



Estimating the effect of differing assumptions on the population health impact of introducing a Reduced Risk Tobacco Product in the USA



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ABSTRACT

We use Population Health Impact Modelling to assess effects on tobacco prevalence and mortality of introducing a Reduced Risk Tobacco Product (RRP). Simulated samples start in 1990 with a US-representative smoking prevalence. Individual tobacco histories are updated annually until 2010 using estimated probabilities of switching between never/current/former smoking where the RRP is not introduced, with current users subdivided into cigarette/RRP/dual users where it is. RRP-related mortality reductions from lung cancer, IHD, stroke and COPD are derived from the histories and the assumed relative risks of the RRP.

A basic analysis assumes a hypothetical RRP reduces effective dose 80% in users and 40% in dual users, with an uptake rate generating ~10% RRP and ~6% dual users among current users after 10 years. Sensitivity study changes in tobacco prevalence and mortality from varying effective doses, current smoking risks, quitting half-lives and rates of initiation, switching, re-initiation and cessation. They also study extreme situations (e.g. everyone using RRP), and investigate assumptions which might eliminate the RRP-related mortality reduction. The mortality reduction is proportional to the dose reduction, increasing rapidly with time of follow-up. Plausible increases in re-initiation or dual users' consumption, or decreased quitting by smokers would not eliminate the drop.

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1. Introduction

We have described (Weitkunat et al., 2015) an approach for assessing the population health impact of introducing a Reduced Risk Tobacco Product (RRP). As described there, the model involves two stages. The first stage starts with a defined group of individuals of a given sex and age range with a known initial distribution of conventional cigarette (CC) smoking habits that is representative of the population at a given time point. The population is then

followed over a number of discrete time intervals under two Scenarios. In the Null Scenario, RRP's are not introduced and the smoking status of each individual (never, current, former) is updated at each interval based on a set of tobacco transition probabilities (TTPs) appropriate for CC use. In the RRP Scenario, RRP's are introduced and the status of each individual (never, current CC, current RRP, current dual use, former) is updated at each interval based on a set of TTPs assumed to be appropriate for this scenario. Note that "current CC smokers" and "current RRP users" refer to those who predominantly use the relevant product, with "dual users" being those with a substantial use of both products. Note also that the term "tobacco use" as used relates only to CC smoking and/or RRP use. At the end of this stage, each individual thus has a complete tobacco product use history over the follow-up period.

In the second stage, the tobacco histories are used to estimate relative risks (RR), compared to never tobacco users, of the four major smoking-related diseases - lung cancer, ischaemic heart

Abbreviations: CC, Conventional cigarette; COPD, chronic obstructive pulmonary disease; D, number of deaths; ED, equivalent dose; H, half-life; IHD, ischaemic heart disease; P, proportion of deaths attributed to tobacco; RE, relative exposure; RED, RE for dual use; REM, RE for RRP use; RR, relative risk; RRP, Reduced Risk Tobacco Product; S, population size; SAD, smoking attributable deaths; TTP, tobacco use transition probability; VNP, vaporized nicotine products.

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disease (IHD), stroke, and chronic obstructive pulmonary disease (COPD) - under the two Scenarios. For each individual, and for each period of follow-up, the RR is estimated using the negative exponential model. The model was originally used to describe the decline in excess relative risk ($= RR - 1$) by time quit, and it has been shown to provide a good fit to data for the four smoking-related diseases (Fry et al., 2013; Lee et al., 2014a, 2012b, 2014b). These publications provided estimates for each disease of the half-life (H) of the excess relative risk, that is the time after quitting when it reaches half that for continuing smokers. Quitting may be regarded as switching from a relative exposure (RE) of 1 unit to 0 units, and a simple adaptation of the negative exponential model allows the excess relative risk to be estimated for switching to a reduced exposure, and has been shown (Lee et al., 2015) to adequately describe reductions in risk of lung cancer following reductions in amount smoked (Lee, 2013). In this paper we describe a further extension of the negative exponential model allowing more generally for multiple changes in effective dose that may result from initiation, quitting, re-initiation, and upward or downward switching of exposure.

The average RRs for each disease for individuals of a given sex and age group under each Scenario are then calculated for each follow-up year, from which the proportions of tobacco-attributable deaths from each of the four diseases are then derived. Using national estimates of numbers of deaths by disease for that sex, age group and year, numbers attributable to tobacco use are also derived. Differences in numbers and proportions between Scenarios then quantify the changes resulting from introducing the RRP. As noted elsewhere (Weitkunat et al., 2015), these estimates can be corrected for differing survival under the two Scenarios.

The work described here aims at understanding the sensitivity of the prevalence of tobacco use and mortality from smoking-associated diseases to the various parameters and assumptions used. To predict the population health impact of introducing a specific product, the model requires product-specific information. This includes population- and disease-specific mortality rates by sex, age and year, as well as estimates of the effective dose of the product relative to CCs and of the rate of product uptake. It should be noted that none of these estimates are intended to reflect likely effective doses and uptake rates for any specific RRP.

2. Methods

2.1. Population at baseline

The comparisons are based on counterfactual analyses. Representative samples of the US population in 1990 are generated, and then followed assuming either that the RRP had not been introduced in that year (Null Scenario) or that it had been (RRP Scenario). Thus the Null Scenario describes the factual situation, and the RRP Scenario the counterfactual situation. Analyses are carried out for males and females, the population followed up being initially aged 10–79 years. Each member of the sample is randomly allocated at baseline to a year of age, based on the age distribution of the population of the given sex for that time point as given in the United Nations website (United Nations, 2013). Given age and sex, each member is then randomly assigned to be a never, current or former smoker, based on published data on their relative frequencies (Forey et al., 2002; Forey and Lee, 2002; Lee et al., 2009). For former smokers, the age of quitting is then randomly allocated, assuming it cannot be less than 18 years, based on National Health Interview Survey data for 2006 (www.cdc.gov/nchs/nhis.htm). Table 1 presents the age-specific distributions of population and of smoking habits used to assign the initial status of each member of the simulated populations.

In the basic analysis and in all of the sensitivity analyses described below, the populations followed up of each sex, under both the Null and RRP Scenarios, are initially identical and of size 10,000. Exceptionally, in one analysis, in order to give insight into the magnitude of variation between simulations, 10 different populations of 10,000 of each sex were studied.

2.2. Estimation of histories of tobacco use

Under each Scenario, the tobacco use status of each member of the simulated population is estimated at each year of follow-up until the year 2010 (or age 79 if that came earlier).

Under the Null Scenario, the same set of TTPs, shown in Table 2, is used in all the analyses conducted. They are defined by the probabilities P_{NC} (initiation, from Never to Current smoking), P_{CF} (quitting, from Current to Former smoking) and P_{FC} (re-initiation, from Former to Current smoking). It is assumed that in each year of follow-up only one change of state can occur. The probabilities (expressed per million to assist readability) were derived initially from educated guesses which produced not unreasonable estimates of current and former smoking during follow-up. Comparison with rates calculated from data presented recently for a follow-up of a representative US sample (Weinberger et al., 2014) suggested that the initiation and quitting rates were reasonable, but the re-initiation rates had to be increased to those given in Table 2. TTPs are assumed to be independent of period of follow-up and of sex. Initiation rates are assumed to be zero at age 35+ years. Based on the US sample (Weinberger et al., 2014), re-initiation rates are assumed to be 48% of quitting rates. Note that the TTP for quitting, P_{CF} , is multiplied by TTP factor 2 (taken as 2 in the basic analysis) if the individual has previously quit. Also the TTP for re-initiation, P_{FC} , is multiplied by TTP factor 3 (taken as 2 in the basic analysis) if the individual is a short-term quitter (taken as up to 2 years in the basic analysis).

Under the RRP Scenario, there are 15 TTPs due to the additional possible states M (current RRP use) and D (current dual use). Three TTPs refer to initiation (P_{NC} , P_{NM} , P_{ND}), three to quitting (P_{CF} , P_{MF} , P_{DF}), three to re-initiation (P_{FC} , P_{FM} , P_{FD}) and six to switching product use (P_{CM} , P_{CD} , P_{MC} , P_{MD} , P_{DC} , P_{DM}). The TTPs were developed so that, 10 years after RRP introduction, approximately 84% of current product users would be CC smokers, 10% RRP users, and 6% dual users. The TTPs were also designed to reflect the fact that younger people may be less likely than older people to switch to RRP, because of cost. These TTPs were designed to study the effects of not implausible uptake rates for a hypothetical RRP. They may not apply, of course, to any specific RRP.

To ensure comparability with the TTPs in Table 2, various constraints were applied: the sum of the three TTPs for initiation should be equal to that for P_{NC} in the Null Scenario; the sum of the three TTPs for re-initiation should be equal to that for P_{FC} in the Null Scenario; and the three TTPs for quitting should each be equal to that for P_{CF} in the Null Scenario.

In the RRP Scenario TTP factors 2 and 3, as defined above, also apply to, respectively, all three quitting rates and all three re-initiation rates. However, two other TTP Factors are also relevant. The TTP associated with the switch P_{MC} is multiplied by TTP Factor 1 (taken as 2 in the basic analysis) if the individual has previously used CCs, except as noted below. The TTPs associated with the switches P_{MC} and P_{MD} are multiplied by TTP Factor 4 (taken as 0 in the basic analysis) if the individual has used RRP continuously for more than a defined period (taken as 2 years in the basic analysis). Note that if TTP Factor 4 is set to a value and an individual uses RRP continuously for more than the defined period, TTP Factor 1 is not applied. However, the user can choose to ignore (not set) TTP Factor 4, in which case TTP Factor 1 is relevant regardless of how long RRP

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