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Estimated Public Health Gains From German Smokers Switching to Reduced-Risk Alternatives: Results From Population Health Impact Modelling *

by

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SUMMARY

Background: Smoking is associated with cancer and cardio-respiratory mortality. Reducing smoking prevalence will lead to fewer deaths and more life-years. Here, we estimate the impact of hypothetical introduction of reduced-risk products (heat-not-burn products and e-cigarettes) in Germany from 1995 to 2015 on mortality from lung cancer, chronic obstructive pulmonary disease, ischaemic heart disease, and stroke in men and women aged 30–79 years.
Methods: We used a previously described population health impact model, with individuals with a defined baseline cigarette smoking distribution followed under a "Null Scenario", with reduced-risk products never introduced, and various "Alternative Scenarios" where they are. Transition probabilities allow product use to change annually, with the individual product histories allowing estimation of risks, relative to never users, which are then used to estimate reductions in deaths and life-years lost for each Alternative Scenario.
Results: In the Null Scenario, we estimated 852,000 deaths from cigarette smoking (42,600 per year), with 8.61 million life-years lost. Had everyone ceased smoking in 1995, and with no use of reduced-risk products, these numbers would reduce by 217,000 and 2.88 million. Compared to the Null Scenario, the estimated reductions would be 159,000 and 2.06 million with an immediate complete switch to heat-not-burn products and 179,000 and 2.34 million with 50% of smokers immediately switching to heat-not-burn products and 50% to e-cigarettes. In four Scenarios with a more gradual switch, the estimated decreases were 39,800–81,000 deaths and 0.50–1.05 million life-years, representing 17.5%–37.5% of the effect of immediate cessation in 1995. These estimates assume that switching to heat-not-burn products and e-cigarettes involves risk decreases of 80% and 95% of those from quitting, respectively. The reductions in mortality would be greater with more diseases and a wider age range considered or with a longer follow-up period, as the decreases increased markedly with time. Various limitations are discussed, none affecting the conclusion that introducing these new products into Germany in 1995 could have substantially reduced deaths and life-years lost.
Conclusions: Deaths from cigarette smoking could be substantially reduced not only by cessation but additionally by switching to reduced-risk products. Respective public health campaigns might increase such switching. [Contrib. Tob. Nicotine Res. 31 (2022) 35–51]

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KEYWORDS

Smoking; public health; modelling; lung cancer; chronic obstructive pulmonary disease; ischaemic heart disease; stroke; e-cigarettes; heat-not-burn product; Germany;

ZUSAMMENFASSUNG

Hintergrund: Rauchen ist mit Krebs und kardiorespiratorischer Mortalität verbunden. Eine Verringerung der Raucherprävalenz würde die Todesfälle reduzieren und die Lebensjahre erhöhen. Hier schätzen wir die Auswirkung der hypothetischen Einführung von Produkten mit geringerem Risiko (Tabakerhitzer und E-Zigaretten) zwischen 1995 und 2015 in Deutschland auf die Mortalität durch Lungenkrebs, chronisch obstruktive Lungenerkrankung, ischämische Herzkrankheit und Schlaganfall bei 30- bis 79-jährigen Männern und Frauen.
Methoden: Wir verwendeten ein zuvor beschriebenes Modell zur Beurteilung der Auswirkungen auf die Gesundheit der Bevölkerung, in welchem Individuen mit einer zum Ausgangszeitpunkt definierten Verteilung des Zigarettenrauchens in einem „Null-Szenario", in dem Produkte mit geringerem Risiko nie eingeführt wurden, und verschiedenen „alternativen Szenarien", in denen diese eingeführt wurden, nachbeobachtet werden. Übergangswahrscheinlichkeiten ermöglichen einen jährlichen Wechsel in der Produktnutzung, wobei individuelle Nutzungshistorien die Einschätzung der Risiken im Vergleich zu Nienutzern ermöglichen. Hierdurch lässt sich die Abnahme der Todesfälle und der verlorenen Lebensjahre für jedes alternative Szenario schätzen.
Ergebnisse: Im Null-Szenario wurde die Anzahl der Todesfälle durch Zigarettenrauchen auf 852.000 (42.600 pro Jahr) und die der verlorenen Lebensjahre auf 8,61 Millionen geschätzt. Wenn 1995 alle Personen mit dem Rauchen aufgehört und keine Produkte mit geringerem Risiko genutzt hätten, würden sich diese Zahlen um 217.000 bzw. 2,88 Millionen reduzieren. Im Vergleich zum Null-Szenario würden die geschätzten Rückgänge bei einem sofortigen und kompletten Umstieg auf Tabakerhitzer 159.000 bzw. 2,06 Millionen und bei einem sofortigen Umstieg von 50% der Raucher auf Tabakerhitzer sowie 50% auf E-Zigaretten 179.000 bzw. 2,34 Millionen betragen. In vier Szenarien mit einem graduelleren Umstieg lag die geschätzte Abnahme der Todesfälle bei 39.800–81.000 und die der Lebensjahre bei 0,50–1,05 Millionen, was 17,5–37,5% des Effekts des sofortigen Rauchstopps im Jahr 1995 entspricht. Diese Schätzungen gehen davon aus, dass der Umstieg auf Tabakerhitzer bzw. E-Zigaretten mit einer Risikoreduzierung von 80% bzw. 95% in Bezug auf diejenige des Rauchstopps einhergeht. Der Rückgang in der Mortalität wäre größer, wenn mehr Krankheitsarten und ein breiterer Altersbereich oder ein längerer Nachbeobachtungszeitraum berücksichtigt würden, da der Rückgang im Zeitverlauf deutlich ansteigt. Es werden verschiedene Einschränkungen diskutiert, wovon keine die Schlussfolgerung beeinflusst, dass die Einführung dieser neuen Produkte 1995 in Deutschland die Todesfälle und die verlorenen Lebensjahre erheblich verringert haben könnte.
Schlussfolgerungen: Die Anzahl der Todesfälle durch Zigarettenrauchen könnte nicht nur durch den Rauchstopp, sondern zusätzlich auch durch den Umstieg auf Produkte mit geringerem Risiko erheblich gesenkt werden. Entsprechende Aufklärungskampagnen der öffentlichen Gesundheit könnten einen solchen Umstieg begünstigen. [Contrib. Tob. Nicotine Res. 31 (2022) 35–51]

RESUME

Contexte: Le tabagisme est associé à la mortalité par cancer et par maladie cardiorespiratoire. Une réduction de la prévalence du tabagisme entraînera une réduction des décès et une augmentation du nombre d'années de vie. Dans cet article, nous estimons l'impact de l'introduction hypothétique de produits à risque réduit (produits de tabac chauffé et cigarette électronique) en Allemagne entre 1995 et 2015 sur la mortalité par cancer des poumons, bronchopneumopathie chronique obstructive, cardiomyopathie ischémique et accident vasculaire cérébral chez des hommes et des femmes âgés de 30 à 79 ans.
Méthodes: Nous avons utilisé un modèle d'impact sur la santé publique précédemment décrit: des sujets présentant un niveau de consommation de cigarettes déterminé lors de leur inclusion dans ce modèle, ont été suivis soit selon un « Scénario Nul » (sans introduction de produits à risque réduit) soit plusieurs « Scénarios Alternatifs » (avec introduction de produits à risque réduit). Les probabilités de transition permettent un changement annuel des produits utilisés. L'historique des produits utilisés par chaque sujet permet d'évaluer les risques par rapport à des sujets n'ayant jamais utilisé ces produits, et ainsi d'estimer la réduction du nombre de décès et d'années de vie perdues pour chaque scénario alternatif.
Résultats: Dans le Scénario Nul, nous avons estimé à 852.000 le nombre de décès dus au tabagisme par cigarette (42.600 par an) et à 8,61 millions le nombre d'années de vie perdues. Si tous les fumeurs avaient arrêté de fumer en 1995, sans qu'aucun n'ait consommé de produits à risque réduit, ces chiffres auraient baissé de 217.000 et de 2,88 millions. Par rapport au Scénario Nul, le nombre de décès et le nombre d'années de vie perdues auraient baissé de 159.000 et de 2,06 millions en cas de conversion immédiate et totale aux produits de tabac chauffés ; ces baisses auraient été de 179.000 et de 2,34 millions si 50% des fumeurs avaient remplacé la cigarette par le tabac chauffé et 50% par la cigarette électronique. Dans les quatre scénarios prévoyant une conversion plus progressive, les réductions étaient comprises entre 39.800 et 81.000 pour les décès et entre 0,50 et 1,05 million pour les années de vie, soit 17,5 % à 37,5 % comparé à l'effet de l'arrêt immédiat du tabagisme en 1995. Ces estimations reposent sur l'hypothèse que le passage aux produits de tabac chauffé et à la cigarette électronique est associé à une diminution des risques de respectivement 80% et 95% par rapport à la baisse observée avec l'arrêt du tabagisme. Les baisses de la mortalité seraient plus importantes si davantage de maladies et une tranche d'âge plus large étaient prises en compte, ou si la période de suivi était plus longue car ces diminutions s'accentuent nettement avec le temps. Plusieurs limites sont abordées dans la discussion, mais aucune ne modifie la conclusion selon laquelle l'intro-

duction de ces nouveaux produits en Allemagne en 1995 aurait pu réduire considérablement le nombre de décès et d'années de vie perdues.
Conclusions: Le nombre de décès liés au tabagisme par cigarette pourrait être sensiblement réduit, non seulement grâce à l'arrêt du tabagisme mais également grâce au passage à des produits à risque réduit. Ce passage pourrait être favorisé par des réglementations et des campagnes de santé publique. [Contrib. Tob. Nicotine Res. 31 (2022) 35–51]

ABBREVIATIONS	
CC	conventional cigarette
COPD	chronic obstructive pulmonary disease
DD	drop in deaths
ECig	e-cigarette
E-component	epidemiologic component
H	half-life
HnB	heat-not-burn
IHD	ischaemic heart disease
LC	lung cancer
NEM	negative exponential model
P-component	prevalence component
PHIM	population health impact modelling
RR	relative risk
RRP	reduced-risk product
SRD	smoking-related deaths
TP	transition probability
WHO	World Health Organization
YLL	years of life lost
YLS	years of life saved

INTRODUCTION

Smoking represents the greatest avoidable risk factor for health (1, 2). Nevertheless, the World Health Organization (WHO) estimates there will be 1.1 billion smokers globally in 2025 (3). In Germany, smoking prevalence is around 28%, with no change since 2016 (4), and numbers of quit attempts are currently decreasing (5). In 2013, an estimated 125,000 people died from smoking-related diseases in Germany (6).
Clearly, smokers would best quit all nicotine and tobacco use at once, but many do not. Recently, increasing numbers of public health experts institutions have embraced tobacco harm reduction as a complementary tool to existing control efforts (7–12). This is directed at adults who would otherwise continue to smoke conventional cigarettes (CCs), aiming to encourage them to switch to smoke-free alternatives such as snus, the e-cigarette (ECig), or the heat-not-burn product (HnB). The aerosols of ECigs and HnBs have been shown to contain toxicant levels lower by an average of > 90% compared with cigarette smoke (13–15).
The proof of principle for tobacco harm reduction comes from epidemiological findings spanning decades from Swedish smokers switching to snus, so that smoking rates and smoking-related mortality in Sweden are the lowest in Europe (16). The efficacy of ECigs in randomized controlled trials to support abandoning CCs (17), coupled with their high acceptance by smokers wishing to replace CCs, could explain the observation that ECigs have contributed to 50,000 to 70,000 additional smokers abandoning cigarettes in the UK per year (18). At the same time, youth initiation continues to be low in the UK and New Zealand (19, 20), and there seems to exist an inverse relationship between youth vaping and smoking (21), with common liabilities suggesting ECigs may have replaced CC smoking (22). In Japan, 20% of smokers have switched to HnBs, which plausibly contributes to the unprecedented drop in cigarette sales seen there (23). These facts suggest that both ECigs and HnBs could help to reduce smoking-attributed morbidity and mortality.
In Germany, ECigs have been available since 2007, current users now forming about 1–3% of the population aged 14 or over [(4), https://www.debra-study.info/], with a 30-day prevalence of 6.9% among young adults (24). HnB products only became available later, in 2016, with numbers of users estimated to have risen from about 36,000 in 2017 to 300,000 in 2019, then forming about 0.4% of the population aged 18 or over, according to Philip Morris market research, with others reporting 0.3% for overall current use (25) and 1.3% for 30-day prevalence among 18- to 25-year-old young adults (24), respectively. Both ECigs and HnBs are predominantly used by current or former smokers, and only by few never-smokers (4). Among 12- to 17-year-olds, use in the last 30 days, not necessarily a good marker for regular use, remains low at 4.1% for ECigs and 0.1% for HnBs (26).
Our main objective is to estimate the population health impact of introducing HnBs or ECigs into Germany during 1995–2015 under various assumptions about their rate of uptake. We compare our estimates to a set of extreme scenarios, including those derived assuming the whole population ceased smoking cigarettes immediately. The estimated effect sizes could inform cost-benefit assessments by German public health authorities and regulators on tools aimed at steering smokers away from cigarettes, preferably by cessation, but, for smokers continuing to smoke, also by switching to reduced risk products (RRPs). To avoid uncertainty about the future, including the effect on future mortality rates of factors such as medical progress and disease epidemics, we use a "hindcasting" approach, in which individuals start in 1995, with a nationally representative distribution of cigarette smoking, then being followed until 2015 under various assumptions. This approach has previously been used to assess the population health impact of introducing HnBs into the US (27, 28) and Japanese (29) markets. Here, we have considered both HnBs and ECigs. Both can be termed RRPs – products considered likely to present less risk of harm to cigarette smokers who switch to them.
The approach generates estimates of numbers of smoking-related deaths (SRD) and number of years of life lost (YLL) in scenarios where RRPs are or are not introduced, the difference between the two scenarios being termed the drop in deaths (DD) and number of years of life saved (YLS). These are calculated separately for the main diseases related to cigarette smoking, lung cancer (LC), chronic obstructive pulmonary disease (COPD), ischaemic heart disease (IHD), and stroke. While the term SRD normally refers to the additional deaths arising from cigarette

smoking, here it is used to refer to the additional deaths arising from the use of cigarettes, HnBs, or ECigs.

MATERIALS AND METHODS

Outline of the approach used in population health impact modelling (PHIM)

The basic method used for estimating the impact of introducing an RRP into a country is as described earlier (30), and involves two components, the Prevalence (P-) component and the Epidemiologic (E-) component.

The P-component starts in a specified year with individuals of a given sex and age range with a defined cigarette smoking distribution. This group is then followed over discrete time intervals under a "Null Scenario" and various "Alternative Scenarios", by using different sets of transition probabilities (TPs). In the Null Scenario, RRPs are never introduced, and each individual's cigarette smoking status (never, current, or former) is updated yearly. In each Alternative Scenario, RRPs are introduced during follow-up, and the TPs allow for switching between six groups (never user, current exclusive cigarette smoker, current exclusive HnB user, current exclusive ECig user, current multiple product user, and former product user). "Never users" have never used cigarettes or either of the two RRPs considered. "Current multiple product users" currently use two or three of the products considered, while "former product users" have previously used at least one product but currently do not use any. At the end of the P-component, each individual has a complete history of product use over the follow-up period under each scenario. The modelling ignores products other than cigarettes, ECigs, and HnBs.

The E-component then uses the product histories to estimate, for each individual, the relative risk (RR), compared to never users, of LC, COPD, IHD, and stroke for each follow-up year and scenario. The estimation involves an extension of the negative exponential model (NEM), allowing for multiple changes in use, fully described elsewhere (27). The NEM requires estimates of the RR for continued smoking for each of the four diseases, the quitting half-life (H) – i.e., the time from quitting when the excess relative risk (RR−1) declines to half of that for continuing smokers – and also estimates of the effective doses for current exclusive HnB use, exclusive ECig use, and multiple product use relative to that for current cigarette smoking (taken as one unit). The decline of the excess relative risk by time since quitting cigarette smoking is well described using a NEM for LC (31), COPD (32), IHD (33), and stroke (34).

The estimation of the RR for an individual does not specifically take into account the amount smoked, but the effective dose for multiple product users may be set to reflect a reduced cigarette consumption. A discussion of how the effective dose may be quantified for an RRP is given elsewhere (30).

For each scenario, the average RR for each disease for individuals of a given sex and age group is then calculated for each follow-up year, from which the proportions of SRD can be derived. These are then converted to numbers using national mortality estimates by sex, age group, and year. The differences in estimated numbers and proportions between the scenarios then quantify the effect of RRP introduction.

For a given scenario, YLL is estimated using the method of GARDNER and SANBORN (35). YLS is then calculated from the difference in YLL between the Alternative and Null Scenarios.

Each of the individuals in each scenario is followed up over the whole period considered, with no removals for death. While, the estimates of DD and YLS assume that the size of the populations of risk remains the same during follow-up, with no correction for differential survival, a correction can be made if required (30).

The methodology can also compare the Null Scenario with Alternative Scenarios where RRPs are not introduced but where different sets of TPs for cigarette smoking are used.

The modelling starts with a population aged 10–79 years, individuals dropping out of the calculations as they reach 80 years of age. This is partly because cause of death certification is unreliable at an older age and partly as our estimates of population health impact also include YLS, which is unaffected by deaths above the age of 74 years.

Common features of each simulation

Each simulation involved follow-up of 100,000 individuals in 1-year intervals from 1995, with the product use status of each individual estimated at each year of follow-up until the year 2015 (or age 79, if that came earlier). For each situation described, separate simulations were conducted for each sex.

Population at baseline

As previously described (27), each individual in a simulation is allocated at the start of the P-component to a year of age, then to a cigarette smoking group (never, current, or former), and, then, for former smokers, to an age of quitting, based on random numbers and the relevant distributions for Germany.

The sex-specific age distributions used for Germany for 1995 are as published by the United Nations (36).

Sex- and age-specific distributions of current and former smoking prevalence for Germany for individual years from 1995 to 2015 were derived by combining data from three sources: International Smoking Statistics (37), which provides results by 5-year age groups from 1980–2015 for current smoking; a report by FOREY and LEE (2012) (38), which provides results by 15-year age groups from 1980–2005 for former smoking; and the German Socioeconomic Panel (39), which provides data for 2002 and 2012 for current and former smoking.

The sex- and age-specific distribution of time quit for former smokers used for the baseline population in 1995 was taken, in the absence of alternative data, from estimates for 2002 derived from the German Socioeconomic Panel (39). Because this source only provided data for age groups 20–24 and above, data for younger age groups were taken from US estimates for 2006 (27).

Additional File S1 gives further details on the derivation of the data on current and former smoking prevalence and

time quit. It also includes tables summarizing the age-specific distribution of the population and the data on smoking habits used to assign the initial status of each member of the simulated population in 1995.

Estimation of histories of cigarette smoking for the Null Scenario

The sex- and age-specific TPs used in the P-component for developing the histories of cigarette smoking for the Null Scenario were derived as described in Additional File S2 and are shown in Table 1. To test the validity of the TPs, the prevalences predicted by using them were compared with the estimates for Germany derived for years up to 2015 as described in Additional File S1.

Estimation of histories of product use for the Alternative Scenarios

Seven different Alternative Scenarios were tested and are summarized in Table 2; Scenarios 1 to 3 are termed "Extreme Scenarios" and Scenarios 4 to 7 "Pragmatic Scenarios". Together with the Null Scenario, which reflects the actual observed smoking prevalence in Germany in 1995-2015, the Extreme Scenarios calculate theoretical maximum effects of immediate cessation or immediate switch to RRPs. The Pragmatic Scenarios were designed to reflect a range of more gradual potential uptake rates of HnBs and ECigs, loosely based on early market data for Germany and international RRP uptake dynamics by 2019, with Scenario 4 (the "Conservative Scenario") being a more pessimistic one, Scenario 5 (the "Dynamic Scenario") an intermediate one and Scenarios 6 (the "Conversion Scenario") and 7 (the "Full Conversion Scenario") more optimistic ones. Exclusive RRP users are defined as the estimated number of Legal Age (over 18 years old) users that used the RRP for 100% of their daily nicotine product consumption over the past 7 days.

No RRP is introduced in Alternative Scenario 1. For the other six Alternative Scenarios, the effective doses are assumed to be 0.2 for exclusive HnB use and 0.05 for exclusive ECig use, in contrast to an effective dose of 1 for exclusive cigarette smoking. The value for HnBs was based on biomarkers and clinical findings (40), and for ECigs on a published expert opinion (41). For multiple product use, the effective dose is assumed to be the mean of the three effective doses (i.e., 0.42).

The TPs used in the P-component for developing usage histories in the Alternative Scenario are presented in Additional File S3. Note that, for each Alternative Scenario, the sum of the initiation TPs (for a given sex, age, and follow-up period) was constrained to equal the corresponding initiation TP for the Null Scenario. The same constraint was applied to the re-initiation TPs. Each cessation TP in the Alternative Scenario was also constrained to equal the cessation TP in the Null Scenario. These constraints were applied so that the various Alternative Scenarios considered only the effect of the RRPs introduced on the distribution of current effect sizes, without any effect on overall initiation, cessation, or re-initiation rates.

Estimating relative risks on the basis of product use histories

For each disease, the estimates of RR for continued cigarette smoking and of H were derived from published meta-analyses. The estimates and sources are given in Table 3.

The sex- and age-specific data on national population size for Germany for 1995 to 2015 are as published by the UNITED NATIONS DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS POPULATION DIVISION (36).

The data on numbers of deaths in Germany from LC, COPD, IHD, and stroke come from the WHO (42). The data on population size and numbers of deaths for Germany for 1995 to 2015 are presented in Additional File S4, which gives fuller details on sources and disease definitions.

The method of estimating the number of deaths and increase in death rates associated with tobacco is as described earlier (27). Unless indicated, results are presented without adjustment for changes in population size associated with each Alternative Scenario.

RESULTS

Comparing smoking prevalences simulated in the Null Scenario and those derived for Germany

Figure 1 compares never, current, and former smoking prevalence estimates for Germany by sex for years up to 2015 and for age groups 30–34, 50–54, and 70–74 years as simulated in the Null Scenario (broken lines) with those derived as described in the Methods section (solid lines). The fit is generally very good, though there is some tendency for the Null Scenario current smoking estimates to be lower than the derived estimates at age 70–74 years.

Predicted prevalence of tobacco product use for the Alternative Scenarios

Figure 2 presents the simulated estimates of product usage in the Conversion Scenario by sex, age (30–34, 50–54, and 70–74 years), and year (1995, 2000, 2005, 2010, and 2015). In 1995, the estimates for current, never and former product use are identical, as expected, to those for cigarette smoking in the Null Scenario shown in Fig 1. The proportions of never and former product users in Figure 1 and Figure 2 remain very similar over the whole time period. While in the Null Scenario, the current product users all smoke cigarettes, in the Conversion Scenario, they fall into four groups. Over the first 15 years, there is a large decline in exclusive cigarette smoking and a corresponding increase in the other three current product use categories. This pattern flattens out between 2010 and 2015, with some decline in some of the groups. Further details for the Conversion Scenario as well as other Pragmatic Scenarios are shown in Additional File S5.

Additional File S6 summarizes the current product use distributions in 2005 for all the scenarios. With regard to the distributions in 2005, after 10 years follow-up, there were, as expected, no current product users at all in Scenario 1, with all HnB users in Scenario 2 and half HnB and half ECig users in Scenario 3.

Table 1. Yearly transition probabilities (per million) in the Null Scenario for Germany.

Period (years)		Initiation (P_{NC})		Quitting (P_{CF})		Re-initiation (P_{FC})	
	Age	Men	Women	Men	Women	Men	Women
1–5	10–14	50,351	40,762	28,960	17,309	13,903	8,308
	15–19	67,051	77,814	46,165	82,605	22,164	39,653
	20–24	8,903	35,760	16,045	58,582	7,701	28,119
	25–29	6,699	8,653	24,172	37,175	11,602	17,840
	30–34	2,637	4,288	30,186	30,128	14,495	14,459
	35–39	0	0	26,610	9,641	12,765	4,634
	40–44	0	0	23,808	18,902	11,424	3,080
	45–49	0	0	27,218	19,232	9,796	1,559
	50–54	0	0	36,677	25,626	5,291	1,032
	55–59	0	0	40,739	33,146	2,912	684
	60–64	0	0	40,265	40,970	1,427	420
	65–69	0	0	55,101	26,610	960	264
	70–74	0	0	90,546	223,260	684	192
	75–79	0	0	90,546	223,260	684	192
6–10	10–14	42,977	35,249	24,477	26,200	11,756	12,575
	15–19	63,577	60,793	57,559	83,602	27,628	40,127
	20–24	6,174	23,515	11,626	60,079	5,578	28,832
	25–29	14,672	11,436	38,461	51,426	18,454	24,676
	30–34	3,953	5,649	35,122	29,264	16,860	14,045
	35–39	0	0	22,246	10,770	10,675	5,172
	40–44	0	0	20,917	25,907	9,558	3,104
	45–49	0	0	27,066	27,745	7,200	1,667
	50–54	0	0	43,070	31,795	5,172	960
	55–59	0	0	48,060	32,086	2,888	684
	60–64	0	0	46,430	39,282	2,529	420
	65–69	0	0	67,962	47,417	1,858	252
	70–74	0	0	55,785	177,670	1,367	180
	75–79	0	0	55,785	177,670	1,367	180
11+	10–14	34,053	24,583	21,858	42,274	10,497	20,281
	15–19	64,469	54,133	72,396	106,963	34,750	51,335
	20–24	3,869	9,165	6,914	53,403	3,319	25,626
	25–29	22,974	13,772	57,718	70,086	27,698	33,646
	30–34	5,948	6,783	42,366	24,888	20,328	11,946
	35–39	0	0	17,321	11,079	8,308	5,315
	40–44	0	0	18,489	36,711	7,152	4,407
	45–49	0	0	30,676	35,749	4,574	2,792
	50–54	0	0	49,103	35,458	3,678	2,170
	55–59	0	0	54,714	28,960	2,050	1,655
	60–64	0	0	51,438	32,040	1,954	876
	65–69	0	0	87,902	27,523	1,631	492
	70–74	0	0	18,737	63,915	432	372
	75–79	0	0	18,737	63,915	684	192

The first period relates to 5 years starting from 1995, the second to 5 years starting from 2000, and the third to 10 years starting from 2005. The transition probabilities between the three states N (never), C (current), and F (former) are described by P followed by two subscripts, the first representing the state changed from and the second the state changed to.
Note that RRPs are not introduced in the Null Scenario.

Table 3. Assumed relative risk for continued smoking and quitting half-life by disease for Germany.

	Age (years)	LC	COPD	Stroke	IHD
Relative risk	Any	8.68	3.31	–	–
	to 54	–	–	2.48	3.38
	55–64	–	–	2.13	2.32
	65–74	–	–	1.39	1.70
	75–79	–	–	1.06	1.27
Half-life	Any	–	13.32	4.78	–
	to 49	6.98	–	–	1.47
	50–59	10.39	–	–	5.22
	60–69	10.60	–	–	7.48
	70–79	12.99	–	–	13.77

See (27) for the sorces of these estimates.

In the Pragmatic Scenarios, the proportions of exclusive cigarette smokers decrease and those of exclusive HnB and ECig users increase from Scenarios 4 to 7. Relative to Scenario 5, the proportions of multiple product users decline in Scenarios 6 and 7. In 2010 (and also at other time points) the overall prevalence of current product users is essentially the same in each of Scenarios 2 to 7. This represents a drop of about 25% in men and 12% in women relative to the proportions in 1995.

Smoking-related deaths and loss of life in the Null Scenario

As estimated by the E-component of PHIM, 852,000 deaths from LC, COPD, IHD, and stroke combined for both sexes, were attributed to cigarette smoking over the period of 20 years from 1995 to 2015, in the absence of any switching to HnBs or ECigs and with the patterns of prevalence of cigarette smoking as existing in Germany (our Null Scenario).

Table 2. The Alternative Scenarios.

Scenario Number	Name	Summary description and comments
Extreme Scenarios		
1	Complete cessation	In 1995, all current cigarette smokers immediately stop smoking. There is no further initiation or re-initiation of cigarettes, HnB, or ECig use.
2	Complete switch to RRPs (HnBs)	In 1995, all current cigarette smokers immediately switch to HnBs. The subsequent initiation, re-initiation, and quitting rates are as in the Null Scenario, but only involve transfers in or out of HnBs.
3	Complete switch to RRPs (50% HnBs and 50% ECigs)	In 1995, all current cigarette smokers immediately switch to either HnBs or ECigs with equal probability. The subsequent rates are as in the Null Scenario, but only involve transfers involving the new products.
Pragmatic Scenarios		
4	Conservative Scenario	HnB: The market share in 2005 is 9% of that in 1995 for cigarette smoking, with 67% exclusive users. ECig: The market share in 2005 is 27% of that in 1995 for cigarette smoking, with 40% exclusive users. The calculated target distributions for 2005 are: Never / Cig only / HnB only / ECig only / Multiple use / Former use *Men*: 35.46 / 24.22 / 2.28 / 4.09 / 7.25 / 26.70 *Women*: 60.56 / 15.64 / 1.47 / 2.64 / 4.68 / 15.01 Note: Multiple (product) users currently use at least one of the three products, while former (product) users have used at least one of the products, but do not currently use an). The sum of the TPs for initiation and the sum of the TPs for re-initiation are the same as that for the Null Scenario. Each quitting TP is as for the Null Scenario. The difference between the four Pragmatic Scenarios only relates to the rates of switching among the three products.
5	Dynamic Scenario	The market shares in 2005 increase to 15.5% for HnBs and 36.4% for ECigs. The proportions of exclusive users are as in the Conservative Scenario. The calculated target distributions for 2005 are: Never / Cig only / HnB only / ECig only / Multiple use / Former use *Men*: 35.46 / 18.20 / 3.93 / 5.51 / 10.20 / 26.70 *Women*: 60.56 / 11.75 / 2.54 / 3.56 / 6.59 / 15.01 The rates of switching from exclusive cigarette smoking are increased from those in the Conservative Scenario.
6	Conversion Scenario	The same as the Dynamic Scenario, except that the proportions of exclusive users rise to 84% for both RRPs. The calculated target distributions for 2005 are: Never / Cig only / HnB only / ECig only / Multiple use / Former use *Men*: 35.46 / 18.20 / 4.93 / 11.57 / 3.14 / 26.70 *Women*: 60.56 / 11.75 / 3.18 / 7.47 / 2.03 / 15.01 Relative to the Dynamic Scenario, all 12 possible rates of switching vary, except those of switching from exclusive use of one RRP to exclusive use of the other.
7	Full Conversion Scenario	The same as the Dynamic Scenario, except that the proportions of exclusive users rise to 100% for both RRPs. The calculated target distributions for 2005 are: Never / Cig only / HnB only / ECig only / Multiple use / Former use *Men*: 35.46 / 18.20 / 5.87 / 13.87 / 0.00 / 26.70 *Women*: 60.56 / 11.75 / 3.79 / 8.89 / 0.00 / 15.01 The comment for the Conversion Scenario applies here as well.

Abbreviations used: Cig = cigarette; ECig = e-cigarette; HnB = heat-not-burn; TP = transition probability;

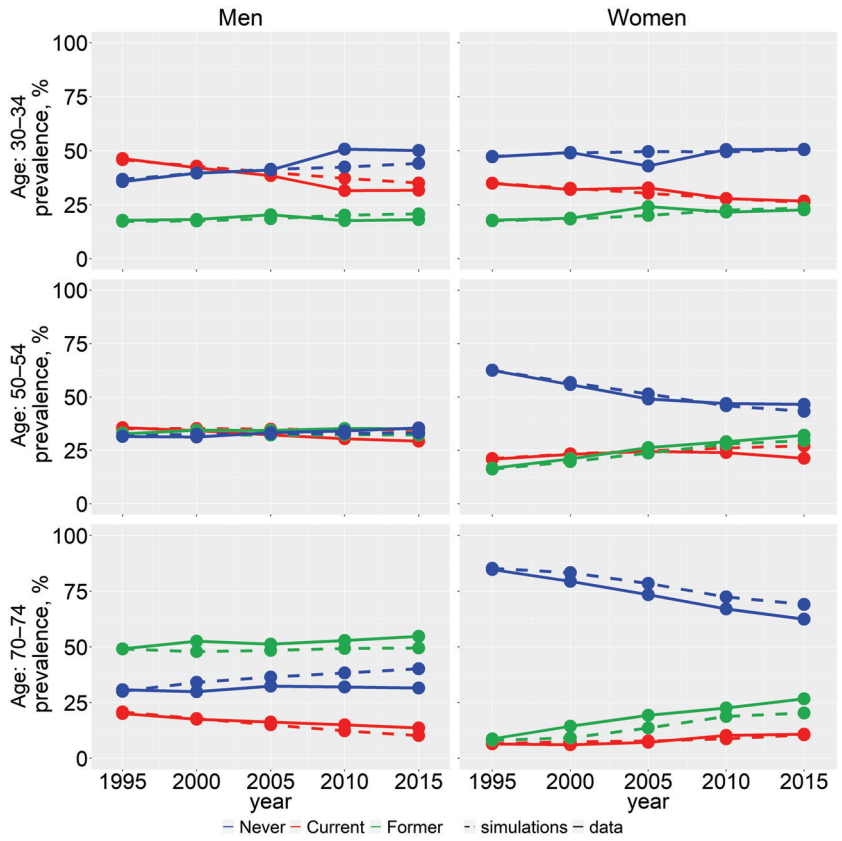


Figure 1. Comparison of Null Scenario and derived estimates of current smoker prevalence.

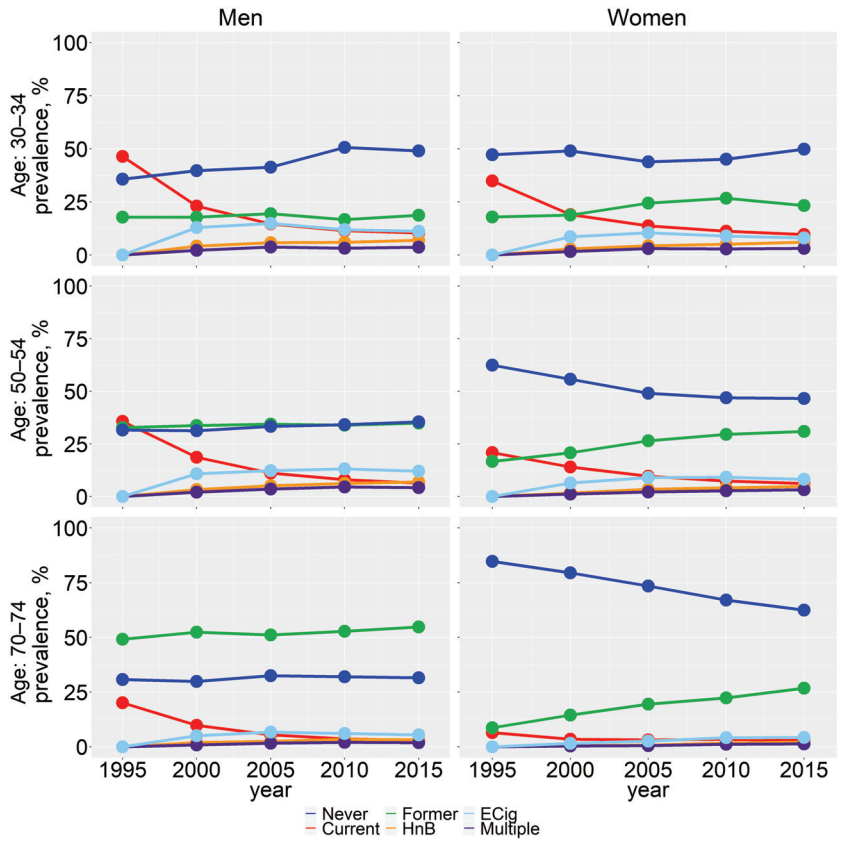


Figure 2. Product usage in the Conversion Scenario. Abbreviations used: ECig = e-cigarettes; HnB = heat-not-burn;

Table 4. Drop in deaths in Germany over the whole follow-up period for the seven Alternative Scenarios.

		Drop in deaths					% Drop in deaths				
	Sex/Scenario	LC	IHD	Stroke	COPD	All four diseases	LC	IHD	Stroke	COPD	All four diseases
Men											
1	Complete cessation	48,092	83,798	15,429	14,166	161,485	13.38	45.26	46.06	16.48	24.32
2	Complete switch to RRPs (HnBs)	34,148	61,591	11,783	10,820	118,342	9.50	33.27	35.17	12.59	17.82
3	Complete switch to RRPs (50% HnBs; 50% ECigs)	38,967	69,431	13,111	12,038	133,547	10.84	37.50	39.14	14.01	20.11
4	Conservative Scenario	8,316	16,144	3,286	2,969	30,714	2.31	8.72	9.81	3.46	4.63
5	Dynamic Scenario	13,437	25,533	5,136	4,680	48,785	3.74	13.79	15.33	5.44	7.35
6	Conversion Scenario	15,950	30,276	6,004	5,425	57,655	4.44	16.35	17.92	6.31	8.68
7	Full Conversion Scenario	17,210	32,734	6,431	5,777	62,153	4.79	17.68	19.20	6.72	9.36
Women											
1	Complete cessation	23,231	18,101	7,345	6,487	55,165	22.01	45.20	50.02	23.22	29.31
2	Complete switch to RRPs (HnBs)	16,617	13,670	5,649	5,000	40,936	15.74	34.14	38.47	17.89	21.75
3	Complete switch to RRPs (50% HnBs; 50% ECigs)	18,882	15,245	6,261	5,534	45,923	17.89	38.07	42.64	19.81	24.40
4	Conservative Scenario	3,476	3,089	1,369	1,169	9,104	3.29	7.71	9.32	4.19	4.84
5	Dynamic Scenario	5,605	4,934	2,141	1,859	14,540	5.31	12.32	14.58	6.66	7.72
6	Conversion Scenario	7,014	6,035	2,616	2,277	17,942	6.64	15.07	17.81	8.15	9.53
7	Full Conversion Scenario	7,530	6,404	2,783	2,424	19,140	7.13	15.99	18.95	8.67	10.17

Abbreviations used: COPD = chronic obstructive pulmonary disease, ECig = e-cigarette, HnB = heat-not-burn, IHD = ischaemic heart disease, LC = lung cancer;

77.9% of these were in males, with the percentages by disease being 54.6% for LC, 26.4% for IHD, 13.4% for COPD and 5.7% for stroke.

In the Null Scenario, 8.61 million YLL were attributed to cigarette smoking. 76.2% of these were in males, with the percentages by disease being 51.6% for LC, 31.8% for IHD, 8.4% for COPD and 8.2% for stroke. The percentages by disease, compared to those given above for attributable deaths, reflect the higher proportion of deaths at younger ages for IHD and stroke than for LC and COPD.

Smoking-related deaths and loss of life in the Alternative Scenarios

We explored a wide range of scenarios assessing the possible effect of RRP introduction on the population health in Germany in 1995–2015.

Our Extreme Scenarios (1–3) estimated theoretical maximum effects. As expected, the greatest impact would have occurred had all cigarette smokers quit in 1995, with no further use of cigarettes, HnBs, or ECigs (Scenario 1), resulting in a DD of about 217,000 and 2.88 million YLS. This extreme scenario has been designed to demonstrate the maximum potential risk reduction for the German population, and it can be considered a point of reference for every other scenario investigated.

Substantial reductions would also have occurred had cigarette smoking in Germany been immediately replaced by either HnB use (Scenario 2; 159,000 DD and 2.06 million YLS) or equally by either HnB or ECig use (Scenario 3; 179,000 DD and 2.34 million YLS), with the greater numbers for Scenario 3 reflecting the assumed lower effective dose for ECigs (0.05) compared with HnBs (0.2).

Four Pragmatic Scenarios revealed more plausible estimates by moving gradually a proportion of cigarette smokers to use HnBs and ECigs.

Table 4 presents the estimated DD values at age 30–79 years over the whole follow-up period for all seven scenarios. These are shown for each disease separately and combined. The results are expressed both as numbers and percentages of all SRD.

The DDs are lower in the Pragmatic Scenarios, because the transition from cigarettes to HnBs and ECigs is less rapid. As would be predicted from the patterns of uptake by scenario shown in Table 2, the greatest DDs are seen in the Full Conversion Scenario, where smokers switch gradually to the RRPs – they are about 40% of the DDs associated with Complete Cessation, where smokers quit smoking immediately in 1995.

The patterns of DDs for the individual diseases are similar to that for the four diseases combined. Among men, the largest absolute DDs are for IHD, with LC next, followed by stroke and COPD with lower and similar DDs. Among women, the DDs for LC are higher than those for IHD, reflecting the lower overall IHD rate among women. As a proportion of all SRDs, the DDs in both sexes are substantially higher for IHD and stroke than for LC and COPD, reflecting the shorter H values for IHD and stroke (i.e., the more rapid reduction in cardiovascular disease risk after smoking cessation or switching to RRPs).

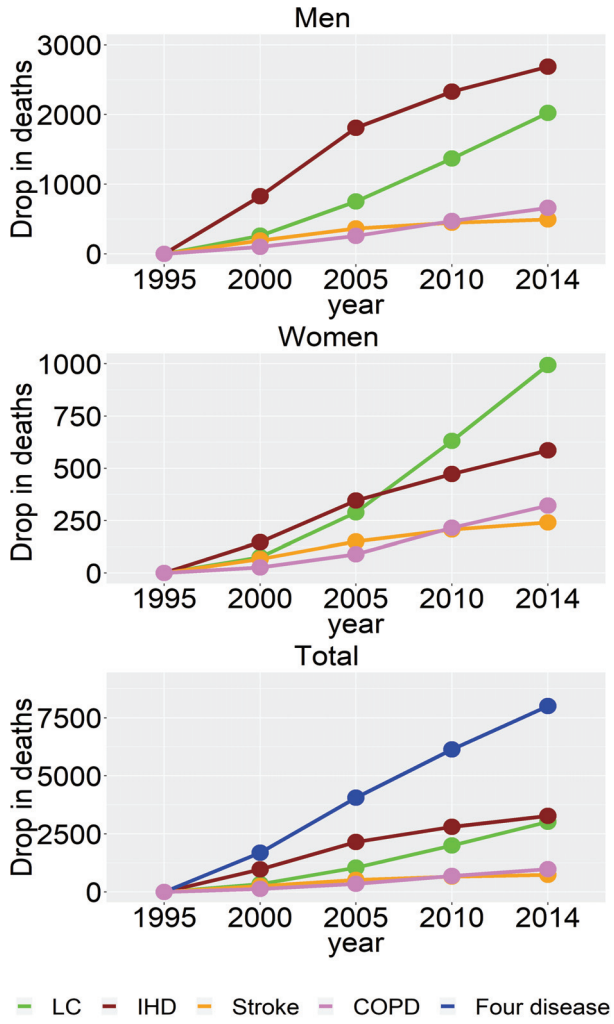


Figure 3. DDs in the Conversion Scenario over the whole follow-up period. Abbreviations used: COPD = chronic obstructive pulmonary disease; IHD = ischaemic heart disease; LC = lung cancer;

The DDs in the Conversion Scenario are also shown by disease over the whole follow-up period in Figure 3.

As is shown for the Conversion Scenario (Figure 3), but as is also evident from Additional File S5 for the other scenarios, an increase in DDs is seen with time in both sexes. This is due partly to the time needed for take-up of HnBs and ECigs and partly to the time required for the resulting decline in risk. This trend suggests that the DDs would have been substantially greater had the follow-up period been extended.

Table 5 and Figure 4 summarize the results for the seven scenarios with regard to YLS by age 75 over the whole follow-up period. The relative values for the different scenarios are very similar to those for DD seen in Table 4. Indeed, on the basis of the results for the four diseases combined in Tables 4 and 5, the sex- and scenario-specific ratios of YLS to DD can be estimated to only vary between 12.5 and 13.4.

The analyses summarized above do not take into account the increase in population size associated with the reduced mortality in the Alternative Scenarios relative to that in the Null Scenario. As shown in the detailed results in Additional File S5, this had little effect on the estimated DD or YLS. For example, for the Conversion Scenario, where the overall unadjusted DDs were 57,655 (8.68% of all SRD) in men and 17,942 (9.53% of SRD) in women, the corresponding adjusted DDs were 57,026 (8.59%) and 17,892 (9.51%), respectively. Full results of the analyses are available in Additional File S5.

DISCUSSION

We estimated the possible population health effect of introducing HnBs or ECigs into Germany during 1995–2015 by exploring a wide range of scenarios with various assumptions about their rate of uptake. Clearly, quitting all tobacco use brings the greatest benefits to the health of a population as a whole and can result in 2.88 million YLS and 217,000 DD upon total elimination of smoking after 20 years. Substantial reductions would also occur if, instead of quitting, CC smoking were immediately replaced by either HnB use or equally by either HnB or ECig use and these scenarios produced drop in deaths that were 74% and 83% of that for total cessation, respectively. Although these are the extreme scenarios and very unlikely to become reality, the simulated results provide the estimates of the highest theoretical benefits.

More plausible are the estimates associated with our Pragmatic Scenarios in which a proportion of cigarette smokers move gradually to use HnBs and ECigs. These scenarios aim to reflect potential effect sizes under less or more favorable conditions for the uptake of RRPs in Germany, rather than reflecting actual or expected RRP uptake dynamics. They are used to estimate how the uptake of ECigs and HnBs by smokers could have affected DDs and YLS in Germany in 1995–2021. Scenarios 4 to 7 vary in the extents to which uptake of these RRPs occurs and to which RRP users fully convert to exclusive RRP use, rather than becoming multiple users of cigarettes and RRPs. However, each scenario shows a positive population health impact, with DD varying, between Scenarios 4 and 7, from 39,800 to 81,300 and YLS from 0.50 to 1.05 million. The different Pragmatic Scenarios would thus have achieved 18–38% for DD and 17–36% for YLS of the effect of immediate cessation (Scenario 1). These estimates could inform public health authorities' cost-benefit assessments on programs aimed at reducing the rate of CC smoking.

The Pragmatic Scenarios could be considered optimistic as they postulate market shares of the CC market in 2005 after ten years of 9 to 15.5% for HnB and 27 to 36.4% for ECig. They could also be considered pessimistic when compared to population health impact models by other authors. For example, Levy *et al.* (43) assumed CC smoking in the US was largely replaced by ECig use within 10 years.

There are four reasons why our calculated estimates, based on the scenarios chosen, may be too low. The first is that we only considered deaths from the four main smoking-related diseases due to lack of reliable data on RR and H for each smoking-associated disease. As estimated elsewhere (30), our estimates of deaths saved would have to be multiplied by about 1.52 to yield an estimate for all smoking-related diseases.

Table 5. Years of life saved (thousands) by age 75 over the whole follow-up period in Germany.

		Men					Women				
	Scenario	LC	IHD	Stroke	COPD	All four diseases	LC	IHD	Stroke	COPD	All four diseases
1	Complete cessation	520	1,329	213	98	2,160	292	258	118	52	720
2	Complete switch to RRPs (HnBs)	357	943	160	74	1,534	203	189	89	40	521
3	Complete switch to RRPs (50% HnBs; 50% ECigs)	412	1,077	180	83	1,752	233	213	99	44	589
4	Conservative Scenario	83	241	43	20	387	42	43	21	10	116
5	Dynamic Scenario	134	379	68	31	612	67	68	33	15	183
6	Conversion Scenario	161	461	80	37	739	84	84	40	18	226
7	Full Conversion Scenario	176	506	86	39	807	90	89	43	19	241

Abbreviations used: COPD = chronic obstructive pulmonary disease; ECig = e-cigarette; HnB = heat-not-burn; IHD = ischaemic heart disease; LC = lung cancer; RRP = reduced risk product;

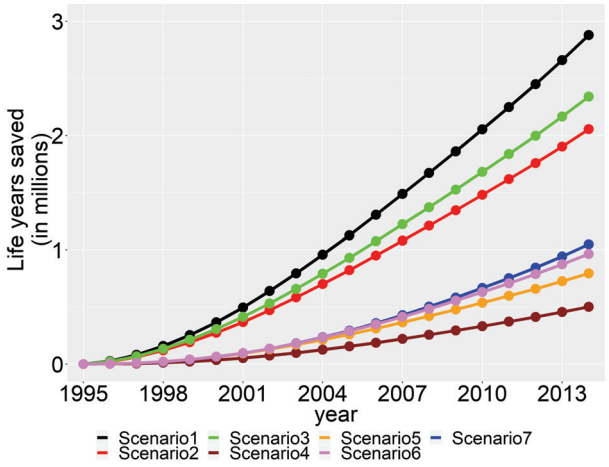


Figure 4. YLS by Scenario over the whole follow-up period. See Table 2 for a description of the scenarios.

Another reason is that we limited attention to deaths up to age 79, partly to avoid the uncertainty of cause of death certification at older ages. Had we not done so, our estimates of deaths saved would have been higher.

A third and very important reason is that we only considered a 20-year follow-up period, as we did not wish to project into the future, where disease rates might be affected by various exogenous factors. The results in Figure 3 show that the DD values increase rapidly over time, particularly from LC and COPD, where quitting takes a long time to reduce risk.

The final reason is that we did not account for the possibility that cigarette smokers who take up ECigs or HnBs might be more likely to quit cigarette smoking than those who continued to exclusively smoke cigarettes. Evidence from the US shows that use of ECigs is associated with increased cessation rates (44).

Our analyses are limited by various factors shown previously (27) to have only a modest effect on estimates of population health impact. These include failure to consider pipe and cigar smoking, use of smokeless tobacco or nicotine replacement therapy, ignoring exposure from environmental tobacco smoke, and not allowing TPs to vary by previous product use history. Though the NEM has been validated on the basis of extensive data on quitting as well as limited data on changes in the number of cigarettes smoked (45), the accuracy of its predictions on more complex changes in usage over time has not been formally tested.

Our results for the introduction of RRPs will be affected by the effective doses chosen. For ECigs, we used an estimate of 0.05 on the basis of expert opinion (41), although this was derived based on chemistry and short-term toxicological results. For HnBs, our estimate of 0.20 was based on biomarker and clinical data (40), with results for a number of endpoints suggesting a lower effective dose. Elsewhere (27), we have demonstrated that the estimated DD is linearly related to the assumed values of the effective dose used, with DD increasing as the effective dose decreases. While the estimated effective dose is an important factor when smokers switch to RRPs like ECigs and HnBs, other factors also play a role. These include changes in the frequency of use and the extent to which cigarettes are completely abandoned.

A possible limitation of our modelling is that we considered people who simultaneously used two or three out of cigarettes, ECigs, and HnBs as multiple-product users, with their effective dose taken as the mean of 1, 0.05, and 0.20. Those who are dual users of cigarettes with either ECigs or HnBs might have a higher effective dose than the mean, while those who are dual users of ECigs and HnBs might have a lower one. However, the proportion of multiple product users is quite low, particularly for the Conversion and Full Conversion Scenarios, so the overall effect of this limitation on the results seems likely to be modest.

The rate at which smokers switch to ECigs and HnBs is likely to depend on product risk perception, much evidence having already shown this to be the case for ECigs. For instance, accurately perceiving ECigs as less harmful than cigarettes predicted subsequent ECig use among British smokers (46) and continues to correlate with ECig use among UK smokers (47). German smokers were more likely to use ECigs for smoking cessation if they perceived them as less harmful than cigarettes (48). US adult dual

users of ECigs and cigarettes who perceived ECigs as less harmful than cigarettes were more likely to switch to exclusive ECig use 1 year later (49). However, correct risk perceptions of ECigs remain low and are getting worse over time, both internationally (46, 47) and in Germany, where more than half of the population perceives ECigs (50, 51) as at least as harmful as cigarettes. Even among ever-users of HnBs in Germany, only just over half of them accurately perceived HnBs as less harmful than cigarettes (52). Public health experts in the UK, the US, and Germany are, therefore, calling for better access to fact-based information (9, 46, 53, 54). Educational campaigns via trusted public health institutions are likely the most effective tool (55). While such campaigns exist in the UK, they are virtually absent in Germany.

Intuitively, maximizing the beneficial population health impact of introducing ECigs and HnBs will require a combination of high uptake among smokers, with many ultimately becoming exclusive RRP users. Our modelling results support this notion, with the DD and YLS increasing between Scenarios 4 and 5, when uptake was increased, and between Scenarios 5 and 7, when exclusive product use was increased. As discussed above, RR perceptions for ECig/HnB *vs*. smoking are potential drivers for both product uptake and exclusive product use, with health policy actions like public education campaigns being a recommended tool. Other factors likely to have an impact include risk-proportionate regulation in general (56) – such as product health warnings (57) – and local smoking cessation guidelines and healthcare professional recommendations (58) as well as media headlines (59). Moreover, fiscal policies can have an impact on relative product use. Recent US retail panel data suggest that ECig taxation increased cigarette sales (60).

Many other publications have estimated the population health impact of introducing RRPs. These include estimates based on our methodology, but applied to the USA (27, 28) or Japan (29), as well as attempts using different methodology, supported by other tobacco companies (61–67) or by public funding (43, 68–73). Despite methodological differences, most modellers have assumed the risk from RRP use, relative to that from cigarette smoking, is low and have concluded as we have that introduction of RRPs is likely to have a beneficial impact. For example, LEVY *et al.* (43) concluded that a strategy including replacing CC smoking by ECig use would yield substantial health gains, even under pessimistic assumptions regarding cessation, initiation and relative harm.

As noted in the introduction, the number of smoking-attributable deaths estimated by MONS and BRENNER to have occurred in Germany in 2013 is 125,000 (6). In the Null Scenario, in 2013, the number of SRD was estimated to be 39,600. There are three main reasons for this discrepancy. First, we only considered four diseases, which form only about 67.5% of the total number of smoking-related diseases (2). Second, we only considered the deaths of people aged 30–79 years, whereas the published estimate was related to age 35 years or above. Third, the disease-specific RRs used by MONS (2) were derived from specific US studies, whereas ours were derived from detailed meta-analyses (see Table 5). While the RRs from the two studies were quite similar for both IHD and stroke, those for LC (23.26 for men and 12.69 for women *vs*. 11.68 for both sexes) and COPD (10.58 for men and 13.08 for women *vs*. 4.56 for both sexes) were markedly higher in the previous study. Had we considered more diseases, a wider age range, or higher RRs, the estimated DD and YLS would, of course, have increased.

Overall, our results provide insight into how much the introduction of the two RRPs considered might affect the distribution of usage in Germany and the mortality related to cigarette smoking. Policies and regulation can accelerate switching to these RRPs, including calling for a more risk-proportionate approach and for the best available information on RRPs to be available to adult smokers. This will help increase the perception of the harm-reduction capabilities of RRPs and encourage switching, make alternatives to cigarettes more attractive for smokers, and help maintain product standards for building consumer trust in RRPs. Rather than any single measure, an integrated tobacco control strategy is likely to be more successful in encouraging smokers to switch to RRPs and thus result in an overall public health gain.

CONCLUSIONS

Based on estimates of the rate of uptake of two RRPs (HnBs and ECigs) in Germany and their effective dose compared with cigarettes, it is estimated that there would have been a drop in SRDs from LC, COPD, IHD, and stroke of approximately 40,000 to 81,000, with 0.50 to 1.05 million life years saved, corresponding to 17–38% of the effect of immediate cessation (Scenario 1). While cessation is the best option for smokers, we estimate that introducing RRPs and encouraging smokers who would otherwise continue to smoke cigarettes to switch to them will result in a substantial population health benefit in Germany, even under what may be considered more pessimistic assumptions about their relative harm and rate of uptake. These estimated effect sizes could help inform German public health authorities' cost-benefit assessments on programs aimed at reducing the rate of CC smoking.

DECLARATIONS

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable

CONSENT FOR PUBLICATION

Not applicable

AVAILABILITY OF DATA AND MATERIAL

The data on population size, mortality, and smoking prevalence used in this study are publicly available at the sources described in the paper. The sources of data used for the RR and H values are also shown.

COMPETING INTERESTS

JSF and PNL are independent consultants in statistics and advisers in epidemiology to several tobacco companies. AK and EB acted as consultants for Philip Morris International. SD is a former employee and AKN and RR are current employees of Philip Morris International.

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All the work described in the paper was funded by Philip Morris International. The authors are wholly responsible for designing the study, conducting the analyses, interpreting the results, and writing the manuscript.

AUTHORS' CONTRIBUTIONS

The work described here was conceived by RR, SD, AKN, and PNL. Some of the data required were extracted by AK and EB. The analyses were run by JSF, RR, and SD, and checked by PNL. The manuscript was drafted by PNL, with contributions from AKN, and developed according to comments from RR, SD, EB, and JSF. All authors read and approved the final manuscript.

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SUPPLEMENTARY INFORMATION

Additional File S1.pdf
Title: Cigarette smoking habits in Germany.
Description: This document describes the derivation of estimates of combustible cigarette smoking habits for Germany.

Additional File S2.pdf
Title: Derivation of TPs for the Null Scenario.
Description: This document describes the derivation of the TPs for the Null Scenario for Germany.

Additional File S3.pdf
Title: TPs for each Alternative Scenario.
Description: This document presents the TPs for each Alternative Scenario for Germany.

Additional File S4.pdf
Title: Data on population, and number of deaths by sex, age, and year.
Description: This file presents the data used for Germany on population size and on numbers of deaths per year from LC, COPD, IHD and stroke. Data are shown by sex, year (1995, 1996, …, 2015), and age group (30–34, 35–39, …, 75–79).

Additional File S5.pdf
Title: Full output for each scenario.
Description: This document provides the full computer output relating to the estimated DDs and YLS, preceded by a description of the contents of the output.

Additional File S6.pdf
Title: Product use distributions.
Description: This document provides current product use distributions in 2005 for all scenarios and the overall prevalence of current product users in 2010.