Juul Labs

The Real-World Impact of ENDS for Adult Smokers: Tobacco Harm Reduction Through Real-World Data and Evidence

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Executive Summary

Smoking-related disease from the use of combustible cigarettes causes nearly one-in-five premature deaths in the United States. Half of the individuals who continue to smoke will die from related illnesses — about 480,000 Americans each year, more than 1,300 every day.

It is widely understood that the best option for adult smokers to reduce the risks to their health from combustible cigarettes is to quit tobacco and nicotine products altogether.

This white paper is intended to provide a discussion of current science and evidence concerning the many individuals using combustible products that have not successfully quit. For these individuals, because cigarette smoking is so extraordinarily harmful, the body of evidence that we discuss in this white paper suggests that switching completely to a noncombustible alternative can significantly reduce their exposure to harmful constituents in smoke and their risk of smoking-related disease.

In particular, this white paper responds to multiple calls for data and evidence showing the real-world, public-health benefit of electronic nicotine delivery systems (ENDS) — sometimes referred to as e-cigarettes or vapor products — for adult smokers as less harmful, noncombustible alternatives to combustible cigarettes. For example, in October 2021, Cohen et al. challenged 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 "¹

Important Disclosures:

This information is intended for members of the scientific and public health communities, regulators, and policymakers. It is not intended for advertising or promotional purposes or intended for a consumer audience.

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.

Any and all sources cited in this white paper, including their authors and publishers, do not, in any way, constitute an endorsement of JLI or any of its products.

¹ Cohen J.E., et al. (2022). "Balancing Risks and Benefits of E-Cigarettes in the Real World," *American Journal of Public Health* 112, no. 2: pp. e1-e2.

Our review of evolving market data and research indicates that not only are ENDS products helping adult smokers achieve reduced risk at the individual level, but at the population level these products are likely to enable a reduction in the harms caused by cigarette smoking. We organize this review along four lines of evidence that we see as reinforcing 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 adult smokers transitioning and completely switching from combustible cigarettes to ENDS products;
- Economic data demonstrating ENDS products as substitutes to combustible cigarettes; and
- Population models demonstrating reductions in tobacco-related death and disease as ENDS use increases.

The bottom line of our review: Real-world data and evidence discussed in this white paper demonstrate that — while ENDS are not without risk — adult smokers are transitioning and completely switching from combustible cigarettes to ENDS products resulting in reduced individual harm from tobacco use and a net benefit to public health.

In the United States, these lines of evidence have emerged despite, and not facilitated by, the current regulatory and policy environment. An environment that over recent years has proven to be quite negative toward less harmful, noncombustible products while unintentionally and unfortunately propping up the deadliest form of tobacco — the combustible cigarette.

Juul Labs, Inc. (JLI) supports risk-proportionate policy and regulation for ENDS and other noncombustible products. Such a policy framework, at its core, applies the most stringent regulations to the riskiest products (e.g., combustible cigarettes) and encourages adult consumers to switch to less harmful, noncombustible alternatives. This policy framework is not a veiled effort to achieve lighter regulations for their own sake — to the contrary, it entails, among other things, comprehensive, evidence-based interventions to address underage use of all tobacco and nicotine products. But a comprehensive, riskproportionate policy and regulatory approach that also prioritizes switching adult smokers to less harmful products can accelerate the end of combustible cigarettes and realize significant public-health gains.

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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 progress made to both help adult smokers quit and prevent new users from initiation, including youth, approximately 31 million Americans continue to smoke combustible cigarettes.^{2,3}

Smoking-related disease causes nearly one in five premature deaths in the U.S.,⁴ and half of those who continue to smoke will die from a smoking-related illness — about 480,000 Americans each year, more than 1,300 every day.⁵ Smoking affects "nearly every organ in the body,"⁶ as depicted in Figure 1 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."⁷

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."**⁸

The best option for adult smokers 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,⁹ fewer than 10% actually succeed in quitting cigarettes.¹⁰

² CDC (2022, March 17). *CDC Current Cigarette Smoking Among Adults in the United States.* CDC. <u>https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm</u>.

³ CDC (2022, March 18). CDC Morbidity and Mortality Weekly Report. CDC. / 71(11);397-405.

http://dx.doi.org/10.15585/mmwr.mm7111a1.

⁴ CDC (2022, March 18).

⁵ U.S. Department of Health and Human Services (2014). <u>The Health Consequences of Smoking—50 Years of</u> <u>Progress: A Report of the Surgeon General</u>. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

⁶ U.S. Department of Health and Human Services (2014).

 ⁷ 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.

⁸ U.S. Department of Health and Human Services (2014).

⁹ Babb S. (2017). Quitting smoking among adults—United States, 2000-2015. *MMWR Morb Mortal Wkly Rep.*, 65.

¹⁰ Cullen K.A., Gentzke A.S., Sawdey M.D. et al. (2018). E-Cigarette Use Among Youth in the United States, 2019. *JAMA*, 322(21):2095-2103.

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 adult smokers can have a significant public-health benefit.

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

Tobacco Harm Reduction 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."¹¹

This statement summarizes the rationale behind tobacco harm reduction: Adults who smoke seek nicotine, but the vast majority of harm associated with smoking comes not from nicotine but from other chemicals. These include tobacco-specific nitrosamines and the thousands of compounds in smoke created through *combustion* (the burning and production of smoke), including carbon monoxide and volatile organic compounds.

¹¹ 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) 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.¹²

Since 2017, FDA's level of commitment-by-action to the Comprehensive Framework has been less sanguine, and a recent external review of CTP by the Reagan-Udall Foundation found that "the Center's current goals and priorities are unclear."¹³ Nevertheless, this harm-reduction approach remains a viable regulatory and policy framework that is founded in real-world data and evidence and positions the agency to achieve its mission of reducing the death and disease caused by tobacco use.

The FDA's Comprehensive Framework envisions reducing nicotine in combustible cigarettes 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).

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.

Figure 2: The Continuum of Risk for Nicotine Delivery



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

¹² Gottlieb S., Zeller M. (2017). A nicotine-focused framework for public health. *N Engl J Med.,* [Emphasis added].

¹³ 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.

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 precedent 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 harms¹⁴

This regulatory approach is also consistent with the demands of adult smokers looking for alternatives to combustible cigarettes — over half of adults who smoke have expressed interest in less harmful products.¹⁵ 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.¹⁶ 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.¹⁷

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.¹⁸

ENDS as a Critical Tool for Harm Reduction in Policy and Practice

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.¹⁹ proposed a "Three-Dimensional Framework for Harm Minimization" (Figure 3) that organizes "alternative nicotine delivery devices" (referred to as "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

¹⁴ Hatsukami D.K., Carroll D.M. (2020). Tobacco harm reduction: Past history, current controversies and a proposed approach for the future. *Prev Med.*,106099.

¹⁵ 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.

¹⁶ Dawkins L.E., McRobbie H. (2017). Changing behaviour: Electronic cigarettes. *British Psychological Society*. https://www.bps.org.uk/psychologist/changing-behaviours.

¹⁷ Dawkins (2017).

¹⁸ 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.

¹⁹ 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.

to envision how to optimize ANDS product use to successfully compete with and replace smoking."²⁰





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 likely will have used for years if not decades — ENDS products must provide sufficient appeal and nicotine delivery.²¹ 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]."²² Nicotine replacement therapies (NRTs), such 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

- ²⁰ Abrams (2018).
- ²¹ Abrams (2018).

²² Abrams (2018).

this sweet spot because some smokers have found an e-cigarette with sufficient appeal for them to sustain use and quit smoking." $^{\prime\prime23}$

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.²⁴ 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."²⁵

Public-Health Experts Urge a Balanced Approach to ENDS

Advancing harm reduction for adult smokers while addressing underage use of all tobacco and nicotine products requires a balanced approach. 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."²⁶

In response to Dr. Balfour et al., Dr. Cohen et al.²⁷ 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 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.²⁸ 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.²⁹

²³ Abrams (2018).

²⁴ 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.

²⁵ Warner (2023).

²⁶ 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.

²⁷ Cohen (2022).

 ²⁸ 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.
 ²⁹ Fagerström (2022).

The "Nearly Invisible" Adult Smoker

Despite decades of progress to decrease cigarette use and initiation, around 31 million American adults still smoke, leading to the approximately 480,000 smoking-related deaths in the U.S. each year.

Reaching these 31 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.³⁰

CTP Director Dr. Brian King recently observed as well that "among persons who smoke, progress hasn't been experienced equitably. Smoking disproportionately affects communities including, but not limited to, certain racial and ethnic populations, low-income populations, people living with mental health conditions, and LGBTQI+ individuals."³¹

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."³² 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."³³ 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."³⁴

³⁰ Balfour (2021). [Emphasis added].

³¹ King, B. (2022). Bringing Health Equity to the Forefront of Tobacco Product Regulation. HPHR. 2022;61. DOI: 10.54111/0001/III2.

³² Warner, K. (2019). "Who's Smoking Now and Why It Matters," *The Conversation*.

https://theconversation.com/whos-smoking-now-and-why-it-matters-109605.

³³ Warner (2019). [Emphasis added].

³⁴ Balfour (2021). [Emphasis added].

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



Source: JLI analysis of public use data, 2020 National Health Interview Survey.

Income: Adults earning less than \$35,000 annually are more than 3x as likely to smoke compared to adults earning \$100,000+.

Education: Adults who did not graduate from high school or have a GED are 4-6x as likely to smoke compared to adults with a 4-year college or graduate degree.

Race/Ethnicity: American Indians/Alaskan Natives are more than 3x as likely to smoke as Hispanics or Asians.

Region: Adults in the Midwest or South are approximately 50% more likely to smoke compared to adults in the Northeast or West.

Sexual Orientation: Adults who identify as gay, lesbian, or bisexual are significantly more likely to smoke compared to adults who identify as straight.³⁵

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

Proposed Ban on Menthol Cigarettes: A Case Study

To illustrate Dr. Warner's point, we look to pending CTP policy. In his recent essay *Bringing Health Equity to the Forefront of Tobacco Product Regulation,* CTP Director Dr. King referenced the agency's proposed ban on menthol cigarettes as one that "would help

³⁵ JLI analysis of 2020 National Health Interview Survey public use data (2020). Data available at https://www.cdc.gov/nchs/nhis/index.htm.

³⁶ Warner (2019).

³⁷ Warner (2019). [Emphasis added].

address longstanding health disparities related to smoking menthol cigarettes."³⁸ He continued:

Included among those who are more likely to smoke menthol cigarettes are Black Americans, other racial and ethnic minority groups, youth and young adults, female adults, persons with less than a high school diploma, and individuals who identify as lesbian, gay, or bisexual. Scientific evidence indicates that menthol cigarettes have historically been and continue to be disproportionately marketed in underserved communities. For example, nearly 85 percent of all non-Hispanic Black adults who smoke use menthol cigarettes, compared to 30 percent of non-Hispanic White adults who smoke.³⁹

In his essay, CTP Director King went on to state that "[p]ublished modeling studies estimate that if menthol cigarettes were no longer available in the U.S., we could see a 15 percent reduction in smoking overall within these same 40 years; it would also avoid 324,000 to 654,000 smoking attributable deaths over the course of 40 years, 92,000 to 238,000 of those among Black Americans."⁴⁰

While not explicit in his piece, but implicit in his citation of the model that underwrites the agency's proposed rule to ban menthol cigarettes,⁴¹ CTP Director King acknowledged the need for ENDS products to serve as a "complementary tool"⁴² (as characterized by Dr. Warner) to FDA policy.

This model not only projected the public-health upside —the 654,000 smoking attributable deaths that may be reduced,238,000 of which are projected to be among Black Americans — but it did so under the assumption of a robust, legal market of tobacco- and menthol-flavored ENDS products in the United States:

[Among] current menthol smokers aged 18-24, 10.1% switch to illicit menthol combustibles, 48.0% switch to non-menthol combustibles, 24.2% switch to NVPs [i.e., ENDS products] and 17.7% quit all product use.⁴³

These transitions are applied to menthol smokers through age 30. Among current menthol smokers aged 35–54, 8.8% switch to illicit menthol cigarettes and cigars, 59.1% switch to non-menthol tobacco use, 17.3% switch to NVPs and 14.7% quit all product use.⁴⁴

Adult smokers deserve opportunities to have access to viable, less harmful alternatives, and ENDS may present a tool that can allow all adult smokers to minimize the risks of disease and death that accompany continued cigarette smoking.

³⁸ King (2022).

³⁹ King (2022).

⁴⁰ King (2022).

⁴¹ FDA (2022). Proposed Rule on Tobacco Product Standard for Menthol in Cigarettes. 87 FR 26454. https://www.federalregister.gov/d/2022-08994.

⁴² Warner (2019).

⁴³ FDA Proposed Rule (2022).

⁴⁴ FDA Proposed Rule (2022).

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

Noncombustible products can provide adult smokers with a less harmful alternative and 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 long-term smokers will die prematurely from smoking-related disease.⁴⁵

ENDS products are just one example of noncombustible alternatives available to adult smokers. Others include smokeless tobacco products, heated tobacco products, and oral tobacco-derived nicotine products (e.g., nicotine pouches). And all 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.

Evolving market data and research demonstrates that not only are ENDS helping adult smokers 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 5: Four Lines of Evidence Showing the Positive Real-World Impact of ENDS Products for Adult Smokers



Source: JLI analysis.

⁴⁵ U.S. Department of Health and Human Services (2014).

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 6).⁴⁶ 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.⁴⁷



Figure 6: 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*.

⁴⁶ 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.

⁴⁷ Altria (2019). *Altria's Third-Quarter 2019 Earnings Conference Call* at 13. <u>https://bit.ly/38RF3Vr</u>.

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?

That ENDS sales are specifically responsible for displacing cigarette sales is supported by population-level data showing that adult smokers are transitioning and completely switching to ENDS products.

An 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.⁴⁸ Results showed that actual smoking prevalence from 2010–2019 was significantly lower than predictions, 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.⁴⁹

The 2022 update to the Cochrane review of ENDS products concluded that there is highcertainty evidence that ENDS are effective for promoting the discontinuation of cigarette smoking.⁵⁰ This conclusion is based on a meta-analysis of randomized controlled trials of adults who stopped smoking combustible cigarettes using ENDS products.⁵¹

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.⁵²

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**

⁴⁸ Foxon, F., Selya, A., Gitchell, J. et al. (2022). Population-level counterfactual trend modelling to examine the relationship between smoking prevalence and e-cigarette use among US adults. *BMC Public Health* 22, 1940. https://doi.org/10.1186/s12889-022-14341-z.

⁴⁹ Foxon, Selya, Gitchell (2022).

⁵⁰ Hartmann-Boyce J., Lindson N., Butler A.R., et al. (2022). Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews*, Issue 11. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub7.

⁵¹ Hartmann-Boyce (2022).

⁵² 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.

who subsequently began using ENDS daily, 28.0% quit smoking cigarettes.⁵³ In contrast, among baseline adult smokers not planning to quit who reported no subsequent use of ENDS, only 5.8% quit smoking cigarettes (Figure 7).

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 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).⁵⁴



Figure 7: Daily ENDS Use Increases Cigarette-Smoking Cessation and Reduces Cigarette Consumption Among Adult Smokers Not Planning to Quit

Source: 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.

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.⁵⁵ Together, these analyses show a substitution effect of ENDS products for combustible cigarettes.

⁵³ 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.

⁵⁴ Kasza (2021).

⁵⁵ 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.

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.⁵⁶ 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."⁵⁷

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.⁵⁸

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

⁵⁶ Levy D. et al. (2021). Public Health Implications of Vaping in the USA: The Smoking and Vaping Simulation Model, *Popul Health Metr* 19, 19.

⁵⁷ Abouk (2023).; see also 87 Fed. Reg. at 26481.

⁵⁸ Foxon, Selya, Gitchell (2022).

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."⁵⁹

Dr. Wagner and Dr. Clifton similarly examined the relationship between cigarette-smoking and ENDS-use prevalence and predicted, as demonstrated in Figure 8 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.⁶⁰



Figure 8: 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.⁶¹ 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 years.⁶² 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 2052.⁶³

⁵⁹ 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.

⁶⁰ 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.

⁶¹ Levy (2021).

⁶² Levy (2021).

⁶³ Levy (2021).

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.

All tobacco products, including ENDS, present risk. However, the scientific evidence shows that ENDS products are likely to present substantially lower health risk than combustible cigarettes for adult smokers who switch completely.

Because ENDS are relatively novel products that have not been used for extended periods, the FDA, the Surgeon General, and the Centers for Disease Control and Prevention (CDC) have not reached a consensus on their long-term health effects. We defer to their expertise.

While long-term data on ENDS use are not available yet, multiple lines of evidence support that ENDS products are expected to 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 are likely to 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. ⁶⁴

United States public-health bodies have issued similar statements:

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 delivery system, either en route to quitting tobacco completely or even as a long-term alternative, the risks of tobacco-related diseases would be

⁶⁴ 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.

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.⁶⁵ 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.

It is not surprising, therefore, that FDA places a heavy priority on HPHC reductions when it considers 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 to use this comparison in its determination of whether permitting the marketing of the product would be APPH.⁶⁶

 ⁶⁵ FDA (2012). Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke: Established List. <u>https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/harmful-and-potentially-harmful-constituents-tobacco-products-and-tobacco-smoke-established-list</u>.
 ⁶⁶ FDA (2021). Premarket Tobacco Product Applications and Recordkeeping Requirements, 86 Fed. Reg.

⁵⁵³ FDA (2021). Premarket Tobacco Product Applications and Recordkeeping Requirements, 86 Fed. Reg. 55300. *Available at*, <u>https://www.federalregister.gov/documents/2021/10/05/2021-21011/premarket-tobacco-product-applications-and-recordkeeping-requirements</u>.

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.⁶⁷

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, indicate that BOEs representing thirteen volatile organic compounds and three heavy metals were significantly lower in ENDS users than in cigarette smokers.⁶⁸ In fact, levels of exposure to these harmful constituents in ENDS users approach levels measured in adults who have never used tobacco products.⁶⁹

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-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."⁷⁰

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.

⁶⁷ 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.

⁶⁸ Holt, N.M., Shiffman, S., Black, R.A., et al. (2023). Comparison of Biomarkers of Exposure to Volatile Organic Compounds, Metals and Nicotine among US Adult Smokers, Users of Electronic Nicotine Delivery Systems, Dual Users and Nonusers in PATH Wave 5. [Submitted for Publication].
⁶⁹ Holt (2023).

⁷⁰ 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.

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.⁷¹

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.⁷²

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.^{73,74}

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)⁷⁵: "We did not find a significant difference in the cardiovascular risk of exclusive e-cigarette use compared with nonuse of cigarettes and e-cigarettes."

Hirschtick et al. (2022)⁷⁶: "ENDS use was not associated with a statistically significant increase in CVD outcomes."

Falk et al. (2022)⁷⁷: "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

⁷¹ U.S. Department of Health and Human Services (2014).

⁷² 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.

⁷³ 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.

⁷⁴ FDA (2012).

⁷⁵ 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.

⁷⁶ 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.

⁷⁷ 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.

compared to non-users. The current analysis extended previous research findings regarding associations between ENDS and CVD."

Farsalinos et al. (2019)⁷⁸: "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)⁷⁹: "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 "ecigarette 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.^{80,81} To reflect this, Canada now refers to EVALI as "Vaping-Associated Lung Illness" (VALI), excluding "e-cigarette" from the official title.⁸²

The reality is likely different than 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 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.⁸³

A recent working paper from Dr. Kenkel et al.⁸⁴ found no evidence that current or former ENDS use is associated with respiratory disease among adults who have never

⁷⁸ 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.

 ⁷⁹ 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.
 ⁸⁰ 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. ⁸¹ Pesko, M.F., Cummings, K.M., Douglas, et al. (2023). United States public health officials need to correct ecigarette health misinformation. *Addiction*. <u>https://doi.org/10.1111/add.16097.</u>

⁸² 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. <u>https://doi.org/10.24095/hpcdp.42.1.06.</u>

⁸³ 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-evidencereview/evidence-review-of-e-cigarettes-and-heated-tobacco-products-2018-executive-summary [Note: OHID was referred to as Public Health England in 2018].

⁸⁴ 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, <u>https://www.nber.org/papers/w27507</u>.

smoked. In other studies that find correlations between ENDS use and respiratory disease, these relationships are often confounded by former combustible use.⁸⁵ 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.⁸⁶

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.⁸⁷ 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 being a transitory state** from cigarette smoking to complete ENDS use.⁸⁸

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 reductions in cigarette consumption.⁸⁹ In fact, substantial declines in cigarette consumption (50% and higher) are associated with significantly lower exposure to HPHCs⁹⁰ and reductions in disease outcomes.⁹¹

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 "associated with four times the probability of sustained 12-month smoking abstinence compared to no current e-cigarette use over two

⁸⁵ 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.

⁸⁶ 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.

⁸⁷ Coleman, S.R.M., Piper, M.E., Byron, M.J. et al. (2022). Dual Use of Combustible Cigarettes and Ecigarettes: a Narrative Review of Current Evidence. *Curr Addict Rep* 9, 353–362. https://doi.org/10.1007/s40429-022-00448-1.

⁸⁸ Balfour (2021).

⁸⁹ 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.

⁹⁰ 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.

⁹¹ 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.

years of follow-up."⁹² Additionally, participants who reported non-daily ENDS use were 72% less likely to achieve cigarette-smoking abstinence than non-users.⁹³

The relationship between statistically increased rates of cigarette-smoking abstinence and ENDS use in the U.S. requires additional research, although a recent study found that ENDS use coincided with a period of higher rates of discontinuing cigarette smoking.⁹⁴

Thus, dual use, while not the optimal state, should be viewed as a necessary transitionary state to 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."⁹⁵

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

And second, anti-risk-proportionate policies (both contemplated and enacted) at the federal, state, and municipal levels have created marketplaces that unintentionally

⁹² 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.
⁹³ Harlow (2022).

⁹⁴ Kasza K.A., Tang Z., Xiao H., et al. (2022). National longitudinal tobacco product cessation rates among US adults from the PATH Study: 2013-2019 (waves 1-5). *Tob Control.* 2022 Jul 25:tobaccocontrol-2022-057323. Doi: 10.1136/tc-2022-057323. Epub ahead of print. PMID: 35879095.

⁹⁵ 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.

advantage combustible cigarettes while simultaneously disadvantaging less harmful, noncombustible products like ENDS.

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 Wave 4 of the National Institute of Health (NIH) and FDA's PATH Study, 68.3% of respondents answered "definitely yes" or "probably yes" in response to the statement "nicotine in cigarettes causes most of the cancer caused by smoking."⁹⁶

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.⁹⁷

In a follow-up study, the same group conducted a survey among physicians to understand the impact of question wording on estimates of nicotine risk.⁹⁸ Specifically, these researchers randomly fielded two versions of a survey item about nicotine risk. Version 1 was: "Please indicate the extent to which you agree or disagree that nicotine directly contributes to the development of the following health problems by selecting your choice"; while version 2 was more specific, reading: "Please indicate the extent to which you agree or disagree that nicotine on its own directly contributes to the development of the following health problems by selecting your choice."

Large majorities of respondents to both versions of the question strongly agreed that nicotine directly contributes to the development of cancer, COPD, and cardiovascular disease. However, version 2 of the question, which included the phrase "nicotine on its own," elicited less strong agreement compared to the responses to version 1. For example, 85% of respondents to version 1 strongly agreed that nicotine directly contributes to cancer compared to 69.6% of respondents to version 2. The researchers concluded that "even after accounting for question version, the proportion of surveyed physicians who believe that nicotine directly contributes to these health outcomes is alarmingly high."

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

⁹⁶ Delinger-Apte R., et al. (2021). Risk Perceptions of Low Nicotine Cigarettes and Alternative Nicotine Products Across Priority Smoking Populations, *International Journal of Environmental Research and Public Health* 18, 5311.

⁹⁷ Steinberg M., et al. (2020). Nicotine Risk Misperception Among US Physicians, *Journal of General Internal Medicine*.

⁹⁸ Manderski B., et al. (2021). Persistent Misperceptions About Nicotine Among US Physicians: Results from a Randomized Survey Experiment, International Journal of Environmental Research and Public Health 18(14):7713.

medium term, vaping poses a small fraction of the risks of smoking."⁹⁹ 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.¹⁰⁰

Researchers at FDA analyzed the Health Information National Trends Survey (HINTS) and found that 49% 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 24% of respondents were unsure.¹⁰¹ These researchers further stratified their analysis by smoking status and reported that among adult smokers planning to quit, 48% agreed or strongly agreed that nicotine causes most of the cancer caused by smoking, 17% were unsure, and only 35% disagreed or strongly disagreed.¹⁰² Nicotine misperceptions among recent smoking quitters were more imbalanced: 64% of this group agreed or strongly agreed that nicotine causes most of the cancer caused by smoking, 7% were unsure, and only 28% disagreed or strongly disagreed.¹⁰³

Misperceptions on Relative Risk

The public maintains significant misperceptions about the relative risks of a broad range of noncombustible alternatives relative to combustible cigarettes, including ENDS products. These misperceptions have 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.¹⁰⁴ Only 17.4% of current established adult smokers perceive ENDS as less harmful than cigarettes, with 70% perceiving ENDS products to be as harmful as cigarettes, and 12.3% perceiving ENDS products to be *more* harmful than cigarettes.

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 be lower risk compared to combustible cigarettes.¹⁰⁵ Yet less than 10% of U.S. adults correctly endorse that such

⁹⁹ 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.
¹⁰⁰ Office for Health Improvement & Disparities (2022).

¹⁰¹ O'Brien E., et al. (2017). U.S. Adults' Addiction and Harm Beliefs About Nicotine and Low Nicotine Cigarettes, *Preventive Medicine* 96, 94.

¹⁰² O'Brien (2017).

¹⁰³ O'Brien (2017).

¹⁰⁴ 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.

¹⁰⁵ 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),

products are less harmful than cigarettes.¹⁰⁶ In one study specifically evaluating risk perceptions of snus products, which have received a modified-risk order from FDA,¹⁰⁷ 55% of respondents reported snus to be as harmful as cigarettes with an additional 20% reporting snus to be *more* harmful than cigarettes.¹⁰⁸

While data on the potential long-term health risks associated with ENDS products are not yet established, multiple lines of evidence support that ENDS products are expected to carry far lower individual health risk than combustible cigarettes.¹⁰⁹ Thus, public-health authorities have recognized the potential for ENDS products to reduce the significant and established harms of cigarette smoking among smokers.¹¹⁰

Figure 9: Risk Perceptions of ENDS Products Relative to Combustible Cigarettes; PATH Study Waves 1-5, All Adults



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.

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.

¹⁰⁶ 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*.

¹⁰⁷ FDA (2019, Oct. 22). "FDA Grants First-Ever Modified Risk Orders to Eight Smokeless Tobacco Products, available at <u>https://bit.ly/3pbvyWR</u>.

¹⁰⁸ Wackowski O., et al. (2019). Smokers' Perceptions of Risks and Harm from Snus Relative to Cigarettes: A Latent Profile Analysis Study, *Addictive Behaviors*.

¹⁰⁹ NASEM (2018).

¹¹⁰ Office on Smoking and Health, Electronic Cigarettes (2021, July 12). *National Center for Chronic Disease Prevention and Health Promotion*. <u>https://bit.ly/3vk4tBX</u>; Gottlieb S., Zeller M. (2017). A Nicotine-Focused Framework for Public Health, *New England Journal of Medicine*.

A real and glaring hurdle to realizing the harm-reduction potential of ENDS products is the misperception of relative risk between these noncombustible alternatives and their counterpart — combustible cigarettes. For example, analysis of Wave 3 (2015–16) of the PATH Study found that 72.7% of U.S. adults perceive ENDS products to be as harmful or more harmful than cigarettes.¹¹¹ Analysis of the 2017 HINTS survey yielded similar results: (i) the proportion of adults who perceived ENDS products as less harmful than cigarettes declined from 50.7% in 2012 to 34.5% in 2017; (ii) the proportion of adults who perceived ENDS products as more harmful than cigarettes increased from 46.4% in 2012 to 55.6% in 2017; and (iii) the proportion of adults who perceived ENDS products as more harmful than cigarettes increased from 2.8% in 2012 to 9.9% in 2017.¹¹²

Worse yet, perceptions of the relative risk of ENDS products compared to combustible cigarettes have degraded over time. Multiple surveys show the proportion of respondent who believe ENDS products are as harmful or more harmful than cigarettes steadily increased.¹¹³ 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 products compared to combustible cigarettes.¹¹⁴ Based on analysis of PATH data, 43.8% of current adult smokers perceived ENDS products to be at least as harmful as cigarettes in Wave 1 (2013–2014), increasing to 68.4% in Wave 3 (2015–2016).¹¹⁵

Figure 11 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 to younger adults,¹¹⁶ suggesting that correcting misperceptions among this population may be helpful in providing a harm-reduction alternative to older adult smokers.

^{III} Malt L., et al. (2020). Perception of the Relative Harm of Electronic Cigarettes Compared to Cigarettes Amongst US Adults from 2013 to 2016: Analysis of the Population Assessment of Tobacco and Health (PATH) Study Data, *Harm Reduction Journal* 17:65.

¹¹² Huang J. et al. (2019). Changing Perceptions of Harm of E-cigarette vs Cigarette Use Among Adults in 2 US National Surveys from 2012 to 2017, *JAMA Network* 2(3):e191047.

¹¹³ 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 Ecigarettes Predicts Future Product Switching Among US Adult Cigarette and E-cigarette Dual Users, *Addiction* 114, 2197; Malt L. (2020); Huang (2019).

¹¹⁴ Malt (2020); Huang (2019).

¹¹⁵ Malt (2020); Huang (2019).

¹¹⁶ 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.



Figure 10: Perception of Equal Risk of ENDS and Combustible Cigarettes Correlates with Increased Cigarette Use

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.





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 advancing tobacco harm reduction and realizing FDA's mandate to reduce tobacco-related death and disease. By one example, FDA proposes to increase access to, and the use of, medicinal nicotine products for tobacco cessation (NRTs). 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.¹¹⁷

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 alternative and less harmful sources."¹¹⁸ 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 ecigarettes 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 2015-16.¹¹⁹

Anti-Risk-Proportionate Public Policy: Taxation

As we write above, we see two clear reasons why adult smokers are not switching to less harmful ENDS products. The first is related to misperceptions on nicotine and relative risk. The second is anti-risk-proportionate public policy.

¹¹⁷ 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.

¹¹⁸ 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 <u>https://bit.ly/3vjsE3z</u>.

¹¹⁹ Persoskie (2019).

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.¹²⁰**

In a separate, new 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.¹²¹

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."¹²²

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.)¹²³

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 approximately 2.75 million adult smokers from transitioning from combustible cigarettes in a ten-year period.¹²⁴

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*:

¹²⁰ Pesko (2020).

 ¹²¹ 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.
 ¹²² 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.

¹²³ 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.

¹²⁴ Saffer, H. et al. (2020). E-cigarettes and adult smoking: Evidence from Minnesota. *J Risk Uncertain* 60, 207–228. <u>https://doi.org/10.1007/s11166-020-09326-5.</u>

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.¹²⁵

Policymakers' goal should be to enact fiscal policy that advances tobacco harm reduction 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.¹²⁶

Anti-Risk-Proportionate Public Policy: Product Restrictions

Prohibitions and bans are blunt public-policy tools that rarely achieve their desired outcome and often have unintended consequences detrimental to public health. For instance:

- Massachusetts banned all ENDS products from September 24 through December 11, 2019, and data suggest the impact of this action led to a likely 7.5% higher-than-expected weekly cigarette sales per capita and possibly 1.7 million more packs of cigarettes sold but for the ENDS ban.¹²⁷ On June 1, 2020, Massachusetts banned all flavored tobacco products including all non-tobacco flavors for ENDS and menthol cigarettes which researchers found led to a 58.6% relative increase in cigarette smoking by Black females.¹²⁸
- Rhode Island banned flavored ENDS products for four months beginning October 4, 2019, which led to a likely 5% higher-than-expected weekly cigarette sales per capita and possibly 281,000 more packs of cigarettes sold after the ENDS ban.¹²⁹

¹²⁷ Xu Y. et al. (2022). "The Impact of Banning Electronic Nicotine Delivery Systems on Combustible Cigarette Sales: Evidence From US State-Level Policies." *Value in Healt*h. https://doi.org/10.1016/j.jval.2021.12.006.
 ¹²⁸ Asare S, Majmundar A, Xue Z, et al. (2013). Association of Comprehensive Menthol Flavor Ban With Current Cigarette Smoking in Massachusetts From 2017 to 2021. *JAMA Intern Med.* Published online February 27, 2023. doi:10.1001/jamainternmed.2022.6743.

 ¹²⁵ 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.
 ¹²⁶ Warner K. (2021). "Build Back Better's e-cigarette tax will make people smoke more," *The Washington Post*, November 22, 2021.

¹²⁹ Xu (2022).

- Washington (state) banned flavored ENDS products for 120 days and estimates suggest that this led to a likely 5% higher-than-expected weekly cigarette sales per capita and possibly 1 million more packs of cigarettes sold but for the ENDS ban.¹³⁰
- San Francisco's ban on flavored tobacco sales was associated with increased cigarette smoking among high school students relative to other school districts.¹³¹

Like taxation, heavily restricting less harmful products relative to combustible cigarettes not only defies the science but also has unintended and negative consequences for public health. As shown above, states that have implemented product restrictions (such as bans) for ENDS products have resulted in increases in cigarettes sales and smoking. Such policies run counter to science, evidence, and public-health objectives and have real-world effects that set back tobacco-control efforts.

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 adult smokers 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 that advances harm reduction principles 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.

¹³⁰ Xu (2022).

¹³¹ Friedman A.S. (2021/2022). A Difference-in-Differences Analysis of Youth Smoking and a Ban on Sales of Flavored Tobacco Products in San Francisco, California. *JAMA Pediatr.* 2021 Aug 1;175(8):863-865. doi: 10.1001/jamapediatrics.2021.0922. Erratum in: *JAMA* Pediatr. 2022 Sep 1;176(9):948. PMID: 34028507; PMCID: PMC8145156.