

# The Harm Reduction Potential of Oral Tobacco Products: Past, Present and Future

Jason W. Flora, Ph.D.

Altria Client Services, LLC



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— FAMILY OF COMPANIES —



# Agenda



## PAST

Brief history of  
Smokeless Tobacco (ST)

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Risk differential of  
cigarettes compared to  
ST, including snus

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Harm reduction success  
in Sweden



## PRESENT

Harm reduction opportunity  
of ST and snus in the U.S.

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Continuum of risk

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Misperceptions of risk



## FUTURE

Emerging Oral Tobacco  
Derived Nicotine (OTDN)  
product category

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Harm reduction  
opportunity of OTDNs

---

Where are we headed?



# Smokeless Tobacco – A VERY Brief History

← PAST



6000 BC

Native Americans are believed to be the first people to smoke, chew and snuff tobacco<sup>1</sup>



Christopher Columbus first encountered tobacco as a gift from Native Americans<sup>1,2</sup>

1492



Tobacco chewing was widespread in parts of Central and South America<sup>3</sup>



Jean Nicot grew and promoted tobacco in Europe<sup>2</sup>

1550s

Ambassador to Portugal and is associated with the early popularity of tobacco in Europe.

Genus *Nicotiana* was named after him

Chewing tobacco became popular among British sailors when smoking was forbidden on boats due to the fire hazard<sup>4</sup>



1800s

Smokeless tobacco became popular in the U.S.<sup>5</sup>



1. History of Tobacco in the World — Tobacco Timeline (tobaccofreelife.org)
2. Christen A.G., Swanson B.Z., Glover E.D., Henderson A.H. Smokeless tobacco: The folklore and social history of snuffing, sneezing, dipping, and chewing. J. Am. dent. Assoc. 1982
3. Voges E. The pleasures of tobacco — How it all began and the whole story. Tob. J. int. 1984;1:80–82.
4. NCBI Monograph Smokeless Tobacco and Some Tobacco-specific N-Nitrosamines
5. Gottsegen, J.J. (1940) A Study of Its Consumption in the United States, New York, Pitman, pp. 3.



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# Smokeless Tobacco Today – A VERY Diverse Category



PRESENT



TODAY, OVER

**300**

MILLION PEOPLE

consume  
ST globally<sup>1</sup>



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1. Siddiqi et. al., "A Policy Perspective on the Global Use of Smokeless Tobacco" *Curr Addict Rep* (2017) 4:503–51



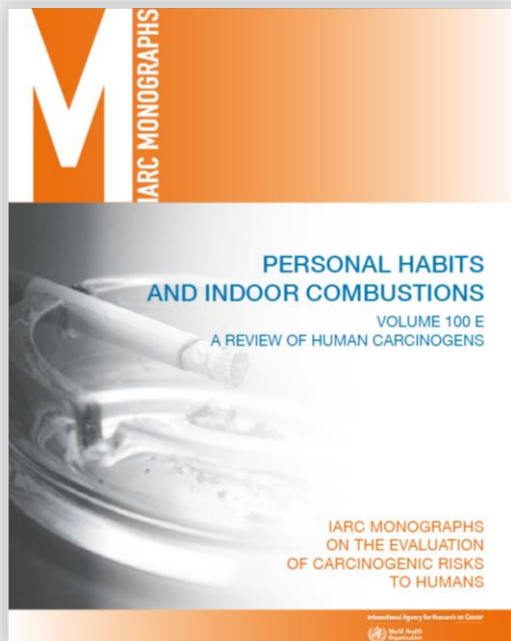
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# Smokeless Tobacco Today – A VERY Diverse Category



PRESENT



## 5. Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of smokeless tobacco. Smokeless tobacco causes cancers of the oral cavity, oesophagus and pancreas.

There is *sufficient evidence* in experimental animals for the carcinogenicity of smokeless tobacco.

Smokeless tobacco is *carcinogenic to humans (Group 1)*.

**Should all  
Smokeless  
Tobacco be  
classified  
together?**



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# Smokeless Tobacco Today – A VERY Diverse Category

PRESENT

Researchers at the U.S. Centers for Disease Control, Harvard University and the University of Pretoria tested smokeless tobacco products (e.g., TSNAs) from 5 WHO regions in 2011<sup>1</sup>

“ These data have important implications for risk assessment because they show that **very different exposure risks may be posed through the use of these chemically diverse oral tobacco products.** ”

“ Because of the wide chemical variation, **oral tobacco products should not be categorised together when considering the public health implications of their use.** ”

Emphasis added

1. Stanfill et al. Tobacco Control 2011



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Research paper

## Global surveillance of oral tobacco products: total nicotine, unionised nicotine and tobacco-specific *N*-nitrosamines

Stephen B Stanfill,<sup>1</sup> Gregory N Connolly,<sup>2</sup> Liqin Zhang,<sup>1</sup> Lily T Jia,<sup>3</sup> Jack E Henningfield,<sup>4</sup> Patricia Richter,<sup>5</sup> Tameka S Lawler,<sup>1</sup> Olalekan A Ayo-Yusuf,<sup>6</sup> David L Ashley,<sup>1</sup> Clifford H Watson<sup>1</sup>

### ABSTRACT

**Objective** Oral tobacco products contain nicotine and carcinogenic tobacco-specific *N*-nitrosamines (TSNAs) that can be absorbed through the oral mucosa. The aim of this study was to determine typical pH ranges and concentrations of total nicotine, unionised nicotine (the most readily absorbed form) and five TSNAs in selected oral tobacco products distributed globally.

**Methods** A total of 53 oral tobacco products from 5 World Health Organisation (WHO) regions were analysed for total nicotine and TSNAs, including 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), using gas chromatography or liquid chromatography with mass spectrometric detection. Unionised nicotine concentrations were calculated using product pH and total nicotine concentrations. Fourier transform infrared spectroscopy was used to help categorise or characterise some products.

**Results** Total nicotine content varied from 0.16 to 34.1 mg/g product, whereas, the calculated unionised nicotine ranged from 0.05 to 31.0 mg/g product; a 620-fold range of variation. Products ranged from pH 5.2 to 10.1, which translates to 0.2% to 99.1% of nicotine being in the

products. In addition to its addictiveness, oral tobacco may contribute to diabetes, high blood pressure, cardiovascular disease, oral diseases, and cancers of the oral cavity and pancreas.<sup>1-3</sup> Oral tobacco use is also associated with increased risk of death from myocardial infarction and increased risk of premature birth and pre-eclampsia.<sup>4,5</sup>

Oral tobacco products range from simple cured tobacco to elaborate products containing many non-tobacco ingredients; these products can be handmade or commercially made by using simple or very complex manufacturing processes.<sup>1,5,6</sup> Some oral tobacco products contain significant amounts of plant material (betel leaf, areca nut, catechu, etc.); moreover, additives such as sweeteners, flavour agents and spices (saffron, cardamom, camphor, eucalyptus, etc.) are commonly added. Alkaline modifiers, including certain inorganic salts, slaked lime and ashes produced by burning certain wood (eg, Willow, Mamón) or fungi,<sup>1,5,6</sup> are also added to some oral tobacco products. Unprocessed tobacco is mildly acidic (approx. pH 5–6.5);

Tob. Control: first published as 10.1136/tc.2010.037465 on 25 November 2010. Downloaded from <http://tobaccocontrol.bmj.com/> on 05/11/2022 at 14:52:00. Copyright: © 2011 British Association of Tobacco Dealers. All rights reserved.



# A Recent Systematic Review of Epidemiological Data on the Health Risks of ST Worldwide – 113 Countries

PRESENT

Siddiqi et al. BMC Medicine (2015) 13:194  
DOI 10.1186/s12916-015-0484-2

Medicine for Global Health

RESEARCH ARTICLE

BMC Medicine

Open Access

## Global burden of disease due to smokeless tobacco consumption in adults: analysis of data from 113 countries

Kamran Siddiqi<sup>1\*</sup>, Sawar Shah<sup>1</sup>, Syed Muslin Abbas<sup>1</sup>, Aishwarya Vijayagopal<sup>1</sup>, Mohammed Jawad<sup>1</sup>, Omara Dogra<sup>1</sup> and Atiq Sheikh<sup>1</sup>

### Abstract

**Background:** Smokeless tobacco is consumed in most countries in the world. In view of its widespread use and increasing awareness of the associated risks, there is a need for a detailed assessment of its impact on health. We present the first global estimates of the burden of disease due to consumption of smokeless tobacco by adults.

**Methods:** The burden attributable to smokeless tobacco use in adults was estimated as a proportion of the disability-adjusted life years (DALYs) lost and deaths reported in the 2010 Global Burden of Disease study. We used the comparative risk assessment method, which evaluates changes in population health that result from modifying a population's exposure to a risk factor. Population exposure was stratified from country-specific prevalence of smokeless tobacco consumption, and changes in population health were estimated using disease-specific risk estimates (relative risk/disease rates) associated with it. Country-specific prevalence estimates were obtained through systematically searching for all relevant studies. Disease-specific risks were estimated by conducting systematic reviews and meta-analyses based on epidemiological studies.

**Results:** We found adult smokeless tobacco consumption figures for 113 countries and estimated burden of disease figures for 113 of these countries. Our estimates indicate that in 2010, smokeless tobacco use led to 1.7 million DALYs lost and 62,283 deaths due to cancers of mouth, pharynx and oesophagus and, based on data from the benchmark 57 country INTERHEART study, 4.7 million DALYs lost and 204,309 deaths from ischaemic heart disease. Over 85% of this burden was in South-East Asia.

**Conclusions:** Smokeless tobacco results in considerable, potentially preventable, global morbidity and mortality from cancer estimates in relation to tobacco; heart disease need to be interpreted with more caution, but nonetheless suggest that the likely burden of disease is also substantial. The World Health Organization needs to consider incorporating regulation of smokeless tobacco into its Framework Convention for Tobacco Control.

### Background

Smokeless tobacco (SLT) consists of a number of products containing tobacco, which are consumed—without burning—through the mouth or nose [1]. A diverse range of SLT products are available worldwide, varying in their composition, methods of preparation and consumption, and associated health risks (Table 1). Its use is most prevalent in South and South-East Asia where one-third of tobacco is consumed in smokeless form [2, 3].

Wrapped in a betel leaf with areca nut, slaked lime, and catechu, SLT is often served at social occasions in this region. Other products (e.g. gutkas, khaini) contain slaked lime, areca nut, flavourings, and aromatic substances [3]. A number of products based on powdered tobacco (e.g. snuff) are also consumed in Nordic countries and North America. In other parts of the world, the most commonly used SLT products (Table 1) include Chimo (Venezuela), Nas (Uzbekistan, Kyrgyzstan), Tambak (Sudan, Chad), and Snuff (Nigeria, Ghana, South Africa).

In addition to nicotine, SLT products contain over 30 carcinogens [5] including tobacco-specific nitrosamines

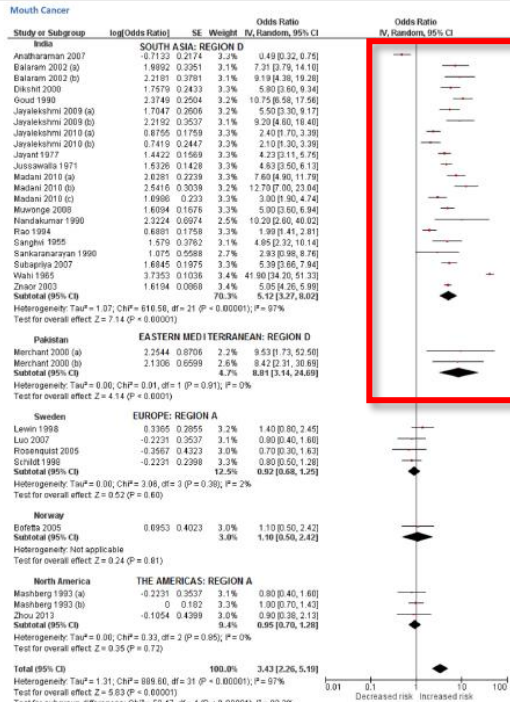
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## Odds Ratio – Mouth Cancer Risk



INDIA

PAKISTAN

SWEDEN

NORWAY

NORTH AMERICA

Balarum 2002 (a): Among never drinkers adjusted for smoking  
Balarum 2002 (b): Among never smokers adjusted for alcohol



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**Keywords:** Global burden of disease, DALYs, Disability-adjusted life-years, Tobacco, Cancer, Heart disease, Mortality

**Background**

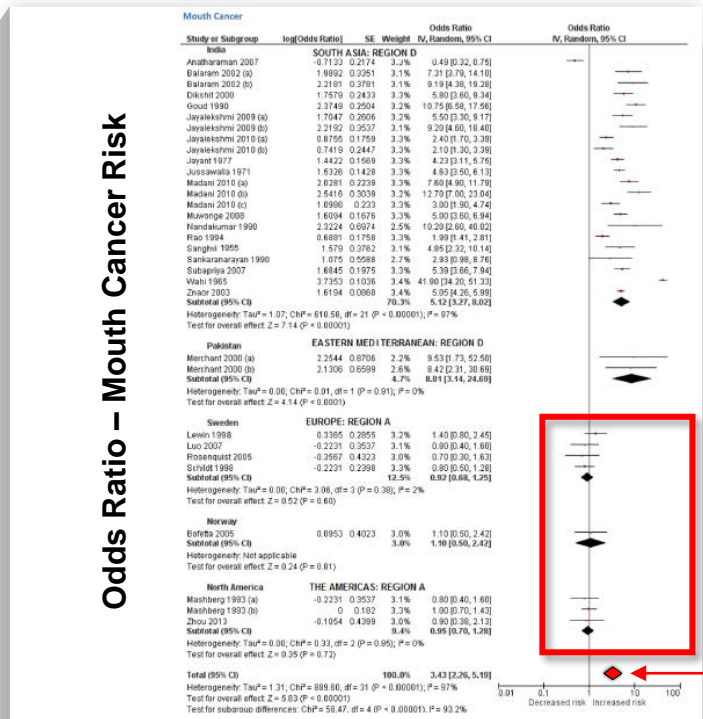
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**Footnotes:**

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INDIA

PAKISTAN

SWEDEN

NORWAY

NORTH AMERICA

**GLOBAL AVERAGE**  
3.43 [2.26, 5.19]

Balararam 2002 (a): Among never drinkers adjusted for smoking  
 Balararam 2002 (b): Among never smokers adjusted for alcohol



# Smokeless Tobacco Today – A VERY Diverse Category

PRESENT



TODAY, OVER  
**300 MILLION PEOPLE**  
consume ST globally<sup>2</sup>

**A** Snus (Sweden)  
~ **1 MILLION USERS**<sup>3</sup>

**E** MST (U.S.)  
~ **6 MILLION USERS**<sup>4</sup>

I: Products containing tobacco\*

II: Products containing tobacco with various alkaline modifiers\*\*

III: Products containing tobacco, slaked lime (as the alkaline modifier) and areca nut\*\*\*

\* These products may also contain spices, sweeteners, flavor chemicals, and low levels of alkaline modifiers.  
\*\* These products may also contain spices, sweeteners, flavor chemicals, and substantial amounts of alkaline modifiers that may include sodium bicarbonate, slaked lime, ashes from fungi or plants, or inorganic salts that increase product pH.  
\*\*\* These products may also contain piper betel leaf, catechu, and various spices.

1. Stanfill et al. *Tobacco Control* 2011
2. Siddiqi et. al., "A Policy Perspective on the Global Use of Smokeless Tobacco" *Curr Addict Rep* (2017) 4:503–510
3. <https://en.wikipedia.org/wiki/Snus>
4. Source: Altria Client Services LLC Adult Tobacco Consumer Tracker (ALCS ATCT), Q1, 2022



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# From this Long History, We have Extensive Epidemiology

Epidemiological evidence for **moist smokeless tobacco (MST)** in the U.S. and **snus** in Sweden and Norway demonstrates that:



**MST / SNUS**

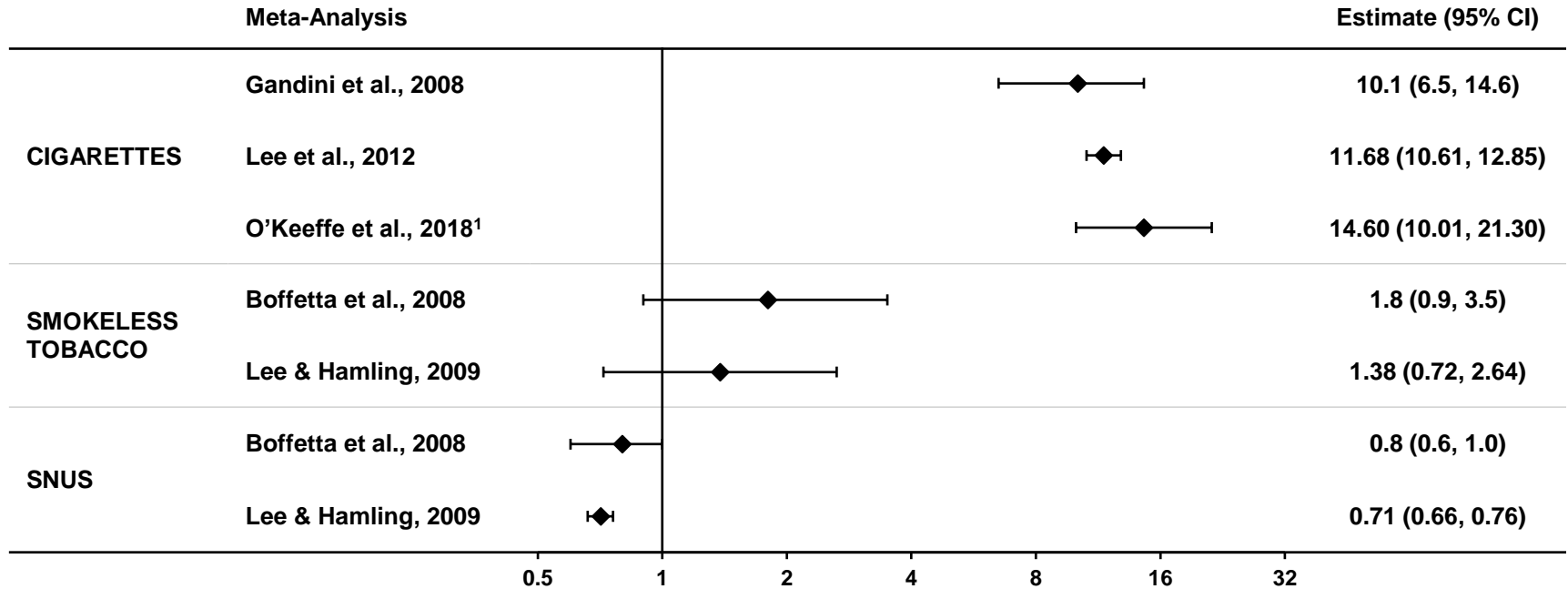
SUBSTANTIALLY  
**LESS HARMFUL**  
COMPARED TO CIGARETTES

**LOWER RISK**  
COMPARED TO CIGARETTE SMOKING

- Lung cancer
- Mouth cancer
- COPD
- Smoking-related heart diseases

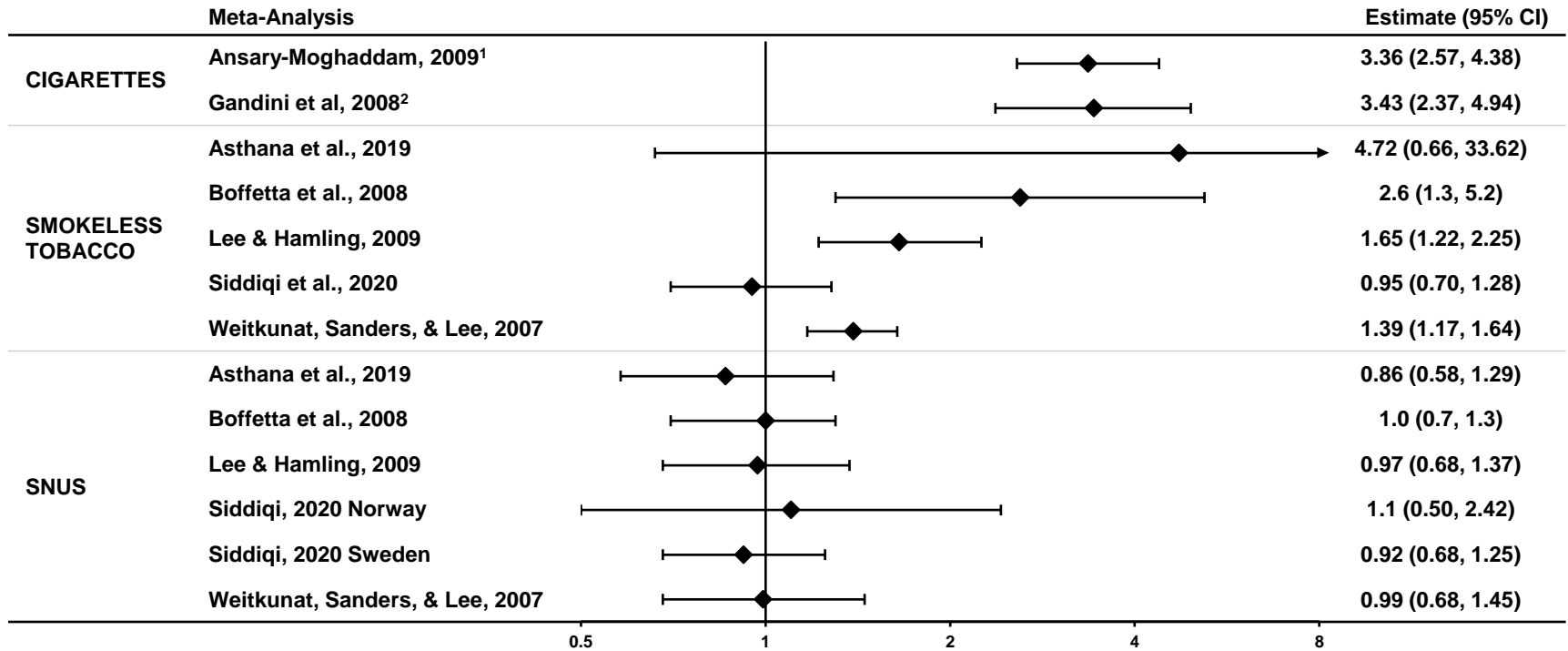


# Epidemiological Data Demonstrates that MST and Snus Users Have Lower Risk of Lung Cancer Compared to Cigarette Smokers



1. ALCS Pooled estimates for studies conducted in the US using a random-effect meta-analysis model.

# Epidemiological Data Demonstrates that MST and Snus Users Have Lower Risk of Mouth Cancer Compared to Cigarette Smokers

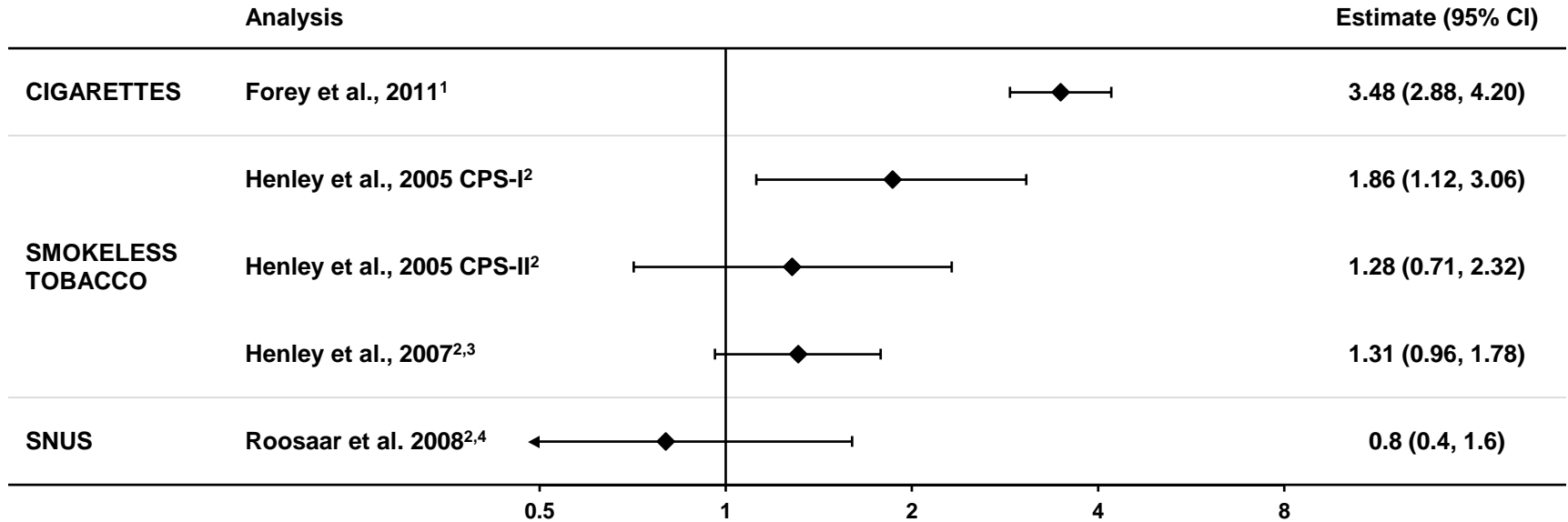


1. ALCS pooled estimates for studies conducted in the US using a random-effect meta-analysis model.

2. Estimate shown in the plot from the Gandini et al. study was for oral cavity cancers; the pooled estimate for pharynx cancers was 6.76 (95% CI=2.86 to 15.98). All other estimates shown in the plot were for oral cavity and pharynx cancers combined.

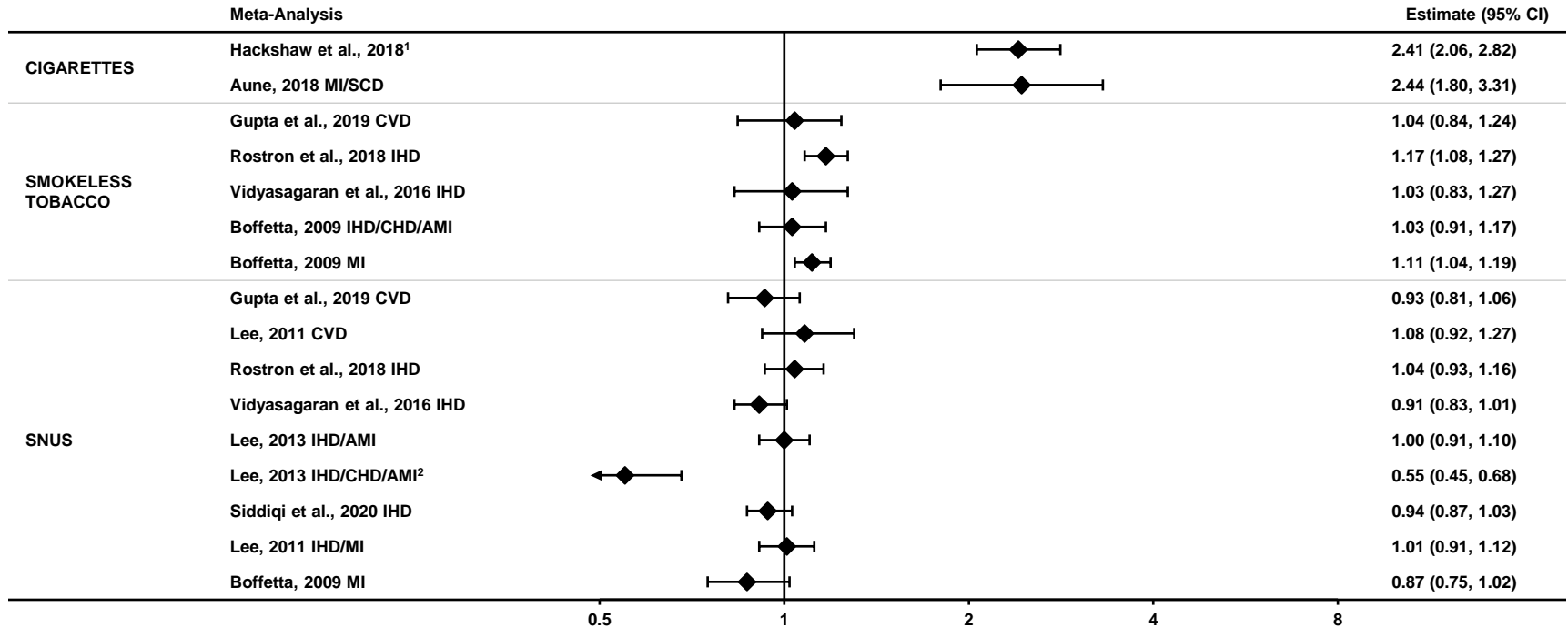


# Epidemiological Data Demonstrates that MST and Snus Users Have Lower Risk of COPD Compared to Cigarette Smokers



1. Meta-analysis. Study was on morbidity and RRs were expressed relative to never smokers (or near equivalent).
2. Study was on mortality with HRs relative to never use of ST. Estimates for ST and snus are from individual studies because no meta-analyses were identified from the literature search.
3. Study investigated the risk of COPD among switchers from cigarettes to ST compared to no tobacco use. Switchers were defined as smokers who were former exclusive cigarette smokers and were currently using ST and having begun doing so at the time of or after they quit exclusive cigarette smoking
4. The outcome of the Roosaar et al. study is respiratory death, which includes COPD.

# Epidemiological Data Demonstrates that MST and Snus Users Have Lower Risk of Smoking Related Heart Disease Compared to Cigarette Smokers



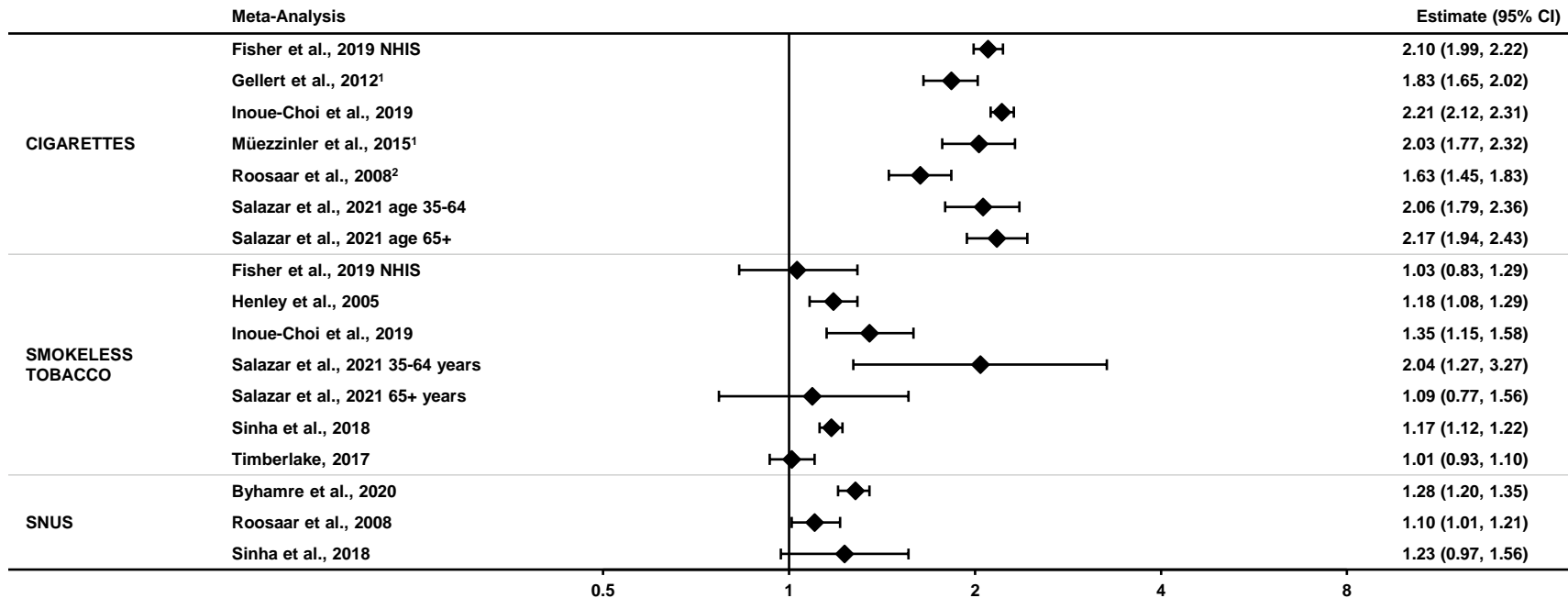
1. ALCS pooled estimates for studies conducted in the US using a random-effect meta-analysis model.

2. Study investigated the risk of heart disease among switchers from cigarettes to snus. The estimate compares individuals who were current snus users who formerly smoked to individuals who continued to smoke.





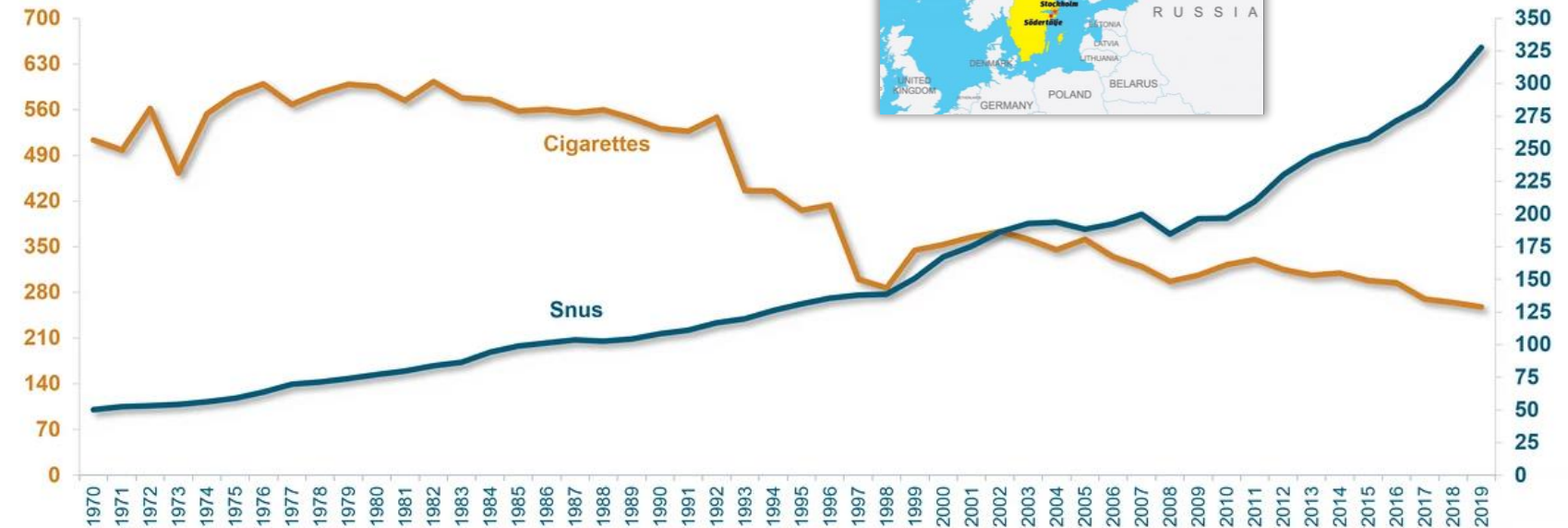
# Epidemiological Data Demonstrates that MST and Snus Users Have Lower Risk of All-Cause Mortality Compared to Cigarette Smokers



1. 60 years and older  
2. Age <75 years

# Harm Reduction Success – Swedish Experience

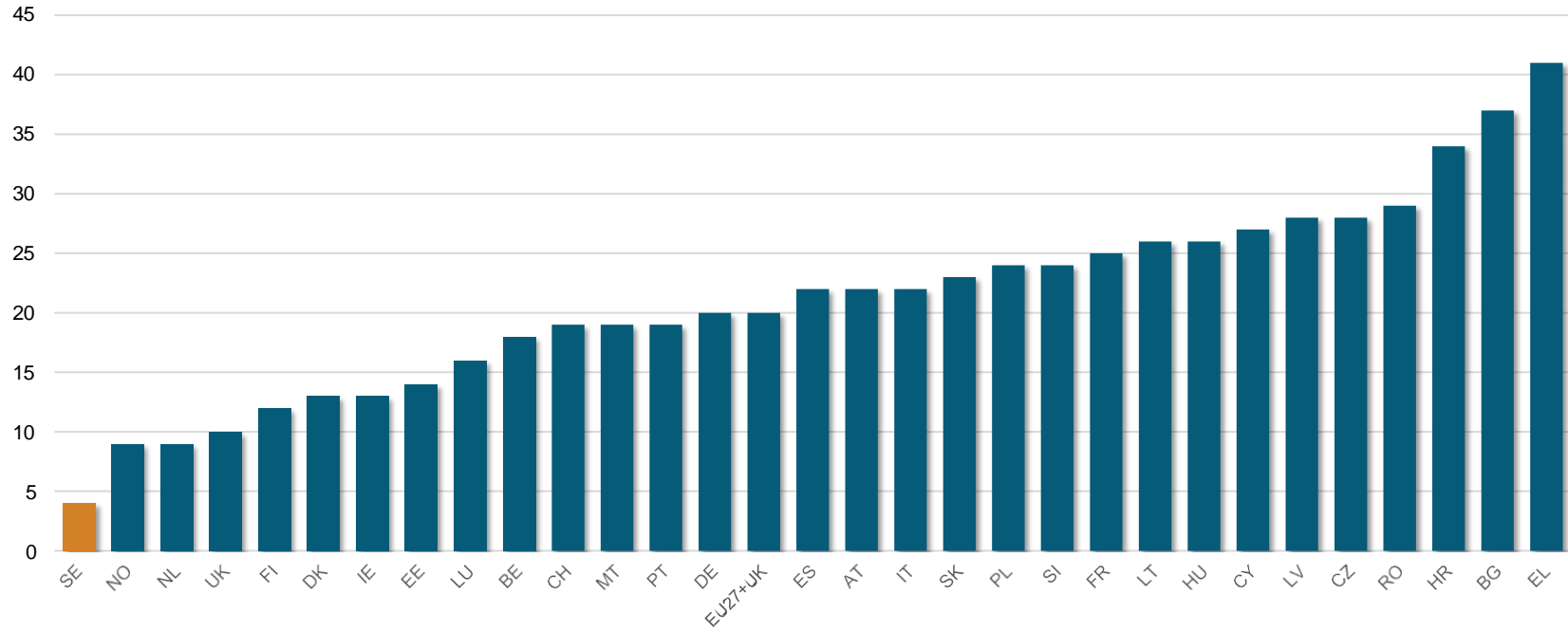
**Cigarettes**  
(million packs)



Source: <https://www.swedishmatch.com/Snus-and-health/Tobacco-use/Tobacco-use-in-figures/> accessed 8/24/21

# Harm Reduction Success – Swedish Experience

## Smoking prevalence in Sweden is the lowest among EU countries



Source: [https://www.swedishmatch.com/globalassets/documents/presentations/2021\\_companypresentation\\_swedishmatch\\_en.pdf](https://www.swedishmatch.com/globalassets/documents/presentations/2021_companypresentation_swedishmatch_en.pdf) accessed 8/24/21



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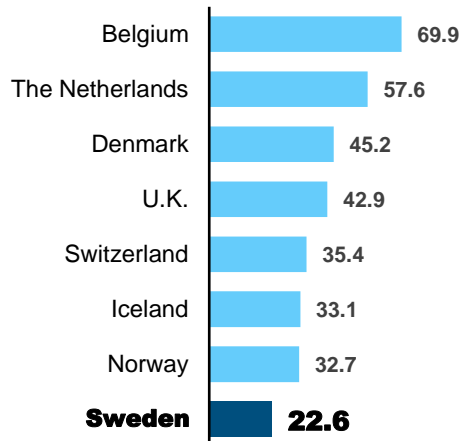
# Harm Reduction Success – Swedish Experience

## Smoking-related disease in Sweden is correspondingly low

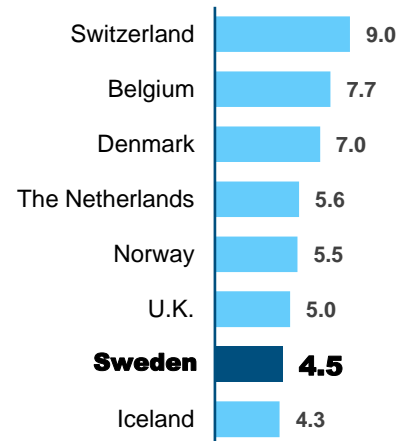
“ We have very good evidence that harm reduction is operating and is contributing to less death and disease from tobacco... ”

said Swedish scientist and consultant Dr Karl Fagerström at Addiction Conference 2021

Lung Cancer mortality rates among European men<sup>1</sup>



Oral Cancer incidence rates among European men<sup>1</sup>



1. per 100,000 by country; Rates are 2002 data and age-standardized (world population)  
Source: International Agency for Research on Cancer



# In the U.S., There is Scientific Consensus That Smokeless Tobacco has Lower Risk Compared to Cigarettes

“

...smokers unable or uninterested in quitting should consider switching to a less hazardous smoke-free tobacco/ nicotine product for as long as they feel the need for such a product.

”

---

**American Association of Public Health Physicians - Principles to Guide AAPHP Tobacco Policy**

(Adopted 9/12/2011)

“

...if smokers who cannot or will not quit their dependence on nicotine switched completely to smokeless tobacco products, they would likely experience a reduction in tobacco-caused mortality and morbidity.

”

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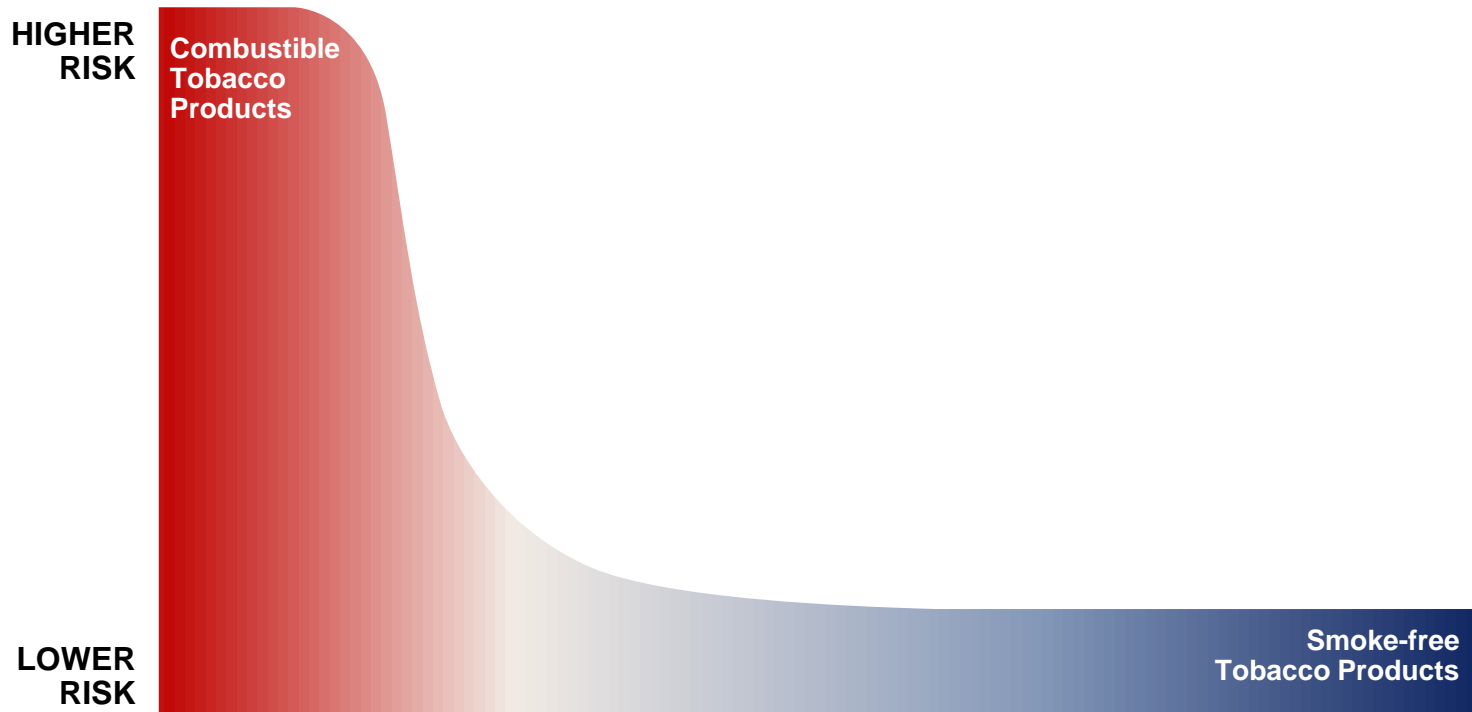
**The Strategic Dialogue on Tobacco Harm Reduction: a vision and blueprint for action in the U.S.**

Tobacco Control, 2009

M. Zeller, D. Hatsukami, and the Strategic Dialogue on Tobacco Harm Reduction Group



# Risk Cliff Between Combustible & Smoke-free Tobacco

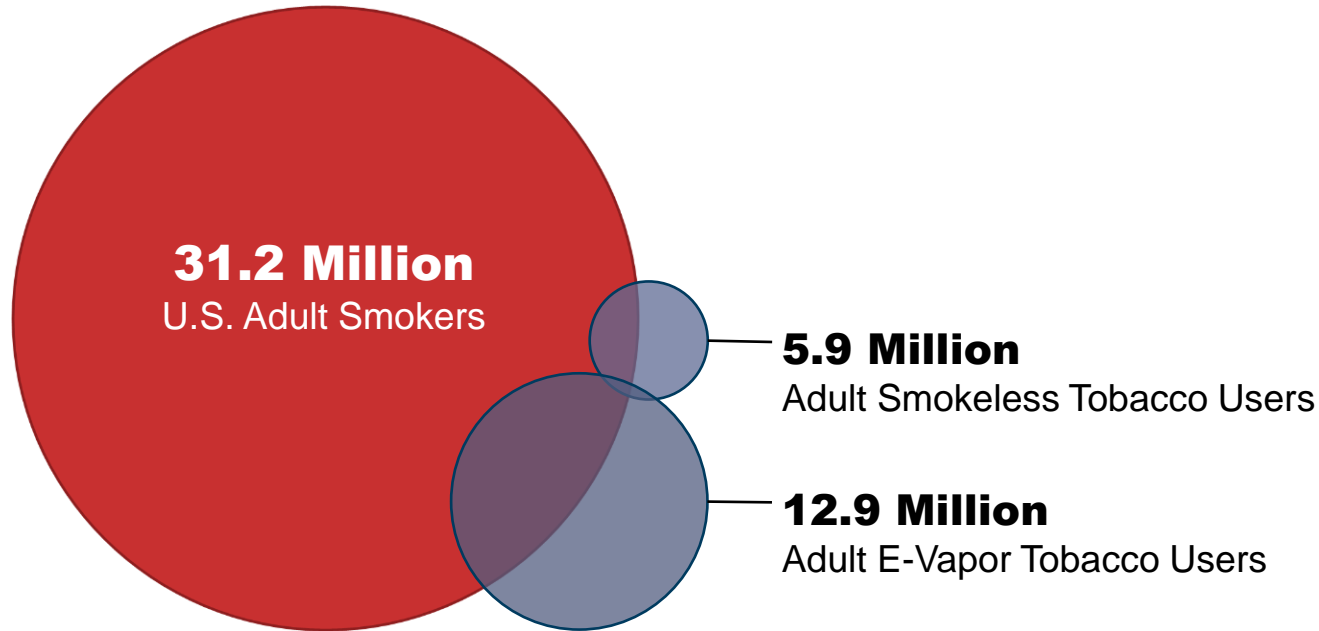


Adapted from Nutt, et. al Estimating the Harms of Nicotine-Containing Products Using the MCDA Approach. *Eur. Addict Res* 2014; 20:218-225.



# Distribution of Adult\* Tobacco Consumers

Altria Client Services LLC Adult Tobacco Consumer Tracker Q1, 2022



Source: [Altria Client Services LLC Adult Tobacco Consumer Tracker \(ALCS ATCT\), Q1, 2022](#)

\*Age 21 or older.

Cigarette smokers include those who report having smoked at least 100 cigarettes in their lifetime and now smoking every day or some days. Smokeless Tobacco users include those who report having used smokeless tobacco (such as dip, spit, moist snuff, pouches, chewing tobacco or snus) fairly regularly and now using smokeless tobacco every day or some days. E-Vapor users include those who report having used e-vapor fairly regularly in their lifetime and now using e-vapor every day or some days.



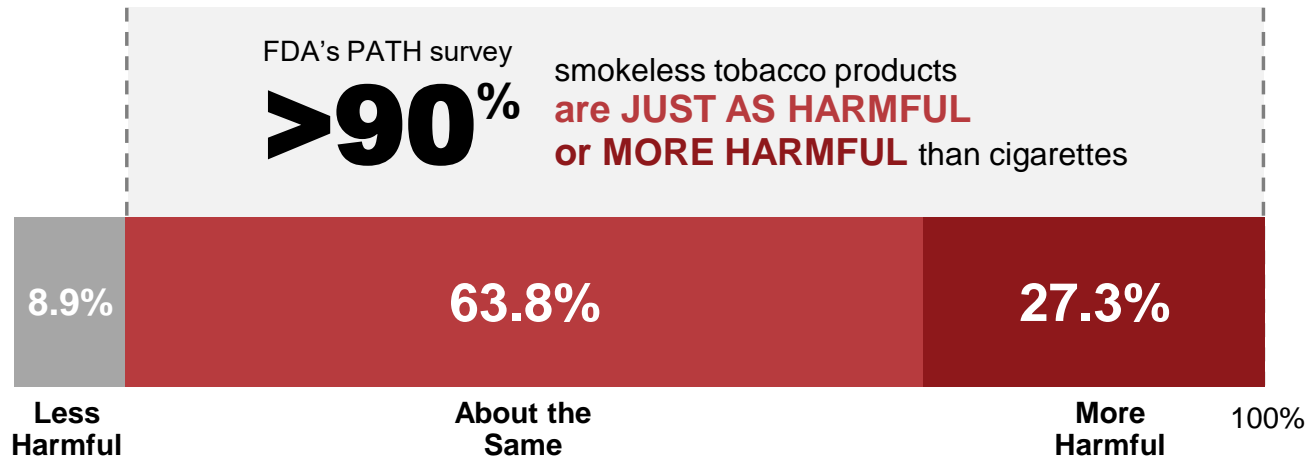
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# In the U.S., there are Widespread Misperceptions of the Risk of ST Products Relative to Cigarettes



Is using smokeless tobacco less harmful, about the same, or more harmful than smoking cigarettes?



ALCS Analysis of PATH Wave 1 (Sept. '13 – Dec. '14).



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# Prevailing Nicotine Misperceptions Among Doctors

September 8, 2020

RUTGERS TODAY

Explore Topics

Health Care

## Rutgers-Led National Survey Uncovers Doctors' Misconceptions About Nicotine Risks

83%

Strongly believed that nicotine directly contributed to heart disease

81%

Thought nicotine contributed to COPD

80%

Incorrectly believe nicotine causes cancer

Steinberg, M.B., Bover Manderski, M.T., Wackowski, O.A. et al. Nicotine Risk Misperception Among US Physicians. *J GEN INTERN MED* (2020). <https://doi.org/10.1007/s11606-020-06172-8>.



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# ST and Snus Modified Risk Tobacco Product Applications (MRTPAs)

PRODUCT	CLAIM(S)
<b>General Snus</b> <i>Submitted 6/2014</i> <i>Market Granted Order 10/2019</i> Source: <a href="#">MRTPA Order Letter</a>	“Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.”
<b>Camel Snus</b> <i>Submitted 3/2017</i> <i>Pending</i> Source: <a href="#">TPSAC Applicant Briefing Book 2018</a>	<p><b>Claim #1:</b> Smokers who <b>switch completely</b> from cigarettes to Camel SNUS can significantly reduce their risk of lung cancer, oral cancer, respiratory disease, and heart disease.</p> <p><b>Claim #2:</b> Smokers who <b>SWITCH COMPLETELY</b> from cigarettes to Camel SNUS can greatly reduce their risk of lung cancer, oral cancer, respiratory disease, and heart disease.</p> <p><b>Claim #3:</b> Smokers who <b>SWITCH COMPLETELY</b> from cigarettes to Camel SNUS can greatly reduce their risk of lung cancer and respiratory disease.</p>
<b>Copenhagen Snuff Fine Cut</b> <i>Submitted 3/2018</i> <i>Pending</i> Source: <a href="#">TPSAC Applicant Briefing Book 2019</a>	“IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer.”



# Emerging Landscape of Oral Tobacco Derived Nicotine (OTDN) Products

FUTURE

OTDN products contain no tobacco



Nicotine Pouches



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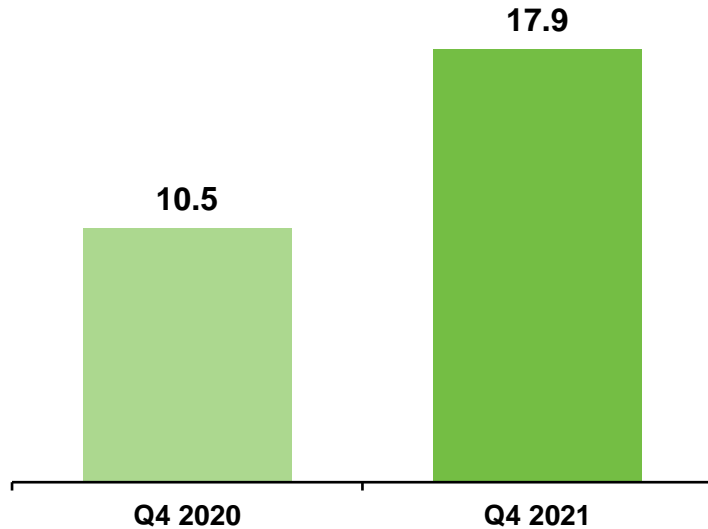
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# Oral Nicotine Pouch (ONP) Category

(share of total U.S. oral tobacco category)

> FUTURE

## ONP Share



**There are now  
~1 million adult  
oral nicotine pouch  
consumers\***

Sources:

IRI InfoScan Oral Tobacco MOC, We 01/02/22

ATCT 12MM as of September 2020, Awareness Study and Innovative Products Study

\*Based on responses for Oral Tobacco Derived Nicotine Products.



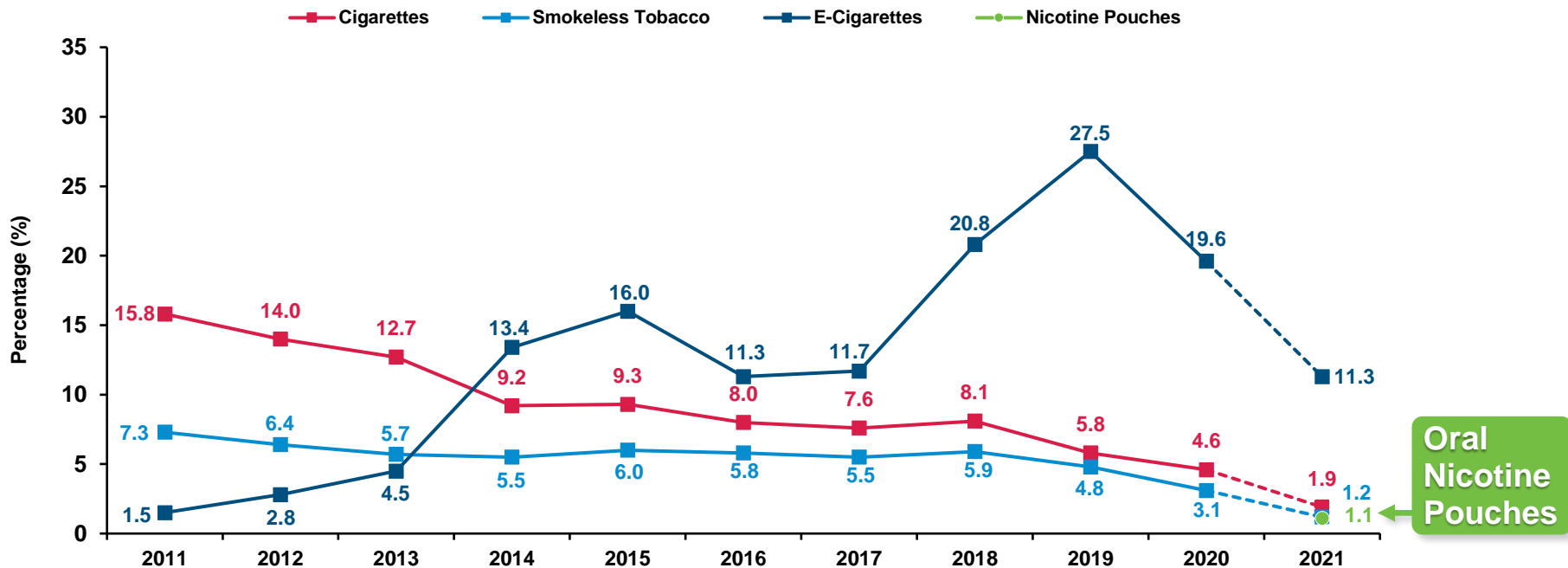
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Jason Flora | Regulatory Affairs | Altria Client Services LLC | 75th Tobacco Science Research Conference, September 12, 2022



# Current Tobacco Product Use Among High School Students

## National Youth Tobacco Survey, 2011-2021



Sources: [Tobacco Product Use Among Middle and High School Students — United States, 2011–2018](#); [Tobacco Product Use and Associated Factors Among Middle and High School Students — United States, 2019](#); [Tobacco Product Use Among Middle and High School Students — United States, 2020](#); and [Tobacco Product Use and Associated Factors Among Middle and High School Students — United States, 2021](#).

Note: Any tobacco use is past 30-day use of cigarettes, cigars, smokeless tobacco, electronic cigarettes, hookahs, pipe tobacco, and/or bids, in addition to heated tobacco products (2020-2021) and nicotine pouches (2021) on ≥ 1 day in the past 30 days.  
 Note: in 2014 and 2015, modifications were made to the e-cigarette measure to enhance its accuracy, which may limit the comparability of these estimates to those collected in previous years. In 2019, modifications were made to the survey, as well as the e-cigarette measure through inclusion of a brand example (JUUL); authors caution against comparisons to prior years. For smokeless tobacco, 2015 and prior years data are not comparable due to methodological changes into 2015. In 2015 smokeless tobacco includes chewing tobacco/snuff/dip, snus, and dissolvable tobacco because of limited sample sizes. Prior to 2015, smokeless tobacco included only chewing tobacco/snuff/dip. In 2021, the survey was conducted online during the COVID-19 pandemic with an overall lower participation rate than during previous years. Due to differences in data collections procedures, any comparison of the 2021 NYTS estimates to previous NYTS survey years that were primarily conducted on school campuses should be interpreted with caution. Dashed lines from 2020-2021 represent these differences.

# Oral Nicotine Pouches Have Lower HPHCs Compared to ST and Snus



Article

## Market Survey of Modern Oral Nicotine Products: Determination of Select HPHCs and Comparison to Traditional Smokeless Tobacco Products

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**Abstract:** In an effort to combat the risks associated with traditional tobacco products, tobacco product innovation has been redirected towards reducing the consumer's potential exposure to harmful or potentially harmful constituents (HPHCs). Among these innovations are modern oral nicotine products (MONPs). This product class aims to deliver nicotine while limiting the consumer's potential toxicant exposure. This body of work sought to investigate the potential for select HPHC exposure (tobacco-specific nitrosamines, carbonyls, benzoflpyrene, nitrite, and metals) from MONPs and to compare it to that from traditional tobacco products. This work expands on previously published studies both in terms of diversity of products assessed and analytes tested. In total, twenty-one unique MONPs were assessed and compared to four traditional tobacco products. We found that there was a difference in the potential exposure based on the MONP filler—plant material vs. granulate/powder. Typically, the HPHC levels observed in plant-based MONPs were higher than those observed for granulate/powder products, most notably within the metals analysis for which the levels were occasionally greater than those seen in traditional smokeless tobacco products. Generally, the overall HPHC levels observed in MONP were at or below those levels observed in traditional tobacco products.

**Keywords:** modern oral nicotine products; HPHCs; reduced-risk products; product characterizations

### 1. Introduction

It is generally acknowledged that use of tobacco products is associated with risks. In an effort to combat these risks, tobacco science and production have refocused their efforts to provide consumers with products that may limit their potential exposure to harmful or potentially harmful constituents (HPHCs). In 2009, the Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act") was passed in which control over regulatory oversight was given to the US Food and Drug Administration (FDA) [1,2]. Included in this act were specific requirements for the language to be included on warning labels for various tobacco products and the need for scientific rigor when making claims for any modified risk profile a product may offer [3]. To be able to claim a modified risk profile, manufacturers must submit scientific evidence to support the claim as part of a Modified-Risk Tobacco Product (MTRP) application, and FDA permission must be received. The Tobacco Control Act further required the FDA to establish a list of harmful or potentially harmful constituents to human health found in mainstream smoke and tobacco products (referred to as the "HPHC list") [1].

Reducing the consumer's exposure to compounds on the HPHC list is one way that risk can conceivably be lowered. Given that combustion is the main source for many of the HPHC compounds, alternative means of delivering nicotine are being promoted and developed. Examples of such products are electronic nicotine delivery systems (ENDS) and heated tobacco products (HTP), which both produce aerosolized nicotine for inhalation.

“

Generally, the overall HPHC levels observed in MONP were at or below those levels observed in traditional tobacco products.

Overall, the MONPs appear to pose a much-reduced exposure risk compared to STPs...

”

Emphasis added



Citation: Jablonski, J.J.; Cheetham, A.G.; Martin, A.M. Market Survey of Modern Oral Nicotine Products: Determination of Select HPHCs and Comparison to Traditional Smokeless Tobacco Products. *Separations* 2022, 9, 65. <https://doi.org/10.3390/separations9030065>

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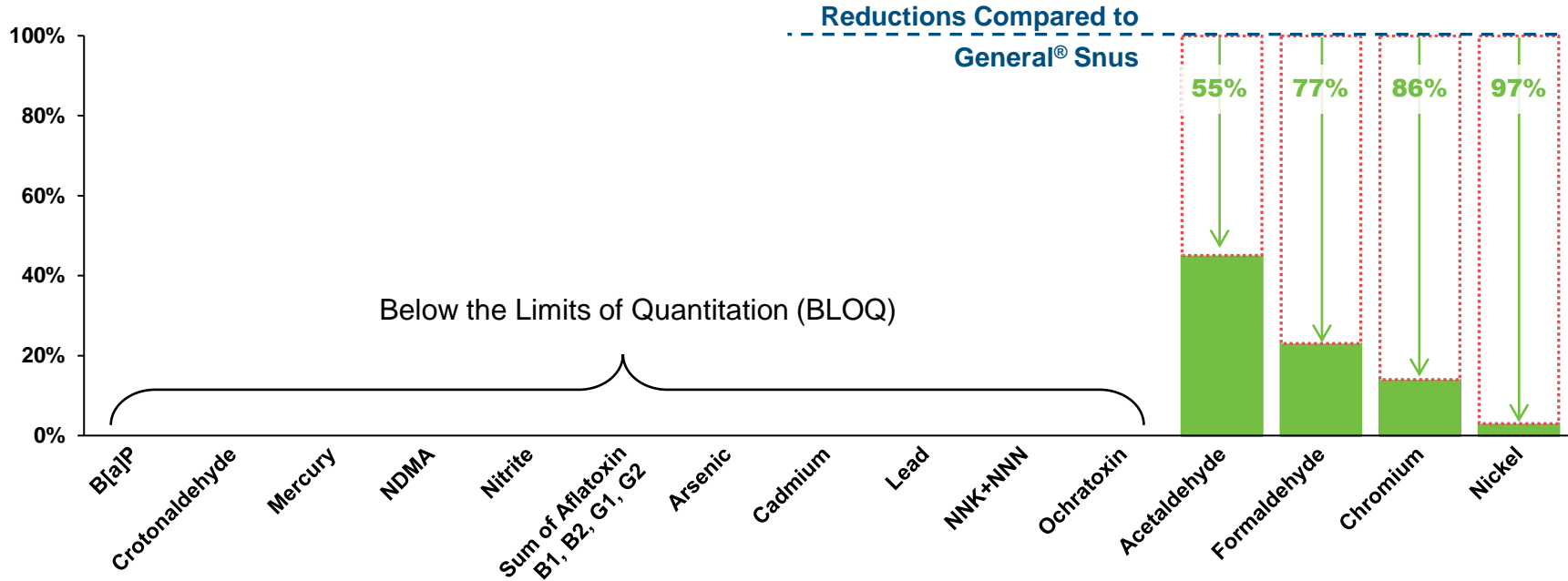
*Separations* 2022, 9, 65. <https://doi.org/10.3390/separations9030065>

<https://www.mdpi.com/journal/separations>

Jablonski, J. J., Cheetham, A. G., & Martin, A. M. (2022). Market Survey of Modern Oral Nicotine Products: Determination of Select HPHCs and Comparison to Traditional Smokeless Tobacco Products. *Separations*, 9(3), 2297-8739. doi:10.3390/separations9030065



# Percent Reduction in HPHCs — Maximum Levels in on!® Compared to Mean Levels in General® Snus<sup>1</sup>



See Karl Wagner's Poster

1. Data source: Mean HPHC level determined in the four MRTP authorized General® snus products tested for this study. The four General® snus products include General Portion Original Large, General Mint Portion White Large, General Portion White Large, General Wintergreen Portion White Large.



# FDA has Determined That a OTDN is Appropriate for the Protection of Public Health – Verve®

## FDA Permits Marketing of New Oral Tobacco Products through Premarket Tobacco Product Application Pathway

Data Show Youth, Non-Smokers, and Former Smokers Are Unlikely to Initiate or Reinitiate Tobacco Use with These Products

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For Immediate Release: October 19, 2021

Today, the U.S. Food and Drug Administration (FDA) announced that it has approved the marketing of four new oral tobacco products under the premarket tobacco product (PMTA) scientific evaluation pathway. This is the first time an agency has used the PMTA pathway to approve new tobacco products. The FDA is committed to ensuring that tobacco products on the market are safe and effective. While there is still a risk for youth and young adults from using tobacco products, the FDA is committed to ensuring that tobacco products on the market are safe and effective. The FDA is committed to ensuring that tobacco products on the market are safe and effective.



**U.S. FOOD & DRUG ADMINISTRATION**

U.S. Food & Drug Administration  
10902 New Hampshire Avenue  
Silver Spring, MD 20993  
www.fda.gov

### PMTA Scientific Review: Technical Project Lead (TPL)

New Tobacco Products Subject of this Review <sup>1</sup>	
STN	PM0000470-PM0000473
<b>Common Attributes</b>	
Submission Date	July 23, 2018
Receipt Date	July 23, 2018
Applicant	U.S. Smokeless Tobacco Company LLC
Product manufacturer	U.S. Smokeless Tobacco Company LLC
Application Type	Standard
Product category	Other
Product subcategory	Other
<b>Cross-Referenced Submission</b>	
All new tobacco products	(b) (4)
<b>Supporting FDA Memoranda Relied Upon in this Review</b>	
All new tobacco products	None
<b>Recommendation</b>	
Issue Marketing Order Letters	

DISCIPLINES REVIEWED	Primary Reviewers	DATE OF REVIEW
Behavioral and Clinical Pharmacology	Babita Das, Kia Jackson	June 26, 2020
Chemistry	Lida Oum	July 14, 2020
Environmental Science	Ronald Edwards	June 25, 2020

“

...evidence shows these products could help addicted smokers who use the most harmful combusted products completely switch to a product with potentially fewer harmful chemicals.

”

### Excerpt from CTP 10/19/21 FDA News Release

<https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-new-oral-tobacco-products-through-premarket-tobacco-product-application>

“

...Due to minimal HPHC exposure, the new **products likely present lower public health concern for tobacco-related diseases than cigarette smoking** or other smokeless tobacco products, and the health effects of the candidate products would likely be similar to those of current NRT products, including nicotine gum.

”

### Excerpt from CTP Technical Project Lead Review 10/08/21

[https://ecm.pmusa.net/ecm/lisapi.dll/fetch/2000/1902072/5827717/75496706/75760731/117388143/98884138/112534725/113019630/Verve\\_PMTA\\_TPL\\_October\\_2021\\_Redacted.pdf?nodeid=115043336&vernum=-2](https://ecm.pmusa.net/ecm/lisapi.dll/fetch/2000/1902072/5827717/75496706/75760731/117388143/98884138/112534725/113019630/Verve_PMTA_TPL_October_2021_Redacted.pdf?nodeid=115043336&vernum=-2)

Emphasis added



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# Bridging to the Epidemiological Evidence of ST Products, Including Snus to Demonstrate the Long-Term Health Effects

## FORMAT

ONP have format similarities and differences compared to ST (U.S.) and snus (Sweden and Norway)

**on!®**  
Mint 4mg



22.6X13.6 mm

**General Snus**  
White Wintergreen



33.7X18.6 mm

**Copenhagen Pouch (ST)**  
Wintergreen



42.3X19.7 mm

*Note: Most ST epidemiology is based on loose products*

## EXPOSURE

Based on our studies and the scientific literature, on!® nicotine pouches compared to ST (U.S.) and snus (Sweden and Norway)

- Used in a similar manner (held between the lip and gum) with lower or comparable frequency and duration of use
- Share a similar route of administration
- Lower or comparable nicotine and free nicotine levels
- Substantially lower levels of HPHCs (except for nicotine)





## PAST

# SUMMARY

People have been smoking and chewing tobacco **for a really long time**

This long history provides us with extensive epidemiological evidence demonstrating that **the use of MST or snus compared to smoking cigarettes presents:**

### LOWER RISK OF

Lung cancer

Mouth cancer

COPD

Smoking-related heart diseases



The Swedish Experience shows that encouraging adult smokers to switch to smoke-free products (e.g., snus) is **a proven harm reduction approach**







# PRESENT

## SUMMARY

A scientific consensus exists in the U.S. that there is a continuum of risk among tobacco products and that

**ST products are substantially lower risk compared to cigarettes**



ST products present a harm reduction opportunity for adult smokers unable or unwilling to quit all tobacco



The emerging OTDN category may offer an even greater harm reduction opportunity



Widespread misperceptions of risk form barriers to tobacco harm reduction





# FUTURE

## SUMMARY

### We can accelerate tobacco harm reduction

by providing adult smokers with a portfolio of satisfying, FDA-authorized smoke-free alternatives and accurate and truthful communications about their relative risk



Satisfying smoke-free tobacco products that appeal to adult smokers



Scientifically accurate relative risk communications to adult smokers

## Meaningful tobacco harm reduction in the U.S.





# Thank You

Special  
thanks to

Karl Wagner, Ph.D.

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Mohamadi Sarkar, M.Pharm., Ph.D., FCCP

