(22.1)	1.09 (0.79-1.50)	1.24 (0.88-1.73)	1.23 (0.87-1.73)
27.5-<30.0	348	76	(21.8)	1.08 (0.76-1.52)	1.11 (0.77-1.61)	1.10 (0.75-1.60)
30.0-<32.5	223	53	(23.8)	1.20 (0.82-1.77)	1.38 (0.92-2.09)	1.30 (0.85-1.98)
≥32.5	224	63	(28.1)	1.51 (1.04-2.19)	1.82 (1.22-2.72)	1.67 (1.11-2.52)
Ptrend				0.11	0.01	0.04
Men (n=1 709)						
<22.5	132	46	(34.9)	Ref.	Ref.	Ref.
22.5-<25.0	334	118	(35.3)	1.02 (0.67-1.56)	0.93 (0.60-1.44)	0.86 (0.551.34)
25.0-<27.5	479	167	(34.9)	1.00 (0.67-1.50)	0.96 (0.63-1.45)	0.92 (0.61-1.41)
27.5-<30.0	410	153	(37.3)	1.11 (0.74-1.67)	1.03 (0.67-1.56)	0.98 (0.64-1.51)
30.0-<32.5	214	76	(35.5)	1.03 (0.65-1.62)	0.98 (0.61-1.56)	0.96 (0.60-1.54)
≥32.5	140	55	(39.3)	1.21 (0.74-1.98)	1.10 (0.66-1.82)	1.09 (0.65-1.83)
Ptrend				0.49	0.54	0.45

Diskusjon/kommentarer

Study design: Cross-sectional study
Is the topic question of the study formulated clearly? **Yes.**
Is a prevalence study a suitable method for answering the topic question? **Yes**.
Is the population from which the sample is taken clearly defined? **Yes.**
Was the sample included in the study in a satisfactory way? **Yes.**
Has it been explained whether the respondents differ from those who have not responded? **No, but all participants were recruited from a population-based study**.
Is the response rate high enough? **No, the response rate was 65.7%.**
Does the study use measurement methods that are reliable (valid) for what you want to measure? **Yes**.
Is the data collection standardized? **Yes**.
Is the data analysis standardized? **Yes**.
What is the result of this study? **Young and premenopausal women with higher BMI and WC have increased odds of *S.aureus* nasal colonization independent of pre-diabetes and diabetes.**
Can the results be due to chance? **No**.
Can the results be transferred to practice? **Yes**.
Does the results of this study coincide with the results of other available studies? **Yes**.

Strengths:
- Large study population (n=12 984)
- Confounding factors have been taken into account
- Significant results

Weaknesses:
- The cross-sectional study design is not capable of establishing or refuting a causal relationship between obesity and *S.aureus* nasal colonization
- Although important risk factors for nasal colonization were adjusted for, uncontrolled or residual confounding might have influenced the results.

Referanse: Esposito S, Terranova L, Macchini F, Bianchini S, Biffi G, Viganò M, et al. Staphylococcus aureus colonization and risk of surgical site infection in children undergoing clean elective surgery. Medicine (Baltimore). 2018;97(27).

Design: Cohort study

Dokumentasjonsnivå: IIb

GRADE: ⊕⊕

Formål

The main aim of this study was to evaluate whether children carrying *S. Aureus* admitted to the hospital for clean elective surgery have an increased risk of postoperative surgical infections.

Konklusjon

Children undergoing clean elective surgery do not need to be screened for *S. aureus* colonization because, although positive, they have no increased risk of surgical site infection.

Land

Italy

År data innsamling

June 2016 – December 2016

Materiale og metode

Recruitment:
Infants and children scheduled for clean elective surgery procedures in the Unit of Pediatric Surgery, Fondazione IRCCS Ca' Granada Ospedale Maggiore Policlinico, Milan, Italy were enrolled.

Exclusion criteria:
Children with a known, chronic underlying disease and those who had been treated with antibiotics in the previous three weeks were excluded.

Data:
At enrollment, a questionnaire was administered to collect demographic data and medical, family and social history. Carriage of *S. aureus* was evaluated on the day of the intervention and 5 days after it. Both anterior nares and pharyngeal swabs were collected. The swabbing was performed by a group of specifically trained pediatric residents supervised by a pediatrician. *S. aureus* was identified using the RIDAGENE MRSA system,

Statistical methods:
The prevalence of positive cultures was compared between subjects with or without surgical site infection using Fischer's exact test. P<.05 was considered statistically significant.

Resultater

A total of 393 children (77.1% males; mean age ± standard deviation, 7.6 ± 4.5 years) were enrolled. At admission, 138 children were screened positive for *S. aureus*. Among these, 42 (33.3%), 35 (27.8%) and 49 (38.9%) children were positive only for the nasal swab, only for the pharyngeal swab, and for both swabs, respectively (12 subjects had missing values in nasal or pharyngeal swab results). MRSA was identified in 40 (29.0% of *S. aureus* positive subjects) cases: 28 (77.8%) in the nose, 4 (11.1% in the pharynx, and 4 (11.1%) in both sites. The carriage rates of *S. aureus* and MRSA varied considerably with age, and in children < 2 years old, the rate was significantly lower than in any other age group (P<.05).

Surgical site infection was demonstrated in 4 out of 109 (3.7%) children who were initially colonized by *S. aureus* and in 5 out of 201 (2.5%) children with a negative screening, without any statistically significant difference between groups (P=.72).

Characteristic	At admission (n=393)		At day 5 (n=298)
Age, years	n (%)		n (%)
<2	51 (13.1)		42 (14.1)
2-4	70 (18.0)		52 (17.5)
5-9	158 (40.5)		114 (38.4)
≥10	111 (28.5)		89 (30.0)
Mean age + SD	7.6 + 4.5		7.6 + 4.6
Sex			
Male	303 (77.1)		225 (75.5)
Female	90 (22.9)		73 (24.5)
***S. aureus* carriage**		Site infection after surgery (n=9)*	
Negative	255 (64.9)	5/201 (25)	180 (60.4)
Positive	138 (35.1)	4/109 (3.7)	118 (39.6)
Nasal carriage only*	42 (11.0)		36 (12.3)
Pharyngeal carriage only*	35 (9.2)		29 (9.9)
Both*	49 (12.9)		47 (16.1)
MRSA positive only	40 (10.2)	0/32 (0)	44 (14.8)
Nasal carriage only*	28 (7.4)		26 (8.9)
Pharyngeal carriage only*	4 (1.1)		6 (2.1)
Both*	4 (1.1)		9 (3.1)

*The sum and percentage do not add up to the total because of 12 missing values in nasal or pharyngeal swab results at enrollment, and of 6 missing values at day 5.
†Follow-up information on surgery site infection was available in 310 out of 393 subjects (78.9%)

Diskusjon/kommentarer

Study design: Cohort study
Is the purpose of the study clearly defined? **Yes.**
Were the subjects recruited to the cohort in a satisfactory way? **Yes.**
Was exposure measured precisely? **Yes.**
Was outcome measured precisely? **Yes.**
Have the authors identified all important confounding factors? **No, no confounding factors are mentioned – one could be type of procedure for instance.**
Have the authors taken into account known, possible confounding factors in design and/or analysis? **No.**
Were a sufficient amount of the subjects followed up? **Yes (78.5%).**
Was the follow-up of the subjects done after a sufficient amount of time? **Yes.**
What was the results of this study? **No statistical significant difference in regards to surgical site infections between those colonized with *S. aureus* and those not colonized.**
How precise are the results and how precise is the risk estimate? **There was no difference between the groups (P=.72).**
Do you believe in the results? **Not completely, because of the small sample size and because the authors do not refer to other studies that support their results. It is not completely clear what the statistical analysis consists of.**
Can the results be transferred to practice? **Yes.**
Do the results of this study coincide with results from other studies? **No, at least the authors do not refer to any such studies.**

Strengths:
- The data was collected in a satisfactory way

Weaknesses:
- Small population (n=393)
- Have not accounted for confounding factors
- Statistical analysis not thoroughly explained
- Shows no support from other studies

Referanse: Williamson DA, Ritchie S, Keren B, Harrington M, Thomas MG, Upton A, et al. Persistence, Discordance and Diversity of Staphylococcus aureus Nasal and Oropharyngeal Colonization in School-aged Children. The Pediatric Infectious Disease Journal. 2016;35(7):744-8.	**Design:** Cross-sectional study
	Dokumentasjonsnivå: IIb
	GRADE: ☺

Formål	Materiale og metode	Resultater	Diskusjon/kommentarer
The aim of this study is to assess the prevalence, persistence and molecular epidemiology of *S. aureus* colonization in the nares and oropharynx of Maori and Pacific children, a population with strikingly high rates of *S. aureus* infection. **Konklusjon** Oropharyngeal *S. aureus* colonization represents a significant reservoir of *S. aureus* and it is possible that the oropharynx may represent a protected anatomical niche, enabling persistent colonization with the same *S. aureus* strain. **Land** New Zealand **År data innsamling** October - November 2013	**Recruitment:** For a 1-month period, between October 14, 2013 and November 15, 2013, we performed a cross-sectional study of children (aged 5-13 years) attending 5 schools in central Auckland. Swabs were taken from the nares and oropharynx. Sampling was repeated from the same schools in October 2014. **Inclusion criteria:** Schools were selected for inclusion on the basis of their high proportion of Maori and Pacific students, and geographic location in low socioeconomic neighborhoods. **Data:** The following demographic information was obtained about each child: age, gender, ethnicity and socioeconomic status. Rayon tipped swabs were taken from the anterior nares and oropharynx, and transported in Amies gel transport agar. Specimens were transported to LabTests community pathology laboratory and plated onto blood agar within 24 hours of collection. Identification of *S. aureus* isolates was performed using a MALDI-TOF MS Biotyper. All *S. aureus* isolates underwent antimicrobial susceptibility testing and *spa* typing. **Statistical methods:** Categorical variables were compared using the $[chi]^2$ or Fischer Exact Test as appropriate. Nonparametric data were compared using the Mann-Whitney *U* test.	Of the 893 children sampled in 2013, 815/893 (91%) were either Maori or Pacific, and 821/893 (92%) resided in areas of high socioeconomic deprivation. A total of 506/893 (56.7%) were colonized with *S. aureus* in the anterior nares, oropharynx or at both sites. The median age of colonized children was significantly higher than that of non-colonized children (9.2 years vs. 8.4 years; $P < 0.01$), although the prevalence of colonization did not differ significantly by ethnicity or NZDep score. Overall, the prevalence of oropharyngeal colonization was significantly higher than the prevalence of nasal colonization (41.1% vs. 31.5%; $P < 0.001$). Interestingly, of the 367 children with oropharyngeal colonization, 225/367 (61.3%) did not have nasal colonization, and were colonized exclusively in the oropharynx. Therefore, the addition of oropharyngeal swabs increased the detection of *S. aureus* colonization by 38.7%. There were no significant associations between the prevalence of colonization at each anatomical site and age, ethnicity or NZDep score (sosioeconomic value). Among the 680 isolates recovered in 2013, 671 were available for *spa* typing. A total of 120 *spa* types were identified. The most common *spa* type among MRSA was t002, and the most common *spa* type among MSSA was t127. Interestingly, of the 142 children who has concurrent nasal and oropharyngeal colonization in 2013, 57 children (40.1%) has disconcordant isolates on the basis of *spa* typing. A total of 911 children were sampled in 2014, although only 683 of these children (76.1%) were sampled in both 2013 and 2014. Of these, 278/683 children (40.7%) were colonized in both 2013 and 2014. Of the children who were sampled in both years, children with exclusive oropharyngeal colonization were significantly more likely to remain colonized after 1 year than children with exclusive nasal colonization (42.5% vs. 26.5%; $P < 0.01$). In addition, children with exclusive oropharyngeal colonization were significantly more likely to be colonized with the same *S. aureus spa* type after 1 year than children with exclusive nasal colonization (67.6% vs. 37.0%; $P = 0.01$).	**Study design**: Cross-sectional study Is the topic question of the study clearly formulated? **Yes**. Is a prevalence study a suitable method for answering the topic question? **Yes**. Is the population that the sample is taken from clearly defined? **Yes.** Was the sample included in the study in a satisfactory way? **Yes**. Has it been explained whether the respondents differ from those who have not responded? **No**. Is the response rate high enough? **It is not specified.** Does the study use measurement methods that are reliable (valid) for what you want to measure? **Not specified.** Is the data collection standardized? **Yes.** Is the data analysis standardized? **Yes.** What is the result of this study? **Colonization prevalence was significantly higher in the oropharynx than the nares.** Can the results be due to chance? **No.** Can the results be transferred to practice? **Yes.** Does the results of this study coincide with the results of other available studies? **Yes.** **Strengths**: - The results is in keeping with other studies - Significant results **Weaknesses**: - The cross-sectional study design - Lack of information about other risk factors - 1/3 of children sampled in 2013 did not have repeat sampling in 2014 - The study population was predominantly (91% Maori or Pacific children in an area of socioeconomic deprivation