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Original Investigation

Tobacco Use and Uptake of COVID-19 Vaccinations in Finland: A Population-Based Study

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Abstract

Introduction: People who smoke are at higher risk of Coronavirus Disease-2019 (COVID-19) hospitalizations and deaths and might benefit greatly from high COVID-19 vaccination coverage. Studies on tobacco use and COVID-19 vaccine uptake in the general population are lacking.

Aims and Methods: We conducted a cohort study utilizing linked data from 42 935 participants from two national surveys in Finland (FinSote 2018 and 2020). Exposures were smoking and smokeless tobacco (snus) use. The primary outcome was the uptake of two COVID-19 vaccine doses. Secondary outcomes were the uptake of one COVID-19 vaccine dose; three COVID-19 vaccine doses; time between the first and second dose; and time between the second and third dose. We examined the association between tobacco use and COVID-19 vaccine uptake and between-dose spacing in Finland.

Results: People who smoke had a 7% lower risk of receiving two COVID-19 vaccine doses (95% confidence interval [CI] = 0.91; 0.96) and a 14% lower risk of receiving three doses (95% CI = 0.78; 0.94) compared to never smokers. People who smoked occasionally had a lower risk of receiving three vaccine doses. People who currently used snus had a 28% lower uptake of three doses (95% CI = 0.56; 0.93) compared to never users but we did not find evidence of an association for one or two doses. We did not find evidence of an association between tobacco use and spacing between COVID-19 vaccine doses.

Conclusions: People who smoke tobacco products daily, occasionally, and use snus had a lower uptake of COVID-19 vaccines. Our findings support a growing body of literature on lower vaccination uptake among people who use tobacco products.

Implications: People who smoke or use snus might be a crucial target group of public health efforts to increase COVID-19 vaccinations and plan future vaccination campaigns.

Clinical Trials Registration Number: NCT05479383

Background

The Coronavirus Disease-2019 (COVID-19) pandemic has resulted in more than 772 million cases and more than 6.9 million deaths worldwide by December 6, 2023.[1] Rapid viral dissemination in many parts of the world has led to the emergence of several variants of concern, with greater transmissibility and severity.[2,3]

During 2020, many countries resorted to strict public health and social measures as means to curb the pandemic, including large-scale lockdowns, closure of schools and public spaces, traveling restrictions, and facemasks mandates. In 2021, most high-income countries began rolling out COVID-19 vaccinations, with the promise of reducing incident COVID-19 infections and preventing hospitalizations and deaths. Achieving high vaccination coverage is crucial for several reasons: (i) to reduce the number of new COVID-19 cases,[4] (ii) to prevent severe COVID-19 outcomes, such as intensive care hospitalizations and deaths,[5] (iii) to potentially reduce the risk of post-acute COVID-19 symptoms,[6] and (iv) to diminish selective pressures leading to the emergence of new variants of concern.[7]

People who smoke are at higher risk of COVID-19 hospitalizations and deaths[8] and might thus particularly benefit from high vaccination coverage. However, evidence suggests that they may be less likely to be vaccinated as those who smoke are less likely to adhere to preventive measures in general and have lower adherence to other vaccination programs.[9–11] Reports of an inverse association between

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smoking and the risk of COVID-19 infection might have also reduced the perceived risks of being infected.[12] Evidence regarding tobacco use and COVID-19 vaccine hesitancy is mixed. Some studies have shown greater mistrust in COVID-19 vaccine benefits[12–15] and greater vaccine hesitancy and lower vaccine acceptance compared to people who do not smoke,[12,16,17] while other studies have reported no differences by smoking status or lower levels of vaccine hesitancy in smokers compared to those who do not smoke.[18–21] Spacing between vaccine doses is also relevant, as a growing body of literature suggests that people who smoke develop a weaker immune response to COVID-19 vaccines.[22]

Vaccine uptake, however, is a dynamic process influenced not only by trust and risk perception but also by convenience factors such as the reliability of the vaccine supply and the convenience of the vaccination schedule.[23] To our knowledge, three studies have examined vaccination uptake by smoking status.[24,25] Two studies from convenience samples in Singapore and Palestine showed that those who smoke had higher odds of being vaccinated.[24,25] However, a study of Israeli insurance patients reported that people who smoke had lower odds of being vaccinated.[26] These studies, however, are not representative of the general population and the first two relied on self-reported vaccination status, resulting in a higher risk of selection and information bias. To our knowledge, the uptake of COVID-19 vaccines among smokeless tobacco users has not been studied.

Finland developed a national COVID-19 vaccination strategy and the vaccine rollout started on December 27, 2020. Vaccinations started with priority groups (health and social care personnel, those aged 70 and over, and people at high risk of severe COVID-19) and expanded in descending order by age groups.[27] Vaccination rollout proceeded quickly during 2021 and, by June 2021, persons older than 16 years old could receive the first dose. The second dose was recommended after 6–12 weeks from the first dose. The third dose rollout started in the last trimester of 2021. COVID-19 vaccines are provided free of charge and delivered nationwide by each municipality. Finland has administered primarily mRNA vaccines.[27]

We examined the association between tobacco use and COVID-19 vaccine uptake and between-dose spacing in Finland until December 31, 2021. Our study expands current knowledge by examining two forms of tobacco use in Finland—smoking and smokeless tobacco use (snus)—and by analyzing the spacing between vaccine doses. We used data from national population surveys in Finland linked to vaccination registries, which reduces the risk of selection and information bias.

Method

The study protocol has been written in close accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement for cohort studies.[28] The study was registered in ClinicalTrials.gov (registration NCT05479383). The only change after registration was to modify the third secondary outcome from 7 months to 20 weeks, given that the recommended spacing was 6–12 weeks. This was done because data was sparse as too few participants exceeded the 7-month threshold.

Study Design

The study design was a cohort study of national health surveys linked to COVID-19 vaccination data, using a unique personal identification number assigned to all residents in Finland.

Setting and Participants

We used data from cross-sectional population health surveys in Finland, FinSote 2018 and 2020.

Participants in the FinSote 2018 Survey were adults aged 20 years and above derived from the Population Register of Statistics Finland, which comprises all permanent residents in Finland. This sampling frame includes also people living in institutions and military conscripts.[29] The survey was based on stratified random sampling. In 2017, 3300 people were invited to participate from each of 18 provinces (2300 adults aged 20–74 and 1000 adults aged 75+, a total sample size 59 400). Data were collected between October 2, 2017, and March 3, 2018. Participants received a self-administered questionnaire in Finnish, Swedish, English, or Russian, which could be returned on paper or filled in electronically. The participation rate was 45%, resulting in a total of 26 422 participants.[29] Participants were asked for consent to registry linkage (56% provided consent), resulting in an analytical sample of 14 736 subjects.

Participants in the FinSote 2020 Survey were adults aged 20 years and older derived from the Digital and Population Data Services Registry, created in January 2020 after the merge between the Population Register of Statistics Finland and local register offices.[30] This sampling frame includes all permanent residents in Finland. The survey was based on a stratified random sample of each of 22 wellbeing areas (2000 adults aged 20–74, 800 adults aged 75+, total sample size of 61 600). Data were collected from September 14, 2020, to February 8, 2021. Participants received a self-administered questionnaire in Finnish, Swedish, English, or Russian, which could be returned on paper or filled in electronically. The analytical sample comprised 28 199 participants, with a participation rate of 46%. In 2020, consent to register linkages was included in the overall consent, and as a result, we were able to link all participants.

Outcomes

Our prespecified primary outcome was the uptake of at least two doses of a COVID-19 vaccine. We chose this outcome given the importance of a full immunization scheme to reduce the COVID-19 burden but also because it suited the study timeframe. We examined four prespecified secondary outcomes:

(1) uptake of at least one dose of a COVID-19 vaccine,
(2) uptake of the complete COVID-19 vaccination scheme (two doses and a booster dose),
(3) proportion of participants with more than 20 weeks days between the first and second COVID-19 dose (recommended spacing was 6–12 weeks), and
(4) proportion of participants with more than 30 weeks between the second dose and booster dose (recommended spacing was 3–4 months for those 60 years and above and 4–6 months for those under 60 years).

We linked separately FinSote 2018 and 2020 data to the Finnish Registry of Primary Care Visits maintained by the Finnish Institute for Health and Welfare using a unique identifier assigned to all residents in Finland. Follow-up was between December 27, 2020 (the date of the first COVID-19 vaccination in the country) and December 31, 2021. We included any approved COVID-19 vaccination in Finland[31]: COVID-19 mRNA vaccines (Comirnaty and Spikevax), recombinant vaccines (Vaxzevria, COVID-19 vaccine Janssen, COVISHIELD, Nuvaxovid, COVOVAX), and inactivated vaccines (BIBP/Sinopharm, COVAXIN, Coronavac). Four participants who received the COVID-19 vaccine Janssen were considered as having two doses after receiving one dose. We used a structured procedure to identify all COVID-19 vaccination doses and date of administration, see the Supplementary Appendix for details. Figure 1 shows a graphic timeline of data collection and assessment of COVID-19 vaccination and incident infections.

Exposures

We examined two forms of tobacco use: smoking and smokeless tobacco (snus) use. We assessed smoking status with the following question: Do you smoke currently (cigarettes, cigars, or pipe)? (a) yes, daily, (b) occasionally, (c) not at all, (d) I have never smoked. We created a categorical variable with the following categories: have never smoked, used to smoke, smokes occasionally, and smokes daily.

We assessed snus use with the following question: Do you currently use any of the following products? Snus (Swedish type moist stuff) (a) yes, daily, (b) occasionally, (c) not at all, and (d) I have never used. We created a categorical variable with the following categories: have never used, used to use, and currently use (daily and occasional combined). Data on smoking status is available for all participants, while data on snus use was available for participants aged 20–74 years old.

In addition, we examined people who used combustible tobacco and snus combined or alone (see Supplementary Appendix for definitions).

Potential Confounders

We used a directed acyclic graph to identify potential sociodemographic confounders (Figure S1). We adjusted for age, sex (men or women), marital status (married or in a registered relationship or cohabiting versus those separated or divorced, widowed, or single), educational level (years of education divided into tertiles), mother tongue (Finnish, Swedish, or other) and participation in social activities (no participation, occasional participation, and active participation). The harmonization protocol can be found in the Supplementary Appendix.

Incident COVID-19 Infections

A special concern was the occurrence of a COVID-19 infection, as it can influence either the willingness or the indication to vaccinate. For FinSote 2018, we considered the incidence of a COVID-19 infection a mediator between tobacco uses and the first dose of the COVID-19 vaccine (C_1). For FinSote 2020, the incidence of a COVID-19 infection might affect tobacco use and it would therefore be considered a confounder. Incident cases after the first vaccine dose are considered mediators (Figure S1) and adjusting for them could result in collider-stratification bias (see the Supplementary Appendix for a detailed discussion). Based on the infection date, we categorized incident cases as occurring prior to the first dose of the COVID-19 vaccine (C_1), in between the first and second dose (C_2), and in between the second and third dose (C_3). For those participants who did not receive any COVID-19 vaccine, we consider the start date of vaccine rollout for their corresponding age group using the rollout at the municipality of Helsinki as a reference.

We obtained COVID-19 infection data until December 31, 2021, from the Finnish National Infectious Disease Register maintained by the Finnish Institute for Health and Welfare. Testing of SARS-CoV-2 with RT-PCR was free and with extensive coverage in Finland throughout the study period. Reporting COVID-19-positive cases was mandatory for laboratories and physicians throughout the study period.[32]

Effect Modifiers

We examined potential effect modification by reporting stratified results by age (as a categorical variable), sex, and educational level. In post hoc analyses, we ran stratified analyses by vaccine type (see Supplementary Appendix for details).

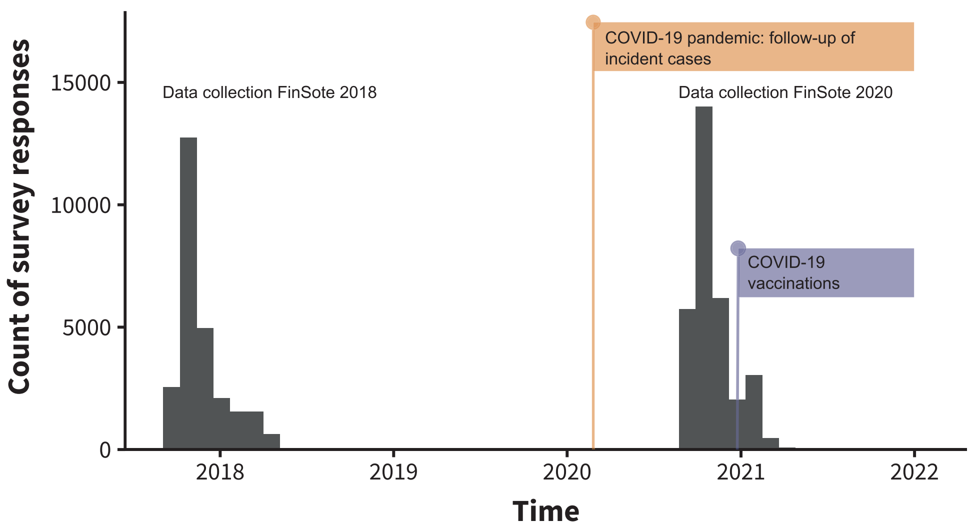

Figure 1. Graphic timeline of data collection and follow-up of COVID-19 vaccinations and incident infections.

Statistical Analyses

We used a Poisson regression with robust standard errors to estimate the relative risk of COVID-19 vaccination uptake. We modeled each outcome as a binary variable. We fitted the following Poisson model:

$$log\ \mu_i\ = \beta_0\ +\ \beta_1 S_i\ + \beta_x X_i^*\ +\ \rho_1 R_a \tag{1}$$

where i denotes the individual, β_0 is the intercept; β_1 is the coefficient of interest for exposure to tobacco S; a vector of covariates X^* (ie, sex, age, marital status, years of education, mother tongue, and participation in social activities); and $\rho_1 R_a$ an indicator for each wellbeing area a. We reported the exponentiated coefficient as the relative risk estimate for a basic model adjusted for sex and age (model 1) and adjusted for all potential confounders (model 2) with their corresponding 95% confidence intervals (CI).

Our primary method to handle missing data was multiple imputation, given that a missing at-random assumption is most likely in our data. We examined patterns of missing data and used multiple imputations using chained equations (MICE). We created fifteen datasets and pooled them taking the complex survey design into account. An annotated statistical code is available in the Supplementary Appendix.

We used age as a continuous variable and tested nonlinearity by comparing the linear model with penalized smoothing splines[33] using a likelihood ratio test with the Wald method.[34] The results showed a better fit when using the penalized smoothing splines. The variable years of education were modeled as categorical to be able to account for secular changes in years of education during the study years. We, therefore, categorized the data into tertiles within each survey wave.

To examine the role of COVID-19 cases, we adjusted for incident cases before the COVID-19 vaccine (C_1). We estimated the percent change in the estimate (ie, the relative risk) after adjusting for C_1 (model 3) compared to the fully adjusted model (model 2). Additionally, we simulated the effect of extreme situations by assuming (1) that all persons who had COVID-19 were vaccinated and (2) that all persons who had COVID-19 were not vaccinated. We calculated percent attenuation (% attenuation) in the β_1 coefficient of tobacco use compared with the reference model in equation 1 as follows.

$$(\beta_{Model2}\ - \beta_{Model3})/\beta_{Model2}) * 100 \tag{2}$$

We examined potential effect modification by reporting stratified analyses by age, sex, and educational level. We tested for multiplicative interactions if there were noticeable differences. We introduced the interaction terms one by one for each of the examined interactions. We used a likelihood ratio test to compare the model with and without the interaction. A p value lower than .05 in the likelihood ratio test was used as an indication of the presence of an interaction.

We carried out additional post hoc analyses examining combinations of combustible tobacco and snus use and several sensitivity analyses to check the robustness of our results: (i) we reported estimates using complete case analyses (ie, taking only the complex sampling design into account); (ii) we excluded participants who participated in FinSote 2020 survey after the start of the vaccination campaign; (iii) we excluded participants that received the vaccination before February 8, 2021 (see earlier); (iv) we re-run the main analyses restricting the follow-up time to when vaccination coverage reached 60% and 80%, to understand whether these associations changed over time and provide estimates that might be comparable to countries with lower vaccination coverage, thus increasing the external validity of our estimates; (v) we restricted analyses using data from FinSote 2020 to examine misclassification exposure bias; (vi) we excluded participants who have had a COVID-19 infection; and (vii) we modeled the data as time-to-event using Cox proportional hazards models.

We used the *MICE* package to conduct the multiple imputation. We took the complex sampling design into account and used inverse probability weights to correct for nonparticipation (see Supplementary Appendix for details). All analyses were carried out using R version 4.1.1. The statistical code is available as Supplementary Appendix 2.

Results

We analyzed data on smoking from 42 935 participants (and 29 192 participants aged 20–74 years old for snus use). Prevalence of daily smoking was 10.7% and current snus use was 4.7%. Baseline characteristics of participants by smoking status are shown in Table 1. People who smoked daily were more often men, younger, separated, single or widowed, had lower education, and reported lower levels of participation in social activities. Table S1 shows baseline characteristics by snus use. We observed overall vaccination rates of 90.1% for the first dose, 87.5% for the second dose, and 31.0% for the third dose by December 31, 2021. The progression of the COVID-19 vaccination uptake was relatively equal between those who smoked and those who had never smoked over time (Figure 2). Around 0.5% of participants experienced a COVID-19 infection before the first vaccine dose.

People who smoked daily had a 7% lower risk (95% CI = 0.91; 0.96) of receiving two doses of a COVID-19 vaccine than those who have never smoked in fully adjusted models (Table 2). We did not find evidence of an association between participants who smoked occasionally or previously smoked and the uptake of two doses of a COVID-19 vaccine. We also did not find evidence of an association between current or former use of snus and the uptake of two doses of a COVID-19 vaccine. We obtained very similar findings regarding the uptake of one dose of a COVID-19 vaccine.

In fully adjusted models, people who smoked daily had a 15% lower risk (95% CI = 0.78; 0.94) of receiving three doses of a COVID-19 vaccine compared to never smokers. Those who smoked occasionally also had a lower risk of receiving three doses of a COVID-19 vaccine (relative risk 0.87, 95% CI = 0.77; 0.99) than those who have never smoked. Our results for those who used to smoke were compatible with a wide range of associations. Current users of snus had a 26% lower risk (95% CI = 0.54; 1.0) of the uptake of three vaccine doses, while former users of snus had a 12% lower risk (RR = 0.88, 95% CI = 0.80; 0.97) of receiving three doses of a COVID-19 vaccine in fully adjusted models.

Regarding between-dose spacing, we observed no evidence of an association between all exposure categories, and the proportion of those exceeding 20 weeks between the first and second dose and 30 weeks between the second and third dose of the COVID-19 vaccine, as the observed associations were compatible with a wide range of values.

People who used both combustible and smokeless tobacco showed similar associations to those who smoked daily (Table S2). We found evidence of an association between dual

Table 1. Baseline Characteristics of the 42 935 FinSote Participants by Smoking Status

Categories		Smoking status			
	Total	Never smoked	Used to smoke	Smoked occasionally	Smoked daily
Smoking prevalence	100	37.9	40.1	7.0	10.7
Vaccination uptake					
First dose (%)	90.1	90.7	91.7	87.9	84.5
Second dose (%)	87.5	88.7	89.3	84.5	80.7
Third dose (%)	31.0	32.7	35.5	17.0	21.3
Between dose-spacing					
More than 20 weeks between the first and second dose (%)	0.7	0.8	0.7	1.0	1.0
More than 30 weeks between second and third dose (%)	3.6	4.1	3.5	2.1	3.2
COVID-19 cases					
Before first dose (%)	0.5	0.5	0.4	0.5	1.0
Between first and second dose (%)	0.4	0.3	0.3	0.3	0.5
Between second and third dose (%)	1.3	1.4	1.3	1.7	0.6
Sociodemographic variables					
Sex, % women	51.4	59.7	47.3	41.9	46.4
Mean age (SD)	50.0 (18.3)	50.4 (19.4)	52.9 (17.7)	40.9 (15.2)	47.0 (15.5)
Marital status, % separated, single, or widowed	34.7	36.6	29.8	41.3	41.6
Educational levels (%)					
Low	17.4	16.1	19.8	9.1	19.5
Intermediate	37.2	31.5	37.9	42.9	50.6
High	45.4	52.5	42.3	48.0	29.9
Mother tongue (%)					
Finnish	93.1	94.3	91.6	93.1	94.0
Swedish	4.9	3.7	6.2	5.0	4.2
Other	2.0	2.0	2.2	1.9	1.8
Participation in social activities (%)					
No participation	50.6	45.3	50.2	53.7	68.3
Occasional	26.5	30.6	26.7	22.9	14.4
Active	22.9	24.1	23.1	23.3	17.2

Data are percentages or mean (SD). All values take the complex sampling design into account.

use and higher interval spacing between the first and second doses of the COVID-19 vaccine.

Adjusting for incident COVID-19 infections before the first COVID-19 vaccine dose (Table 3) resulted in a minimal change in the estimates for people who smoked daily, translating to less than 2% attenuation. Simulation results were consistent with these findings (Table S3). The change in estimates for other exposure categories was also minimal. The percent attenuation was mostly small (less than 10%), with a few exceptions where the unexponentiated estimate was so close to zero that any minimal change resulted in large percent attenuations.

In stratified analyses, we did not find substantive differences in the association between smoking and snus and COVID-19 vaccine uptake by sex, age, or educational level (Tables S4–S6). We did not observe differences by vaccine type, with the exception that those who received two doses of mRNA vaccines or one dose of mRNA vaccines and one dose of Vaxzevria were less likely to receive a third dose of COVID-19 vaccine than those who received two doses of Vaxzevria (Table S7).

Sensitivity analyses using complete case analyses (Table S8), excluding participants who either responded to FinSote 2020 after the start of the vaccination campaign (Table S9) or were vaccinated during FinSote 2020 data collection yielded very similar results (Table S10). Restricting follow-up time until the sample reached 60% and 80% coverage resulted in similar results (Tables S11 and S12). Excluding participants from FinSote 2020 to examine misclassification bias in the exposure was consistent with the main findings (Table S13). Likewise, excluding participants who were infected with COVID-19 (Table S14) did not materially affect the results. We also obtained consistent results by using time-to-event analyses (Table S15).

Discussion

We examined the association between tobacco use (smoking and snus use) and the uptake of COVID-19 vaccinations. We found that people who smoked daily had a lower risk of receiving one, two, or three doses of the COVID-19 vaccines compared to those who have never smoked. People who smoked occasionally or used snus were substantially at lower risk of receiving the third COVID-19 vaccine dose. We did not find evidence of an association between tobacco use and delays in COVID-19 vaccinations.

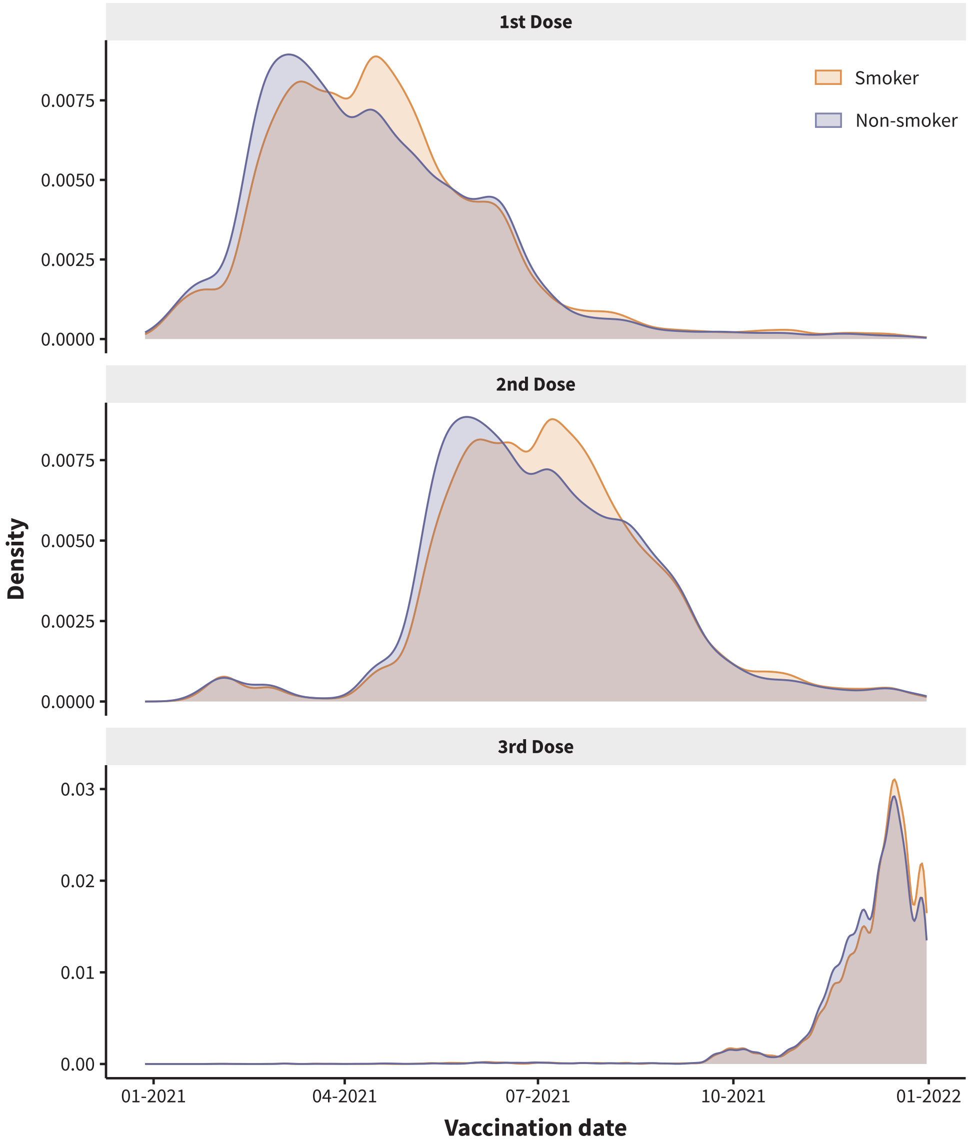

Figure 2. Density plots of COVID-19 vaccination uptake in smokers versus never smokers. Smokers include daily, occasional, and former smokers.

Our findings show that people who smoked daily had lower vaccination uptake of all doses of COVID-19 vaccines. These findings are in contrast with the studies in Singapore and Palestine showing higher COVID-19 vaccine uptake among people who smoked. This difference could be explained by the differences in study populations and in the classification of the exposure. The Singaporean study was carried out in a convenience sample of highly educated individuals (41% had a postgraduate degree),[35] while participants in the Palestinian study were health care workers.[25] Our findings are more consistent with previous studies showing greater vaccine hesitancy in people who smoked compared to those who do not smoke.[12,16,17]

We found a substantial reduction in vaccination uptake for the third dose for people who smoked daily or occasionally as well as those who currently used snus or used to. One potential explanation for these findings could be delays in receiving the vaccination, as our follow-up period ended on December 31, 2021. This would explain the results only if there were differences in between-dose spacing between those who have never smoked and other smoking categories. However, our sensitivity analyses restricting follow-up time to 60% and 80% of vaccination coverage did not show important differences and we found no evidence of differences in the spacing of COVID-19 vaccines. In addition, there are important differences in COVID-19 vaccine uptake in Finland between the second and third doses that persist to date. By February 12, 2023, the uptake of a second dose was 87% compared to 66.1% of a third dose.[36] A second explanation can be a lower perception of risk from COVID-19 after receiving two vaccine doses. In other words, participants might have perceived that two vaccine doses provided enough protection against a COVID-19 infection and associated adverse outcomes. Finland has high levels of trust in public institutions and in the authorities' preparedness to handle the COVID-19 emergency,[37] which might have helped to overcome hesitancy among smokers and snus users for the first two doses but not enough to motivate a third dose. A third explanation can be personal experiences with the virus and vaccination (eg, the experience of side effects) might have reduced the willingness to receive a third dose. We consider this explanation as unlikely as in Finland vaccine acceptance increased from 64% prior to the start of the vaccination rollout (November/December 2020) to 74% in April 2021.[38] Likewise, a small proportion of participants experienced a COVID-19 infection

Table 2. Relative Risk (and 95% Confidence Intervals) of Primary and Secondary Outcomes by Tobacco Use in 42 935 FinSote Participants (29 192 by Snus Use)

Tobacco uses category	Outcome	
	Model 1: adjusted for sex and age	**Model 2: adjusted for all confounders**
Primary outcome (two doses of COVID-19 vaccination)		
Smoking		
Currently smokes daily	0.91 (0.89; 0.94)	0.93 (0.91; 0.96)
Currently smokes occasionally	0.97 (0.94; 1.01)	0.98 (0.95; 1.01)
Used to smoke	1 (0.98; 1.01)	1 (0.98; 1.01)
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	1 (0.95; 1.04)	0.99 (0.95; 1.04)
Used to use	1 (0.98; 1.03)	1 (0.98; 1.02)
Has never used	Ref.	Ref.
Secondary outcome one (one dose of COVID-19 vaccination)		
Smoking		
Currently smokes daily	0.94 (0.92; 0.96)	0.95 (0.93; 0.98)
Currently smokes occasionally	0.99 (0.96; 1.02)	0.99 (0.97; 1.02)
Used to smoke	1.01 (0.99; 1.02)	1.01 (1; 1.02)
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	1.01 (0.97; 1.05)	1.01 (0.96; 1.05)
Used to use	1.01 (0.99; 1.03)	1.01 (0.99; 1.03)
Has never used	Ref.	Ref.
Secondary outcome two (three doses of COVID-19 vaccination)		
Smoking		
Currently smokes daily	0.79 (0.72; 0.87)	0.85 (0.78; 0.94)
Currently smokes occasionally	0.85 (0.75; 0.97)	0.87 (0.77; 0.99)
Used to smoke	1.01 (0.97; 1.05)	1.02 (0.98; 1.06)
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	0.73 (0.54; 0.99)	0.74 (0.54; 1.00)
Used to use	0.87 (0.79; 0.95)	0.88 (0.8; 0.97)
Has never used	Ref.	Ref.
Secondary outcome three (interval spacing between first and second dose)		
Smoking		
Currently smokes daily	1.54 (0.72; 3.30)	1.64 (0.76; 3.51)
Currently smokes occasionally	1.67 (0.77; 3.59)	1.68 (0.79; 3.54)
Used to smoke	0.88 (0.64; 1.20)	0.89 (0.64; 1.23)
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	2.21 (0.6; 8.11)	2.2 (0.6; 8.10)
Used to use	0.9 (0.49; 1.65)	0.91 (0.50; 1.67)
Has never used	Ref.	Ref.
Secondary outcome four (interval spacing between second and third dose)		
Smoking		
Currently smokes daily	1.04 (0.77; 1.41)	1.2 (0.87; 1.64)
Currently smokes occasionally	0.77 (0.52; 1.13)	0.82 (0.56; 1.22)
Used to smoke	1.02 (0.88; 1.18)	1.06 (0.91; 1.22)
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	1 (0.56; 1.80)	1.03 (0.57; 1.86)
Used to use	0.79 (0.59; 1.05)	0.82 (0.62; 1.09)
Has never used	Ref.	Ref.

Data are relative risk with 95% confidence intervals. Models for smoking include 42 935 participants aged 20+. Models for snus include 29 192 participants aged 20–74 years old. Model 1 is adjusted for sex and age (as penalized smoothing spline). Model 2 is adjusted for sex, age (as penalized smoothing spline), marital status, educational level, mother tongue, and participation in social activities. All models are based on multiple imputation that take the complex sampling design into account.

Table 3. Relative Risk and Percent Attenuation of Primary and Secondary Outcomes by Tobacco Use After Adjusting for Incident COVID-19 Cases Before First Vaccination Dose (C_1)

Tobacco uses category	Outcome	
	Model 3: adjusted for confounders and C1	**Percent attenuation**
Primary outcome (two doses of COVID-19 vaccination)		
Smoking		
Currently smokes daily	0.93 (0.91; 0.96)	1.3
Currently smokes occasionally	0.98 (0.95; 1.01)	−2.6
Used to smoke	1.00 (0.98; 1.01)	−20.0
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	0.99 (0.95; 1.04)	−9.5
Used to use	1.00 (0.98; 1.03)	−700.0
Has never used	Ref	Ref.
Secondary outcome one (one dose of COVID-19 vaccination)		
Smoking		
Currently smokes daily	0.95 (0.93; 0.98)	0.4
Currently smokes occasionally	0.99 (0.97; 1.02)	−3.3
Used to smoke	1.01 (1; 1.02)	0.0
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	1.01 (0.96; 1.05)	1.8
Used to use	1.01 (0.99; 1.03)	−2.8
Has never used	Ref.	Ref.
Secondary outcome two (three doses of COVID-19 vaccination)		
Smoking		
Currently smokes daily	0.85 (0.78; 0.94)	0.2
Currently smokes occasionally	0.87 (0.77; 0.99)	−0.4
Used to smoke	1.02 (0.98; 1.06)	0.0
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	0.74 (0.54; 0.99)	−0.3
Used to use	0.88 (0.8; 0.97)	0.8
Has never used	Ref.	Ref.
Secondary outcome three (interval spacing between first and second dose)		
Smoking		
Currently smokes daily	1.64 (0.77; 3.52)	−0.6
Currently smokes occasionally	1.67 (0.79; 3.53)	0.6
Used to smoke	0.89 (0.64; 1.23)	−0.8
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	2.18 (0.59; 8.05)	0.7
Used to use	0.91 (0.5; 1.67)	4.1
Has never used	Ref.	Ref.
Secondary outcome four (interval spacing between second and third dose)		
Smoking		
Currently smokes daily	1.20 (0.87; 1.64)	−0.7
Currently smokes occasionally	0.82 (0.56; 1.22)	−0.9
Used to smoke	1.06 (0.91; 1.22)	1.6
Has never smoked	Ref.	Ref.
Snus use		
Currently uses	1.03 (0.57; 1.86)	11.8
Used to use	0.82 (0.62; 1.09)	−0.1
Has never used	Ref.	Ref.

Data are relative risk with 95% confidence intervals. Models for smoking include 42 935 participants aged 20+. Model 3 is adjusted for sex, age (as penalized smoothing spline), marital status, educational level, mother tongue, and participation in social activities and incident COVID-19 cases before first vaccination dose (C_1). All models are based on multiple imputation that take the complex sampling design into account.

during the study period. Our mediation analyses showed that experiencing an incident COVID-19 infection explained a minimal proportion of the association between tobacco use and COVID-19 vaccine uptake.

Major strengths of our study included pre-registered analyses, for which we provide information and code to allow full replication of our results. We used directed-acyclic graphs to help us identify the causal structure of our study design, allowing us to transparently recognize confounders and mediators. We used data from large national health surveys in Finland using a sampling frame that included people living in institutions and conscripts, reducing the risk of selection bias. Data on vaccinations was obtained from a nationwide registry with a very low risk of selection and misclassification bias. We measured exposure to tobacco use before the outcome, reducing the risk of reverse causality. Our sensitivity analyses excluding participants who received the COVID-19 vaccination before the end of data collection or who participated in FinSote after the start of the vaccination campaign were consistent with the main analyses.

However, some limitations are noted. First, we relied on self-reported assessment of tobacco use, which is subject to information bias. In addition, participants in FinSote 2018 might have changed their tobacco use since data collection, resulting in a misclassification bias of the exposure. This bias is likely small, as the time lag is relatively short, and our sensitivity analyses did not show important differences. Second, nonparticipation in FinSote surveys was relatively high and threatened the internal validity of our findings. We used inverse probability weights to account for nonparticipation and reduce the risk of selection bias, but we cannot rule out that some bias persists. Third, we considered the incidence of COVID-19 cases during the study period. Incident COVID-19 cases are, however, likely to be underestimated. This underestimation was larger during the first months of the COVID-19 pandemic when testing was restricted to health workers and hospitalized patients. In May 2020, PCR testing became widely available and free of access, decreasing drastically the risk of underestimation. Reporting of COVID-19 cases was mandatory throughout the study period and rapid antigen tests only became widely used during January 2022 and thereafter. Fourth, we were not able to adjust for important confounders such as comorbidity or personality traits. Thus, our results remain primarily descriptive. Fifth, the external validity of our findings is limited to settings with relatively high vaccination rollout and where tobacco users have not been included in priority groups.

The public health implications of our study are twofold. First, the study clearly identified people who smoked daily as a risk group for lower COVID-19 vaccination uptake, which was observed for all vaccination doses. Vaccination among those who smoke daily could be supported with targeted informational campaigns, as well as reinforcing vaccination opportunities in communities or professions with higher smoking rates. Second, lower uptake of the third dose of COVID-19 vaccines among other groups of users of tobacco (ie, people who smoked occasionally or currently use snus) reinforces the need to address potential vaccination fatigue among people who use tobacco. The uptake of third and fourth doses in Finland has remained below the levels of the second dose; public health authorities should implement targeted interventions for users of tobacco to both reduce the risk of COVID-19 adverse outcomes in this population group and increase overall vaccination rates.

Conclusion

People who smoked daily had lower COVID-19 vaccination uptake for all three doses compared to those who had never smoked. We found lower uptake of the third vaccine dose among people who smoke occasionally or use snus compared to those who have never used it. Further research could triangulate these findings in other settings and populations, explore whether tobacco use is associated with reduced effectiveness of COVID-19 vaccines, and use sales and population data to identify areas or occupational groups with higher smoking rates for planning targeted interventions.

Supplementary Material

Supplementary material is available at *Nicotine and Tobacco Research* online .

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Declaration of Interests

None declared.

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Author Contributions

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Data Availability

The data used in this study are not publicly available but can be accessed with a research proposal and an approved user authorization application from the Finnish Social and Health Data Permit Authority (Findata). For more information, please visit https://findata.fi/en/.

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