Article

Modeling the Population Health Impact of Introducing a Modified Risk Tobacco Product into the U.S. Market

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Abstract: Philip Morris International (PMI) has developed the Population Health Impact Model (PHIM) to quantify, in the absence of epidemiological data, the effects of marketing a candidate modified risk tobacco product (cMRTP) on the public health of a whole population. Various simulations were performed to understand the harm reduction impact on the U.S. population over a 20-year period under various scenarios. The overall reduction in smoking attributable deaths (SAD) over the 20-year period was estimated as 934,947 if smoking completely went away and between 516,944 and 780,433 if cMRTP use completely replaces smoking. The reduction in SADs was estimated as 172,458 for the World Health Organization (WHO) 2025 Target and between 70,274 and 90,155 for the gradual cMRTP uptake. Combining the scenarios (WHO 2025 Target and cMRTP uptake), the reductions were between 256,453 and 268,796, depending on the cMRTP effective dose. These results show how a cMRTP can reduce overall population harm additionally to existing tobacco control efforts.

Keywords: public; tobacco; risk; modified; reduced; nicotine; non-combustible; health; smoking; harm

1. Introduction

Worldwide, there are approximately 1.1 billion smokers, and nearly 6 million deaths are attributed to smoking annually [WHO 2014]. A number of serious diseases are associated with tobacco smoking that result in smoking-related mortality, including cardiovascular diseases, lung cancer, and chronic obstructive pulmonary disease (COPD). For many years, preventing smoking initiation and promoting smoking cessation were the primary strategies for reducing the harm associated with cigarette smoking. Although smoking prevalence has declined over the last 40 years, those declines have flattened in many countries in the last 10 years [WHO 2014].

Smoking cessation is clearly the most effective strategy for smokers to reduce their risk of harm and disease. However, the number of former smokers who relapse is high. Approximately 80% of smokers who attempt to quit smoking return to smoking within one month, and annually, approximately 5% of smokers quit successfully [Tashkin 2015]. PMI is developing non-combustible tobacco and nicotine containing products that have the potential to present less risk of harm to smokers who switch to these products versus continued smoking. We refer to these products as cMRTPs. Harm reduction is, by definition, a strategy used in medicine and social policy to minimize harm to individuals and/or wider society from hazardous behaviors or practices that cannot be completely avoided or prevented [Royal College of Physicians 2016].

In this context, a complementary approach to existing strategies to reduce smoking prevalence, is starting to gain support from a range of stakeholders, including public health organizations, healthcare professionals, and regulators. According to the Royal College of Physicians, embracing

such an approach could offer a means to prevent millions of deaths [Royal College of Physicians 2007] and to hasten our progress to a tobacco-free society [Royal College of Physicians 2016].

In 2012, the U.S. Food and Drug Administration (FDA) released a draft guidance for MRTP applications that described the evidentiary requirements for claims of reduced exposure and reduced risk [FDA 2012]. An cMRTP is defined by the U.S. Family Smoking Prevention and Tobacco Control Act as "any tobacco product that is sold or distributed for use to reduce harm or the risk of tobacco related disease associated with commercially marketed tobacco products." At PMI, cMRTP is the term used to refer to products that present, are likely to present, or have the potential to present less risk of harm to smokers who switch to these products versus continued smoking. PMI has a range of cMRTPs in various stages of development, scientific assessment, and commercialization. Because the cMRTPs do not burn tobacco, they produce far lower quantities of harmful and potentially harmful compounds than found in cigarette smoke.

In 2016, PMI filed an MRTP application for its Tobacco Heating System (THS) [FDA 2017[, with aerosol containing lower levels of harmful and potentially harmful toxicants than found in cigarette smoke, thus offering reduced exposure to these toxicants, reduced toxicity, and reduced health risks to consumers compared with continued cigarette smoking. In 2017, the Committee on Toxicology (COT) released a statement that THS investigations show a decrease in the harmful and potentially harmful constituents (HPHC), of approximately 50% for some HPHCs and more than 90% for others, with many constituents below the limits of detection in the aerosol generated by the device compared to smoke from a conventional cigarette [COT 2017].

Population harm reduction depends both on the availability of lower-risk products and on a significant number of adult smokers being willing to accept and switch to these products. Conversely, low product acceptance could theoretically offset even substantial, product-specific risk reduction. Concerns have been raised that the benefits of alternative products could be offset by an increase in unintended consequences, such as smoking initiation, interference with quitting among smokers, or encouraged re-initiation in former smokers.

One difficulty is that population-level data on consumer product use and behaviors cannot be collected prior to marketing a cMRTP, so the impact of marketing the product on the health of the population as a whole cannot be assessed fully. Therefore, PMI has implemented a comprehensive pre-market product assessment program [Smith et al. 2016] based on FDA's draft Guidance (2012) as well as an applicable post-market research program to assess the impact of marketing products on the population as a whole.

Initially, this model will use assumptions to predict what may happen following the launch of the product. However, data from the post-market assessment program can serve as input into the model (replacing the initial assumptions with actual market-derived data) and can also be used to refine the assumptions moving forward.

PMI has developed the PHIM to quantify, in the absence of epidemiological data, the effect that marketing a cMRTP may have on the health of the population as a whole [Weitkunat et al. 2015; Lee et al. 2017]. This activity is accompanied by an increasing number of publications on alternative modeling approaches for estimating the population health impact following changes in the nicotine and tobacco product landscape [Bachand and Sulsky 2013; Vugrin et al. 2015; Hill and Camacho 2017; Poland and Teischinger 2017]. The FDA acknowledges the inherent difficulties of such models, as they require assumptions about how today's consumers, both users and non-users of tobacco products, will modify their future behavior in response to the market entry of an cMRTP. Therefore, it is of key importance to describe these assumptions, and how variation in them affects the estimated population health impact, clearly.

2. Materials and Methods

The methodology of the PHIM has been described in detail [Weitkunat et al. 2015] and is summarized below. It was designed to assess the population-level health impact of marketing a cMRTP as a function of the risk or toxicity of the product to the individual user and the product use prevalence distribution in the population.

2.1. Estimating tobacco use histories

In the application of the PHIM described here, simulated samples of 10,000 males and 10,000 females start aged 10-79 in 1990 with a U.S.-representative distribution of smoking prevalence and no use of a cMRTP. Individual tobacco histories are then updated each year until 2010 based on two alternative sets of estimated "transition probabilities" of switching between tobacco groups, referred to as "scenarios." In the null scenario, the tobacco groups are never, current, and former smokers, and the probabilities are set so as to produce smoking prevalence distributions comparable to those observed in the U.S. In various alternative scenarios, described below, differing sets of probabilities are used. Where an alternative scenario involves the introduction of a cMRTP, there are five tobacco groups: never tobacco users, current cigarette smokers, current cMRTP users, current dual users, and former tobacco users. Note that any individual reaching age 80 drops out of the population, so by 2010, smoking prevalence refers to those aged 30-79.

2.2. Estimating relative risks

Separately for the null and alternative scenarios, the PHIM then derives estimates of the relative risk (compared to never users) for lung cancer, COPD, ischemic heart disease, and stroke for every individual of each sex at each year of follow up. The estimation uses a negative exponential model that has been described elsewhere [Lee et al. 2017]. It requires not only knowledge of each individual's tobacco use at each year but also estimates of the "effective dose" corresponding to the tobacco use pattern. The effective dose (f-factor) takes the value 0 when an individual is not using tobacco (a never or former user), 1 for cigarette smoking, the f for a current cMRTP user, and $(1+f)/2$ for a dual user. A dual user is an individual whose tobacco use pattern consists of a substantial use of both products, cigarettes and cMRTPs. At the population level, for a given scenario, sex, disease, and follow-up year, the PHIM then estimates the mean relative risk ($\bar{RR}$) for individuals in each five-year age group from 30-34 to 75-79.

2.3. Estimating deaths attributable to tobacco use

To estimate the absolute numbers of deaths attributable to tobacco product use for each scenario in those aged 30-79 years, published U.S. sex- and age-specific numbers of deaths for each of the four diseases are multiplied by $(\bar{RR}-1)/\bar{RR}$, and the total number of SADs from the four diseases combined are obtained by simple addition. The population health impact is then derived by subtracting the numbers under the alternative scenario from those under the null scenario. As equal population size is assumed under both scenarios, an adjustment can be made for the decrease in death rates in the alternative scenario [Weitkunat et al. 2015; Lee et al. 2017]. However, the simulations presented in this paper do not use this adjustment, as it had a small effect and did not affect the overall picture.

2.4. Null scenario

The derivation of the smoking histories under the null validation scenario uses the set of transition probabilities described in Table 2 of our earlier publication [Lee et al. 2017]. That publication demonstrates that there was a reasonably good fit between the smoking distributions generated by PHIM across all these ages in 1990 and 1995, though the estimates for the older age groups do not correspond as strongly with the International Smoking Statistics (ISS) data. Exact correspondence between these two estimates was not expected for various reasons, such as variation due to the simulation process, inaccuracies in the ISS estimates, and ISS estimates for the U.S. population not being available past 2005 (so that 2005 estimates were used for later years).

The null scenario and all of the alternative scenarios use the disease and age-specific estimates of the relative risk for continued cigarette smoking and of the half-life for quitting smoking provided in Table 5 of our earlier paper [Lee et al. 2017] and justified there.

Estimates of SADs derived from the null scenario have been compared previously with estimates published by the U.S. Surgeon General [U.S. Department of Health and Human Services 2014] and

in the Morbidity and Mortality Weekly Report [CDC 2015]. The results for most diseases were similar when compared with the Surgeon General estimates [Lee et al. 2017]. However, there is a notable difference for COPD, with the null scenario estimates much lower in both sexes. This difference mainly arises due to the much lower current smoking ‾RR estimate of 4.56 for both sexes incorporated in the PHIM. The other estimates were higher, particularly for 2005-2009 [U.S. Department of Health and Human Services 2014], assumed as 29.69 at age 65-74 and 23.01 at age 75+ for males and 38.89 at age 65-74 and 20.96 at age 75+ for females. Given that our estimate was based on a published meta-analysis [Lee et al. 2017] involving 39 North American studies, with the 95% confidence interval for our estimate as narrow as 3.69 to 5.62, it seems likely that the Surgeon General's ‾RR estimate is far too high.

2.5. Alternative scenarios

Eight different alternative scenarios have been used. Some estimate the health impact of introducing a cMRTP onto the market, while others illustrate the effect of alternative methods of risk reduction for comparative purposes.

2.5.1. No further smoking

As smoking cessation is the "gold standard" for the maximum risk reduction that can be achieved, this scenario is one in which all current smokers immediately stop smoking, with no further initiation or re-initiation of tobacco use.

2.5.2. Smoking totally replaced by cMRTP use

This scenario illustrates the maximal impact of introducing a cMRTP into the U.S. market. Here, all current smokers in 1990 immediately switch to the cMRTP. Unlike the first alternative scenario, in which initiation and re-initiation are eliminated, it is assumed here that initiation, re-initiation, and quitting rates are the same as in the null scenario but only involve switches to or from the cMRTP. To understand the potential impact of the cMRTP range of effective doses (*f*-factors) between *f*=0.1 and *f*=0.3 are generally considered. In order to derive estimate the *f*-factor, the non-clinical and clinical data collected during the product assessment programs were examined. PMI developed a multivariate *f*-factor distribution based on objective Bayesian statistics using the set of biomarkers of exposure and clinical risk endpoints collected in the studies (submitted for publication). In the absence of data to inform the model, we assumed that the *f*-factor is distributed uniformly between 0 (smoking cessation) and 1 (continued smoking) and normality of the conditional distribution of each biomarker given the product use. The relative changes in the parameters provide information on the *f*-factor using a link function of an unknown, multi-endpoint biomarker that ensures the sufficiency of the selected set of biomarkers. The *f*-factors, which are derived from aerosol chemistry and biomarker data, are intended to indicate the highest (90%) and medium (70%) plausible reductions in effective dose for the cMRTP.

2.5.3. WHO 2025 Target

The WHO's 2015 "Global Report on Trends in Tobacco Smoking 2000-2025" [WHO 2015] states, "If the 194 WHO Member States collectively achieved a 30% reduction from the 2010 level of 22.1%, they would be expected to reach a prevalence level of 15.4% in 2025" (i.e., they target a 30% reduction in the prevalence of tobacco smoking between 2010 and 2025). To examine the impact that such a reduction in smoking prevalence might have on the health of the U.S. population, the third scenario used a set of transition probabilities aimed at reducing smoking prevalence by 30% between 1990 and 2005, with the smoking prevalence being allowed to continue to decline over the last five years of the follow up.

2.5.4. WHO 2025 Projection

The WHO report referenced above goes on to state, "At this stage, it is projected that the prevalence level in 2025 will be 18.9%, or 3.5 percentage points above the target. This would represent a 14% relative reduction overall." The fourth scenario uses transition probabilities aimed at reducing smoking prevalence by 14% between 1990 and 2005.

2.5.5. cMRTP uptake case

For this scenario, the transition probabilities were designed so that within 10 years of marketing the product, 17% of the smoking population uses the cMRTP (15% cMRTP users and 2% dual users), as if the cMRTP was launched in 1990. We aimed for the target but continued to simulate over the next 10 years of follow up.

2.5.6. cMRTP uptake case in addition to the WHO 2025 Target

This scenario examines the effects of combining a 30% reduction in smoking prevalence in 15 years with the addition of 17% of the remaining adult smokers using an cMRTP within 10 years, with both continuing to decline at the same rates for the remainder of the 20-year period.

2.5.7. cMRTP uptake case in addition to the WHO 2025 Projection

Similarly, this scenario examines the effects of combining a 14% reduction in smoking prevalence in 15 years with the addition of 17% of the remaining adult smokers using a cMRTP within 10 years.

2.5.8. Extreme increase in dual use

In this scenario, majority of cMRTP use occurs in a dual use pattern (12.5% of dual users and 5% of cMRTP users) within 10 years of marketing the cMRTP.

The sets of transition probabilities used in the different scenarios can be found in Appendix A.

3. Results

In the application of the PHIM described here, simulated samples of 10,000 males and 10,000 females start aged 10-79 in 1990 with a US-representative distribution of smoking prevalence, and no use of a cMRTP. Individual tobacco histories are then updated each year until 2010 based on two alternative sets of estimated "transition probabilities" of switching between tobacco groups, referred to as "scenarios". The null scenario and various alternative scenarios are described fully in Section 4. The results for each scenario are described below.

3.1. No further smoking

While the smoking prevalence remains at zero throughout the 20-year follow-up period, the risks of the four smoking-related diseases following smoking cessation do not diminish instantaneously; instead, the decline is gradual over time, at a rate that is dependent on the disease-specific half-life of excess risk. As shown in Figure 1, the initial annual reduction in SADs is relatively small (approximately 5,500 for both sexes and all ages combined in 1991), but this increases annually as the excess risk declines. By the end of the period, in 2009, the annual reduction is over 83,000 per year. Over the 20-year period combined, the total elimination of smoking is estimated to result in 934,947 fewer SADs. Clearly, this number would have continued to increase sharply had follow up been continued for more than 20 years. In the sections that follow, we compare this estimate of the maximal effect achievable in 20 years (934,947 total SADs) with those from other alternative scenarios.
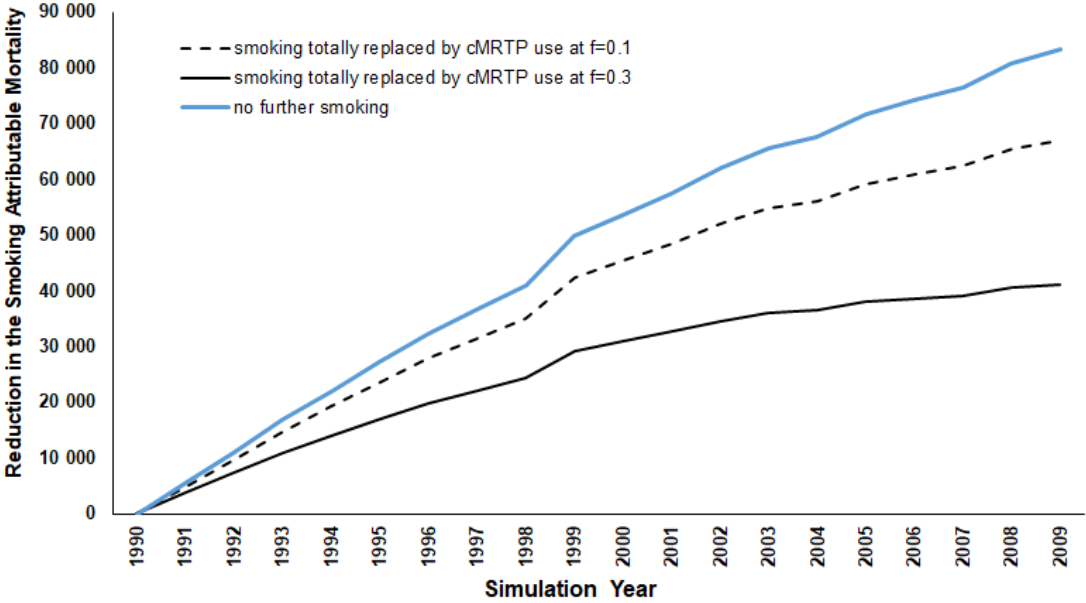
Figure 1. Annual reduction in SADs from 1990 to 2009 for alternative for alternative scenario 1, "No further smoking," and scenario 2 "Smoking totally replaced by cMRTP use at *f*=0.1 and *f*=0.3." For all years combined, the reductions are 516,944 and 780,433 deaths. The line for the "no further smoking "scenario is superimposed.

3.2. Smoking totally replaced by cMRTP use

As in the first scenario, the initial years show a marginal reduction in SADs, between 3,726 (*f*-value=0.30) and 4,907 (*f*-value=0.10) in 1991 (see Figure 2). However, by the end of the period, the introduction of the cMRTP resulted in a cumulative reduction in SADs between 516,944 and 780,433 (55% to 83% of the results seen for no further smoking).
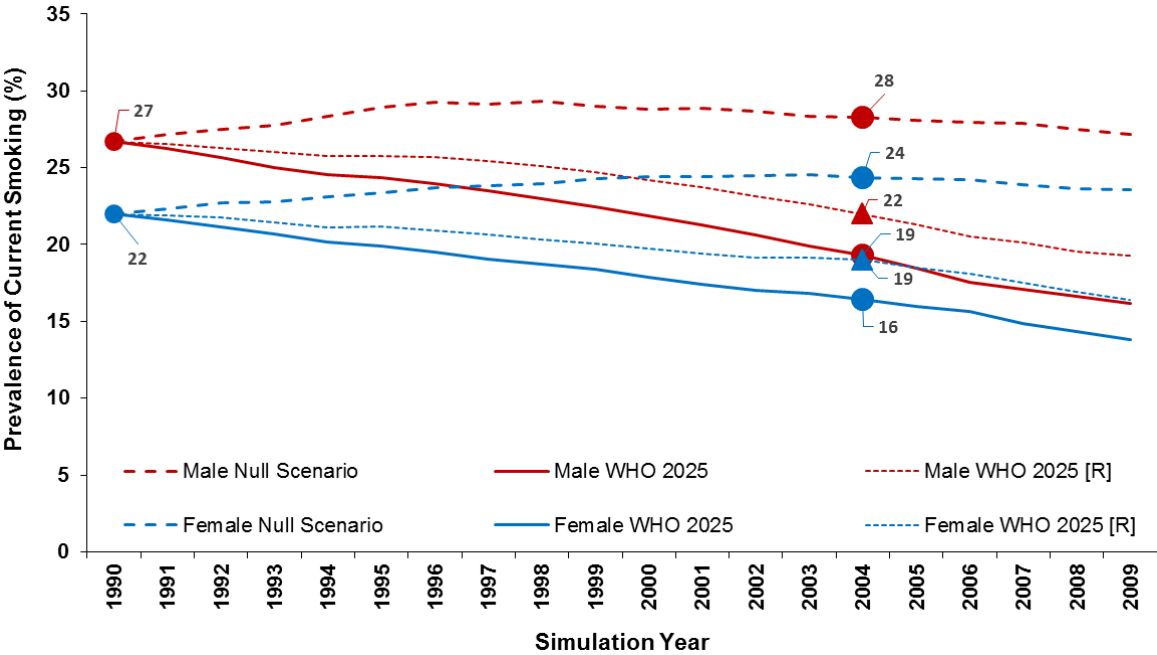
Figure 2. Reduction in smoking prevalence between 1990 and 2005 under the null scenario and the WHO 2025 projections (WHO 2025 reflects the initial estimates of a 30% reduction, WHO 2025 [R] reflects the revised projections).

3.3. WHO 2025 Target

At baseline in 1990, smoking prevalence was 26.7% in males and 22.0% in females. In the null scenario, smoking prevalence (at ages up to 79 years) remained relatively constant over the 20-year period – 26.8% in males and 23.5% in females in 2009. In the WHO 2025 Target scenario (30% reduction in 15 years), the transition probabilities produced smoking prevalence in 2005 of 18.5% in males and 16% in females. These were equivalent to 30.7% and 27.3% reductions, respectively, quite close to the 30% reductions the WHO sought to achieve. This scenario resulted in a cumulative total of 172,458 fewer SADs over the 20-year period (108,637 in males and 63,820 in females).

3.4. WHO 2025 Projection

In the WHO 2025 Projection scenario (14% reduction in 15 years), the transition probabilities used produced smoking prevalence of 21.3% in males and 18.5% in females in 2005. These were equivalent to 20.2% and 15.7% reductions, respectively, somewhat greater than the 14% reduction they were designed to produce. Here, there was a cumulative total reduction of 111,102 fewer SADs (69,042 in males and 42,060 in females). Figure 3 illustrates the trends in smoking prevalence in the two WHO scenarios as compared to the null scenario.
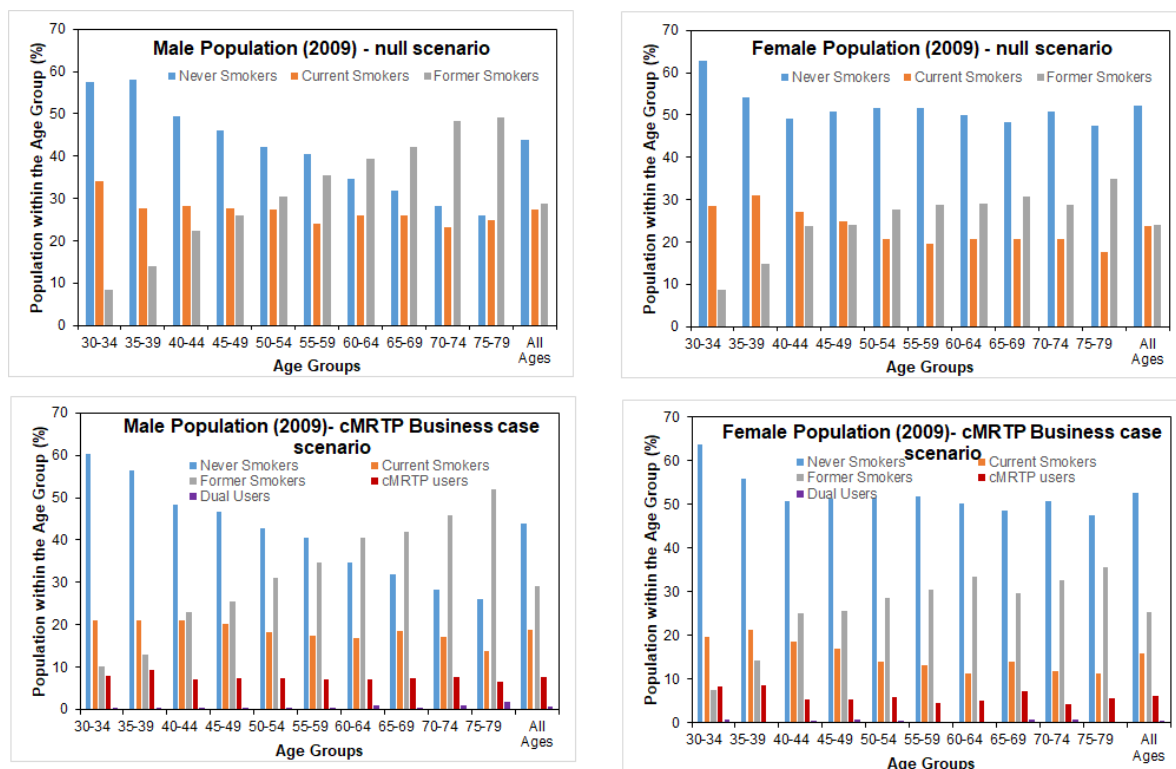
Figure 3. Distribution of smoking patterns by age and sex in 2009 in the null scenario and in the cMRTP uptake case scenario.

3.5. cMRTP uptake case

Here, there was very little change in the prevalence of never smokers and former smokers between the null scenario and the cMRTP scenario, as the majority of cMRTP users and dual users transitioned to this state from the cigarette smoking state. By the end of follow up, the initial smoking prevalence of 26.6% in males had become 18.3% current cigarette smokers, 7.9% cMRTP users, and 0.5% dual users. In females, 21.6% of initial smokers had become 15.3% current cigarette smokers, 6.2% cMRTP users, and 0.5% dual users (see Figure 4).
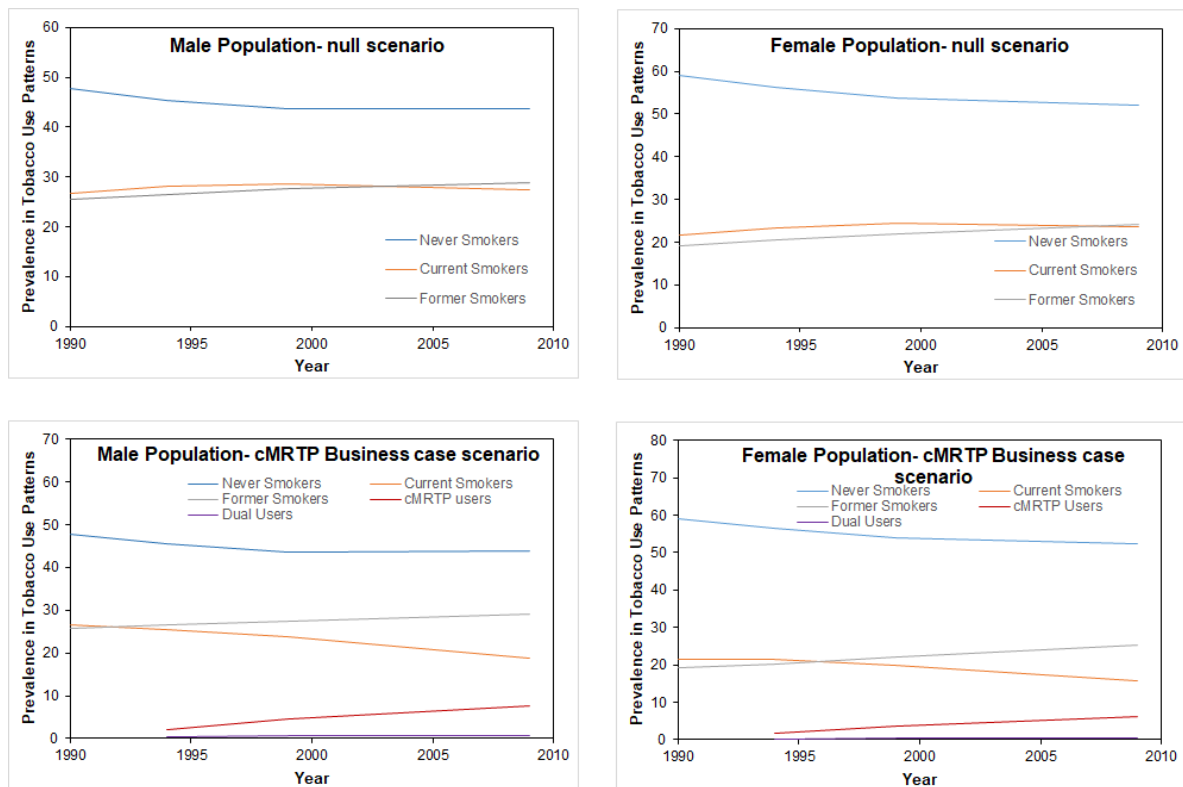
Figure 4. Change in smoking prevalence patterns by sex over the period 1990 to 2009 in the null scenario and in the cMRTP uptake case scenario by sex.

In this scenario, there were 90,156 fewer cumulative SADs up to 2009 for an *f*-value of 0.1 and 70,275 fewer for an *f*-value of 0.3. In an additional alternative in which the rates of switching were the same but the cMRTP was assumed to have an *f*-value of 0, there were 100,235 fewer cumulative SADs (67,151 in the male population and 33,083 in the female population). This is the case in which the same consumers were switched to smoking cessation.

3.6. cMRTP uptake case in addition to the WHO 2025 Target

In this case, the modeling simulation resulted in between 256,453 and 268,796 fewer SADs over the 20-year period for a cMRTP with an effective dose between *f*=0.1 and 0.3.

3.7. cMRTP uptake case in addition to the WHO 2025 Projection

Here, the combination of tobacco prevention and cMRTPs resulted in estimated reductions in cumulative total SADs of 186,876 (*f*=0.1) and 170,026 (*f*=0.3). This scenario and the previous one demonstrate how cMRTPs such as the THS can complement existing efforts to reduce SADs.

3.8. Extreme increase in dual use

In this scenario, after 10 years, there is still 17.5% of cMRTP use in the smoking population. However, 5% are mainly using cMRTPs, while 12.5% are dual users. Despite this increase in the prevalence of dual use, simulation results show reduction in cumulative total SADs between 45,802 and 59,840 over the 20-year period for an *f*-value between 0.1 and 0.3

To summarize the above, Table 1 summarizes smoking prevalence at the end of the 20-year period for the various alternative scenarios, while Table 2 compares the reductions in cumulative SADs. Fuller details of the trends in smoking prevalence can be found in Appendix B.

Table 1. Summary of smoking prevalence after the 20-year period for the null and alternative scenarios.

Modeling scenario	Never smokers (%)	Current smokers (%)	cMRTP users (%)	Dual users (%)	Former smokers (%)
Males, all ages					
Null scenario	44.0	27.6	0.0	0.0	28.3
1. No further smoking	52.3	0.0	0.0	0.0	47.7
2. Smoking replaced by cMRTP	44.1	0.0	27.4	0.0	28.4
3. WHO 2025 Target	45.8	15.7	0.0	0.0	38.5
4. WHO 2025 Projection	45.8	18.8	0.0	0.0	35.4
5. cMRTP uptake case	44.1	18.4	7.9	0.6	29.1
6. cMRTP uptake + WHO Target	43.2	10.3	5.0	0.0	41.5
7. cMRTP uptake + WHO Projection	45.8	13.5	5.4	0.4	35.0
8. Extreme increase in dual use	43.9	21.0	2.3	4.2	28.6
Females, all ages					
Null scenario	52.3	23.7	0.0	0.0	24.0
1. No further smoking	60.2	0.0	0.0	0.0	39.8
2. Smoking replaced by cMRTP	52.6	0.0	23.6	0.0	23.8
3. WHO 2025 Target	54.4	13.3	0.0	0.0	32.3
4. WHO 2025 Projection	54.4	16.1	0.0	0.0	29.6
5. cMRTP uptake case	52.6	15.4	6.2	0.5	25.4
6. cMRTP uptake + WHO Target	52.1	8.6	4.5	0.0	34.9
7. cMRTP uptake + WHO Projection	54.4	11.3	4.4	0.3	29.5
8. Extreme increase in dual use	52.5	17.7	1.9	3.4	24.4

The null scenario values are the same or very similar for all eight modeling scenarios.

Table 2. Reduction in cumulative SADs for the various alternative scenarios (data for both sexes and the four diseases combined)

Modeling scenario	Cumulative SADs	f-factor	Reduction in cumulative SADs	% Drop in SADs
Null scenario	3,581,652		-	-
Alternative scenarios				
1. No further smoking		NA	934,947	26.1
2. Smoking replaced by cMRTP		$f = 0.1$	780,433	21.8
		$f = 0.3$	516,944	14.4
3. WHO 2025 Target		NA	172,458	4.8
4. WHO 2025 Projection		NA	111,102	3.1
5. cMRTP uptake case		$f = 0.1$	90,155	2.5
		$f = 0.3$	70,274	2.0
6. cMRTP uptake + WHO Target		$f = 0.1$	268,796	7.5
		$f = 0.3$	256,453	7.2
7. cMRTP uptake + WHO Projection		$f = 0.1$	186,876	5.2
		$f = 0.3$	170,026	4.7
8. Extreme increase in dual use		$f = 0.1$	59,840	1.7
		$f = 0.3$	45,802	1.3

4. Discussion

Clearly, cessation brings the greatest benefits to the health of a population as a whole and can result in a significant number of lives saved, with 934,947 fewer SADs estimated to occur in the U.S. upon total elimination of smoking after 20 years. This number will increase further in subsequent years. Although this is an extreme scenario and very unlikely to become reality, it has been designed and tested to demonstrate the maximum potential risk reduction for the U.S. population, and it can be considered a point of reference for every other scenario investigated.

In scenarios where a cMRTP is introduced to the U.S. population, the extreme case, in which smoking is immediately and totally replaced by cMRTP use, produced reductions in SADs that were 55% to 83% of that for total cessation, depending on the cMRTP effective dose. In scenarios that are less extreme and could become reality, reductions were less marked but still important and relevant. The WHO 2025 Projection of a 14% reduction in smoking prevalence in 15 years can lead to 3.1% fewer SADs in the U.S. over a 20-year period. If cMRTPs are introduced into the market as defined in the cMRTP uptake case, this percentage will increase 4.7% to 5.2% further depending on the cMRTP effective dose. Introducing cMRTPs similarly increases the reductions in prevalence in line with the WHO 2025 Target.

Overall, in every scenario considered, whether it involves complete or partial elimination of smoking or a replacement of some or all smokers with cMRTP users, a benefit on population health

is shown, as quantified by a reduction in SADs. Even the extreme increase of dual use scenario, which can be considered as the worst scenario given the increased relative exposure for dual use (*f*-value range 0.55 to 0.65) as compared with cMRTP use (*f*-value range 0.1 to 0.3), resulted in a small reduction in SADs, and the higher the prevalence of dual use, the less SADs decline will be observed. Therefore, it is important that consumers of cMRTPs understand that the product is more effective when is not combined with cigarettes.

The negative exponential model we use to estimate relative risks from tobacco histories would benefit from the large study data collecting extensive information on changes in tobacco use over time as a part of ongoing refinement process.

The model assumes that individuals only smoke cigarettes and/or use cMRTPs and does not account for other forms of tobacco use. Smokeless tobacco and nicotine replacement therapy are believed to have little or no effect on the risk of the diseases studied. Ignoring e-cigarettes may also not be important, if claims [Nutt et al. 2014] that any health effects are less than 5% of those from cigarettes are correct. Ignoring cigar and pipe smoking may seem more relevant. The model effectively assumes that cigar and pipe smoking carry the same risk as cigarette smoking, as the initial smoking status of the populations followed is based on the prevalence of smoking any product rather than only cigarettes. Had we allocated initial smoking status based on estimates of prevalence of cigarette smoking, we would instead have effectively assumed that cigar and pipe smokers have the same risk as never smokers, which would clearly be a less appropriate assumption. The problem, of course, is that extending the tobacco groups to include pipe and cigar smokers (and possibly also cigarette smokers with differing consumption levels) would require estimation of a huge number of transition probabilities, which would be difficult or impossible to do reliably. In the context of the U.S., our treatment of pipe and cigar smoking is probably unimportant, as cigarette smokers form the vast majority of all smokers.

The 30% and 14% reductions referred to by the WHO are presumably related to populations of the same or similar age, and we have applied them in situations where the simulated population is ageing. Given that in the null scenario, smoking prevalence (at ages up to 79 years) remained relatively constant over the 20-year period, the results we have produced in scenarios 3, 4, 6, and 7 should still provide a good illustration of the effects of the different scenarios. The fact that the chosen set of transition probabilities produces reductions in smoking prevalences that did not exactly align with the WHO reductions also seems unimportant for analyses that are intended to provide a broad indication of the relative effects of the alternative scenarios.

We do not account for environmental tobacco smoke (ETS) exposure, where we showed earlier [Weitkunat et al. 2015] that whether or not the cMRTP reduces the risk from ETS exposure would have little effect on the estimated drop in mortality associated with cMRTP introduction.

In the absence of reliable available estimates on relative risk and half-lives for all of the diseases associated with smoking, we have limited attention to the four major smoking-associated diseases. We estimated earlier [Weitkunat et al. 2015] that overall estimates of deaths saved due to the introduction of the cMRTP would have to be increased by approximately 50% to give an estimate for all smoking-related diseases combined. Our estimates of deaths saved may be in error if those who switch from cigarette smoking to cMRTP use tend to be atypical in some ways (e.g., having a duration of smoking markedly different from those who do not switch) or change their distribution of other risk factors (e.g., their degree of alcohol consumption).

More importantly, our analyses have limited attention to a 20-year follow up, particularly if the introduction of the cMRTP has an effect on the initiation of tobacco use by adolescents and young men and women. While the increase in prevalence would be clear after 20 years, any effect on mortality would be minimal, as the great majority of the additional tobacco users would be less than 50 years old.

Despite these reservations, we believe that the results summarized here provide a good insight into the extent to which introduction of a cMRTP might affect the distribution of tobacco use and the number of deaths associated with tobacco and clarify the assumptions that are most critical to the predictions.

The closeness of the null scenario predictions to actual epidemiological and authoritative statistics from the U.S. population across the 20-year study period provides a solid basis for assessing the potential population benefit of a cMRTP [Lee et al. 2017]. As shown in that paper, the introduction of a cMRTP would result in fewer SADs in all but the most unlikely situations. The degree to which SADs are reduced is influenced primarily by the prevalence of cMRTP use, maximized in the scenario in which there is complete switching by adult smokers with no influence on non-smokers. In the real world, consumers will need to understand the relative health benefits of switching from cigarettes to cMRTPs. It will take time to determine this precisely, as a meaningful number of smokers will first have to convert to cMRTPs. During this time, it will be important to conduct post-market surveillance and studies that would provide additional insights and encourage switching behavior among smokers.

5. Conclusions

Overall, based on the scenario assumptions within the various PHIM simulations, introducing a cMRTP into the U.S. population will lead to a net public health benefit in terms of reduced tobacco-related mortality.

Appendix A: The sets of transition probabilities used in the different scenarios

For the null scenario, the probability of transition between the three states (N = never, C = current and F = former) is described by P followed by two subscripts, the first representing the state changed from, and the second representing the state changed to.

For the alternative scenarios, the probability of transition between the five states (N = never, C = current conventional cigarettes, T = current cMRTP, D = current dual, and F = former) is described by P followed by two subscripts, the first representing the state changed from, and the second representing the state changed to.

Table A1. Monthly tobacco transition probabilities (per million) under the null scenario.

Age	Initiation P_{NC}	Quitting P_{CF}	Re-initiation P_{FC}
10-14	2000	500	240
15-19	3500	1500	720
20-24	2000	2000	960
25-29	1000	2000	960
30-34	500	2000	960
35-39	0	2000	960
40-44	0	2000	960
45-49	0	2000	960
50-54	0	2000	960
55-59	0	2500	1200
60-64	0	2500	1200
65-69	0	3000	1440
70-74	0	3500	1680
75-79	0	4000	1920

Table A2. Monthly tobacco transition probabilities (per million) under the "No further smoking" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	0	0	0	1000000	0	0	0	0	0
	15-19	0	0	0	1000000	0	0	0	0	0
	20-24	0	0	0	1000000	0	0	0	0	0
	25-29	0	0	0	1000000	0	0	0	0	0
	30-34	0	0	0	1000000	0	0	0	0	0
	35-39	0	0	0	1000000	0	0	0	0	0
	40-44	0	0	0	1000000	0	0	0	0	0
	45-49	0	0	0	1000000	0	0	0	0	0
	50-54	0	0	0	1000000	0	0	0	0	0
	55-59	0	0	0	1000000	0	0	0	0	0
	60-64	0	0	0	1000000	0	0	0	0	0
	65-69	0	0	0	1000000	0	0	0	0	0
	70-74	0	0	0	1000000	0	0	0	0	0
	75-79	0	0	0	1000000	0	0	0	0	0
25+	10-14	0	0	0	1000000	0	0	0	0	0
	15-19	0	0	0	1000000	0	0	0	0	0
	20-24	0	0	0	1000000	0	0	0	0	0
	25-29	0	0	0	1000000	0	0	0	0	0
	30-34	0	0	0	1000000	0	0	0	0	0
	35-39	0	0	0	1000000	0	0	0	0	0
	40-44	0	0	0	1000000	0	0	0	0	0
	45-49	0	0	0	1000000	0	0	0	0	0
	50-54	0	0	0	1000000	0	0	0	0	0
	55-59	0	0	0	1000000	0	0	0	0	0
	60-64	0	0	0	1000000	0	0	0	0	0
	65-69	0	0	0	1000000	0	0	0	0	0
	70-74	0	0	0	1000000	0	0	0	0	0
	75-79	0	0	0	1000000	0	0	0	0	0

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	0	0	0	0	0	0
	15-19	0	0	0	0	0	0
	20-24	0	0	0	0	0	0
	25-29	0	0	0	0	0	0
	30-34	0	0	0	0	0	0
	35-39	0	0	0	0	0	0
	40-44	0	0	0	0	0	0
	45-49	0	0	0	0	0	0
	50-54	0	0	0	0	0	0
	55-59	0	0	0	0	0	0
	60-64	0	0	0	0	0	0
	65-69	0	0	0	0	0	0
	70-74	0	0	0	0	0	0
	75-79	0	0	0	0	0	0

Table A3. Monthly tobacco transition probabilities (per million) under the "Smoking totally replaced by cMRTP use" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	0	2000	0	0	0	0	0	240	0
	15-19	0	3500	0	0	0	0	0	720	0
	20-24	0	2000	0	0	0	0	0	960	0
	25-29	0	1000	0	0	0	0	0	960	0
	30-34	0	500	0	0	0	0	0	960	0
	35-39	0	0	0	0	0	0	0	960	0
	40-44	0	0	0	0	0	0	0	960	0
	45-49	0	0	0	0	0	0	0	960	0
	50-54	0	0	0	0	0	0	0	960	0
	55-59	0	0	0	0	0	0	0	1200	0
	60-64	0	0	0	0	0	0	0	1200	0
	65-69	0	0	0	0	0	0	0	1440	0
	70-74	0	0	0	0	0	0	0	1680	0
	75-79	0	0	0	0	0	0	0	1920	0
25+	10-14	0	2000	0	0	0	0	0	240	0
	15-19	0	3500	0	0	0	0	0	720	0
	20-24	0	2000	0	0	0	0	0	960	0
	25-29	0	1000	0	0	0	0	0	960	0
	30-34	0	500	0	0	0	0	0	960	0
	35-39	0	0	0	0	0	0	0	960	0
	40-44	0	0	0	0	0	0	0	960	0
	45-49	0	0	0	0	0	0	0	960	0
	50-54	0	0	0	0	0	0	0	960	0
	55-59	0	0	0	0	0	0	0	1200	0
	60-64	0	0	0	0	0	0	0	1200	0
	65-69	0	0	0	0	0	0	0	1440	0
	70-74	0	0	0	0	0	0	0	1680	0
	75-79	0	0	0	0	0	0	0	1920	0

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	1000000	0	0	0	0	1000000
	15-19	1000000	0	0	0	0	1000000
	20-24	1000000	0	0	0	0	1000000
	25-29	1000000	0	0	0	0	1000000
	30-34	1000000	0	0	0	0	1000000
	35-39	1000000	0	0	0	0	1000000
	40-44	1000000	0	0	0	0	1000000
	45-49	1000000	0	0	0	0	1000000
	50-54	1000000	0	0	0	0	1000000
	55-59	1000000	0	0	0	0	1000000
	60-64	1000000	0	0	0	0	1000000
	65-69	1000000	0	0	0	0	1000000
	70-74	1000000	0	0	0	0	1000000
	75-79	1000000	0	0	0	0	1000000

Table A4. Monthly tobacco transition probabilities (per million) under the "WHO 2025 Target" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	1800	0	0	1042	0	0	115	0	0
	15-19	3300	0	0	3125	0	0	346	0	0
	20-24	1800	0	0	4167	0	0	461	0	0
	25-29	800	0	0	4167	0	0	461	0	0
	30-34	300	0	0	4167	0	0	461	0	0
	35-39	0	0	0	4167	0	0	461	0	0
	40-44	0	0	0	4167	0	0	461	0	0
	45-49	0	0	0	4167	0	0	461	0	0
	50-54	0	0	0	4167	0	0	461	0	0
	55-59	0	0	0	5208	0	0	576	0	0
	60-64	0	0	0	5208	0	0	576	0	0
	65-69	0	0	0	6250	0	0	691	0	0
	70-74	0	0	0	7292	0	0	806	0	0
	75-79	0	0	0	8333	0	0	922	0	0
25+	10-14	1800	0	0	1042	0	0	115	0	0
	15-19	3300	0	0	3125	0	0	346	0	0
	20-24	1800	0	0	4167	0	0	461	0	0
	25-29	800	0	0	4167	0	0	461	0	0
	30-34	300	0	0	4167	0	0	461	0	0
	35-39	0	0	0	4167	0	0	461	0	0
	40-44	0	0	0	4167	0	0	461	0	0
	45-49	0	0	0	4167	0	0	461	0	0
	50-54	0	0	0	4167	0	0	461	0	0
	55-59	0	0	0	5208	0	0	576	0	0
	60-64	0	0	0	5208	0	0	576	0	0
	65-69	0	0	0	6250	0	0	691	0	0
	70-74	0	0	0	7292	0	0	806	0	0
	75-79	0	0	0	8333	0	0	922	0	0

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	0	0	0	0	0	0
	15-19	0	0	0	0	0	0
	20-24	0	0	0	0	0	0
	25-29	0	0	0	0	0	0
	30-34	0	0	0	0	0	0
	35-39	0	0	0	0	0	0
	40-44	0	0	0	0	0	0
	45-49	0	0	0	0	0	0
	50-54	0	0	0	0	0	0
	55-59	0	0	0	0	0	0
	60-64	0	0	0	0	0	0
	65-69	0	0	0	0	0	0
	70-74	0	0	0	0	0	0
	75-79	0	0	0	0	0	0

Table A5. Monthly tobacco transition probabilities (per million) under the "WHO 2025 Projection" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	1800	0	0	833	0	0	144	0	0
	15-19	3300	0	0	2500	0	0	432	0	0
	20-24	1800	0	0	3333	0	0	576	0	0
	25-29	800	0	0	3333	0	0	576	0	0
	30-34	300	0	0	3333	0	0	576	0	0
	35-39	0	0	0	3333	0	0	576	0	0
	40-44	0	0	0	3333	0	0	576	0	0
	45-49	0	0	0	3333	0	0	576	0	0
	50-54	0	0	0	3333	0	0	576	0	0
	55-59	0	0	0	4167	0	0	720	0	0
	60-64	0	0	0	4167	0	0	720	0	0
	65-69	0	0	0	5000	0	0	864	0	0
	70-74	0	0	0	5833	0	0	1008	0	0
	75-79	0	0	0	6667	0	0	1152	0	0
25+	10-14	1800	0	0	833	0	0	144	0	0
	15-19	3300	0	0	2500	0	0	432	0	0
	20-24	1800	0	0	3333	0	0	576	0	0
	25-29	800	0	0	3333	0	0	576	0	0
	30-34	300	0	0	3333	0	0	576	0	0
	35-39	0	0	0	3333	0	0	576	0	0
	40-44	0	0	0	3333	0	0	576	0	0
	45-49	0	0	0	3333	0	0	576	0	0
	50-54	0	0	0	3333	0	0	576	0	0
	55-59	0	0	0	4167	0	0	720	0	0
	60-64	0	0	0	4167	0	0	720	0	0
	65-69	0	0	0	5000	0	0	864	0	0
	70-74	0	0	0	5833	0	0	1008	0	0
	75-79	0	0	0	6667	0	0	1152	0	0

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	0	0	0	0	0	0
	15-19	0	0	0	0	0	0
	20-24	0	0	0	0	0	0
	25-29	0	0	0	0	0	0
	30-34	0	0	0	0	0	0
	35-39	0	0	0	0	0	0
	40-44	0	0	0	0	0	0
	45-49	0	0	0	0	0	0
	50-54	0	0	0	0	0	0
	55-59	0	0	0	0	0	0
	60-64	0	0	0	0	0	0
	65-69	0	0	0	0	0	0
	70-74	0	0	0	0	0	0
	75-79	0	0	0	0	0	0

Table A6. Monthly tobacco transition probabilities (per million) under the "cMRTP uptake case" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	1660	260	80	500	500	500	144	48	48
	15-19	2905	455	140	1500	1500	1500	432	144	144
	20-24	1660	260	80	2000	2000	2000	576	192	192
	25-29	830	130	40	2000	2000	2000	576	192	192
	30-34	415	65	20	2000	2000	2000	576	192	192
	35-39	0	0	0	2000	2000	2000	576	192	192
	40-44	0	0	0	2000	2000	2000	576	192	192
	45-49	0	0	0	2000	2000	2000	576	192	192
	50-54	0	0	0	2000	2000	2000	576	192	192
	55-59	0	0	0	2500	2500	2500	720	240	240
	60-64	0	0	0	2500	2500	2500	720	240	240
	65-69	0	0	0	3000	3000	3000	864	288	288
	70-74	0	0	0	3500	3500	3500	1008	336	336
	75-79	0	0	0	4000	4000	4000	1152	384	384
25+	10-14	1416	484	100	500	500	500	96	96	48
	15-19	2478	842	180	1500	1500	1500	288	288	144
	20-24	1416	484	100	2000	2000	2000	384	384	192
	25-29	708	230	60	2000	2000	2000	384	384	192
	30-34	354	116	30	2000	2000	2000	384	384	192
	35-39	0	0	0	2000	2000	2000	384	384	192
	40-44	0	0	0	2000	2000	2000	384	384	192
	45-49	0	0	0	2000	2000	2000	384	384	192
	50-54	0	0	0	2000	2000	2000	384	384	192
	55-59	0	0	0	2500	2500	2500	480	480	240
	60-64	0	0	0	2500	2500	2500	480	480	240
	65-69	0	0	0	3000	3000	3000	576	576	288
	70-74	0	0	0	3500	3500	3500	672	672	336
	75-79	0	0	0	4000	4000	4000	768	768	384

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	600	1	600	1	10000	400
	15-19	600	1	600	1	10000	400
	20-24	600	1	600	1	10000	400
	25-29	1200	1	600	1	10000	400
	30-34	1200	1	600	1	10000	400
	35-39	1200	1	600	1	10000	400
	40-44	1200	1	600	1	10000	400
	45-49	1200	1	600	1	10000	400
	50-54	1200	1	600	1	10000	400
	55-59	1200	1	600	1	10000	400
	60-64	1200	1	600	1	10000	400
	65-69	1200	1	600	1	10000	400
	70-74	1200	1	600	1	10000	400
	75-79	1200	1	600	1	10000	400

Table A7. Monthly tobacco transition probabilities (per million) under the "cMRTP uptake case in addition to the WHO 2025 Target" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	1494	135	5	1042	1042	1042	69	23	23
	15-19	2739	406	14	3125	3125	3125	207	69	69
	20-24	1494	542	18	4167	4167	4167	276	92	92
	25-29	664	542	18	4167	4167	4167	276	92	92
	30-34	249	542	18	4167	4167	4167	276	92	92
	35-39	0	0	0	4167	4167	4167	0	0	0
	40-44	0	0	0	4167	4167	4167	0	0	0
	45-49	0	0	0	4167	4167	4167	0	0	0
	50-54	0	0	0	4167	4167	4167	0	0	0
	55-59	0	0	0	5208	5208	5208	0	0	0
	60-64	0	0	0	5208	5208	5208	0	0	0
	65-69	0	0	0	6250	6250	6250	0	0	0
	70-74	0	0	0	7292	7292	7292	0	0	0
	75-79	0	0	0	8333	8333	8333	0	0	0
25+	10-14	1274	252	6	1042	1042	1042	46	46	23
	15-19	2336	752	18	3125	3125	3125	138	138	69
	20-24	1274	1008	23	4167	4167	4167	184	184	92
	25-29	566	958	28	4167	4167	4167	184	184	92
	30-34	212	967	28	4167	4167	4167	184	184	92
	35-39	0	0	0	4167	4167	4167	0	0	0
	40-44	0	0	0	4167	4167	4167	0	0	0
	45-49	0	0	0	4167	4167	4167	0	0	0
	50-54	0	0	0	4167	4167	4167	0	0	0
	55-59	0	0	0	5208	5208	5208	0	0	0
	60-64	0	0	0	5208	5208	5208	0	0	0
	65-69	0	0	0	6250	6250	6250	0	0	0
	70-74	0	0	0	7292	7292	7292	0	0	0
	75-79	0	0	0	8333	8333	8333	0	0	0

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	600	1	600	1	10000	400
	15-19	600	1	600	1	10000	400
	20-24	600	1	600	1	10000	400
	25-29	1200	1	600	1	10000	400
	30-34	1200	1	600	1	10000	400
	35-39	1200	1	600	1	10000	400
	40-44	1200	1	600	1	10000	400
	45-49	1200	1	600	1	10000	400
	50-54	1200	1	600	1	10000	400
	55-59	1200	1	600	1	10000	400
	60-64	1200	1	600	1	10000	400
	65-69	1200	1	600	1	10000	400
	70-74	1200	1	600	1	10000	400
	75-79	1200	1	600	1	10000	400

Table A8. Monthly tobacco transition probabilities (per million) under the "cMRTP uptake case in addition to the WHO 2025 Projection" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	1494	234	72	833	833	833	86	29	29
	15-19	2739	429	132	2500	2500	2500	259	86	86
	20-24	1494	234	72	3333	3333	3333	346	115	115
	25-29	664	104	32	3333	3333	3333	346	115	115
	30-34	249	39	12	3333	3333	3333	346	115	115
	35-39	0	0	0	3333	3333	3333	346	115	115
	40-44	0	0	0	3333	3333	3333	346	115	115
	45-49	0	0	0	3333	3333	3333	346	115	115
	50-54	0	0	0	3333	3333	3333	346	115	115
	55-59	0	0	0	4167	4167	4167	432	144	144
	60-64	0	0	0	4167	4167	4167	432	144	144
	65-69	0	0	0	5000	5000	5000	518	173	173
	70-74	0	0	0	5833	5833	5833	605	202	202
	75-79	0	0	0	6667	6667	6667	691	230	230
25+	10-14	1274	436	90	833	833	833	58	58	29
	15-19	2336	794	170	2500	2500	2500	173	173	86
	20-24	1274	436	90	3333	3333	3333	230	230	115
	25-29	566	184	48	3333	3333	3333	230	230	115
	30-34	212	70	18	3333	3333	3333	230	230	115
	35-39	0	0	0	3333	3333	3333	230	230	115
	40-44	0	0	0	3333	3333	3333	230	230	115
	45-49	0	0	0	3333	3333	3333	230	230	115
	50-54	0	0	0	3333	3333	3333	230	230	115
	55-59	0	0	0	4167	4167	4167	288	288	144
	60-64	0	0	0	4167	4167	4167	288	288	144
	65-69	0	0	0	5000	5000	5000	346	346	173
	70-74	0	0	0	5833	5833	5833	403	403	202
	75-79	0	0	0	6667	6667	6667	461	461	230

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	600	1	600	1	10000	400
	15-19	600	1	600	1	10000	400
	20-24	600	1	600	1	10000	400
	25-29	1200	1	600	1	10000	400
	30-34	1200	1	600	1	10000	400
	35-39	1200	1	600	1	10000	400
	40-44	1200	1	600	1	10000	400
	45-49	1200	1	600	1	10000	400
	50-54	1200	1	600	1	10000	400
	55-59	1200	1	600	1	10000	400
	60-64	1200	1	600	1	10000	400
	65-69	1200	1	600	1	10000	400
	70-74	1200	1	600	1	10000	400
	75-79	1200	1	600	1	10000	400

Table A9. Monthly tobacco transition probabilities (per million) under the "Extreme increase in dual use" scenario – probabilities of initiation, cessation, and re-initiation.

Period of follow up	Age	Initiation			Cessation			Re-initiation		
		P_{NC}	P_{NT}	P_{ND}	P_{CF}	P_{TF}	P_{DF}	P_{FC}	P_{FT}	P_{FD}
1-24	10-14	1660	260	80	500	500	500	144	48	48
	15-19	2905	455	140	1500	1500	1500	432	144	144
	20-24	1660	260	80	2000	2000	2000	576	192	192
	25-29	830	130	40	2000	2000	2000	576	192	192
	30-34	415	65	20	2000	2000	2000	576	192	192
	35-39	0	0	0	2000	2000	2000	576	192	192
	40-44	0	0	0	2000	2000	2000	576	192	192
	45-49	0	0	0	2000	2000	2000	576	192	192
	50-54	0	0	0	2000	2000	2000	576	192	192
	55-59	0	0	0	2500	2500	2500	720	240	240
	60-64	0	0	0	2500	2500	2500	720	240	240
	65-69	0	0	0	3000	3000	3000	864	288	288
	70-74	0	0	0	3500	3500	3500	1008	336	336
	75-79	0	0	0	4000	4000	4000	1152	384	384
		1416	484	100	500	500	500	96	96	48
25+	10-14	2478	842	180	1500	1500	1500	288	288	144
	15-19	1416	484	100	2000	2000	2000	384	384	192
	20-24	708	230	60	2000	2000	2000	384	384	192
	25-29	354	116	30	2000	2000	2000	384	384	192
	30-34	0	0	0	2000	2000	2000	384	384	192
	35-39	0	0	0	2000	2000	2000	384	384	192
	40-44	0	0	0	2000	2000	2000	384	384	192
	45-49	0	0	0	2000	2000	2000	384	384	192
	50-54	0	0	0	2500	2500	2500	480	480	240
	55-59	0	0	0	2500	2500	2500	480	480	240
	60-64	0	0	0	3000	3000	3000	576	576	288
	65-69	0	0	0	3500	3500	3500	672	672	336
	70-74	0	0	0	4000	4000	4000	768	768	384
	75-79	1660	260	80	500	500	500	144	48	48

Probabilities of product switching

Period of follow up	Age	Switching between current tobacco use groups					
		P_{CT}	P_{CD}	P_{TC}	P_{TD}	P_{DC}	P_{DT}
Any	10-14	600	313	6000	100000	10000	0
	15-19	600	313	6000	100000	10000	0
	20-24	600	313	6000	100000	10000	0
	25-29	1200	625	6000	100000	10000	0
	30-34	1200	625	6000	100000	10000	0
	35-39	1200	625	6000	100000	10000	0
	40-44	1200	625	6000	100000	10000	0
	45-49	1200	625	6000	100000	10000	0
	50-54	1200	625	6000	100000	10000	0
	55-59	1200	625	6000	100000	10000	0
	60-64	1200	625	6000	100000	10000	0
	65-69	1200	625	6000	100000	10000	0
	70-74	1200	625	6000	100000	10000	0
	75-79	1200	625	6000	100000	10000	0

Appendix B: Smoking prevalence over the simulation period in the alternative scenarios

Table B1. No further smoking.

Sex	Age	Scenario	Year	Never smokers (%)	Current smokers (%)	Former smokers (%)	Scenario	Never smokers (%)	Current smokers (%)	cMRTP users (%)	Dual users (%)	Former smokers (%)
Male	All ages	null	1990	47.7	26.6	25.6	alternative	47.7	26.6	0	0	25.6
	All ages	null	1991	47.1	27.0	25.9	alternative	47.8	0	0	0	52.2
	All ages	null	1992	46.6	27.4	26.0	alternative	47.9	0	0	0	52.1
	All ages	null	1993	45.8	28.1	26.1	alternative	48.0	0	0	0	52.0
	All ages	null	1994	45.3	28.2	26.4	alternative	48.1	0	0	0	51.9
	All ages	null	1995	44.9	28.3	26.8	alternative	48.3	0	0	0	51.7
	All ages	null	1996	44.6	28.6	26.8	alternative	48.5	0	0	0	51.5
	All ages	null	1997	44.3	28.7	27.0	alternative	48.7	0	0	0	51.3
	All ages	null	1998	44.0	28.7	27.2	alternative	49.0	0	0	0	51.0
	All ages	null	1999	43.8	28.8	27.5	alternative	49.2	0	0	0	50.8
	All ages	null	2000	43.6	28.6	27.7	alternative	49.4	0	0	0	50.6
	All ages	null	2001	43.5	28.6	27.9	alternative	49.7	0	0	0	50.3
	All ages	null	2002	43.5	28.6	28.0	alternative	50.0	0	0	0	50.0
	All ages	null	2003	43.4	28.7	27.9	alternative	50.2	0	0	0	49.8
	All ages	null	2004	43.4	28.7	27.9	alternative	50.5	0	0	0	49.5
	All ages	null	2005	43.4	28.4	28.2	alternative	50.7	0	0	0	49.3
	All ages	null	2006	43.5	28.2	28.4	alternative	51.0	0	0	0	49.0
	All ages	null	2007	43.5	28.2	28.3	alternative	51.3	0	0	0	48.7
	All ages	null	2008	43.6	27.8	28.6	alternative	51.5	0	0	0	48.5
	All ages	null	2009	43.8	27.7	28.5	alternative	51.9	0	0	0	48.1
	All ages	null	2010	44.0	27.6	28.3	alternative	52.3	0	0	0	47.7
Female	All ages	null	1990	59.2	21.6	19.3	alternative	59.2	21.6	0	0	19.3
	All ages	null	1991	58.3	22.2	19.5	alternative	59.1	0	0	0	40.9
	All ages	null	1992	57.4	22.7	19.9	alternative	59.0	0	0	0	41.0
	All ages	null	1993	56.6	23.2	20.2	alternative	58.9	0	0	0	41.1
	All ages	null	1994	56.1	23.4	20.5	alternative	58.9	0	0	0	41.1
	All ages	null	1995	55.3	23.9	20.7	alternative	58.8	0	0	0	41.2
	All ages	null	1996	54.8	24.0	21.1	alternative	58.8	0	0	0	41.2
	All ages	null	1997	54.3	24.4	21.3	alternative	58.9	0	0	0	41.1
	All ages	null	1998	53.9	24.5	21.7	alternative	58.9	0	0	0	41.1
	All ages	null	1999	53.6	24.6	21.8	alternative	59.0	0	0	0	41.0
	All ages	null	2000	53.4	24.4	22.2	alternative	59.0	0	0	0	41.0
	All ages	null	2001	53.1	24.4	22.5	alternative	59.1	0	0	0	40.9
	All ages	null	2002	52.8	24.6	22.5	alternative	59.1	0	0	0	40.9

All ages	null	2003	52.6	24.7	22.6	alternative	59.2	0	0	0	40.8
All ages	null	2004	52.5	24.4	23.0	alternative	59.3	0	0	0	40.7
All ages	null	2005	52.4	24.5	23.1	alternative	59.4	0	0	0	40.6
All ages	null	2006	52.3	24.6	23.1	alternative	59.6	0	0	0	40.4
All ages	null	2007	52.3	24.2	23.4	alternative	59.8	0	0	0	40.2
All ages	null	2008	52.3	24.1	23.6	alternative	59.9	0	0	0	40.1
All ages	null	2009	52.2	24.1	23.7	alternative	60.0	0	0	0	40.0
All ages	null	2010	52.3	23.7	24.0	alternative	60.2	0	0	0	39.8

Table B2. Smoking totally replaced by cMRTP use.

Sex	Age	Scenario	Year #	Never smoker (%)	Current smoker (%)	Former smoker (%)	Scenario	Never smoker (%)	Current smoker (%)	cMRTP users (%)	Dual users (%)	Former smoker (%)
Male	All ages	null	1990	47.7	26.6	25.6	alternative	47.7	26.6	0	0	25.6
	All ages	null	1991	47.1	27.0	25.9	alternative	46.9	0	28.0	0	25.2
	All ages	null	1992	46.6	27.4	26.0	alternative	46.5	0	28.0	0	25.5
	All ages	null	1993	45.8	28.1	26.1	alternative	46.0	0	28.0	0	25.9
	All ages	null	1994	45.3	28.2	26.4	alternative	45.6	0	28.0	0	26.0
	All ages	null	1995	44.9	28.3	26.8	alternative	45.0	0	29.0	0	26.3
	All ages	null	1996	44.6	28.6	26.8	alternative	44.5	0	29.0	0	26.4
	All ages	null	1997	44.3	28.7	27.0	alternative	44.1	0	29.0	0	26.5
	All ages	null	1998	44.0	28.7	27.2	alternative	43.9	0	29.0	0	26.6
	All ages	null	1999	43.8	28.8	27.5	alternative	43.6	0	29.0	0	27.0
	All ages	null	2000	43.6	28.6	27.7	alternative	43.4	0	29.0	0	27.1
	All ages	null	2001	43.5	28.6	27.9	alternative	43.3	0	29.0	0	27.3
	All ages	null	2002	43.5	28.6	28.0	alternative	43.3	0	29.0	0	27.4
	All ages	null	2003	43.4	28.7	27.9	alternative	43.4	0	29.0	0	27.5
	All ages	null	2004	43.4	28.7	27.9	alternative	43.3	0	29.0	0	27.6
	All ages	null	2005	43.4	28.4	28.2	alternative	43.3	0	29.0	0	27.7
	All ages	null	2006	43.5	28.2	28.4	alternative	43.5	0	29.0	0	27.7
	All ages	null	2007	43.5	28.2	28.3	alternative	43.6	0	28.0	0	28.1
	All ages	null	2008	43.6	27.8	28.6	alternative	43.6	0	28.0	0	28.3
	All ages	null	2009	43.8	27.7	28.5	alternative	43.9	0	28.0	0	28.4
	All ages	null	2010	44.0	27.6	28.3	alternative	44.1	0	27.4	0	28.4
Female	All ages	null	1990	59.2	21.6	19.3	alternative	59.2	21.6	0	0	19.3
	All ages	null	1991	58.3	22.2	19.5	alternative	58.5	0	22.7	0	18.9
	All ages	null	1992	57.4	22.7	19.9	alternative	57.7	0	23.0	0	19.3
	All ages	null	1993	56.6	23.2	20.2	alternative	56.9	0	23.6	0	19.5
	All ages	null	1994	56.1	23.4	20.5	alternative	56.4	0	23.8	0	19.8
	All ages	null	1995	55.3	23.9	20.7	alternative	55.6	0	24.4	0	20.0
	All ages	null	1996	54.8	24.0	21.1	alternative	55.1	0	24.7	0	20.2
	All ages	null	1997	54.3	24.4	21.3	alternative	54.8	0	24.7	0	20.5
	All ages	null	1998	53.9	24.5	21.7	alternative	54.4	0	24.8	0	20.8
	All ages	null	1999	53.6	24.6	21.8	alternative	54.1	0	24.9	0	21.0
	All ages	null	2000	53.4	24.4	22.2	alternative	53.8	0	25.0	0	21.2
	All ages	null	2001	53.1	24.4	22.5	alternative	53.4	0	25.1	0	21.5
	All ages	null	2002	52.8	24.6	22.5	alternative	53.3	0	25.0	0	21.7
	All ages	null	2003	52.6	24.7	22.6	alternative	53.1	0	24.9	0	22.0
	All ages	null	2004	52.5	24.4	23.0	alternative	53.0	0	24.8	0	22.3

All ages	null	2005	52.4	24.5	23.1	alternative	52.8	0	24.6	0	22.6
All ages	null	2006	52.3	24.6	23.1	alternative	52.7	0	24.4	0	22.8
All ages	null	2007	52.3	24.2	23.4	alternative	52.7	0	24.2	0	23.1
All ages	null	2008	52.3	24.1	23.6	alternative	52.6	0	23.9	0	23.4
All ages	null	2009	52.2	24.1	23.7	alternative	52.5	0	23.9	0	23.6
All ages	null	2010	52.3	23.7	24.0	alternative	52.6	0	23.6	0	23.8

Table B3. WHO 2025 Target.

Sex	Age	Scenario	Year #	Never smoker (%)	Current smoker (%)	Former smoker (%)	Scenario	Never smoker (%)	Current smoker (%)	cMRTP users (%)	Dual users (%)	Former smoker (%)
Male	All ages	null	1990	47.9	26.7	25.4	alternative	47.9	26.7	0	0	25.4
	All ages	null	1991	47.2	27.1	25.6	alternative	47.4	26.3	0	0	26.4
	All ages	null	1992	46.7	27.5	25.8	alternative	47.0	25.7	0	0	27.4
	All ages	null	1993	46.3	27.8	25.9	alternative	46.7	25.0	0	0	28.3
	All ages	null	1994	45.6	28.3	26.0	alternative	46.2	24.5	0	0	29.3
	All ages	null	1995	45.0	28.9	26.0	alternative	45.5	24.3	0	0	30.1
	All ages	null	1996	44.6	29.3	26.1	alternative	45.1	23.9	0	0	30.9
	All ages	null	1997	44.3	29.1	26.5	alternative	44.8	23.5	0	0	31.7
	All ages	null	1998	44.1	29.3	26.6	alternative	44.6	23.0	0	0	32.4
	All ages	null	1999	44.0	29.0	27.0	alternative	44.4	22.5	0	0	33.1
	All ages	null	2000	43.9	28.8	27.3	alternative	44.4	21.9	0	0	33.8
	All ages	null	2001	43.8	28.8	27.4	alternative	44.3	21.3	0	0	34.4
	All ages	null	2002	43.8	28.7	27.6	alternative	44.4	20.6	0	0	35.0
	All ages	null	2003	43.9	28.3	27.8	alternative	44.5	19.9	0	0	35.6
	All ages	null	2004	43.9	28.3	27.8	alternative	44.6	19.3	0	0	36.1
	All ages	null	2005	44.1	28.1	27.9	alternative	44.8	18.5	0	0	36.7
	All ages	null	2006	44.2	27.9	27.9	alternative	45.0	17.6	0	0	37.5
	All ages	null	2007	44.3	27.9	27.8	alternative	45.1	17.1	0	0	37.8
	All ages	null	2008	44.4	27.5	28.1	alternative	45.3	16.6	0	0	38.1
	All ages	null	2009	44.6	27.1	28.3	alternative	45.5	16.1	0	0	38.4
	All ages	null	2010	44.8	26.8	28.3	alternative	45.8	15.7	0	0	38.5
Female	All ages	null	1990	59.8	22.0	18.3	alternative	59.8	22.0	0	0	18.3
	All ages	null	1991	59.0	22.3	18.7	alternative	59.1	21.6	0	0	19.3
	All ages	null	1992	58.4	22.7	18.9	alternative	58.5	21.2	0	0	20.4
	All ages	null	1993	57.9	22.8	19.3	alternative	57.9	20.6	0	0	21.5
	All ages	null	1994	57.3	23.1	19.6	alternative	57.3	20.1	0	0	22.6
	All ages	null	1995	56.7	23.4	19.9	alternative	56.7	19.9	0	0	23.4
	All ages	null	1996	56.3	23.7	19.9	alternative	56.3	19.5	0	0	24.3
	All ages	null	1997	55.9	23.8	20.3	alternative	55.9	19.0	0	0	25.1
	All ages	null	1998	55.5	23.9	20.6	alternative	55.4	18.7	0	0	25.9
	All ages	null	1999	55.1	24.3	20.7	alternative	55.0	18.4	0	0	26.6
	All ages	null	2000	54.8	24.4	20.7	alternative	54.8	17.8	0	0	27.3
	All ages	null	2001	54.6	24.4	21.0	alternative	54.7	17.4	0	0	27.9
	All ages	null	2002	54.3	24.5	21.2	alternative	54.4	17.0	0	0	28.6
	All ages	null	2003	54.2	24.5	21.3	alternative	54.4	16.8	0	0	28.8
	All ages	null	2004	54.0	24.3	21.7	alternative	54.2	16.4	0	0	29.3

All ages	null	2005	53.9	24.3	21.8	alternative	54.1	16.0	0	0	29.9
All ages	null	2006	53.8	24.2	22.0	alternative	54.1	15.6	0	0	30.2
All ages	null	2007	53.8	23.9	22.3	alternative	54.2	14.9	0	0	31.0
All ages	null	2008	53.6	23.6	22.7	alternative	54.2	14.3	0	0	31.5
All ages	null	2009	53.7	23.5	22.8	alternative	54.3	13.8	0	0	31.9
All ages	null	2010	53.7	23.5	22.8	alternative	54.4	13.3	0	0	32.3

Table B4. WHO 2025 Projection.

Sex	Age	Scenario	Year #	Never smoker (%)	Current smoker (%)	Former smoker (%)	Scenario	Never smoker (%)	Current smoker (%)	cMRTP users (%)	Dual users (%)	Former smoker (%)
Male	All ages	null	1990	47.9	26.7	25.4	alternative	47.9	26.7	0	0	25.4
	All ages	null	1991	47.2	27.1	25.6	alternative	47.4	26.5	0	0	26.1
	All ages	null	1992	46.7	27.5	25.8	alternative	47.0	26.3	0	0	26.8
	All ages	null	1993	46.3	27.8	25.9	alternative	46.7	26.0	0	0	27.3
	All ages	null	1994	45.6	28.3	26.0	alternative	46.2	25.8	0	0	28.1
	All ages	null	1995	45.0	28.9	26.0	alternative	45.5	25.8	0	0	28.7
	All ages	null	1996	44.6	29.3	26.1	alternative	45.1	25.7	0	0	29.2
	All ages	null	1997	44.3	29.1	26.5	alternative	44.8	25.4	0	0	29.8
	All ages	null	1998	44.1	29.3	26.6	alternative	44.6	25.1	0	0	30.2
	All ages	null	1999	44.0	29.0	27.0	alternative	44.4	24.7	0	0	30.9
	All ages	null	2000	43.9	28.8	27.3	alternative	44.4	24.2	0	0	31.5
	All ages	null	2001	43.8	28.8	27.4	alternative	44.3	23.7	0	0	32.0
	All ages	null	2002	43.8	28.7	27.6	alternative	44.4	23.2	0	0	32.5
	All ages	null	2003	43.9	28.3	27.8	alternative	44.5	22.6	0	0	32.9
	All ages	null	2004	43.9	28.3	27.8	alternative	44.6	22.0	0	0	33.5
	All ages	null	2005	44.1	28.1	27.9	alternative	44.8	21.3	0	0	33.9
	All ages	null	2006	44.2	27.9	27.9	alternative	45.0	20.5	0	0	34.5
	All ages	null	2007	44.3	27.9	27.8	alternative	45.1	20.1	0	0	34.8
	All ages	null	2008	44.4	27.5	28.1	alternative	45.3	19.6	0	0	35.1
	All ages	null	2009	44.6	27.1	28.3	alternative	45.5	19.2	0	0	35.3
	All ages	null	2010	44.8	26.8	28.3	alternative	45.8	18.8	0	0	35.4
Female	All ages	null	1990	59.8	22.0	18.3	alternative	59.8	22.0	0	0	18.3
	All ages	null	1991	59.0	22.3	18.7	alternative	59.1	21.9	0	0	19.0
	All ages	null	1992	58.4	22.7	18.9	alternative	58.5	21.7	0	0	19.8
	All ages	null	1993	57.9	22.8	19.3	alternative	57.9	21.5	0	0	20.6
	All ages	null	1994	57.3	23.1	19.6	alternative	57.3	21.1	0	0	21.6
	All ages	null	1995	56.7	23.4	19.9	alternative	56.7	21.2	0	0	22.2
	All ages	null	1996	56.3	23.7	19.9	alternative	56.3	20.9	0	0	22.8
	All ages	null	1997	55.9	23.8	20.3	alternative	55.9	20.6	0	0	23.5
	All ages	null	1998	55.5	23.9	20.6	alternative	55.4	20.3	0	0	24.3
	All ages	null	1999	55.1	24.3	20.7	alternative	55.0	20.1	0	0	24.9
	All ages	null	2000	54.8	24.4	20.7	alternative	54.8	19.7	0	0	25.4
	All ages	null	2001	54.6	24.4	21.0	alternative	54.7	19.4	0	0	25.9
	All ages	null	2002	54.3	24.5	21.2	alternative	54.4	19.2	0	0	26.4
	All ages	null	2003	54.2	24.5	21.3	alternative	54.4	19.1	0	0	26.5
	All ages	null	2004	54.0	24.3	21.7	alternative	54.2	19.0	0	0	26.8

All ages	null	2005	53.9	24.3	21.8	alternative	54.1	18.5	0	0	27.3
All ages	null	2006	53.8	24.2	22.0	alternative	54.1	18.1	0	0	27.7
All ages	null	2007	53.8	23.9	22.3	alternative	54.2	17.5	0	0	28.4
All ages	null	2008	53.6	23.6	22.7	alternative	54.2	16.9	0	0	28.9
All ages	null	2009	53.7	23.5	22.8	alternative	54.3	16.4	0	0	29.3
All ages	null	2010	53.7	23.5	22.8	alternative	54.4	16.1	0	0	29.6

Table B5. cMRTP uptake case.

Sex	Age	Scenario	Year #	Never smoker (%)	Current smoker (%)	Former smoker (%)	Scenario	Never smoker (%)	Current smoker (%)	cMRTP users (%)	Dual users (%)	Former smoker (%)
Male	All ages	null	1990	47.7	26.6	25.6	alternative	47.7	26.6	0.0	0.0	25.6
	All ages	null	1991	47.1	27.1	25.8	alternative	46.9	26.7	0.5	0.1	25.8
	All ages	null	1992	46.6	27.6	25.9	alternative	46.5	26.4	1.0	0.2	26.0
	All ages	null	1993	45.8	28.2	26.0	alternative	46.0	25.9	1.5	0.3	26.3
	All ages	null	1994	45.3	28.3	26.4	alternative	45.6	25.4	2.1	0.4	26.5
	All ages	null	1995	45.0	28.3	26.7	alternative	45.0	25.1	2.6	0.5	26.7
	All ages	null	1996	44.6	28.6	26.8	alternative	44.5	25.0	3.3	0.5	26.7
	All ages	null	1997	44.3	28.6	27.1	alternative	44.1	24.8	3.9	0.6	26.6
	All ages	null	1998	44.0	28.6	27.3	alternative	43.9	24.4	4.4	0.6	26.8
	All ages	null	1999	43.8	28.6	27.6	alternative	43.6	23.9	4.6	0.6	27.4
	All ages	null	2000	43.6	28.5	27.9	alternative	43.5	23.5	5.0	0.5	27.6
	All ages	null	2001	43.5	28.4	28.1	alternative	43.3	23.0	5.4	0.5	27.8
	All ages	null	2002	43.5	28.4	28.2	alternative	43.3	22.6	5.8	0.5	27.8
	All ages	null	2003	43.4	28.5	28.1	alternative	43.4	22.0	6.1	0.5	28.1
	All ages	null	2004	43.4	28.5	28.1	alternative	43.3	21.5	6.4	0.5	28.3
	All ages	null	2005	43.4	28.2	28.4	alternative	43.3	21.3	6.7	0.5	28.2
	All ages	null	2006	43.5	27.9	28.6	alternative	43.5	20.8	7.0	0.6	28.2
	All ages	null	2007	43.5	27.8	28.6	alternative	43.6	20.2	7.3	0.5	28.4
	All ages	null	2008	43.6	27.4	29.0	alternative	43.6	19.6	7.5	0.6	28.7
	All ages	null	2009	43.8	27.4	28.9	alternative	43.9	18.9	7.6	0.6	29.1
	All ages	null	2010	44.0	27.2	28.8	alternative	44.1	18.4	7.9	0.6	29.1
Female	All ages	null	1990	59.2	21.6	19.3	alternative	59.2	21.6	0.0	0.0	19.3
	All ages	null	1991	58.3	22.2	19.5	alternative	58.5	21.6	0.4	0.1	19.5
	All ages	null	1992	57.4	22.7	19.9	alternative	57.7	21.6	0.8	0.1	19.8
	All ages	null	1993	56.6	23.3	20.1	alternative	56.9	21.6	1.2	0.2	20.1
	All ages	null	1994	56.1	23.4	20.5	alternative	56.4	21.4	1.7	0.2	20.4
	All ages	null	1995	55.3	23.9	20.8	alternative	55.6	21.2	2.2	0.4	20.7
	All ages	null	1996	54.8	24.0	21.2	alternative	55.1	21.0	2.6	0.4	20.9
	All ages	null	1997	54.3	24.4	21.3	alternative	54.8	20.6	2.9	0.4	21.3
	All ages	null	1998	53.9	24.4	21.8	alternative	54.4	20.3	3.2	0.4	21.8
	All ages	null	1999	53.6	24.5	21.9	alternative	54.1	19.9	3.6	0.4	22.0
	All ages	null	2000	53.4	24.3	22.3	alternative	53.8	19.8	3.9	0.4	22.2
	All ages	null	2001	53.1	24.3	22.7	alternative	53.4	19.5	4.3	0.4	22.3
	All ages	null	2002	52.8	24.5	22.7	alternative	53.3	19.1	4.6	0.4	22.7
	All ages	null	2003	52.7	24.5	22.8	alternative	53.1	18.6	4.8	0.5	23.0

All ages	null	2004	52.5	24.2	23.2	alternative	53.0	18.0	5.2	0.5	23.4
All ages	null	2005	52.4	24.2	23.4	alternative	52.8	17.5	5.5	0.4	23.8
All ages	null	2006	52.3	24.3	23.4	alternative	52.7	16.8	5.7	0.4	24.3
All ages	null	2007	52.3	23.8	23.9	alternative	52.7	16.4	5.9	0.4	24.6
All ages	null	2008	52.3	23.7	24.1	alternative	52.6	15.9	6.0	0.5	24.9
All ages	null	2009	52.2	23.7	24.1	alternative	52.5	15.8	6.1	0.4	25.2
All ages	null	2010	52.3	23.3	24.5	alternative	52.6	15.4	6.2	0.5	25.4

Table B6. cMRTP uptake case in addition to the WHO 2025 Target.

Sex	Age	Scenario	Year #	Never smoker (%)	Current smoker (%)	Former smoker (%)	Scenario	Never smoker (%)	Current smoker (%)	cMRTP users (%)	Dual users (%)	Former smoker (%)
Male	All ages	null	1990	47.9	26.7	25.4	alternative	47.9	26.7	0.0	0.0	25.4
	All ages	null	1991	47.2	27.1	25.6	alternative	47.3	25.7	0.5	0.0	26.5
	All ages	null	1992	46.7	27.5	25.8	alternative	46.8	24.6	0.8	0.0	27.8
	All ages	null	1993	46.3	27.8	25.9	alternative	46.4	23.5	1.3	0.0	28.7
	All ages	null	1994	45.6	28.3	26.0	alternative	45.9	22.5	1.9	0.0	29.7
	All ages	null	1995	45.0	28.9	26.0	alternative	45.1	21.7	2.4	0.0	30.7
	All ages	null	1996	44.6	29.3	26.1	alternative	44.6	20.8	2.8	0.0	31.7
	All ages	null	1997	44.3	29.1	26.5	alternative	44.1	19.8	3.3	0.0	32.7
	All ages	null	1998	44.1	29.3	26.6	alternative	43.8	18.9	3.7	0.1	33.6
	All ages	null	1999	44.0	29.0	27.0	alternative	43.3	18.1	4.0	0.0	34.5
	All ages	null	2000	43.9	28.8	27.3	alternative	43.1	17.1	4.3	0.0	35.4
	All ages	null	2001	43.8	28.8	27.4	alternative	42.9	16.2	4.6	0.1	36.2
	All ages	null	2002	43.8	28.7	27.6	alternative	42.8	15.3	4.8	0.1	36.9
	All ages	null	2003	43.9	28.3	27.8	alternative	42.8	14.7	4.9	0.1	37.6
	All ages	null	2004	43.9	28.3	27.8	alternative	42.8	14.0	5.0	0.1	38.2
	All ages	null	2005	44.1	28.1	27.9	alternative	42.8	13.2	5.0	0.1	38.9
	All ages	null	2006	44.2	27.9	27.9	alternative	42.8	12.4	5.2	0.1	39.6
	All ages	null	2007	44.3	27.9	27.8	alternative	42.9	11.8	5.3	0.1	40.0
	All ages	null	2008	44.4	27.5	28.1	alternative	42.9	11.3	5.2	0.0	40.5
	All ages	null	2009	44.6	27.1	28.3	alternative	43.0	10.8	5.2	0.1	41.0
	All ages	null	2010	44.8	26.8	28.3	alternative	43.2	10.3	5.0	0.0	41.5
Female	All ages	null	1990	59.8	22.0	18.3	alternative	59.8	22.0	0.0	0.0	18.3
	All ages	null	1991	59.0	22.3	18.7	alternative	59.0	21.0	0.4	0.0	19.5
	All ages	null	1992	58.4	22.7	18.9	alternative	58.3	20.2	0.9	0.0	20.6
	All ages	null	1993	57.9	22.8	19.3	alternative	57.7	19.3	1.3	0.0	21.6
	All ages	null	1994	57.3	23.1	19.6	alternative	56.9	18.6	1.8	0.0	22.6
	All ages	null	1995	56.7	23.4	19.9	alternative	56.2	18.0	2.2	0.0	23.6
	All ages	null	1996	56.3	23.7	19.9	alternative	55.6	17.2	2.7	0.0	24.5
	All ages	null	1997	55.9	23.8	20.3	alternative	55.1	16.4	3.0	0.0	25.5
	All ages	null	1998	55.5	23.9	20.6	alternative	54.5	15.8	3.3	0.0	26.4
	All ages	null	1999	55.1	24.3	20.7	alternative	54.0	15.2	3.6	0.0	27.2
	All ages	null	2000	54.8	24.4	20.7	alternative	53.7	14.4	3.8	0.0	28.1
	All ages	null	2001	54.6	24.4	21.0	alternative	53.5	13.7	3.8	0.0	28.9
	All ages	null	2002	54.3	24.5	21.2	alternative	53.0	13.0	4.1	0.0	29.8
	All ages	null	2003	54.2	24.5	21.3	alternative	52.8	12.5	4.2	0.0	30.5
	All ages	null	2004	54.0	24.3	21.7	alternative	52.6	11.9	4.3	0.0	31.2

All ages	null	2005	53.9	24.3	21.8	alternative	52.3	11.3	4.3	0.1	32.0
All ages	null	2006	53.8	24.2	22.0	alternative	52.2	10.7	4.3	0.0	32.8
All ages	null	2007	53.8	23.9	22.3	alternative	52.1	10.2	4.4	0.0	33.3
All ages	null	2008	53.6	23.6	22.7	alternative	52.0	9.7	4.5	0.0	33.8
All ages	null	2009	53.7	23.5	22.8	alternative	52.0	9.0	4.6	0.0	34.4
All ages	null	2010	53.7	23.5	22.8	alternative	52.1	8.6	4.5	0.0	34.9

Table B7. cMRTP uptake case in addition to the WHO 2025 Projection.

Sex	Age	Scenario	Year #	Never smoker (%)	Current smoker (%)	Former smoker (%)	Scenario	Never smoker (%)	Current smoker (%)	cMRTP users (%)	Dual users (%)	Former smoker (%)
Male	All ages	null	1990	47.9	26.7	25.4	alternative	47.9	26.7	0.0	0.0	25.4
	All ages	null	1991	47.2	27.1	25.6	alternative	47.4	26.1	0.4	0.1	26.0
	All ages	null	1992	46.7	27.5	25.8	alternative	47.0	25.4	0.7	0.2	26.9
	All ages	null	1993	46.3	27.8	25.9	alternative	46.7	24.5	1.2	0.3	27.4
	All ages	null	1994	45.6	28.3	26.0	alternative	46.2	23.8	1.7	0.2	28.1
	All ages	null	1995	45.0	28.9	26.0	alternative	45.5	23.3	2.2	0.3	28.7
	All ages	null	1996	44.6	29.3	26.1	alternative	45.1	22.6	2.6	0.3	29.4
	All ages	null	1997	44.3	29.1	26.5	alternative	44.8	21.9	3.1	0.3	29.8
	All ages	null	1998	44.1	29.3	26.6	alternative	44.6	21.2	3.5	0.4	30.3
	All ages	null	1999	44.0	29.0	27.0	alternative	44.4	20.5	3.8	0.4	30.9
	All ages	null	2000	43.9	28.8	27.3	alternative	44.4	19.7	4.1	0.3	31.5
	All ages	null	2001	43.8	28.8	27.4	alternative	44.3	19.1	4.4	0.3	31.9
	All ages	null	2002	43.8	28.7	27.6	alternative	44.4	18.4	4.6	0.3	32.3
	All ages	null	2003	43.9	28.3	27.8	alternative	44.5	17.7	4.7	0.4	32.8
	All ages	null	2004	43.9	28.3	27.8	alternative	44.6	17.0	4.8	0.4	33.2
	All ages	null	2005	44.1	28.1	27.9	alternative	44.8	16.2	4.9	0.4	33.8
	All ages	null	2006	44.2	27.9	27.9	alternative	45.0	15.3	5.0	0.4	34.3
	All ages	null	2007	44.3	27.9	27.8	alternative	45.1	14.8	5.2	0.4	34.4
	All ages	null	2008	44.4	27.5	28.1	alternative	45.3	14.3	5.3	0.4	34.6
	All ages	null	2009	44.6	27.1	28.3	alternative	45.5	13.9	5.3	0.4	34.9
	All ages	null	2010	44.8	26.8	28.3	alternative	45.8	13.5	5.4	0.4	35.0
Female	All ages	null	1990	59.8	22.0	18.3	alternative	59.8	22.0	0.0	0.0	18.3
	All ages	null	1991	59.0	22.3	18.7	alternative	59.1	21.5	0.3	0.1	19.0
	All ages	null	1992	58.4	22.7	18.9	alternative	58.5	20.9	0.8	0.1	19.8
	All ages	null	1993	57.9	22.8	19.3	alternative	57.9	20.2	1.2	0.2	20.6
	All ages	null	1994	57.3	23.1	19.6	alternative	57.3	19.5	1.6	0.2	21.4
	All ages	null	1995	56.7	23.4	19.9	alternative	56.7	19.1	1.9	0.2	22.1
	All ages	null	1996	56.3	23.7	19.9	alternative	56.3	18.5	2.3	0.2	22.7
	All ages	null	1997	55.9	23.8	20.3	alternative	55.9	17.9	2.6	0.2	23.4
	All ages	null	1998	55.5	23.9	20.6	alternative	55.4	17.5	2.8	0.2	24.1
	All ages	null	1999	55.1	24.3	20.7	alternative	55.0	17.0	3.1	0.2	24.6
	All ages	null	2000	54.8	24.4	20.7	alternative	54.8	16.4	3.4	0.2	25.1
	All ages	null	2001	54.6	24.4	21.0	alternative	54.7	15.9	3.5	0.3	25.6
	All ages	null	2002	54.3	24.5	21.2	alternative	54.4	15.3	3.7	0.3	26.3
	All ages	null	2003	54.2	24.5	21.3	alternative	54.4	14.9	3.8	0.3	26.6
	All ages	null	2004	54.0	24.3	21.7	alternative	54.2	14.5	4.0	0.3	27.0

All ages	null	2005	53.9	24.3	21.8	alternative	54.1	14.0	4.1	0.3	27.4
All ages	null	2006	53.8	24.2	22.0	alternative	54.1	13.6	4.2	0.3	27.8
All ages	null	2007	53.8	23.9	22.3	alternative	54.2	12.9	4.3	0.3	28.4
All ages	null	2008	53.6	23.6	22.7	alternative	54.2	12.4	4.3	0.3	28.8
All ages	null	2009	53.7	23.5	22.8	alternative	54.3	11.9	4.4	0.3	29.2
All ages	null	2010	53.7	23.5	22.8	alternative	54.4	11.3	4.4	0.3	29.5

Table B8. Extreme increase in dual use.

Sex	Age	Scenario	Year #	Never smoker (%)	Current smoker (%)	Former smoker (%)	Scenario	Never smoker (%)	Current smoker (%)	cMRTP users (%)	Dual users (%)	Former smoker (%)
Male	All ages	null	1990	47.7	26.6	25.6	alternative	47.7	26.6	0.0	0.0	25.6
	All ages	null	1991	47.1	27.1	25.8	alternative	46.9	26.5	0.5	0.2	25.9
	All ages	null	1992	46.6	27.6	25.9	alternative	46.5	26.0	0.6	0.9	26.1
	All ages	null	1993	45.8	28.2	26.0	alternative	46.0	25.4	0.8	1.4	26.5
	All ages	null	1994	45.3	28.3	26.4	alternative	45.6	24.9	0.8	2.0	26.7
	All ages	null	1995	44.9	28.3	26.7	alternative	45.0	24.6	1.0	2.5	26.8
	All ages	null	1996	44.6	28.6	26.8	alternative	44.5	24.4	1.4	2.9	26.7
	All ages	null	1997	44.3	28.6	27.1	alternative	44.1	24.5	1.4	3.3	26.6
	All ages	null	1998	44.0	28.6	27.3	alternative	43.9	24.2	1.5	3.6	26.8
	All ages	null	1999	43.8	28.6	27.6	alternative	43.6	24.1	1.4	3.6	27.3
	All ages	null	2000	43.6	28.5	27.9	alternative	43.4	23.8	1.7	3.6	27.5
	All ages	null	2001	43.5	28.4	28.1	alternative	43.3	23.6	1.7	3.8	27.6
	All ages	null	2002	43.5	28.4	28.2	alternative	43.3	23.3	1.9	3.8	27.7
	All ages	null	2003	43.4	28.5	28.0	alternative	43.4	22.8	1.9	3.9	28.0
	All ages	null	2004	43.4	28.5	28.1	alternative	43.3	22.6	2.1	4.1	28.0
	All ages	null	2005	43.4	28.2	28.4	alternative	43.3	22.5	2.0	4.1	28.0
	All ages	null	2006	43.5	27.9	28.6	alternative	43.5	22.3	2.1	4.1	28.1
	All ages	null	2007	43.5	27.8	28.6	alternative	43.6	22.0	2.4	3.9	28.1
	All ages	null	2008	43.6	27.4	29.0	alternative	43.6	21.5	2.5	4.0	28.4
	All ages	null	2009	43.8	27.4	28.9	alternative	43.9	21.0	2.3	4.2	28.6
	All ages	null	2010	44.0	27.2	28.8	alternative	44.1	20.6	2.6	4.1	28.4
Female	All ages	null	1990	59.2	21.6	19.3	alternative	59.2	21.6	0.0	0.0	19.3
	All ages	null	1991	58.3	22.2	19.5	alternative	58.5	21.4	0.4	0.3	19.4
	All ages	null	1992	57.4	22.7	19.9	alternative	57.7	21.3	0.5	0.8	19.7
	All ages	null	1993	56.6	23.3	20.1	alternative	56.9	21.3	0.7	1.1	20.0
	All ages	null	1994	56.1	23.4	20.5	alternative	56.4	21.1	0.8	1.4	20.2
	All ages	null	1995	55.3	23.9	20.8	alternative	55.6	21.0	1.0	1.9	20.5
	All ages	null	1996	54.8	24.0	21.2	alternative	55.1	20.8	1.0	2.2	20.9
	All ages	null	1997	54.3	24.4	21.3	alternative	54.8	20.4	1.0	2.6	21.2
	All ages	null	1998	53.9	24.4	21.8	alternative	54.4	20.2	1.1	2.8	21.5
	All ages	null	1999	53.6	24.5	21.9	alternative	54.1	19.9	1.2	3.1	21.7
	All ages	null	2000	53.4	24.3	22.3	alternative	53.8	19.8	1.4	3.2	21.9
	All ages	null	2001	53.1	24.3	22.7	alternative	53.4	19.7	1.5	3.4	22.0
	All ages	null	2002	52.8	24.4	22.7	alternative	53.3	19.5	1.5	3.6	22.2
	All ages	null	2003	52.6	24.5	22.8	alternative	53.1	19.1	1.5	3.6	22.6
	All ages	null	2004	52.5	24.2	23.2	alternative	53.0	18.8	1.6	3.7	23.0

All ages	null	2005	52.4	24.2	23.4	alternative	52.8	18.5	1.9	3.6	23.2
All ages	null	2006	52.3	24.3	23.4	alternative	52.7	18.1	1.8	3.7	23.7
All ages	null	2007	52.3	23.8	23.9	alternative	52.7	18.0	1.8	3.6	23.9
All ages	null	2008	52.3	23.7	24.1	alternative	52.6	17.8	1.8	3.7	24.1
All ages	null	2009	52.2	23.7	24.1	alternative	52.5	17.7	1.9	3.4	24.4
All ages	null	2010	52.3	23.3	24.5	alternative	52.6	17.4	2.1	3.4	24.5

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