

Research report



A conceptual framework for assessing the public health effects from snus and novel non-combustible nicotine products Nordic Studies on Alcohol and Drugs 2021, Vol. 38(6) 586–604 © The Author(s) 2021 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/14550725211021248 journals.sagepub.com/home/nad



Karl Erik Lund

Norwegian Institute of Public Health, Oslo, Norway

Tord Finne Vedøy

Norwegian Institute of Public Health, Oslo, Norway

Abstract

Objective: The tobacco industry plans to base their future earnings on the production of non-combustible nicotine products. These might replace or come in addition to the more harmful cigarettes that historically have dominated the nicotine market in the Nordic countries. The authorities in each country must decide whether the products should have market access and, in that case, how strictly they should be regulated. Our aim is to present a framework that can assist the health authorities to make a regulation where benefits will outweigh the harms. Method: In a public health perspective, health gains from substitution must be weighed against the health loss from additional use. The main elements of the weighing will be based on the information about the absolute risk of the products, their relative risk compared to conventional cigarettes and how the users are composed according to smoking status. We apply the framework on snus as used in Norway – a product with an established usage pattern and epidemiologically assessed health risks. Results: The framework consists of (i) a comprehensive set of specific user patterns that may result in health deterioration and user patterns that may result in health benefits, (ii) an estimation of the number of people with health-augmenting and health-impairing user patterns, respectively, and (iii) an estimation of the degree of health deterioration or health benefit that will affect the persons with the different user patterns. Conclusion: The net effect on public health will appear

Submitted: 27 October 2020; accepted: 12 May 2021

Corresponding author:

Karl Erik Lund, Norwegian Institute of Public Health, PO 222, Skøyen, Oslo, 0213, Norway. Email: kelu@fhi.no



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/

by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

as an overall result of the number of people with positive and negative user patterns, respectively, in combination with the magnitude of the change in health status these people will experience. The use of an explicit framework highlights how a political decision may affect nicotine use and health-related outcomes. The framework breaks open a large and complex question into smaller pieces and requires the authorities to expose and explain the kind of evidence and reasoning behind regulations of novel nicotine products.

Keywords

e-cigarettes, nicotine, preventive work, public health, snus, tobacco

The nicotine marked is changing rapidly. In a 50-year period after the Second World War, the Nordic tobacco market was dominated by two types of combustible products: factory made cigarettes and rolling and pipe tobacco. Eventually, snus increased its market share at the expense of these combustible products especially in Norway and Sweden. Gradually, e-cigarettes have been added to the nicotine market, and more recently heated tobacco products, so-called heat-not-burn technology (HNB), and tobacco-free - yet nicotine-containing pouches for oral use. Without combustion, snus, e-cigarettes, HNB products and nicotine pouches release less of the toxic substances that are the main cause of smoke-related morbidity and mortality. The tobacco industry will, within a few years, launch even more varieties of noncombustible nicotine products to the market and claims to turn production away from cigarettes (Gharib, 2020).

Non-combustible nicotine products are not without health risk for consumers, but they are considered to be significantly less harmful compared to cigarettes (National Academies of Sciences, Engineering, and Medicine (NASEM), 2018; Royal College of Physicians, 2007). The products are used for smoking cessation, but with their variation in flavour, fancy packaging and functionality, they resemble consumer products more than medicinal products for therapeutic purposes. Consequently they appeal to many other than the small group of smokers who use nicotine medication to treat

their nicotine addiction. The products can potentially oust cigarettes among those who are – or would have become – smokers and therefore dramatically reduce the detrimental health consequences in this group. At the same time, due to the broader appeal, these products gain access to groups – primarily adolescents – who would otherwise refrain from all nicotine use. In this specific group, the products may lead to an increased health risk.

The weighting principle

It has become a challenge for the health authorities to balance the consideration of these products' harm-reducing function among smokers against prevention of use among young people. Potential health benefits from substitutional use must be weighed against the potential health deterioration from additional use - hereinafter referred to as the weighting principle. If the products are supposed to reduce damage from smoking more than they increase health damage among new users, the authorities can achieve a net health benefit by allowing such products, taxing them at a lower rate than cigarettes or giving other competitive advantages to channel nicotine use from cigarettes to less harmful products (risk proportional policies). If the net effect is reversed, the authorities may prefer to impose sales bans, tax them highly, regulate the area of use or induce strong marketing restrictions. In this article, we will present a framework that can be used to weigh the

advantages and disadvantages when the authorities are designing regulation.

The procedure presupposes that we have fairly accurate - although not complete - information about the risks the products may pose, information about the risk-difference in relation to cigarettes and information about smoking status in the user population. This information should ideally be obtained from empirical observations after long-time use, but for new products, input has to be based on expectations regarding risks and different scenarios of use patterns. Rather than presenting a numerical calculation of the public health effect, our ambition is to present a framework that identifies which factors should be included in a weighting model. We will base our example on snus - an established alternative nicotine product to cigarettes in Norway – because this is where we have the most accurate information about health risks and use patterns.

Competing principles for regulating novel products

Nordic tobacco control policies on novel nicotine products have been based on other considerations than weighting of advantages and disadvantages Typically, public reports and governmental strategy plans highlight three guiding principles from medical ethics when discussing novel nicotine products: The do no harm principle requires that the authorities should advise against the use of nicotine products that, due to its toxic content, may lead to consequential damage. The precautionary principle cautions against use of products where it cannot be ruled out that undetected consequential damages may occur in the future. The loss of autonomy principle warns against use of products that may be addictive (Helse- og omsorgs departementety, 2015, p. 72). Based on sole use of these principles, it would be most appropriate to ban new nicotine products. However, we argue that more emphasis should be given to the weighting principle and a policy aiming at maximising public health effects. Ideally, a justification for any

regulation should demonstrate that it would add to the protection of public health, and that it is reasonable to expect that the benefits will outweigh the harms.

The framework outline

In short, an assessment of the public health effect from regulating novel nicotine products (restrictive vs. liberal) should contain three elements. First, we have to identify user patterns that may result in health deterioration and user patterns that may result in health benefits. Second, we have to estimate the number of people with health-augmenting and health-impairing user patterns, respectively. Finally, we have to estimate the degree of health deterioration or health benefit that will affect the persons with the different user patterns. Thus, the net effect on public health will appear as an overall result of the number of people with positive and negative user patterns, respectively, in combination with the magnitude of the change in health status these people will experience.

In order to imbue the framework with data, we will need in particular three types of information. Social scientists must provide data on *usage patterns* and user trajectories for a particular nicotine product. In addition, from biomedicine and epidemiology we must have data on *absolute risk* from using this nicotine product as compared to absence of use. Finally, we have to know what kind of reduction in health damage – if any – the product may lead to among those who would otherwise use cigarettes. To illustrate and show other necessary components, we will now apply the framework to snus.

The framework as applied to snus

Identification of positive and negative use patterns

Inspired by Levy, Borland et al. (2017), we can illustrate how access to snus may affect the transitions in nicotine use in a health-augmenting and a health-impairing way

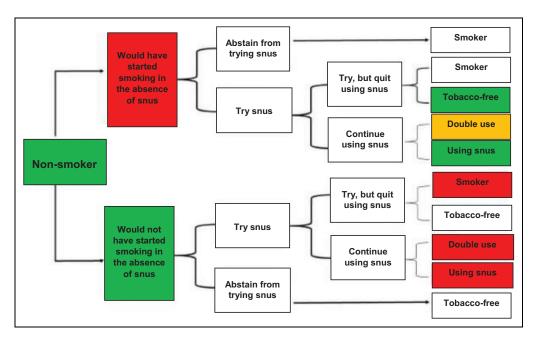


Figure 1. Public health effect of snus use where the baseline is non-smokers.

(Figures 1–3). The point of departure in Figure 1 is those who do not smoke. If snus was not available, this population could either start smoking or abstain from all kinds of nicotine use. The key point in the figure is that access to snus can ultimately result in a different outcome than would have been in a hypothetical absence of snus. In the upper part of the figure, we see the consequences of snus for those who would start smoking in any case. In the presence of snus, some of these would try snus. Among these, some would dislike snus. They may then end up as smokers anyway, or they may become tobacco-free if the use of snus caused them to "loose the taste" for tobacco. On the other hand, among those who like snus and continue, the use of snus can either replace or be an addition to the smoking they would otherwise do. In the bottom part of Figure 1, we see how the availability of snus can affect those who would not have started smoking. Some of them would try snus, and this would expose them to the risk of becoming persistent snus users or "waking the

appetite" for tobacco in general and move them towards smoking or dual use.

The colour codes for the boxes in the last column symbolise the assumed contribution from snus use to the public health balance. The white boxes give no contribution in either in a positive or negative direction because the snus use does not have any influence on the endpoint. Green boxes symbolise that the user pattern of snus will make a beneficial contribution to health. Red boxes show that the user pattern of snus makes a negative contribution to health. In the yellow boxes (double use), the contribution to the public health balance will depend on how much snus affects the intensity of smoking (consumption of cigarettes). Note that the colour of a box depends on what you would otherwise do. In the last column, snus use is marked in red for those who otherwise would not smoke, while it is green for those who otherwise would smoke cigarettes. Such figures can be reproduced for those who already smoke and for those who have stopped smoking (Figures 2 and 3).

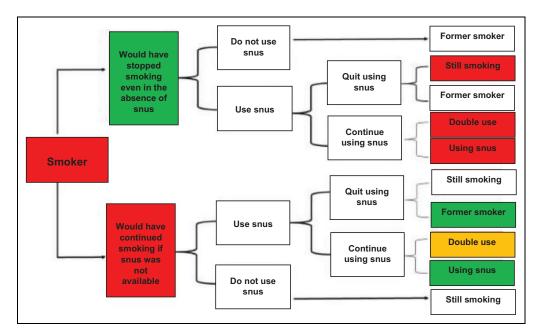


Figure 2. Public health effect of snus use where the baseline is smokers.

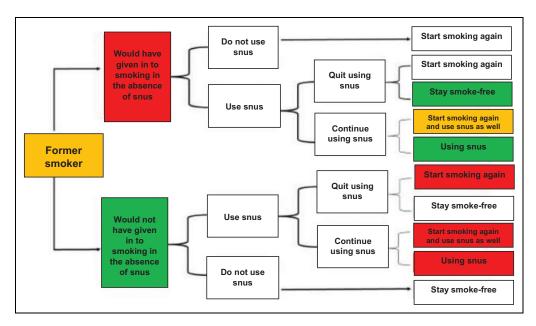


Figure 3. Public health effect of snus use where the baseline is former smokers.

An alternative way of illustrating how different user patterns of snus could affect public health is shown in Table 1. As above, we have divided a user's trajectory of use into a start-up phase (I), a user phase (II) and a cessation phase (III). The last column presents the direction

Table I. Snus user configuration.

Cell type (CT)	Transitions	Description	Effect on public health
I. Start-up pha	ise		
1	Snus start-up among persons who would	New nicotine	Negative
	never have started smoking	consumption	.
la	with following progression to smoking due to prior snus use	The gateway hypothesis	Negative
Ib	with following cessation after use for	Experimenting	None
	a short period	Experimenting	110110
2	Snus start-up among persons who would	The diversion hypothesis	Positive
	otherwise have started smoking	,,	
2a	with following (but delayed) progression	Delayed smoke start-up	Positive
21	to smoking	.	. .
2b	with following cessation after use for	Experimenting	None
II. User phase	a short period		
3	Continued snus use among persons who		Negative
	would otherwise not be smoking		
4	Continued snus use among persons who	Total substitution	Positive
	would otherwise be smoking		
5 _	Combined use of snus and cigarettes	Dual use	_
5a	with a reduction in smoking intensity	Partial substitution	Positive
5b	with no reduction in smoking intensity	No substitution	Negative
5c	where additional use of snus shortens	Accelerated smoking	Positive
	the smoking phase (accelerates smoking	cessation	
	cessation)		
5d	where additional use of snus prolongs	Delayed smoking	Negative
	the smoking phase	cessation	
III. Cessation		A saidantal anaskins	Danisira
0	Transition to snus use among smokers who have no intention to quit smoking	Accidental smoking cessation	Positive
7	Transition to snus use among "smoking	Cessation	
	quitters" who would have continued		
	smoking without snus use		
7a	with following permanent use of snus	Exclusive snus use	Positive
- .			
7b	with following relapse to smoking where	Relapse	Negative
	resumption may be due to temporary snus use		
7c	with following being nicotine-free which	Abstinence	Positive
, c	may be due to temporary snus use	Abstinctice	1 Osicive
8	Transition to snus among "smoking quitters"	Unnecessary snus use	Negative
	who would have stopped smoking without	•	
	snus use		
8a	with following relapse to smoking where		Negative
	resumption may be due to temporary snus		
	use		

(positive/negative) the different transitions could conceivably have in a public health balance.

On one hand, there will be a negative contribution to the public health balance if: (i) nonsmokers (who would otherwise never have started using nicotine) start using snus (CT-1) and if this snus use is what causes them to start smoking (the gateway hypothesis) (CT-1a); (ii) smokers who start using snus continue to smoke as much as before (CT-5b) or remain as smokers for a longer period of time (e.g., because the snus will help with abstinence at work or in places where smoking is forbidden) (CT-5d), these are also negative contributions to population health; (iii) ex-smokers start using snus and therefore relapse to smoking (CT-7b) or if those who quit smoking switch to snus instead of quitting all kind of tobacco (CT-8).

On the other hand, there will be a positive contribution to the public health balance if: (i) snus were to be used by young people who would otherwise have started smoking (the diversion hypothesis) (CT-2) or postpones the start of smoking (CT-2a); (ii) additional snus use leads to a reduction of cigarette consumption among smokers (CT-5a) or leads to a shorter smoking career (CT-5c); (iii) smokers with no intentions to quit accidentally "stumble across" snus and change product (CT-6 – accidental quitting smoking) or if snus would be the only way smokers manage to quit smoking (CT-7a). For other user patterns and transition types, the impact on the public health will be less significant (e.g., CT-1b and 2b).

For products which have no or a very short history of use – such as tobacco-free pouches (e.g., ZYN) and products using heat-not-burn technology (e.g., IQOS) – there will be greater uncertainty around the estimates for both the degree of risk (absolute and relative) and use patterns. For other products, such as e-cigarettes, that have been on the market for over 10 years, there will be a better observational basis for user patterns and risk. In models used for calculation of the public health effects of novel nicotine products, researchers typically

use input from constructed scenarios of user patterns (see, e.g., Cherng et al., 2016; Hill & Camacho, 2017; Kalkhoran & Glantz, 2015; Lee et al., 2017; Levy, Borland, et al., 2017; Levy, Cummings, et al., 2017; NASEM, 2018; Soneji et al., 2018; Vugrin et al., 2015; Warner & Mendez, 2019; Weitkunat et al., 2015). However, a 10-year history of use is too short a period to make precise estimates of the (absolute and relative) risk of using e-cigarettes. In the absence of epidemiological studies on long-term use, the estimates of the risks of e-cigarettes must thus be based on analyses of chemical content, animal studies and acute physiological reactions in humans – like, e.g., Public Health England does in their reports (McNeil et al., 2018).

For snus, the preconditions for assessing the public health effect are far better. Use of snus has a long tradition in Norway and Sweden and snus use among people with varied smoking status can be documented decades back in time. Moreover, risk estimates can be derived from epidemiological studies of long-time use.

User pattern of snus

In a recent report from the Norwegian Institute of Public Health (Folkehelseinstituttet (NIPH), 2019), ever use of snus was distributed according to smoking status for the period 2004–2018. With the authors' permission (ourselves) we reproduce these findings in Figures 4 (men) and 5 (women).

Among both women and men the majority of snus users are made up of ever smokers consisting of: (i) current smokers (double users – blue), (ii) former smokers (purple) and (iii) persons who have quit both snus and cigarettes (yellow). In these three groups (who have experience with both snus and cigarettes), 70% among men and 84% among women had started their tobacco consumption with cigarettes (NIPH, 2019). From this, we can conclude that a majority of snus users have a history of smoking, and that snus consequently *may* have played a role in their smoking cessation.

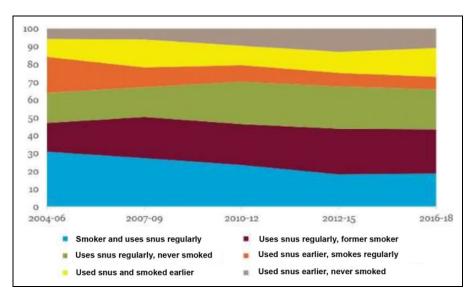


Figure 4. Percentage of men aged 16–74 years who used snus regularly or previously, by smoking status in the period 2004–2018; three years intervals. Age-standardised numbers (reference year 2017). *Source*: Statistics Norway, NIPH (2019).

This hypothesis is supported by research that, i.a., shows that snus is the most widely used method for smoking cessation in Norway (after unassisted attempts) (NIPH, 2018), that the smoking cessation rate is generally higher among snus users than among smokers who do not use snus (Lund et al., 2010; Lund & Lund, 2014), that dual users of snus and cigarettes more often see themselves as being smokefree five years into the future compared to smokers who do not use snus (Lund et al., 2017) and that dual users more often than exclusive smokers become smoke-free after five years (Lund & Christiansen, 2020). In addition, among ex-smokers who used snus at the time of the survey, as many as 82.7% stated that snus was in fact the aid they used when they stopped smoking (Lund et al., 2017).

However, although snus may have helped many to become smoke-free, it is also possible that snus may contribute to delayed smoking cessation for some dual users (blue segment, CT-3 in Table 1). Among former smokers (purple segment), some would have quit all nicotine use, in the hypothetical absence of access to

snus (CT-8 in Table 1). There is no reliable data that can identify the magnitude of these groups.

Nevertheless, we have data that show that the consumption of cigarettes is 30% lower in smokers who also use snus (blue segment) (Lund et al., 2017; NIPH, 2019) (CT-5a in Table 1). For diseases with a dose-response relationship with smoking, such as lung cancer, a reduced smoking intensity will be of significance. However, for other diseases such as cardiovascular diseases, smoking intensity will be less important (Bjartveit & Tverdal, 2005). A systematic overview funded by the tobacco industry (Lee, 2013) showed that dual users of snus and cigarettes had a lower incidence of diseases than exclusive cigarette smokers. However, based on our cross-sectional data, we cannot assume that lower consumption of cigarettes among dual users is an effect of additional snus use.

Likewise, we do not have sufficient information about the group of snus users without former use of cigarettes (green and grey segments in Figures 4 and 5) that is likely relevant to the public health balance. Based on the figures, we know that the proportion of snus users who

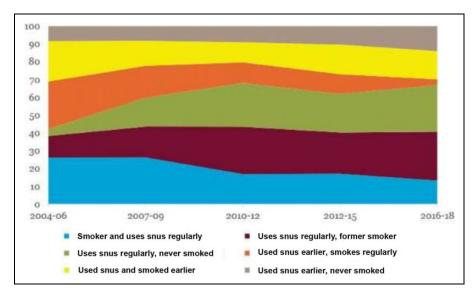


Figure 5. Percentage of women aged 16–74 years who used snus regularly or previously, by smoking status in the period 2004–2018; three years intervals. Age-standardised numbers (reference year 2017). *Source*: Statistics Norway, NIPH (2019).

have never been smokers has increased over time – and that this increase has been greatest among women. Of ever snus users, interviewed during the period 2016–2018, 33% of the men and 40% of the women had no former experience with smoking. This was an increase from the period 2004–2006, when 23% of the men and 12\% of the women who were ever snus users had never smoked (NIPH, 2019, p. 50). Without access to snus, it is possible that some of these snus users would have remained tobacco-free - often referred to as the abstinence hypothesis. In this case, snus would contribute negatively to the public health balance (CT-1 in Table 1). This would also be the case if snus were to act as a gateway to subsequent smoking - the so-called gateway hypothesis. Such a gateway mechanism can then be effective in a segment that appears to increase over time. This is potentially alarming.

However, we do not know how many users started to smoke because of their experience with snus – that is, whether snus use is a causal reason for starting to smoke (CT-1a in Table 1). Some studies show that young people who are

using snus have an increased statistical probability of subsequent smoking (Grøtvedt et al., 2019; Grøtvedt et al., 2013; Joffer et al., 2014; Lund & Scheffels, 2014 – if snus debut took place before the age of 15 years). It is, however, uncertain whether this can actually be attributed to their previous use of snus or whether it is because snus users also have characteristics that predispose them to smoking onset - often referred to as the common liabilities hypothesis (Kim & Selya, 2019). Examples of underlying characteristics that dispose to both smoking and snus are involvement in other sorts of risk behaviour (truancy, early sexual debut, shoplifting, binge-drinking etc.) or certain personality traits (such as impulsiveness or sensation-seeking behaviour).

However, research on snus as a risk factor for smoking onset is not unambiguous. Other studies have not found any statistical association (Galanti et al., 2008; Larsen et al., 2012), and some have found that snus reduces the likelihood of smoking onset (Furberg et al., 2005; Lund & Scheffels, 2014 – if snus debut took place after the age of 15 years; Ramström et al., 2016; Ramström & Foulds, 2006).

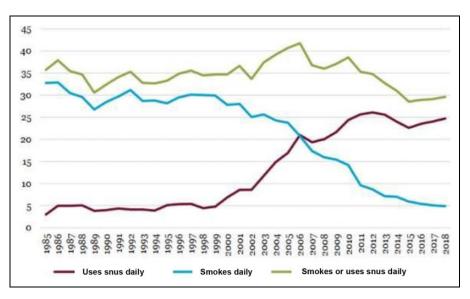


Figure 6. Percentage who smoke and use snus on a daily basis, and the proportion who use snus or smoke on a daily basis among men in the age group 16–24 years in the period 1985–2017. Three-year moving average. Age-standardised numbers (reference year 2017). Source: NIPH (2019, p. 45).

Moreover, some might have started smoking in a hypothetical absence of access to snus – often referred to as *the diversion hypothesis*. In this case, snus will have had a positive effect on the public health balance (CT-2 in Table 1).

Thus, the use of snus may both increase the risk of smoking onset for some (gateway) and protect against smoking onset for others (diversion). In order to confidently claim that snus is a causal cause of smoking, we will need to show that these persons would not have started smoking if it had not been for their previous experience with snus. Correspondingly – if snus is a causal cause of reduced smoking onset, we must show that these persons would have started smoking even if they had not started using snus (see, e.g., Kim & Selya, 2019; Philips, 2015; Vanyukov et al., 2012; Vedøy, 2016 for a more detailed discussion of the abstinence hypothesis, the gateway hypothesis, the diversion hypothesis and the common liabilities hypothesis).

Yet, even if a gateway mechanism exists, it is not reflected in ecological data at the aggregated level. The Figures 6 and 7 show that the proportion of smokers among young adults has declined at the same time as the proportion of snus users has increased. The inverse correlation between snus use and smoking seems to occur approximately from the year 2000. Thus, the figures can be interpreted in support of the diversion hypothesis, postulating that snus use could have a preventive effect that deters combustible tobacco cigarette use. For "high-risk" youth with a disposition toward risk-taking behaviour (e.g., impulsive personality, novelty-seeking tendency) who are susceptible to smoking initiation, snus may provide a diversion that prevents them from experimenting with harmful combustible tobacco products (Etter, 2017; Kozlowski & Warner, 2017). Because some youth possess an elevated drive to engage in exploratory and risk-taking behaviour, the availability of snus allows such young people to satisfy their curiosity and drive for novelty seeking without needing to resort to combustible tobacco products to satisfy the desire for exploration.

Figures 6 and 7 do not conclusively prove a diversion effect, but they do show that

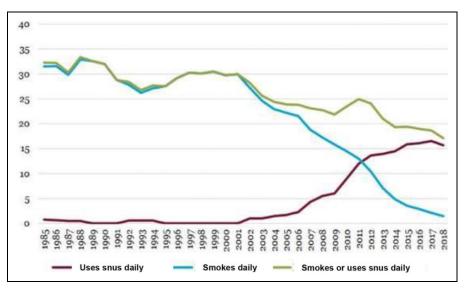


Figure 7. Percentage who smoke and use snus on a daily basis, and the proportion who use snus or smoke on a daily basis among women in the age group 16–24 years in the period 1985–2017. Three-year moving average. Age-standardised numbers (reference year 2017).

Reference: NIPH (2019, p. 46).

population-level trends are much better explained by a net diversion effect, and are very inconsistent with a net catalyst effect. Recently, this was also observed for the trends in e-cigarette use among young persons in the US (Selya & Foxon, 2021).

Absolute risk of snus

In the comprehensive report *Health risks from* snus use (NIPH, 2019), the main focus was to identify the difference in harm between using snus and not using any form of tobacco – that is, the absolute risk. Knowledge from several kinds of biomedical studies was compiled: health risk evaluations of the contents of snus (toxicological studies), how these substances affect animals in experimental studies (e.g., cytological studies), which acute physiological reactions are activated in humans from snus use (clinical studies) and studies comparing development of diseases among snus users and persons who do not use tobacco (epidemiological studies). The report could not detect any

correlation between snus and cancer in organs with direct exposure such as the oral cavity and throat. Still, compared to persons who remain tobacco-free, the report concluded that persons who use snus were likely to have an increased risk of oesophageal and pancreatic cancer. Moreover, high blood pressure, increased mortality in the aftermath of a heart attack or stroke, type 2 diabetes when consuming more than four boxes per week, and risk of premature birth among pregnant women were also likely negative outcomes from snus use. For a number of other health consequences, the report concluded that there was a possible increased risk from snus use. This concerned gastric and rectal cancer, increased mortality after a cancer diagnosis, reduced vascular cell function and reduced diastolic function, risk of non-affective psychosis, risk of increased weight and obesity, as well as risk of stillbirths, reduced birth weight, C-section, short-term respiratory arrest and lip/palate defects in new-borns.

Thus, non-smokers who start using snus must therefore anticipate a certain risk for some

outcomes, and smokers who replace cigarettes with snus can still not expect a totally risk-free use of tobacco.

Risk-difference between snus use and smoking

In the NIPH report, the health risk from snus use was not compared with the risks from smoking. However, several international publications have discussed different nicotine products along a risk continuum, and emphasise that the most important factor is whether the tobacco product is combusted or not, and that the differences in risk between combustion-free nicotine products will be very small in comparison (British Medical Association (BMA), 2018; Cancer Research UK (CRUK)/Royal College of General Practitioners (RCGP), 2017; Gottlieb & Zeller, 2017; Institute of Medicine, 2001; McNeill et al., 2018; NASEM, 2018; Public Health England, 2015; Royal College of Physicians (RCP), 2016; US Department of Health and Human Services, 2014).

The Royal College of Physicians (RCP, 2007) describe the difference in harm between snus and cigarettes as follows:

On toxicological and epidemiological grounds, some of the Swedish smokeless products appear to be associated with the lowest potential for harm to health.... Therefore, in relation to cigarette smoking, the hazard profile of the lower risk smokeless products is very favourable. (p. 161)

... for most of the major health effects of tobacco, smoking is many times more dangerous than smokeless tobacco use. (p. 156)

The large risk difference between snus and cigarettes has been emphasised in systematic reviews (Broadstock, 2007; FDA, 2019; Roth et al., 2005; Scientific Committee on Emerging and Newly Identified Health Risks (SCE-NIHR), 2008) and in recent population studies (Fisher et al., 2019; Rodu & Plurphanswat, 2019).

The magnitude of the risk difference between smoking and snus use will vary for different diseases. The use of snus is neither associated with lung cancer or respiratory diseases, conditions which together are responsible for half of all smoking-related deaths (NIPH, 2011). Nor does there appear to be any evidence that snus use increases the risk of developing cardiovascular diseases, which is the second main group of smoking-related deaths. On the other hand, studies indicate an increased risk of sudden death among those who already have a heart disease. For some other diseases, such as diabetes or pancreatic cancer, the differences in the increased risk between snus use and smoking are assumed to be smaller, but since these conditions are far less common, they also play a smaller part in an overall assessment. If snus primarily reduced the risk of diseases smokers rarely got anyway, the health benefit of switching would be minimal. Because use of snus eliminates the risk of major and central causes of death resulting from smoking, the harm reduction appears to be a real opportunity to improve the population's health.

Two scientific committees have estimated that the aggregated degree of harm from snus use was 5% (Nutt et al., 2014) and 10% (Levy et al., 2004), respectively, when compared to the harms from smoking. The aggregated degree of harm was assessed based on an estimate of the difference in harm between snus use and smoking for a number of individual diseases, combined with the importance of each of these diseases for the total smoking-attributed mortality.

An authoritative confirmation on the difference in harm between snus use and smoking was received in an announcement by the FDA in October 2019. After a long-last processing (four years) and extensive analysis of the health risk for the products, the FDA stated that eight snus products of the type which is common in Scandinavia should be given the status of a so-called modified risk tobacco product (MRTP). This meant that a manufacturer (Swedish

Match) for the first time was granted the right to market a tobacco product as a harm-reducing alternative to cigarettes. The FDA (2019) announced in their press release that this applied to typical smoking diseases such as cancer in the oral cavity, lung cancer, stroke, emphysema and chronic bronchitis.

Based on data from the Global Burden of Disease Study, Ramström (2020a) showed that tobacco-related mortality in Swedish men, who consume most tobacco as snus, was lower than men in any other EU country where to the tobacco normally is smoked. This was the case in spite of the fact that the per capita consumption was similar.

Overall, it seems to be a medical consensus that the difference in harm (relative risk) between snus use and smoking is large. Thus, smokers who switch from cigarettes to snus can expect a large health benefit, while snus users who switch from snus to cigarettes (gateway) can expect a large health deterioration.

Use-and-risk equilibrium

The importance of snus for the population's health will thus be a result of a complex interaction of tobacco-use patterns among different groups of snus users, the relative size of these groups and the health benefit or health deterioration that these groups will experience under different regulatory regimes. However, even for an established product such as snus, we must acknowledge that we do not have all the information needed to fully assess the public health balance. We have, i.a., a limited possibility of identifying previous product trajectories among tobacco users and nearly no possibility of uncovering the causal role that snus may have had in transitions between different usage patterns.

Even though important data are missing, it is still possible to outline some probable outcomes from a public health assessment of snus use in Norway. An appropriate starting point is to use a use-and-risk equilibrium (Kozlowski et al., 2001) where we pose the question: Given

Table 2. Conditions of use between smokers and non-smokers that will result in snus having as large negative as positive consequences for public health given different levels of harm when using snus compared to smoking.

Degree of damage from snus in relation to cigarettes (percentage)	Number of people choosing snus instead of cigarettes	Number of nicotine-free people needed to start using snus to equalise the health benefit
1	1	100
2	1	50
5	1	20
10	1	10
15	1	6.7
20	1	5
25	I	4

different levels of degree of harm for snus compared to cigarettes, how many nicotine-free persons must start using snus to equalise the health benefit of each person who chooses snus instead of cigarettes? This is illustrated in Table 2.

If, as a starting point, we set the degree of harm from snus to approximately 5% of the degree of harm from cigarettes (column 1), the health benefit of snus will be positive as long as there are fewer than 20 non-smokers starting with snus (column 3) for each person who chooses snus instead of cigarettes (column 2). We have previously referred to expert groups who believe that the true level of harm for snus relative to cigarettes is probably somewhere between 5% and 10%. Given that snus should amount to 10% of the degree of harm from cigarettes, the net public health effect according to the table will only be negative if more than 10 non-smokers start using snus for each smoker who switches to snus, and would otherwise have continued smoking.

Data from Norway indicate that the proportion that switches from smoking to snus is probably higher than the proportion that started with snus without previous smoking. Figures 4 and 5 showed that non-smokers have been a *minority*

among snus users. Given the current knowledge about (the moderate), (i) health damages from snus use (absolute risk), (ii) the estimates on the harm difference between snus use and smoking (relative risk), and (iii) the compositions of the snus users by smoking status (the user pattern), it is likely that access to snus has generated a net gain to public health over the past decades. This is because the total number of persons who have quit smoking or reduced their cigarette consumption with snus has likely been higher than the total number of persons who have started with snus without previous experience with smoking. The health benefit of tobacco substitution has probably been greater than the health deterioration affecting the proportion of snus users assuming they would have been tobacco-free if snus had not been available on the market in Norway. This conclusion harmonises with observations from Sweden (Ramström et al., 2016), a modelling performed by Australian researchers (Gartner et al., 2007) and being in line with what was claimed by the aforementioned expert group appointed by the EU (SCENIHR, 2008, p. 116):

In northern Sweden, the availability of snus and the way in which it has been used may have been beneficial to public health since the harm to health caused by any use of snus as a gateway into smoking may have been more than outweighed numerically by the numbers quitting smoking for snus.

In fact, Ramström et al. (2016) set out for a more stringent evaluation of this balance based on data on the relative number of snus users with potential positive and potential negative pathways. In their original paper, the authors identified 13 pathways of transition from one status of tobacco use to another. In October 2020, a specifically edited description of these pathways showed that 15% of the respondents were on pathways in which snus may have been harmful, while 74% were on pathways in which snus may have been beneficial (Ramström, 2020b).

From positive to negative public health effect?

Although the net effect of snus use has probably been positive for public health up until now, this will not necessarily be the case in the future. As the proportion of smokers in the population decreases, snus' role as a therapeutic substitute to cigarettes will diminish. With reduced smoking prevalence, there will be fewer smokers to aid with snus. Moreover, as smoking becomes increasingly de-normalised in society, cigarettes as a distinction marker for trendiness among youth will fade. At this point, snus will also lose its role as an alternative tobacco product that can divert youth away from cigarettes.

With declining smoking prevalence, the most important reservoir of potential snus users – smokers - will shrink. This may in turn contribute to a reduction in the prevalence of snus users, and thereby reduced overall tobacco consumption. Another consequence from declining smoking might be that the relative proportion of non-smokers will continue to increase at the expense of the proportion using snus as a substitute or alternative product to cigarettes. Such a shift may - if it becomes large enough - tilt the public health effect of snus in a negative direction. Thus, the framework has to be dynamic, in the sense that it has to take into account that the relative composition of smokers and nonsmokers in the user group of new nicotine products may change over time.

Limitations

In this article, we have presented a framework that may guide an assessment of the health-related benefits and disadvantages of various forms of market access and regulation of nicotine products. The framework is only intended to consider consequences on narrowly understood medical outcomes, i.e., medical conditions and mortality risk. We acknowledge that there are wider definitions of health that include both physical, mental and social welfare. We

share the view that a comprehensive evaluation of a political change should also consider these broader outcomes – as well as additional non-medical conditions, e.g., related to dependency and autonomy.

Furthermore, weighting implies that different population groups are assessed against each other, which raises the question whether certain groups should be considered to be more important than others. Policies that help one demographic group can harm another. Some may argue that the negative consequences of nicotine use among young non-smokers should be regarded as especially important, given their life expectancy. Others would argue that the positive consequences of replacing cigarettes with presumed less dangerous products among smokers should be emphasised, because smoking is more prevalent in groups with lower socioeconomic status, and because smokers are a vulnerable group and at increased risk for many diseases. Discussing prioritisation of different population groups has been outside the scope of our paper.

Opponents of the weighting principle claim that the tobacco industry will utilise the identification of beneficial usage patterns for nicotine products for propaganda purposes. In addition, some fear that the self-imposed transformation of the tobacco industry from cigarettes to noncombustible nicotine products may be a bluff (Daube et al., 2017). Within the tobacco control movement, the weighting principle meets additional resistance from those who pursue a totally nicotine-free society. This goal, in turn, reflects an absolutist/prohibitionist mindset that rules out use of any non-pharmaceutical nicotine product for tobacco harm reduction (Fugelli, 2005). Thus, there is little acceptance of a perspective where certain patterns of use are considered to give a positive contribution in the context of public health. In this article we do not address these questions.

Conclusion

Our primary objective has been to launch a framework that may be used to identify and

assess desired and undesirable consequences of various types of market regulations of new nicotine products such as e-cigarettes, tobaccofree snus and combustion-free cigarettes. We encourage the authorities to use a weighting principle when drawing up regulations for market access for these products. Exclusive use of the non-harm principle, the absence of autonomy principle and the precautionary principle – which until now have been the basis for much of the tobacco control policy - should, in our opinion, be supplemented with an approach that weighs advantages against disadvantages from various regulatory alternatives in a more holistic context. The main elements of the weighing procedure are information about the absolute risk of the products, their relative risk compared to conventional cigarettes and their user composition. Input on risk will have to be retrieved from medical studies – epidemiological or toxicological – while input on user composition and user careers must be retrieved from population surveys. There will be uncertainty related to these data, but this is not sufficient for rejecting the weighing principle as an approach. The use of an explicit framework highlights various ways in which a political decision can affect nicotine use and health-related outcomes. It breaks down a large and complex question into smaller pieces and requires us to state the assumptions for each element. This makes it easier to investigate what kind of evidence is used as a basis for tobacco control policies.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Karl Erik Lund https://orcid.org/0000-0002-4015-1167

References

- Bjartveit, K., & Tverdal, A. (2005). Health consequences of smoking 1–4 cigarettes per day. *Tobacco Control*, *14*(5), 315–320. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1748107/https://doi.org/10.1136/tc.2005.011932
- British Medical Association (BMA). (2018). *Ecigarettes: Balancing risks and opportunities. A position paper*. BMA. https://www.bma.org.uk/collective-voice/policy-and-research/public-and-population-health/tobacco/e-cigarettes https://www.bma.org.uk/media/2083/e-cigarettes-position-paper-v3.pdf
- Broadstock, M. (2007). Systematic review of the health effects of modified smokeless tobacco products. *New Zealand Health Technology Assessment Report*, 10(1), 1–129. http://nzhta.chmeds.ac.nz/publications/smokeless_tobacco.pdf
- Cancer Research UK (CRUK)/Royal College of General Practitioners (RCGP). (2017). Position statement on the use of electronic nicotine vapour products (e-cigarettes). Cancer Research UK. https://www.cancerresearchuk.org/sites/default/files/rcgp_e-cig_position_statement_approved_060917_clean_copy.pdf
- Cherng, S. T., Tam, J., Christine, P. J., & Meza, R. (2016). Modeling the effects of e-cigarettes on smoking behavior: Implications for future adult smoking prevalence. *Epidemiology*, 27(6), 819–826. https://doi.org/10.1097/EDE. 0000000000000000497
- Daube, M., Moodie, R., & McKee, M. (2017). Towards a smoke-free world? Philip Morris International's new Foundation is not credible. *Lancet*, 390(10104), 1722–1724. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17) 32561-8/fulltext https://doi.org/10.1016/s0140-6736(17)32561-8
- Etter, J. F. (2017). Gateway effects and electronic cigarettes. *Addiction*, *113*(10), 1776–1783. 10.1111/add.13924.
- Fisher, M. T., Tan-Torres, S. M., Gaworski, C. L., Black, R. A., & Sarkar, M. A. (2019). Smokeless tobacco mortality risks: An analysis of two contemporary nationally representative longitudinal

- mortality studies. *Harm Reduction Journal*, *16*(1), 27. https://doi.org/10.1186/s12954-019-0294-6
- Folkehelseinstituttet (NIPH). (2011). Hvor dødelig er røyking? Beregninger for 2009. Oppdatering av tabell A2 [How Deadly is Smoking? Calculations for 2009. Update of table A2], FHI rapport 2006:4. https://www.fhi.no/publ/eldre/hvor-dode lig-er-royking-rapport-om-/
- Folkehelseinstituttet (NIPH). (2018, 19 June). Tobakkmarkedets sammensetning og endring [Composition and change of the tobacco market.]. https://www.fhi.no/nettpub/tobakkinorge/bruk-av-tobakk/tobakkmarkedets-sammenset ning-og-endring/
- Folkehelseinstituttet (NIPH). (2019, 9 October). *Helserisiko ved snusbruk* [Health risk from snus use]. Nettrapport. https://www.fhi.no/nyheter/2019/helserisiko-ved-snus/
- Food and Drug Administration (FDA). (2019, 22 October). FDA grants first-ever modified risk orders to eight smokeless tobacco products. FDA. https://www.fda.gov/news-events/press-announcements/fda-grants-first-ever-modified-risk-orders-eight-smokeless-tobacco-products
- Fugelli, P. (2005). *0-Visjonen. Essays om helse og frihet* [The 0-Vision. Essays on health and freedom]. Universitetsforlaget. ISBN: 9788215009407
- Furberg, H., Bulik, C. M., Lerman, C., Lichtenstein, P., Pedersen, N. L., & Sullivan, P. F. (2005). Is Swedish snus associated with smoking initiation or smoking cessation? *Tobacco Control*, 14(6), 422–424. https://doi.org/10.1136/tc.2005.012476
- Galanti, M. R., Rosendahl, I., & Wickholm, S. (2008).
 The development of tobacco use in adolescence among "snus starters" and "cigarette starters":
 An analysis of the Swedish "BROMS" cohort.
 Nicotine & Tobacco Research, 10(2), 315–323.
 https://doi.org/10.1080/14622200701825858
- Gartner, C., Hall, W. D., Vos, T., Bertram, M. Y., Wallace, A. I., & Lim, S. S. (2007). Assessment of Swedish snus for tobacco harm reduction: An epidemiological modelling study. *The Lancet*, 369(9578), 2010–2014. https://doi.org/10.1016/ s0140-6736(07)60677-1

- Gharib, S. (2020, 30 January). Philip Morris CEO aims for a "smoke-free future". *Fortune*. https://fortune.com/2020/01/30/philip-morris-ceo-aims-for-a-smoke-free-future-the-faster-the-better/
- Gottlieb, S., & Zeller, M. (2017). A nicotine-focused framework for public health. *New England Journal of Medicine*, 377(12), 1111–1114. https://doi. org/10.1056/NEJMp1707409
- Grøtvedt, L., Forsén, L., Ariansen, I., Graff-Iversen, S., & Lingaas Holmen, T. (2019). Impact of snus use in teenage boys on tobacco use in young adulthood: A cohort from the HUNT Study Norway. *BMC Public Health*, 19(1), Article 1265. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6743150/ https://doi.org/10.1186/s12889-019-7584-5
- Grøtvedt, L., Forsén, L., Stavem, K., & Graff-Iversen, S. (2013). Patterns of snus and cigarette use: A study of Norwegian men followed from age 16 to 19. *Tobacco Control*, 22(6), 382–388. https://www.ncbi.nlm.nih.gov/pubmed/22634571 https://doi.org/10.1136/tobaccocontrol-2011-050158
- Helse- og omsorgsdepartementet (HOD). (2015). Folkehelsemeldingen. Mestring og muligheter (Meld. St. 19 (2014–2015) [Public health reports. Mastery and opportunities]. Regjeringen. https://www.regjeringen.no/no/dokumenter/meld.-st.-19-2014-2015/id2402807/
- Hill, A., & Camacho, O. M. (2017). A system dynamics modelling approach to assess the impact of launching a new nicotine product on population health outcomes. *Regulatory Toxicol*ogy and *Pharmacology*, 86, 265–278. https://doi. org/10.1016/j.yrtph.2017.03.012
- Institute of Medicine. (2001). Clearing the smoke:

 Assessing the science base for tobacco harm reduction. The National Academies Press. https://www.nap.edu/read/10029/chapter/1
- Joffer, J., Burell, G., & Bergström, E. (2014). Predictors of smoking among Swedish adolescents. BMC Public Health, 14, 1296. https://doi.org/10.1186/1471-2458-14-1296
- Kalkhoran, S., & Glantz, S. A. (2015). Modeling the health effects of expanding e-cigarette sales in the United States and United Kingdom: A Monte Carlo analysis. *JAMA Internal Medicine*,

- 175(10), 1671–1680. https://doi.org/10.1001/jamainternmed.2015.4209
- Kim, S., & Selya, A. S. (2019). The relationship between electronic cigarette use and conventional cigarette smoking is largely attributable to shared risk factors. *Nicotine & Tobacco Research*, Article ntz157. https://doi.org/10.1093/ntr/ntz157
- Kozlowski, L. T., Strasser, A. A., Giovino, G. A., Erickson, P. A., & Terza, J. V. (2001). Applying the risk/use equilibrium: Use medicinal nicotine now for harm reduction. *Tobacco Control*, 10(3), 201–203. https://doi.org/10.1136/tc.10.3.201
- Kozlowski, L. T., & Warner, K. E. (2017). Adolescents and e-cigarettes: Objects of concern may appear larger than they are. *Drug and Alcohol Dependence*, 174, 209–214.
- Larsen, E., Rise, J., & Lund, K. E. (2012). The relationship between snus use and smoking cognitions. Addiction Research & Theory, 20(6), 447–455. https://doi.org/10.3109/16066359. 2012.665521
- Lee, P. N. (2013). The effect on health of switching from cigarettes to snus: A review. *Regulatory Toxicology and Pharmacology*, 66(1), 1–5. https://doi.org/10.1016/j.yrtph.2013.02.010
- Lee, P. N., Fry, J. S., Hamling, J. F., Sponsiello-Wang, Z., Baker, G., & Weitkunat, R. (2017). Estimating the effect of differing assumptions on the population health impact of introducing a reduced risk tobacco product in the USA. Regulatory Toxicology and Pharmacology, 88, 192–213. https://doi.org/10.1016/j.yrtph.2017.06.009
- Levy, D. T., Borland, R., Villanti, A. C., Niaura, R., Yuan, Z., Zhang, Y., Meza, R., Holford, T. R., Fong, G. T., Cummings, K. M., & Abrams, D. B. (2017). The application of a decision-theoretic model to estimate the public health impact of vaporized nicotine product initiation in the United States. *Nicotine & Tobacco Research*, 19(2), 149–159. https://doi.org/10.1093/ntr/ ntw158
- Levy, D. T., Cummings, K. M., Villanti, A. C., Niaura, R., Abrams, D. B., Fong, G. T., & Borland, R. (2017). A framework for evaluating the public health impact of e-cigarettes and other

vaporized nicotine products. *Addiction*, *112*(1), 8–17. https://doi.org/10.1111/add.13394

- Levy, D. T., Munford, E. A., Cummings, M., Gilpin, E. A, Giovino, G., Hyland, A., Sweanor, D., & Warner, K. E. (2004). The relative risks of a low-nitrosamine smokeless tobacco product compared with smoking cigarettes: Estimates of a panel of experts. *Cancer Epidemiology, Biomarkers & Prevention*, 13(12), 2035–2042. http://cebp.aacrjournals.org/content/13/12/2035
- Lund, I., & Christiansen, S. G. (2020). Association between snus use over time and smoking cessation in Norwegian smokers. *Addiction*, 115(1), 170–174. https://doi.org/10.1111/add.14809
- Lund, I., & Lund, K. E. (2014). How has the availability of snus influenced cigarette smoking in Norway? International Journal of Environmental Research and Public Health, 11(11), 11705–11717. https://doi.org/10.3390/ijerph111111705
- Lund, I., & Scheffels, J. (2014). Smoking and snus use onset: Exploring the influence of snus debut age on the risk for smoking uptake with cross-sectional survey data. *Nicotine & Tobacco Research*, 16(6), 815–819. https://doi.org/10.1093/ntr/ntu001
- Lund, K. E., Scheffels, J., & McNeill, A. (2010). The association between use of snus and quit rates for smoking: Results from seven Norwegian crosssectional studies. *Addiction*, 106(1), 162–167. https://doi.org/10.1111/j.1360-0443.2010.03122.x
- Lund, K. E., Vedøy, T. F., & Bauld, L. (2017). Do never smokers make up an increasing share of snus users as cigarette smoking declines? Changes in smoking status among male snus users in Norway 2003–15. Addiction, 112(2), 340–348. https://doi.org/10.1111/add.13638
- McNeill, A., Brose, L. S., Calder, R., Bauld, L., & Robson, D. (2018). Evidence review of e-cigarettes and heated tobacco products 2018. A report commissioned by Public Health England. Public Health England. https://www.gov.uk/government/publications/e-cigarettes-and-heated-tobacco-products-evidence-review/evidence-review-of-e-cigarettes-and-heated-tobacco-products-2018-executive-summary#authors-and-citation

- National Academies of Sciences, Engineering, and Medicine (NASEM). (2018, 23 January). 19, Modeling of e-cigarette use. In Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Review of the Health Effects of Electronic Nicotine Delivery Systems; Eaton DL, Kwan LY, & Stratton K (Eds.), *Public health consequences of e-cigarettes*. National Academies Press (US). https://www.ncbi.nlm.nih.gov/books/NBK507162/
- Nutt, D. J., Phillips, L. D., Balfour, D., Curran, H. V., Dockrell, M., Foulds, J., Fagerstrom, K., Letlape, K., Milton, A., Polosa, R., Ramsey, J., & Sweanor, D. (2014). Estimating the harms of nicotine-containing products using the MCDA approach. *European Addiction Research*, 20(5), 218–225. https://doi.org/10.1159/000360220
- Phillips, C. V. (2015). Gateway effects: Why the cited evidence does not support their existence for low-risk tobacco products (and what evidence would). *International Journal of Environmental Research and Public Health*, *12*(5), 5439–5464. https://doi.org/10.3390/ijerph120505439
- Public Health England (PHE). (2015, 15 September). E-cigarettes: An emerging public health consensus. Joint statement on e-cigarettes by Public Health England and other UK public health organisations. https://www.gov.uk/government/news/e-cigarettes-an-emerging-public-health-consensus
- Ramström, L. (2020a). *Tobacco-related mortality Sweden & EU: Easier readable charts*. Researchgate. https://www.researchgate.net/publication/345643346_Tobacco-related_mortality_SwedenEU_easier_readable_charts?channel=doi&linkId=5fa9c 1ad458515157bf7823f&showFulltext=true DOI: 10.13140/RG.2.2.29008.12806
- Ramström, L. (2020b). Pathways of transition from one status of tobacco use to another, men in Sweden (n = 28,302). Researchgate. https://www.researchgate.net/publication/344397311_Pathways_of_transition_from_one_status_of_tobacco_use_to_another_men_in_Sweden_n_28302?channel=doi&linkId=5f709114299bf1b53ef74996&showFulltext=true
- Ramström, L., Borland, R., & Wikmans, T. (2016).

 Patterns of smoking and snus use in Sweden:
 Implications for public health. *International*

- Journal of Environmental Research and Public Health, 13(11), 1110. https://doi.org/10.3390/ijerph13111110
- Ramström, L. M., & Foulds, J. (2006). Role of snus in initiation and cessation of tobacco smoking in Sweden. *Tobacco Control*, 15(3), 210–214. https://doi.org/10.1136/tc.2005.014969
- Rodu, B., & Plurphanswat, N. (2019). Mortality among male smokers and smokeless tobacco users in the USA. *Harm Reduction Journal*, 16, Article 50. https://doi.org/10.1186/s12954-019-0321-7
- Roth, H. D., Roth, A. B., & Liu, X. (2005). Health risks of smoking compared with Swedish snus. *Inhalation Toxicology*, 17(13), 741–748. https:// doi.org/10.1080/08958370500224698
- Royal College of Physicians (RCP). (2007, October). Harm reduction in nicotine addiction: Helping people who can't quit. A report by the Tobacco Advisory Group of the Royal College of Physicians. https://shop.rcplondon.ac.uk/products/harm-reduction-in-nicotine-addiction-helping-people-who-cant-quit?variant=6509405637
- Royal College of Physicians (RCP). (2016, 28 April). *Nicotine without smoke: Tobacco harm reduction*. RCP. https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction-0
- Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). (2008, 6 February). Scientific opinion on the health effects of smokeless tobacco products. https://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_013.pdf
- Selya, A. S., & Foxon, F. (2021). Trends in electronic cigarette use and conventional smoking: Quantifying a possible "diversion" effect among US adolescents. *Addiction*, PMID 33394529. Advance online publication. 10.1111/add.15385.
- Soneji, S. S., Sung, H. Y., Primack, B. A., Pierce, J. P., & Sargent, J. D. (2018). Quantifying population-level health benefits and harms of e-cigarette use in the United States. *PLoS ONE*,

- 13(3), Article e0193328. https://doi.org/10.1371/journal.pone.0193328
- US Department of Health and Human Services. (2014). *The health consequences of smoking–50 years of progress: A report of the Surgeon General*. Centers for Disease Control and Prevention (US). https://doi.org/10.1037/e510072014-001 https://www.surgeongeneral.gov/library/reports/50-years-of-progress/index.html
- Vanyukov, M. M., Tarter, R. E., Kirillova, G. P., Kirisci, L., Reynolds, M. D., Kreek, M. J., Conway, K. P., Maher, B. S., Iacono, W. G., Bierut, L., Neale, M. C., Clark, D. B., & Ridenour, T. A. (2012). Common liability to addiction and "gateway hypothesis": Theoretical, empirical and evolutionary perspective. *Drug and Alcohol Dependence*, 123(Suppl 1), S3–S17. https://doi.org/10.1016/j.drugalcdep.2011.12.018
- Vedøy, T. F. (2016). Fra snus til rus fordom eller fakta? [From snus to abuse – prejudice or fact?] *Tidsskrift for Den norske legeforening*, 136(6), 544–546. https://tidsskriftet.no/2016/04/kronikk/ fra-snus-til-rus-fordom-eller-fakta https://doi. org/10.4045/tidsskr.15.0737
- Vugrin, E. D., Rostron, B. L., Verzi, S. J., Brodsky, N. S., Brown, T. J., & Choiniere, C. (2015). Modeling the potential effects of new tobacco products and policies: A dynamic population model for multiple product use and harm. *PLoS ONE*, 10(3), Article e0121008. https://doi.org/10.1371/journal.pone.0121008
- Warner, K. E., & Mendez, D. (2019). E-cigarettes: Comparing the possible risks of increasing smoking initiation with the potential benefits of increasing smoking cessation. *Nicotine & Tobacco Research*, 21(1), 41–47. https://doi.org/10.1093/ntr/nty062
- Weitkunat, R., Lee, P. N., Baker, G., Sponsiello-Wang, Z., González-Zuloeta Ladd, A. M., & Lüdicke, F. (2015). A novel approach to assess the population health impact of introducing a modified risk tobacco product. *Regulatory Toxicology and Pharmacology*, 72(1), 87–93. https://doi.org/10.1016/j.yrtph.2015.03.011