

Report



How non-combustible nicotine alternatives can accelerate tobacco control and harm reduction, to save millions of adult smokers' lives.

Report by International and Local Tobacco Harm Reduction (THR) Experts

2024

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Executive Summary

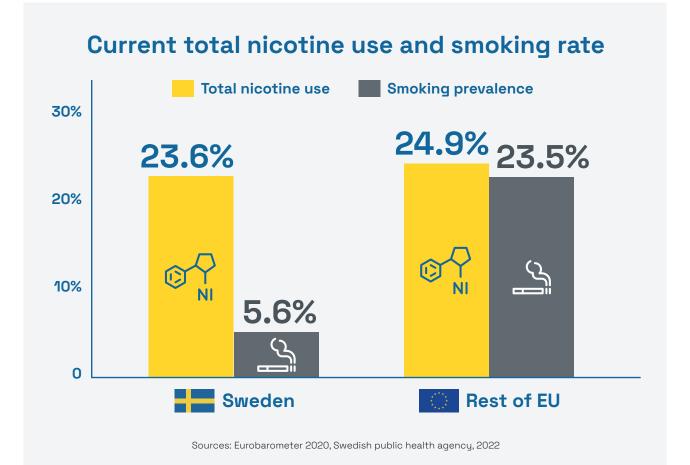
In Sweden, almost one in four adults use nicotine daily. That is the same level of nicotine consumption as is found across Europe. Yet Sweden's incidence of cancer is 41% lower than the European average and it suffers less than half of the tobacco-related deaths experienced by 24 of its 26 EU neighbours.

What is the reason for this remarkable disparity, and what can the rest of Europe, and the world, learn from this Scandinavian success story?

Well, quite simply, Swedes have learned to consume their nicotine in a different – and much safer manner.

Sixty years ago, 49% of Swedish men smoked cigarettes. By 2022, Sweden's public health agency reported that only 5.6% of Swedish adults continue to do so. Swedes have switched their preference to alternative, smokeless products – such as snus, vapes, oral nicotine pouches and heat-not-burn devices – and they have thereby spawned a smoke free generation.

By enabling this transition to safer alternatives, Sweden has virtually eradicated combustible, deadly cigarettes. Although the smoke free generation uses nicotine at much the same rate as other high-consuming nations, they incur a fraction of the tobacco-related disease and the burden on public health is minimal.



This report investigates this startling divergence to emphasise these important truths:

- Despite widespread misperceptions, nicotine does not cause cancer and has minimal, if any, contribution to tobacco-related disease
- There will always be people who wish to consume nicotine, like those who consume caffeine
- Total nicotine use in Sweden is equivalent to other EU countries, but because smoke free nicotine products are allowed, this country has significantly less tobacco-related disease and premature deaths
- Enabling consumers to use nicotine in less risky ways will save millions of lives

Worldwide, even after decades of tobacco control measures, 1.1 billion people still smoke. While consumption has been on a downward trend, this has been at far too slow a rate. To this day, every year nearly 8 million people die globally due to tobacco-related (largely combustion-related) diseases. This highlights a huge opportunity for public health, in terms of the numbers of lives that could be saved if smokers switched to less risky products.

Sweden has already seized this opportunity. Its successful reduction in smoking rates over the years has been facilitated by education, tobacco control measures, and the adoption of safer, smokeless alternatives.

Sweden's early progress was assisted by the traditional use of snus – a smoke free oral tobacco product. The introduction of modern tobacco-free alternatives, such as vaping in 2015 and next-generation oral nicotine pouches in 2018, significantly accelerated this progress. Consequently, smoking rates

in Sweden have plummeted by an impressive 55% over the last decade.

When that smoking rate falls below 5% later this year, Sweden will become the first developed nation to achieve official 'smoke free' status.

The public health benefits of Sweden's strategy are profound. Compared to the rest of the European Union, Sweden boasts 44% fewer tobacco-related deaths, a 41% lower cancer rate, and 38% fewer deaths attributable to any cancer.

Comparisons on 'male-only' data in 2020 show even more pronounced differences. Sweden had 52% fewer tobacco-related male deaths than Poland and 57% fewer than Romania. For male lung cancer, Sweden had 55% fewer deaths than France and Germany, 57% fewer than Italy and 69% fewer than Poland.

Sweden is the manifestation of 'No Smoke, Less Harm' and a beacon of inspiration for all nations seeking to reduce the deadly toll of cigarettes.

Although nicotine may be dependence-forming, it does not cause cancer. Studies have long established this fact. Tragically, significant myths about nicotine persist among physicians and the public alike. The misperception of nicotine's harms among healthcare professionals is unacceptable and not in the best interest of their patients.

If health professionals don't understand nicotine, how can we expect the public to know that nicotine does not cause disease? Consider, for example, that in the UK, 40% of the public believes that nicotine causes smoking-related cancers, despite the NHS's own public health advice stating, "Nicotine itself does not cause cancer, lung disease, heart disease or stroke and has been used safely for many years in medicines to help people stop smoking."



The NHS concludes: "Although nicotine is addictive, it is relatively harmless to health."

While caffeine and nicotine are both dependence-forming, caffeine is widely accepted despite its effects as it is perceived to be relatively harmless. This report suggests comparing their dependence levels to create riskbased regulations for both. This report also serves as a call to the World Health Organization (WHO) and global public health communities to recognise that it is products of combustion that cause harm to smokers, and not nicotine itself. There are, in fact, significantly less risky forms of nicotine that can be consumed without causing premature death. This report will shed light on nicotine's low-risk profile when consumed in smoke free products.

It urges policymakers to:

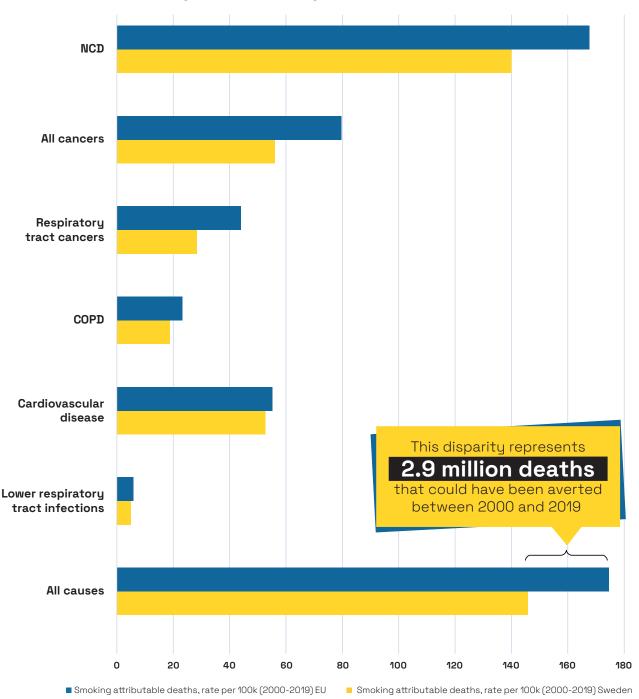
- Recognize the potential of Tobacco Harm Reduction (THR) in reducing harm
- Implement THR provisions within existing tobacco control frameworks
- Regulate nicotine products based on their relative risk profile
- Encourage healthcare professionals to embrace THR as a harm reduction strategy
- Empower THR users to advocate for supportive policies

THE REPORT DEMANDS SEVERAL ACTIONS:

- There should be increased THR awareness and adoption. The "No Smoke, Less Harm" principle should be employed by fundamentally differentiating between smoked and smoke free products.
- WHO should formally add the 4th pillar of THR to tobacco control policy.
- Member states should adopt a risk-proportionate regulatory framework for all nicotine products, based on the risk continuum.
- Nicotine disinformation should be actively eliminated.
- All stakeholders should be building THR evidence through research.
- The ethical framework of THR should be recognised and the consumer's fundamental human right to health respected.
- WHO and member states should step up monitoring and evaluation of THR.

Source: IHME GBD.

Smoking-Attributable Death Rates by Cause: Sweden vs EU (2000-2019)





Introduction

Smoke kills, not the nicotine. Where there is No Smoke, there is Less Harm.

Smoking is one of the most harmful addictions, with more than 8 million premature deaths being recorded annually from smoking-related diseases, according to the WHO. While nicotine is the main substance linked to dependence, harm is predominantly caused by combustion products or other harmful compounds present in cured tobacco. Due to the difficulty in quitting smoking and the relatively low effectiveness of smoking cessation medications, the concept of tobacco harm reduction, a strategy of providing a cleaner form of nicotine, has come to the fore as a potential lifesaver for adult smokers, who cannot or will not quit smoking.

1. Historical Perspective: Limits of Tobacco Control

Since the 1960s, when the first reports from the Royal College of Physicians in the UK1 and the Surgeon General in the United States were released,² it has been well established that smoking is a major preventable risk factor for a variety of diseases and an addictive habit responsible for substantial morbidity and mortality. The World Health Organization reports that 22.7% of the global population above the age of 15 were smokers in 2015, which translates to approximately 1.1 billion people.³ Even more worryingly, 1 billion people are expected to die prematurely from smoking-related diseases during the 21st century. In the United States, it has been estimated that approximately 480,000 people die annually from smoking-related diseases, while the respective death toll in Europe is estimated at 700,000.4,5

This substantial health, economic and social burden of smoking has resulted in intense efforts to regulate tobacco cigarettes, with the main purpose being to minimise addictiveness, appeal and use by the population. A landmark, global, coordinated effort was the Framework Convention on Tobacco Control (FCTC), established in 2005 and comprising 168 signatory countries.⁶ The goal and responsibility of the FCTC was to provide proper guidance and a strategic plan for policies that could be implemented globally. In that context, the MPOWER was created in 2008, with the core principles being to develop policies to prevent smoking initiation and promote smoking cessation, educate people about the risks of smoking, ban marketing and advertising of tobacco products, and raise taxes as a measure to discourage use.⁷ While these efforts were key in reducing prevalence, smoking remains a prevailing public health issue.

^{1.} Royal College of Physicians. <u>Smoking and health. A report of the Royal College of Physicians on smoking in relation to cancer of the lung and other diseases</u>, 1962

^{2.} United States Surgeon General's Advisory Committee on Smoking and Health. <u>Smoking and Health: Report of the Advisory Committee to the</u> <u>Surgeon General of the Public Health Service</u>, 1964

^{3.} World Health Organization Global Health Observatory (GHO) data. Prevalence of tobacco smoking.

^{4.} U.S. Department of Health and Human Services. The Health Consequences of Smoking-50 Years of Progress, 2014

^{5.} European Commission Eurobarometer 429. Attitudes of Europeans towards tobacco and electronic cigarettes, 2014

^{6.} WHO. Framework Convention on Tobacco Control, 2003

^{7.} World Health Organization. MPOWER: Six policies to reverse the tobacco epidemic

The Tobacco Endgame

Eradicating a Worsening Epidemic

MPOWER provides a roadmap for the Tobacco Endgame



policies

Report

<mark>o Smoke</mark> ess Harm



people from

Offering help to quit tobacco use tobacco smoke



tobacco



Enforcing

advertising,

promotion and sponsorship

bans on

tobacco



Raising taxes on tobacco for effective tobacco control

Figure 1: The WHO uses the acronym MPOWER to describe their tobacco control method, working towards the "Tobacco Endgame".⁶

Tobacco Harm Reduction (THR) 2.

Harm reduction initially referred to policies, programs and practices that aim to attenuate negative health, social and legal impacts related to drug use, drug policies and drug laws.⁹

Harm reduction is fundamentally based on justice and human rights, focusing on positive change and on working with people without judgement, coercion, discrimination, or requiring that they stop using drugs as a precondition of support. Some characteristic interventions are the needle and syringe exchange programs and opioid substitution therapy for intravenous drug users. Such measures have been actively endorsed by authorities such as the World Health Organization and the Red Cross and several countries through national legislation.^{10, 11}

These measures are known to reduce the risk of blood-borne infectious diseases such as hepatitis and HIV, are cost-effective and result in improved quality of life.^{12, 13, 14} However, the harm reduction concept has a much wider perspective and is applicable even in common daily activities. The use of helmets and seatbelts is a typical case of a harm reduction approach since it does not eliminate the risk of injury or death in an accident, but it reduces the risk.

Even medicine could be considered as a harm reduction science since, except for some infections which can be cured, most diseases are only treated but not cured. This means that therapeutic measures are applied to reduce symptoms, reduce the consequenc-

^{8.} WHO Report on the global tobacco epidemic. MPOWER, 2023

^{9.} Harm Reduction International. What is harm reduction?

^{10.} World Health Organization, United Nations Office on Drugs and Crime, Joint United Nations Program on HIV/AIDS.HO, UNODC, UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment, and care for injecting drug users: 2012 revision. Harm Reduction International. Global state of harm reduction, 2014

^{12.} Marshall BDL, Wood E. Toward a comprehensive approach to HIV prevention for people who use drugs, 2010.

Beyrer C, Malinowska-Sempruch K, Kamarulzaman A, Kazatchkine M, Sidibe M, Strathdee SA. Time to act: a call for comprehensive responses 13. to HIV in people who use drugs, 2010.

^{14.} Wilson DP, Donald B, Shattock AJ, Wilson D, Fraser-Hurt N. The cost-effectiveness of harm reduction. Int J Drug Policy, 2015



es, reduce the decline in quality of life, and reduce the inability to deal with diseases.

Similarly to the generalised concept of harm reduction, tobacco harm reduction refers to the reduction of harm associated with the use of combustible tobacco products. It was initially conceived by the British scientist Prof. Michael A.H. Russell, who mentioned in 1976 that "smokers smoke for nicotine but die from tar".¹⁵This statement is closely linked to the distinction between the dependence potential of smoking, in which nicotine plays an important role, and the harm caused by smoking, which is mainly caused by combustion products and other toxins present in cured tobacco leaves.

The need for tobacco harm reduction is linked to the difficulty in quitting smoking and the limited effectiveness and appeal of smoking cessation interventions. Such medications have been available for many years. While all available medications are relatively safe and effective compared to placebo^{16,17,18,19,20} their long-term success rate is limited. A systematic review and meta-analysis of the effectiveness of nicotine replacement therapies found that < 7% of smokers remained abstinent for one year.²¹ Cohort studies of real-world use of these medications available over the counter raise further doubts about their effectiveness compared to quit attempts without the use of any aid.²² Pharmaceutical nicotine products characteristically deliver nicotine much slower compared to tobacco cigarettes. At the same time, they do not address the psycho-behavioural aspect of smoking dependence.^{23,24,25,26} Although better than pharmaceutical nicotine, oral smoking cessation medications still have a relatively low success rate.²⁶ In real-world clinical use, their effectiveness may be even lower.²⁷

Added to the above, a substantial proportion of smokers are not willing to use medications or professional assistance for smoking cessation. As a result, quitting without any aid remains a popular but ineffective smoking cessation method.^{28,29} Therefore, most smokers are unwilling or unable to quit smoking with currently approved methods, while others want to continue experiencing the "positive" effects of smoking (in terms of the behavioural experience and nicotine intake) and are unlikely to use medications that do not provide the "pleasure" perceived from smoking.³⁰

This led to suggestions that a tobacco harm reduction strategy be applied using smokeless tobacco products.^{31,32} A characteristic example of such products is Sweden, where there is a high prevalence of snus use among

^{15.} Russell MA. Low-tar medium-nicotine cigarettes: a new approach to safer smoking, 1976

^{16.} Stead LF, Perera R, Bullen C, et al. <u>Nicotine replacement therapy for smoking cessation</u>, 2012

^{17.} Eisenberg MJ, Filion KB, Yavin D, et al. Pharmacotherapies for smoking cessation: a meta-analysis of randomised controlled trials, 2008

Cahill K, Stevens S, Perera R, Lancaster T. <u>Pharmacological interventions for smoking cessation: an overview and network meta-analysis</u>, 2013
 Wu P, Wilson K, Dimoulas P, Mills EJ. <u>Effectiveness of smoking cessation therapies: a systematic review and meta-analysis</u>, 2006

^{20.} Suissa K, Larivière J, Eisenberg MJ, Eberg M, Gore GC, Grad R, Joseph L, Reynier PM, Filion KB. <u>Efficacy and Safety of Smoking Cessation Inter-</u> ventions in Patients With Cardiovascular Disease: A Network Meta-Analysis of Randomised Controlled Trials, 2017

^{21.} Moore D, Aveyard P, Connock M, Wang D, Fry-Smith A, Barton P. <u>Effectiveness and safety of nicotine replacement therapy assisted reduction</u> to stop smoking: systematic review and meta-analysis, 2009

^{22.} Kotz D, Brown J, West R. 'Real-world' effectiveness of smoking cessation treatments: a population study, 2014

Benowitz NL. <u>Pharmacology of nicotine: addiction, smoking-induced disease, and therapeutics</u>, 2009
 Caggiula AR, Donny EC, Chaudhri N, Perkins KA, Evans-Martin FF, Sved AF. <u>Importance of nonpharmacological factors in nicotine self-administration</u>, 2002

^{25.} Bevins RA, Palmatier MI. Extending the role of associative learning processes in nicotine addiction, 2004.

^{26.} Rigotti NA, Pipe AL, Benowitz NL, Arteaga C, Garza D, Tonstad S. Efficacy and safety of varenicline for smoking cessation in patients with cardiovascular disease: A randomised trial, 2010

^{27.} Casella G, Caponnetto P, Polosa R. Therapeutic advances in the treatment of nicotine addiction : present and future, 2010

^{28.} Farsalinos KE, Poulas K, Voudris V, Le Houezec J. <u>Electronic cigarette use in the European Union: analysis of a representative sample of 27 460</u> Europeans from 28 countries, 2016

^{29.} Edwards SA, Bondy SJ, Callaghan RC, Mann RE. <u>Prevalence of unassisted quit attempts in population-based studies: a systematic review of the literature</u>, 2014

^{30.} Farsalinos KE, Stimson GV. Is there any legal and scientific basis for classifying electronic cigarettes as medications?, 2014.

^{31.} Russell MAH, Jarvis MJ, Feyerabend C. <u>A new age for snuff?</u> 1980

^{32.} Kirkland LR. The nonsmoking uses of tobacco, 1980

men.^{33,34} While tobacco use among Swedish men has not been eliminated, most men use snus instead of smoking tobacco cigarettes. Still, the death rates from cardiovascular disease, lung cancer and any type of cancer in Swedish men is the lowest in the European Union.³⁵ This example of best practice in "No Smoke, Less Harm, will be covered in Chapter 1.

However, despite the overall acceptability of the harm reduction principles for daily activities or for intravenous drug users, tobacco harm reduction remains a controversy within the public health community.^{36,37,38,39}

3. Why is THR controversial?

Unfortunately, harm reduction has also evoked many emotional debates and some controversy.³⁹ There will always be people who engage in risky behaviours, no matter what the consequences might be to themselves or others. Those who support the principles of harm reduction seek to reduce or mitigate the health risks associated with these risky behaviours, rather than eliminate them.

There are two sides to the debate. Nearly everyone in the public health community still advocates abstinence as the only defendable goal. Here, the underlying philosophy is that we should all work for a drug-free or tobacco-free world. In their recent study, Alderman, Dollar, and Kozlowski noted that public health ethics tend to emphasise social justice concerns to the exclusion of other moral perspectives that value scientific authority, professional loyalty, and bodily purity.⁴⁰Their views emphasise the need for greater awareness of the different emotional reactions and underlying moral motivations in the harm reduction debate. However, the number of those who support the concept of harm reduction is growing. The pragmatists usually embrace the concept first, as they come to appreciate that for some people, abstinence is an unrealistic qoal. Some individuals will always engage in risky behaviour such as smoking or using drugs, so it is preferable to try to mitigate the consequences for them and others affected by that behaviour. One of the first principles of medical ethics coined by Hippocrates is "first, do no harm". While many would say the Greek physician's meaning was not: "first, do less harm", there is clearly a moral imperative to act to reduce harm if that is the only option available. Inaction justified by an unrealistic goal of eliminating harm may, in fact, result in continuous harm. Such inaction constitutes harm. This is, after all, the principle of pain reduction in the terminally ill, where physicians use medication to alleviate suffering even when the condition is incurable. No one would suggest withholding treatment simply because a condition is untreatable.

39. Harm Reduction International. What is harm reduction?

^{33.} Wikipedia. Snus

^{34.} Lee PN, Epidemiological evidence relating snus to health-an updated review based on recent publications. 2013

^{35.} Ramström L, Wikmans T. <u>Mortality attributable to tobacco among men in Sweden and other European countries: an analysis of data in a WHO report</u>, 2014

^{36.} Gray NJ, Henningfield JE. <u>A long-term view of harm reduction</u>, 2004

^{37.} Sumner W 2nd. Permissive nicotine regulation as a complement to traditional tobacco control, 2005

^{38.} Bates C, Fagerström K, Jarvis MJ, Kunze M, McNeill A, Ramström L. <u>European Union policy on smokeless tobacco: a statement in favour of evidence based regulation for public health</u>, 2003

^{40.} Alderman J, Dollar KM, Kozlowski LT. <u>Understanding of anger, contempt, and disgust in public health policy disputes: Applying moral psychology to harm reduction debates</u>, 2010



4. Individual versus Community Interests in Harm Reduction

Harm reduction highlights the frequent conflict between societal and individual interests in public health and medical practice. Harm reduction itself can be achieved at the individual and the societal level. For example, health professionals advising a patient to substitute smoking cigarettes with using a less toxic substance such as snus may result in a net decrease of harm in that patient. However, this may not necessarily achieve a net increase in benefit to society. If there is a significant reduction in risk, however, there is likely to be a public health benefit despite a large increase in use. In this regard, Kozlowski, and colleagues argue that: "Public health concerns should trump individual rights only when there is clear and convincing evidence of harm to society. Lacking that evidence, individual rights should prevail."41

Harm reduction highlights the frequent conflict between societal and individual interests in medical practice. Harm reduction itself can be achieved at the individual and the societal level.

5. The Evolution of THR

Against the background of competing forces, it is interesting to study the evolution of tobacco control and harm reduction:

- **From 1960-2010**, the focus was mainly on "traditional" tobacco control, targeting the supply of tobacco products to consumers and mitigating the significant marketing power of tobacco manufacturers.
- The era **from 2000-2030** has seen the emergence of non-combustible nicotine alternatives on the global market, where consumers themselves have driven the growth and use of these products, mainly to help mitigate the harms caused by smoking. This demand-based trend has been hampered by slow or no risk-proportionate regulation in most countries, except for countries such as the United Kingdom, New Zealand, Sweden, and Canada. Currently, there are up to 130 million consumers of smoke free alternatives worldwide and this is growing.⁴²
- An exciting era awaits, probably between **2020 and 2040**, where we are expecting a fundamental re-evaluation of nicotine. Preferably based on solid science, society will have the opportunity to consider the acceptance (or not) of nicotine as a socially acceptable stimulant, much like coffee (the active molecule being caffeine).

1960-2010 Tobacco control

How do we stop tobacco use and fight Big Tobacco?

2000-2030 Tobacco harm reduction

How do we reduce harms caused by smoking?

Rethinking nicotine

Can nicotine be accepted and regulated as a socially acceptable stimulant?

Figure 2: The Epochs of Tobacco and Nicotine Control

^{41.} Kozlowski LT, O'Connor RJ, Edwards BQ. <u>Some practical points on harm reduction: What to tell your lawmaker and what to tell your brother</u> about Swedish snus, 2003.

^{42.} Global State of Tobacco Harm Reduction. <u>The Right Side of History</u>, 2022.

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6. Key Benefits of THR

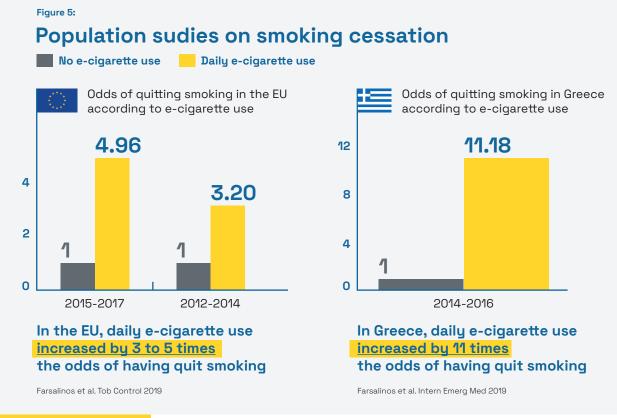
Individual benefits:

Adult smokers can use THR for smoking cessation through substitution. The benefits for individuals who smoke are that THR reduces death and disease caused by toxicants in tobacco smoke. For those who don't smoke, THR prevents second-hand smoke and avoids smoking role models, which are a powerful influence on young people.



Figure 4: THR as an effective smoking cessation approach





Societal benefits:

THR can benefit society in several ways:

- Reducing tobacco-related disease, disability, and premature death.
- Reducing loss of productivity and poverty due to smoking.
- Reducing health costs.
- Reducing the human cost of adverse effects; and
- Reducing fires through careless actions by smokers.^{43,44,45}

7. Lives Saved by THR

The overarching message of this report is "No Smoke, Less Harm". This report argues that current global approaches to tobacco control have failed to halt the devastating toll of tobacco-related deaths, with the World Health Organization (WHO) estimating 8 million annual tobacco-related deaths. This figure is projected to increase to 10 million, before eventually declining.

Recent modelling efforts have demonstrated the potential health gains from the adoption of THR products, including e-cigarettes, oral nicotine pouches, snus, and heated tobacco

^{43.} American Association of Public Health Physicians. <u>AAPHP resolution and white paper: The case for harm reduction for control of tobacco-re-</u> lated illness and death, 2008.

^{44.} Royal College of Physicians. <u>Harm reduction in nicotine addiction: Helping people who can't quit</u>, 2007.

^{45.} Stratton K, Shetty P, Wallace R, Bondurant S, editors. Clearing the smoke: Assessing the science base for tobacco harm reduction - executive summary, 2001

products.⁴⁶ In 2018, Levy et al. used a simulation modelling process to demonstrate the potential deaths averted in the USA by replacing cigarettes with e-cigarettes.⁴⁷ They acknowledge that the tobacco control community has been divided regarding the role of e-cigarettes in tobacco control.⁴⁸ However, according to their projections, a strategy of replacing cigarette smoking with vaping would yield substantial life-year gains, even under pessimistic assumptions regarding cessation, initiation, and relative harm.

Derek Yach and a panel of international authors calculated the potential lives to be saved in selected lower- and middle-income countries. The study's key findings indicate that many lives can be saved in these countries through the widespread adoption of THR and related measures. For instance, Kazakhstan could prevent 165,000 premature deaths in the next four decades, while South Africa, Bangladesh and Pakistan could save 320,000, 920,000, and 1,200,000 lives, respectively.⁴⁹

A similar report "Saving Lives like Sweden" used a retrospective modelling method to calculate how much more effective tobacco control in selected EU countries would have been if they had adopted a similar strategy as Sweden. This country facilitated the increased access for consumers to reduced – risk smoke free products, in a way that was acceptable and affordable.⁵⁰ The report found that potentially 2,9 million tobacco-related deaths could have been averted in the European Union, during the years 2000-2019 had the EU employed the Swedish approach to tobacco control.

8. Call for Action through "No Smoke, Less Harm"

This report demands the recognition of less harm by cutting out combustion-generated smoke. Member States at COP10 should have activated the harm reduction provisions of the WHO Framework Convention on Tobacco Control (FCTC).^{51,52} A former Director at WHO, Dr Derek Yach⁵³, states that: **"The expected deaths associated with tobacco use could be dramatically reduced by hundreds of millions between now and 2060 through measures that improve cessation and harm reduction support among adults". The WHO needs to be held accountable for supporting** policy positions that undermine population health. Governments need to regulate nicotine products proportionately to the risk they pose to health. Physician leadership is needed to better understand nicotine, to better support their patients and policymakers about the benefits of THR. THR users need to galvanise into a powerful movement that advocates for pro-THR policies. If these key steps are implemented, a scenario of "No Smoke, Less Harm" would be possible. It will save lives.

^{46.} Abrams DB. Promise and peril of e-cigarettes: Can disruptive technology make cigarettes obsolete?, 2014.

^{47.} Levy DT, Borland R, Lindblom EN, Goniewicz ML, Meza R, Holford TR et al. <u>Potential deaths averted in USA by replacing cigarettes with e-cigarettes</u>, 2017

^{48.} Maziak W. Potentials and pitfalls of e-cigarettes – reply, 2014

^{49.} Yach D, et al. Lives Saved, 2023.

^{50.} Smoke Free Sweden. <u>Saving Lives Like Sweden</u>, 2023

^{51.} Letter to Dr Margaret Chan, Director General WHO. <u>Reducing the toll of death and disease from tobacco – tobacco harm reduction and the</u> <u>Framework Convention on Tobacco Control</u>. 2014

^{52.} US Department of Health and Human Services. <u>The health consequences of smoking - 50 years of progress: A report of the surgeon general</u>, 2014

^{53.} Yach D. Accelerating an end to smoking: a call to action on the eve of the FCTC's COP9. <u>https://www.emerald.com/insight/content/doi/10.1108/</u> DAT-02-2020-0012/full/html



Chapter 1: No Smoke Less Harm

1.1. Sweden is on the cusp of becoming smoke free

Tobacco remains a leading cause of preventable death worldwide. In the past two decades, there has been a concerted effort to reduce smoking levels globally, notably through the World Health Organisation's (WHO) Framework Convention on Tobacco Control (FCTC) which started in 2003^{54} . The FCTC has resulted in the introduction of a range of tobacco control measures, with interventions ranging from price increases for cigarettes, indoor smoking bans and the introduction of plain packaging legislation.

Two decades on, there has been a decrease in levels of tobacco consumption across the globe. However, as we will explore in more detail later, this reduction is not necessarily due to the measures that have been recommended by the FCTC. Particularly in Europe, smoking rates remain stubbornly high, averaging 23,9% in 2020⁵⁵. That same year, the WHO, during its seventh Conference of the Parties (COP), committed to reducing the prevalence of tobacco use by 30% by 2025⁵⁶, a target that is set to be missed by some margin.

Sweden stands out as an outlier in this European trend of high smoking rates. With an official smoking rate of 5.6% in 2022^{57} The Scandinavian country is soon set to become the first European country to meet the WHO's official threshold of 'smoke free', meaning less than 5% of the adult population smoke tobacco. Thus, Sweden is likely to not only achieve the bloc's 2040 smoke free target but meet it a staggering 16 years early.

Sweden has seen an 80% reduction in the overall number of smokers since 1963, when records first became available, despite a 30% population increase over the same period. In 1963, <u>36%</u> of adults smoked, including around half (<u>49%</u>) of men⁵⁸.

1.2. The Swedish context: a long history of openness to alternatives

The key to Sweden's success, as we wrote in The Swedish Experience: The Road Map to a Smoke Free Society last year, is its long history of being open to safer alternatives and innovation. This first started with snus, a traditional oral tobacco product that has been used in Sweden for centuries. Unlike cigarettes, snus is a non-combustible form of tobacco that users place between the lips and gum. Snus is particularly popular amongst Swedish men, with official data from Statistics Sweden showing that since 1980 snus use amongst Swedish men has grown as smoking rates have simultaneously declined⁵⁹.

However, in the last 15 years, the introduction of new smoke free alternative products such as vapes in 2015 or oral nicotine pouches in 2018 has allowed the country's smoke free journey to gain new momentum.

^{54.} World Health Organization, Framework convention on tobacco control, 2003

^{55.} Eurobarometer 2020. https://europa.eu/eurobarometer/surveys/detail/2240

^{56.} World Health Organization, Global Strategy to Accelerate Tobacco Control: Advancing Sustainable Development through the Implementation of the WHO FCTC 2019–2025

^{57.} The Public Health Agency of Sweden, Use of tobacco and nicotine products (self-reported) by age, gender and year, 2022.

^{58.} The Public Health Agency of Sweden, Use of tobacco and nicotine products (self-reported) by age, gender and year, 2022.

^{59.} The Public Health Agency of Sweden, Use of tobacco and nicotine products (self-reported) by age, gender and year, 2022.

As these products have become more readily available, Sweden's smoking rate has tumbled further from 15% in 2008 to 5.6% today⁶⁰.

Figure 6: Transition from smoking to snus in Sweden

Tobacco use changes among men in Sweden				
Age	Prevalence	e of <mark>Daily smoking</mark>	Prevalence	e of <mark>Daily snus use</mark>
group:	1988/89	2004/05	1988/89	2004/05
35-44	33%	13%	19%	31%
45-54	32%	21%	11%	24%
55-64	28%	21%	9%	18%

Similar overall tobacco and nicotine use in men in Sweden compared to the rest of the EU. But most are using snus and very few smoke tobacco cigarettes

Ramstrom & Wikmans, Tob Induc dis 2014

Between 2006 and 2020, Sweden saw the steepest drop in smoking rates compared to any other EU country, by a staggering $60\%^{61}$. This is more than twice as large as the 25% reduction in other EU member states during this same period⁶².

The increasing use of safer alternative products as a path to quitting cigarettes has also helped close the gender gap in smoking. Until recently, Swedish women smoked in much higher numbers than men. Smoking rates for women have declined by 6.1% in the past decade whilst at the same time their use of snus and nicotine pouches has risen by 3.5%⁶³.

Sweden is a case study of tobacco harm reduction in practice. Alternative nicotine products are widely used throughout the country, meaning Swedes consume similar amounts of nicotine per capita to their European counterparts. Yet, the country has the lowest level of tobacco related diseases in Europe.

1.3. Sweden's pragmatic approach to reducing smoking rates: using all available tools.

Like many other developed countries, Sweden has enacted several stringent tobacco control measures introduced as part of a global public health push against smoking spearheaded by the WHO FCTC. These measures include setting high excise taxes on tobacco products, mandating the use of plain packaging, banning the advertisement of tobacco products, as

^{60.} The Public Health Agency of Sweden, Use of tobacco and nicotine products (self-reported) by age, gender and year, 2022.

^{61.} The Public Health Agency of Sweden, Use of tobacco and nicotine products (self-reported) by age, gender and year, 2022.

^{62.} European Commission, <u>Special Eurobarometer 506</u>, 2021.

^{63.} The Public Health Agency of Sweden, Use of tobacco and nicotine products (self-reported) by age, gender and year, 2022.



well as running public health campaigns that seek to improve education about the harms of smoking and ways to guit.

Yet, many other countries, and most of Sweden's European counterparts have implemented all the above measures and have not even come close to achieving the same results. What has Sweden done differently that made all the difference?

The answer lies in the country's pragmatic approach to regulating alternative products and their openness to using them to help smokers quit. This has resulted in a growing number of Swedes turning away from cigarettes and instead using smoke free alternatives, ultimately quitting smoking.

This sort of openness to alternatives is in some part cultural and historic – indeed, the country has a long history of using snus, and receiving an exemption from an EU-wide ban was a condition of its accession to the bloc

Figure 6: Swedish Prime Minister comments on snus*



but anything we can do to reduce cigarette consumption is a good thing.

Ulf Kristersson Swedish Prime Minister

in 1995⁶⁴. Swedish public health authorities and policymakers have had numerous opportunities over the years to heavily restrict these alternative products, as has been done in several other countries, but have chosen not to do so with good reason.

Instead, successive Swedish governments have proactively embraced harm reduction in a way that complements other tobacco control and educational initiatives. For example, Sweden differentiates between traditional cigarettes and alternative forms of tobacco and nicotine through taxation, which reflects the relative risk of each product. The country also permits advertising and communication about less harmful alternatives whilst restricting it to cigarettes.

Though originally a consumer-led revolution, this approach and recognition at the highest levels of government have endured and increased.

In 2023, announcing plans to raise cigarette taxes by 9% and at the same time cut the tax on snus by 20%, Swedish Prime Minister Ulf Kristersson commented that "anything we can do to reduce and avoid smoking is good"65. On several occasions, Swedish MPs have voted to officiallu recognise tobacco harm reduction. with Minister for Public Health Jakob Forssmed commenting that "in relation to snus, cigarettes and smoking tobacco represent a relatively greater health hazard"66.

64. European Commission, <u>REPORT FROM THE COMMISSION TO THE COUNCIL on the implementation by the Kingdom of Sweden of the measures</u> necessary to ensure that oral tobacco is not placed on the market in other Member States /* COM/2010/0399 final, 2010.

65. Ulf Kristersson, <u>Instagram post</u>, 6 September 2023.

66. Riksdagen. Answer to written question 2023/24:595, 2024.

1.4. Key insight: The way nicotine is consumed can save lives.

The Swedish smoking rates are indisputable proof of what Sweden has achieved. But what is remarkable is the fact that while smoking rates have dropped significantly (and together with their mortality, cancer rates, and other negative health outcomes), total nicotine consumption levels have remained largely unaffected. This negative correlation cements the proof that nicotine is not the problem but that the way in which nicotine is delivered matters enormously.

In contrast, other European countries such as Germany have smoking incidences almost five times as high as Sweden's (at $23.8\%^{67}$ in 2022), with the bulk of nicotine consumption driven by cigarette smoking. This has precipitated vastly different health outcomes.

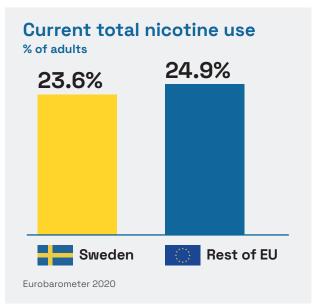


Figure 8: Total Nicotine Use in Sweden

1.5. Lessons for the rest of the world: No Smoke equals Less Harm

With tobacco prematurely killing nearly half of its users according to the WHO⁶⁸, the Swedish people have reaped the benefits of the country's smoking prevalence falling to record lows as it lies on the brink of eliminating the habit completely.

Worldwide, even after decades of tobacco control measures, 1.1 billion people still smoke⁶⁹ and while consumption has been on a downward trend, this has been at far too slow a rate. To this day, every year, nearly 8 million people die worldwide due to tobacco-related diseases⁷⁰.

Sweden's success in reducing smoking has led to the lowest tobacco-related death rate in Europe, 39.6% lower than the EU average⁷¹.

Meanwhile, its incidence of cancer is 41% lower than its European counterparts⁷² including the lowest lung cancer incidence in Europe at only 17.7 per 100,000 across both sexes⁷³.

Out of the other 26 EU Member States, 24 have a tobacco-related mortality rate at least twice as high as Sweden⁷⁴.

The EU has set the objective to achieve a smoke free society by 2040, a target that most of its member states are set to miss by some margin without urgent action.

Sweden offers an example in practice of how tobacco control measures can be successfully combined with harm reduction policies to help eliminate smoking and, with it, reduce mortality from smoking-related diseases and save millions of lives.

^{67.} German Federal Ministry for Health, <u>Smoking</u>, 2022.

^{68.} World Health Organisation, <u>Tobacco</u>

^{69.} The Lancet, The global burden of tobacco, 2021.

^{70.} World Health Organisation, <u>Tobacco</u>

^{71.} Data extracted from <u>Global Burden of Disease Database</u>, 2019.

^{72.} Ramström, L. "Institute for Tobacco Studies. Death rates per 100,000 attributable to tobacco – Sweden and the rest of the EU in 2019. Compiled from The Global Burden of Disease Study", 2020.

^{73.} WHO International Agency for Research on Cancer, Estimated age-standardised incidence rates, 2022.

^{74.} Snus Commission. Snus saves lives: A study of snus and tobacco-related mortality in the EU, 2017.



Figure 9: Population Health Outcomes in Sweden and the European Union

Population health outcome

Death rates (per 100,000) attributable to tobacco

MEN	Sweden	European Un Min	ion Member Sta Median	tes other than Sweden Max
Lung cancer	87	91	220	399
Other cancer	63	41	105	217
All cardiovascular	72	107	170	618
All causes	222	378	550	1388

Result: Swedish men have by far the lowest (about 3-times lower) tobaccorelated death rates from cancer and heart disease compared to the EU

Ramström & Wikmans, Tob Induc dis 2014

Our own estimates from the **Saving Lives like Sweden** report found that in Europe, nearly 2.9 million lives could have been saved between 2000 and 2019 if the EU had the same smoking-related mortality rate as Sweden⁷⁵. This figure alone should spur policymakers into action to prevent the same loss of life in the coming decades.

Individual countries should do their part, too. Taking the case of Germany, our modelling, which considered current smoking and vaping habits, showed that between 2013 and 2060, 300,000 deaths could be avoided, and 4.7 million life years saved if adult smokers were to switch to nicotine vaping products⁷⁶. Similarly, our research found that in the US this would equate to preventing over 1.8 million deaths and gaining 38.9 million life years saved if adult smokers were to switch to nicotine vaping products⁷⁷.

The rest of the world has an opportunity to replicate Sweden's success in displacing smoking with other smoke free alternatives, thus preventing millions of incidences of tobacco related diseases and avoiding millions of premature deaths each year.

^{75.} Smoke Free Sweden. Saving Lives Like Sweden, 2023

^{76.} Smoke Free Sweden. Saving Lives Like Sweden, 2023

^{77.} Smoke Free Sweden. Saving Lives Like Sweden, 2023

Chapter 2: Explaining Nicotine

2.1. Nicotine – A Misunderstood Molecule

Although nicotine may cause dependence, it does not cause disease.⁷⁸ Studies have long established this fact, and nicotine has been used in pharmaceutical formulations for decades. Therefore, as a harm-reduction tool, nicotine is an extremely useful substitute for combustible tobacco.

The UK's National Health Service (NHS) declares: "Although nicotine is addictive, it is relatively harmless to health.

"Nicotine itself does not cause cancer, lung disease, heart disease or stroke and has been used safely for many years in medicines to help people stop smoking."⁷⁹

In addition, nicotine may have therapeutic effects. "In human studies, acute administration of nicotine can have positive effects on cognitive processes, such as improving attention, fine motor coordination, concentration, memory, speed of information processing, and alleviation of boredom or drowsiness. Some nicotine users benefit from self-medication effects for alleviation of stress, anxiety, depression, and other mental health and medical conditions, including schizophrenia and Parkinson's disease.⁸⁰

As a harm-reduction tool, nicotine is an extremely useful substitute for combustible tobacco. World-renowned researcher in human nicotine pharmacology and a veteran in tobacco control at the Center for Tobacco Control Research and Education at the University of California, Dr Neal Benowitz, states, **"Nicotine plays a minor role, if any, in causing smoking-induced diseases."**^{81,82}



Nicotine consumers are not only those who are trying to quit smoking with the help of nicotine replacement therapy. It is also those who find nicotine useful to improve productivity, enhance focus and reduce anxiety. Some people with mental health conditions use nicotine to help cope with depression, attention deficit disorders and schizophrenia.

Still, the biggest public health problem is that almost one-fifth of all people consume nicotine by smoking cigarettes. Although the hazards of smoking are well documented, smokers still choose to continue the habit, notwithstanding high taxes, restrictions of use, broad social disapproval, and the knowledge that they do harm to their own and others' health.

^{78.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{79.} NHS. UK.2024. https://www.nhs.uk/better-health/quit-smoking/vaping-to-quit-smoking/vaping-myths-and-the-facts/

^{80.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{81.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{82.} Benowitz NL. <u>Nicotine addiction</u>, 2010.



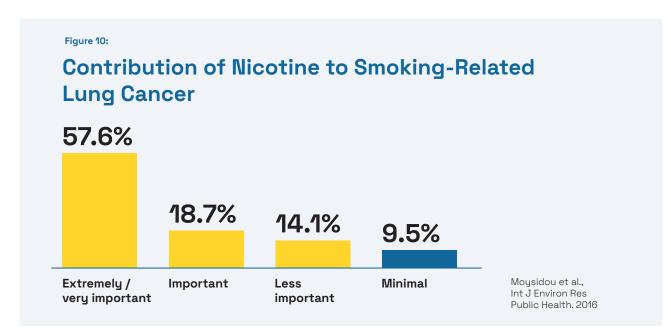
2.2. Nicotine Misperceptions

Tragically, significant myths about nicotine persist among physicians and the public alike.⁸³ The misperception of nicotine's harms among healthcare professionals is unacceptable and not in the best interest of their patients.

Patel et al.'s^{84,85} 2013 survey at the University of Louisville, KY consisted of 826 full-time faculty members in the schools of medicine, public health, dentistry and nursing (57% male respondents). Of the participants, 38% believed that even separate from smoking, nicotine is a high-risk factor for heart attack and stroke. Furthermore, 50% regarded nicotine itself as a moderate risk factor.

For cancers, 38% of the faculty deemed nicotine a high-risk factor and 37% a moderate risk factor. These percentages were 32% and 40% respectively for oral cancer. The male professor respondents appeared moderately better informed than their female counterparts, as male professors were more likely to rate cigarettes as riskier than nicotine (by odds ratios of 1.88 to 2.30).^{86,87}

In 2016, Moysidoulet et al.⁸⁸ examined the perceptions of 262 Greek healthcare professionals about nicotine's association with smoking-related disease. Approximately 80% of participants reported that the contribution of nicotine to smoking-related lung cancer and cancer in other organs is important, very important, or extremely important, despite nicotine not being classified as a carcinogen. Similar responses were given about the contribution of nicotine to smoking-related cardiovascular disease.



^{83.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{84.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{85.} Patel D, Peiper N, Rodu B. Perceptions of the health risks related to cigarettes and nicotine among university faculty, 2012.

^{86.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{87.} Patel D, Peiper N, Rodu B. Perceptions of the health risks related to cigarettes and nicotine among university faculty, 2012.

^{88.} Moysidou A, et al. <u>Knowledge and Perceptions about Nicotine, Nicotine Replacement Therapies and Electronic Cigarettes among Healthcare Pro-</u><u>fessionals in Greece</u>, 2016.

In 2019, Ferrara et al.^{89,90} completed an online survey of 256 European Union residents in public health (143 female/106 male). Of the respondents, 62% held that nicotine itself causes cancer and more than 72% believed that atherosclerosis is caused by nicotine.

If health professionals don't understand nicotine, how can we expect the public to know that nicotine does not cause disease? Consider, for example, that in the UK, 40% of the public believes that nicotine causes smoking-related cancers.^{91,92}

Male and female smokers equally hold a widespread misperception that nicotine causes disease. This could partly explain the comparatively low utilisation of Nicotine Replacement Therapy (NRT).^{93,94}

A 2016 study of 1,047 clients at the UK stop-smoking services found that even among smokers who chose NRT for treatment, as low as 6.0% (Cl 4.3, 8.3) were using NRT at the oneyear follow-up, which indicates the limited success of NRT for substitution.^{95,96}

According to Abrams et al.^{97,98}, it is critical to separate the consequences of nicotine addiction from concerns regarding the harm caused to smoking adults: "The mistaken public beliefs that nicotine is the cause of disease risk and cancer, rather than the smoke from combustion, must be dispelled."

Figure 11:

Misperceptions Among US Physicians Regarding Nicotine

National Survey

- 926 physicians were randomized to receive 1 of 2 versions of a questionnaire
- In 1 version, participants were asked about the extent to which they agree or disagree that "nicotine, on its own" directly contributed to health effects
- N = 465 US physicians in 3 specialties
 - Family medicine, internal medicine, obstetrics /qynecology

Distribution of Responses to Nicotine Questions

Condition	Agree, %	Strongly Agree, %	Agree or Strongly Agree, %
Birth defects	32.0	39.0	71.0
COPD	10.2	67.3	77.5
CVD	11.9	78.2	90.1
Cancer	12.7	69.6	82.3

91. O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{89.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{90.} Ferrara P, Shantikumar S, Cabral Veri'ssimo V, Ruiz-Montero R, Masuet-Aumatell C, Ramon-Torrell JM. <u>Knowledge about e-cigarettes and tobacco</u> harm reduction among public health residents in Europe, 2019.

^{92.} McNeill A, Brose LS, Calder R, Bauld L, Robson, D. Evidence review of e-cigarettes and heated tobacco products 2018: A report commissioned by Public Health England, 2018.

^{93.} O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century</u>, 2020.

^{94.} Black A, Beard E, Brown J, Fidler J, West R. <u>Beliefs about the harms of long-term use of nicotine replacement therapy: Perceptions of smokers in England</u>, 2012.

^{95.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{96.} Shahab L, Dobbie F, Hiscock R, McNeill A, Bauld, L. <u>Prevalence, and impact of long-term use of nicotine replacement therapy in UK stop-smoking</u> services: Findings from the ELONS study, 2016.

^{97.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{98.} Abrams DB, Glasser AM, Pearson JL, Villanti AC, Collins, LK, Niaura, RS. <u>Harm minimization and tobacco control: Reframing societal views of nicotine use to rapidly save lives</u>, 2018.



As mentioned before, physicians remain profoundly misinformed about the actual risk of nicotine. This is true, even within the most developed countries, such as the USA. In 2021, Bover Manderski et al. performed a national survey to test 926 US physicians' perception of the link between nicotine and certain conditions, showing alarming ignorance.⁹⁹

Without question, there is an urgent need for health professionals and the public to have access to accurate information about the risk profile and evidence base for therapeutic and recreational nicotine.¹⁰⁰

It is critical that these misperceptions are corrected through primary and ongoing professional education. to avoid:

- Suboptimal advice on smoking cessation, not explaining the efficacy of smoke free nicotine alternatives as cessation tools.
- Unscientific advice about the risks of nicotine (e.g. that nicotine does not cause cancer).
- Unscientific advice on smoke-free nicotine alternatives, such as oral nicotine pouches, e-cigarettes, and heated tobacco products.

2.3. Origins and biochemistry of nicotine

Nicotine is found in several plants, including tomatoes, aubergines and even potatoes. However, the largest quantities are found in the tobacco plant. It is interesting to note that, despite centuries of tobacco use, scientists were only able to identify the active ingredient of the tobacco plant in the laboratory during the early 1800s.

Two researchers, Cerioli and Vauquelin, successfully extracted an oily substance from the plant, first naming it "nicotanine" after Jean Nicot. Later, in 1828, Posselt and Reimann, two researchers from the Uni-

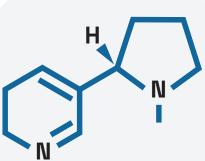


Figure 12: Biochemical Structure of Nicotine

versity of Heidelberg, purified the extract and called it "Nikotin". In its pure form, nicotine is a colourless or pale-yellow oily liquid. The chemical formula for nicotine, $C_{10}H_{11}N_{2}$, was established in 1840 and since then, it has been possible to synthesise the compound in a laboratory.

> Tobacco products contain hundreds of substances, while the smoke produced when setting it alight contains more than 4,000 substances or toxi-

cants. However, the one common factor found in all types of tobacco products is nicotine, whether in the smoked or the smokeless forms.^{101,102}

^{99.} Manderski B. Persistent Misperceptions about Nicotine among US Physicians: Results from a Randomised Survey Experiment, 2021. 100. O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{101.} Ghoshen OA, Dwoskin LP, Miller DK, Crooks PA. Accumulation of nicotine and its metabolites in rat brain after intermittent or continuous peripheral administration of [2'- (14) C] nicotine, 2001.

^{102.} Crooks PA, Dwoskin LP. Contribution of CNS nicotine metabolites to the neuropharmacological effects of nicotine and tobacco smoking, 1997.

2.4. How the Body Absorbs Nicotine

The main effect of nicotine in the body is due to its direct action on nicotinic acetylcholine receptors that are present in the adrenal medulla, central nervous system, and skeletal muscle.

Because of the overall positive effect of nicotine on the brain – especially concerning sharpness, alertness, and concentration - it can be problematic to force some patients who perform high-performance jobs, such as pilots, surgeons, and heavy machinery operators to guit cold turkey. The loss of concentration and alertness combined with withdrawal symptoms can be quite dangerous.¹⁰³ As nicotine undergoes extensive metabolism in the body, the breakdown of nicotine into six metabolites (mainly in the liver), enables scientists to measure the success of tobacco cessation objectively when combined with nicotine use cessation. Cotinine has the largest concentration of nicotine metabolites in the blood and is often used to verify whether a patient has truly stopped smoking. It also has a longer plasma half-life than nicotine (16-20 hours), so requesting this laboratory test when appropriate is useful.¹⁰⁴

Nicotine act on nicotinic cholinergic receptors, triggering the release of dopamine, producing rewarding psyhoactive effects.



Figure 13: Nicotine Action on the Brain

2.5. Why Nicotine Replacement Therapy (NRT) is an ineffective cessation tool.



Although nicotine replacement therapy (NRT) is included on the WHO List of Essential Medicines, it remains a relatively ineffective method for smoking cessation, in part due to the way it is slowly absorbed by the body, compared with the relatively fast absorption of nicotine, when it is inhaled.

A recent Cochrane Review (2024) analysing 88 completed studies, found strong evidence that nicotine e-cigarettes are more effective than traditional nicotine-replace-

^{103.} Giannakoulas G, Katramados, A, Melas N, Diamantopoulos I, Chimonas E. <u>Acute effects of nicotine withdrawal syndrome in pilots during flight</u>, 2003. 104. Benowitz NL, Kuyt F, Jacob P, Jones RT, Osman AL. <u>Cotinine disposition and effects</u>, 1983.



ment therapy (NRT) in helping people quit smoking.

"Evidence also suggested that nicotine e-cigarettes led to higher quit rates than e-cigarettes without nicotine, or no stop smoking interventions, but less data contributed to these analyses." ¹⁰⁵

The National Health Service website in the UK states that "Evidence shows that nicotine vapes are more effective than nicotine replacement therapies, like patches or gum.

Some people find vaping helps them because the hand-to-mouth action is like smoking, plus you get similar sensations and satisfaction.¹⁰⁶

In contrast, the various forms of medicinal nicotine (NRTs or nicotine replacement therapy) deliver nicotine much slower.¹⁰⁷ NRTs were specifically designed to minimise their addiction potential.

2.6. Evaluating the Risks of Nicotine in NRT, Snuff and Snus

The use of nicotine replacement therapy (NRT) over the last 20 years or more has offered the best evidence in clinical trials and observational study settings that nicotine is a safe drug.^{108,109}

While NRTs may have some local adverse effects (such as skin irritation), these are rather linked to the form of nicotine intake.

While there is no clear evidence that nicotine can induce acute cardiovascular effects; it has been associated with minor cardiovascular adverse effects such as palpitations, which are not considered as having long-term adverse prognostic value.^{110,111}

Various studies have shown no increased risk of cardiovascular disease among people who continue to smoke while using medicinal nicotine, or in cardiovascular patients who use medicinal nicotine.¹¹²:

Likewise, several studies show that nicotine in snus products do not contribute to heart disease or stroke. Huhtasaari et al¹¹³ reported that **"the risk of myocardial infarction (MI) is not increased in snuff dippers and that nicotine is probably not an important contributor to ischemic heart disease in smokers".**

Hansson et al¹¹⁴ found that the use of snus was not associated with the risk of stroke (whether haemorrhagic, thrombotic or non-specified). Hence, **"nicotine is unlikely to contribute importantly to the pathophysiology of stroke."**

Wennberg et al.¹¹⁵ found no increased risk for MI amongst snuff users without a previous history of smoking. They found that for snuff users with a previous history of smoking, **"the tendency towards an increased risk for MI may reflect the residual risk from former smoking"**.

A study by Hansson et al.¹¹⁶ found no association between the use of snus and the development of acute myocardial infarction (AMI). **"Hence, toxic components other than nicotine appear to be implicated in the pathophysiology of smoking-related ischemic heart disease".**

106. NHS, Vaping myths and the facts

^{105.} Lindson N, et al. Electronic Cigarettes for Smoking Cessation. Cochrane Library. (2024).

^{107.} Hukkanen J, Jacob P, Benowitz NL. Metabolism and disposition kinetics of nicotine, 2005

^{108.} West R, DiMarino ME, Gitchell J, McNeill A. Impact of UK policy initiatives on use of medicines to aid smoking cessation, 2005.

^{109.} Silagy C, Lancaster T, Stead L, Amant D, Fowler G. <u>Nicotine replacement therapy for smoking cessation</u>, 2004

^{110.} Zevin S, Jacob P, Benowitz NL. Dose-related cardiovascular and endocrine effects of transdermal nicotine, 1998.

Dacosta A, Guy JM, Tardy B, Gonthier R, Denis L, Lamaud M, et al. <u>Myocardial infarction and nicotine patch: A contributing or causative factor?</u> 1993.
 Benowitz NL, editor. <u>Nicotine safety and toxicity</u>, 1998

^{113.} Huhtasaari F. Smokeless tobacco as a possible risk factor for myocardial infarction: a population-based study in middle-aged men, 1999.

^{114.} Hansson J, et al. Snus (Swedish smokeless tobacco) use and risk of stroke: pooled analyses of incidence and survival, 2014.

^{115.} Wennberg P, et al. <u>The risk of myocardial infarction and sudden cardiac death amongst snuff users with or without a previous history of smoking</u>, 2007.

^{116.} Hansson J, et al. Snus (Swedish smokeless tobacco) use and risk of stroke: pooled analyses of incidence and survival, 2014.

2.7. Does Nicotine Cause Cancer in Humans?

In the UK, the National Health Service "Better Health" website states that "Nicotine itself does not cause cancer, lung disease, heart disease or stroke and has been used safely for many years in medicines to help people stop smoking."¹¹⁷

To date, there are no relevant studies in humans on the carcinogenic effects of medicinal pure nicotine.¹¹⁸ Furthermore, the 2014 Surgeon General Report states that "the evidence is inadequate to infer the presence or absence of a causal relationship between exposure to nicotine and the risk of cancer.¹¹⁹ Nicotine itself is not a carcinogen.¹²⁰

Even more persuasive is the ground-breaking 2007 report of the Royal College of Physicians, "Harm Reduction in Nicotine Addiction: Helping people who can't quit". They conclude: **"There is no direct evidence that NRT therapy is carcinogenic or influences the risk of other common smoking-related diseases in humans."**¹²¹

The Swedish snus experience mitigates against nicotine being carcinogenic. Lee et al.¹²²provides a meta-analysis of the epidemiological evidence relating snus to health. They found that **"there are no clear associations evident in never smokers, with any possible risk from snus being much less than from smoking. "Snuff-dipper's lesion" does not predict oral cancer. Snus users have increased weight, but diabetes and chronic hypertension seem unaffected".**

In another meta-analysis, Lee et al.¹²³ performed a systematic review of the relationship between smokeless tobacco and cancer in Europe and North America. They conclude: **"An increased risk of oropharyngeal cancer is evident most clearly for past (before 1990) smokeless tobacco use in the USA, but not for Scandinavian snuff and not in studies after 1990. Effects of smokeless tobacco use on other cancers are not clearly demonstrated".**

2.8. Is Nicotine Linked to Chronic Disease?

More extensive epidemiological data on the association between nicotine intake and cancer or cardiovascular disease are available from studying snus use. Snus users obtain equal or higher amounts of nicotine¹²⁴ on a daily basis compared to smokers.¹²⁵ However, snus use,

especially Scandinavian snus, which is a low-nitrosamine smokeless tobacco product, carries a very low risk of developing cancer compared to smoking. Luo et al. found that **"the risk of oral and lung cancer among snus users was like never smokers, while only pancreatic cancer**

^{117.} NHS, Vaping myths and the facts

^{118.} Sanner T, et al. Nicotine: Carcinogenicity and Effects on Response to Cancer Treatment - A Review, 2015.

^{119.} US Department of Health and Human Services. The Health Consequences of Smoking - 50 Years of Progress, 2014

^{120.} Sanner T, et al. Nicotine: Carcinogenicity and Effects on Response to Cancer Treatment - A Review, 2015.

^{121.} Royal College of Physicians. Harm reduction in nicotine addiction: Helping people who can't quit, 2007.

^{122.} Lee PN. Summary of the epidemiological evidence relating snus to health, 2011.

^{123.} Lee PN, Hamling J. Systematic review of the relation between smokeless tobacco and cancer in Europe and North America, 2009.

^{124.} Wennmalm A., et al. Relation between tobacco use and urinary excretion of thromboxane A2 and prostacyclin metabolites in young men, 1991.

^{125.} Holm H., Jarvis M.J., Russell M.A.H., Feyerabend C. Nicotine intake and dependence in Swedish snuff takers, 1992.



risk was elevated in current snus users and those using more than 10 grams per day".¹²⁶

A systematic review of the relation between snus use and cancer concluded that if the smoking population was using snus instead, only 1.1% of the smoking-attributed cancers would occur,¹²⁷ showing that the risk for cancer is higher than non-use but minimal compared to smoking. Similar evidence exists for the association between snus use and cardiovascular disease. A retrospective case-control study in Sweden found that the risk for acute myocardial infarction was similar between snus users and never-smokers.¹²⁸ An analysis of eight prospective studies also found no association between snus use and acute myocardial infarction.¹²⁹

Similarly, an analysis of eight prospective cohort studies on stroke risk (ischemic and haemorrhagic), with more than 130,000 non-smoking men participating, found no association between snus use and risk of stroke ¹³⁰. These studies have shown that nicotine is highly unlikely to contribute significantly to smoking-related cancer and cardiovascular disease.

2.9. Why do people use nicotine?

2.9.1. Smoking Cessation

Nicotine replacement therapy and other forms of nicotine are used by consumers to quit smoking. There is scientific and social consensus that this is a valid use of nicotine. Bell et al.¹³¹ argue that "by delivering nicotine in way that resembles the visual spectacle and bodily pleasures of smoking, but without the harms of combustible tobacco, e-cigarettes highlight the complex status of nicotine as both a poison and remedy in contemporary public health and tobacco control".

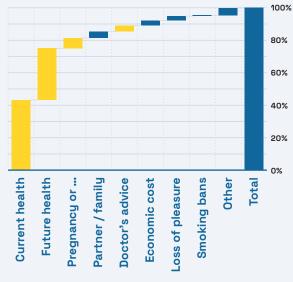
It is also important to understand why they want to quit, mostly using nicotine-based products.

2.9.2. Other reasons such as for mood control¹³² and cognitive enhancement¹³³

Consumers use nicotine for other reasons as well, including mood control and cognitive enhancement. More research and evidence-based debate is needed to identify and validate these supplementary uses.

Nicotine without harm: Why do people quit?

Stated reasons for quitting smoking



Gallus S, Muttarak R, Franchi M, et al. Why do smokers quit? Eur J Cancer Prev 2013;22(1):96–101.

Figure 14: Why do People Quit Smoking?

^{126.} Luo J, et al. Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: A retrospective cohort study, 2007.

^{127.} Lee P.N., Hamling J. <u>Systematic review of the relation between smokeless tobacco and cancer in Europe and North America,</u> 2009. 128. Huhtasaari F, et al. <u>Smokeless tobacco as a possible risk factor for myocardial infarction: A population-based study in middle-aged men,</u> 1999.

^{129.} Hansson J, et al. Use of snus and acute myocardial infarction: Pooled analysis of eight prospective observational studies, 2012.

^{130.} Hansson J, et al. Snus (Swedish smokeless tobacco) use and risk of stroke: pooled analyses of incidence and survival, 2014.

^{131.} Bell K. International Journal of Drug Policy, 2012. https://www.sciencedirect.com/science/article/abs/pii/S0955395912000072?via%3Dihub

^{132.} Benowitz NL. Pharmacology of Nicotine: Addiction, Smoking-Induced Disease, and Therapeutics, 2008.

^{133.} Newhouse PA. Therapeutic Applications of Nicotinic Stimulation: Successes, Failures, and Future Prospects, 2018.

Why do people use nicotine?

Mood control

In humans, nicotine from tobacco induces stimulation and pleasure, and reduces stress and anxiety. Smokers come to use nicotine to modulate their level of arousal and for mood control in daily life.



Figure 15: Nicotine Role in Mood Control



Figure 16: Nicotine Role in Cognitive Enhancement

attention/response mechanisms as well as enhancing working memory in humans.



2.10. Caffeine

When considering the regulation of nicotine, we always present the case for dependence. But why do we never discuss the dependence on caffeine? Because caffeine does not cause harm. Public health is about disease and death, not about a moralistic judgment of behaviours and lifestyle choices. Therefore, nicotine regulation should be based on the public health argument of harm caused by different products, since nicotine itself is associated with minimal harm.

Dr. Konstantinos Farsalinos Nicotine Researcher

Caffeine is a naturally occurring chemical compound found in plant constituents such as coffee and cocoa beans, tea leaves, guarana berries, and the kola nut. It has a long history of human consumption. When consumed by humans, caffeine stimulates the central nervous system, and in moderate doses increases alertness and reduces sleepiness.

Caffeine consumption in the European Union is significant. The European Food Safety Authority (EFSA) reports¹³⁴ that coffee was the predominant source of caffeine for adults, contributing between 40% and 94% of total intake. Tea was the main source in Ireland and the United Kingdom, contributing 59% and 57% of total caffeine intake respectively.

Few studies have compared the dependence on different tobacco and nicotine products. Even less is known about how it relates to dependence on other common drugs, e.g. caffeine. In a study by Dr Karl Fagerstrom¹³⁵ the degree of dependence was compared between snus, cigarettes, nicotine replacement therapy (NRT), electronic cigarettes and coffee. Dependence on traditional cigarettes and snus seem to be relatively similar, while NRT was rated lower and coffee lowest. Since the prevalence of caffeine use in all forms is more prevalent than nicotine, there might be more people in society that are heavily dependent on caffeine.

Figure 19:

Average intake of caffeine in the European Union

Very elderly (75 years and above)	22-417mg
Elderly (65-75 years)	23-362mg
Adults (18-65 years)	37-319mg
Adolescents (10-18 years)	0.4-1.4mg/kg bw
Children (3-10 years)	0.2-2.0mg/kg bw
Toddlers (12-36 months)	0-2.1mg/kg bw

Implication: Tobacco products are likely more dependence forming than nicotine replacement products and coffee, although there might be more people dependent on caffeine. The addiction to coffee or caffeine is seldom discussed in society probably because of the little or no harm it causes. This is also reflected in the vastly differing regulatory focus on caffeine, as opposed to nicotine. The authors would suggest that more comparative studies be done to provide a more evidence-based and risk-proportionate regulation of these two social psychoactive drugs.

134. EFSA. <u>Caffeine</u>

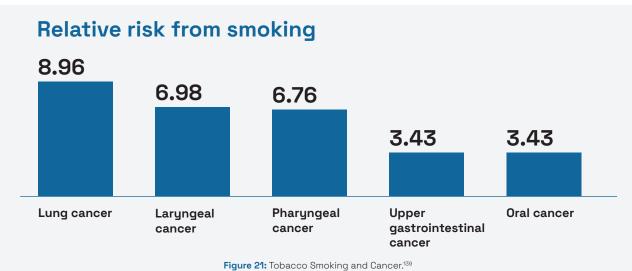
^{135.} Fagerstrom. A Comparison of Dependence across Different Types of Nicotine Containing Products and Coffee, 2018.

Chapter 3: Combustion versus Non-combustible Nicotine

3.1. Combustible Tobacco Products

"No Smoke Less Harm" highlights the fundamental difference between harm linked to combustible and non-combustible tobacco and nicotine products. Traditional combustible cigarettes are probably the most commercially successful "fast moving consumer product, but sadly, they are also one of the deadliest products of all time.

- **Distribution:** Cigarettes are the most widely consumed tobacco product and nicotine-delivery vehicle. Of all the tobacco products sold, 92% are cigarettes (approximately 6.3 trillion cigarettes are consumed per year). Although most cigarettes are manufactured commercially, some are hand-rolled. Over 15 billion cigarettes are smoked worldwide every day. One in three cigarettes smoked in the world today is smoked in China.
- Mode of action: Cigarettes are set alight, and the smoke is inhaled into the lungs, where it is very rapidly absorbed into the bloodstream. Physiologically, this means that nicotine enters the arterial blood supply and reaches the brain within seconds. A cigarette delivers a potent 'hit' or 'rush' for the smoker – much more effectively and faster than any other nicotine delivery device –, which greatly enhances its addictive potential.^{136,137} Each cigarette has, on average, 10-12 mg of nicotine content.
- **Risk profile:** Cigarettes are the most hazardous nicotine delivery system on the market, causing harm to almost every part of the body. Cigarettes are responsible for 90% of all cancers, 30% of all heart disease, and 30% of all chronic obstructive lung disease.¹³⁸



136. Henningfield JE, et al. <u>Higher levels of nicotine in arterial than in venous blood after cigarette smoking</u>, 1993.

137. Gourlay SG, et al. Determinants of plasma concentrations of nicotine and cotinine during cigarette smoking and transdermal nicotine treatment. 1997.

138. NTP (National Toxicology Program). <u>Report on carcinogens.</u> 14th ed, 2016.

139. Gandini S, et al. Tobacco smoking and cancer: a meta-analysis, 2008.



• **Smoking cessation benefits:** Quitting smoking is one of the most effective ways of reducing future health risks, both in the context of primary and secondary prevention. Evidence suggests that smoking cessation is more effective in terms of the number needed to treat (NNT) than interventions that have been considered revolutionary in medicine, such as the use of ACE-inhibitors in heart failure or the use of statins in coronary artery disease.

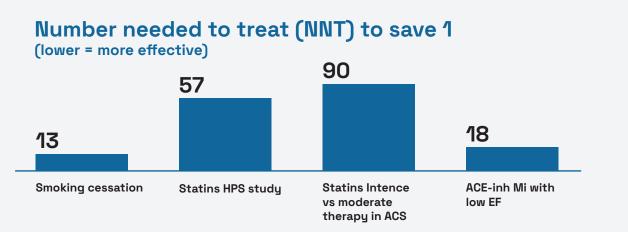


Figure 22: "Number needed to treat" in the prevention of future health risk: Benefits of Smoking Cessation,¹⁴⁰ Statins,¹⁴¹ Statins vs Moderate therapy¹⁴² and ACE inhibitors¹⁴³

"A cigarette delivers a potent hit or rush for the smoker – much more effectively and faster than any other nicotine-delivery device – which greatly enhances its addictive potential."

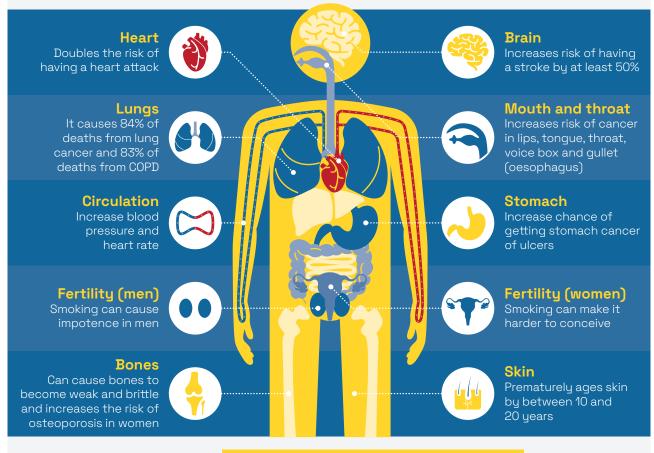
140. Wu AD, et al. Smoking cessation for secondary prevention of cardiovascular disease, 2022

141. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial, 2002.
142. Afilalo J, Majdan AA, Eisenberg MJ. Intensive statin therapy in acute coronary syndromes and stable coronary heart disease: a comparative

142. Afilalo J, Majdan AA, Eisenberg MJ. Intensive statin therapy in acute coronary syndromes and stable coronary heart disease: a comparative meta-analysis of randomised controlled trials. 2007.

143. Flather MD, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group, 2000.

Figure 23: How smoking combustible cigarettes harm the body



Smoking prematurely **kills around 96,000 annually** in the UK ...more than obesity, alcohol, road accidents, drug misuse and HIV combined

Public Health England, "Health Matters", 2022

3.2. Fire escape: Non-combustible nicotine-based products

Over the last decade, several categories of non-combustible nicotine alternatives have been developed and widely used. There is a significant difference in risk profile between these products and combustible cigarettes.

We are standing on the cusp of a quickening of nicotine product disrupters. Consumers are demanding new, less harmful, user-friendly, effective, and fast-acting nicotine products, which can be used as substitutes for cigarettes.

Dr Kgosi Letlape,

President, Africa Harm Reduction Alliance (AHRA)



"Epidemiological studies show us that tobacco products delivering nicotine vary considerably in harmfulness. Within each product category, there is a (sometimes wide) variation of dose and manner of use, but the extreme ends of the spectrum differ in harmfulness by orders of magnitude."

Vapour products (otherwise known as electronic nicotine delivery systems, or ENDS, or electronic cigarettes) use a battery to heat liquid containing pharmaceutical-grade nicotine, an inert diluent (such as propylene glycol) and flavourings. They create an aerosol of tiny nicotine-containing droplets, which the user then inhales, absorbing nicotine through the mouth, throat, and lungs. The design and efficiency in nicotine delivery of e-cigarettes have improved substantially since they were introduced into the market in 2006.¹⁴⁶ There are currently three e-cigarette designs/generations:¹⁴⁷

- A disposable product.
- A reusable, refillable device that users fill with liquid from a tank system; and
- A reusable device which attaches to prefilled cartridges ('carts' or 'pods')

Heated tobacco products use a battery or other heating source to heat tobacco and create a vapour that carries nicotine and flavours from the tobacco. These products aim to mimic the experience of smoking closely, but with much lower risk. Heated tobacco products are gaining popularity globally, especially in Japan and South Korea.¹⁴⁸ Japan has 90% of the global market for heated tobacco products.^{149,150} However, in 2018, the prevalence of past-month users was only 2.7% of the population, with men being the predominant users (76.0% male vs 24.0% female).^{151,152}

Japanese smokers find heated tobacco products especially appealing since they eliminate the smell of second-hand smoke and the social disapproval that accompanies it.^{153, 154,155} Evidence¹⁵⁶ has shown that the reduction in cigarette sales in Japan has accelerated considerably since the introduction of heated tobacco products in the market, from a yearly percentage decline of -3.10% across 2011-2015 to -16.38% across 2016–2019. Another study reported that the per capita cigarette sales in Japan were increasing at a rate of 0.10 to 0.14 per month before the introduction of heated tobacco products, but they declined at a rate of 0.63 to 0.66 cigarettes per month after their introduction.¹⁵⁷ Other major markets for heated tobacco products have also seen a rapid increase in sales from 2017 to 2018 - for example, by 300% in Italy and over 500% in Russia.¹⁵⁸

151. O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century</u>, 2020.

156. Cummings KM, Nahhas GJ, Sweanor DT. <u>What Is Accounting for the Rapid Decline in Cigarette Sales in Japan?</u> 2020.

^{144.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{145.} Gray N, et al. Towards a comprehensive long-term nicotine policy, 2005.

^{146.} O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century</u>, 2020.

^{147.} O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century</u>, 2020.

^{148.} O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century</u>, 2020.

^{149.} O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century</u>, 2020.

^{150.} Filter Magazine. Rise of heat-not-burn products coincides with a decrease in cigarette sales, 2019.

^{152.} Sutanto E, et al. <u>Prevalence, use behaviours, and preferences among users of heated tobacco products: findings from the 2018 ITC Japan survey</u>, 2019.

^{153.} O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century,</u> 2020.

^{154.} Hair EC, et al. Examining perceptions about 100S heated tobacco product: Consumer studies in Japan and Switzerland, 2018.

^{155.} Tabuchi T, et al. <u>Heat-not-burn tobacco product use in Japan: Its prevalence, predictors and perceived symptoms from exposure to second-hand heat-not-burn tobacco aerosol</u>, 2018.

^{157.} Stoklosa M, et al. Effect of IQOS introduction on cigarette sales: evidence of decline and replacement, 2020.

^{158.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

Smokeless tobacco products are sucked or chewed instead of smoked. Risks from smokeless tobacco arise from impurities or hazardous agents in the tobacco itself; however, these can be controlled in the curing and pasteurisation process.

Novel nicotine products can deliver nicotine in various forms, including gum, lozenges, transdermal patches, films, liquids, and oral nicotine pouches. Modern oral nicotine products, are white, pre-portioned little bags comprising a nicotine-containing carrier material, are considered the advanced, cleaner version of Swedish snus, a pasteurized oral tobacco that is available as loose products or pouches and is credited with helping Sweden achieve its record-low smoking prevalence by offering smokers a less harmful way to consume nicotine.

According to Euromonitor International,¹⁵⁹ global sales of nicotine pouches grew from 17.09 billion units in 2022 to an estimated 20.77 billion units in 2023. The overwhelming majority of sales, however, take place in the U.S., where an estimated 14.97 billion units were sold in 2023 compared to 12.61 billion units in 2022. Sweden ranks second, with 1.8 billion units sold in 2022 and an estimated 2.2 billion units sold in 2023.

Swedish Snus has been used in Sweden and other Scandinavian countries for more than 200 years. Resembling a small teabag, snus itself is an oral tobacco product that contains processed, normally pasteurised tobacco in a paper pouch. The user places the pouch in the mouth between the gum and cheek. Note that snus is not the same as loose snuff, chewing

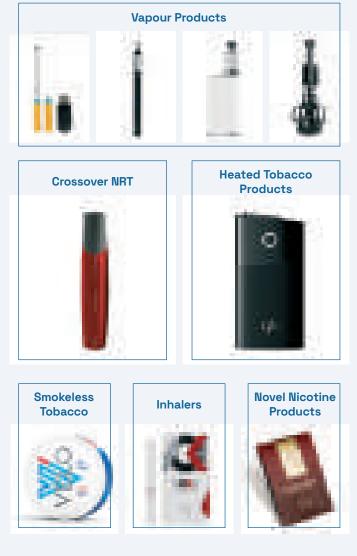


Figure 24: Types of non-combustible nicotine products

or dip tobacco. Because of the pasteurisation, snus contains a greatly reduced level of nitrosamines and tobacco compounds that cause tobacco-related diseases.^{160,161}

It does not generate second-hand smoke exposure and has a proven harm reduction potential. In a comparative case study, Ram-

^{159. &}lt;u>https://www.euromonitor.com/tobacco-free-oral-nicotine</u>

^{160.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{161.} O'Connor RJ, et al. <u>Surveillance methods for identifying, characterising, and monitoring tobacco products: Potential reduced exposure products as an example</u>, 2009.



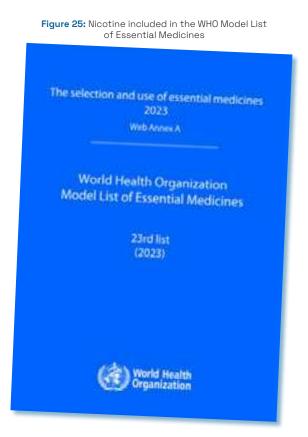
ström and Wikmans¹⁶² compared rates for smoking-related mortality between males in Sweden (where snus is available) and in European countries (where snus is banned). Analysing 2004 data from the WHO Global Report on Mortality Attributable to Tobacco, they found that both populations had a similar prevalence of daily tobacco use. However, Swedish men aged between 60-69 years not only had lower rates of lung cancer deaths (87 per 100 000) than the European Union average (220 per 100 000), but also lower rates of cardiovascular death (72 vs 170 per 100 000). 163,164

On 22 October 2019, the United States Food and Drug Administration (USFDA) validated the harm reduction value of snus by granting Swedish Match USA a 'modified risk order' for eight general brand snus products.^{165,166}

The US FDA announced, **"The available scientific evidence, including long-term** epidemiological studies, shows that relative to cigarette smoking, exclusive use of these specific smokeless tobacco products poses a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis."¹⁶⁷

Nicotine Replacement Therapies (NRTs) is a key element of smoking cessation.^{168,169} The World Health Organization has encouraged physicians and health professionals worldwide to offer medical help to those patients who want to quit smoking. NRTs are on the WHO List of Essential Medicines.¹⁷⁰

The World Health Organization (WHO) has classified nicotine as a component of nicotine replacement therapy for smoking cessation in the WHO Model List of Essential Medicines



^{162.} Ramstrom L, Wikmans T. Mortality attributable to tobacco among men in Sweden and other European countries: An analysis of data in a WHO report, 2014.

^{163.} O'Leary R, Polosa R. <u>Tobacco harm reduction in the 21st century</u>, 2020.
164. Ramstrom L, Wikmans T. <u>Mortality attributable to tobacco among men in Sweden and other European countries: An analysis of data in a WHO</u> report, 2014.

^{165.} O'Leary R, Polosa R. Tobacco harm reduction in the 21st century, 2020.

^{166.} US Food and Drug Administration. FDA grants first-ever modified risk orders to eight smokeless tobacco products, 2019.

^{167.} US Food and Drug Administration. FDA grants first-ever modified risk orders to eight smokeless tobacco products, 2019.

^{168.} The Lung Association. <u>Making quit happen: Canada's challenges to smoking cessation in 2008</u>, 2008.

^{169.} Fiore MC, et al. Treating tobacco use and dependence, 2008.

^{170.}

3.3. Risk Continuum

To place the aforementioned products into the context of their relative harm, the harm continuum (Fig. 26) was developed first by Nutt et al.,¹⁷¹ and modified with permission by Abrams et al.¹⁷² The harm continuum powerfully illustrates the point that none of these products are completely safe. Rather, that e-cigarettes are significantly less harmful than combustible cigarettes. NRTs are safe enough that most medicine regulatory bodies have approved their use as an acceptable strategy to quit smoking, thereby reducing morbidity and mortality from smoking.



^{171.} Nutt et al. Estimating the Harms of Nicotine-Containing Products Using the MCDA Approach, 2014.

^{172.} Abrams et al. Harm Minimization and Tobacco Control: Reframing Societal Views of Nicotine Use to Rapidly Save Lives, 2020.



Chapter 4: The Ethical Basis for the Adoption of Harm Reduction

During her closing address to COP10, the Head of the Secretariat of the WHO FCTC, Dr Adriana Blanco Marquizo quoted a line from the published statement of young activists at COP10: "The interests of the tobacco industry, or even of smokers, should never serve as justification for legitimising products that could send even a single child down the path of addiction." By publicly recognising this statement and leading the applause for the "guardians of the future", she was in fact making a very significant statement on the ethics of tobacco control.¹⁷³

There is no doubt that the preferred future of tobacco control and harm reduction should shield, as far as possible, young people from initiating or using tobacco or nicotine products. However, juxtaposing the interests of a "single" child against that of the 1,3 billion adult smokers, is ethically questionable.

"Smokers have become invisible. Public health ignores their rights to information and choice of less harmful nicotine alternatives. This is ethically and medically unacceptable.

Dr Kgosi Letlape, <mark>President Africa Harm</mark> Reduction Alliance The ethical elements of harm reduction have largely been ignored in the tobacco control debate. Many tobacco-related health problems involve multifaceted ethical dilemmas with no easy answers. Along with science, ethics needs to be central in the consideration of the inclusion of THR in tobacco control.

So, what exactly is ethics and how can it support THR through "No Smoke, Less Harm"? In simple terms, ethics is the study of morality – of what is right and wrong. It involves the careful and systematic reflection on and analysis of moral decisions and behaviour, whether past, present, or future. Applied to tobacco harm reduction, ethical analysis provides some valuable insights.

4.1. Values in medical ethics

There are six values in health ethics relevant to the THR ethics debate:

- Autonomy: Recognition of a person's right to self-determination, i.e. the right to refuse or choose their treatment.
- **Beneficence:** Act in a manner that promotes the well-being of others. In the medical context, this means taking actions that serve patients' best interests.
- Non-malfeasance: "First, do no harm".
- **Justice:** Concerns the distribution of scarce health resources and the decision of who receives scarce treatments (fairness and equality).
- **Dignity:** The patient (and the treating health professional) has the right to dignity.
- **Truthfulness and honesty:** To enable persons to make informed choices.

^{173.} WHO FCTC. Closing Address to COP10, Dr Adriana Blanco Marquizo, 2024.

These values represent a framework of thinking as opposed to offering clear-cut answers to ethical dilemmas. In evaluating whether tobacco harm reduction is "ethical" or not, it should be applied within a meaningful context. Health professionals and public health leaders are expected to exemplify these values, in addition to compassion, competence, and health professional autonomy.

4.2. Basic ethical principles

The **United Nations Universal Declaration of Human Rights**¹⁷⁴ is an example of a basic human right relevant to THR. WHO also acknowledges access to information and tools for health promotion as a fundamental right.

Tobacco Ha	arm Reduction is a human rights issue
WE	IO Ottawa Charter for Health Promotion 1986
±	not achieve their fullest health potential unless they are control of those things which determine their health"
ensure pe	ent in public health ople's <u>access to information</u> on public health issues ople's <u>access to tools (products)</u> that help them promote their

Adult smokers have a right to know that there are smokeless products that are safer than cigarettes, and their physicians should tell them.^{176,177}

One argument made against tobacco harm reduction is that, although it might benefit the individual smoker, it will **potentially** lead to greater risk for society. This report argues that the use of smoke-free nicotine alternatives will lead to net societal benefits, as has been shown in Sweden.

^{174.} United Nations. <u>The universal declaration of human rights</u>, 1948

^{175.} WHO. Ottawa Charter for Health Promotion. 1986.

^{176.} Kozlowski LT, O'Connor RJ, Edwards BQ. <u>Some practical points on harm reduction: What to tell your lawmaker and what to tell your brother</u> <u>about Swedish snus</u>, 2003.

^{177.} Kozlowski LT. <u>Harm reduction, public health, and human rights: Smokers have a right to be informed of significant harm reduction options,</u> 2002.



4.3. Public Health vs. Individual Health

There is sometimes conflict between 'public health' and 'individual health'. In tobacco harm reduction, a divide is clearly visible. Swedish citizens are allowed (and even recommended) to use snus as a cessation or substitute product for combustible tobacco. In other EU countries, this is not possible, as snus is forbidden. In applying this principle to tobacco harm reduction, Kozlowski comes with a clear recommendation as to whose rights should prevail: **"Public** health concerns should trump individual rights only when there is clear and convincing evidence of harm to society. Lacking that evidence, individual rights should prevail".^{478,479}

4.4. Ethical arguments in favour of the tobacco harm reduction approach

In concert with tobacco control, THR can reduce tobacco use. Ethically, the following principles need to be considered:

Autonomy and individual rights

People have a right to make informed choices about their own health and that authorities are therefore obliged to provide health information to enable individuals to make a reasoned decision. The WHO Ottawa Charter for Health Promotion, 1986, clearly states that "People cannot achieve their fullest health potential unless they are able to take control of those things which determine their health."

Beneficence/paternalism

Restriction of access to smoked tobacco or increased access to low-risk nicotine can be seen as paternalistic.

Consequentialist perspectives

There is solid evidence that the use of smoke free nicotine products reduces the harm to individuals.

• Justice

If only smoked tobacco were to be restricted, with no balancing increase in the availability and access to low-risk nicotine products, it could be regarded as unfair.

In reflecting on THR through "No Smoke, Less Harm, ethical considerations are an important component of the debate. Good ethical practice should be a central pillar in the development of evidence based THR policy.

^{178.} Mann JM. <u>Medicine and public health, ethics, and human rights. In: Mann J, Gruskin S, Grodin M, Annas G, eds. Health and human rights</u>, 1997 179. Kozlowski LT, O'Connor RJ. <u>Apply federal research rules on deception to misleading health information: An example on smokeless tobacco</u> <u>and cigarettes</u>, 2003.

Chapter 5: Regulatory Perspectives on THR

For smoke-free nicotine alternatives to be an effective harm reduction and tobacco cessation public health strategy, a robust and proportionate regulatory framework is a requirement.

The best example of a comprehensive and fully implemented regulatory framework on electronic cigarettes exists in the European Union: The Tobacco Products Directive, promulgated in 2014 and adopted into national legislation of all member states in 2016.^{171,180}

The Tobacco Products Directive integrates electronic cigarettes into the regulation for tobacco products, but under a separate section that does not classify them as tobacco products. This is appropriate because they do not contain any tobacco. While nicotine in electronic cigarettes is derived from the tobacco plant, as is nicotine in pharmaceutical nicotine replacement therapies, this cannot scientifically justify the classification as a tobacco product in the same way that biodiesel cannot be considered a vegetable product because it is derived from plants.¹⁸¹ Products cannot be characterized and classified based on the source of one of their ingredients.

For specific cases, the Tobacco Products Directive allows the regulation of electronic cigarettes as medicinal products, but in almost all cases, they are marketed as consumer products. Electronic cigarettes are excluded from many of the restrictions on combustible tobacco products, including the prohibition of flavours and the placement of health warning messages and pictorials on the packaging. The regulation includes quality standards, nicotine concentration and volume limits in electronic cigarette liquids and prefilled cartridges, marketing restrictions, and a defined registration process for all products. Product sales are monitored and reported to an adverse effects registry. To minimise the uptake of electronic cigarettes by youth, the regulation includes a ban on sales to minors below the age of 18. The Tobacco Products Directive is being continuously assessed with the goal of revising it every few years based on the monitoring process. The TPD, although not perfect, is realistic and largely applicable to any other country.

The UK has adopted a more aggressive approach in supporting electronic cigarettes in a tobacco harm reduction strategy. The National Institute of Clinical Excellence actively recommends that healthcare workers advise smokers about the potential utility of e-cigarettes as smoking cessation modalities,¹⁸² Meanwhile, the UK Parliament Science and Technology Committee recommended an even more liberal regulatory framework for e-cigarettes to strengthen their effect as a smoking cessation measure.¹⁸³

Moreover, the government has launched an innovative new program, called "Swop to Stop", a pioneering initiative to encourage and effectively fund one million smokers in England to switch from cigarettes to vaping products (electronic nicotine delivery systems or ENDS).¹⁸⁴

Finally, smoking cessation services have adopted the use of e-cigarettes as smoking cessation aids.

These positions indicate the acceptability of current evidence on the safety and efficacy of these products and the valuable prospects of strengthening tobacco control measures through a harm reduction strategy with e-cigarettes.

182. NICE. <u>Tobacco: Preventing Uptake, Promoting Quitting and Treatment Dependence</u>, 2021. 183. UK Parliament. <u>Conclusions and Recommendations</u>, 2018.

^{180.} Official Journal of the European Union. <u>DIRECTIVE 2014/40/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL</u>, 2014.

^{181.} Farsalinos K, Barbouni A. Association between electronic cigarette use and smoking cessation in the European Union in 2017: analysis of a representative sample of 13057 Europeans from 28 countries, 2020.

^{184.} GOV UK. Smokers urged to swap cigarettes for vapes in the world first scheme, 2023.



Regulation of tobacco and nicotine products should clearly differentiate smoke-free nicotine alternatives (e.g. oral nicotine pouches and electronic cigarettes) from combustible tobacco cigarettes and consider these products as a valuable tool and an ally in smoking control.

5.1. Preferred Regulatory Principles

In that respect, we suggest that regulatory initiatives for smoke free nicotine products should follow at least 6 basic principles:

5.1.1 Regulation should be clearly based on the risk-proportionate principle.

This represents the only proper approach and has been commonly applied to the regulation of any product. Evidence on risk determines the levels of restrictions that need to be implemented.

5.1.2 Regulation should be realistic, ensure product availability and accessibility, and allow for innovation and rapid adoption of technological evolution.

It would make little sense to create a requlation that would be expensive or difficult to implement and comply. This would result in the elimination of smoke-free nicotine alternatives or the creation of an uncontrolled black market, as has been the case in Australia, Belgium, India, and South Africa. Both consequences will end up protecting tobacco cigarette sales while no quality standards can be expected from illicitly traded black market products. Rapid technological evolution has resulted in improvements in the performance, efficacy, and safety of oral nicotine pouches and electronic cigarettes. Currently, available products are safer and more effective as smoking substitutes than the products available a few years ago because of using

better materials, providing a better experience for smokers, and being more effective in alleviating smoking and nicotine cravings. Hurdles to the availability, accessibility and acceptability of oral nicotine pouches and electronic cigarettes are unintentionally protecting tobacco cigarette sales.

5.1.3 Regulation should ensure that the marketing of smoke free nicotine alternatives is not banned but is carefully regulated to only target smokers.

The regulation should include a ban on the sales of these products to people younger than 18 years old. Heavy fines and other consequences should be adopted for those violating this rule.

5.1.4 Regulation should create a competitive advantage for smoke free nicotine alternatives compared to tobacco cigarettes.

Regulation should ensure that smokers are motivated to switch to electronic cigarette use and completely quit smoking. Product cost is a major motive for smokers to try and use alternatives to smoking products. Therefore, any taxation policy should ensure that they remain substantially cheaper than tobacco cigarettes. A recent study by United States scientists found that taxing electronic cigarette results in an increase in tobacco cigarette sales.¹⁸⁵ Additionally, smokers should have easier access to electronic cigarettes

^{185.} Cotti CD, Courtemanche CJ, Maclean JC, Nesson ET, Pesko MF, Tefft N. The Effects of E-Cigarette Taxes on E-Cigarette Prices and Tobacco Product Sales : Evidence from Retail Panel Data, 2020.

than to tobacco cigarettes. A regulated and, thus, carefully controlled marketing strategy for these products is essential to target, inform and educate smokers about the existence and value of smoke free nicotine alternatives in improving their health. Additionally, products should contain enough nicotine; otherwise, consumers will simply continue to smoke to obtain the nicotine they need. Nicotine and flavours were found to be the two major determinants of the attractiveness of electronic cigarettes among adult smokers.¹⁸⁶

5.1.5 Regulation should classify smoke free nicotine alternatives as consumer products with specific rules and restrictions.

The success of electronic cigarettes as smoking substitutes is based on their use as consumer products. They are used according to smokers' preferences and needs, while choice also depends on personal taste and preference. This can only be ensured through a regulatory framework of characterising these products as consumer products with the restrictions mentioned above, but with a clear differentiation between smoke free nicotine alternatives and combustible tobacco cigarettes.

5.1.6 Regulation should introduce reduced-risk labelling or, at least, reduced exposure messages in smoke free nicotine alternatives.

The main incentive for smokers to guit is to reduce health risks. The current environment is characterised by gross misinformation and misperceptions among the population, especially smokers, about the relative risk of electronic cigarettes compared to smoking. Most smokers wrongly believe that electronic cigarettes are equally or even more harmful than smoking. This is unacceptable and harmful to public health. Regulatory authorities should consider adding messages that clearly differentiate these products from tobacco cigarettes and present the reduced risk potential for cancer and other disease conditions. There is already evidence that inappropriate health warnings may inadvertently deter smokers from initiating use and substituting their tobacco smoking for electronic cigarette use,¹⁸⁷ while a message that electronic cigarettes are much less harmful than smoking encourages more smokers to switch without resulting in increased uptake among non-smokers.¹⁸⁸

5.2. How can the World Health Organization show leadership in accelerating tobacco control through THR?

Harm reduction seems to be the orphan in the elaboration and implementation of the FCTC, despite it being explicitly mentioned as part of tobacco control in Article 1(d) of that treaty.¹⁸⁹

Dr Derek Yach,¹⁹⁰ former WHO Director who led the development of WHO's Framework Convention on Tobacco Control (FCTC), states: "Leaders in public health have long recognized that the fastest way to reduce deaths from tobacco is to address cessation. However, clinical, personalized, and medicated solutions were not prioritized in the original FCTC, which instead focused on population-scale policies, such as tax increases, smoke-free

^{186.} Gades MS, Alcheva A, Riegelman AL, Hatsukami DK. <u>The Role of Nicotine and Flavor in the Abuse Potential and Appeal of Electronic Cigarettes</u> for Adult Current and Former Cigarette and Electronic Cigarette Users: A Systematic Review, 2022.

^{187.} Kimber C, Frings D, Cox S, Albery IP, Dawkins L. <u>Communicating the relative health risks of E-cigarettes: An online experimental study exploring</u> the effects of a comparative health message versus the EU nicotine addiction warnings on smokers' and non-smokers' risk perceptions and <u>behavioural intentions</u>, 2020.

^{188.} Kimber C, Frings D, Cox S, Albery I, Dawkins L. <u>The effects of the European e-cigarette health warnings and comparative health messages on</u> <u>non-smokers</u>' and <u>smokers</u>' risk perceptions and behavioural intentions</u>, 2018

^{189.} WHO. Framework Convention on Tobacco Control, 2003

^{190.} Yach D. Accelerating an end to smoking: a call to action on the eve of the FCTC's COP9, 2020.



spaces, advertising bans and educational programs. While these strategies have successfully reduced long-term trends in youth uptake, their impact on adult smokers has been marginal. To cut death and disease rates within two decades, we must consider new strategies for accelerating adult cessation. In particular, we must embrace empathetic tactics that encourage individual smokers to quit or switch – including the use of harm reduction products (HRPs)".

There are other glimmers of hope. During the COP10 meeting in Panama (November 2023), the government of Saint Kitts and Nevis not only argued that the WHO needs to define harm reduction¹⁹¹ but also introduced a proposal that Article 1(d) should be considered in

deliberations over other FCTC articles. It also called for an inter-sessional working group to be established on harm reduction strategies in tobacco control. The working group is to provide guidance on the role of novel and emerging tobacco and nicotine products as a less harmful substitute to conventional cigarettes in the process of developing tobacco control policies. This included the study of best practices, research, and experience covering the reliable and most effective evidence-based interventions to reduce tobacco and nicotine-associated harm.

A formal decision is yet to be made on whether this working group is to be established, but at least some courageous countries are asking the right questions.

St Kitts and Nevis statement at FCTC COP10

St. Kitts and Nevis is very pleased to be part of the global tobacco control community, aiming at protecting present and future generations from the devastating health, social, environmental, and economic consequences of tobacco consumption. And so we are very pleased to be part of this debate today.

At our own domestic situation, we have seen a reduction in smoking prevalence to below 9%. But despite this, globally, we have seen the proliferation of a number of products. One of the concerns that we have really is that when dealing with novel and emerging tobacco and nicotine products that are used commonly by the tobacco industry.

There is the misuse of the so-called harm production or reduced risk.

And this is claiming to attract both smokers and non-smokers to its new products by saying that these novel products expose their users to less harmful constituents, which eventually lead to the renormalization of smoking.

And so although the convention that guides us itself describes tobacco control as a range of supply, demand, and harm reduction strategies.

The public health community must define these terms in a more detailed manner. It is important to note, however, that the proven concept of harm reduction plays a significant role in other areas of public health, such as sexually transmitted infections, HIV AIDS, drug and alcohol addiction, and in fact, air pollution.

And I want to associate myself personally with this because of my earlier experience as being the spokesman for the Caribbean region on matters of health inclusive of HIV AIDS pandemic.

Therefore, the tobacco control community should not reject the idea of harm reduction per se but we should learn from the best practices of proven public health oriented measures while preventing the tobacco industry from hijacking that important term.

Figure 28: Statement by St Kitts and Nevis at COP10

^{191.} COP10. St Kitts and Nevis Statement to the FCTC, 2023

Chapter 6: Conclusions

As a society, our biggest health problem is posed not by nicotine, but by the way that nicotine is consumed. This report offers a pathway for smoke free nicotine alternatives to displace combustible cigarettes and help prevent tobacco-related disease, disability, and premature death.

To achieve a net public health benefit, the trend towards switching from high-risk smoked products, such as cigarettes, to low-risk, smoke free products, such as e-cigarettes, heated tobacco products, smokeless tobacco, and oral nicotine pouches, should be accelerated. This approach is known as 'tobacco harm reduction' (THR) and is based on the idea that 'people smoke for the nicotine but die from the tar'. It works because almost all the disease risk attributable to smoking arises from the smoke, which contains particles of tar and toxic gases that are inhaled from burning process.

Tobacco control and tobacco harm reduction are falsely regarded as opposites. These two methodologies are in fact complementary, not contradictory.

This harm reduction concept is endorsed in Article 1 (d) of the World Health Organization Framework Convention on Tobacco Control (FCTC) and is supported by many scientists and policy experts worldwide. It is a complement, not an alternative, to established tobacco control approaches. Its success lies in giving smokers additional and more appealing options to quit smoking.

Tobacco control strategies should therefore embrace and integrate the concept of harm reduction. Effective regulation involves striking a balance – ensuring products are legally available, but that they are primarily bought by adult smokers in search of a less harmful alternative.

As an international panel of experts, we offer the following recommendations to accelerate THR and the use of smoke free nicotine alternatives to prevent and control tobacco-related disease, disability, and premature death:

Recommendation 1:

Actively eliminate nicotine disinformation.

As important as the measures to combat disinformation during the Covid pandemic, urgent action is needed to tackle disinformation related to nicotine and tobacco harm reduction. It cannot be tolerated that nicotine can still be wrongly perceived as a cause of cancer. Nicotine is not the problem or the cause of cancer. Organisations that propagate false, misleading and deceptive messages about harm reduction and nicotine should be held accountable. Likewise, bad or fake science needs to be confronted and retractions demanded. All efforts should be made to eliminate the original lies, which often live on in policy briefs or headlines worldwide and are seen by many as fact.

Recommendation 2:

Increase THR awareness and adoption.

Stakeholders of all kinds, from national governments to health professionals, private industry, and global health institutions, need to recognize THR as a part of sound practice of public health and a fundamental human right to health (which includes harm reduction) for all individuals and societies affected by tobacco use. There needs to be a concerted effort to stimulate debate on how THR can benefit communities worldwide, as the government of St Kitts and Nevis recently advocated at COP10.

Increased awareness will result in increased political will and opportunities for action. Health professionals have a pivotal role to play in this process, as their patients are often the consumers of tobacco products. We need to develop specific and realistic goals for intervention strategies that are custom-



ised to individuals, local settings, and larger communities. Evidence-based policies and programs will be able to extend the success of THR in Sweden to other countries. Ongoing evaluation of implemented strategies will allow policymakers and other stakeholders to assess the effectiveness of THR interventions and direct any future adjustments to the overall strategy and priorities.

Recommendation 3:

No Smoke, Less Harm – fundamentally differentiate between combustible and smoke free products.

A comprehensive regulatory framework should cover all forms of consumer nicotine products. Total nicotine use should be calculated in countries as well as their delivery systems. The key differentiator for policy purposes is whether the product is combustible and is smoked or a smokeless product. Smoke free tobacco and nicotine products can displace smoking and greatly reduce health burdens. It follows that they should be treated differently to smoked products – reflecting opportunity as well as risk.

Recommendation 4:

Tobacco control policy should include THR.

Awareness of THR is not enough. The WHO must incorporate THR into tobacco control as a 'fourth pillar.' This 'policy push' is essential to making a difference in the lives of the 1.1 billion people who smoke as well as those exposed to second-hand smoke.

The FCTC needs to formally elaborate Article 1(d) of the FCTC and recognize THR. Health professionals and public health advocates must place pressure on global health institutions and governments to introduce harm reduction principles into the FCTC and national public policy.

Recommendation 5:

Adopt a risk-proportionate regulatory framework for all nicotine products based on the risk continuum.

Countries need to establish a regulatory framework to regulate all products that contain nicotine (medicinal or tobacco-based). This will enable coherent and consistent regulation relevant to the risk of each product including the conditions under which it can be sold. Regulation must be based on the level of risk or hazard the tobacco or nicotine product poses.

Recommendation 6: Accelerate THR research.

As was requested by several member states during COP10, policymakers, researchers, health professionals and local policy implementers at both the global and local levels need to build on the knowledge derived from existing best practices in tobacco control to expand the current evidence base on THR.

Recommendation 7:

THR should be recognised as a fundamental ethical and human right.

Recognition and defence of the fundamental human right of consumers to accurate information and the choice of less harmful nicotine alternatives.

Recommendation 8:

Report and monitor progress on THR.

Progress on THR requires that all stakeholders better coordinate their efforts, define clear goals, identify reasonable success metrics, and share their learnings through open channels of communication and the identification of best practices such as the Swedish '3A' approach.

Annex A

Selected positions and statements on tobacco harm reduction

A1) Policymakers

THR Statements from Politicians

1. Ulf Kristersson, Swedish Prime Minister

"I no longer use snus myself, but anything we can do to reduce cigarette consumption is a good thing."

https://www.instagram.com/kristerssonulf/p/ Cw3FINssizI/

Jakob Forssmed, Minister for Social Affairs and Public Health (Sweden)

"In this context, I would also like to emphasise that in relation to snus, cigarettes and smoking tobacco represent a relatively greater health hazard. This approach is reflected in the taxation of these products in Sweden, a diversification that the Government has proposed to reinforce".

https://www.riksdagen.se/sv/dokument-ochlagar/dokument/svar-pa-skriftlig-fraga/forbudmot-nikotinportioner_hb12595/ 2. Casey Costello, Associate Minister of Health (New Zealand)

"I think Sweden was one of the first countries in Europe to reach below that 5 percent threshold. And how much oral nicotine products contributed to that - I'm really interested to understand how that worked."

https://www.nzherald.co.nz/nz/snuff-andchewing-tobacco-could-be-legalised-to-helpsmokers-quit-but-researchers-sceptical-aboutbenefits/.

3. Senator Hollie Hughes (Australia)

"Sweden has made less harmful alternatives to cigarettes accessible, affordable and socially acceptable. Products such as snus, oral nicotine pouches and vaping products were introduced and embraced, leading to a health revolution. In just 14 years from 26 2006 to 2020 these alternatives contributed to a striking 60 percent decrease in Swedish smoking rates"

https://www.youtube.com/ watch?v=1kLDG014J9A

4. MEP Sara Skyttedal (EPP, Sweden)

"Strong message today from the EP on #harm reduction and the need to evaluate tobacco vs new nicotine products in the #NCDreport. I expect @EU_Health to listen to us and learn from Sweden - the first country in the EU to become smoke free."

https://twitter.com/skyttedal/ status/1734953438180446478



5. MP Craig Whittaker (UK)

"In Japan, where 18.6 million people smoke, 25% of ex-smokers quit using heated tobacco, and Japan is already seeing the health benefits through its health system. Similarly, more than half of the ex-smokers in the countru with the lowest smoking rate in the world, Sweden, have guit using something called snus, which is already banned here in the UK. Ironically, the Government have put all their eggs into the vaping scene for cessation but 30% of those people who vape still smoke cigarettes."

https://hansard.parliament.uk/ commons/2024-04-16/debates/EDBAAEB6-8690-4448-83D3-1C0EAD384ABE/ TobaccoAndVapesBill

6. MP Brendan Clarke-Smith (UK)

"We must also appreciate the role of vaping. As has been pointed out, Sweden is a world leader in this. It is down to 5.6%, and when a country gets down to the 5% target it is classed as smoke free. Yes, it used things such as snus, which was outlawed throughout the rest of the European Union. It had special exemptions, and I believe an opportunity has been missed over the years to use that to cut down on the number of smokers, but vaping has of course provided a highly effective alternative."

https://hansard.parliament.uk/ commons/2024-04-16/debates/EDBAAEB6-8690-4448-83D3-1C0EAD384ABE/ TobaccoAndVapesBill

7. MP Gareth Johnson (UK)

"Sweden has been so enthusiastic about allowing people alternatives to tobacco that it currently has the lowest smoking rate in the world and, moreover, the lowest rate of lung cancer in the world".

https://hansard.parliament.uk/ commons/2024-04-16/debates/ EDBAAEB6-8690-4448-83D3-1C0EAD384ABE/TobaccoAndVapesBill

8. MEP Johan Nissinen (ECR, Sweden)

"Sweden has the lowest proportion of smokers in the EU, with only around 6% of people smoking daily. The EU average is around 18%. A smoke-free Sweden would therefore appear to be an increasingly realistic prospect."

https://www.europarl.europa.eu/doceo/ document/E-9-2022-003907_EN.html

9. Joint European Parliamentary question from MEPs Sara Skyttedal (EPP, Sweden), Peter Liese (EPP, Germany), Jessica Polfjärd (EPP, Sweden), Tomislav Sokol (EPP, Croatia)

https://www.europarl.europa.eu/doceo/ document/P-9-2023-003001_EN.html

A2) Organizations



British Medical Association:

"Significant numbers of smokers are using e-cigarettes (electronic cigarettes), with many reporting that they are helpful in quitting or cutting down cigarette use. There are clear potential benefits to their use in reducing the substantial harms associated with smoking, and a growing consensus that they are significantly less harmful than tobacco use."



Royal College of General Practitioners

Royal College of General Practitioners:

"The evidence so far shows that e-cigarettes have significantly reduced levels of key toxicants compared to cigarettes, with average levels of exposure falling well below the thresholds for concern."



Royal College of Physicians:

"Although it is not possible to precisely quantify the long-term health risks associated with e-cigarettes, the available data suggest that they are unlikely to exceed 5% of those associated with smoked tobacco products, and may well be substantially lower than this figure... E-cigarettes are effective in helping people to stop smoking."



Cancer Research UK:

"While the long-term health consequences of e-cigarette use are uncertain, the evidence so far suggests that e-cigarettes are far less harmful than smoking. ...There is also growing evidence to suggest that e-cigarettes can work successfully as an aid to cessation. ...There is insufficient evidence to support a blanket indoor ban on e-cigarette use, either on the basis of renormalisation of smoking or harm to bystanders from second-hand vapour."



British Lung Foundation:

"Experts have reviewed all the research done on e-cigarettes over the past few years, and found no significant risks for people using e-cigarettes. ...Swapping cigarettes for an e-cig can improve your symptoms of lung conditions like asthma and COPD."



Public Health England:

"Our new review reinforces the finding that vaping is a fraction of the risk of smoking, at least 95% less harmful, and of negligible risk to bystanders. Yet over half of smokers either falsely believe that vaping is as harmful as smoking or just don't know."



Royal Society for Public Health:

"RSPH has welcomed a new comprehensive evidence review on e-cigarettes published by Public Health England (PHE). The report reflects an up-to-date evidence base that is increasingly pointing in the same direction: not only that vaping is at least 95% less harmful than smoking, but also that it is helping increasing numbers of smokers to quit."

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Action on Smoking and Health UK:

"It has been estimated that e-cigarettes are 95% less harmful than ordinary cigarettes. There is negligible risk to others from second-hand e-cigarette vapour. ...The lifetime cancer risk of vaping has been assessed to be under 0.5% of the risk of smoking. [But] Public understanding of the relative harms of e-cigarettes [vs smoking cigarettes] have worsened over time and are less accurate today than they were in 2014."



US Food & Drug Administration:

"Make no mistake. We see the possibility for ENDS products like e-cigarettes to provide a potentially less harmful alternative for currently addicted individual adult smokers who still want to get access to satisfying levels of nicotine without many of the harmful effects that come with the combustion of tobacco."



US Centers for Disease Control:

"E-cigarettes have the potential to benefit adult smokers who are not pregnant if used as a complete substitute for regular cigarettes and other smoked tobacco products."



Cochrane Tobacco Addiction Group (Cochrane TAG):

"No serious side effects were associated with [the use of e-cigarettes] (up to two years)."



French National Academy of Pharmacy:

"The World Health Organization's [anti-e-cigarette] position is incomprehensible. Tobacco is responsible for 73,000 deaths in France. The e-cigarette helps people quit smoking. Its components are obviously less harmful than tobacco." NOTE: This is a Tweet from the Académie Nationale de Pharmacie. Not an official statement.



Government of Canada:

"Vaping is less harmful than smoking. Completely replacing cigarette smoking with vaping will reduce your exposure to harmful chemicals. There are short-term general health improvements if you completely switch from smoking cigarettes to vaping products."



The Royal Australasian College of Physicians

Royal Australian College of Physicians:

"The RACP acknowledges that e-cigarettes may have a potential role in tobacco harm reduction and smoking cessation for smokers unable or unwilling to quit."



Royal Australian & New Zealand College of Psychiatrists:

"Research shows that 70% of people with schizophrenia and 61% of people with bipolar disorder smoke compared to 16% of those without mental illness. ...E-cigarettes and vaporizers provide a safer way to deliver nicotine to those who are unable to stop smoking, thereby minimizing the harms associated with smoking tobacco and reducing some of the health disparities experienced by people with mental illness."

Report Smoke ss Harm

NATIONAL Sciences ACADEMIES Medicine

Engineering

US National Academies of Sciences, **Engineering and Medicine:**

"While e-cigarettes are not without health risks, they are likely to be far less harmful than combustible tobacco cigarettes."



New Zealand Ministry of Health:

"The regulatory controls in the Smoke-free Environments Act 1990 were designed primarily for tobacco products that are smoked. They are inadequate for vaping and smokeless tobacco products, which are less harmful to users. There is an opportunity, through better regulation (and public information), to support smokers to switch to significantly less harmful alternatives, substantially reducing the risks to their health and those around them."



American Association of Public Health **Physicians:**

"Smoke-free tobacco/nicotine products, as available on the American market, while not risk-free, carry substantially less risk of death and may be easier to quit than cigarettes. ... Smokers who have tried, but failed to quit using medical guidance and pharmaceutical products, and smokers unable or uninterested in quitting, should consider switching to a less hazardous smoke-free tobacco/nicotine product for as long as they feel the need. Such products include pharmaceutical Nicotine Replacement Therapy (NRT) products used, off-label, on a long term basis, electronic "e" cigarettes, dissolvables (sticks, strips and orbs), snus, other forms of moist snuff, and chewing tobacco."



National Health Service Scotland consensus statement on e-cigarettes:

"Smoking kills. Helping people to stop smoking completely is our priority. ... There is now agreement based on the current evidence that vaping e-cigarettes is definitely less harmful than smoking tobacco."

This statement was created and endorsed by: Action on Smoking & Health Scotland • Cancer Research UK • Chest Heart & Stroke Scotland • Chief Medical Officer for Scotland • NHS Ayrshire and Arran • NHS Greater Glasgow and Clyde • NHS Lothian • NHS Tayside Roy Castle Lung Cancer Foundation
 Royal College of General Practitioners • Royal College of Physicians of Edinburgh • Royal College of Physicians and Surgeons of Glasgow • Royal Environmental Health Institute of Scotland • Scottish Collaboration for Public Health Research and Policy • Scottish Consultants in Dental Health • Scottish Thoracic Society • UK Centre for Tobacco & Alcohol Studies • University of Edinburgh • University of Stirling



American Cancer Society:

"Based on currently available evidence, using current generation e-cigarettes is less harmful than smoking cigarettes."

NOTE: This was the official statement from 2018-2019. As of November 2019, ACS no longer recommends e-cigarettes as a smoking cessation tool. Their stated reason for this change was "e-cigarette use by young people." Illegal under-age use is undesirable, but does not change the original finding that nicotine vaping is less harmful than smoking.



A3) Consumers

Consumer views on THR: Real people and their stories



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Autors and the

Helio, I'm terry, I guit accidentally. Had given up trying to guit. Simoked for over 3D years. Guit almost 5 years ago. Feel like a different person. Thanks to vanifie oustand. And thanks to all who made this happen. And our advocates.

Different rate of some factor in the local

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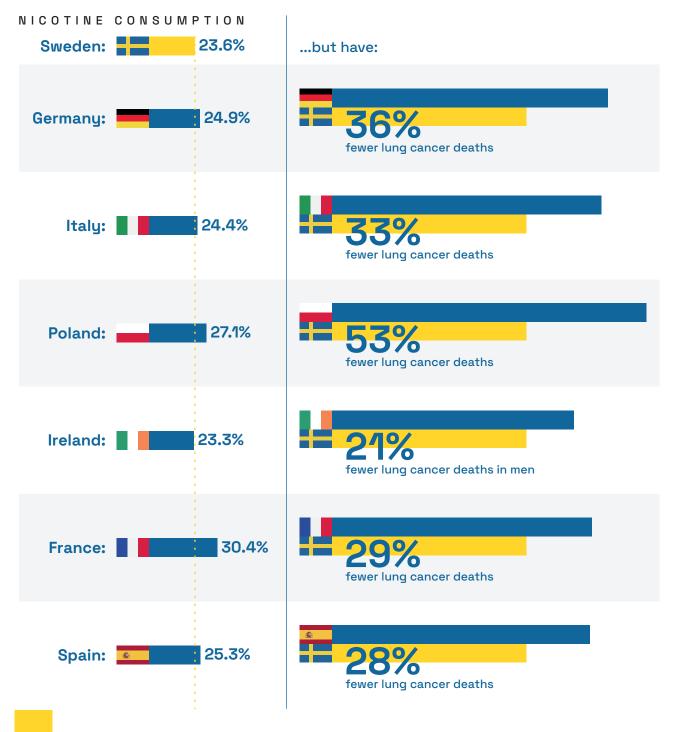


My name is Rich. I started vaping with apple fritter flavoured nicotine about 9 years ago, and have been cigarette free aince. My mother pecced from lang cancer, and I guit because I cidn't want to put my kids through that.

SERVE My R. SEC. When in Proc.

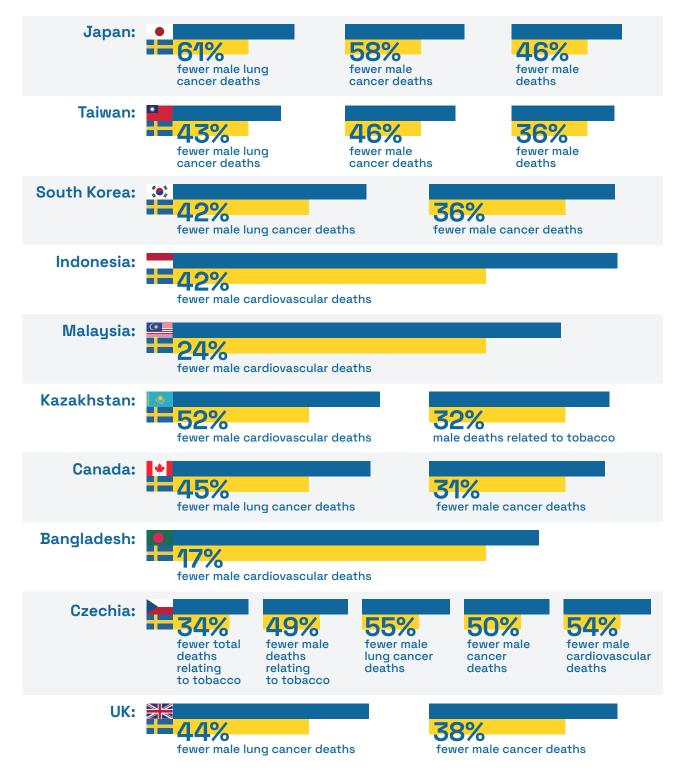
Annex B

Swedes consume similar levels of nicotine to other Europeans, but have better health outcomes, because they use smoke free nicotine alternatives





Due to their use of smoke free nicotine alternatives, Swedes have better health outcomes than many countries



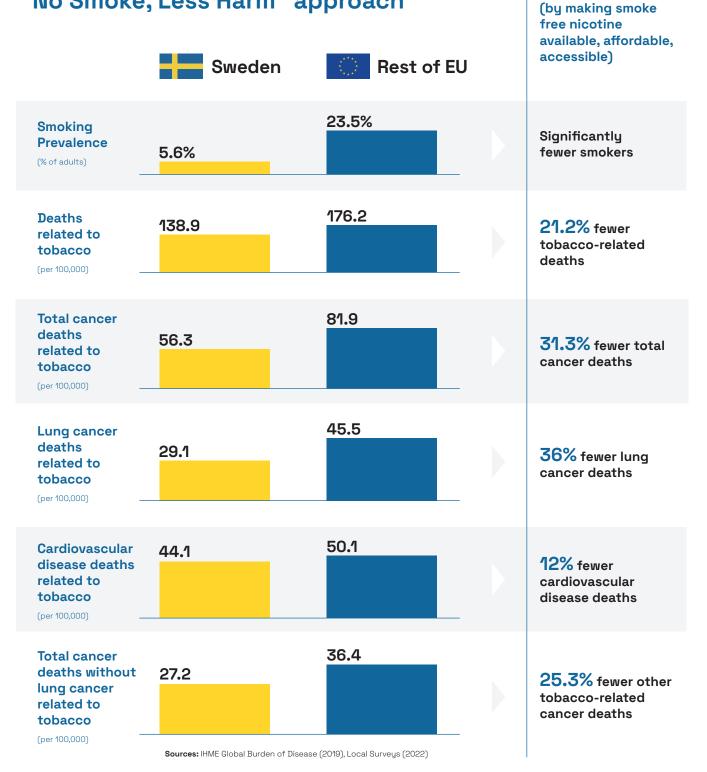
*All data refers to tobacco-attributed deaths and diseases

Smoke Free Sweden superiority despite

equivalent total nicotine use

No Smoke Less Harm

Demonstrating the benefit for Public Health of Sweden's "No Smoke, Less Harm" approach

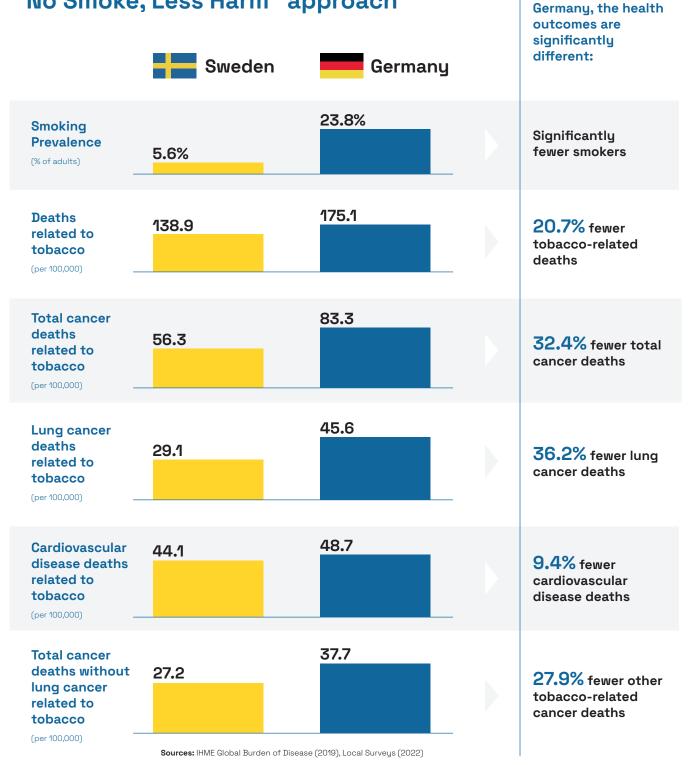




While people in Sweden consume

similar amounts of nicotine to those in

Demonstrating the benefit for Public Health of Sweden's "No Smoke, Less Harm" approach



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While people in

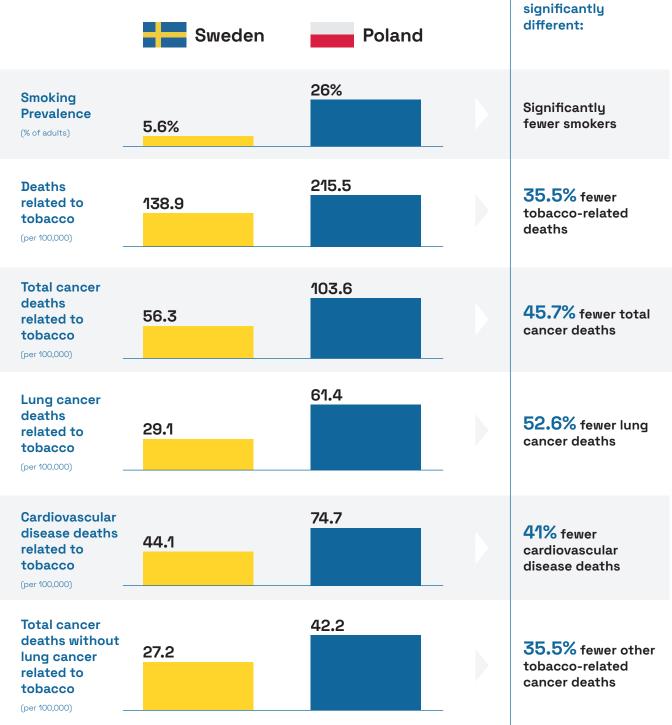
Sweden consume

similar amounts of nicotine to those in

Poland, the health outcomes are

No Smoke Less Harm

Demonstrating the benefit for Public Health of Sweden's "No Smoke, Less Harm" approach



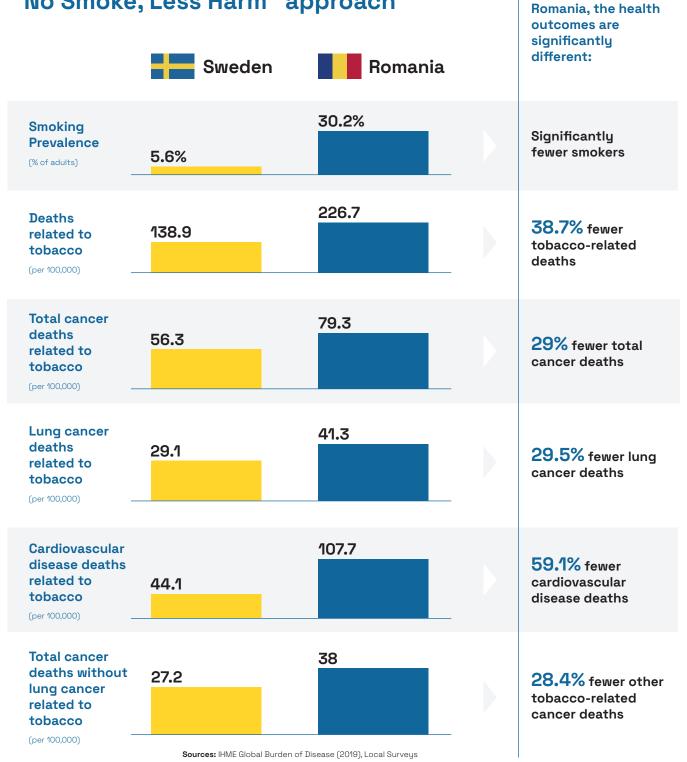
Sources: IHME Global Burden of Disease (2019), Local Surveys (2022)



While people in Sweden consume

similar amounts of nicotine to those in

Demonstrating the benefit for Public Health of Sweden's "No Smoke, Less Harm" approach



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Annex C: Resources

- Letter to WHO by 100 top scientists
- Position Statement by 15 former Presidents of the Society for <u>Research on Tobacco and Nicotine (SRNT)</u>
- The Swedish Experience
- Saving Lives like Sweden Report
- Learnings from Smoke-Free Sweden: A Global Consultation
- <u>COP 10 Scorecard</u>
- Lives Saved in LMICs
- Lives Saved (Brazil)
- THR E-Book (on thr.net)
- Oral Nicotine Commission Report (on oralnicotine.com)
- Snus Commission Reports



About the Authors



KONSTANTINOS FARSALINOS, MD, MPH IS A PHYSICIAN AND A RE-SEARCH ASSOCIATE AT THE UNIVERSITY OF PATRAS AND THE UNI-VERSITY OF WEST ATTICA IN GREECE.

His field of expertise is Public Health. He has been conducting laboratory, clinical and epidemiological research on smoking, tobacco harm reduction and nicotine products as principal investigator since 2011. He authored the first systematic review on e-cigarette safety/risk profile, published in 2014. Additionally, he has performed research and published studies on heated tobacco products. His findings have been presented in major international scientific congresses and his studies were used in preparing the regulatory framework on e-cigarettes by the European Union in 2014. As of early 2024, he has published more than 100 studies and articles in international peer-reviewed scientific journals, mostly about smoking, tobacco harm reduction and alternative-to-smoking nicotine products. He has presented in more than 80 international conferences, and he was the handling editor and author of a book titled "Analytical assessment of e-cigarettes", published by Elsevier in 2017. In November 2020, he was declared a Highly Cited Researcher 2019 by the Web of Science, a list of researchers (6200 scientists out of 9 million examined) with the highest impact in global science in 21 scientific fields in the past decade. During the COVID-19 pandemic, he has published 10 peer-reviewed articles and several pre-prints about COVID-19, including the association between smoking, nicotine and COVID-19.



PROF. KARL-OLOV FAGERSTRÖM - SWEDEN

Prof. Karl Fagerström is a psychologist and founding member of the Society for Research on Nicotine and Tobacco (SRNT). He was awarded the World Health Organization medal in 1999 for his outstanding work in tobacco control. In 2013 he was the recipient of the Award on Clinical Science from the Society for Research on Tobacco and Nicotine. He has been part of the early development of the Nicotine Replacement products and developed the first non-tobacco nicotine pouch.



DR. ANDERS MILTON - SWEDEN

Dr. Milton is a physician with extensive experience in public service, a highly sought-after consultant in the healthcare sector and a former chair of the WMA. Currently the owner and CEO of Milton Consulting and current chair of the Snus Commission. He is the Chairman of the Board of three foundations that work with education for children and adolescents and several for-profit companies in the field of life science. Dr. Milton's resumé also includes stints as President and CEO of the Swedish Medical Association (SMA), and as President of the Swedish Red Cross, the People and Defence Foundation and the Swedish Confederation of Professional Associations (SACO).



DR. DELON HUMAN - SOUTH AFRICA, FRANCE

Dr. Delon Human is a specialist family physician, global health advocate, published author, international speaker and health care consultant specialising in global health strategy, harm reduction and health communication. He is the former Secretary-General of the World Medical Association, International Food and Beverage Alliance and Co-founder of the African Harm Reduction Alliance (AHRA). He has acted as an adviser to three WHO Directors-General and to the UN Secretary-General on global public health strategies.



PROF. MIHAELA RĂESCU - ROMANIA

Prof. Dr. Răescu (Dentist) teaches Oral and Dental Prevention at the Faculty of Dental Medicine of the "Titu Maiorescu" University in Bucharest, Romania since 2003 and has been a tenured professor since 2015, in addition to being an active practitioner and a Specialty Doctor, Dr. Răescu has authored and co-authored numerous studies and publications and has been a guest speaker at various professional conferences.



DR. S. ABBAS RAZA - PAKISTAN

Dr. Raza is currently a Consultant Endocrinologist at Shaukat Khanum Hospital and Research Center in Pakistan and National Defence Hospital in Lahore, Pakistan, since 2004. He received his medical degree from Allama Iqbal Medical College, Lahore, and was Chief Medical Resident at Atlantic City Medical Center, NJ, USA. Fellowship in Diabetes, Endocrinology and Metabolism was completed at University Wisconsin, Madison, USA. Dr Raza is American Board Certified in Internal Medicine, and in Endocrinology, Diabetes and Metabolism. He has presented extensively on diabetes and endocrinology throughout his career and has received numerous awards in recognition of his contributions to this field. He has been Awarded Tamghae-Imtiaz by the President of Pakistan for services in the field of Medicine. Dr Raza is an Executive Member (since 2004) and President of International Society of Endocrinology (2022- 2024), Past-President of the Pakistan Endocrine Society (PES), South Asian Federation of Endocrine Societies (SAFES) and Pakistan Chapter of American Association of Clinical Endocrinologist. He was also previously on the Board of Directors for the American Association of Clinical Endocrinologists (AACE) (2003– 2004).



DR. GINTAUTAS- YUOZAS KENTRA - KAZAKHSTAN

Dr. Kentra is a Cardiologist and Deputy Chairman of the Council and member of the Expert. Council of the Densaulyk ULL, which is the Harm Reduction Association of Kazakhstan, focusing on the institutionalisation of harm reduction in non-communicable diseases.





DR. KGOSI LETLAPE - SOUTH AFRICA

Dr. Kgosi Letlape is an ophthalmologist from South Africa and is currently a founding member of the Africa Harm Reduction Alliance (AHRA), a former president of the Health Professions Council and chairman of the Medical and Dental Board of South Africa. He is the current president of the Africa Medical Association and president of the Association of Medical Councils of Africa. He is also past chairman of the board of the South African Medical Association (SAMA) and past president of the World Medical Association (WMA), the global representative body for physicians. He was admitted as a fellow of the College of Surgeons of South Africa in April 1988 and as a fellow of the Royal College of Surgeons of Edinburgh for ophthalmology in May 1988. He has the distinction of being the first black African to qualify as an ophthalmologist in Southfield, South Africa, and the first to become president of the WMA. Internationally, Dr. Letlape has been closely involved in policy on a range of issues – from the ethics of clinical research to health care systems and the FCTC. During the last decade, he has focused on harm reduction policy and science. He brings to the table superior, world-class skills of leadership, advocacy and policy insight.



PROF. SOLOMON TSHIMONG RATAEMANE - SOUTH AFRICA

Prof Solomon Tshimong Rataemane is the former head of Department of Psychiatry at the University of Limpopo (MEDUNSA CAMPUS in Pretoria). He has special interest in child psychiatry, mood disorders and addiction medicine. He has served as deputy chairperson and chairperson of the Central Drug Authority of South Africa from 1995 to 2005. He is currently involved with UCLA Substance Abuse Program in collaborative research to improve Cognitive Behavior Therapy for counsellors at SANCA Clinics in South Africa. He is a Board member of ICAA (International Council on Alcohol and Addictions) and serves on the Health Committee of the Health Professions of South Africa assisting in physicians' health management. He is currently the Interim Executive Dean of the Health Sciences Faculty of the University of Limpopo. The current engagements include an effort to develop policy and protocols for management of substance abuse. He was appointed Deputy Chair of the Medical Research Council of South Africa for the triennium 2007 -2010 and serves a third term as member of the Colleges of Psychiatry. He is a member of the following organisations, including the South African Society of Psychiatrists, Health Professions Council of South Africa, International Council on Alcohol and Addictions, World Psychiatric Association and the World Association for Social Psychiatry.



DR. DIEGO VERRASTRO - ARGENTINA

Dr. Diego Verrastro is a general surgeon, specialising in emergency medicine, abdominal mini-invasive surgery, ultrasonography and obesity. He is also spokesperson for RELDAT, The Latin American network for the reduction of tobacco-associated harm. In this role, he has called for further discussion of the merits of harm reduction in Latin America, drawing attention to the examples provided by other countries - including the UK, New Zealand and Sweden.



PROF. HEINO STÖVER - GERMANY

Prof. Stöver is a social scientist and Professor of Social Scientific Addiction Research at the Frankfurt University of Applied Sciences in Germany, Faculty of Health and Social Work. Since 2009 he has been the director of the Institute of Addiction Research. Heino Stöver's main fields of research and project development expertise are health promotion for vulnerable and marginalised groups, drug services, prison health care and related health issues (especially HIV/AIDS, Hepatitis C, drug dependence, and gender issues), and the potential of e-cigarettes. His international research and consultancy expertise includes working as a consultant for the European Commission, United Nations Office on Drugs and Crime (UNODC), World Health Organization (WHO), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), International Committee of the Red Cross (ICRC) and Open Society Institute (OSI) in various contexts.



DR. ANOOP MISRA - INDIA

Dr. Anoop Misra is an Indian endocrinologist and a former honorary physician to the Prime Minister of India. He is the chairman of Fortis Centre for Diabetes, Obesity and Cholesterol (C-DOC) and heads, National Diabetes Obesity and Cholesterol Foundation (NDOC). A former Fellow of the World Health Organization at the Royal Free Hospital, UK, Misra is a recipient of the Dr. B. C. Roy Award, the highest Indian award in the medical category. The Government of India awarded him the fourth highest civilian honour of the Padma Shri, in 2007, for his contributions to Indian medicine.



DR. HIROYA KUMAMARU - JAPAN

Cardiovascular surgeon. Hiroya Kumamaru is vice director of AOI International Hospital in Kawasaki, Japan, a position he has held since April 2013. A graduate from the School of Medicine at Keio University, Kumamaru studied cardiovascular surgery in Europe and the United States. His professional experience includes time spent as director of the K.I. Akihabara Clinic (July2008 to March 2013), chief surgeon of the department of cardiovascular surgery at Kawasaki Municipal Hospital, Kanagawa (July 2005 to March 2008) and senior cardiovascular medical director and group leader of clinical scientific affairs at Pfizer Japan (April 1996 to June 2005). His current major project is to determine how preventive medicine can minimize future health care costs. www.smokefreesweden.org







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