



GTNF 2024

Advancing Responsible Innovation

24 – 26 September 2024 | Athens, Greece

Nicotine Science

Mohamadi Sarkar, M. Pharm., PhD., FCP

Fellow, Scientific Strategy, Regulatory Affairs

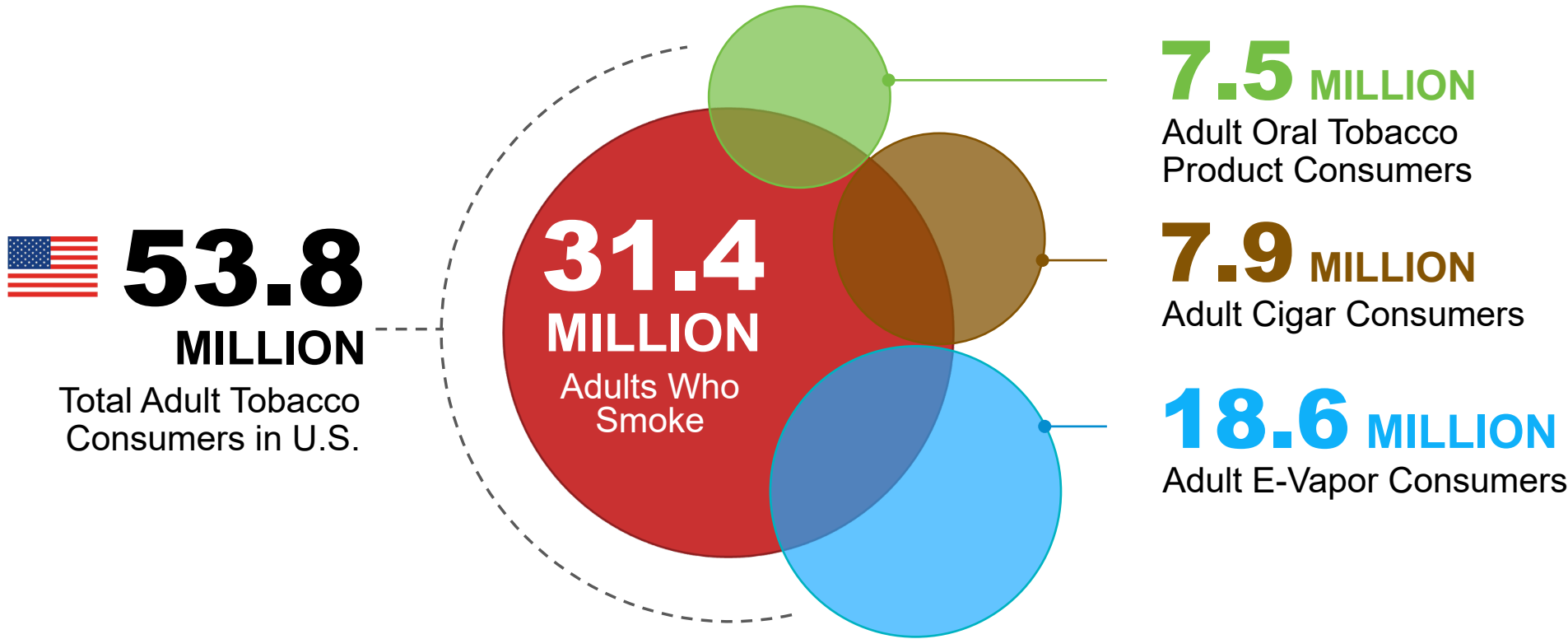
Altria Client Services LLC.

Professor of Clinical Pharmacology

VCU School of Pharmacy

Richmond, VA

Population of Adults Who Use Tobacco Is Still Sizeable



Source: ALCS Adult Tobacco Consumer Tracker 2014 - Q2 2024 Annual Prevalence Estimates.
Prevalence is calculated based on reported past 30-day usage of cigarette, e-vapor and oral tobacco products. We began to include oral nicotine products in the oral tobacco product category since 2020.
Overlaps do not represent real number of dual users



1.25 BILLION Adult Tobacco Consumers Worldwide

According to latest estimates by WHO. WHO Press [Release](#), 16 January 2024



Less Harmful Alternative Nicotine Delivery Products Can Help Reduce Smoking-Related Morbidity and Mortality



**PROFESSOR MICHAEL ANTHONY
HAMILTON RUSSELL**
(1932–2009)

“ People smoke for nicotine
but die from the tar. ”

[Emphasis added]

Less Harmful Alternative Nicotine Delivery Products Can Help Reduce Smoking-Related Morbidity and Mortality



**PROFESSOR MICHAEL ANTHONY
HAMILTON RUSSELL**
(1932–2009)

“ People smoke for nicotine
but die from the tar. ”

[A]lternative nicotine delivery products for cessation would need to be **promoted actively** to smokers for them to compete with cigarettes, that **these products** would need to be **available and acceptable to smokers**, and that they would **need to deliver nicotine** sufficiently in order **to satisfy cravings**.

Russell, M.A.H. The future of nicotine replacement.
British Journal of Addiction, 86:653-658 (1991)

[Emphasis added]

Harmful Effects of Cigarette Smoke Should Not be Conflated with Nicotine



The NEW ENGLAND
JOURNAL of MEDICINE

Perspective

A Nicotine-Focused Framework for Public Health

Scott Gottlieb, M.D., and Mitchell Zeller, J.D.

“The availability of potentially less harmful tobacco products could reduce risk while delivering satisfying levels of nicotine for adults who still need or want it.”

A Nicotine-Focused Framework for Public Health. Gottlieb S, Zeller M. *N Engl J Med*. 2017 Sep 21;377(12):1111-1114

[Emphasis added]



Altria

Altria Client Services | M. Sarkar GTNF Panel Discussion | September 25th, 2024

Harmful Effects of Cigarette Smoke Should Not be Conflated with Nicotine



The NEW ENGLAND
JOURNAL of MEDICINE

Perspective

A Nicotine-Focused Framework for Public Health

Scott Gottlieb, M.D., and Mitchell Zeller, J.D.

“The availability of potentially less harmful tobacco products could reduce risk while delivering satisfying levels of nicotine for adults who still need or want it.”

“Nicotine, though not benign, **is not directly responsible for the tobacco-caused cancer, lung disease, and heart disease that kill hundreds of thousands of Americans each year.**”

A Nicotine-Focused Framework for Public Health. Gottlieb S, Zeller M. *N Engl J Med*. 2017 Sep 21;377(12):1111-1114

[Emphasis added]



Altria

Altria Client Services | M. Sarkar GTNF Panel Discussion | September 25th, 2024

Major Health Concerns for Nicotine*

*Informed by statements from peer reviewed publications and statements from authoritative bodies e.g. IARC, USSG Reports.
References can be found at the end of the presentation



Major Health Concerns for Nicotine*



2024 | Athens, Greece

**Nicotine is addictive
and not risk-free**



**Potentially less risky than cigarettes
when delivered without combustion**

*Informed by statements from peer reviewed publications and statements from authoritative bodies e.g. IARC, USSG Reports. References can be found at the end of the presentation



Altria

Altria Client Services | M. Sarkar GTNF Panel Discussion | September 25th, 2024

Major Health Concerns for Nicotine*



2024 | Athens, Greece

**Nicotine is addictive
and not risk-free**

→ **Potentially less risky than cigarettes
when delivered without combustion**



Reproductive toxicity

Can harm the baby
if pregnant or nursing¹



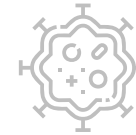
Adolescent brain development²

Youth should not use
any tobacco products



Cardiovascular disease

Not likely to cause CVD
but has acute effects and
can exacerbate CVD events
in at-risk individuals³



Cancer

Not a human carcinogen⁴
May function as a tumor
promotor, but evidence is
inadequate to infer the
presence or absence of a
causal relationship⁵



COPD

**Not likely to
cause COPD⁶**

Nicotine is **NOT directly responsible for
major smoking related cardiovascular disease, cancer and COPD⁷**

*Informed by statements from peer reviewed publications and statements from authoritative bodies e.g. IARC, USSG Reports. References can be found at the end of the presentation



Altria

Altria Client Services | M. Sarkar GTNF Panel Discussion | September 25th, 2024

FDA Conclusions Regarding Long-Term Oral Nicotine Use from NRTs



FEDERAL REGISTER

The Daily Journal of the United States Government



N Notice

Modifications To Labeling of Nicotine Replacement Therapy Products for Over-the-Counter Human Use

A Notice by the [Food and Drug Administration](#) on 04/02/2013



“ We have reviewed the published literature on this longer-term use of NRT products and **have not identified any safety risks associated with such use.** ”

[Emphasis added]

“ Upon reviewing the published reports of these and other studies, we have determined that the concomitant use of OTC NRT products with cigarettes or with other nicotine-containing products **does not raise significant safety concerns.** ”



Altria

Altria Client Services | M. Sarkar GTNF Panel Discussion | September 25th, 2024

Potential Beneficial Effects of Nicotine*



2024 | Athens, Greece



Therapeutic Benefits

Ulcerative colitis⁸

Neurodegenerative
disease^{9,10,11}



Source: <http://mindstudy.org/> Accessed 5/30/22



Functional Benefits

Cognitive Function^{12,13}

Relaxation / Stimulant¹⁴

Pleasure¹⁵

Other

**MOST IMPORTANT
BENEFIT**



Nicotine delivered without combustion can potentially
**reduce population harm from smoking
combustible cigarettes**

*Informed by peer reviewed publications

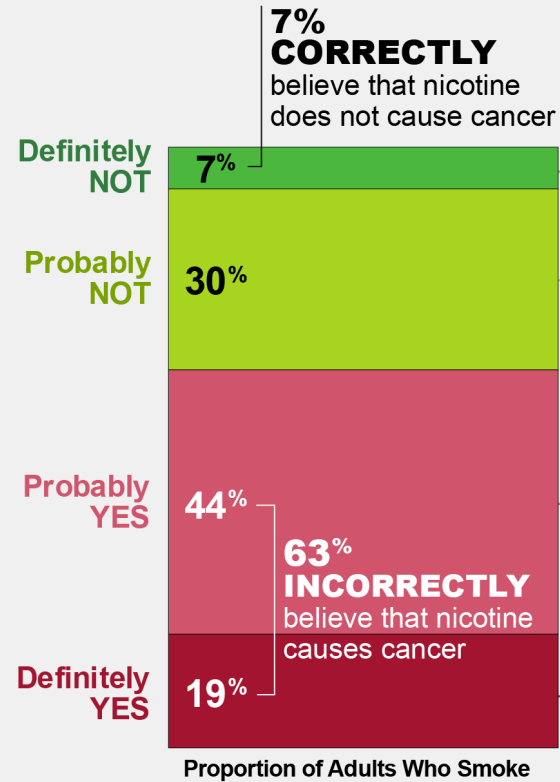


Altria

Altria Client Services | M. Sarkar GTNF Panel Discussion | September 25th, 2024

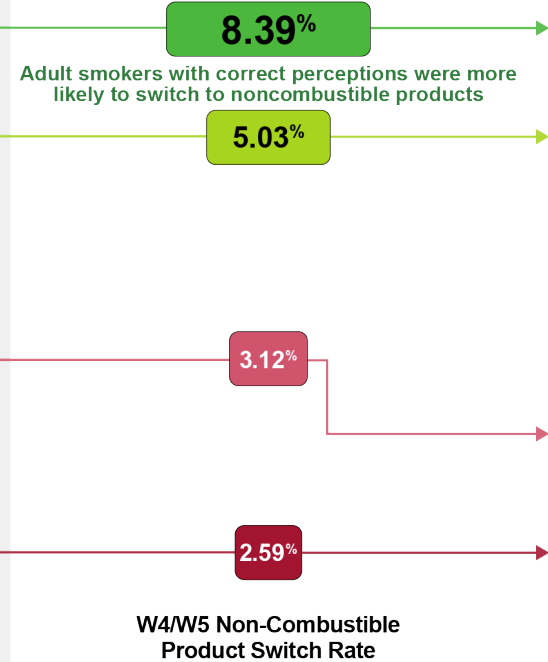
Majority of Adults Who Smoke Believe that “Nicotine Causes Cancer”

Perceptions

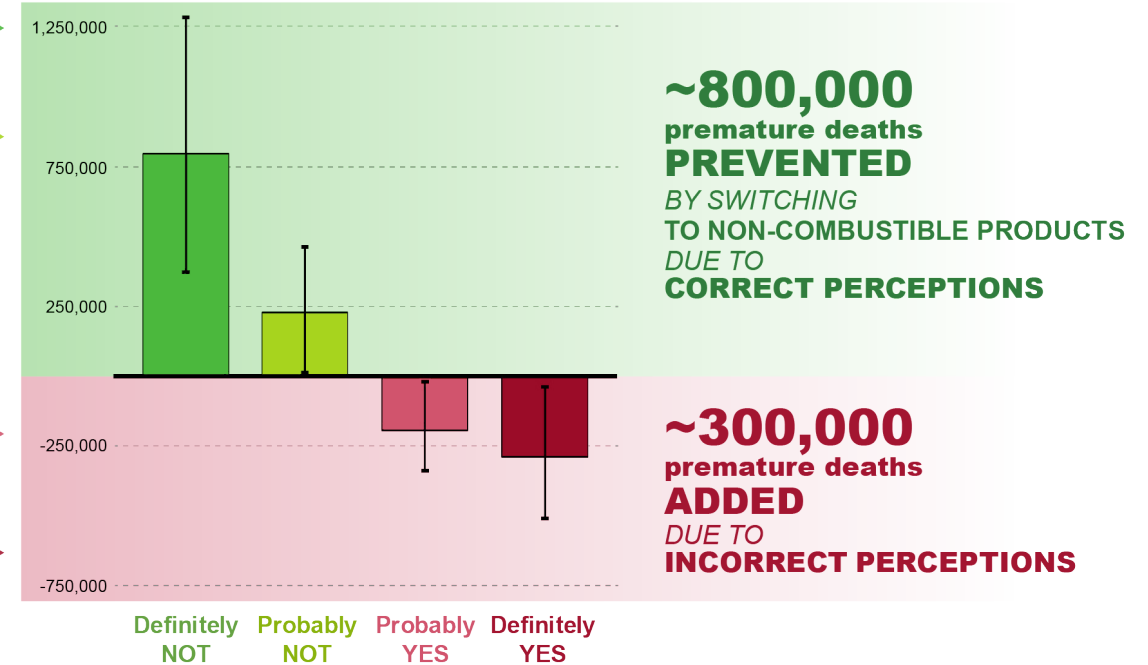


OUTCOMES Based on Adult Smokers' Nicotine Perception

Likelihood of Adult Smokers Switching to Non-combustible Products



Cumulative Premature Deaths Prevented Over 75 Years (Ages 35-85) Effects of Perception on Premature Deaths in Adult Smokers



Hannel T, Wie L, Muhmmad-Kah RS, Largo EG and Sarkar M., *Harm Reduction J*, 21:145 (2024)



Altria

Altria Client Services | M. Sarkar GTNF Panel Discussion | September 25th, 2024

Call to Action

➤ Adults who smoke combustible cigarettes may **benefit by switching to less harmful alternative nicotine delivery systems**

➤ **Correcting misperceptions of nicotine harm** may promote switching and achieve significant public health benefit

➤ **Failure to do so can cause harm**

The main concern is to
REDUCE tobacco-related
diseases

Russell, M.A.H. The future of nicotine replacement.
British Journal of Addiction, 86:653-658 (1991)

References



2024 | Athens, Greece

1. U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion. Office on Smoking and Health. A Report of the Surgeon General (2001). Women and Smoking.
2. U.S. Department of Health and Human Services. E-cigarette Use Among Youth and Young Adults: A Report of the Surgeon General. Centers for Disease Control and Prevention; 2016. Accessed Feb 14, 2024.
3. U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion. A Report of the Surgeon General (2000).
4. International Agency for Research on Cancer – European Code Against Cancer: <https://cancer-code-europe.iarc.fr/index.php/en/ecac-12-ways?id=199#:~:text=No.%20Nicotine%20is%20a%20common%20chemical%20compound%20found,to%20the%20carcinogens%20in%20smoked%20or%20smokeless%20tobacco.>
5. U.S. Department of Health and Human Services (2014), Chapter 5 Conclusions - page 5 and 126.
6. Scherer G, Pluym N and Scherer M. Literature Review on Nicotine's Role in Human Health. *Contributions to Tobacco & Nicotine Research*, 33 (2024): Issue 1 (February 2024).
7. Gottlieb S, Zeller M. A Nicotine-Focused Framework for Public Health. *N Engl J Med*. 2017 Sep 21;377(12):1111-1114.
8. R D Pullan, J Rhodes, S Ganesh, V Mani, J S Morris, G T Williams, R G Newcombe, M A Russell, C Feyerabend, G A Thomas, et al. Transdermal nicotine for active ulcerative colitis. *N Engl J Med* 1994 Mar 24;330(12):811-5.
9. D J Balfour, K O Fagerström. Pharmacology of nicotine and its therapeutic use in smoking cessation and neurodegenerative disorders. *Pharmacol Ther*. 1996;72(1):51-81.
10. P A Newhouse, M Kelton. Nicotinic systems in central nervous systems disease: degenerative disorders and beyond. *Pharm Acta Helv*. 2000 Mar;74(2-3):91-101.
11. J M Rusted, P A Newhouse, E D Levin. Nicotinic treatment for degenerative neuropsychiatric disorders such as Alzheimer's disease and Parkinson's disease. *Behav Brain Res*. 2000 Aug;113(1-2):121-9.
12. A Alhowail. Molecular insights into the benefits of nicotine on memory and cognition (Review). *Mol Med Rep*. 2021 Jun;23(6):398.
13. C S Myers, R C Taylor, E T Moolchan, S J Heishman. Dose-related enhancement of mood and cognition in smokers administered nicotine nasal spray. *Neuropsychopharmacology*. 2008 Feb;33(3):588-98.
14. B Silverstein. Cigarette smoking, nicotine addiction, and relaxation. *J Pers Soc Psychol*. 1982 May;42(5):946-50.
15. N L Benowitz. Pharmacology of Nicotine: Addiction, Smoking-Induced Disease, and Therapeutics. *Annu Rev Pharmacol Toxicol*. 2009; 49: 57–71.





GTNF 2024

Advancing Responsible Innovation

24 – 26 September 2024 | Athens, Greece

Any questions?