

Review

Does Dual Use Jeopardize the Potential Role of Smokeless Tobacco in Harm Reduction?

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Abstract

Introduction: The use of smokeless tobacco as part of a strategy to reduce the harm from cigarette smoking is a topic of debate within the tobacco control and public health communities. One concern voiced regarding endorsement of such a tactic is the possibility of actually increasing harm should current smokers adopt dual cigarette/smokeless tobacco use (dual use), which could lead to unintended consequences by perpetuating cigarette smoking, diminishing tobacco cessation, or increasing tobacco-related harm.

Methods: Here, we review the available literature on health effects and trajectories of use among dual users from a variety of U.S. and European epidemiological studies.

Results: These data suggest that there are not any unique health risks associated with dual use of smokeless tobacco products and cigarettes, which are not anticipated or observed from cigarette smoking alone. Furthermore, studies show that dual users smoke fewer cigarettes than exclusive smokers, and studies of tobacco use patterns over time (tobacco use trajectory data) indicate that dual users are more likely than exclusive cigarette smokers to cease smoking.

Conclusions: Overall, the concern about dual use appears to be contradicted by the evidence in the literature that dual use of smokeless tobacco and cigarettes may result in reduction in smoking-related harm as smoking intensity is decreased and smoking cessation increases.

Introduction

Several thought provoking reviews and commentaries on the public health implications of placing smokeless tobacco within a harm-reduction strategy has recently been published (Gartner, Hall, Chapman, & Freeman, 2007; Hall & Gartner, 2009; Savitz, Meyer, Tanzer, Mirvish, & Lewin, 2006; Zeller & Hatsukami, 2009). Frequently, these articles raise questions regarding what effect the use of smokeless tobacco may have on the success

of smoking cessation interventions, what will be the impact of using smokeless tobacco on the amount of smoking among continuing smokers, and how effective might smokeless tobacco be as a path away from cigarette smoking in comparison with pharmaceutical nicotine?

Here, we wish to highlight one area that continues to draw attention when the topic of smokeless tobacco is mentioned in regard to cigarette smoking, namely dual use (Henningfeld, Rose, & Giovino, 2002). These issues have recently moved from the theoretical to the practical in the United States as major tobacco manufacturers have developed and marketed smokeless tobacco products intended for adult smokers (Biener & Bogen, 2009; Parascandola, Augustson, O'Connell, & Marcus, 2009). Furthermore, dual use of smokeless tobacco forms currently in the U.S. market and cigarettes is already noted to occur in the U.S. population (Tomar, Alpert, & Connolly, 2010) so that a discussion of dual use is relevant to both traditional and newer U.S. smokeless tobacco products, such as snus. If smokeless tobacco products appeal to current adult smokers, it is likely that some sort of period of dual use may occur, and a discussion of the implications is necessary. Stated broadly, the issues typically raised regarding dual use of smokeless tobacco and cigarettes center on unique health risks and on the impact on cigarette usage either increased initiation or reduced cessation.

Dual use at this point in time has no established definition. Loosely, it captures that period of time when people will smoke cigarettes concomitantly with the use of smokeless tobacco products. It does not mean simultaneous use of the two tobacco product types but rather subsumes either a transition period from one predominant type to another or a period where people use both products interchangeably without trending toward either product. For smokers switching to smokeless tobacco, this may mean the period where smokeless products are used in place of cigarettes smoked. On the other end of this spectrum is the possibility that smokeless tobacco results in continued cigarette use. Compounding the lack of clarity regarding the definition of "dual use" is the criteria used to capture a "user" since individual investigators have developed individual criteria. For the purposes of this review, we have accepted the definition of

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dual use and dual users as applied by the various authors cited herein.

In this report, we review the published literature related to the interplay between cigarette smoking and smokeless tobacco use over time (trajectories of dual use behavior) and relevant information from epidemiological studies, which provide insights into the relationship between dual use and disease risk as compared with exclusive use of cigarettes or smokeless tobacco. The scope of the review concentrates on the major types of tobacco products sold in North America and Scandinavia, including traditional fermented moist smokeless tobacco products as well as snus products since this is where the wealth of information resides. This information is typically presented as secondary data within epidemiological studies focused primarily on examining associations between smokeless tobacco use and specific disease outcomes. In most of these studies, dual use is not the primary assessment parameter of interest, and in many cases, dual use is not mentioned by the study authors in the article title or abstract. For this reason, traditional key word-searching approaches using databases like PubMed or SCOPUS are not well suited for identifying health effects data related to dual use. We therefore identified relevant studies by reviewing available epidemiological studies investigating associations between smokeless tobacco use and disease outcomes to determine which ones also contained data related to dual use. Using this approach, we identified 17 epidemiological studies containing quantitative data or other qualitative information related to health effects associated with dual use. Disease outcomes investigated in these studies included oral cancer, lung cancer, esophageal and stomach cancer, pancreatic cancer, ischemic heart disease (IHD), gastrointestinal disorders, stroke, myocardial infarction (MI), any cancers, respiratory disease, and all-cause mortality. Similarly, studies are not readily identifiable regarding the longitudinal tobacco use patterns of dual users per se. Therefore, studies that included tobacco use patterns of smokers and smokeless tobacco users were reviewed to identify those that contained data specific to dual users. Although such search methodology may be more stochastic in nature than more typical key word searches, we believe that the studies reviewed regarding both health effects and tobacco use trajectories are representative of the extant data.

What Are the Transitional Patterns and Reasons For Dual Use?

The published data from both the United States and Sweden indicate that most dual users come from the category of exclusive cigarette smokers. Very few people initiate tobacco use with both cigarette smoking and smokeless tobacco use. According to the 2008 National Survey on Drug Use and Health report (Office of Applied Studies, 2008), of those who had used both cigarettes and smokeless tobacco at some point in their life, 65.5% used cigarettes first, 31.8% used smokeless tobacco first, and only 2.7% started out using both cigarettes and smokeless tobacco. One recent U.S. study found that 2.2% of exclusive smokers and 1.8% of exclusive smokeless tobacco users at baseline became dual users at a 1-year follow-up (Zhu et al., 2009). In Sweden, there is a similar pattern of initiating tobacco use with cigarettes alone: 75% of dual users were smokers first (Furberg, Lichtenstein, Pedersen, Bulik, &

Sullivan, 2006), and snus users were significantly less likely to initiate smoking as compared with non-snus users (Ramstrom & Foulds, 2006).

Data from about 3,000 men from the northern Sweden MONICA study, which included population-based surveys conducted in 1986, 1990, 1994, and 1999, were used to develop prevalence estimates of categories of tobacco use and changes over time (Rodu & Phillips, 2008; Rodu, Stegmayr, Nasic, & Asplund, 2002). Between 1986 and 1999 in Sweden, the percentage of men who were smokers was reduced from 23% to 14%. The estimated prevalence of dual use of cigarettes and snus did not grow, but the percentage of men who were snus users increased from 22% to 30% between 1984 and 1999, primarily due to the increase in current snus users who were formerly smokers. Although these data are cross-sectional, it suggests that many male smokers in Sweden used both cigarettes and snus for a period of time before becoming exclusive snus users. Lundqvist, Sandstrom, Ohman, and Weinehall (2009) examined data from 16,486 individuals in the Vasterbotten Intervention program, including a 10-year follow-up study of smoking and snus use. In that study, 7.4% of smokers were dual users at follow-up and 3.2% of snus users were dual users at follow-up. More than 60% of smokers at baseline were smokers at follow-up, while only 4.4% of snus users at baseline were smokers (either exclusively or dual users) at the 10-year follow-up.

People may become dual users for a variety of reasons. Established adult smokers who become dual users may use smokeless products when they cannot smoke or may use it intentionally to reduce or stop smoking (Gilljam & Galanti, 2003; Rodu & Phillips, 2008). Among younger adults, particularly males, use of multiple forms of tobacco may occur through experimentation and therefore be a part of overall risk-taking behavior (Timberlake, Huh, & Lakon, 2009; Wagner, 2001). In a survey of current and former Swedish smokers who ever used snus, the number one reason for using snus, reported by about 20% of those surveyed, was to “help to stop smoking” and 7.1% of those surveyed cited “smoking reduction” (Gilljam & Galanti, 2003). Other reported reasons for using snus included health concerns, use as an alternative to nicotine replacement therapy (NRT), that they were curious, that they found it pleasant, and due to social circumstances (such as smoking restrictions).

Published studies from the United States and Sweden demonstrate that dual users are more likely than exclusive smokers to cease smoking. However, most studies also suggest that dual users may be less likely to become completely tobacco abstinent because of continued use of smokeless tobacco. A recent study in the United States calculated population-weighted rates of switching and quitting smoking after 1-year follow-up and reported that a higher percentage of dual users quit smoking and ceased all tobacco use as compared with exclusive smokers (Zhu et al., 2009). After the follow-up in male dual users, 45% continued to use both, 37% stopped using smokeless and only smoked cigarettes, 4.9% quit smoking but continued smokeless tobacco, and 13% stopped both smoking and smokeless tobacco use (18% smoking cessation rate overall). In contrast, the percentage of male exclusive smokers who quit smoking 1 year later was 11.6%, and the percentage who did not smoke or use smokeless tobacco 1 year later was 11.3%. Continued usage was most stable for exclusive cigarette smoking followed by exclusive

smokeless tobacco use and was least stable for dual users. In another U.S. study, the National Cancer Institute Working Well Trial assessed 4,886 men for tobacco use by survey at baseline and then conducted a follow-up after 4 years (Wetter et al., 2002). At the 4-year follow-up, 28.7% of dual users ceased smoking as compared with 17.1% of exclusive smokers at baseline who ceased smoking. At follow-up, 11.3% of baseline dual users were tobacco abstinent, while 15.7% of exclusive smokers discontinued all tobacco use. Almost 80% of exclusive smokers continued to exclusively smoke, while only 27% of dual users became exclusive smokers. For both of the above studies, demographic variables typically associated with reduced likelihood of smoking cessation were more prevalent among the category of dual users (Agrawal, Sartor, Pergadia, Huizink, & Lynskey, 2008).

In Swedish studies that track dual use trajectories over longer periods of time, most dual users reduce or quit smoking and either switch to only smokeless tobacco use or quit all forms of tobacco. Using a 2001–2002 survey of 6,752 adult Swedes, Ramstrom and Foulds (2006) reported that 28% of primary smokers became dual users and subsequently 88% of those who became dual users ceased daily smoking, whereas 56% of smokers who did not use snus ceased daily smoking (Ramstrom & Foulds, 2006). In another Swedish study, those smokers who used snus had statistically significant decreased odds of being a daily cigarette smoker (odds ratio [OR] = 0.67, 95% CI: 0.51–0.87) as compared with those who did not use snus (Lindstrom & Isacson, 2002).

Furberg et al. (2006) used data from the Swedish Twin Registry to estimate tobacco use trajectories for males, which was reconstructed based on reported former and current tobacco habits. Interviews were conducted from 1998 to 2002 and included those who were born between 1935 and 1958 (transition data were estimated for about 14,424 males). Of the 3,083 who transitioned to dual use, 14.3% remained dual users, 7.4% were exclusive smokers, 47.7% were exclusive snus users, and 30.6% did not use any tobacco at the time of the interview. In a separate study that included an 8-year follow-up, 19% of dual users became tobacco abstinent as compared with 23% of smokers (Tillgren, Haglund, Lundberg, & Romelsjö, 1996). However, smoking cessation in this study was much higher among dual users, with 50% of dual users quitting smoking as compared with only 28% of smokers quitting during the 8-year follow-up.

Smokeless tobacco has been reportedly used as a smoking cessation and reduction aid. Ramstrom and Foulds (2006) reported that snus was the most commonly reported smoking cessation aid, reported by 58% of participants in their study (Ramstrom & Foulds, 2006). Sixty-five percent of men who used snus were successful in quitting smoking, while 51% of those who used nicotine gum and 34% of those using the nicotine patch were successful. Fifty-eight percent of women who used snus successfully quit smoking as compared with 34% of those who used nicotine gum and 27% of those who used nicotine patches. Those who used snus in their latest cessation attempt were also more likely than those who used NRT to reduce their smoking from daily to occasionally, and they were least likely to continue daily smoking. Gilljam and Galanti (2003) reported that men who used snus had a statistically significant increased odds of being a former smoker, OR = 1.72 (95% CI: 1.30–2.28) for ever-users, and OR = 1.81 (95% CI: 1.31–2.53) for current snus users, as compared with those who did not use snus.

Another study from Furberg et al. (2005) found that snus use was a statistically significant factor in smoking cessation and reported that smokers who were regular snus users had an age-adjusted odds for smoking cessation of OR = 3.7 (95% CI: 3.3–4.2).

Analysis of U.S. data from the 2000 National Health Interview Survey also suggests that the majority of those who use smokeless tobacco as a smoking cessation method successfully quit smoking (Rodu & Phillips, 2008). The percentage who became former smokers was 73% for those who switched to smokeless tobacco, 64% for those who stopped all at once (most common method), and 34%–35% for those who used nicotine gum or patch. Close to 50% of those who reported using a clinic/program or that they gradually decreased cigarettes were former smokers at the time of the survey. Although smokeless tobacco use is less prevalent in the United States than in Sweden, the available data describing transitional patterns of use between cigarettes and smokeless tobacco are generally concordant among the studies conducted in the two countries.

Are the Health Effects of Smoking Increased By Dual Use?

With the potential for dual use to occur among smokers, it is important to understand the impact of such behavior on tobacco-related disease risk. The U.S. Surgeon General has determined that both cigarettes and smokeless tobacco products are addictive and cause serious diseases. However, a number of national and international health advisory groups have reviewed the scientific evidence and have concluded that use of snus and moist smokeless tobacco products poses a significantly lower risk of lung cancer and chronic obstructive pulmonary disease than cigarette smoking, while recognizing that smokeless tobacco is not risk free (Institute of Medicine, 2001; Royal College of Physicians of London, 2007; Scientific Committee on Emerging and Newly Identified Health Risks, 2008).

Although dual use exists among some tobacco users, the question of disease risk related to dual use is only occasionally addressed in the smoking and smokeless tobacco literature. Even when studies contain data relevant to the analysis of dual use, it may not be discussed in any length by the study authors. The available epidemiological data, however, are useful in assessing disease risk using a weight-of-evidence evaluation. For the purposes of our analysis, risk estimates of exclusive smokers were compared with those of dual users.

Oral Cancer

The risk of oral cancer is often cited in discussions of smokeless tobacco; however, the most recent estimates indicate that risk of oral cancer from the use of smokeless tobacco is less than that from cigarette smoking (Lee & Hamling, 2009). With respect to dual use, Schildt, Eriksson, Hardell, and Magnuson (1998) surveyed 410 patients with oral cancer and 410 matched controls between 1980 and 1989 in Sweden and found that the strongest risk for oral cancer was related to alcohol consumption. Current snuff users who were current or former smokers had no significant increased odds of oral cancer as compared with never users of snuff or tobacco (Table 1).

Table 1. Epidemiological Studies That Included Cancer Risk Estimates For Dual Use Sample Sets

Study	Health effect	Described tobacco use	Risk estimate	
			OR	95% CI
Schildt et al. (1998)	Oral cancer	Never snuff/never-smoker	1	ref
		Never snuff/ex-smoker	0.9	0.6–1.4
		Never snuff/active smoker	1.7	1.1–2.6
		Ex-snuff/never-smoker	1.8	0.9–3.5
		Ex-snuff/ex-smoker	1.6	0.8–3.4
		Ex-snuff/active smoker	3.1	1.4–6.8
		Active snuff/never-smoker	0.7	0.4–1.2
		Active snuff/ex-smoker	0.6	0.3–1.3
		Active snuff/active smoker	1.2	0.6–2.4
Winn et al. (1981)	Oral and pharyngeal cancer		RR	95% CI
		No smoking/no dipping (White race)	1	ref
		No smoking/current dipping (White race)	4.2	2.6–6.7
		Current smoking/no dipping (White race)	2.9	1.8–4.7
		Current smoking/current dipping (White race)	3.3	1.4–7.8
		No smoking/no dipping (Black race)	1	ref
		No smoking/current dipping (Black race)	1.5	0.5–4.8
		Current smoking/no dipping (Black race)	2.6	0.8–8.7
		Current smoking/current dipping (Black race)	3	0.7–13.8
Accortt et al. (2002)	Lung cancer		HR	95% CI
		Nontobacco users	1	ref
		Exclusive smokeless tobacco users	0	
		Exclusive smokers	13.2	4.5–38.2
		Current exclusive smokers	24.7	8.3–73.5
		Former exclusive smokers	7	2.1–23.2
		Current smokeless/smoking	22.6	6.4–80.3
		Current smokeless/current smoking	33.9	8–143.7
	All cancer	Current smokeless/former smoking	9	2–40.8
		Nontobacco users	1	ref
		Exclusive smokeless tobacco users	1	0.3–2.5
		Exclusive smokers	1.3	0.8–2.1
		Current exclusive smokers	1.8	1.1–3.1
		Former exclusive smokers	1	0.5–1.8
		Current smokeless/ever smoking	1.6	0.9–2.7
		Current smokeless/current smoking	2.2	1.2–3.7
		Current smokeless/former smoking	0.9	0.4–1.8
Accortt et al. (2005)	Lung cancer Note: each group compared with nontobacco users		HR	95% CI
		Exclusive smokeless users	0.0	0/8
		Exclusive smokers	13.2	5.5–31.8
	All cancer Note: each group compared with nontobacco users	Combined users	22.3	7.5–66.3
		Exclusive smokeless users	0.8	0.4–1.6
		Exclusive smokers	1.4	0.9–1.9
		Combined users	1.3	0.9–2.0
Zendehdel et al. (2008)	Esophageal adenocarcinoma		RR	95% CI
		Ever-smokers/non snus users	1	ref
	Esophageal squamous cell carcinoma	Ever-smokers/snus use	1	0.6–1.5
		Ever-smokers/non–snus users	1	ref
	Stomach cancer—cardia	Ever-smokers/snus use	0.8	0.6–1.2
		Ever-smokers/non–snus users	1	ref
	Stomach cancer—noncardia	Ever-smokers/snus use	0.9	0.7–1.3
		Ever-smokers/non–snus users	1	ref
Hassan et al. (2007)	Pancreatic cancer		AOR	95% CI
		Smokers/never snuff use	1	ref
		Smokers/ever snuff use	0.7	0.3–1.4

Note. Tobacco use and risk estimates data were extracted from individual study as noted. See indicated reference for additional specific information on study design, sample characteristics, statistical methods, and adjustments. Data considered to be relevant to dual use are marked in bold italics. AOR = adjusted odds ratio; HR = hazards ratio; OR = odds ratio; RR = relative risk.

Even the frequently cited Winn study (Winn et al., 1981), which identified an elevated risk of oral cancer with snuff use in a select population, contains data regarding dual use. In this case-control study involving 255 women with oral and pharyngeal cancer and 502 controls in North Carolina, it was reported that snuff use and the combined effects of alcohol consumption and cigarette smoking were risk factors for oral cancer (actual form of snuff is not defined in this paper, but in a later study by the same authors, it is described as dry snuff). Both Black women and White women who were dual users had a relative risk that was not significantly different than Black women and White women dip-only users or exclusive smokers (overlapping 95% CI; Table 1).

Lung Cancer

Accortt, Waterbor, Beall, and Howard (2002) reported the results of a 20-year mortality follow-up of subjects who took part in the First National Health and Nutrition Examination Survey (NHANES 1) conducted in the United States between 1971 and 1975. While higher hazard ratios (HRs) for lung cancer mortality among male dual users as compared with male exclusive smokers were reported (Table 1), the author concluded that “combined use of smokeless tobacco and cigarettes did not increase overall mortality beyond that expected from use of the individual products.” In a separate publication by the same authors and using the same data, it was concluded that “no synergistic effect was observed between ST (smokeless tobacco) and cigarette smoking among male combined users for the major cancers.” (Accortt, Waterbor, Beall, & Howard, 2005).

Esophageal and Stomach Cancer

In a retrospective cohort study of 336,381 male construction workers in Sweden (surveillance between 1971 and 1993), Zendejdel et al. (2008) found no significant increased relative risk of esophageal cancer (adenocarcinoma or squamous cell carcinoma) or stomach cancer (cardia or noncardia) for those who ever smoked plus used snus as compared with ever-smokers who did not use snus (Table 1). The incidence rates of esophageal and stomach cancers (per 100,000 person years) were the same or slightly lower among those with a history of dual use as compared with those who had ever smoked and never used snus. The point estimates of the relative risk of cancer among the dual use group, as compared with the exclusive smoking group, ranged from 0.8 to 1.0 for the esophageal and stomach cancers.

Pancreatic Cancer

Based on a study by Boffetta, Aagnes, Weiderpass, & Andersen (2005), the International Agency for Research on Cancer has established a causal relationship between smokeless tobacco and pancreatic cancer (International Agency for Research on Cancer, 2007). Regarding dual use, Hassan et al. (2007) calculated adjusted odds ratios of pancreatic cancer for chewing tobacco and snuff among smokers, nonsmokers, and the total population in a hospital-based case-control study of 808 pancreatic adenocarcinoma cases and 808 healthy controls in Texas. Consistent with previous observations, they found an association between active smoking and increased risk for pancreatic cancer. Use of either chewing tobacco or snuff resulted in no further increase in risk for pancreatic cancer among cigarette smokers (Table 1).

Any Cancers, Respiratory Disease, Cardiovascular Disease, All-cause Mortality, and Gastrointestinal Disorders

While data in this area are limited, Roosaar, Johansson, Sandborgh-Englund, Axell, and Nyren (2008) recently reported the results of a cohort of 9,976 men in Sweden who were part of a population-based survey in 1973–1974 with follow-up in January 2002. While not specific to dual use and confounded by classifications of tobacco use, the authors found no increased HR for ever daily snus (ca. 40% of cases had history of ever smoking) for “any cancer” or “smoke-related cancer” compared with never daily snus use (ca. 70% of cases had a history of ever smoking). HR for cancer, respiratory disease, cardiovascular disease, and all-cause mortality were lower among ever snus users (this group included smokers who ever used snus) than among ever-smokers. The HR for respiratory disease among ever daily snus users >80 years of age was similar to the that for ever daily smokers overall.

One small Swedish case-control study reported a “synergistic” relationship for risk of Crohn’s disease and ulcerative colitis among ever oral moist snuff users who were also current cigarette smokers (Persson, Hellers, & Ahlbom, 1993). While neither exclusive smokers nor exclusive moist snuff users were found to have statistically significant elevated relative risk estimates for either Crohn’s disease or ulcerative colitis, among users of both products, the relative risk for Crohn’s disease was estimated to be 3.7 (95% CI: 1.1–13.1) and for ulcerative colitis 3.3 (95% CI: 1.0–10.9). To our knowledge, the reported findings have never been replicated, and there are several factors that challenge the relevance of the results. These issues include a disparate classification status, which precludes an independent assessment of consistency of results or dose-response relationships between the two groups (smokers were classified as “never,” “former,” and “current,” whereas moist snuff users were classified as “never” and “ever” with former and current users combined into the single “ever” classification), and wide CIs, suggesting significant variation and lower bound CI at or close to 1.0.

IHD and Stroke

Haglund, Eliasson, Stenbeck, and Rosen (2007) linked records from the 1988–1989 Survey of Living Conditions with the Swedish hospital Discharge and Cause of Death Registers to evaluate incidence and mortality from IHD and stroke. The study included 5,002 males and covered 14–16 years (follow-up through 2003). The analysis was controlled for age, physical activity, socioeconomic status, and other variables. Among dual users, the IHD incidence rate ratio and mortality ratio CIs included the null value. There was no statistically significant difference between dual use and exclusive smoking for IHD or stroke (Table 2). The authors report a significantly elevated risk for stroke mortality among dual users as compared to no tobacco, however this risk estimate was based on three cases. The authors stated that there are no excess risks of mortality or hospitalization from IHD or stroke among snuff users and conclude that “if there is a risk associated with snuff, it is evidently much lower than those associated with smoking.”

In another study, Johansson, Sundquist, Qvist, and Sundquist (2005) carried out a follow-up study on the Swedish Annual Level-of-Living Survey conducted annually by the

Table 2. Epidemiological studies That Included IHD and Stroke Risk Estimates For Dual Use Sample Sets

Study	Health effect	Described tobacco use	Risk estimate	
			IRR	95% CI
Haglund et al. (2007)	IHD (incidence)	No tobacco	1	ref
		Smoke	1.74	1.41–2.14
		Snuff	0.77	0.51–1.15
		Smoke and snuff	1.64	0.96–2.79
	IHD (mortality)	Tobacco occasionally	0.8	0.46–1.40
		No tobacco	1	ref
		Smoke	1.98	1.35–2.91
		Snuff	1.15	0.54–2.41
		Smoke and snuff	1.69	0.52–5.46
	Stroke (incidence)	Tobacco occasionally	0.91	0.28–2.91
		No tobacco	1	ref
		Smoke	1.4	1.03–1.91
		Snuff	1.07	0.65–1.77
		Smoke and snuff	1.98	1.00–3.95
	Stroke (mortality)	Tobacco occasionally	1.52	0.83–2.75
		No tobacco	1	ref
		Smoke	1.02	0.50–2.05
		Snuff	1.01	0.35–2.92
		Smoke and snuff	4.3	1.22–15.1
		Tobacco occasionally	1.33	0.31–5.64
Hansson et al. (2009)	IHD	Never smoking/never snus	1	ref
		Never smoking/former snus	1.07	0.56–2.03
		Never smoking/current snus	0.85	0.51–1.41
		Former smoking/never snus	1.34	1.10–1.64
		Former smoking/former snus	1.65	1.14–2.39
		Former smoking/current snus	1.22	0.82–1.74
		Current smoking/never snus	1.99	1.59–2.50
		Current smoking/former snus	2.18	0.99–4.79
		Current smoking/current snus	1.5	0.73–3.08
	Stroke	Never smoking/never snus	1	ref
		Never smoking/former snus	1.35	0.65–2.82
		Never smoking/current snus	1.18	0.67–2.08
		Former smoking/never snus	1.01	0.78–1.30
		Former smoking/former snus	1.12	0.67–1.87
		Former smoking/current snus	0.77	0.46–1.29
		Current smoking/never snus	1.61	1.22–2.13
		Current smoking/former snus	1.65	0.59–4.64
	All cardiovascular disease	Current smoking/current snus	1.45	0.58–3.62
		Never smoking/never snus	1	ref
		Never smoking/former snus	1.21	0.75–1.97
		Never smoking/current snus	1	0.69–1.46
		Former smoking/never snus	1.17	1.00–1.38
		Former smoking/former snus	1.44	1.06–1.95
		Former smoking/current snus	1.04	0.78–1.39
		Current smoking/never snus	1.86	1.56–2.22
		Current smoking/former snus	1.82	0.95–3.48
		Current smoking/current snus	1.51	0.86–2.65

Table 2. Continued

Table 2. Continued

Study	Health effect	Described tobacco use	Risk estimate	
			IRR	95% CI
			HR	95% CI
Johansson et al. (2005)	Coronary heart disease	Never-smoker	1	ref
		Former smoker	1.47	1.07–2.03
		Daily smoker	2.3	1.66–3.19
		Daily snuffer/never-smoker	1.41	0.61–3.28
		Daily snuffer/former smoker	1.18	0.67–2.06
		Daily snuffer and smoker	2.73	1.35–5.53
Accortt et al. (2002)	IHD	Nontobacco users	1	ref
		Exclusive smokeless tobacco users	0.6	03–1.2
		Exclusive smokers	1.5	1.1–2.1
		Current exclusive smokers	2.0	1.4–2.8
		Former exclusive smokers	1.2	0.8–2.0
		Current smokeless/smoking	1	0.6–1.7
		Current smokeless/current smoking	0.8	0.5–1.5
		Current smokeless/former smoking	1.1	0.6–2.1

Note. Tobacco use and risk estimates data were extracted from individual study as noted. See indicated reference for additional specific information on study design, sample characteristics, statistical methods, and adjustments. Data considered to be relevant to dual use are marked in bold italics. HR = hazards ratio; IHD = ischemic heart disease; IRR = incidence rate ratio; RR = relative risk.

Swedish statistics bureau, which included men aged 30–74 years who had been previously surveyed in 1988 and 1989. In order to identify coronary heart disease (CHD) events, the data were linked to the Swedish National Hospital Discharge Register and the Cause-of-Death Register. While the authors reported that the highest HR was among dual users, there was no indication of a synergistic effect of smoking and use of snuff on CHD (Table 2). Using three different risk models for cardiovascular disease adjusted for confounding risk factors, the HRs associated with dual use were less than the added effects of smoking and snuffing in two of the models and were just additive in the third model.

More recent data from a study of 1,642 Swedish twins participating in the Screening Across the Lifespan Twin Study conducted in 1998–2002 investigated the association between snus use and the risk for IHD, stroke, and all cardiovascular disease (Hansson et al., 2009). Statistically significant elevated risks for IHD, stroke, and all cardiovascular disease were observed for current smokers who were never snus users, with no elevated risks for these diseases observed among current snus users who were never-smokers (Table 2). Among dual users (current smokers who were also current snus users), no statistically significant elevated risks were observed for IHD, stroke, or all cardiovascular disease, suggesting a possible risk reduction effect of concurrent snus use among smokers.

Data from NHANES I also indicated no increased risk for IHD among dual users (Table 2; Accortt et al., 2002).

Myocardial Infarction

There are four published epidemiological studies from Sweden on exclusive and dual use of smokeless tobacco and of cigarettes and the incidence of MI. Huhtasaari, Asplund, Lundberg,

Stegmayr, and Wester (1992) examined a subset of data from a Northern Sweden population as part of the broader World Health Organization's Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO MONICA) project. The study population included 585 cases of MI, which occurred during a study period from April 1989 to April 1991, with a control population of 589 randomly selected men who had not had an MI. While specific ORs for MI incidence associated with dual use were not presented in this study report, among MI cases, 29% were exclusive smokers, whereas, among controls, 19% were exclusive smokers. Among MI cases, 10% were exclusive snuff users as compared with 15% among controls. By comparison, among MI cases, 6% were dual users, whereas, among controls, 5% were dual users. In another study, Huhtasaari, Lundberg, Eliasson, Janlert, and Asplund (1999) examined 687 MI cases occurring during the study period from May 1, 1991 to December 31, 1993 along with 687 control subjects matched for age and residence. Compared with nonsmokers, the OR for MI among current smokers (no current snuff use) was 3.65 (97% CI: 2.67–4.99) (Table 3). By comparison, the OR for MI among current snuff users who were also smokers was 2.66 (95% CI: 1.24–5.71). Hergens, Ahlbom, Andersson, and Pershagen (2005) published a case-control study of 1,432 MI cases and 1,810 controls matched for age, hospital area, and smoking in two Swedish counties. Compared with nonsmokers, the OR for MI among current smokers (never snuff users) was comparable with current snuff users who were also current smokers (Table 3). Similarly, Wennberg et al. (2007) conducted a prospective incident case-referent study in northern Sweden (525 MI cases and 1,798 matched controls) and found comparable OR for MI among current smokers (no current snuff use) and dual users (Table 3).

In 2007, Lee (2007) published a meta-analysis of five studies relevant to joint effects of smokeless tobacco use and smoking in

Table 3. Epidemiological Studies That Included MI Risk Estimates For Dual Use Sample Sets

Study	Health effect	Described tobacco use	Risk estimate	
			OR	95% CI
Huhtasaari et al. (1999)	MI	Never users of tobacco	1	ref
		Current snuff/no smoking	0.96	0.65–1.41
		Current smoking/no snuff	3.65	2.67–4.99
		Current concomitant user	2.66	1.24–5.71
		Former snuff/never smoking	1.23	0.54–2.82
		Former smoker/never snuff	1.05	0.77–1.43
		Former smoker/former snuff	0.99	0.62–1.59
Hergens et al. (2005)	MI		OR	95% CI
		Never snuff/never smoking	1	ref
		Never snuff/former smoking	1.3	1.1–1.6
		Never snuff/current smoking	2.8	2.3–3.4
		Former snuff/never smoking	1.2	0.46–3.1
		Former snuff/former smoking	1.1	0.73–1.7
		Former snuff/current smoking	5.3	2.7–10.6
		Current snuff/never smoking	0.73	0.35–1.5
Wennberg et al. (2007)	MI	Current snuff/former smoking	1.6	1.1–2.2
		Current snuff/current smoking	2.3	1.6–3.4
			OR	95% CI
		Never used tobacco	1	ref
		Never smoked/current snuff	0.82	0.46–1.43
		Former smoker/current snuff	1.25	0.80–1.96
		Current smoker/no snuff	2.60	1.91–3.54
		Current smoker/current snuff	2.14	1.28–3.60
		Never smoked/former snuff	0.66	0.32–1.34
		Former smokers/never snuff	1.18	0.82–1.70
		Former smoker/former snuff	1.34	0.84–2.12

Note. Tobacco use and risk estimates data were extracted from individual study as noted. See indicated reference for additional specific information on study design, sample characteristics, statistical methods, and adjustments. Data considered to be relevant to dual use are marked in bold italics. MI = myocardial infarction; OR = odds ratio.

Western populations, including evidence related to circulatory disease and smokeless tobacco. The OR from the meta-analysis conducted was 1.01 (95% CI: 0.87–1.18), indicating no interactive or enhanced effect from dual use compared with exclusive cigarette use for risk of MI.

Is There Evidence For Reduced Risk Among Dual Users Compared With Exclusive Smokers?

As indicated in the previous few paragraphs, many of the ORs found for sample sets in the dual use category are less than those found for exclusive smoking, although not always statistically significantly different. Data from two recent comprehensive studies indicate that snus use among smokers (dual use) results in reduced cigarette smoking and, thereby, reduced smoking-related health risks relative to exclusive smoking (Boffetta, Aagnes, Weiderpass, & Andersen, 2005; Luo et al., 2007). Both

studies reported significant reductions in smoking-related diseases among dual users compared with smokers who do not use snus. While Boffetta et al. do not suggest the use of smokeless tobacco as a strategy for reducing tobacco-related harm; their report shows that risk of some cancers is lower among snus users who smoke as compared with exclusive smokers. Luo et al. report that among smokers, the "... net effect of snus use in the studied population might be a reduced risk of cancer" as compared with those who do not use snus. In their analysis of all cohort members, the "adjusted relative risks for cancer in ever users of snus, compared with never users, were 0.7 (95% CI 0.5–0.9) for oral, 0.7 (95% CI: 0.6–0.7) for lung, and 0.9 (95% CI: 0.7–1.2) for pancreatic cancer."

Discussion

In their 2001 review of harm reduction in smoking, the Institute of Medicine stated that "a product is harm reducing if it lowers total tobacco-related mortality and morbidity even though use of that product may involve continued exposure to tobacco-related toxicants." (Institute of Medicine, 2001). Many

have argued that smokeless tobacco products offer a potential harm-reduction strategy for smokers who are unable or unwilling to quit using tobacco (Fagerstrom & Ramstrom, 1998; Kozlowski, O'Connor, & Edwards, 2003; Levy et al., 2006; Rodu, 1994; Rodu & Godshall, 2006; Savitz et al., 2006). However, others would counter that the potential for continued use of tobacco with some risk potential, even one with overall lower health risk compared with cigarette smoking, remains a risk that is too high to accept, given the potential for unintended consequences and the efficacy of existing tobacco control measures (Tomar, Fox, & Severson, 2009).

In this review, we have attempted to address two fundamental questions regarding the possible role of smokeless tobacco use in a harm-reduction strategy:

- Are there any unique health risks (either qualitative or quantitative) associated with dual use of smokeless tobacco products and cigarettes not anticipated or observed from single use of either product?
- What is the potential effect of dual use on future tobacco harm?

Regarding the first question, the evidence is sufficient and clear that there are no unique health risks (either qualitative or quantitative) associated with dual use of cigarettes and smokeless tobacco products, which are not anticipated or observed from single use of these products for the major health effects associated with smoking and smokeless tobacco. This conclusion is based on the review of 17 studies that addressed dual use in some format, 4 of these studies were from the United States and 13 studies were from Europe, primarily Sweden. Endpoints in these studies included various cancers

and cardiovascular diseases. Furthermore, some data indicate that the risks of dual use are lower than those of exclusive smoking.

With respect to Question 2, the current evidence suggests that smokeless tobacco use can contribute to reducing smoking-related harm and that the potential for dual use of both products should not be a barrier to using smokeless tobacco in harm-reduction strategies. Dual users are more likely to reduce smoking intensity or to cease smoking cigarettes than exclusive smokers. This is despite the fact that, at least for the U.S. cohorts assessed herein, dual users as a group have higher prevalence of demographic variables that are typically associated with lower rates of smoking cessation, such as younger age, lower educational attainment (a strong correlate with poverty), and unmarried status (Agrawal et al., 2008). For example, dual users in the cohort examined by Zhu et al. (2009) were on average younger than exclusive smokers (dual users: 62.5% aged 25–44 year and 22.4% aged 45–64 years and exclusive smokers: 46.1% aged 25–44 years and 34.3% aged 45–64 years). Dual users in the Zhu study also tended to be less educated (dual users: 63.4% ≤12-year education and exclusive smokers: 57.5% ≤12-year education). In the cohort studied by Wetter et al. (2002), dual users on average were younger than exclusive smokers (average age 35.5 and 39.5 years, respectively), were less educated, and were more likely to live with others in the household who smoke. A comparison of demographic variables among dual users is not available for the Swedish studies assessed here; however, similar demographic factors are associated with continued smoking in, for example, the Tillgren study (Tillgren et al. 1996). Our analysis has primarily concentrated on risks other than nicotine dependence, thus leaving open the important question of how

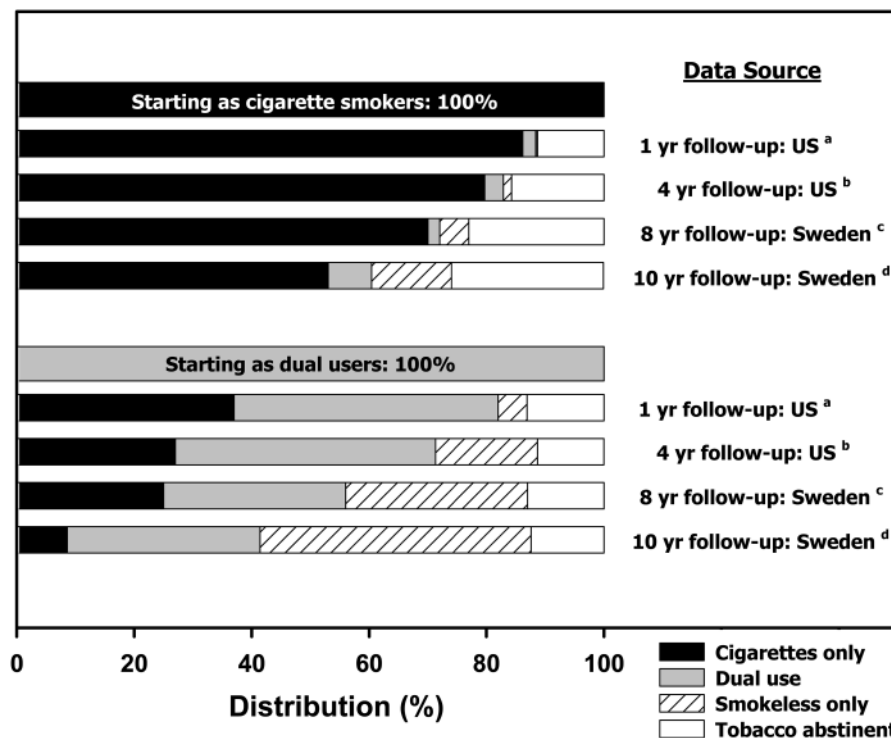


Figure 1. Distribution of tobacco usage drawn from four independent studies conducted in the United States or Sweden: (a) Zhu et al. (2009), (b) Wetter et al. (2002), (c) Tillgren et al. (1996), (d) Lundqvist et al. (2009). Data represent the reported use of tobacco at the start of the study as either cigarettes or dual use (smoking and smokeless) as well as the final reported use of tobacco in one of four categories (cigarettes, dual use, smokeless, or tobacco abstinent).

to balance the potential risks of nicotine dependence with the potential benefits of reducing other serious diseases. Clearly, nicotine dependence remains a serious concern among any tobacco user population, and the impact of dual use is of course relevant, particularly as some studies suggest greater levels of nicotine dependence among dual users (Post, Gilljam, Rosendahl, Bremberg, & Galanti, 2010). Nonetheless, the collective trajectory data from four independent studies, which included follow-up periods from 1 to 10 years (Figure 1), suggest that, while over time, dual users are less likely to stop all tobacco use altogether, they are more likely to reduce smoking intensity (i.e., transition away from cigarettes). Overall tobacco abstinence rates at follow-up were only slightly higher in initial cigarette smokers compared with initial dual users. The fact that a greater proportion of smokers who switch to smokeless tobacco continue to use tobacco products (primarily in the form of smokeless tobacco) compared with smokers who do not is greatly mitigated by the substantial risk differential between the two product categories (Fagerstrom & Ramstrom, 1998; Kozlowski et al., 2003; Levy et al., 2006; Rodu, 1994; Rodu & Godshall, 2006; Savitz et al., 2006).

We are aware that concerns may be raised when comparing typical U.S. smokeless tobacco products and Swedish products due to differences in manufacturing, tobacco types, and constituent levels (Rodu & Jansson, 2004; Schwartz et al., 2010; Stepanov, Jensen, Hatsukami, & Hecht, 2008; Stepanov et al. 2010). However, a detailed discussion of these differences and their potential relevance to health is beyond the scope of this paper. We believe the critical point is that the currently available epidemiology for both product types clearly demonstrates the disparate risk between smoking and use of either Swedish or U.S. smokeless tobacco products. Virtually, all published literature that we are aware of demonstrates that when smokers shift away from continued cigarette consumption, there are substantial benefits to health.

We recognize several caveats regarding the generalizability of the data reviewed in this manuscript. First, there is the broad definitional question regarding dual use; specifically, the lack of a consistent definition applied across studies. For our purposes, dual users were considered to be anybody who used both types of tobacco products concomitantly for any period of time. While this definition broadens the available data regarding dual use behavior and health effects, it may mask underlying differences among subgroups.

Additionally, this review concentrated on the major types of smokeless tobacco products used by populations in North America and Scandinavia, including traditional fermented moist tobacco smokeless products as well as snus products. Although smokeless tobacco is used elsewhere, such as North Africa and Asia, products typical of those areas have been shown to have different health risk profiles compared with North American and Scandinavian products. Therefore, the health effects associated with dual use may differ in magnitude and type from those discussed here. Environmental and cultural differences between North America/Scandinavia and other places where smokeless tobacco use is prevalent also may alter the interplay between smokeless tobacco use and smoking among tobacco using populations. Similarly, because very few dual tobacco users are female, the data reviewed here are exclusive to males; these findings may not extend to females. Also, it seems

likely that the population of dual users is nonhomogeneous in terms of their motivations for dual use, and therefore, average usage patterns may not apply at the individual level. For example, dual use behavior among young males may be related to propensity for risk-taking behavior and not a desire to reduce or quit smoking cigarettes (O'Connor, Flaherty, Quinio, & Kozlowski, 2003; Timberlake et al., 2009; Wagner, 2001). However, when such a group is considered in the context of smokers who use smokeless tobacco and compared with smokers who do not, it seems reasonable that the overall trajectories of tobacco use behavior could be similar to those described herein. Additionally, the analyses of trajectories of tobacco use rely on self-reported usage and in some cases on usage patterns interpolated from self-reports on historical tobacco usage. Nonetheless, self-reported tobacco use information is generally accepted as informative (Brigham et al., 2008). Perhaps more importantly, the tobacco use patterns discussed may have been influenced by environmental and cultural factors different from those experienced by current tobacco users in which case the impact of smokeless tobacco use on smoking behavior could be different than that described here.

No one can describe with certainty the extent and impact of adoption of smokeless tobacco products marketed to adult smokers. However, even with the limitations discussed above, the primary finding from the data reviewed, that dual users are more likely to quit smoking cigarettes than exclusive smokers, is strikingly consistent in terms of tobacco use patterns for dual users over time despite the fact that the data are derived from studies of individuals from varying backgrounds, different countries, and at different points in time.

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Declaration of Interests

All authors are employees of Altria Client Services.

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