

# Snus and Alcohol: Mutually Rewarding Effects in the Brain? A Matched Controlled Population Study

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## ABSTRACT

**BACKGROUND:** The use of moist smokeless tobacco (snus) is increasing in the U.S. and other Western countries, and especially among young people. Snus is associated with several health problems, but the relationship between use of snus and alcohol is scarcely explored. Neuro-cognitive and psychological research suggest an association due to possible mutually rewarding effects in the limbic brain. We investigated this issue in a matched controlled population study.

**METHODS:** Matched control group design where drinking habits and alcohol consumption in a group of users of snus ( $n = 1043$ , mean age = 35.20;  $n$  men = 749,  $n$  women = 294) were compared to a control group of non-users matched on age and gender ( $n = 1043$ , mean age = 35.65;  $n$ men = 749,  $n$ women = 294). In addition, we registered background variables such as level of education, income, self-perceived general, dental health, mental health, current depressive symptoms, and BMI. In estimation of alcohol consumption, the background variables were used as covariates in factorial analyses of variance (ANCOVA).

**RESULTS:** Users of snus had lower level of education, lower income, poorer general, dental, and mental health status than non-users, but there were no differences in BMI. Differences in mental health status were related to drinking habits. Users of snus had a higher frequency of drinking, higher frequency of intoxication, and showed more excess drinking. Controlled for background variables users of snus had a 25.2% higher estimated yearly consumption of alcohol in terms of standard units of alcohol on the weekdays, 26.4% higher on weekends and a 60.2% higher yearly excess consumption.

**CONCLUSION:** Users of snus had an elevated alcohol consumption and another drinking style than non-users. The findings are discussed according to neuro-cognitive and psychopharmacological mechanisms, reward learning and conditioning. The results have implications for prevention, treatment and rehabilitation of alcohol and nicotine dependence.

**KEYWORDS:** Snus, smoking, alcohol, addiction, reward

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## Introduction

Moist smokeless tobacco, snus (sometimes denoted Swedish snus) is a psychoactive substance containing nicotine with rewarding and cognitive effects mainly caused by nicotine acting on the nicotinic ACh receptors (nAChRS) in the nervous system and other internal organs in the body with ACh receptors.<sup>1,2</sup> Snus also contains several other constituents including water, salt, humectants, tobacco-specific nitrosamines etc. Nicotine causes increased psychological reward and probably withdrawal relief<sup>3</sup> and is strongly addictive.<sup>4</sup> Physical tolerance and dependency develops quickly.<sup>5</sup> In Scandinavia, snus is taken orally in small portions (pads). The daily dosage for men and women in the age 16 to 74 is typically 10 portions, yielding a total exposition in the mouth of approximately 63 to 80 mg nicotine,<sup>6</sup> that is, ca. 3650 portions per year for 1 person. The pads are taken out after some time and become waste, which also could create an environmental problem. More than 100 million boxes containing over 2 billion portions were consumed in Norway last year.<sup>7</sup> The use of snus seems to increase in Western and Nordic countries, whereas tobacco smoking shows a decreasing trend.<sup>6,8,9</sup>

Snus is prohibited in EU member states, except Sweden, but not in the US and Norway. Use of snus will probably increase also in the US in the coming years due to increased availability, more smokeless products and marketing.<sup>10,11</sup>

In Norway snus use has been increasing since the late 1990's and especially among young people. There is male preponderance and today 20% of adult men and 5% of women are daily users of snus, whereas in the age group 16 to 24, 25% of the men and 15% of the women use snus daily.<sup>6</sup> The increase among young adults is not surprising since snus use is linked to norm-challenging behaviour, risk-related life-style and team sports,<sup>12,13</sup> clearly showing the impact of cultural factors. Use of snus is also associated with sociodemographic factors such as lower income and lower level of education.<sup>14</sup> However, twin-studies suggest that snus initiation is also influenced by genetic factors.<sup>15</sup>

Snus seems to have a positive effect on quitting smoking,<sup>16</sup> and probably a harm reduction effect on tobacco-related diseases.<sup>17</sup> On the other hand, mental health problems are linked to snus, and especially among young people,<sup>18</sup> as well as increased drinking.<sup>19</sup> Several other health problems are also



reported. A recent review of the research literature describes cardiovascular, malignant, dental, gastro-intestinal, diabetic, metabolic, mental disorders, and pregnancy outcomes.<sup>6</sup> Alcohol habits of users of snus were not discussed in that review, which was unexpected since a large longitudinal Swedish community study (10 years follow-up) on a middle aged cohort ( $n = 21\,037$ ) found that snus users had an increased risk for development of alcohol dependence.<sup>20</sup> These results strongly suggest an elevated alcohol consumption among snus users. Moreover, many users of snus are former and dual users of tobacco,<sup>21</sup> which also is linked to increased drinking, a relationship that has been known for years. For instance, general population studies have shown that tobacco smokers drink almost twice as much as non-smokers,<sup>22</sup> findings also corroborated from other research areas such as clustered health risk habits,<sup>23-25</sup> lifestyle choice<sup>26</sup> and health behaviour.<sup>27</sup>

The widespread combined use of nicotine and alcohol suggests enhanced reward learning, since brain areas affected by alcohol and nicotine such as nucleus accumbens, striatum and prefrontal cortex and involving dopamine systems<sup>28-30</sup> also are involved in reward learning.<sup>31</sup> Nicotine and alcohol seem to increase dopamine production in targeted brain areas.<sup>32</sup> Furthermore, psychopharmacological evidence proposes that nicotine reduces the intoxicative and sedative effects of alcohol, which, again, might potentiate mutual rewarding effects.<sup>33,34</sup>

However, the combined use of nicotine and alcohol in the general population might be a more complex issue than effects of neuro-cognitive and psychopharmacological mechanisms. The syndrome model of addiction suggested by Shaffer et al<sup>35</sup> could be a useful point of departure to understand better this addictive behaviour. This theoretical approach describes three common superordinate categories: distal antecedents (eg, genetic and neurobiological risk, psychosocial risk factors), pre-morbid factors (eg, proximal antecedents such as psychosocial events) and shared manifestations, but different expressions for various types of addictions such as smoking, drinking, gambling, and drug use. This syndrome model also includes neurobiological factors such as the dopaminergic reward systems, neuro-cognitive and memory systems, and mental health issues.

The psychosocial and neurobiological antecedents seem to be especially relevant for understanding the use of snus and alcohol in the general population. For instance, lower education among snus users could be regarded as a distal psychosocial antecedent, that is, creating risk factors in terms of social norms, sociocultural closeness, social modelling and positive attitudes toward use snus, comparable to what has been seen in smoking.<sup>36,37</sup> Likewise, meso-limbic dopaminergic structures could be seen as distal neurobiological antecedents since these systems convey the neuro-cognitive interaction between nicotine and alcohol in the limbic brain, which could result in a dual use of alcohol and snus due to mutual rewarding effects.<sup>33</sup> Taken together, the presented evidence suggests that increased alcohol consumption is to be expected among snus users and their drinking habits specifically should be subject to further empirical research.

The aim of the current study was to investigate alcohol consumption and drinking habits in a sample of users of snus compared to a sample of non-users matched on age and gender. We examined frequency of drinking in the weekdays (Monday-Thursday), in the weekends (Friday-Sunday), frequency of intoxication and frequency of excess drinking (more than 6 standard units of alcohol per drinking occasion). In addition, we estimated the yearly alcohol consumption in terms of units of alcohol for weekdays, for weekends, and the yearly excess consumption controlled for health-related and sociodemographic background variables.

## Methods

### *Participants and procedure*

Data was extracted from the Norwegian Survey on Living Conditions – Health, Care, Social Relations 2015 ( $n = 8164$ ) administered by the Norwegian Centre for Research Data (NSD). The survey was conducted by computer assisted telephone interviews (CATI) and comprised a wide range of topics, including living conditions, labour, health, education, economy, and is representative of the almost Caucasian adult Norwegian population.<sup>38</sup> That survey also included one question about how often they were using snus. The answers were registered on a Likert scale: 1 = Daily, 2 = Now and then, 3 = Never, 4 = Will not answer, 5 = Do not know. Totally, 741 reported that they were using snus daily (9.1%), 302 (3.7%) now and then, 26 (0.3%) would not answer the question and 7 (0.1%) did not know. To get a better distribution of age and gender, we included both the daily users and the now-and-then users in the snus sample, total  $n = 1043$ ;  $n$  men = 749 (71.8%),  $n$  women = 294 (28.2%);  $M_{\text{age}} = 35.20$  years,  $SD = 14.03$ .

The majority of the total sample,  $n = 7088$  (86.8%), never used snus;  $n$  men = 3345 (47.2%),  $n$  women = 3743 (52.8%). In addition, 26 would not answer the question (0.3%) and 7 did not know (0.1%).  $M_{\text{age}}$  for the total sample was 49.5 years,  $SD = 18.6$ . Due to the differences in age and gender between the users and non-users of snus, we randomly selected (the random sampling procedure from the Statistical Package for the Social Sciences) from that sample ( $n = 7088$ ) a control group of non-users matched with the snus group on age and gender, total  $n = 1043$ ,  $n$  men = 749 (71.8%),  $n = 294$  (28.2%),  $M_{\text{age}} = 35.65$ ,  $SD = 11.53$ .

### *Measures*

*Alcohol and smoking habits.* Firstly, the participants were asked if they had an alcoholic drink of any kind or smoked the last 12 months. The answers were registered on a dichotomic scale: 1 = Yes, 2 = No.

Secondly, they were asked about the frequency of drinking alcohol the last 12 months. The answers were registered on a 4-point Likert scale: 1 = Daily, 2 = Weekly, 3 = Several times a month, 4 = Less than monthly.

The third question assessed the frequency of drinking in the weekdays Monday to Thursday. The answers were registered

on a 5-point Likert scale: 1 = All 4 days, 2 = On 3 of 4 days, 3 = 2 of 4 days, 4 = 1 of 4 days, 5 = None of the days.

Fourthly, they were asked about the number of standard units of alcohol consumed on weekdays (volume and category explained more detailed to the respondents): 1 = 16 or more units, 2 = 10-15 units, 3 = 6-9 units, 4 = 4-5 units, 5 = 3 units, 6 = 2 units, 7 = 1 unit, 8 = 0 units. This scale was transformed to another interval scale to give a more direct estimate of units of alcohol using the arithmetic mean values of the intervals as estimates. For instance, the interval 2 = 10-15 units was transformed into 12.5, resulting in the following final scale: 1 = 16 units, 2 = 12.5 units, 3 = 7.5 units, 4 = 4.5 units, 5 = 3 units, 6 = 2 units, 7 = 1 unit, 8 = 0 units. One standard unit is comparable to 1 small bottle of beer (0.33 l), 1 glass of wine, or 1 drink of liquor and corresponds to 1.5 cl or 12.5 g pure alcohol.<sup>39</sup> We estimated the amount of weekdays consumption according to this QF-formula (Quantity x Frequency): Number of units typically consumed in the weekdays x frequency of drinking: 1 = All 4 days, 2 = 3 of the 4 days, 3 = 2 of the 4 days, 4 = 1 of 4 days, 5 = None of the days. Yearly weekday consumption was calculated as weekday consumption x 52 (number of weeks).

The fifth question registered the frequency of drinking in weekends (Friday-Sunday): 1 = All 3 days, 2 = On 2 of 3 days, 3 = 1 of 3 days, 4 = None of the days.

The sixth question assessed the amount of alcohol typically consumed on a weekend day in terms of standard units of alcohol: 1 = 16 or more units, 2 = 10-15 units, 3 = 6-9 units, 4 = 4-5 units, 5 = 3 units, 6 = 2 units, 7 = 1 unit, 8 = 0 units. This scale was also transformed to the same interval scale as used in question 4: For instance, the interval 2 = 10-15 units was transformed into 12.5, resulting in the following final scale: 1 = 16 units, 2 = 12.5 units, 3 = 7.5 units, 4 = 4.5 units, 5 = 3 units, 6 = 2 units, 7 = 1 unit, 8 = 0 units. From the answers we estimated the amount of alcohol consumption in the weekends in terms of standard units of alcohol according to the following QF measure: Number of units typically consumed on a weekend drinking occasion x frequency of weekend drinking: 1 = All 3 days, 2 = On 2 of 3 days, 3 = 1 of 3 days, 4 = None of the days. The yearly weekend alcohol consumption was calculated as weekend consumption x 52.

The seventh question registered how often they had been drinking so much that they got a clear sense of intoxication: 1 = Daily, 2 = Weekly, 3 = Monthly – several times, 4 = Less than monthly, 5 = Never.

The eighth questions registered excess alcohol consumption by asking how often they had been drinking 6 standard units of alcohol or more: 1 = Daily, 2 = Weekly, 3 = Several times a month, 4 = Monthly or less, 5 = Never. From the answers we estimated the yearly amount of excess consumption according to this QF-formula: 6 units x frequency of drinking: 1 = Daily (almost every day – 340 days), 2 = Weekly (2-3 times a week – 130 days), 3 = Several times a month (approximately once a week – 52 days), 4 = Monthly or less (12 days) and 5 = Never (0 days).<sup>22</sup> For example, drinking 6 units daily will result in a

yearly estimated excess consumption of 2040 units of alcohol (6 x 340 days).

When we calculated the yearly consumption in the weekdays, weekends and excess consumption we first included both those who reported drinking and no drinking (0 units), that is, the total samples in both groups. Secondly, we included only those who reported drinking (more than 1 unit ie, selected samples). Thus, respondents who did not drink were excluded from the second analyses. In the Table 5 we present the results for both analyses.

*Body mass index and self-perceived general and dental health status.* Body Mass Index (BMI) is a frequently used screening method for weight classification and is related to a number of disease outcomes, including depression.<sup>40</sup> BMI was calculated as self-reported weight in kilograms divided by the square of height in metres (kg/m<sup>2</sup>).

Self-perceived health is a valid and widely used indicator of general health status in many research areas.<sup>41-44</sup> In the current study self-perceived General health and Dental health status were assessed with the questions 'How is your health in general. Is it. . .' and 'How is your dental health. Is it. . .' The answers were registered on a 5-point Likert scale 1 = Very good, to 5 = Very bad.<sup>38,45</sup>

*General mental health and depressive symptoms.* The Symptom Check List-10 (SCL-10) was used for assessment of general mental health (last 2 weeks). This is a shorter form of SCL-25, and has been shown to be valid, reliable and as a screening instrument almost as good as the SCL-25 version. The answers were registered on a 4-point Likert scale: 1 = Not at all, 4 = Very much. Clinical cut-off is set at a score above 1.75.<sup>46</sup>

Current depressive symptoms (last 2 weeks) was registered according to the adapted European version (PHQ-8) of the depression scale taken from the Patient Health Questionnaire (PHQ-9) by Spitzer et al.<sup>47</sup> The 8 questions were answered on a 4-point Likert scale: 1 = Not at all to 4 = Nearly every day and calculated into a clinical index: 1 = None, 2 = Mild, 3 = Moderate, 4 = Moderately severe, 5 = Severe.<sup>45</sup>

*Educational status and monthly income.* Level of education was registered according to the Norwegian Standard Classification of Education<sup>48</sup> using the following scale: 0 = No education; 1 = Elementary school, 1-7 years; 2 = Secondary school, 8-10 years; 3 = College, 11-12 years; 4 = College + 1 year; 5 = College and supplementary education; 6 = University, high school, 14-17 years; 7 = University, high school, 18-19 years; 8 = PhD.

Information about income in NOK (Norwegian krone; 1 USD = p. t. approximately 8.5 NOK) was retrieved from the Norwegian Tax Administration (2014) and calculated as net monthly income (HHINCOME) according to the standard set by the European Union.<sup>49</sup> The monthly income was registered on an interval scale: 1 = NOK 0-19999, 2 = NOK 20 000-39 999, 3 = NOK 40 000-59 999 etc. This scale was recoded into

**Table 1.** Sociodemographic and health-related background variables for users and non-users of snus.

	USERS OF SNUS		NON-USERS		P VALUE
	MEAN	SD	MEAN	SD	
Self-perceived general health	1.90	0.80	1.79	0.80	.002
Current depression	1.39	0.76	1.24	0.56	.000
Self-perceived dental health	2.15	0.87	1.98	0.85	.000
SCL-10	1.29	0.53	1.22	0.47	.002
BMI	25.29	3.99	25.55	6.95	.302
Education	4.81	1.57	5.06	1.60	.001
Monthly income	48653.85	28694.93	52005.79	27910.29	.007

Self-perceived general health: 1=very good, 5=very bad; current depression: 1=none, 2=mild, 3=moderate, 4=moderately severe, 5=severe; dental health: 1=very good, 5=very bad; education: 0=no education; 1=elementary school, 1 to 7 years; 2=secondary school, 8 to 10 years; 3=college, 11 to 12 years; 4=college + 1 year; 5=college and supplementary education; 6=university, high school, 14 to 17 years; 7=university, high school, 18 to 19 years; 8=PhD; monthly income=mean values in NOK for the households; n users of snus=983 to 1043, n non-users=913 to 1043.

another interval scale by using the arithmetic mean values of each interval to calculate the net monthly income. For instance, 1=0-19999 was recoded as 1=10000, 2=20000-39999 was recoded into 2=30000, 3=40000-59999 was recoded into 3=50000 etc. In this way we could directly show monthly income in NOK.

### Data analyses

We used the SPSS Version 26 to analyse the data and applied Pearson Chi-squares to test differences between the groups for the variables assessing drinking habits in dichotomic scales (eg, drinking alcohol and smoking last 12 months (1=Yes, 2=No) and Likert scales with few intervals (eg, frequency of drinking last 12 months, during the week, during weekends, frequency of feeling intoxicated, excess drinking). Possible differences in socioeconomic and health-related background variables (self-perceived general and dental health status, current depression, SCL-10, educational status, and net monthly income) were tested using factorial analysis of variance (ANOVA) with use of snus as the independent variable (1=Yes, 2=No). Differences in alcohol consumption in terms of estimated standard units of alcohol were tested using factorial analyses of variance controlled for socioeconomic and health-related background variables: smoking, self-evaluated general and dental health status, current depression, general mental health (SCL-10), level of education and net monthly income, using these variables as covariates in a factorial model (ANCOVA). Dependent variables were estimated yearly consumption during weekdays, weekends and yearly excess consumption for the total samples and selected subsamples and the independent variable (fixed factor) was use of snus (1=Yes, 2=No).

### Ethics

All participants consented according to Norwegian law and recommendations. The data applied in the analysis in this

publication are based on 'Health, Care and Social Relations, Survey on Living Conditions, 2015, Regions'. The survey was financed by The Norwegian Directorate of Health. The data are provided by Statistics Norway, and prepared and made available by NSD – Norwegian Centre for Research Data. Neither Statistics Norway, The Norwegian Directorate of Health nor NSD are responsible for the analysis/interpretation of the data presented here.

### Results

Table 1 shows the sociodemographic and health-related background variables for users and non-users of snus.

Compared to non-users the users of snus reported significantly worse self-perceived general health,  $F(1,2083)=9.85$ ,  $P=.002$ ,  $\eta^2=.005$ , Observed Power=.880, self-evaluated dental health  $F(1,2079)=19.35$ ,  $P=.000$ ,  $\eta^2=.009$ , Observed Power=.993, and they had a higher current depression score,  $F(1,2070)=24.71$ ,  $P=.000$ ,  $\eta^2=.012$ , Observed Power=.999. The snus group also had slightly poorer general mental health status (SCL-10),  $F(1,2084)=9.43$ ,  $P=.002$ ,  $\eta^2=.004$ , Observed Power=.866, lower level of education  $F(1,1894)=11.89$ ,  $P=.001$ ,  $\eta^2=.006$ , Observed Power=.931, and lower net monthly income  $F(1,2075)=28$ ,  $P=.007$ ,  $\eta^2=.003$ , Observed Power=.770. There were no significant differences between the groups in BMI,  $F(1,2060)=1.07$ ,  $P=.302$ , but the mean values of both groups were within the overweight category (BMI 25-29.9<sup>50</sup>). The differences in mental health status (SCL-10) between the groups were no longer significant when we controlled for yearly alcohol consumption and drinking habits in ANCOVA (see Table 5):  $F(1,1319)=3.254$ ,  $P=.071$ . However, there were still significant differences in self-perceived general health  $F(1,1312)=5.238$ ,  $P=.022$ ,  $\eta^2=.004$ , Observed Power=.628, dental health (although marginal):  $F(1,1311)=3.994$ ,  $P=.046$ ,  $\eta^2=.003$ , Observed Power=.515, and current depression:  $F(1,1305)=14.768$ ,  $P=.000$ ,  $\eta^2=.011$ , Observed Power=.970.

**Table 2.** Frequency of smoking and drinking alcohol the last 12 months for users and non-users of snus.

	USERS OF SNUS		NON-USERS	
	N	%	N	%
Drinking alcohol	978	93.8	862	88.2
Not drinking	65	6.2	181	17.4
Smoking	261	25.0	207	19.8
Not smoking	782	75.0	836	80.2
Frequency of drinking				
Daily	27	2.8	6	0.7
Weekly	350	35.8	254	29.6
Monthly – several times	336	34.4	570	31.1
Less than monthly	264	27.0	628	34.2

Smoking: Yes/No; drinking alcohol: Yes/No; drinking or smoking last 12 months:  $P = .000$ ; frequency of drinking:  $P = .000$ ; total n users of snus = 1043; total n non-users = 1043.

*Smoking and drinking*

Table 2 shows drinking and smoking for users and non-users of snus the last 12 months (yes/no).

Most of the participants in both groups had been drinking alcohol the last year, but significantly more users (93.8%) than non-users (82.5%),  $\chi^2(1) = 62.01, P = .000$ ; Cramer's  $V = .172$ . Similarly, 25% of the snus users had been smoking last year, compared to 19.8% for non-users  $\chi^2(1) = 8.03, P = .005$ ; Cramer's  $V = .062$ . Users of snus also drank alcohol more frequently than non-users;  $\chi^2(3) = 26.91, P = .000$ ; Cramer's  $V = .121$ . 38.6% of the snus users reported drinking on a daily-weekly basis, compared to 30.3% of the not users, whilst 27% and 34.2% drank less than monthly among users and non-users, respectively.

Table 3 shows the results for drinking habits during the weekdays Monday to Thursday and weekend days Friday to Sunday for users and non-users of snus.

There were no differences in frequency of drinking during the weekdays (Monday-Thursday) between the 2 groups,  $\chi^2(4) = 5.26, P = .262$ , Cramer's  $V = .054$ . However, during the weekend (Friday-Sunday) users of snus tended to drink more frequently than non-users,  $\chi^2(3) = 18.83, P = .000$ , Cramer's  $V = .102$ . For example, 66% were drinking on one of the days, compared to 60.2% of non-users, and only 8% of snus users were not drinking alcohol during weekends, compared to 14.2% of non-users.

*Excess drinking*

Table 4 describes the differences between the groups in drinking style, that is, drinking so much that they felt intoxicated and frequency of excess drinking, that is, 6 units of alcohol or more on a drinking occasion.

**Table 3.** Frequency of drinking alcohol during the weekdays Monday to Thursday and weekend days Friday-Sunday for users and non-users of snus.

	USERS OF SNUS		NON-USERS	
	N	%	N	%
Monday-Thursday				
All 4 days	4	0.4	6	0.2
3 of 4 days	8	0.8	8	0.9
2 of 4 days	39	4.1	24	2.8
1 of 4 days	145	15.3	110	12.9
None of the days	754	79.4	706	82.7
Friday-Sunday				
All 3 days	20	2.1	23	2.7
2 of 3 days	227	23.9	192	22.5
1 of 3 days	627	66.0	517	60.6
None of the days	76	8.0	121	14.2

Monday-Thursday: no significant differences; Friday-Sunday:  $P = .000$ ; total n users of snus = 954 to 1043, total n non-users = 854 to 1043.

**Table 4.** Frequency of consuming an amount of alcohol on a drinking occasion resulting in a feeling of drunkenness and frequency of excess drinking, that is, more than 6 units of alcohol per drinking occasion.

	USERS OF SNUS		NON-USERS	
	N	%	N	%
Felt intoxicated				
Daily	2	0.3	1	0.2
Weekly	38	4.8	10	1.8
Monthly – several times	111	14.1	39	6.9
Less than monthly	559	71.0	434	77.0
Never	77	9.8	80	14.2
More than 6 units				
Daily	3	0.3	2	0.2
Weekly	54	5.6	22	2.6
Monthly – several times	190	19.5	85	9.9
Less than monthly	540	55.6	456	53.1
Never	185	19.0	293	34.1

Felt intoxicated:  $P = .000$ ; more than 6 units:  $P = .000$ ; total n users of snus = 1043, total n non-users = 1043.

Users of snus felt intoxicated significantly more often than non-users,  $\chi^2(4) = 30.10, P = .000$ , Cramer's  $V = .152$ . Totally, 19.2% of the snus users reported being intoxicated on a daily-weekly-monthly basis compared to 8.9% of non-users. 14.2% of

**Table 5.** Estimated yearly alcohol consumption in terms of standard units for weekdays (Monday-Thursday), weekends (Friday-Sunday) and excess drinking (6 units or more) controlled for sociodemographic and health-related background variables (self-perceived general health, dental health, current depression, SCL-10, smoking, level of education, net monthly income). Factorial ANCOVA for the total samples and the selected subsamples of users and non-users of snus.

	USERS OF SNUS			NON-USERS			%	P VALUE
	MEAN	SE	CI 95%	MEAN	SE	CI 95%		
Weekdays total	211.95	14.35	183.80-240.10	169.26	14.78	140.31-198.26	25.2	.039
Weekends total	332.40	9.24	314.27-350.52	262.93	9.93	243.45-282.40	26.4	.000
6 units total	152.98	6.45	139.44-164.73	94.91	7.02	81.15-108.67	60.2	.000
Weekdays selected	1099.85	23.58	1053.46-1146.24	1139.17	27.52	1084.99-1193.34	3.5	.282
Weekends selected	362.27	9.48	343.67-380.87	304.07	10.48	283.52-324.62	19.1	.000
6 units selected	187.27	7.70	172.15-202.38	139.56	9.02	121.51-157.61	34.2	.000

Abbreviations: CI 95%: 95% confidence intervals; SE: standard error; %: percent differences in units of alcohol consumed between the users and non-users of snus; total n users of snus=882 to 1043, total n non-users of snus=765 to 1043; weekdays selected samples: n users of snus=182, n non-users=134; weekend selected samples: n users of snus=808, n non-users=663; 6 units or more selected samples: n users of snus: 741, n non-users=521.

non-users never felt intoxicated compared to 9.8% of snus users. There were also differences in excess drinking. Users of snus consumed 6 units or more frequently than non-users,  $\chi^2(4) = 78.45$ ,  $P = .000$ , Cramer's  $V = .207$ . Totally, 25.4% of users reported excess drinking on a daily-weekly-monthly basis compared to 12.7% of non-users. 19% of the snus group never reported excess drinking, compared to 34.1% among non-users.

#### *Estimated yearly alcohol consumption in weekdays, weekends and total yearly excess consumption*

In Table 5 we present the results of the factorial ANCOVA analyses for the estimated yearly consumption in weekdays (Monday-Thursday), weekends (Friday-Sunday) and the yearly excess consumption (6 units of alcohol or more per drinking occasion) controlled for smoking and sociodemographic and health-related background variables.

Most of the total sample did not drink during weekdays (82.0%), 9.5% did not drink during the weekends, and 22.9% reported no excessive consumption.

Compared to non-users users of snus had 25.2 % higher yearly estimated consumption in the weekdays (42.7 more units),  $F(1,1836) = 4.25$ ,  $P = .039$ , Observed Power = .540; 26.4% higher weekend consumption (69.5 units),  $F(8,1638) = 25.94$ ,  $P = .000$ , Observed Power = .999, and 60.2% higher excess consumption (57.1 units),  $F(8,1671) = 35.60$ ,  $P = .000$ , Observed Power = 1.000. Totally, a significantly higher consumption for all 3 measures when we looked at the total samples. The results for the subsamples (those who did not drink were excluded) confirmed the general picture, except consumption in weekdays (Monday-Thursday) where there was no significant difference between the users of snus and non-users,  $F(1,307) = 1.61$ ,  $P = .282$ . The weekend consumption for the selected samples (Friday-Sunday) was 19.1% higher for the users of snus (58.2 units),  $F(1,1462) = 16.76$ ,

$P = .000$ , Observed Power = .983, and the estimated yearly excess consumption was 34.2% higher (47.7 units),  $F(1,1253) = 15.67$ ,  $P = .000$ , Observed Power = .977.

## Discussion

The current study has investigated alcohol consumption and drinking habits in a sample of users of snus compared to a sample of non-users matched on age and gender. We examined frequency of drinking in the weekdays, in the weekends, frequency of intoxication, and frequency of excess drinking. We also estimated the yearly alcohol consumption in terms of units of alcohol for weekdays, for weekends, and the yearly excess consumption controlled for relevant sociodemographic and health-related background variables.

Most of the findings on socioeconomic and health-related background variables were as expected. Lower level of education and income among users of snus is a common finding in the research literature,<sup>14</sup> evidence suggesting socio-cultural and lifestyle differences between the 2 groups.<sup>13</sup> We also found slightly worse self-perceived general and dental health status and higher current depression scores among users of snus. Since use of snus is associated with several somatic and dental health risks<sup>6,51-53</sup> it is not surprising that their self-perceived general and dental health status is poorer, also after controlling for alcohol consumption.

Users of snus had higher scores on SCL-10 and current depression than non-users, but none of the scores were above clinical cut-off. It is, however, interesting that the differences in SCL-10 disappeared when we controlled for drinking habits, indicating that alcohol consumption accounted for the self-reported reduced mental health. This is not surprising since the association between use of alcohol and mental health disorders is well known from clinical investigations,<sup>54,55</sup> but our findings also show an association at sub-clinical level. An implication of this finding is that alcohol consumption should always be measured

when SCL-10 or comparable screening instruments are used to assess general mental health status in general populations. Drinking habits could influence self-reports of mental health. On the other hand, and somewhat unexpected, differences in current depressive symptoms were not affected by the drinking habits of snus users. However, several studies have shown an association between nicotine and depression, so the finding that users of snus had an elevated depression score could reflect more complex underlying population and genetic factors.<sup>56</sup>

As expected, users of snus showed more dual use of tobacco and alcohol than non-users, they were more often intoxicated, had a higher alcohol consumption and more risky drinking style. Mutual reward learning could be one explanation, as suggested in the model of Shaffer et al<sup>35</sup> emphasizing the role of learning and memory in the hippocampus, emotion regulation in the amygdala and the rewarding role of dopamine-systems interacting with nicotine and alcohol. Since 2004 when the model was presented, there has been a considerable scientific development in psychopharmacology and neuroscience describing these systems, especially in understanding the alcohol-nicotine interaction in the limbic brain. As shown in the thorough review by Adams,<sup>33</sup> alcohol and nicotine have mutual potentiating rewarding effects and, in addition, the intoxication and sedative effects of alcohol seem to be reduced by nicotine. Together, these two mechanisms could cause a powerful reward learning effect that is, the probability of intake of alcohol when using snus increases, or vice versa. Hence, these neuro cognitive and psychopharmacological factors in combination with conditional learning could be essential in maintaining the dual use of snus and alcohol. The underlying neurobiological structures are probably the mesolimbic dopaminergic pathways conveying the cross-reinforcement process (reward) whereas the nicotine acetylcholine receptor (nAChR) in combination with genetic susceptibility factors could induce cross-tolerance.<sup>33</sup> Furthermore, cross-reward and cross-tolerance effects also seem to be influenced by learning and memory. Experimental research indicate a conditioned modulatory effect of drug-associated environmental context in development of cross-tolerance.<sup>57</sup> These findings suggest that situational factors are important. Reward learning is dependent upon activity in the dopaminergic systems, and dopamine agonists enhance reward learning and novelty seeking.<sup>58</sup> Since snus contains nicotine, snus can be regarded as a dopamine agonist. Epidemiological findings lend support to this assumption since snus users have a lowered risk of Parkinson disease,<sup>59</sup> a disorder associated with dopamine dysregulation.<sup>60</sup> Thus, snus could facilitate reward learning which again could lead to increased drinking due to the cross-reward and cross-tolerance effects of nicotine and alcohol.<sup>33</sup>

Snus users are also typically former tobacco smokers and often dual users,<sup>21</sup> as also shown in the current study where 25% of the snus users reported that they had smoked the last 12 months compared to 19.8% among non-users. We would, thereby, expect similar drinking habits among users of snus and

tobacco smokers that is, an elevated alcohol consumption.<sup>22,61,62</sup> Furthermore, it is well documented that nicotine is a very addictive psychoactive substance<sup>63</sup> and development of the full nicotine dependence syndrome (in adolescents) can occur within less than two years of tobacco use onset. Symptoms such as increased tolerance, impaired control and withdrawal reactions are commonly reported.<sup>64</sup> Previous studies have also documented that users of snus have symptoms of nicotine dependence comparable to cigarette smokers, and that dual users report the highest prevalence of withdrawal symptoms.<sup>4</sup> Hence, increased drinking among users of snus in our sample could be related both to positive (reward) and negative reinforcing effects of alcohol (alleviation of withdrawal reactions) in combination with nicotine addiction. This suggestion is supported by recent epidemiological research showing that tobacco use is a preceding correlate of alcohol problems.<sup>65</sup>

Taken together, controlled for background variables related to alcohol consumption the combined effect of cross-reinforcement and cross-tolerance for nicotine and alcohol in combination with learning and conditioning could be underlying common factors explaining a dual use of snus and alcohol. These effects also have implications for treatment and rehabilitation. As shown in the current study, snus users show unhealthy drinking habits (more often felt drunk, more excess drinking) which could place them at risk for development of more severe drinking problems later on in life.<sup>66,67</sup> Doctors and health care workers should be aware of this risk, especially with respect to prevention of alcohol problems. A successful reduction in drinking is probably difficult to obtain if the use of snus or tobacco continues as usual due to the cross-reward and cross-tolerance effects of nicotine and alcohol. It would be hard to reduce the intake of one of the drugs, and not the other; intake of both should be reduced. Similarly, nicotine dependency related to snus or tobacco use could be difficult to treat successfully unless attention also is paid to the users elevated alcohol consumption. As suggested by Adams<sup>33</sup> a combined treatment of tobacco and alcohol dependence could, therefore, be more clinically efficient than focus on the separate drugs.

### Limitations of this study

The sample of snus users were taken from a representative sample of the adult Norwegian population. The sample of snus users is therefore ethnically very homogenous and not biased in terms of selection. We also used a matched control group design, and these two factors make our investigation methodologically robust. However, there are limitations. The participants were white Caucasians, but, to the best of our knowledge, there is no reason to assume that rewarding effects in the limbic system of nicotine and alcohol is linked to ethnicity. We have also rather crude measures of alcohol consumption and more detailed data such as categories of alcohol (e.g., beer, wine, liquor) and amounts consumed in each category would be preferable. Categorical data would allow us to estimate

alcohol consumption more precisely. Assessment of behaviour profiles and mental health status are also quite limited, and it has been shown that personality factors revealing impulsivity and risky behaviour seem to be associated with increased drinking.<sup>68,69</sup> These factors could also be linked to use of snus. Future investigations should, therefore, include a more detailed assessment of mental health, personality factors and behaviour. Finally, although the data were obtained through computer assisted telephone interviews (CATI) and not based on questionnaires completed by the participants, the data were basically self-reported and that is another limitation.

## Conclusion

As expected, there were significant differences between users of snus and non-users in several socioeconomic and health-related background variables (eg, self-perceived general health, dental health, current depression, general mental health, education, and income). The differences in general mental health (SCL-10) were related to drinking habits. More snus users had been smoking and drinking alcohol in the last 12-months than non-users, they had a higher frequency of drinking, higher frequency of intoxication, and higher frequency of excess drinking (6 standard units or more). Controlled for smoking and background variables, users of snus also had a 25.2% higher estimated yearly consumption of alcohol in terms of standard units of alcohol on the weekdays, 26.4% higher on weekends and a 60.2% higher yearly excess consumption. The results also have implications for prevention, treatment and rehabilitation of alcohol and nicotine dependence.

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## Author Contributions

RGW developed the concept for the study and was responsible for the data analyses. VPW contributed to the neuropsychological and clinical analyses. Both authors contributed to the interpretation of the data, edited the final draft of the manuscript, and approved the version to be published.

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