Dissolvable Tobacco Products: Population-Level Effects

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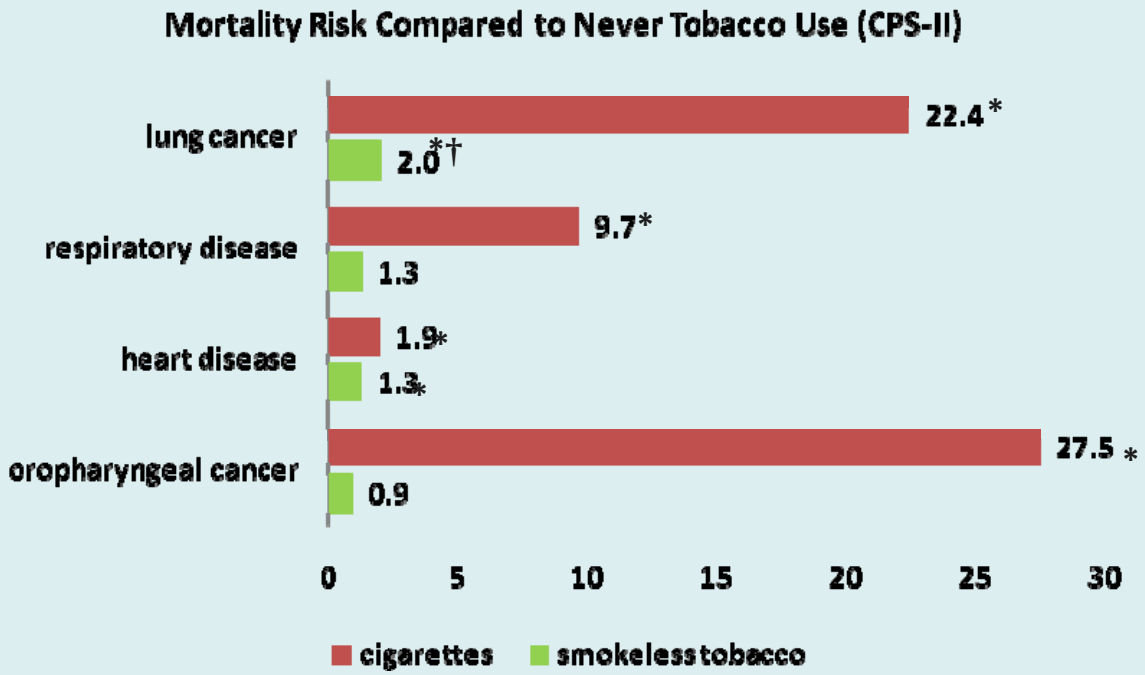
Presentation Outline

- Appropriate context for examining nature and impact of dissolvable tobacco use on public health
- Available science regarding population-level effects with increased smokeless tobacco use (including dissolvable products)
- Models for estimating population-level benefits/deficits with increased smokeless tobacco use (including dissolvable products)

Dissolvable Tobacco Products

- Dissolvable tobacco characterized as low-nitrosamine smokeless tobacco (LN-SLT) product
- Population-level effects (*i.e.* unintended consequences)
  - dissolvable tobacco as starter product (*i.e.* gateway effect)
  - dual use versus complete product switching
  - dissolvable tobacco facilitates continued smoking
- Examination of population-level effects must consider associated disease risk profiles
  - disease risk *significantly influenced* by tobacco product type, as well as frequency, duration and manner of use
  - while no tobacco product shown to be safe, risks associated with smokeless tobacco/nicotine products *significantly less* than cigarettes

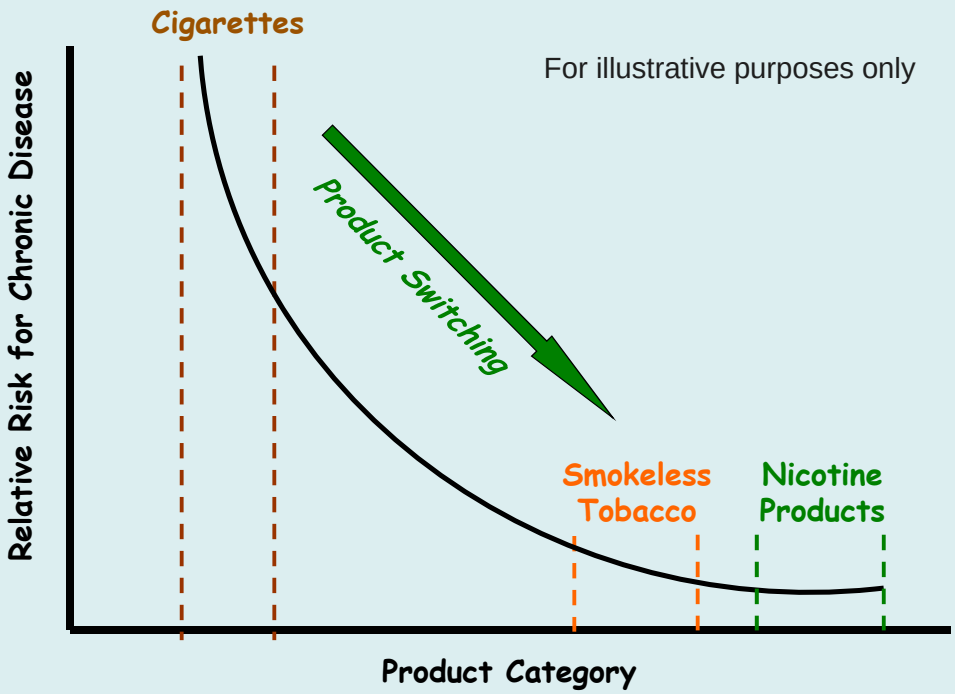
Tobacco Use and Disease Risks



Risks relative to reference population of non-tobacco users (RR = 1.00); asterisk represents statistical difference from non-tobacco users; † not replicated in other studies.

- *substantial reduction* in mortality risks for smokeless tobacco use supported by same US data used to establish disease risks for smoking

Continuum of Risk



Public health organizations recognizing *pronounced continuum of risk,* potential for harm reduction with product switching (*e.g.* LN-SLT)

- **Institute of Medicine (2001)**
- **American Council on Science and Health (2006)**
- **Royal College of Physicians (2002, 2007)**
- **Scientific Committee on Emerging and Newly Identified Health Risks (2007)**
- **Life Sciences Research Office (2008)**
- **American Association of Public Health Physicians (2008)**
- **World Health Organization (2008)**
- **Strategic Dialogue on Tobacco Harm Reduction Group (2009)**

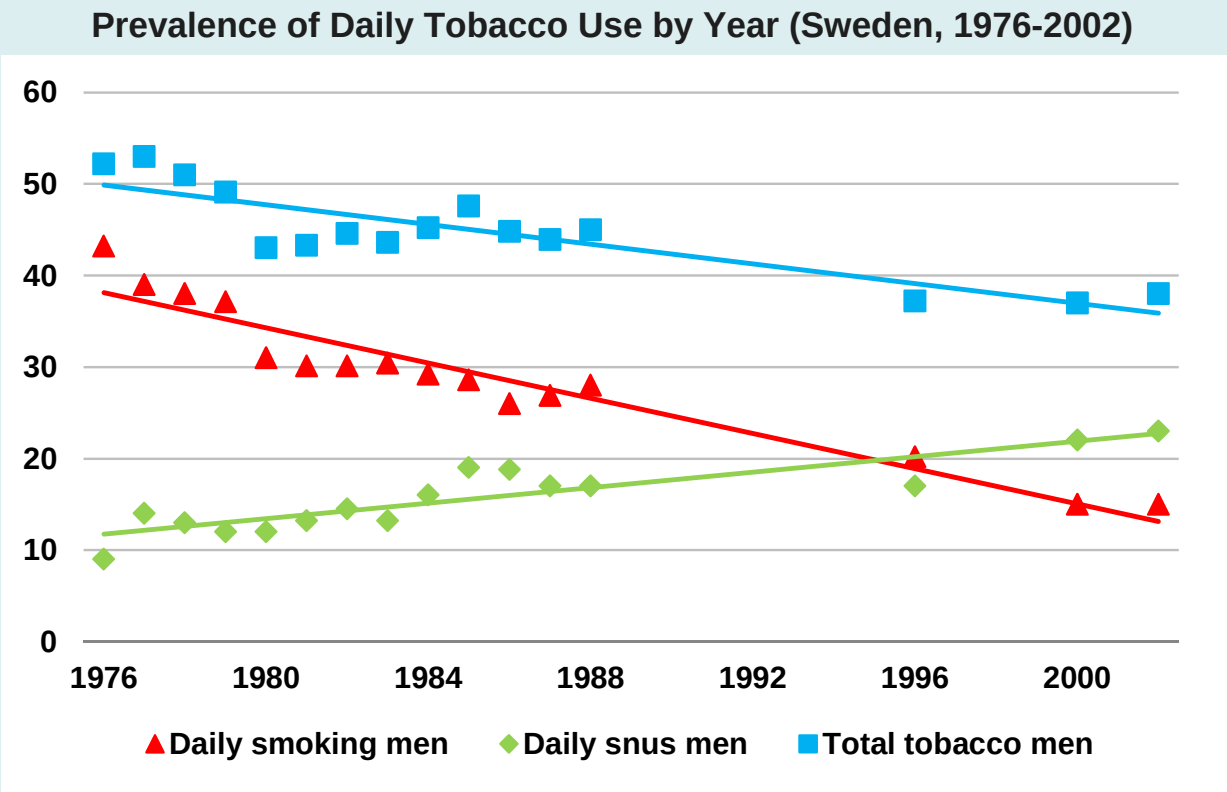
Continuum of Risk

- Smoking *undoubtedly more hazardous* than various forms of smokeless tobacco (Zeller et al., 2009)
  - smokeless tobacco *not associated* with many smoking-related cancers or pulmonary disease
- Median total mortality relative risk associated with LN-SLT use 5%-10% of that associated with smoking (Levy et al., 2004)
  - significant reductions in mortality risk for lung cancer (>96%) and heart disease (90%)
  - panel assumed smokeless tobacco use limited to LN-SLT products, notably dissolvable tobacco and snus
  - estimates based, in part, on epidemiology studies from Sweden

Population-Level Effects

- *Significantly lower risks* associated with smokeless tobacco use compared to smoking must be considered when examining population-level effects
- Available studies from Sweden demonstrate potential to reduce smoking-attributable disease with smokeless tobacco use
  - Sweden only developed country to achieve WHO 2000 target for reducing smoking prevalence to less than 20%
  - during same period, Swedish men exhibited substantial decreases in smoking-attributable disease
    - *lowest incidence of lung cancer among developed nations*
    - *low incidence of oral cancer by international standards*
    - *significant improvement in cardiovascular health*

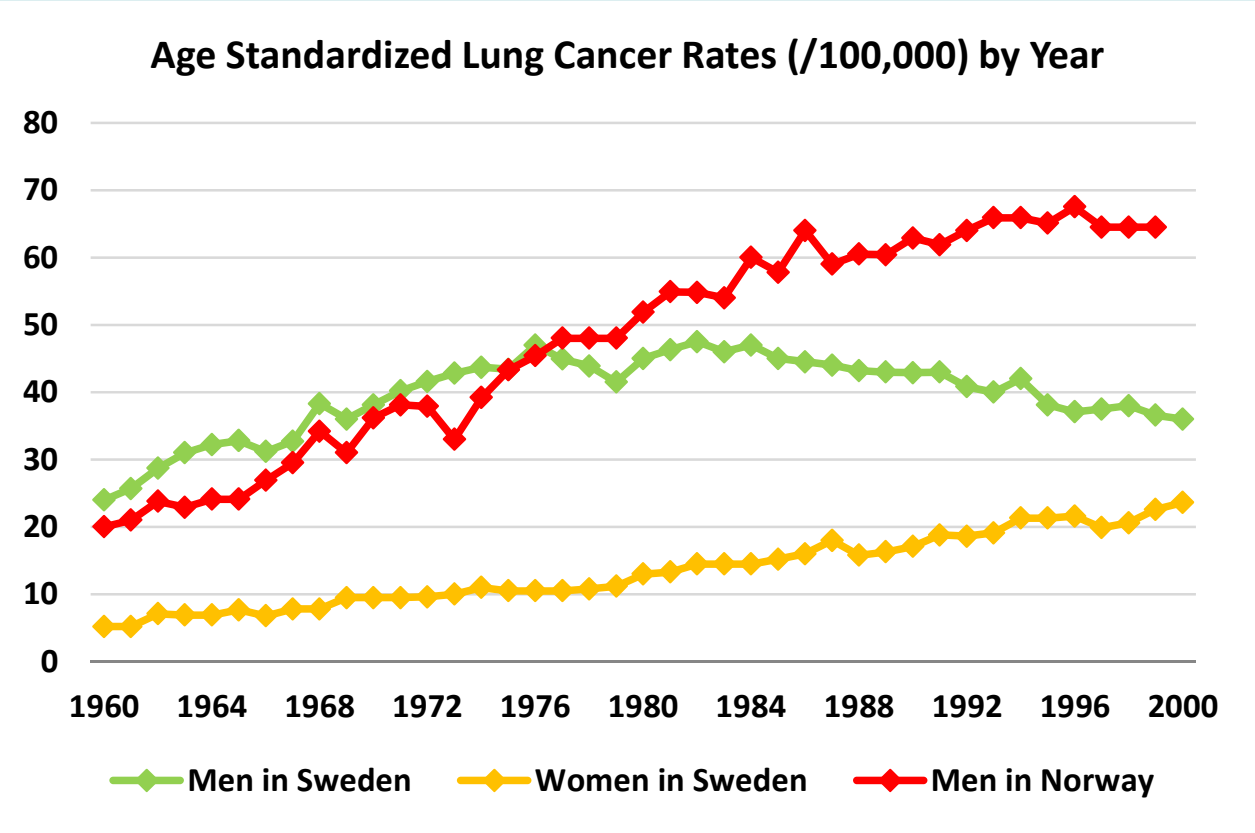
‘Swedish Experience’



Adapted from Foulds *et al.*, 2003

- (1976-2002) daily smoking and total daily tobacco use among Swedish males decreased as daily snus (LN-SLT) use increased

‘Swedish Experience’



no smoking decline similar to Sweden

male smoking, *40% to 15%*; male snus use, *10% to 23%*

Adapted from Foulds *et al.*, 2003

- steady decline in Swedish male lung cancer rates closely parallels decreased smoking and increased snus use

Population-Level Effects

- Opponents of product switching to reduce smoking-attributable risk often cite concerns regarding ‘dual use’ and ‘gateway effect’
  - dual use not associated with reduced smoking frequency, but instead increases toxicant exposure and risk for disease
  - dual use facilitates continued smoking
  - smokeless tobacco use increases smoking initiation
- *However*, available data *do not support* hypotheses regarding unintended consequences associated with increased smokeless tobacco use

Dual Use and Disease Risks

- No increased disease risks associated with dual use
  - no increased risk for *all cancers* among dual users compared with exclusive smokers (Accortt et al., 2005, 2002)
  - no increased risk for *oral cancer* among dual users compared with exclusive smokers (Schildt et al., 1998; Winn et al., 1981)
  - no increased risks for *heart disease, stroke or all cardiovascular disease* among dual users compared with exclusive smokers (Hansson et al., 2009; Haglund et al., 2007; Johansson et al., 2005; Accortt et al., 2002)
  - no increased risk of *myocardial infarction* among dual users compared with exclusive smokers (Wennberg et al., 2007; meta-analysis, Lee, 2007; Hergens et al., 2005; Huhtasaari et al., 1999)

Dual Use and Smoking Frequency

- Dual users *more likely* to reduce smoking frequency compared to exclusive smokers (Sweden, Norway)
  - dual use significant positive predictor (OR 3.01) in regression analysis of “greatly reduced cigarette consumption” (Lund et al., 2010)
  - smokeless tobacco provides sufficient substitute for nicotine to significantly reduce craving and allow smoking reduction of ~40% (Caldwell et al., 2010)
  - inverse relationship between dual use (weekly smokeless tobacco consumption) and cigarettes per day (Gilljam & Galanti, 2003)

[initial literature review did not identify any studies that contradict findings of reduced smoking frequency among dual users compared to exclusive smokers]

Dual Use and Smoking Frequency

- Dual users *more likely* to reduce smoking frequency compared to exclusive smokers (United States)
  - smokers interested in quitting reduced smoking frequency ~40% during *dissolvable tobacco* sampling period that allowed *ad libitum* use of cigarettes (Hatsukami et al., 2011)
  - smokers not interested in quitting reduced cigarette consumption ~25% during trial of smokeless/nicotine products (O'Connor et al., 2011)
    - *stable level of substitution consistent with smokers preferring gradual shift versus immediate changeover for quitting, similar to NRTs*
  - smokers not interested in quitting partially substituted *dissolvable tobacco* for regular smoking; no requirement to abstain, yet smoking frequency reduced ~40% (Carpenter & Gray, 2010)

[Tomar et al., 2010; Wetter et al. 2002]

Dual Use and Toxicant Exposure

- Reduced smoking frequency among dual users likely results in reduced toxicant exposure (United States)
  - product-specific concentrations of NNK (TSNA carcinogen) closely parallel urine concentrations of total NNAL (NNK metabolites) in tobacco users (Hatsukami et al., 2007)
    - *potential for smokers to dramatically reduce toxicant exposure by switching to LN-SLT products*
  - significant reductions in CO, total cotinine (nicotine metabolite) and total NNAL levels during dissolvable tobacco substitution for regular smoking (Mendoza-Baumgart et al., 2007)
    - *LN-SLT products have potential to reduce toxicant exposure, promise for reducing individual disease risk*

Dual Use and Quitting Smoking

- Dual users *more likely* to quit smoking compared to exclusive smokers (Sweden, Norway)
  - consistently higher quit ratio among daily dual users in seven cross-sectional studies (Lund et al., 2011)
  - increased odds (5.5) of quitting smoking among dual users in cohort study (Stenbeck et al., 2009)
  - among 12 main effects, dual use strongest independent correlate of smoking cessation in national survey (Furberg et al., 2008)
  - increased odds (5.7) of quitting smoking among dual users in national sampling (Ramström & Foulds, 2006)
  - increased odds (3.7) of being former smoker with regular dual use in national survey (Furberg et al., 2005)

[Galanti et al., 2008; Tønnesen et al., 2008; Gilljam & Galanti, 2003]

Dual Use and Quitting Smoking

- Dual users *more likely* to quit smoking compared to exclusive smokers (United States)
  - dual use (*dissolvable tobacco*) significantly increased measures of readiness/self-efficacy to quit in pilot study (Carpenter & Gray, 2010)
  - dual use significantly increased past-year quit attempts, seriously considering/levels of interest in quitting; current daily dual users more likely to be former smokers in national surveys (Tomar et al., 2010)
  - male smokers using smokeless tobacco during most recent quit attempt had 2-fold higher proportion of former smokers compared with nicotine patch/gum in national survey (Rodu & Phillips, 2008)
  - dual users (cigarette initiators/moist snuff) 2-fold more likely to have quit smoking in national survey (Kozlowski et al., 2003)

[Tomar, 2003; Wetter et al., 2002]

Smokeless Use and Smoking Initiation

- No evidence of gateway effect, smokeless tobacco use to smoking (Sweden)
  - decreased odds (0.52) of initiating smoking among young smokeless users compared to non-users in cohort study (Stenbeck et al., 2009)
  - *higher lifetime smokeless use (POR 11.7) among young males versus females, with males less likely than females to ever smoke (0.70) or smoke exclusively (0.55) in national survey (Furberg et al., 2008)*
  - smokeless use associated with never versus current smoking in school-based cohort study (Galanti et al., 2008)
  - decreased odds (0.28) of initiating daily smoking among smokeless users compared to non-users in national sampling (Ramström & Foulds, 2006)
  - smokeless use inversely associated with smoking initiation, with decreased odds (0.20) of ever smoking among regular smokeless users compared to non-users in national survey (Furberg et al., 2005)

[*Stegmayr et al., 2005*]

Smokeless Use and Smoking Initiation

- Gateway effect unlikely, smokeless use to smoking (United States)
  - smokeless initiators significantly less likely to be current/daily smokers compared to cigarette initiators in national survey (Rodu & Cole, 2010)
    - *smoking prevalence higher among young smokeless users, lower among adult smokeless users in national surveys (Tomar et al., 2010)*
  - adjusting for baseline differences in risk factors for smoking (propensity scoring), no association between smokeless use and smoking initiation in national adolescent survey (Timberlake et al., 2009)
    - regression analysis suggests smokeless use predictor of subsequent smoking in regional adolescent cohort (Severson et al., 2007)
  - adjusting for non-causal users (product order) and predictors of smoking, smokeless use not predictive of current smoking (O'Connor et al., 2005, 2003)
    - young male smokeless users significantly more likely than never-users to initiate smoking in national survey (Tomar, 2003)

[*Kozlowski et al., 2003*, Haddock et al., 2001]

Population Modeling (smokeless use)

- Life tables methods used to estimate differences in health-adjusted life expectancies, net population harm for different exposure conditions (Gartner et al., 2007)
  - life tables do not account for trajectories, but provide estimated survival under different static exposure distributions; *nonetheless,*
  - little difference for health-adjusted life expectancy of switchers compared to quitters, smokeless users compared to never users
  - 17-21 potential quitters switching to smokeless needed to offset potential health gain from each smoker switching to smokeless
  - 17-20 never smokers initiating smokeless needed to offset potential gain from each new tobacco user using smokeless instead of smoking
- Findings confirmed/extended for US population using dynamic, population-based model that accounted for tobacco exposure trajectories and time-dependent effects of exposure and cessation (Sulsky et al., unpublished)

Population Modeling (smokeless use)

- Recently published dynamic model estimated impact of promoting smokeless use as safer alternative to smoking, suggested no population-level benefit (Mejia et al., 2010)
  - model *overly simplistic*, *e.g.* minimal exposure states and transitions, same rates (initiation, cessation, transition) applied to whole population, health outcome (health index) assumed to be same regardless of duration of tobacco use or cessation
  - initial exposure distributions and *transition probabilities not justified*, *e.g.* assumed smokeless users very unlikely to quit and very likely to switch to smoking or dual use (deficits), while smokers very likely to quit or switch to smokeless and unlikely to initiate dual use (benefits)
  - slight modification of transition probabilities, *i.e.* more realistic assignment based on age, results in *significant population-level benefit*

Population Modeling (smokeless use)

Dynamic model estimates impact on tobacco-related mortality with increased prevalence of reduced risk product

- hypothetical population of never smokers followed from age a_{start} to age a_{end}
- up to 33 different transitions into and out of tobacco exposure states
- mortality based on age-, duration of smoking- and duration of cessation-specific person-years and deaths from population of interest
- at end of each age category, estimates survivors assuming reduced risk product not available (base case), survivors assuming modified risk product used at given frequency (exposure scenario)
- implemented in WinBUGS, allows for estimation of variability of all model outputs

*Poisson model (Bachand & Sulsky, unpublished)

Population Modeling (smokeless use)

Validation of base case and full models

- comparison of age category-specific estimates for numbers of survivors, 2006 US life table (men) versus base case model
  - transition probabilities based on US smoking initiation and cessation rates, 1980
  - conservative excess relative risk (ERR), 0.11 for smokeless versus cigarettes
  - coefficients for mortality based on data from Kaiser Permanente (KP) cohort
  - base case model estimated 671,800 survivors versus 674,217 for US life table (CDC)
- comparison of age category-specific estimates for numbers of survivors, 2006 Swedish life table (men) versus full model
  - transition probabilities based on Swedish data (10-year follow-up periods, 1990-2004), adjusted to approximate tobacco use pattern in early 1980s
  - coefficients for mortality based on KP data, adjusted for differences in background mortality in US and Sweden (1981-2006)
  - full model estimated 759,182 survivors versus 764,275 for Swedish life table (Swedish Statistics)

Population Modeling (smokeless use)

Hypothesis Testing

- comparison of age category-specific estimated numbers of survivors, US tobacco use pattern similar to Sweden
  - Swedish transition probabilities (1980)
    - smokeless initiation versus remaining never users, 0.05
    - smokers switching to smokeless versus quitting, 0.02
    - smokeless initiators switching to smoking/dual use, 0.01/0.03
    - smokeless initiators remaining smokeless/quitting, 0.77/0.19
  - conservative excess relative risk, 0.11 for smokeless versus cigarettes
  - life tables from 2006; model starts with 1,000,000 12-year-old male never users
- estimated 19,340 (95% PI 10,980-27,790) lives potentially saved, US tobacco use pattern among men similar to that of Sweden (1980)
  - significant increase in number of survivors in each age category past age 42

Population Modeling (smokeless use)

	age category	survivors mean difference	95% posterior interval	
Swedish transition probabilities, 1980	33-72	19,340	10,980	27,790
(1) ST initiation versus remaining never users, 0.05 to 0.10 (ages 13-32)	33-72	18,810	9,270	28,300
(2) smokers switching to ST versus quitting, 0.02 to 0.10 (all ages)	33-72	19,260	10,920	27,710
combined (1) and (2)	33-72	18,730	9,216	28,210
(3) ST initiators switching to smoking or dual use, 0.01/0.03 to 0.20 (ages 13-27), ST initiators remaining ST (0.77 to 0.50) or quitting (0.19 to 0.10)	33-72	18,720	9,045	28,200
combined (1) and (2) and (3)	33-72	17,730	4,942	30,040
combined (1) and (2) and (3), with (4) switchers remaining ST, 0.0768 to 0.50, relapsing to smoking, 0.015 to 0.40, or quitting, 0.9082 to 0.10 (all ages)	33-72	14,630	1,787	26,990
combined (1) and (2) and (3) and (4), with ERR for ST versus smoking, 0.11 to 0.50	33-72	12,920	3	25,350
(5) ST initiation versus initiating smoking, 0.05 to 0.10 (ages 13-32)	33-72	20,300	12,030	28,670
(6) smokers continue to smoke, 0.90 to 0.80, switch to ST, 0.05 to 0.10, or switch to dual use, 0.05 to 0.10 (all ages)	33-72	30,240	20,940	39,590

- estimates from population model indicate population-level benefit with increased smokeless use, minimal impact of unintended consequences

Population-Level Effects Summary

- Dual use of smokeless tobacco products (*e.g.* LN-SLT) and cigarettes not associated with increased risk of disease compared to exclusive smoking
  - consideration of comparative disease risks necessary to properly examine nature and impact of smokeless products on public health
- Dual users more likely to reduce (versus increase) smoking frequency, and thereby reduce exposure to smoke toxicants
  - substitution patterns consistent with smokers preferring gradual shift rather than immediate changeover for quitting (similar to NRTs)
- Dual users more likely to quit smoking compared to exclusive smokers; smokeless tobacco users less likely to initiate smoking (*i.e. gateway away from smoking*)
- Population models estimating changes in tobacco-related mortality indicate net population-level benefit with increased smokeless tobacco use, provide necessary insight to counterfactuals

Tobacco Harm Reduction

- Current population-level trends in US and Scandinavia occurring despite misconception regarding comparative risks associated with smokeless tobacco and cigarettes
  - vast majority (~85%) of US tobacco users *incorrectly* perceive disease risks associated with smokeless tobacco use as *similar or greater* than smoking; represents major public health failing (*e.g.* O'Connor *et al*. 2007)
- Nicotine in tobacco products is addictive, but *not* considered significant threat to health; smoke inhaled from burning tobacco poses most significant risk for serious diseases
  - Misconception regarding comparative risks associated with smokeless tobacco and cigarettes has potential to *adversely impact* public health, *i.e.* impacts tobacco use behaviors

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