Juul Labs

2025 Update | Real-World Evidence White Paper: The Demonstrable Public Health Benefits of Smokefree Alternatives to Cigarettes

May 2025

Executive Summary

Cigarette smoking causes nearly one in five premature deaths in the United States — about 450,000 Americans each year, more than 1,200 every day. Half of the people who continue to smoke will die from related diseases.

The best option for adults who smoke cigarettes to reduce their health risks is to quit tobacco and nicotine products altogether.

However, for those adults who continue to use nicotine, switching to a noncombustible alternative can significantly reduce their exposure to harmful constituents in smoke and their risk of smoking-related disease.

In March 2023, Juul Labs published a white paper titled "The Real-World Impact of ENDS for Adult Smokers: Tobacco Harm Reduction Through Real-World Data and Evidence." This white paper offered evidence on the harms of smoking cigarettes and the demonstrable public health benefits of Americans who smoke switching to smokefree alternatives. Given the rapidly growing body of science, our second edition in May 2025 is updated to include recent science that continues to demonstrate these benefits.

This paper and our March 2023 white paper respond to repeated calls for data and evidence showing the real-world, public health benefit of electronic nicotine delivery systems (ENDS) — also referred to as e-cigarettes or vapor products — for adults who smoke. For example, in October 2021, Cohen et al. challenged the scientific community to

Important Disclosures:

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Certain analyses throughout this white paper were sponsored by Juul Labs, Inc. (JLI) as either JLI internal science or through PinneyAssociates, Inc., which provides consulting services on tobacco harm reduction to JLI.

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"consider how e-cigarettes (in all of their heterogeneity of design and use patterns) perform in the real world when making conclusions about their effects . . . ."[1]

Our review of evolving market data and research indicates that ENDS are not only helping adults who smoke reduce their individual risk, but at the population level these products are displacing combustible cigarettes – likely reducing the overall death and disease caused by cigarette smoking. We organize this review along four lines of evidence that reinforce the positive, real-world impact of ENDS products in the United States:

- Market data demonstrating faster-than-anticipated declines in cigarette sales as a result of increasing ENDS availability;
- Population surveys demonstrating that adults who smoke transition and completely switch from cigarettes to ENDS products or significantly reduce their cigarettes smoked per day if they do not switch completely;
- Economic data demonstrating that ENDS products are substitutes for cigarettes; and
- Population models demonstrating reductions in tobacco-related death and disease as ENDS use increases.

Key Takeaway: Real-world data and evidence discussed in this white paper demonstrate that — while ENDS are not without risk — Americans who smoke are transitioning and completely switching from combustible cigarettes to ENDS, resulting in reduced individual risk and a significant net benefit to public health.

In the United States, the regulatory and policy environment has been highly skeptical of less harmful noncombustible products, in part because of misconceptions about the role nicotine itself plays in smoking-caused disease. An unintended consequence of this skepticism has been a regulatory and policy environment that favors the deadliest form of tobacco, the combustible cigarette. Yet the lines of evidence we discuss have emerged despite this challenging environment – a sentiment amplified in a 2021 publication in the *American Journal of Public Health* by fifteen past presidents of the Society for Research on Nicotine and Tobacco who said:

> While evidence suggests that vaping is currently increasing smoking cessation, the impact could be much larger if the public health community paid serious attention to vaping's potential to help adult smokers, smokers received accurate information about the relative risks of vaping and smoking, and policies were designed with the potential effects on smokers in mind.[2]

JLI continues to support risk-proportionate policy and regulation for ENDS and other noncombustible products. Such a policy framework, at its core, applies the most stringent

[1] Cohen J.E., et al. (2022). "Balancing Risks and Benefits of E-Cigarettes in the Real World," *American* [1]*Journal of Public Health* 112, no. 2: pp. e1-e2.
[2] Balfour D.J.K., et al. (2021). "Balancing Consideration of the Risks and Benefits of E-Cigarettes," *American Journal of Public Health* 111, no. 9: pp. 1661-1672.

regulations to the riskiest products – combustible cigarettes – and encourages adults who continue to smoke to switch to less harmful, noncombustible alternatives.

The availability of reduced risk products is a necessary component of any comprehensive plan to transition adult smokers away from cigarettes. Unfortunately, not enough progress has been made to provide Americans who smoke with less harmful FDA-authorized alternatives to cigarettes that they find satisfying enough to switch to completely. Cigarettes continue to dominate the market, while less harmful products remain unauthorized. Through the Premarket Tobacco Product Application (PMTA) process, FDA has the statutory authority and mandate to promote public health by authorizing new, less harmful nicotine and tobacco products to the U.S. market. The statutory standard is "appropriate for the protection of public health," which relies on a weighing of the potential risks to nonusers of tobacco products (particularly those underage) and the benefits for Americans who smoke. This process necessitates science-based decision making, but, more importantly, deciding how to weigh the benefits and risks of these products is a question of policy and values.

FDA has been very cautious in its authorizations so far, despite incontrovertible evidence that these products are much less harmful than smoking and can promote switching.[3] Nicotine products introduced to the American marketplace should be scientifically-validated, responsibly marketed to adults, and made by manufacturers committed to following the law. It is important to note that a product authorization through the PMTA pathway is not permanent. FDA should be less timid in the products it authorizes because of its authority to revoke a product's authorization in post-market surveillance if it is no longer appropriate for the protection of the public health.

The bottom line: Technology allows us to sunder nicotine from tobacco, so Americans who smoke can consume nicotine in satisfying, but much safer, ways. With more innovative alternatives to cigarettes than ever before, no one should die because of how they consume nicotine. ENDS present a historic opportunity to leverage technology to make the combustible cigarette obsolete and end the unnecessary premature death and pervasive chronic illnesses caused by cigarette use.

[3] Lindson N, Butler AR, McRobbie H, Bullen C, Hajek P, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Livingstone-Banks J. Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews. 2024(1). https://doi.org/10.1002/14651858.CD010216.pub8

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Introduction: The Harm Caused by Combustible Cigarettes

Smoking remains the leading cause of preventable disease and premature death in the United States. Despite efforts to promote cessation and prevent initiation, particularly among youth, approximately 28 million Americans continue to smoke combustible cigarettes.[4]

Smoking-related disease causes nearly one in five premature deaths in the U.S.,[5] and half of those who continue to smoke will die from a smoking-related illness — about 450,000 Americans each year, more than 1,200 every day.[6] Smoking affects "nearly every organ in the body,"[7] as depicted in Figure 1 below from the 2014 Surgeon General's Report. An estimated 14 million Americans suffer from smoking-attributable medical conditions, including chronic obstructive pulmonary disease, heart attacks, stroke, lung disease, diabetes, and smoking-related cancers "including acute myeloid leukemia (AML) and cancers of the oral cavity and pharynx; esophagus; stomach; colon and rectum; liver; pancreas; larynx; lung, bronchus, and trachea; kidney and renal pelvis; urinary bladder; and cervix."[8]

The root cause of these smoking-related diseases is well-known: the burning of tobacco and inhalation of smoke, and the thousands of toxicants that come with it. As stated by the Surgeon General: **"The burden of death and disease from tobacco use in the United States is overwhelmingly caused by cigarettes and other combusted tobacco products; rapid elimination of their use will dramatically reduce this burden."**[9]

The best option for adults who smoke to reduce the risk of tobacco-related disease is to quit tobacco and nicotine products altogether**. But despite that nearly seven in ten smokers want to quit and more than 50% try to quit each year,[10] fewer than 10% actually succeed in quitting cigarettes.**[11]

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[4] Cornelius ME, Loretan CG, Jamal A, et al. Tobacco Product Use Among Adults – United States, 2021. MMWR Morb Mortal Wkly Rep 2023;72:475–483. DOI: http://dx.doi.org/10.15585/mmwr.mm7218a1

[5] CDC (2022, March 18).

[6] Le TT, Méndez D, Warner KE. New Estimates of Smoking-Attributable Mortality in the US From 2020 Through 2035. American Journal of Preventive Medicine. 2024 May 1;66(5):877-82. https://doi.org/10.1016/j.amepre.2023.12.017

[7] U.S. Department of Health and Human Services (2014).

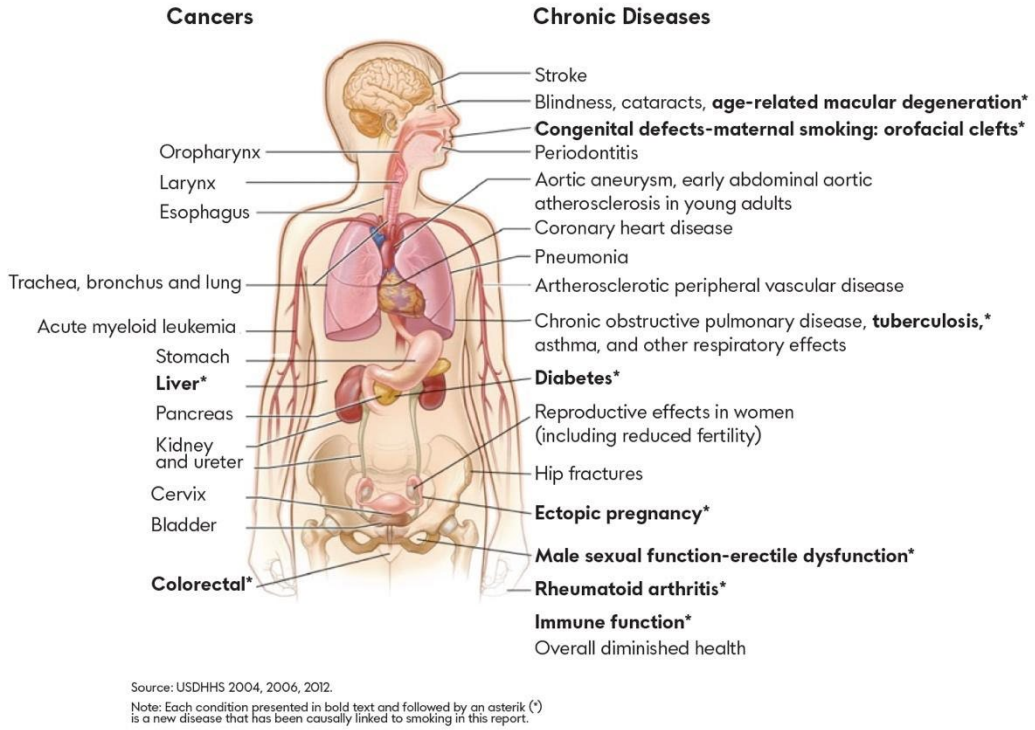
[8] Gallaway M.S., Henley S.J., Steele C.B., et al. (2018). Surveillance for Cancers Associated with Tobacco Use — United States, 2010–2014. MMWR Surveill Summ 2018;67(No. SS-12):1–42. DOI: http://dx.doi.org/10.15585/mmwr.ss6712a1.

[9] U.S. Department of Health and Human Services (2014).

[10] Babb S. (2017). Quitting smoking among adults—United States, 2000–2015. *MMWR Morb Mortal Wkly Rep.,* 65.

[11] VanFrank B, Malarcher A, Cornelius ME, Schecter A, Jamal A, Tynan M. Adult Smoking Cessation — United States, 2022. MMWR Morb Mortal Wkly Rep 2024;73:633–641. DOI: http://dx.doi.org/10.15585/mmwr.mm7329a1.

Figure 1: The Health Consequences Causally Linked to Smoking Cigarettes



Source: U.S. Department of Health and Human Services, *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General.*

Because smoking cigarettes is so extraordinarily harmful, for those who have not successfully quit, switching completely to a noncombustible alternative can significantly reduce their exposure to harmful constituents in smoke and their risk of smoking-related disease. At the population level, widespread, complete switching to noncombustible products by Americans who smoke will improve public health.

In this white paper, we offer evidence that ENDS — as demonstrated by real-world data and evidence — are reducing the prevalence of cigarette smoking and thus likely to reduce the individual- and population-level harms associated with cigarette use.

Ending Cigarette Use and FDA's Comprehensive Framework

In 1976, Dr. Michael Russell, a pioneer in nicotine and tobacco research, noted: "People smoke for the nicotine but die from the tar."[12]

This statement summarizes the rationale behind ending combustible cigarette use: Adults who smoke seek nicotine, but the vast majority of harm associated with smoking comes not from nicotine but from smoke. Smoke contains carcinogenic tobacco-specific nitrosamines and thousands of other compounds created through *combustion* (the burning and production of smoke), including carbon monoxide and volatile organic compounds.

[12] Russell M.A. (1976). Low-tar medium-nicotine cigarettes: a new approach to safer smoking. *Br Med J.,* 1(6023):1430-1433.

In 2017, the Food and Drug Administration (FDA) under President Trump announced a Comprehensive Plan for Tobacco and Nicotine Regulation (Comprehensive Framework) — a multi-dimensional plan that seeks to reduce the death and disease caused by combustible cigarettes, building upon the principle voiced by Dr. Russell more than forty years prior. At the time FDA unveiled its Comprehensive Framework, former Commissioner Scott Gottlieb and former Center for Tobacco Products (CTP) Director Mitch Zeller wrote in the *New England Journal of Medicine*:

> The regulatory framework for reducing harm from tobacco must include nicotine — the chemical responsible for addiction to tobacco products — as a centerpiece. 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. The FDA's approach to reducing the devastating toll of tobacco use must be rooted in this foundational understanding: other chemical compounds in tobacco, and in the smoke created by combustion, are primarily to blame for such health harms.[13]

Since 2017, FDA's proposed commitment to the Comprehensive Framework has yet to come to fruition. A 2022 external review of CTP by the Reagan-Udall Foundation found that "the Center's current goals and priorities are unclear."[14] **Nevertheless, the Comprehensive Framework laid out a powerful roadmap for reducing smoking rates in America and the associated premature death and disease caused by combustible cigarettes.**

The FDA's Comprehensive Framework envisions devaluing the combustible cigarette by reducing nicotine levels to minimally- or non-addictive levels and shifting adult smokers who have not successfully quit to noncombustible alternatives that fall lower on the continuum of risk (Figure 2).

The Comprehensive Plan hinges on having a lawful marketplace of scientifically-validated products that deliver nicotine without smoke and can effectively compete with cigarettes, recognizing that **not all products that deliver nicotine pose the same level of risk.** Products that burn tobacco and produce smoke, such as combustible cigarettes, present the highest risk. Products that deliver nicotine without burning tobacco are likely to present significantly less risk of harm.

[13] Gottlieb S., Zeller M. (2017). A nicotine-focused framework for public health. *N Engl J Med.,* [Emphasis added].
[14] Silvis et al. (2022). Operational Evaluation of Certain Components of FDA's Tobacco Program: A Report of the Tobacco Independent Expert Panel. *Regan Udall Foundation*. https://reaganudall.org/sites/default/files/2022-12/Tobacco%20report%20210pm.pdf.

Figure 2: The Continuum of Risk for Nicotine Delivery

Source: JLI analysis of continuum of risk, *FDA Comprehensive Framework*.

The vision of the Comprehensive Framework has been validated by independent research. One such paper emphasized that a very low nicotine product standard for combustible cigarettes could be complemented by less harmful, noncombustible alternatives:

> Tobacco harm reduction recognizes that tobacco abstinence or never using tobacco is the ideal outcome but accepts alternative ways to reduce harm among tobacco users. Harm reduction does not take precedence over measures that prevent tobacco use and help facilitate the achievement of abstinence, but rather plays a complementary role. Harm reduction has been considered a human rights issue, where all smokers, whether or not they want or are able to quit tobacco use, are provided a means to reduce tobacco-related harms . . . .[15]

This regulatory approach is also consistent with the preferences of adults who smoke who are looking for alternatives to combustible cigarettes — and over half of adults who smoke have expressed interest in less harmful products.[16] In the past decade, product innovation has led to an array of novel, noncombustible products that deliver nicotine without burning tobacco and are acceptable alternatives for millions of adult smokers.[17] The availability of a wide range of nicotine alternatives is likely to substantially improve public health, especially if these products enable complete switching from cigarette smoking.[18]

Indeed, population modeling projects that 8.5 million premature deaths could be averted by 2100 if the use of combustible cigarettes is drastically reduced while shifting demand for nicotine to noncombustible alternatives.[19]

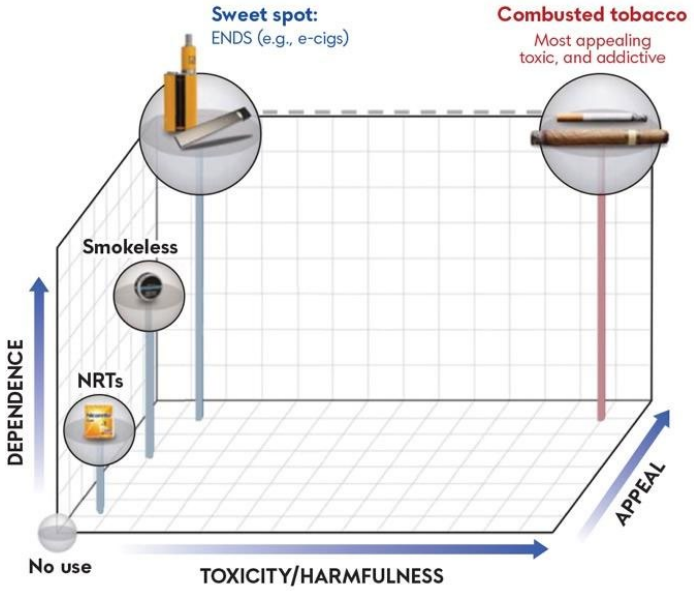
[15] Hatsukami D.K., Carroll D.M. (2020). Tobacco harm reduction: Past history, current controversies and a proposed approach for the future. *Prev Med.*,106099.
[16] Pearson J.L., Johnson A.L., Johnson S.E., et al. (2018). Adult interest in using a hypothetical modified risk tobacco product: findings from wave 1 of the Population Assessment of Tobacco and Health Study (2013-14). *Addiction*, 113(1):113-124.
[17] Dawkins L.E., McRobbie H. (2017). Changing behaviour: Electronic cigarettes. *British Psychological Society*. https://www.bps.org.uk/psychologist/changing-behaviours.
[18] Dawkins (2017).
[19] Apelberg B.J., Feirman S.P., Salazar E., et al. (2018). Potential public health effects of reducing nicotine levels in cigarettes in the United States. *New England Journal of Medicine*, 378(18):1725-1733.

ENDS as a Critical Tool for Making Cigarettes Obsolete

Less harmful alternatives to combustible cigarettes will deliver maximum public health benefit when large numbers of adult smokers switch completely to these products. For that to happen, these less harmful alternatives must be satisfying to adult smokers.

Following the Comprehensive Framework, Dr. Abrams et al.[20] proposed a "Three-Dimensional Framework for Harm Minimization" (Figure 3) that organizes "alternative nicotine delivery devices" (referred to as "ANDS" by Abrams, but "ENDS" in this white paper and other research) around their relative: "(a) harmfulness; (b) appeal; and (c) satisfaction including dependence." As the researchers wrote, this framework "provides a road map with which to envision how to optimize ANDS product use to successfully compete with and replace smoking."[21]

Figure 3: Three-Dimensional Framework for Harm Minimization



Source: Abrams et al., *Harm minimization and tobacco control: reframing societal views of nicotine use to rapidly save lives.* Note: Image modified to the more conventional "ENDS" from the published version, which described the category as "ANDS" (e-cigs=electronic cigarettes; ENDS=electronic nicotine delivery systems; NRTs=nicotine replacement therapies.)

To compete with combustible cigarettes — a highly effective nicotine-delivery product that many adult smokers will have used for years, if not decades — ENDS products must provide sufficient appeal and nicotine delivery.[22] Thus, products towards the front lower left of this framework — low in toxicity/harmfulness but also low in appeal and dependence potential — are unlikely to switch large numbers of adult smokers, despite being far less harmful than cigarettes. The researchers concluded this "has proven to be the case with over-the-counter [nicotine replacement therapies]."[23] Nicotine replacement therapies (NRTs), such

[20] Abrams D.B., Glasser A.M., Pearson J.L., et al. (2018). Harm minimization and tobacco control: reframing societal views of nicotine use to rapidly save lives. *Annu Rev Public Health*, 39:193-213.
[21] Abrams (2018).
[22] Abrams (2018).
[23] Abrams (2018).

as nicotine patches and gums, have proven efficacy for smoking cessation in clinical trials, but have not displaced cigarettes at the population level due to modest uptake and low continued use.

Dr. Abrams et al. argued that to optimize their potential benefit, alternatives to cigarettes must occupy the "sweet spot" in the upper left corner of the chart — on par with the combustible cigarette when it comes to appeal and dependence-potential but delivering relatively far lower toxicity and harm. Products that provide similar behavioral rituals as smoking may contribute to appeal and help adult smokers switch completely. According to Dr. Abrams et al., "some new innovations in e-cigarettes do begin to occupy this sweet spot because some smokers have found an e-cigarette with sufficient appeal for them to sustain use and quit smoking."[24]

Supporting the notion that ENDS products occupy the "sweet spot" of relatively low-harm, high-appeal, and high satisfaction, researchers in a *Nature Medicine* article added that there is abundant evidence that ENDS can increase smoking discontinuation and are much less harmful than combustible cigarettes.[25] In this article, researchers acknowledged that while ENDS "are not the magic bullet that will end the devastation wrought by cigarette smoking . . . they can contribute to that lofty public health goal."[26]

Public Health Experts Urge a Balanced Approach to ENDS

Making the combustible cigarette obsolete by advancing safer alternatives to cigarettes must go hand-in-hand with limiting youth access to and appeal of all tobacco and nicotine products. This balanced approach – protecting kids from starting nicotine use while providing Americans who smoke with the tools and information to make informed decisions about their health – is both feasible and necessary. **Fifteen past presidents of the Society for Research on Tobacco and Nicotine (Balfour et al.) published that "evidence indicates that e-cigarette use can increase the odds of quitting smoking, many scientists . . . encourage the health community, media, and policymakers to more carefully weigh vaping's potential to reduce adult smoking-attributable mortality."**[27]

In response to Dr. Balfour et al., Dr. Cohen et al.[28] urged a more systematic review of the science and, in contrast to characterizations of researchers as "opponents" or "supporters" of ENDS products, strongly encouraged "the scientific community to consider how e-cigarettes (in all of their heterogeneity of design and use patterns) perform in the real world when making conclusions about their effects . . ." because "what matters is how these products perform at the individual and population levels in practice and their effects on reducing tobacco-related disparities."

Evidence suggests that governments that foster a well-regulated market of viable, noncombustible alternatives experience improved public health. Dr. Fagerström

[24] Abrams (2018).
[25] Warner, K.E., Benowitz, N.L., McNeill, A. et al. (2023). Nicotine e-cigarettes as a tool for smoking cessation. *Nat Med*. https://doi.org/10.1038/s41591-022-02201-7.
[26] Warner (2023).
[27] Balfour D.J.K., et al. (2021). "Balancing Consideration of the Risks and Benefits of E-Cigarettes," *American Journal of Public Health* 111, no. 9: pp. 1661-1672.
[28] Cohen (2022).

analyzed cigarette-smoking prevalence in countries with relatively high uptake of noncombustible alternatives, including ENDS, and compared those data to surrounding countries without similar regulatory regimes.[29] The data showed lower smoking rates in countries where alternatives were more widely available, suggesting that embracing harm-reduction policy frameworks can accelerate declines in cigarette smoking across the population.[30]

The "Nearly Invisible" Adult Smoker

Despite decades of progress to decrease cigarette use and initiation, around 28 million American adults still smoke,[31] leading to the approximately 450,000 smoking-related deaths in the U.S. each year.

Reaching these 28 million adult current smokers and offering them a reduced-risk alternative to combustible cigarettes presents a material public health opportunity.

Socioeconomic Disparities Among Adult Smokers

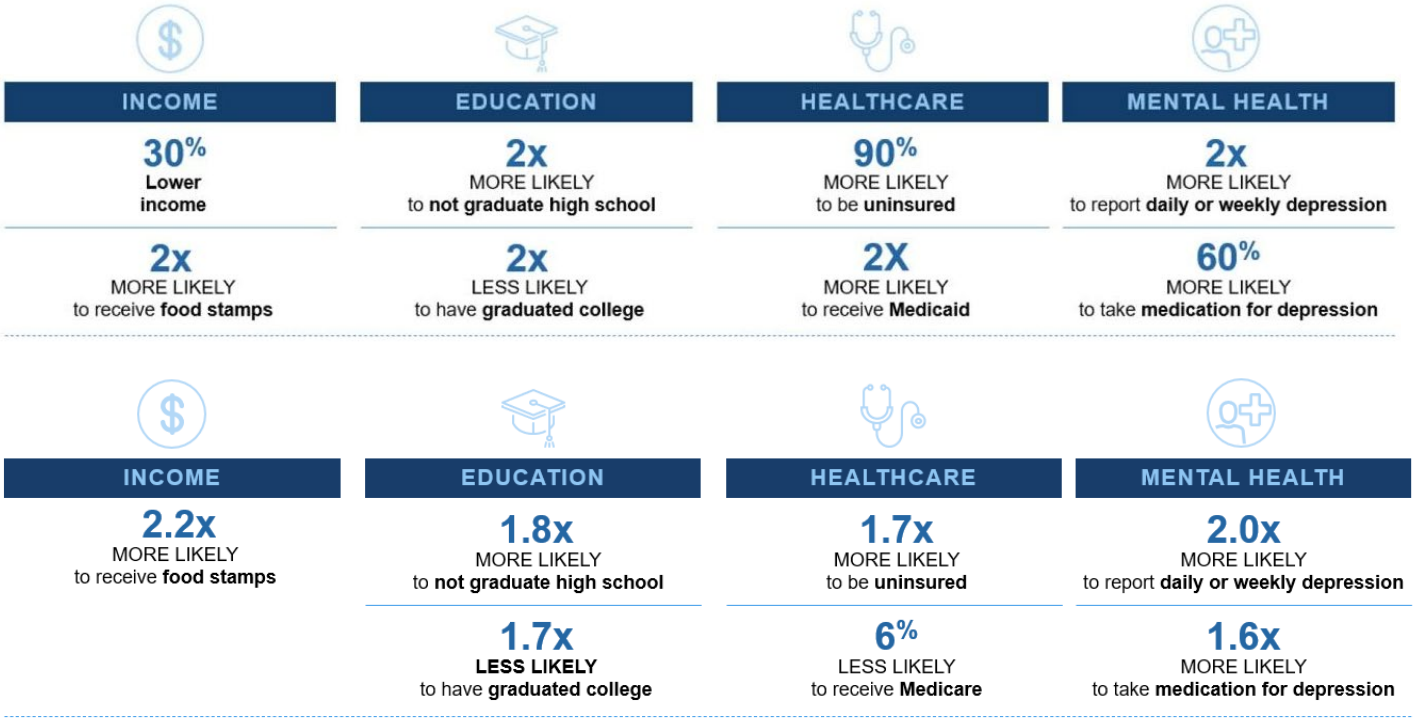
As Dr. Balfour et al. noted, declines in smoking have not been experienced equally:

> To the more privileged members of society, today's smokers may be nearly invisible. Indeed, many affluent, educated US persons may believe the problem of smoking has been largely 'solved.' They do not smoke. Their friends and colleagues do not smoke. There is no smoking in their workplaces, nor in the restaurants and bars they frequent. Yet 1 of every 7 US adults remains a smoker today.[32]

Data elucidate the realities of the current adult smoking population and illustrate the disconnect that Dr. Kenneth Warner described as "[accounting] for the divergence between common perceptions about smoking and the dismal reality."[33] Supported by the data below (Figure 4), **". . . the burden of smoking falls primarily on marginalized populations — the poor, the poorly educated, and those suffering from mental health problems."**[34] And as Dr. Balfour et al. stated, "**the potential lifesaving benefits of e-cigarettes for adult smokers deserve attention equal to the risks to youths**. Millions of middle-aged and older smokers are at high risk of near-future disease and death."[35]

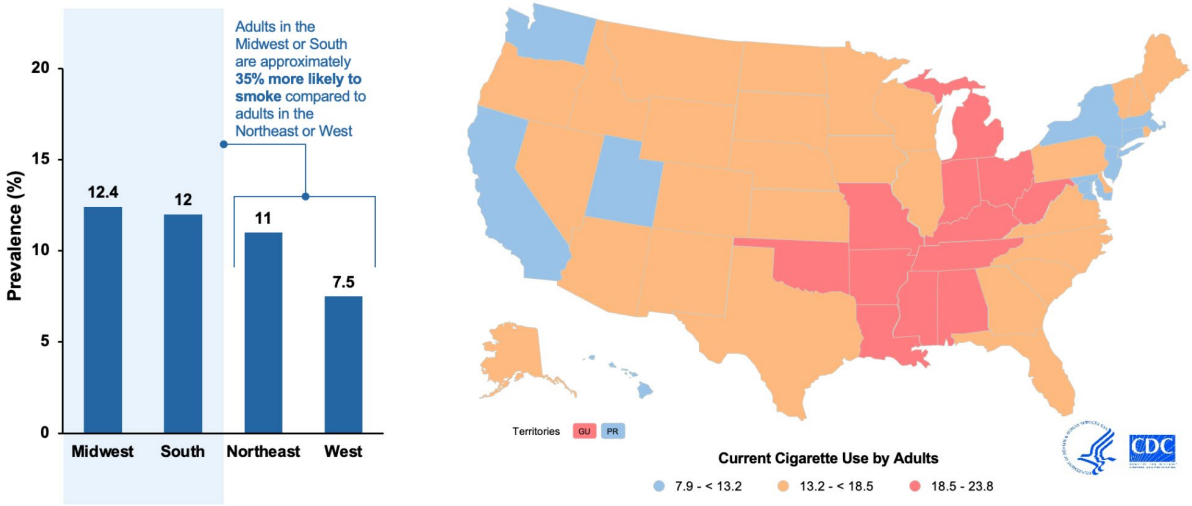
[29] Fagerström K. (2022). Can alternative nicotine products put the final nail in the smoking coffin? Harm Reduct J. 2022 Dec 1;19(1):131. doi: 10.1186/s12954-022-00722-5. PMID: 36456941; PMCID: PMC9714162.
[30] Fagerström (2022).
[31] Cornelius ME. Tobacco product use among adults–United States, 2021. MMWR. Morbidity and mortality weekly report. 2023;72. http://dx.doi.org/10.15585/mmwr.mm7218a1
[32] Balfour (2021). [Emphasis added].
[33] Warner, K. (2019). "Who's Smoking Now and Why It Matters," *The Conversation*. https://theconversation.com/whos-smoking-now-and-why-it-matters-109605
[34] Warner (2019). [Emphasis added].
[35] Balfour (2021). [Emphasis added].

Figure 4: Adult Smokers Are Far More Likely to Experience Socioeconomic Inequities



Source: JLI analysis of public use data, *2023 National Health Interview Survey*.

Figure 5: Adult Smokers Are More Likely to Live in the Midwest or South



Source: JLI analysis of public use data, *2023 National Health Interview Survey*.

According to JLI analysis of public use data from the 2023 National Health Interview Survey:

Education: Adults who did not graduate from high school or have a GED are 1.6-6.2x as likely to smoke compared to adults with a 4-year college or graduate degree.

Race/Ethnicity: American Indians/Alaskan Natives are 1.9-2.8x as likely to smoke as Hispanics or Asians.

Region: Adults in the Midwest or South are 1.4x as likely to smoke compared to adults in the Northeast or West.

Dr. Warner raised a simple but essential question: What can be done to change this?[36] In addition to public education and policy interventions via taxation, advertising and promotion restrictions, and anti-smoking media campaigns, he offered:

> These evidence-based measures are unlikely to be enough, however. A potentially complementary tool may lie in a highly controversial recent development: the emergence of e-cigarettes. Novel reduced-risk nicotine delivery products like e-cigarettes may serve as alternatives to smoking, especially for those otherwise incapable of quitting cigarettes. Vaping may hold the potential to help significant numbers of Americans to quit smoking. The risks of vaping are clearly substantially less than those of smoking.[37]

The 28 million Americans who smoke deserve access to scientifically-validated ENDS products and should be able to make informed choices about their health with honest and accurate information about these products.

Real-World Data and Evidence Demonstrating That ENDS Are Reducing Population Harm from Cigarette Smoking

Noncombustible products provide adults who smoke with a less dangerous alternative to cigarettes and an off-ramp from combustible use. The public health benefits of providing this population with a less harmful form of nicotine delivery can be significant. One out of every two Americans who smoke long-term will die prematurely from smoking-related disease.[38]

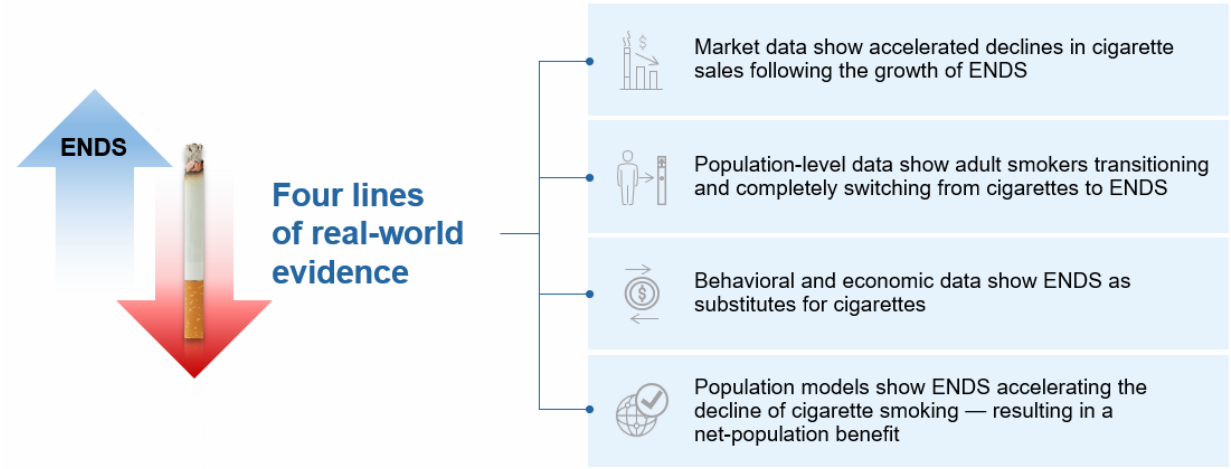
ENDS products are just one example of noncombustible alternatives available to adult smokers. Others include smokeless tobacco products, heated tobacco products, and oral nicotine products (e.g., nicotine pouches). All of these commercially-marketed products are in addition to FDA-approved, nicotine-containing cessation products (e.g., NRTs). The relative risk of any one product depends on a number of factors — such as the product itself, how it's used, and by whom.

The current state of data and evidence on the ENDS category specifically, reinforced by the array of ENDS products determined by FDA to be "appropriate for the protection of public health," helps illustrate how adult smokers who switch to ENDS are likely to reduce their exposure to harmful chemicals compared to combustible cigarettes.

[36] Warner (2019).
[37] Warner (2019).
[38] U.S. Department of Health and Human Services (2014).

Evolving market data and research demonstrates that not only are ENDS helping Americans who smoke achieve reduced risk at the individual level, but at the population level the products are enabling a reduction in the harms caused by cigarette smoking. Importantly, we see four lines of evidence showing the positive real-world impact of ENDS products for adult smokers:

Figure 6: Four Lines of Evidence Showing the Positive Real-World Impact of ENDS Products for Adult Smokers



Source: JLI analysis.

Four Lines of Evidence:

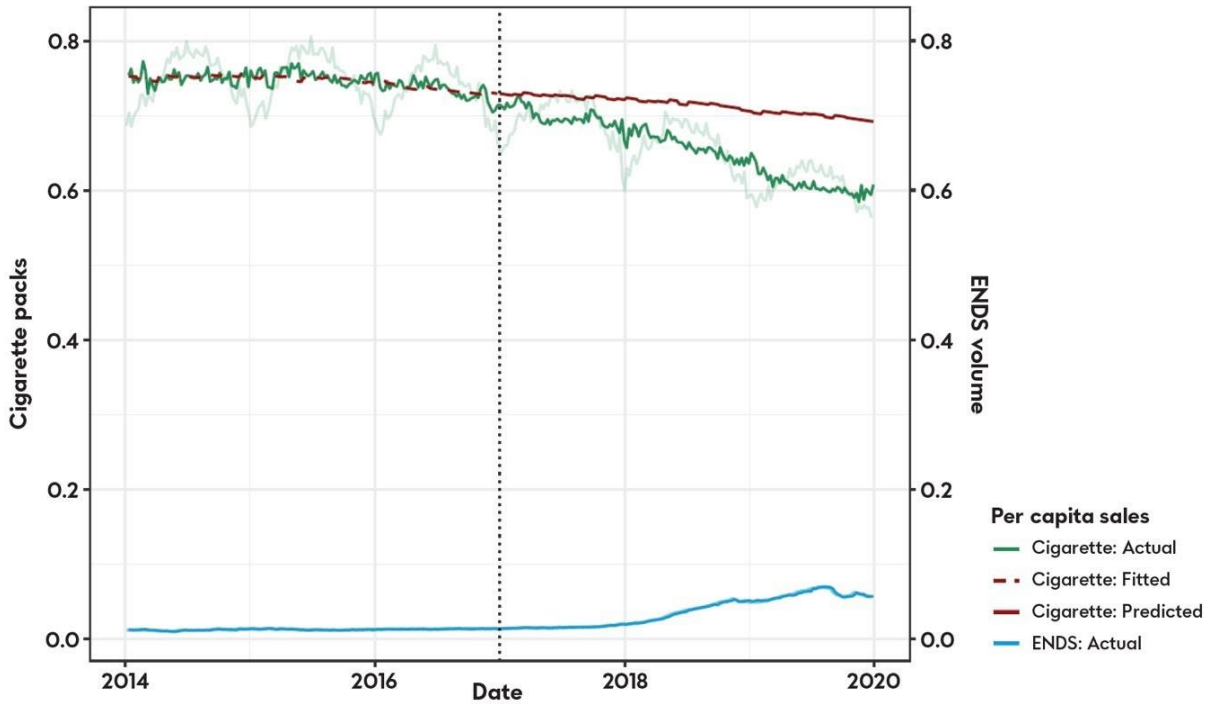
1. Market data demonstrating faster-than-anticipated declines in cigarette sales as a result of increasing ENDS availability.

The first line of evidence is an accelerated decline in the sales of combustible cigarettes over recent years — a steeper decline than what market analysts had originally expected. An analysis of U.S. ENDS and cigarette market data show steeper declines in cigarette-sales volumes over recent years, as ENDS sales have simultaneously increased.

Dr. Selya et al. used Information Resources, Inc. (IRI) data, capturing cigarette and ENDS sales from a national sample of tracked retail outlets, to correlate the changes in cigarette sales with changes in ENDS sales from 2014–2019 (Figure 7).[39] **This analysis found that every unit of ENDS products sold displaced the sale of 1.4–1.5 cigarette packs and that cigarette sales were up to 16% lower over the period from 2017–19 following the growth of ENDS sales than would otherwise have been expected if cigarette sales had continued their anticipated sales trends over 2014–2016**. Consistent with these results, U.S. cigarette manufacturer Altria reported a 5.5% decline from 2018 to 2019 in cigarette-sales volumes and attributed 36% of this decline to displacement by ENDS sales.[40]

[39] Selya A., Wissmann R., Shiffman S., et .al. (2023). Sales of Electronic Nicotine Delivery Systems (ENDS) and Cigarette Sales in the USA: A Trend Break Analysis. *J Consum Policy (Dordr)*, 46(1):79-93. doi: 10.1007/s10603-022-09533-4. Epub 2023 Jan 16. PMID: 36686374; PMCID: PMC9841499.
[40] Altria (2019). *Altria's Third-Quarter 2019 Earnings Conference Call* at 13. https://bit.ly/38RF3Vr.

Figure 7: Actual Sales of Cigarette Packs and ENDS Units Per Capita and Projected Cigarette Sales



Source: Selya A., Wissmann R., Shiffman S., et .al., *Sales of Electronic Nicotine Delivery Systems (ENDS) and Cigarette Sales in the USA: A Trend Break Analysis*.

2. Population surveys demonstrating adult smokers transitioning and completely switching from combustible cigarettes to ENDS products.

The second line of evidence builds on the first. We know that cigarette sales are declining more rapidly than expected. But why?

The sale of ENDS is responsible for displacing cigarette sales–this is supported by population-level data showing that adult smokers are transitioning and completely switching to ENDS products.

A 2024 analysis of National Health Interview Survey (NHIS) trend data for cigarette smoking and ENDS use assessed whether, and how much, smoking prevalence differs from modeling expectations since the introduction of ENDS products.[41] Results showed that actual smoking prevalence from circa 2007 to 2022 was significantly lower than expected based on pre-ENDS-era trends, with the discrepancy being larger in cohorts with greater ENDS prevalence. This evidence suggests that smoking prevalence has dropped faster than expected, correlated with increased ENDS use.

[41] Foxon F, Selya A, Gitchell J, Shiffman S. Increased e-cigarette use prevalence is associated with decreased smoking prevalence among US adults. Harm Reduction Journal. 2024 Jul 18;21(1):136. https://doi.org/10.1186/s12954-024-01056-0

In other analyses of NHIS data, methods used to stop smoking by adults who had successfully stopped were investigated.[42] The authors reported that: "In 2022, an estimated 2.9 million [95% CI 2.5 million–3.2 million] US adults had stopped smoking in the past year… The most popular methods used to stop smoking were nicotine products (53.9% [47.4–60.3%]; 1.5 [1.3–1.8] million adults), especially e-cigarettes in combination with other methods (40.8% [34.4–47.5%]; 1.2 [0.9–1.4] million) and e-cigarettes alone (26.0% [20.4–32.3%]; 0.7 [0.6–0.9] million). Prescription drug products (8.1% [5.3–11.8%]; 0.2 [0.1–0.3] million) and non-nicotine, non-prescription drug methods (6.3% (3.9–9.7%); 0.2 [0.1–0.3] million) were less popular. A further 13.1 [12.2–14.0] million tried but did not stop smoking. Compared to those who tried but didn't stop smoking, those who successfully stopped were more likely to be younger, degree-educated, and to use e-cigarettes to stop smoking."

The 2024 update to the Cochrane review of ENDS products concluded that there is high-certainty evidence that ENDS are effective for promoting the discontinuation of cigarette smoking.[43] This conclusion is based on a meta-analysis of randomized controlled trials of adults who stopped smoking combustible cigarettes using ENDS products.

A formal medicinal cessation approach is unlikely to work for a majority of adult smokers. As we write above, NRTs have proven effective for smoking cessation in clinical trials but have not displaced cigarette smoking at the population level due to modest uptake and low continued use. Furthermore, formal cessation requires an explicit quit attempt, but a large portion of adult smokers (32%) are not willing to quit in the near future.[44]

It is imperative then to understand whether and how ENDS products can play a role in enabling adults to discontinue cigarette smoking even if they are not actively trying to quit. Analysis shows that ENDS use is strongly associated with increased odds of smoking discontinuation among adult smokers who had no intentions to quit smoking cigarettes.

Using Waves 2–5 of FDA's Population Assessment of Tobacco and Health (PATH) Study, Dr. Kasza et al. found that **among baseline adult smokers who did not plan to quit and who subsequently began using ENDS daily, 28.0% quit smoking cigarettes**.[45] In contrast, among baseline adult smokers not planning to quit who reported no subsequent use of ENDS, only 5.8% quit smoking cigarettes (Figure 8).

The researchers found that those adult smokers not planning to quit who subsequently used ENDS daily had eight times higher odds of quitting smoking cigarettes as those who did not use ENDS (adjusted odds ratio (aOR) 8.11, 95% C.I. 3.14–20.97). Further, those who used

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[42] Foxon F, Niaura R. Use of nicotine products, prescription drug products, and other methods to stop smoking by US adults in the 2022 National Health Interview Survey. Internal and Emergency Medicine. 2025. https://doi.org/10.1007/s11739-024-03847-6

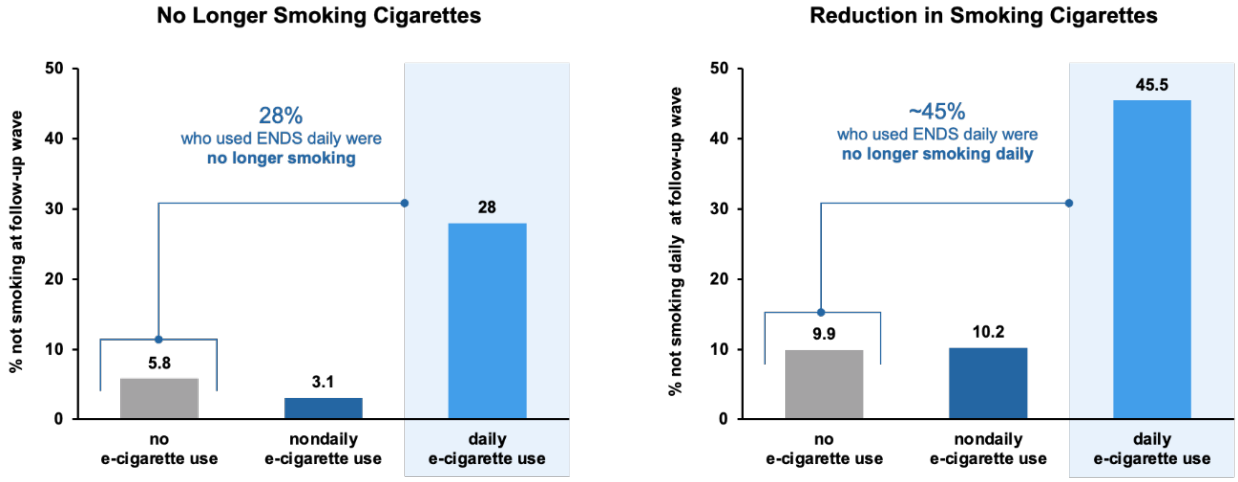
[43] Lindson N, Butler AR, McRobbie H, Bullen C, Hajek P, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Livingstone-Banks J. Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews. 2024(1). https://doi.org/10.1002/14651858.CD010216.pub8

[44] Babb S., Malarcher A., Schauer G. (2017). Quitting Smoking Among Adults - United States, 2000-2015. *MMWR Morb Mortal Wkly Rep*, 6;65(52):1457-1464. doi: 10.15585/mmwr.mm6552a1. PMID: 28056007.

[45] Kasza K.., Edwards K.., Anesetti-Rothermel A., et al. (2022). E-cigarette use and change in plans to quit cigarette smoking among adult smokers in the United States: Longitudinal findings from the PATH Study 2014-2019. Addict Behav;124:107124. doi: 10.1016/j.addbeh.2021.107124. Epub 2021 Sep 22. PMID: 34598012; PMCID: PMC8511329.

ENDS daily had almost ten times higher odds of no longer smoking cigarettes daily as those who did not use ENDS (aOR 9.67, 95% C.I. 4.02-23.25).[46]

Figure 8: Daily ENDS Use Is Associated With Greater Cigarette-Smoking Cessation and Lower Cigarette Consumption Among Adult Smokers Not Planning to Quit



Recreated based on the findings by Kasza KA, Edwards KC, Anesetti-Rothermel A, Creamer MR, Cummings KM, Niaura RS, Sharma A, Pitts SR, Head SK, Everard CD, Hatsukami DK, Hyland A. E-cigarette use and change in plans to quit cigarette smoking among adult smokers in the United States: Longitudinal findings from the PATH Study 2014-2019. *Addict Behav.* 2022.

Not only is ENDS use associated with switching away from cigarettes, but the association has grown stronger over time with recent generations of ENDS products, starting in 2016/17.

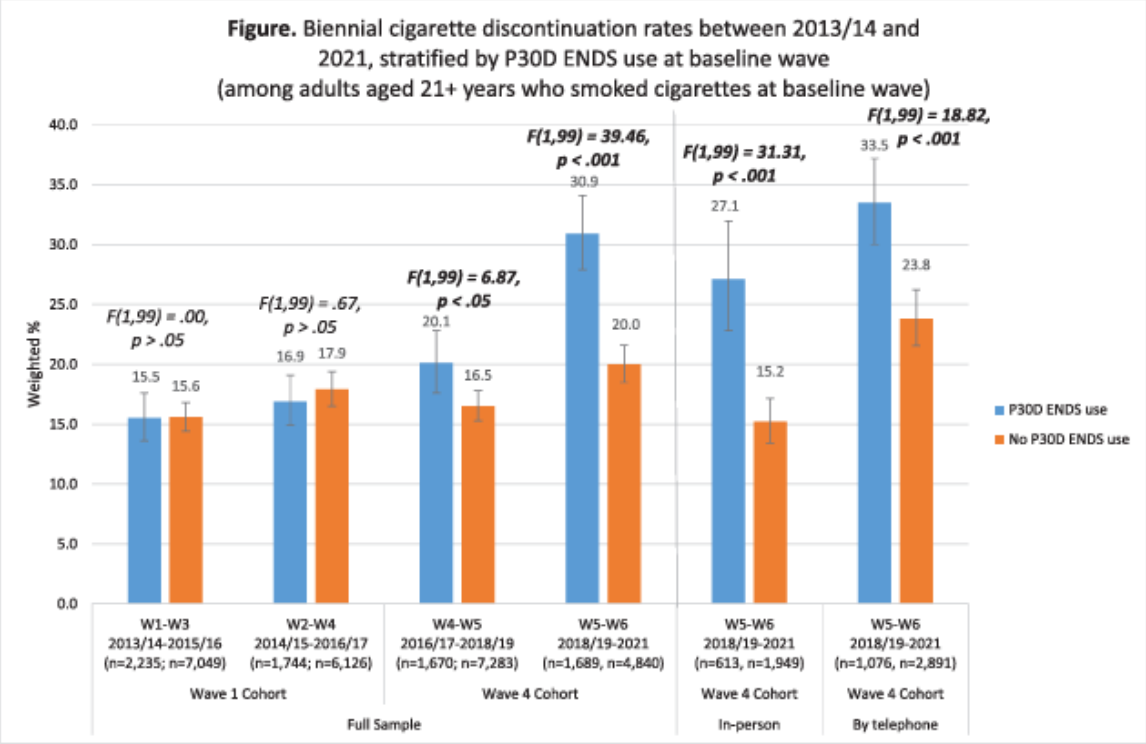
The same research group above more recently analyzed trends between 2013-2021 in rates of cigarette discontinuation among adult ENDS users, again using data from the PATH study.[47] Dr. Kasza and colleagues found that among adults who smoke, those who used ENDS in 2013-16 (Waves 1-3) were no more likely to discontinue smoking in the following year. However, starting in Wave 4 (2016/17), those who used ENDS were significantly more likely to have discontinued smoking the following year, with even larger differences in Wave 5 (Figure 9).

Though this study cannot answer why cigarette discontinuation rates associated with ENDS use increased starting in 2016/17, Dr. Kasza and colleagues offer several possible reasons, including the expanded ENDS marketplace. In particular, they state "[r]esearch has shown that daily use of ENDS is associated with cigarette discontinuation in the population and it is possible that ENDS use frequency increased over the course of our study period, perhaps because of changes in ENDS product features, which could contribute to explaining our findings." **In other words, more satisfying ENDS products on the US market starting in 2016 could have encouraged more engagement with ENDS and might explain the**

[46] Kasza (2021).
[47] Kasza, K.A., Tang Z., Sik Seo Y., et al. (2024). Divergence in Cigarette Discontinuation Rates by Use of Electronic Nicotine Delivery Systems (ENDS): Longitudinal Findings from the United States PATH Study Waves 1-6. Nicotine Tob Res, Epub ahead of print. doi:10.1093/ntr/ntae027. PMID: 38566367

higher – and growing – rates of cigarette discontinuation among adults who smoke and use ENDS.

Figure 9: ENDS Use is Associated with Higher – and Growing – Likelihood of Discontinuing Smoking



Source: Kasza KA, Tang Z, Sik Seo Y, Benson AF, Creamer MR, Edwards KE, Everard C, Chang JT, Cheng Y-C, Das B, Oniyide O, Tashakkori NA, Weidner A-S, Xiao H, Stanton C, Kimmel HL, Compton W, Hyland A. Divergence in cigarette discontinuation rates by use of electronic nicotine delivery systems (ENDS): Longitudinal findings form the United States PATH Study Waves 1-6. *Nicotine Tob Res*, 2024.

3. Economic data demonstrating ENDS products as substitutes to combustible cigarettes.

The third line of real-world evidence comes from a broad array of causal economic analyses that demonstrate the interplay between ENDS and cigarette demand as driven by price. **The findings generally show that increased taxation of ENDS products reduce ENDS sales as intended but also have the unintended effect of increasing cigarette sales. Conversely, higher cigarette taxes lead to increased ENDS use.**[48] A systematic review and meta-analysis of econometric research[49] concluded that:

> "A 10% increase in ENDS price is associated with an 11.5% (9.7%–13.4%) decrease in ENDS sales/purchases, and also decreased ENDS use prevalence. A 10% increase in

[48] Abouk, R. and De, P. and Pesko, M. (2023). Estimating the Effects of Tobacco-21 on Youth Tobacco Use and Sales. *SSRN*: https://ssrn.com/abstract=3737506 or http://dx.doi.org/10.2139/ssrn.3737506.
[49] Selya A, Foxon F, Chandra S, Nealer E. Meta-analysis of e-cigarette price elasticity. F1000Research. 2023 Feb 2;12:121. https://doi.org/10.12688/f1000research.129233.1

> cigarette price is associated with a 9.8% (5.7%–13.8%) increase in ENDS sales/purchases, and also increased ENDS use prevalence. A 10% increase in ENDS price is non-significantly associated with a 1.1% (-0.5%–2.8%) increase in cigarette sales/purchases, and increased ENDS price was associated with increased smoking prevalence, propensity, and number of cigarettes smoked."

Together, these analyses show a substitution effect of ENDS products for combustible cigarettes.

Restrictions placed on ENDS sales via other policy mechanisms have a similar effect. We delve into the impact of both price and product restrictions policies in greater depth below.

4. Population models demonstrating reductions in tobacco-related death and disease as ENDS use increases.

Finally, the use of simulation modeling to generate counterfactual estimates to compare against actual population-level data **demonstrate how the availability and uptake of ENDS products can result in significant declines in cigarette-smoking prevalence, resulting in a net-population benefit**.

Dr. Levy et al. used their Smoking and Vaping Model (SAVM) to estimate the impact of ENDS products on cigarette smoking rates and smoking/ENDS use attributable mortality in the United States by comparing model outcomes between scenarios with and without ENDS products in the U.S. market.[50] The National Health Interview Survey (NHIS) provided cigarette-smoking and ENDS use prevalence inputs and FDA's Population Assessment of Tobacco and Health (PATH) Study provided age-group specific transition probabilities between ENDS products and combustible cigarettes.

These researchers estimated that, without ENDS products, adult smoking prevalence in 2023 would be 17.4% for males and 12.7% for females. In the model specification with ENDS products, adult smoking prevalence in 2023 would be 12.9% for males and 10.1% for females.

The lower smoking prevalence under the scenario with ENDS products resulted in an estimated 7,050 fewer deaths attributable to smoking and ENDS use in 2023 alone compared to the model scenario without ENDS in the U.S. market.

As referenced by FDA in its proposed rule to ban menthol in combustible cigarettes, extending the models from 2013 to 2060 with ENDS products in the market projects that "654,000 premature deaths and 11,300,000 life-years lost averted by 2060."[51]

Supporting this proposition is an analysis by Foxon et al. which found that, considering population-level data, smoking prevalence has dropped faster than expected correlating with increased ENDS use.[52]

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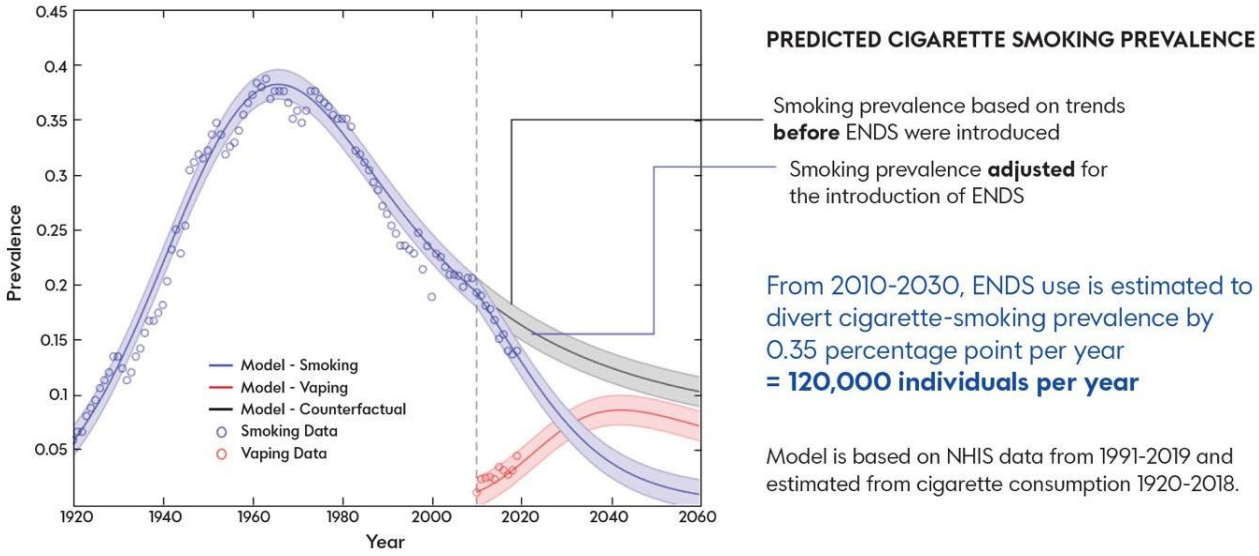
[50] Levy D. et al. (2021). Public Health Implications of Vaping in the USA: The Smoking and Vaping Simulation Model, *Popul Health Metr* 19, 19.
[51] Abouk (2023).; see also 87 Fed. Reg. at 26481.
[52] Foxon, Selya, Gitchell, and Shiffman (2024).

Population modeling also can pull from prior, observed trends to generate reliable predictions of a future state. Researchers used a population simulation model to project the number of what they term "life-years saved (LYS)" attributable to ENDS use between 2018 and 2100. The analysis weighs the ability of ENDS products to serve as a substitute for combustible cigarettes for adults against the known health risks of ENDS use and the possibility that ENDS use will serve as a gateway to cigarette use among young people. **The combination of model assumptions produced 360 possible scenarios, 99% of which yielded positive estimates of LYS due to ENDS use by 2100 ranging from 143,000 LYS to 65 million LYS by the end of the Century. Their paper concluded: "Harm reduction can, and many would say should, be a part of the complex formula that will eventually bring about the demise of smoking."**[53]

Wagner and Dr. Clifton similarly examined the relationship between cigarette-smoking and ENDS-use prevalence and predicted, as demonstrated in Figure 10 below, that **from 2010–2030, ENDS use is estimated to divert adult smoking prevalence by 0.35 percentage points per year, or 120,000 individuals per year.**[54]

Figure 10: Declines in Smoking Prevalence Can Be Attributed to ENDS



Source: Wagner L., Clifton S., *Modeling the Public Health Impact of E-cigarettes on Adolescents and Adults.*

Modeling of prior, observed trends reaffirms the forward-looking simulations by showing that ENDS' displacement of combustible cigarettes already has likely reduced future instances of cigarette-related mortality.[55] Dr. Levy et al. examined the relationship between cigarette-smoking prevalence and ENDS-use prevalence and found that the predicted cigarette-prevalence trends before ENDS were introduced to the market are lower than expected since ENDS were introduced. Since 2012, U.S. adult smoking prevalence rates have been lower than expected, particularly among adults aged eighteen to forty-four

[53] Mendez D., Warner K. (2021). A Magic Bullet? The Potential Impact of E-Cigarettes on the Toll of Cigarette Smoking, *Nicotine & Tobacco Research*, Volume 23, Issue 4, April 2021, Pages 654–661, https://doi.org/10.1093/ntr/ntaa160.
[54] Wagner L., Clifton S. (2021). Modeling the Public Health Impact of E-cigarettes on Adolescents and Adults. *Chaos: An Interdisciplinary Journal of Nonlinear Science*. DOI: 10.1063/5.0063593.
[55] Levy (2021).

years.[56] **And most importantly, this observed decrease in cigarette prevalence from 2012–2018 is projected to avert over 400,000 smoking-attributable deaths in the U.S by 2052.**[57]

The Risk Profile of ENDS Products and Health Effects Relative to Combustible Cigarettes

The best way for adult smokers to reduce their risk of disease is to quit all tobacco and nicotine. ENDS, and other noncombustible nicotine products like nicotine pouches and heated tobacco products, are much less harmful than smoking, but they do have risks.

While long-term data on ENDS use are not available yet, multiple lines of evidence, including clinical studies, support that ENDS products carry far lower individual health risks than cigarettes, which kill one out of every two long-term users.

The scientific literature and findings of public health authorities indicate that for adult smokers who need or want to continue using nicotine, those who switch completely to ENDS can reduce their risk compared to continued cigarette smoking.

Public Health Bodies

In England, the Office for Health Improvement and Disparities in the Department of Health and Social Care (formerly Public Health England) reported that — while emphasizing ENDS are not risk-free — evidence shows significantly lower exposure from ENDS use compared to cigarette smoking in biomarkers for cancer, heart, and lung disease. [58]

United States public health bodies have issued similar statements:

> U.S. FDA (2024): Non-combusted products – such as e-cigarettes and other smokeless tobacco products – generally have lower health risks than cigarettes and other combustible products... For adults who smoke, switching completely from cigarettes to e-cigarettes may reduce exposure to many harmful chemicals present in cigarettes (*FDA 2024*).
>
> U.S. National Academies of Science, Engineering, and Medicine (2018): The evidence about harm reduction suggests that across a range of studies and outcomes, e-cigarettes pose less risk to an individual than combustible tobacco cigarettes (*NASEM 2018*).
>
> U.S. Surgeon General (2016): [C]urrent knowledge of the characteristics of the inhaled aerosol from e-cigarettes suggests that if a current adult smoker of conventional cigarettes or other combustible tobacco products would use e-cigarettes exclusively instead of combustibles as a substitute nicotine

[56] Levy (2021).
[57] Levy (2021).
[58] McNeill A., Simonavičius E., Brose, L.S., et al. (2022). Nicotine vaping in England: an evidence update including health risks and perceptions, September 2022. *A report commissioned by the Office for Health Improvement and Disparities*. London: Office for Health Improvement and Disparities.

> delivery system, either en route to quitting tobacco completely or even as a long-term alternative, the risks of tobacco-related diseases would be reduced substantially compared with the risk imparted by continued smoking of conventional cigarettes (*USDHHS 2016*).

Harmful and Potentially Harmful Constituents

The vast majority of the risks associated with cigarette use come from the inhalation of tobacco smoke. ENDS aerosol is very different from tobacco smoke. **A growing body of evidence supports that ENDS present a substantial reduction in exposure to harmful and potentially harmful constituents (HPHCs) relative to combustible cigarettes and the harmful health endpoints that result from exposure to HPHCs.**

Cigarette smoke contains many of the ninety-three FDA-identified HPHCs at high levels.[59] When a person inhales the smoke from a burning cigarette, they are exposed to these toxicants. Exposure to toxicants triggers molecular changes that disrupt biological mechanisms causing cell and tissue changes, which can lead to smoking-related disease.

FDA considers HPHC reductions in comparison to combustible cigarettes when reviewing applications from manufacturers seeking to introduce new tobacco products in the United States. This process, in which FDA allows for a new product to enter the U.S. market for sale, is called "marketing authorization." The Agency may grant marketing authorization only if it finds that the new product is "appropriate for the protection of public health" (often shorthanded as the "APPH standard").

Through its regulations for premarket tobacco product applications (PMTAs), FDA has provided additional information on its criteria for application review:

> The toxicological profile also includes information regarding the ingredients, additives, and HPHCs, relative to the route of administration and the range of the potential levels of exposure resulting from the use of or other exposure to the product. While FDA is aware of the risk of harm posed by HPHCs generally, understanding the toxicological effects of HPHCs in the product is important to FDA's review because the levels and combinations of HPHCs to which a consumer may be exposed can determine whether, and the severity with which, a user may experience harm. For example, some constituents may only cause harm above certain levels of exposure, while others may have no safe level of exposure.
>
> Additionally, since there are potential complex interactions between HPHCs and each tobacco product can produce a different mixture of these HPHCs, FDA needs to determine the toxicity of the specific mixture of HPHCs in a tobacco product in order to compare that tobacco product to other similar products on the market and

[59] FDA (2012). Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke: Established List. https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/harmful-and-potentially-harmful-constituents-tobacco-products-and-tobacco-smoke-established-list.

to use this comparison in its determination of whether permitting the marketing of the product would be APPH.[60]

Noncombustible alternatives to combustible cigarettes that produce lower levels of toxicants and, in turn, significantly reduce users' exposure to HPHCs are likely to reduce or disrupt the chain of events leading to smoking-related disease.[61]

The closer these reductions are to reductions observed with smoking cessation, the greater the likelihood of reduced individual risk among adult smokers switching completely to these alternatives. Limiting the exposure to these chemicals and toxins is the key to reducing tobacco-related death and disease.

Biomarkers of Exposure

Biomarkers of exposure (BOEs) indicate the extent to which a person has been exposed to a certain substance or chemical. In the case of tobacco products, BOEs measure exposure to specific toxicants (many of which are designated by FDA as HPHCs) that are largely understood to contribute to smoking-related diseases.

Recent analysis of PATH data, a nationally representative longitudinal cohort study, indicates that BOEs representing thirteen volatile organic compounds and three heavy metals were significantly lower in ENDS users than in cigarette smokers.[62] **In fact, levels of exposure to these harmful constituents in ENDS users approach levels measured in adults who have never used tobacco products.**[63]

A systematic review and meta-analysis of biomarkers of potential harm in people switching from smoking tobacco to e-cigarette use [64] concluded that: "Switching from smoking to vaping or dual use appears to reduce levels of biomarkers of potential harm significantly."

These findings, in a real-world sample representative of the U.S. population, confirm and extend findings from other more controlled studies showing that **ENDS use is associated with exposure to much lower levels of many HPHCs associated with smoking-related disease compared to continued cigarette smoking**. Previous findings demonstrated that "smokers who completely substitute combustible cigarettes with e-cigarettes over a short period of time experience reductions in exposure to a number of known harmful tobacco-

[60] FDA (2021). Premarket Tobacco Product Applications and Recordkeeping Requirements, 86 Fed. Reg. 55300. *Available at*, https://www.federalregister.gov/documents/2021/10/05/2021-21011/premarket-tobacco-product-applications-and-recordkeeping-requirements.
[61] Stratton K., Shetty P., Wallace R., et al. (2001). Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction. *Institute of Medicine (US) Committee to Assess the Science Base for Tobacco Harm Reduction*, Washington (DC): National Academies Press (US); 2001. Available from: https://www.ncbi.nlm.nih.gov/books/NBK222375/ doi: 10.17226/10029.
[62] Holt, N. M., Shiffman, S., Black, R. A., Goldenson, N. I., Sembower, M. A., & Oldham, M. J. (2023). Comparison of biomarkers of exposure among US adult smokers, users of electronic nicotine delivery systems, dual users and nonusers, 2018–2019. *Scientific reports*, *13*(1), 7297.
[63] Holt (2023).
[64] Hartmann-Boyce J, Butler AR, Theodoulou A, Onakpoya IJ, Hajek P, Bullen C, Rigotti NA, Lindson N. Biomarkers of potential harm in people switching from smoking tobacco to exclusive e-cigarette use, dual use or abstinence: secondary analysis of Cochrane systematic review of trials of e-cigarettes for smoking cessation. Addiction. 2023 Mar;118(3):539-45. https://doi.org/10.1111/add.16063

related toxicants and carcinogens similar to smokers who quit smoking over the same period of time as measured by urine, blood and exhaled breath BOEs."[65]

ENDS can reduce exposure to HPHCs, which is then reflected in the reductions of BOEs that are associated with the diseases caused by smoking cigarettes. Reducing this exposure is likely to lead to reduced risk of specific diseases associated with smoking cigarettes.

Cardiovascular Disease

Smoking is a leading cause of cardiovascular disease (CVD) and increases the risk of heart attacks, stroke, and many other CVDs. The 2014 U.S. Surgeon General's report concluded that chemical compounds in tobacco smoke, such as oxidizing chemicals, volatile organic chemicals, particulates, and carbon monoxide, are the primary contributors to increased CVD risk associated with cigarette smoking.[66]

Nicotine itself may cause cardiovascular-related conditions, such as increasing heart rate and blood pressure. Separately, inhalation of vapor from ENDS products may aggravate pre-existing heart conditions.[67]

But in the relative sense — when comparing ENDS use to cigarette smoking — the current science indicates that, while nicotine is addictive and carries certain harms, it has not been found to contribute to smoking-related CVD risk and is not classified as an HPHC for CVD by FDA.[68,69]

Furthermore, within the large body of science addressing physiological changes related to ENDS use, a number of studies have found no significant association between ENDS and CVD:

> Berlowitz et al. (2022)[70]: "We did not find a significant difference in the cardiovascular risk of exclusive e-cigarette use compared with nonuse of cigarettes and e-cigarettes."

[65] D'Ruiz, C.D., Graff, D.W. & Robinson, E. (2016). Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes. *BMC Public Health* **16**, 543. https://doi.org/10.1186/s12889-016-3236-1.
[66] U.S. Department of Health and Human Services (2014).
[67] Benowitz N., St Helen G, Liakoni E. (2021). Clinical Pharmacology of Electronic Nicotine Delivery Systems (ENDS): Implications for Benefits and Risks in the Promotion of the Combusted Tobacco Endgame. J Clin Pharmacol. 2021 Aug;61 Suppl 2(Suppl 2):S18-S36. doi: 10.1002/jcph.1915. PMID: 34396553; PMCID: PMC9239851.
[68] Benowitz N.L., Burbank A.D. (2016). Cardiovascular toxicity of nicotine: Implications for electronic cigarette use. *Trends Cardiovasc Med*. 2016 Aug;26(6):515-23. doi: 10.1016/j.tcm.2016.03.001. Epub 2016 Mar 10. PMID: 27079891; PMCID: PMC4958544.
[69] FDA (2012).
[70] Berlowitz J., Xie W., Harlow A. et al. (2022). E-Cigarette Use and Risk of Cardiovascular Disease: A Longitudinal Analysis of the PATH Study (2013–2019). 145:1557–1559. *Circulation*. Originally published 6 May 2022. https://doi.org/10.1161/CIRCULATIONAHA.121.057369.

Hirschtick et al. (2022)[71]: "ENDS use was not associated with a statistically significant increase in CVD outcomes."

Falk et al. (2022)[72]: "There were no differences in diagnoses of stroke, diabetes mellitus, coronary artery disease, or myocardial infarction among exclusive ENDS users compared to non-users; while exclusive use of ENDS was associated with an increased likelihood of having hypertension compared to non-users. The current analysis extended previous research findings regarding associations between ENDS and CVD."

Farsalinos et al. (2019)[73]: "The pooled analysis of the 2016 and 2017 NHIS showed no association between e-cigarette use and myocardial infarction or CHD."

Osei et al. (2019)[74]: "We found no significant association between e-cigarette use and CVD among never combustible cigarette smokers."

Respiratory Disease

The public perception of ENDS use and the associated risks of respiratory disease have been driven largely by the spate of illnesses and deaths in 2019, which was termed as "e-cigarette or vaping product use associated lung injury" (EVALI) — a misnomer coined by CDC. The perceived linkage of "EVALI" to regulated, nicotine-containing ENDS products was ultimately debunked; rather, cases of "EVALI" were strongly linked to tetrahydrocannabinol (THC) vape products from illicit sources and vitamin E acetate.[75,76] To reflect this, Canada now refers to EVALI as "Vaping-Associated Lung Illness" (VALI), excluding "e-cigarette" from the official title.[77]

The reality is likely different from most of the public's perception: risks of lung disease among ENDS users have not been quantified but are likely to be substantially below the risks of cigarette smoking due to decreased exposure to harmful toxicants. According

[71] Hirschtick J.L., Cook S., Patel A., et al. (2022). Longitudinal associations between exclusive and dual use of electronic nicotine delivery systems and cigarettes and self-reported incident diagnosed cardiovascular disease among adults. *Nicotine Tob Res*. 2022 Jul 30:ntac182. doi: 10.1093/ntr/ntac182. Epub ahead of print. PMID: 35907264.
[72] Falk G.E., Okut H., Vindhyal M.R., et al. (2022). Hypertension and Cardiovascular Diseases among Electronic and Combustible Cigarette Users. *Kans J Med*. 2022 Jul 21;15:226-230. doi: 10.17161/kjm.vol15.16752. PMID: 35899059; PMCID: PMC9311785.
[73] Farsalinos K.E., Polosa R., Cibella F., et al. (2019). Is e-cigarette use associated with coronary heart disease and myocardial infarction? Insights from the 2016 and 2017 National Health Interview Surveys. *Ther Adv Chronic Dis*. 2019 Sep 27;10:2040622319877741. doi: 10.1177/2040622319877741. PMID: 31632622; PMCID: PMC6767743.
[74] Osei A.D., Mirbolouk M., Orimoloye O.A., et al. (2019). Association Between E-Cigarette Use and Cardiovascular Disease Among Never and Current Combustible-Cigarette Smokers. *Am J Med*. 2019 Aug;132(8):949-954.e2. doi: 10.1016/j.amjmed.2019.02.016. Epub 2019 Mar 8. PMID: 30853474.
[75] Hall W., Gartner C., Bonevski B. (2020). Lessons from the public health responses to the US outbreak of vaping-related lung injury. *Addiction*, vol. 116 (5), 985-993. doi:10.1111/add.15108.
[76] Pesko, M.F., Cummings, K.M., Douglas, et al. (2023). United States public health officials need to correct e-cigarette health misinformation. *Addiction*. https://doi.org/10.1111/add.16097.
[77] Baker M.M., Procter T.D., Belzak L., et al. (2022). Vaping-associated lung illness (VALI) in Canada: a descriptive analysis of VALI cases reported from September 2019 to December 2020. *Health Promot Chronic Dis Prev Can*. 2022;42(1):37-44. https://doi.org/10.24095/hpcdp.42.1.06.

to a 2018 OHID report, among ENDS users, two studies of biomarker data for acrolein, a potent respiratory irritant, found levels consistent with non-smoking levels.[78]

A recent working paper from Dr. Kenkel et al.[79] found no evidence that current or former ENDS use is associated with respiratory disease among adults who have never smoked. In other studies that find correlations between ENDS use and respiratory disease, these relationships are often confounded by former combustible use.[80] Additionally, in adults with chronic obstructive pulmonary disorder (COPD), data suggest individuals who substantially reduced conventional smoking or achieved abstinence by switching to ENDS products may mitigate some of the effects of COPD, with the benefits appearing to persist over the long-term.[81]

Similarly, longitudinal analyses of PATH data have also found that ENDS use was not significantly associated with developing COPD after adjusting for cumulative smoking history among adults,[82] and exclusive ENDS use was not associated with self-reported respiratory diagnoses among youth.[83]

Dual Use and Transitioning from Combustible Cigarettes to ENDS Products

Public health stakeholders express concern with the prospect of dual use (using both combustible cigarettes and ENDS products), which could diminish the harm-reduction potential of ENDS products among adult smokers.[84] While many studies support the notion that dual use offers a lessened public health benefit, **recent evidence shows that complete switching is a more common endpoint, with dual use usually being a transitory state between cigarette smoking to complete ENDS use**.[85]

And while complete switching is the best outcome, even those who do not completely switch may experience reduced harm given that dual use is often marked by substantial

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[78] McNeill A., Brose L.S., Calder R., et al. (2018). Evidence review of e-cigarettes and heated tobacco products 2018. *A report commissioned by Public Health England*. London: Public Health England. https://www.gov.uk/government/publications/e-cigarettes-and-heated-tobacco-products-evidence-review/evidence-review-of-e-cigarettes-and-heated-tobacco-products-2018-executive-summary [Note: OHID was referred to as Public Health England in 2018].

[79] Kenkel D., Mathios A., Wang H. (2020). E-Cigarettes and Respiratory Disease: A Replication, Exension, and Future Directions. *National Bureau of Economic Research*, Working Paper 27057, July 2020, doi: 10.3386/w27507, https://www.nber.org/papers/w27507.

[80] Sargent, J.D et al. (2022). Tobacco use and respiratory symptoms among adults: Findings from the Longitudinal Population Assessment of Tobacco and Health (PATH) Study 2014-16. *Nicotine & Tobacco Research.* ntac080. https://doi.org/10.1093/ntr/ntac080.

[81] Polosa R., Morjaria J.B., Prosperini U. et al. (2020). COPD smokers who switched to e-cigarettes: health outcomes at 5-year follow up. *Ther Adv Chronic Dis*. 2020 Oct 10;11:2040622320961617. doi: 10.1177/2040622320961617. PMID: 33101622; PMCID: PMC7549158.

[82] Cook S.F., Hirschtick J.L., Fleisher, N.L., et al. (2023). Cigarettes, ENDS Use, and Chronic Obstructive Pulmonary Disease Incidence: A Prospective Longitudinal Study. *Am J Prev Med.* 2023 Aug;65(2):173-181. doi: 10.1016/j.amepre.2023.01.038. PMID: 36890083.

[83] Mukerjee R., Hirschtick, J.L., Zavala Arciniega L., Xie Y., Barnes G.D., Arenberg D.A., Levy D.T., Meza, R., Fleisher N.L., Cook S.F. (2024). *Am J Prev Med.* 2024 May;66(5):789-796. doi: 10.1016/j.amepre.2023.12.005. PMID: 38081374

[84] Coleman, S.R.M., Piper, M.E., Byron, M.J. et al. (2022). Dual Use of Combustible Cigarettes and E-cigarettes: a Narrative Review of Current Evidence. *Curr Addict Rep* 9, 353–362. https://doi.org/10.1007/s40429-022-00448-1.

[85] Brouwer AF, Jeon J, Jimenez-Mendoza E, et al. Changing patterns of cigarette and ENDS transitions in the USA: a multistate transition analysis of adults in the PATH Study in 2017–2019 vs 2019–2021. Tobacco Control Published Online First: 22 August 2024. doi: 10.1136/tc-2023-058453

reductions in cigarette consumption.[86] **In fact, substantial declines in cigarette consumption (50% and higher) are associated with significantly lower exposure to HPHCs[87] and reductions in disease outcomes.**[88]

A study — which evaluated the impact of ENDS use on cigarette-smoking abstinence, smoking reduction, and tobacco-product abstinence by longitudinal patterns of ENDS use frequency — found that daily ENDS use is "positively associated with substantial reduction in cigarette smoking." [89] Additionally, participants who reported non-daily ENDS use were 72% less likely to achieve cigarette-smoking abstinence than non-users.[90]

Dual use, while not the optimal state, should be viewed as a transitionary state for many adults who smoke in switching completely to ENDS products from combustible cigarettes. And the science shows that adult smokers who continue to reduce cigarette consumption during this transition lower their risk of harm.

Impediments to Progress and Barriers to Switching: Worsening Misperceptions of Nicotine and Relative Risk and the Negative Impact of Anti-Risk-Proportionate Policy

The science is increasingly clear: ENDS products present lower risk than combustible cigarettes for adult smokers. A report from the U.S. National Academies of Sciences, Engineering, and Medicine concluded that "there is conclusive evidence that completely substituting e-cigarettes for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes."[91]

So why don't more adult smokers switch to ENDS? We see two reasons.

First, the general public, healthcare professionals, and, critically, adult smokers, harbor worsening misperceptions on the harms of nicotine and relative risk of ENDS products compared to combustible cigarettes.

The current state of public (mis)understanding about the harms of nicotine and relative risk of noncombustible products compared to combustible cigarettes highlights the need for research and messaging development to support accurate, non-misleading information for adult users, particularly those of combustible cigarettes. This information, in turn, can help

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[86] Selya, A., Shiffman, S., Greenberg, M. et al. (2021). "Dual Use of Cigarettes and JUUL: Trajectory and Cigarette Consumption," *American Journal of Health Behavior*. Vol. 45. May 2021, pp. 464-485.
[87] Arnold M., Nollen N., Mayo M. et al. (2021). Harm Reduction Associated with Dual Use of Cigarettes and e-Cigarettes in Black and Latino Smokers: Secondary Analyses from a Randomized Controlled e-Cigarette Switching Trial, *Nicotine & Tobacco Research*, Volume 23, Issue 11, November 2021, Pages 1972–1976. https://doi.org/10.1093/ntr/ntab069.
[88] Godtfredsen N.S., Prescott E., Osler M. (2005). Effect of Smoking Reduction on Lung Cancer Risk. *JAMA*. 2005;294(12):1505–1510. doi:10.1001/jama.294.12.1505.
[89] Harlow A.F., Stokes A.C., Brooks D.R., et al. (2022). Prospective association between e-cigarette use frequency patterns and cigarette smoking abstinence among adult cigarette smokers in the United States. *Addiction*. 2022 Aug 1. doi: 10.1111/add.16009. Epub ahead of print. PMID: 35913015.
[90] Harlow (2022).
[91] National Academies of Sciences, Engineering, and Medicine (NASEM) (2018). *Public Health Consequences of E-Cigarettes*. Washington, DC: The National Academies Press. https://doi.org/10.17226/24952.

move adult smokers down the continuum of risk and support broader regulatory and public health objectives based on the data, science, and evidence.

The harmful consequences of such misperceptions were recognized by then SRNT president Dr. Ben Toll, Dr. Tracy Smith, and then FDA CTP Director Dr. Brian King in a Nature Medicine commentary:[92] "These misperceptions are associated with lower odds of completely transitioning from cigarettes to e-cigarettes... For adults who continue to smoke, healthcare professionals may consider... educating patients that although the long-term risks of e-cigarettes are unknown, exclusive use of e-cigarettes instead of cigarettes would reduce exposure to known toxicants and carcinogens."

Misperceptions on Nicotine

A substantial proportion of U.S. adults incorrectly perceive that nicotine is a significant contributor to the harms of tobacco use and the cause of major smoking-related diseases, including cancer, COPD, and CVD. According to a recent analysis of the National Institute of Health (NIH)'s 2019 Health Information National Trends Survey (HINTS), only 22% of respondents answered "strongly disagree" or "disagree" with the statement "nicotine in cigarettes is the substance that causes most of the cancer caused by smoking."[93]

These misperceptions are not limited to the public writ large – they also are found among healthcare professionals. **In one study, shockingly, over 80% of physicians "strongly agreed" that "nicotine directly contributes to" cancer, COPD, and cardiovascular disease.**[94]

In 2022, the UK Office for Health Improvement and Disparities in the Department of Health and Social Care (formerly Public Health England) released its latest in a series of independent reports on ENDS. The report stated that evidence shows "in the short and medium term, vaping poses a small fraction of the risks of smoking."[95] **The report also noted the public health risk posed by inaccurate perceptions of ENDS use. In 2021, "only 34% of adults who smoked accurately believed that vaping was less harmful than smoking," which needs to be addressed.[96]**

Researchers at FDA analyzed the Health Information National Trends Survey (HINTS) and found that 58% of respondents agreed or strongly agreed with the statement "nicotine is the substance that causes most of the cancer caused by smoking" and an additional 20% of respondents were unsure.[97] These researchers also found that nicotine cancer harm misperception has been growing significantly over several waves of HINTS. [98]

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[92] Toll B.A., Smith, T.T., King, B.A. Nicotine e-cigarettes: considerations for healthcare providers. *Nat Med.* 2024 Jun;30(6):1513-1514. doi: 10.1038/s41591-024-02926-7. PMID: 38627561

[93] Peterson EB, Pitzer L, Zhao X. Disparities in Nicotine Addictiveness and Cancer Harm Perceptions Among U.S. Adults: A Trend Analysis Using the Health Information National Trends Survey. *Nicotine Tob Res.* 2023;25(4):639-647. doi:10.1093/ntr/ntac245

[94] Steinberg M., et al. (2020). Nicotine Risk Misperception Among US Physicians, *Journal of General Internal Medicine*.

[95] Office for Health Improvement & Disparities (2022). Nicotine vaping in England: 2022 evidence update main findings. 2022 Sept 29. https://www.gov.uk/government/publications/nicotine-vaping-in-england-2022-evidence-update/nicotine-vaping-in-england-2022-evidence-update-main-findings.

[96] Office for Health Improvement & Disparities (2022).

[97] Peterson (2023).

[98] Peterson (2023).

Furthermore, multiple disparities were observed, as those with lower educational attainment, older adults, and racial minorities were significantly more likely to report an incorrect nicotine cancer harm perception.[99].

Misperceptions on Relative Risk

Despite evidence showing that ENDS are significantly less harmful and improve public health, harm misperceptions around the ENDS category are widespread[100] and have worsened over time. **These misperceptions are likely having a real impact on the potential public health benefit that ENDS offer because they affect adult smokers' willingness to purchase, try, and eventually switch to ENDS.**[101] Only 17.4% of current established adult smokers correctly perceive ENDS as less harmful than cigarettes.[102]

Adult smokers who believe ENDS present less risk than cigarettes switch at much higher rates compared to those who believe ENDS are more or as harmful as cigarettes. As more adults perceive ENDS as equally or more harmful than cigarettes, fewer adult smokers will successfully switch to ENDS.

This misperception is not unique to ENDS, and applies to other noncombustible alternatives as well. **Smokeless tobacco products in the U.S. are known to pose lower risk compared to combustible cigarettes.[103] Yet less than 10% of U.S. adults correctly believe that such products are less harmful than cigarettes.**[104] In one study specifically evaluating risk perceptions of snus products, which have received a modified-risk order from FDA,[105] 55% of respondents reported snus to be as harmful as cigarettes with an additional 20% reporting snus to be *more* harmful than cigarettes.[106]

A real and glaring hurdle to making cigarettes obsolete is the misperception of relative risk between noncombustible alternatives and their counterpart — combustible cigarettes. Despite evidence showing that ENDS improve public health, harm misperceptions around

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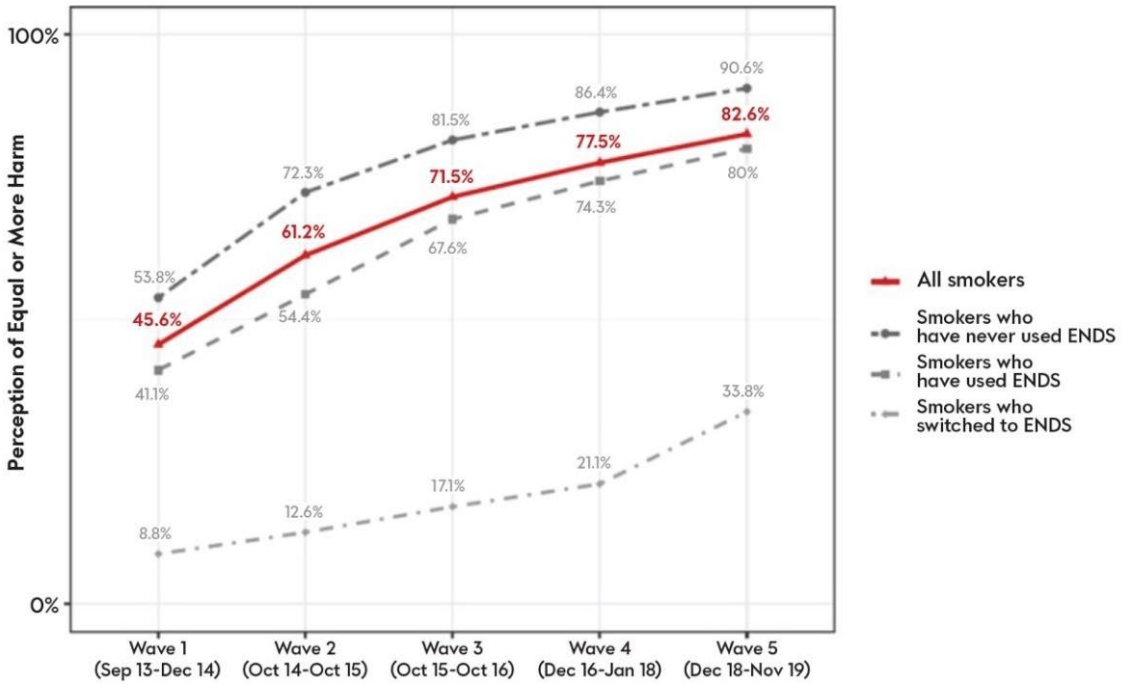
[99] Peterson (2023).
[100] Villanti AC, Naud S, West JC, Pearson JL, Wackowski OA, Niaura RS, Hair E, Rath JM. Prevalence and correlates of nicotine and nicotine product perceptions
in U.S. young adults, 2016. Addict Behav. 2019 Nov;98:106020. doi: 10.1016/j.addbeh.2019.06.009. Epub 2019 Jun 10. PMID: 31238235; PMCID: PMC6947657.
[101] Goldenson N., Holt N., Black R., et al. (2022). Association of Risks Perceptions and Behavioral Intentions of Electronic Nicotine Delivery Systems Among Adult Smokers. *Available at*, https://www.juullabsscience.com/wp-content/uploads/sites/8/2022/08/2022-SBM-Poster_Association-of-Risk-Perceptions-and-Behavioral-Intentions-with-Use-of-Electronic-Nicotine-Delivery-Systems-among-Adult-Smokers-1.pdf.
[102] Kim, S., Shiffman, S. & Sembower, M.A. US adult smokers' perceived relative risk on ENDS and its effects on their transitions between cigarettes and ENDS. BMC Public Health 22, 1771 (2022). https://doi.org/10.1186/s12889-022-14168-8
[103] Fisher M., et al. (2019). Smokeless Tobacco Mortality Risks: An Analysis of Two Contemporary Nationally Representative Longitudinal Mortality Studies, *Harm Reduction Journal* 16:27; Salazar E., et al. (2021), Modeling Mortality Risk Effects of Cigarettes and Smokeless Tobacco: Results from the National Health Interview Survey Linked Mortality File Data, *BMC Public Health* 21:1773.
[104] Feirman S., et al. (2017). Monitoring Harm Perceptions of Smokeless Tobacco Products Among U.S. Adults: Health Information National Trends Survey 2012, 2014, 2015, *Addictive Behaviors*.
[105] FDA (2019, Oct. 22). "FDA Grants First-Ever Modified Risk Orders to Eight Smokeless Tobacco Products, available at https://bit.ly/3pbvyWR.
[106] Wackowski O., et al. (2019). Smokers' Perceptions of Risks and Harm from Snus Relative to Cigarettes: A Latent Profile Analysis Study, *Addictive Behaviors*.

the e-cigarette category are widespread[107] and have worsened over time; 45.6% of adult smokers misperceived e-cigarettes as equally or more harmful than cigarettes in 2013/4, rising to 82.6% in 2018/9 (Figure 11).[108]

Figure 11: The Percentage of Smokers who Perceive ENDS to be at Least as Harmful as Cigarettes has Increased Over Time



Source: Kim S, Shiffman S, Sembower MA. US adult smokers' perceived relative risk on ENDS and its effects on their transitions between cigarettes and ENDS.

Multiple surveys show the proportion of respondents who believe ENDS products are as harmful or more harmful than cigarettes steadily increased.[109] **And these negative and degrading misperceptions occur among adult smokers, the very group most likely to act on and potentially benefit from accurate perceptions of the relative risk of ENDS compared to combustible cigarettes.**[110] Figure 12 age-stratifies risk perceptions for ENDS products among adult smokers and demonstrates that risk perceptions have degraded most among those thirty-five and older. **Notably, adults over the age of thirty-five are less likely to make a quit attempt and less likely to successfully stop smoking compared**

[107] Villanti AC, Naud S, West JC, Pearson JL, Wackowski OA, Niaura RS, Hair E, Rath JM. Prevalence and correlates of nicotine and nicotine product perceptions in U.S. young adults, 2016. Addict Behav. 2019 Nov;98:106020. doi: 10.1016/j.addbeh.2019.06.009. Epub 2019 Jun 10. PMID: 31238235; PMCID: PMC6947657.

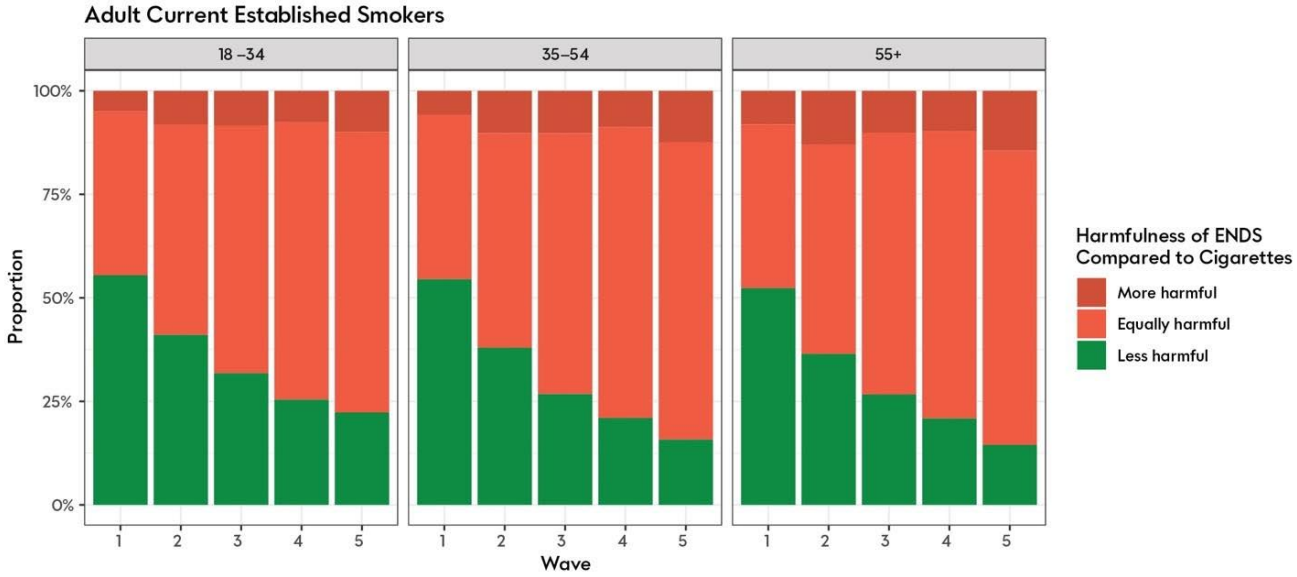
[108] Kim S, Shiffman S, Sembower MA. US adult smokers' perceived relative risk on ENDS and its effects on their transitions between cigarettes and ENDS. BMC Public Health. 2022 Sep 19;22(1):1771. doi: 10.1186/s12889-022-14168-8. PMID: 36123722; PMCID: PMC9484256.

[109] Nyman A., et al. (2019). Perceived Comparative Harm of Cigarettes and Electronic Nicotine Delivery Systems, JAMA Network 2(11):e1915680; Persoskie A., et al. (2019), Perceived Relative Harm of Using E-cigarettes Predicts Future Product Switching Among US Adult Cigarette and E-cigarette Dual Users, *Addiction* 114, 2197; Malt L. (2020); Huang (2019).

[110] Malt (2020); Huang (2019).

to younger adults,[111] suggesting that correcting misperceptions among this population may be helpful in providing a harm-reduction alternative to older adult smokers.

Figure 12: Risk Perceptions of ENDS Products Relative to Combustible Cigarettes; PATH Study, Waves 1–5, Current Established Adult Smokers Stratified by Age



National Institute of Health (NIH) and U.S. Food and Drug Administration's (FDA) Population Assessment of Tobacco and Health (PATH) Study is a national longitudinal study of tobacco use and how it affects the health of people in the United States. Waves (the time span during which the survey was conducted) include: Wave 1 (Sep. 2013–Dec. 2014), Wave 2 (Oct. 2014–Oct. 2015), Wave 3 (Oct. 2015–Oct. 2016), Wave 4 (Dec. 2016—Jan. 2018), and Wave 5 (Dec. 2018–Nov. 2019).

Source: JLI analysis of PATH Waves 1-5 data.

These misperceptions of nicotine and the relative risk of noncombustible products are significant barriers to making the combustible cigarette obsolete and realizing FDA's mandate to reduce tobacco-related death and disease. By one example, in 2023, FDA issued guidance that would increase access to, and the use of, medicinal nicotine products for tobacco cessation (NRTs).[112] Research, however, shows that adult smokers who misperceive medicinal nicotine products to be as harmful as combustible cigarettes are less likely to use these products to support tobacco cessation.[113]

FDA's Comprehensive Framework also recognizes the role of scientifically-substantiated, less harmful noncombustible products to reduce the harms of combustible use and seeks to "ensure that it is possible for current adult smokers who still seek nicotine to get it from

[111] Messer K., et al. (2008). Smoking Cessation Rates in the United States: A Comparison of Young Adult and Older Smokers, *American Journal of Public Health* 98(2):317.
[112] FDA (2023). FDA issues final nicotine replacement therapy drug products guidance. Available at https://www.fda.gov/drugs/drug-safety-and-availability/fda-issues-final-nicotine-replacement-therapy-drug-products-guidance.
[113] Shiffman S., et al. (2008). Perceived Safety and Efficacy of Nicotine Replacement Therapies Among US Smokers and Ex-smokers: Relationship with Use and Compliance, *Addiction* 103(8):1371; Ferguson S., et al. (2011). Providing Accurate Safety Information May Increase a Smoker's Willingness to Use Nicotine Replacement Therapy As Part of a Quit Attempt, *Addictive Behaviors* 36(7):713.

alternative and less harmful sources."[114] Here, too, misperceptions of the relative risk of noncombustible alternatives to combustible products are barriers to the full realization of the Comprehensive Framework.

FDA's own analysis of adult smokers and dual users of cigarettes and ENDS products in the PATH Study concluded:

> [T]hose who perceived e-cigarettes as less harmful than cigarettes were more likely to switch to exclusive e-cigarette use, more likely to remain dual users and less likely to switch to exclusive smoking 1 year later. Our findings highlight the concern that perceptions of e-cigarettes as equally or more harmful than cigarettes could potentially deter complete switching to e-cigarettes among some US adult smokers . . . Based on estimates produced by our weighted analyses, of approximately 10.5 million dual users in 2014–15, nearly 4.3 million did not perceive e-cigarettes as less harmful than cigarettes. Of these 4.3 million, only approximately 115 000 (2.7%) became exclusive e-cigarette users in 2015–16. If these 4.3 million dual users had the same rate of complete switching as those who perceived e-cigarettes as less harmful than cigarettes (7.5%), approximately 205 000 more would have been exclusive e-cigarette users in 2015–16. If their rate of complete switching was the same as those who perceived e-cigarettes as less harmful in both 2014–15 and 2015–16 (11.3%), approximately 370 000 more would have been exclusive e-cigarette users in 2015–16.[115]

The current state of public (mis)understanding about the harms of nicotine and relative risk of ENDS compared to combustible products highlights the need for research and messaging development to support accurate, non-misleading information for Americans who smoke. This information would empower Americans who want to use nicotine to make informed decisions about their health. Without clear communication from trusted sources emphasizing the difference in risk between products that burn tobacco and those that do not, there is less of an incentive to switch away from cigarettes.

FDA efforts on this front to date have been limited, with formative research projected to last years just to share with Americans what is already widely accepted: it is the combustion that makes cigarettes deadly, not the nicotine.

To address the pervasive and entrenched misperceptions held by people who smoke and the public, FDA should make it a priority to refine and disseminate a communications campaign that targets Americans who smoke to dispel misperceptions they have regarding the risk of non-combustible alternatives compared to cigarettes.

[114] FDA (2018, March 15). Transcript of FDA Media Briefing on Pivotal Public Health Step to Explore Dramatically Reducing Smoking Rates by Lowering Nicotine in Combustible Cigarettes to Minimally or Non-Addictive Levels, available at https://bit.ly/3vjsE3z.
[115] Persoskie (2019).

Anti-Risk-Proportionate Public Policy: Taxation

The second likely reason why adult smokers are not switching to less harmful products is anti-risk-proportionate policies (both contemplated and enacted) at the federal, state, and municipal levels. These policies have created marketplaces that unintentionally advantage combustible cigarettes while simultaneously disadvantaging less harmful, noncombustible products like ENDS.

The data show that ENDS products are substitutes for combustible cigarettes and provide adult smokers an off-ramp from combustible use. Public policy should reflect this reality and support this behavior. That is, evidence-based policy should encourage switching to a less harmful product and, as a result, decrease cigarette smoking. The evidence suggests that fiscal policy, in particular, for tobacco and nicotine products can impact public health. For example, in a study utilizing the nationally representative public surveys, Behavioral Risk Factor Surveillance System and National Health Interview Survey, **researchers estimated that a national tax on ENDS products, equivalent to $1.65 per milliliter of e-liquid, would raise the proportion of adult smokers daily by approximately 1 percentage point, translating to 2.5 million additional smokers.**[116]

In a separate systematic review and meta-analysis, researchers found that while a 10% increase in ENDS product price was associated with an 11.5% decrease in ENDS sales and purchases, the price increase also resulted in a 1.1% increase in sales and purchases of combustible cigarettes. Conversely, a 10% increase in cigarette price was associated with a 9.8% increase in ENDS sales and purchases, as well as increased ENDS-use prevalence.[117]

Multiple studies also consider the impact of ENDS taxes on specific population groups. Using comprehensive national surveys, Dr. Abouk et al. found that **ENDS tax increases reduce youth use of ENDS, but also can lead to an increase in youth use of combustible cigarettes due to substitution**: **"We conclude that the unintended effects of ENDS taxation may considerably undercut or even outweigh any public health gains."**[118]

Another study, focusing on young adults (ages 18 to 25 years), found that a one dollar increase in ENDS taxes significantly reduced daily ENDS use but increased recent cigarette smoking and signaled greater dual use (with associations reversing when cigarette taxes are applied.)[119]

At the state level, an analysis examining the effects of an ENDS tax in Minnesota estimated that taxing ENDS products at the same rate as cigarettes nationwide would deter

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[116] Pesko (2020).
[117] Selya A., Foxon F., Chandra S. et al. (2023). Meta-analysis of e-cigarette price elasticity [version 1; peer review: awaiting peer review]. *F1000Research*, 12:121. https://doi.org/10.12688/f1000research.129233.1.
[118] Abouk R., Courtemanche C., Dave D. et al. (2021). Intended and Unintended Effects of E-cigarette Taxes on Youth Tobacco Use. *NBER Working Paper* No 29216.
[119] Friedman A.S., Pesko M.F. (2022). Young adult responses to taxes on cigarettes and electronic nicotine delivery systems. *Addiction*. 2022 Dec;117(12):3121-3128. doi: 10.1111/add.16002. Epub 2022 Jul 29. PMID: 35852452; PMCID: PMC9796020.

approximately 2.75 million adult smokers from transitioning from combustible cigarettes in a ten-year period.[120]

Public health stakeholders agree that differential tax for differential risk would advance the harm-reduction potential of noncombustible alternatives for adult smokers. As researchers wrote in the *New England Journal of Medicine*:

> The rapid evolution of the nicotine-product marketplace suggests that it's time to rethink the idea that similar taxes are best practice. We believe that national, state, and local policymakers should consider an approach that differentially taxes nicotine products in order to maximize incentives for tobacco users to switch from the most harmful products to the least harmful ones.[121]

Policymakers' goal should be to enact fiscal policy that advances making combustible cigarettes obsolete and achieves public health benefits by incentivizing adult smokers to switch to less harmful alternatives. As Dr. Warner wrote in the *Washington Post*, failure to do so could have the opposite, more harmful effect:

> Economic studies demonstrate that cigarettes and e-cigarettes are substitutes for each other. If cigarettes become more costly relative to e-cigarettes, some cigarette smokers will switch to e-cigarettes. Conversely, if e-cigarettes prices rise relative to cigarette prices . . . some people will smoke cigarettes who would otherwise have used e-cigarettes.[122]

Anti-Risk-Proportionate Public Policy in Action: New Zealand and Australia Case Study

A recent study by researchers at the University of Queensland published in the journal *Addiction*[123] provides compelling evidence that a risk-proportionate regulatory framework which provides adults who smoke access to smokefree alternatives, coupled with accurate science-based information about those products versus cigarettes, can lead to faster declines in smoking rates.

The study compared smoking and vaping rates from 2016-2023 across two neighboring countries, Australia and New Zealand, with similar demographics and policy profiles around combustible tobacco. For example, both countries tax cigarettes heavily, have plain packaging and health warnings on cigarette packs, and have similar smokefree goals.

New Zealand has embraced balanced regulation that allows adult consumers to purchase vaping products from licensed retailers, while implementing policies[124] to remove devices like disposables and products with youth-appealing imagery. The country is clear on its

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[120] Saffer, H. et al. (2020). E-cigarettes and adult smoking: Evidence from Minnesota. *J Risk Uncertain* 60, 207–228. https://doi.org/10.1007/s11166-020-09326-5.

[121] Chaloupka F., Sweanor D., Warner K. (2015). Differential Taxes for Differential Risks--Toward Reduced Harm from Nicotine-Yielding Products. *N Engl J Med*. 2015 Aug 13;373(7):594-7. doi: 10.1056/NEJMp1505710.

[122] Warner K. (2021). "Build Back Better's e-cigarette tax will make people smoke more," *The Washington Post*, November 22, 2021.

[123] Mendelsohn, C. P., Beaglehole, R., Borland, R., Hall, W., Wodak, A., Youdan, B., & Chan, G. C. K. Do the differing vaping and smoking trends in Australia and New Zealand reflect different regulatory policies?. *Addiction*.

[124] New Zealand Ministry of Health. (2024). Vaping regulations coming into effect 1 October. Retrieved May 5, 2025, from https://www.health.govt.nz/news/vaping-regulations-coming-into-effect-1-october

stance that vaping can be an effective tool to help adult smokers make the switch from combustible cigarettes, dedicating a government website[125] to providing reliable facts and resources about vaping's role in making cigarettes obsolete.

Australia's vaping policy, by contrast, is one of the most restrictive in the world, based on a prescription-only[126] model that treats e-vapor products akin to controlled substances. Beginning in late 2024, restrictions were lightened slightly to counter a black market[127] that erupted. Still the policy continues to require prescriptions and/or limited over-the-counter pharmacy purchases only which discourages adults who smoke from using vapor products as an alternative to cigarettes.

The results show:

1. **Smoking declined twice as fast in New Zealand**. Between 2016 and 2023, New Zealand's adult daily smoking rate plummeted from 14.5% to 6.8% – a 10% annual decline. Australia's rate fell by just half of that over the same period with 8.3% of adults smoking daily in 2023.

2. **Vaping rates mirror smoking declines**. By 2023, 9.7% of New Zealand adults reported daily use of e-vapor products, compared to only 3.5% of Australian adults – reflecting the differing accessibility of these products as alternatives to combustible cigarettes.

3. **Smoking rates for young adults declined in both countries, and lower socioeconomic groups in New Zealand benefited.** In both countries, smoking declined the most among younger adults, which also reflect higher vaping rates among that population. The lower socioeconomic and indigenous populations in New Zealand - communities often at the highest risk for smoking and smoking-related disease - saw more rapid declines in smoking rates following implementation of New Zealand's vaping policies, suggesting access to alternatives played a role.

4. **Youth vaping rates in New Zealand are higher than Australia but have started to decline since regulations were introduced**. The authors note that most of the rise in youth vaping occurred prior to the 2021 enactment of New Zealand's vaping policies and, since regulation went into effect, daily vaping among youth has decreased from 10.1% in 2022 to 8.7% in 2024. The authors rightly note that the rise in youth vaping raises important public health questions and underlines the importance of balanced regulation, including "restricting the sale of vaping products to licensed retail outlets; strict age verification and use of closed-circuit television at point-of-sale; harsh penalties including the loss of licence for underage sales; restricted advertising and marketing to adolescents; restrictions on disposables; and banning flavour names, images and packaging, which appeal to young people."

[125] Vaping Facts Website. Retrieved May 5, 2025, from https://vapingfacts.health.nz
[126] Hall, W. D. (2024). Will Australia's tightened prescription system reduce nicotine vaping among young people?. *Addiction*, *119*(10), 1682-1688.
[127] Department of Health and Aged Care. (2025*)* About vaping. Australian Government. https://www.health.gov.au/topics/smoking-vaping-and-tobacco/about-vaping

5. **Thriving black market in Australia.** Restrictive policies in Australia have "helped create a thriving and increasingly violent" black market.[128] As one co-author noted, more than 90% of vaping products sold in the country are unauthorized and sold outside of the prescription and pharmacy-only restrictions.

The implications for the U.S. are clear. Effective regulations to protect against youth adoption of alternative nicotine products are essential, but if we aim to end cigarette smoking, policies must also be balanced in a way that provides for access to an array of potentially less harmful alternatives for adult smokers and to be able to compete against the black market.

The U.S. FDA has been restrictive in its approach to authorizing vapor products and has sent mixed messages to adult smokers about the benefit of transitioning from combustibles to ENDS.

This study provides a roadmap for effective tobacco policy: a well regulated market for adult smokers seeking alternatives, accurate and evidence-based information about relative risk, and focused enforcement against both youth access and illegal products. The message here is clear and compelling – if we want to make cigarettes obsolete, we need to follow the roadmap of those countries who are on their way toward achieving that goal.

Conclusion: A Well-Regulated, Science-Based ENDS Market Can Complement Other Tobacco-Control Measures to Accelerate Declines in Cigarette Smoking and Significantly Improve Public Health

The evidence presented in this white paper demonstrates that ENDS products can play a critical role in transitioning and completely switching adults who smoke from combustible cigarettes to noncombustible alternatives. ENDS complement other evidence-based tobacco control interventions that prevent tobacco product initiation and can accelerate the decline of combustible cigarette use across the population. If regulated in a manner based on sound science, coupled with evidence-based policy development, ENDS products can help significantly reduce tobacco-related death and disease and ultimately realize an endgame for combustible cigarettes.

Juul Labs, Inc.'s mission is to transition the world's billion adult smokers away from combustible cigarettes, eliminate their use, and combat underage usage of our products.

For more information on the science and evidence discussed in this white paper, visit juullabsscience.com.

[128] Elks, S., & Thomas, H. (2024). Burning out: How Australia's bid to cut smoking rates exploded into suburban tobacco wars. The Guardian. https://www.theguardian.com/society/2024/nov/02/burning-out-how-australias-bid-to-cut-smoking-rates-exploded-into-suburban-tobacco-wars