Preventive Medicine 150 (2021) 106707

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Assessing quality-adjusted years of life lost associated with exclusive cigarette smoking and smokeless tobacco use

Xin Xu[a,*], Leah Fiacco[b], Brian Rostron[a], Ghada Homsi[b], Esther Salazar[a], Burton Levine[b], Chunfeng Ren[a], James Nonnemaker[b]

[a] *Center for Tobacco Products, Food and Drug Administration, Silver Spring, MD, USA*
[b] *RTI International, Research Triangle Park, NC, USA*

ARTICLE INFO

Keywords:
Quality adjusted life years
Health related quality of life
Mortality
Cigarettes
Smokeless tobacco
National Health Interview Survey

ABSTRACT

The main purpose of this analysis is to quantify quality adjusted life years (QALYs) lost associated with lifetime *exclusive* cigarette or smokeless tobacco use among U.S. adults. Multiple waves of National Health Interview Survey (NHIS) data linked to death certificate records were used to define current *exclusive* cigarette and smokeless tobacco use and associated mortality risks. NHIS data were used to assess health-related quality of life (HRQOL). Regression and Cox proportional hazard modeling were used to adjust HRQOL and mortality risk associated with tobacco use for age, sex, race/ethnicity, body mass index, education, and household poverty level. QALYs were estimated based on adjusted HRQOL and mortality risks. All analyses were initiated in 2019 and completed in 2020. Male current exclusive cigarette smokers, aged 25 to 29 years would lose 8.1 QALYs (SE = 0.09), and male current exclusive smokeless tobacco users aged 25 to 34 would lose 4.1 QALYs (SE = 0.22), compared to never users of tobacco. Current *exclusive* cigarette or smokeless tobacco use is associated with QALY loss. QALYs lost can be lessened through preventing the initiation of tobacco product use or helping tobacco product users quit as early in life as possible.

1. Introduction

Tobacco use, especially cigarette smoking, has repeatedly been identified as the leading risk factor for preventable disease and death in the United States (Lim et al., 2012; Danaei et al., 2009; U.S. Department of Health and Human Services, 2014). To document health consequences associated with cigarette smoking, studies have quantified mortality risks such as the number of premature deaths and resulting years of life that are lost because of cigarette smoking (U.S. Department of Health and Human Services, 2014; Centers for Disease Control and Prevention, 2008; Fenelon and Preston, 2012; Rostron, 2011), while others have estimated morbidity risks such as the number of individuals living with major medical conditions caused by cigarette smoking (Rostron et al., 2014).

In addition, studies have used joint measures, such as quality-adjusted life years (QALYs) and disability adjusted life years (DALYs), which reflect both mortality and morbidity risks to assess health consequences associated with cigarette smoking (Lortet-Tieulent et al., 2017; Reitsma et al., 2017; Forouzanfar et al., 2016; Siddiqi et al., 2020). Although both DALYs and QALYS are useful for documenting the public health burden of tobacco use (Lortet-Tieulent et al., 2017; Reitsma et al., 2017; Forouzanfar et al., 2016; Siddiqi et al., 2020), QALYs are often recommended as a standard measure for economic evaluation and cost-effectiveness studies in the U.S. (Russell et al., 1996; Weinstein et al., 1996; Siegel et al., 1996; Sanders et al., 2016) and thus have been widely used in economic evaluation studies for public health interventions associated with cigarette smoking (Cromwell et al., 1997; Xu et al., 2015; Villanti et al., 2012; Fiscella and Franks, 1996; Holtgrave et al., 2009; Javitz et al., 2004; Keeler et al., 2002; Feirman et al., 2016). Although studies have presented QALYs lost (or gained) associated with cigarette smoking (or cessation) in U.S. adults, such QALY estimates are currently not available for smokeless tobacco (SLT) use.

Among three commonly used approaches (Health Utilities Index (HUI), Quality of Well-being Scale, and EQ-5D) to generate QALY estimates (Feirman et al., 2016; Kaplan et al., 2007; Jia et al., 2013; Jia et al., 2011), the HUI has been the most widely used in population-based tobacco control and prevention studies (Feirman et al., 2016). However, these QALY estimates were based on National Health Interview Survey

* Corresponding author.
E-mail address: xin.xu@fda.hhs.gov (X. Xu).

https://doi.org/10.1016/j.ypmed.2021.106707
Received 19 November 2020; Received in revised form 14 June 2021; Accepted 23 June 2021
Available online 26 June 2021
0091-7435/Published by Elsevier Inc.

(NHIS) data collected 25 year ago, and did not isolate health consequences associated with one tobacco use from others among dual or poly tobacco users, which represents a new phenomenon in the more recent tobacco landscape (Fiscella and Franks, 1996; Erickson et al., 1995).

To address this literature gap, the purpose of this study is twofold: (1) to assess QALYs lost associated with exclusive current and former SLT users as they compare to individuals who have never used any tobacco product (hereafter referred to as "never users"), and (2) to provide an update on QALYs lost associated with exclusive current and former cigarette smoking (Reitsma et al., 2017). To define exclusive cigarette and SLT users and estimate separate QALYs by tobacco use status (current, former, and never), this study used more recent NHIS data and followed the HUI approach (Fiscella and Franks, 1996; Erickson et al., 1995).

2. Methods

2.1. Data sources

To present QALYs lost associated with exclusive SLT and cigarette use, we used NHIS data to construct exclusive tobacco use status and health related quality of life (HRQOL), a HUI measure of morbidity risks, (Erickson et al., 1995) as well as public-use NHIS data linked with death certificate records from the National Death Index to estimate mortality risks.

For morbidity estimates, because the NHIS only collected information on use of non-cigarette tobacco products, including smokeless tobacco use, in a Cancer Control Supplement once every 5 years between 2000 and 2011 and then annually thereafter, we pooled data from the 2000, 2005, 2010, and 2012 to 2017 NHIS adult samples to define exclusive cigarette smoking or SLT use and to estimate HRQOL. For mortality estimates, death certificates were not available for the NHIS between 2015 and 2017. To provide robust estimates for mortality risks by exclusive tobacco use status, especially given limited NHIS samples of exclusive SLT use, we boosted our final sample with data from early waves of the NHIS when information of use of non-cigarette tobacco products was collected. Therefore, mortality risks were estimated based on 1987, 1991, 1992, 1994, 1998, 2000, 2005, 2010, and 2012 through 2014 NHIS linked death certificates.

2.2. Study sample

For the pooled NHIS sample used for HRQOL estimation, we included adults from the civilian, noninstitutionalized population who were 25 or older at time of interview. We excluded individuals with missing health status and health limitation data (n = 138), individuals who reported dual or poly tobacco use (n = 52,678) or use of tobacco products other than cigarettes or SLT (n = 21,516), and those with missing sociodemographic characteristics (n = 1021). The final sample size used to estimate HRQOL was 179,649. The same inclusion criteria were adopted for the NHIS linked death certificates sample. We excluded dual tobacco users of cigarettes and SLT (n = 6016), and poly users or users of other tobacco products (n = 59,964). The final sample used for mortality estimation was 253,539.

2.3. Measures

2.3.1. Tobacco use status

We constructed five tobacco use categories: 1) exclusive current cigarette smokers; 2) exclusive former cigarette smokers; 3) exclusive current SLT users; 4) exclusive former SLT users; and 5) never users of any tobacco product. Current cigarette smokers include individuals who reported ever smoking at least 100 cigarettes in their lifetime and either reported smoking every day or somedays or quit cigarette smoking within the past 2 years at the time of interview. This definition of current cigarette smokers accommodates "sick-quitters," a phenomenon among smokers who quit smoking due to a recent diagnosis of serious smoking-related health conditions (U.S. Department of Health and Human Services, 2014; Centers for Disease Control and Prevention, 2008). Former smokers include individuals who have smoked at least 100 cigarettes in their lifetime and who have quit cigarette smoking for more than 2 years at the time of interview. The NHIS questionnaires define SLT products as chewing tobacco, snuff, dissolvable tobacco, dip, or snus. Current SLT users include individuals who reported ever using SLT and were using SLT every day or some days at time of interview. Former SLT users include individuals who reported ever use of SLT and did not report current use at time of interview. To define exclusive use, cigarette or SLT users who had used any other tobacco product (i.e., cigars, hookah, pipes filled with tobacco, bidis, or electronic cigarettes) in their life time were removed from the analysis sample. Never users include individuals who reported never using tobacco products (i.e., cigarettes, SLT, cigars, hookah, pipes filled with tobacco, bidis, or electronic cigarettes) in their lifetime.

2.3.2. Sociodemographic characteristics

To accommodate sample size differences in cigarette and SLT users, we defined two age variables: a 5-year interval age variable for cigarette smokers and a 10-year interval age variable for SLT users (Fiscella and Franks, 1996). Because of limited exclusive female SLT users in the final sample, we were unable to provide QALY estimates for this subpopulation. Following existing studies (Rostron, 2011; Rostron et al., 2014; Jia et al., 2013; Jia et al., 2011), we included other sociodemographic controls, such as sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other), education (less than high school graduate, high school or GED, some college (without bachelor's or associate's degree), college degree or higher), federal poverty level status (at or above poverty threshold, below poverty threshold), and body mass index (BMI, defined as weight [kg]/height [m] (Danaei et al., 2009): underweight, BMI $<$ 18.5; normal weight, 18.5 $\leq$ BMI $<$ 25; overweight, 25 $\leq$ BMI $<$ 30; obese, BMI $\geq$ 30). Because alcohol use was not collected for the first four years of NHIS (1987, 1991, 1992 and 1994) we used for mortality rate estimation, we did not include alcohol use as a covariate when estimating adjusted health related quality of life and mortality rates.

2.3.3. Health-related quality of life

To qualify morbidity risks, we defined 30 unique health states using responses to perceived health status and activity limitation questions. We classified individuals into one of five categories of perceived health (excellent, very good, good, fair, and poor) and six levels of activity limitations (not limited, limited in other activities, limited in major activity, unable to perform major activity, limited in instrumental activities of daily life, and limited in activities of daily life) Table A1. We assigned HRQOL scores to each of these 30 health states Table A2 (Erickson et al., 1995). Detailed information on activity limitations and HRQOL scores are presented in Appendix Tables A1 and A2.

2.3.4. Mortality rates

To qualify mortality risks, we defined mortality rates as the ratio of "number of weighted deaths" to "weighted person-years" during a mortality follow-up period (i.e., the time of interview to December 31, 2015). We assumed that self-reported tobacco use at the time of interview would remain constant for 10 years to prevent misclassification of tobacco use status during the mortality follow-up period (Fisher et al., 2019a).

2.4. Analyses

To estimate QALYs, we combined adjusted HRQOL scores estimated based on the NHIS samples, and adjusted mortality rates estimated based on the NHIS linked death certificates by sex, age, and tobacco use status (Fiscella and Franks, 1996). We also compared differences in life years and QALYs between current users and never users, current users and former users, and former users and never users. Because the NHIS involves complex, multistage sample designs with stratification and clustering, analytic weights were necessary to present nationally representative estimates for the civilian, noninstitutionalized U.S. population. To account for pooling over multiple waves of the NHIS, analytic weights were divided by the number of combined years in the sample (National Center for Health Statistics, 2018a). Years with the same study design were assigned the same values for the strata and primary sampling unit (PSU) variables to calculate correct variance estimates (National Center for Health Statistics, 2018b). All analyses were initiated in 2019 and completed in 2020.

2.4.1. Adjusted HRQOL scores

We estimated adjusted HRQOL scores by regressing scores by sex, age, and tobacco use on sociodemographic characteristics, including race/ethnicity, education, federal poverty level status, and BMI. Predicted averages and standard errors of HRQOL scores were calculated for each age group, by sex and tobacco use, using a marginal least-squares means approach.

2.4.2. Adjusted mortality rates and abridged life tables

We estimated relative mortality risk for the five tobacco use categories as hazard ratios, using an age- and sex-stratified Cox proportional hazard model after adjusting for sociodemographic characteristics such as race/ethnicity, education, federal poverty level status, and BMI, with never users as a reference group. We estimated adjusted mortality rates for exclusive current and former users of cigarettes and SLT by multiplying the mortality rates for never users by corresponding tobacco use hazard ratios (Rostron, 2011). A Taylor series linearization approach was used to estimate the variance of the mortality rates to account for the nonlinear relationship between mortality rates and population parameters. We calculated abridged life tables by sex, age, and tobacco use status using estimated adjusted mortality rates (Chiang, 1984). Detailed life table calculations are presented in the Appendix.

2.4.3. QALY estimation

We combined adjusted HRQOL scores and abridged life tables generated from adjusted mortality rates to estimate QALYs by sex, age, and tobacco use status Table A3, A4, A5, A6, A7 and A8 (Fiscella and Franks, 1996). Detailed approaches to estimate and test QALYs are provided in the Appendix. We further examined QALY loss associated with tobacco use to assess independent effects of mortality and morbidity (measured by HRQOL). Holding HRQOL scores and mortality rates constant between compared tobacco use categories, QALYs were re-estimated to obtain differences due to mortality and morbidity, respectively (Stewart et al., 2009). For example, when examining differences in QALYs between current users and never users, we held mortality rates for current users at the never user level to examine QALYs lost due to morbidity only (i.e., differences in HRQOL). Finally, we used the Wilcoxon signed-rank test to compare the QALY loss attributed to morbidity and mortality for cigarette smokers and SLT users across all age groups.

3. Results

3.1. Cigarette smoking

QALYs estimated for exclusive current cigarette smokers were less than those estimated for former or never users, while QALYs for exclusive former cigarette smokers were less than never users across all age (Fig. 1) and sex groups (Appendix Tables A3-A5). For example, 35.5 QALYs (SE = 0.046) remained for exclusive current cigarette smokers aged 25–29 years old, while those for former smokers and never users of the same age group were 40.6 (SE = 0.047) and 43.5 (SE = 0.046), respectively (Fig. 1). QALYs declined with increasing age for each cigarette smoking status group ($P < 0.001$). Compared to the 35.5 QALYs remaining for exclusive current smokers aged 25–29 years old, 1.6 (SE = 0.046) QALYs remained for current smokers aged 85 and above, 2.8 (SE = 0.47) for former smokers, and 4.2 (SE = 0.034) for never users of the same age group.

Across all age and sex groups, QALY loss was associated with cigarette smoking (current cigarette smokers vs. never users, and former cigarette smokers vs. never users, $P < 0.001$), while QALY gains were associated with quitting (current cigarette smokers vs. former cigarette smokers, $P < 0.001$) (Table 1).

For those aged 25–29 years old, both male and female current cigarette smokers would lose approximately 8 QALYs, if they continued smoking for the rest of their lives, compared to never users. In contrast, they could reclaim 5 QALYs if they decided to quit at this age. However, they would still lose 3 QALYs compared to those who have never used tobacco products. For those aged 85 years and older, QALY loss for current smokers compared to never users was greater for females than males, at 3 and 2 years, respectively. Quitting at this age was associated with a gain of 1 QALY for males and females. However, former smokers would still lose approximately 1 QALY compared to never users.

3.2. SLT use

Exclusive current SLT users had less estimated QALYs than exclusive former SLT users or never users across all age groups in the overall sample (Fig. 1) and among males (Appendix Tables A6–A8). Also, exclusive former SLT users had less estimated QALYs than never users, with a minimum difference for users aged 85 years and older. For example, 40.1 (SE = 0.167) QALYs were estimated for exclusive current SLT users aged 25 to 34 years old, while those for exclusive former SLT users and never users of the same age group were 43.1 (SE = 0.122) and 43.4 (SE = 0.049), respectively. Approximately 4.0 (SE = 0.065) QALYs were estimated for exclusive current SLT users aged 85 years and older, compared to 4.1 (SE = 0.051) for exclusive former SLT users, and 4.2

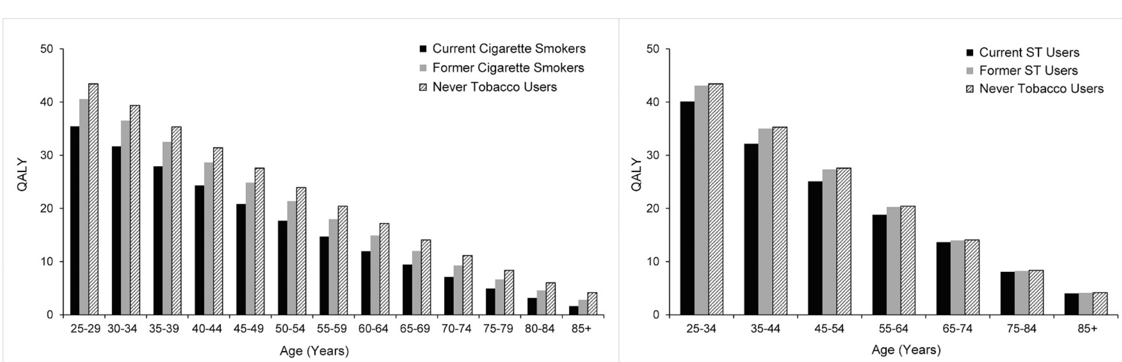

Fig. 1. Estimated QALYs for adults by cigarette smoking and smokeless tobacco use status.

Table 1
Estimated QALYs lost associated with cigarette smoking status, overall and by sex.

Age (years)	Overall			Male			Female		
	Current cigarette smokers vs. never users	Former cigarette smokers vs. never users	Current cigarette smokers vs. former smokers	Current cigarette smokers vs. never users	Former cigarette smokers vs. never users	Current cigarette smokers vs. former smokers	Current cigarette smokers vs. never users	Former cigarette smokers vs. never users	Current cigarette smokers vs. former smokers
25–29	8.0	2.9	5.1	8.1	2.7	5.4	7.7	2.6	5.1
30–34	7.7	2.9	4.9	7.7	2.7	5.1	7.4	2.6	4.9
35–39	7.4	2.8	4.6	7.4	2.6	4.8	7.1	2.5	4.6
40–44	7.1	2.8	4.3	7.1	2.6	4.5	6.8	2.4	4.4
45–49	6.7	2.7	4.0	6.7	2.5	4.2	6.5	2.4	4.1
50–54	6.3	2.6	3.7	6.2	2.4	3.8	6.0	2.3	3.8
55–59	5.7	2.4	3.3	5.6	2.2	3.5	5.6	2.1	3.4
60–64	5.2	2.3	2.9	5.0	2.0	3.1	5.1	2.0	3.1
65–69	4.6	2.1	2.5	4.4	1.8	2.7	4.5	1.8	2.7
70–74	4.0	1.9	2.1	3.8	1.6	2.2	4.0	1.7	2.3
75–79	3.4	1.7	1.8	3.2	1.4	1.8	3.4	1.5	1.9
80–84	2.9	1.5	1.4	2.6	1.2	1.4	2.8	1.3	1.5
85+	2.5	1.4	1.2	2.3	1.1	1.2	2.5	1.2	1.3

(SE = 0.034) for never users of the same age group.

Using SLT was associated with QALY loss among adults (current users vs. never users, $P < 0.0001$; former users vs. never users, P < 0.0001), while quitting was associated with potential QALY gains (current users vs. former users, $P < 0.0001$) (Table 2).

Male SLT users aged 25–34 would lose on average 4 QALYs compared to never users. Estimated QALY loss for 25 to 34-year-olds among all adults was similar to estimated QALY loss among males. Quitting SLT use at this age was associated with a gain of 3 QALYs compared to those who continued SLT use for the rest of their lives. The effects of having ever used SLT at this age were relatively small on average, with a loss of about 1 QALY for males and a minimal effect for former SLT users. For adults aged 85 years and older, SLT current users would lose 1 QALY compared to never users, while former SLT users gained less than 1 QALY from quitting. Former SLT users lose less than 1 QALY because of ever SLT use.

Fig. 2 presents the total QALY loss associated with exclusive current cigarette smoking and SLT use across age groups, by attributable losses in mortality and morbidity as measured by HRQOL. For exclusive current cigarette smokers across all age groups, larger proportions of QALY loss were attributed to smoking related mortality than morbidity ($P < 0.001$). For example, 5.4 out of 8.0 QALYs lost for current cigarette smokers aged 25–29 years old were attributable to increases in mortality, while another 3 QALYs were lost due to increases in morbidity. Exclusive current cigarette smokers aged 85 years and older experienced a total QALY loss of 2.5 years from smoking, 2.4 years of which were attributable to increases in mortality and 0.4 years associated with morbidity changes. For exclusive current SLT users, QALY loss attributed to mortality was not greater than morbidity across all age groups ($P = 0.22$). QALY loss from exclusive current SLT use was mostly attributable to mortality for adults aged 25- to 64-years-old, but only associated with morbidity for adults 65 years or older. It is important to note that the sum of years lost due to mortality and morbidity may not equal to total QALYs lost, since mortality and morbidity are correlated within each tobacco use group.

Table 2
Estimated QALYs Lost Associated with Smokeless Tobacco Use Status, Overall and by Sex.

Age (years)	Overall			Male		
	Current SLT users vs. never users	Former SLT users vs. never users	Current SLT users vs. former SLT users	Current SLT users vs. never users	Former SLT users vs. never users	Current SLT users vs. former SLT users
25–34	3.3	0.4	3.0	4.1	0.8	3.3
35–44	3.2	0.3	2.9	3.9	0.7	3.2
45–54	2.5	0.2	2.2	3.0	0.6	2.4
55–64	1.6	0.2	1.4	2.0	0.4	1.5
65–74	0.4	0.1	0.3	0.6	0.3	0.3
75–84	0.3	0.1	0.2	0.4	0.2	0.2
85+	0.1	0.1	0.1	0.2	0.1	0.1

4. Discussion

Our study reveals that exclusive cigarette smoking and exclusive current SLT use are associated with QALY loss, as results of reductions in both life expectancy and HRQOL. Specifically, for both males and females, current exclusive cigarette smokers aged 25 to 29 could lose 8.1 QALYs compared to never users, if they continue to smoke cigarettes for the rest of their lives. Similarly, current exclusive SLT use is associated with a loss of 4.1 QALYs for males aged 25 to 34 compared to never users, if they continue to use SLT products for the rest of their lives. We were unable to assess QALYs loss for female SLT users because of limited sample sizes.

Our study also offers several methodological and empirical contributions to the existing literature. Using the instruments from multiple waves of NHIS, we can define exclusive cigarette smokers, exclusive SLT users, as well as never users to isolate and identify health risks exclusively related to tobacco product use. By controlling for individual sociodemographic confounding factors, including race/ethnicity, educational, federal poverty level status, and BMI in the regression analysis, we also provide more reliable QALY estimates associated with cigarette smoking and SLT use. We specifically generate the QALY loss associated with SLT use, which, to the best of our knowledge, has not been done previously.

Our study shows that exclusive current and former cigarette smoking are associated with greater risk of all-cause mortality. These estimated proportional hazard ratios (unshown) are generally comparable with existing evidence (U.S. Department of Health and Human Services, 2014; Christensen et al., 2018; Jha et al., 2016). Compared to never users, current exclusive cigarette smokers aged 25 to 29 would lose more than 8 QALYs if they would continue to smoke throughout the rest of their lives. In contrast, those who would quit smoking by ages 45–54 could reclaim approximately 4 QALYs, compared to those who would continue to smoke. These estimated health consequences (and gains) associated with cigarette smoking (and quitting) are largely consistent with the existing evidence on cigarette smoking associated mortality risks, although our data and methodology differ substantially (Jha et al., 2016). For example, estimated QALYs lost due to cigarettes smoking in this analysis are a little less than estimated life years lost in Jha's study (Jha et al., 2016). The differences are likely due to different methods

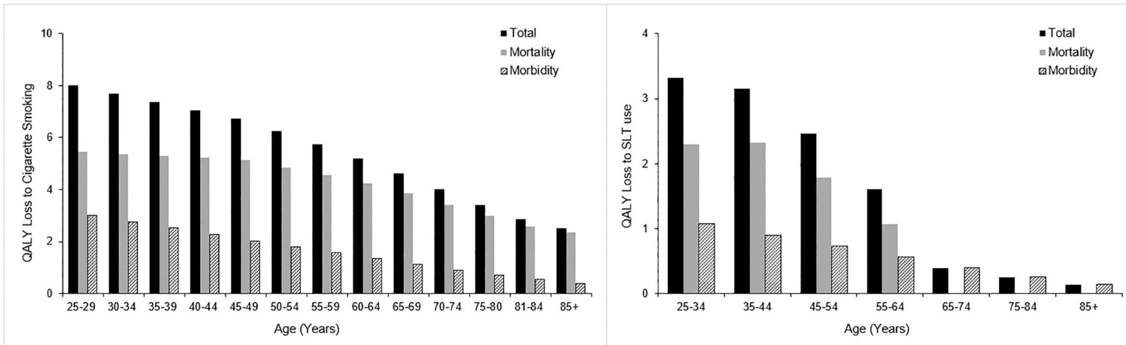

Fig. 2. QALY Loss Due to Current Cigarette Smoking and Current Smokeless Tobacco Use (Overall, and Due to Each of Morbidity and Mortality).

used in these two studies (Jha et al., 2016). First, different definitions of former smokers and never users were adopted. In our analysis, former smokers were those who have quit cigarette smoking for 2 or more years, while former smokers were defined as having quit for 5 or more years in Jha's study (Jha et al., 2016). Different cut-offs for duration of quitting can affect estimated mortality risks of both current and former smokers. Our definition of cigarette smoking is also more restrictive, as it excludes ever-use of any other tobacco products in the life time (Jha et al., 2016). The exclusion of any other tobacco product use in this analysis can affect mortality risks associated with all three cigarette smoking statuses (current, former, and never). For example, regular cigar smoking has contributed to approximately 9000 premature deaths among US adults aged 35 years or older in 2010 (Nonnemaker et al., 2014), while SLT is associated with serious health consequences such as increased risk of cancer and/or DALYs lost resulted from elevated heart disease risk (Siddiqi et al., 2020; Hatsukami et al., 2014). Also, unlike Jha's study, this analysis does not scale up absolute death rates in the NHIS sample to match the U.S. national rates. Finally, compared to Jha's study, our analysis is based on a more recent NHIS sample. Overall, our findings underscore the importance of preventing cigarette smoking initiation, as even ever-use of cigarettes can be associated with substantial increases in both mortality and morbidity risks, and thus reductions in QALYs remaining during a lifetime. In contrast to limited evidence on mortality risk associated with current SLT use (Fisher et al., 2019b), our findings indicate that exclusive current SLT use was associated with substantial QALY loss for all adults. However, we also find that exclusive former SLT use was associated with modest changes in QALYs (Fisher et al., 2019b).

Our study has some limitations. First, tobacco product use and HRQOL measures are constructed based on self-reported information and thus are subject to recall bias. Second, the NHIS sampling frame does not include institutionalized adults. This should not, however, substantially affect the observed QALY differences between exclusive tobacco product users and adults who have never used tobacco in the NHIS. In addition, the NHIS is a cross-sectional survey, and data on tobacco use status were collected only at baseline. Some of the surveyed tobacco users could have quit subsequently, thereby slightly affecting their QALY measures with 10 years of follow-up (Chaiton et al., 2016). Alternatively, if they would continue using tobacco products beyond 10 years of follow-up, the hazards of long-term use of tobacco products could be underestimated (Doll et al., 1994). Similarly, QALY loss associated with former smokers might be overestimated, since some deaths may well reflect mortality among tobacco users who quit because they became ill. Therefore, the true gain of QALYs from the time of cessation would be somewhat greater than we presented. Finally, although individual demographic characteristics were controlled in the analysis, there could be other uncontrolled confounders associated with exclusive cigarette smoking or SLT use.

Despite these limitations, our study provides further evidence that both current exclusive cigarette and exclusive SLT use are associated with reductions in QALYs. This study underscores the importance of preventing the initiation of cigarette smoking and the use of SLT products and providing evidence-based cessation interventions so that users of these products quit as early in life as possible.

Funding

Funding for this study was provided by the Center for Tobacco Products (CTP), U.S. Food and Drug Administration (FDA) under contract HHSF223201510002B to RTI International.

Declaration of Competing Interest

Authors have no conflict of interest to report. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Food and Drug Administration.

Appendix A. Appendix

Table A1
Activity definitions by age.

Age group	Activity level	NHIS activity definitions[a]
18–64 years of age	Major activity	Limited in the kind *or* amount of work one can do because of a physical, mental, or emotional problem Unable to work at a job or business because of a physical, mental, or emotional problem
Both age groups	Instrumental activities of daily living	Needs help in handling *routine needs*, such as everyday household chores, doing necessary business, shopping, or getting around for other purposes because of a physical, mental, or emotional problem
	Activities of daily life	Needs help with *personal care needs*, such as eating, bathing, dressing, or getting around inside their home
	Other activity	Limited in any way in any activities because of a physical, mental, or emotional problem
65 years and older	Major activity [b]	*Major activity is considered to be IADL and ADL activities*

[a] Source: Erickson P, Wilson R, Shannon I. years of healthy life. *Healthy People 2000* statistical notes. 1995; 7:1–15.
[b] Respondents 65 years and older cannot be assigned to the "limited in major activity" category

Table A2
Health states and associated scores.

Activity limitation	Perceived health status				
	Excellent	Very good	Good	Fair	Poor
Not limited	1.00	0.92	0.84	0.63	0.47
Limited in other activities	0.87	0.79	0.72	0.52	0.38
Limited in major activity	0.81	0.74	0.67	0.48	0.34
Unable to perform major activity	0.68	0.62	0.55	0.38	0.25
Limited in IADL	0.57	0.51	0.45	0.29	0.17
Limited in ADL	0.47	0.41	0.36	0.21	0.10

Source: Erickson P, Wilson R, Shannon I. Years of Healthy Life. *Healthy People 2000* Statistical Notes. 1995; 7:1–15.

A.1. Mortality rate estimation

Mortality rates for never users by sex and age were calculated as the ratio of “number of weighted deaths” to “weighted person-years” during the mortality follow-up period. Mortality rates for exclusive former and current users of cigarettes and SLT were estimated as follow: (1) age- and sex-stratified Cox proportional models were first fitted to estimate hazard ratio with never users as reference and adjusting for potential confounders such as race/ethnicity, education, federal poverty level status, and BMI; (2) mortality rates for each tobacco use status were then estimated by multiplying the mortality rates for never users by the corresponding hazard ratio.

A.2. Abridged life table calculation

For each of the five tobacco use categories, we generated an abridged life table by following a hypothetical cohort of 100,000 individuals from the first age group until the last individual in the cohort dies. The following age-specific indexes were defined for each i-th age group category: mortality rate (m_i) (estimated from the NHIS linked mortality data), mortality probability (q_i), number of persons living in each age-interval (l_i), number of person-years (L_i), total survived person-year (T_i), and expected average remaining lifetime (e_i). For $i = 1, \cdots, w$, where w is the number of age-group intervals and d is the age group width (in this analysis $d = 5$ or 10), the following formulas were used:

$$q_i = 1 - e^{-d\, m_i}$$

$$l_0 = 100,000, l_i = l_{i-1}(1 - q_{i-1}), 1 \le i \le w$$

$$L_i = \frac{d\,(l_i + l_{i+1})}{2}, 1 \le i \le w-1, L_w = \frac{l_w}{m_w}$$

$$T_i = \sum_{j \ge i} L_j$$

$$e_i = \frac{T_i}{l_i}$$

A.3. QALY estimation by age, sex, and tobacco use status

Let x represent age within each tobacco use status and sex of interest. For the age interval i, let L_i be the stationary population or the number of person-years, and Q_i the average adjusted HRQOL estimated from the regression model. Allow l_x to be the number of persons living at age x given the first age interval of 100,000 population. Then, the QALY is defined as

$$QALY(x) = \frac{\sum_{i \ge x} L_i Q_i}{l_x}.$$

For each tobacco use status, we calculated QALYs for all adults by sex and age groups. We then calculated the difference in life years and QALYs for current users vs. never users, current users vs. former users, and former users vs. never users. Due to the small sample size of female exclusive SLT users, we limited analyses to males and the overall sample. Standard errors of QALY estimates were calculated using methods from Jia et al. (2011, 2013).[1,2] A detailed approach is described in the Appendix. We computed the Kendall's Tau correlation coefficient and tested the significance for the association between QALYs and age groups. A Kruskal-Wallis test was used to investigate if QALYs were significantly different across tobacco use status for all age groups. Also, a Dunn's post-hoc test for pairwise comparison was used following a significant Kruskal-Wallis test.

A.4. Variance estimation for QALY associated with cigarette smoking and smokeless tobacco

Jia et al. (2011) provides equations for calculating the variance of quality-adjusted life years (QALYs) for age interval i, including equations for calculating the variance of QALY components. These components include the cohort population (l_i) or number of persons living at the beginning of an

[1] Jia H, Zack MM, Thompson WW, et al. Quality-adjusted life expectancy (QALE) loss due to smoking in the United States. *Qual Life Res*. 2013; 22(1):27–35.
[2] Jia H, Zack MM, Thompson WW. State quality-adjusted life expectancy for U.S. adults from 1993 to 2008. *Qual Life Res*, 2011. 20(6): 853–863.

age interval, average HRQOL (Q_i), mortality rate (m_i), and probability of dying (q_i). Jia et al. (2011) also provides equations for calculating the variance of the difference between QALYs for two groups (e.g., exclusive current smokers vs. never users).

This appendix provides annotated Jia's equations within the context of the NCHS Healthy People 2000 paper and explain when and how our methods differ from Jia's. The QALY variance equations in Jia et al. (2011) have been modified to use NCHS terms and fit our 5- and 10-year age intervals, with equations for 5-year age intervals presented below.

To calculate QALYs, let d_i and N_i be the deaths and populations for 5-year age intervals i. The observed age-interval death rate is $m_i = d_i/N_i$, and the probability of dying in the 5-year age interval is $q_i = 1 - e^{-5*m_i}$. Let l_0 be a hypothetical population of 100,000 at the first age interval (i.e., 25–29) and l_i be the number of the population surviving to age interval i ($i>$ age interval 25–29), represented by ($l_{i-1} - l_{i-1} * q_{i-1}$). Assuming those who died during a 5-year age interval lived an average of 2.5 years, the life years between age interval i, L_i, is 2.5 * ($l_i + l_{i+1}$).

Jia's paper provides the following equation to approximate the variance of the estimated QALY:

$$Var(QALY_x) = \frac{\sum_{x\le i\le 80}\left[l_i^2 * \left(\frac{nQ_i}{2} + QALY_{i+1}\right)^2 * VAR(q_i) + l_i^2 n^2 \left(1-\frac{q_i}{2}\right)^2 * VAR(Q_i)\right]}{l_x^2} + \frac{VAR(LE_{85}) * Q_{85}^2 + L_{85}^2 * VAR(Q_{85}) + VAR(LE_{85}) * VAR(Q_{85})}{l_x^2}$$

for $x = 25, 30, 35, \cdots, 80$ and $i = x, x+5, x+10, \cdots, 80$, where each x index indicates the $[x, x+4]$ age groups, respectively, and $x = 85$ indicates the 85+ age group, and the variance of the probability of dying (q_i) is:

$$Var(q_i) = \frac{q_i^2(1-q_i)}{d_i} + (1-q_i)^2 Var(m_i)$$

Jia's paper includes a $Var(m_i)$ term to account for the added variance caused by estimating the death rate (m_i) using model predictions. They say, “For the 2007 and 2008 model predictions, the variance of estimated age-specific mortality, q_i, should be adjusted for the uncertainty of these predictions, where $Var(m_i)$ is the variance of model-based estimates of death rate.” We do not predict death data, and thus will calculate $Var(m_i)$ using a Taylor linearization method to account for the complex NHIS sample design when calculating the variance of q_i. The first term, $q_i^2(1 - q_i)/d_i$, remains as the variance of a binomially distributed variable (probability of dying), as explained in Scherbov and Ediev (2011)[3].[3]

Jia's paper also provides the variance of life expectancy for someone aged 85+, where $n = 5$:

$$Var(LE_{85+}) = \frac{\left(e^{-n\sum_{k<85+} m_k}\right)^2}{d_{85+} m_{85+}^2} l_{25-29}^2$$

A.5. Variance of differences between tobacco use categories

The variance of the difference in QALY estimates for two groups with age interval i is:

$$Var(\Delta_i) = Var\left(QALY_i^0\right) + Var\left(QALY_i^1\right)$$

The formula above indicates that the variance of the difference between QALYs for two groups (e.g., exclusive current smokers vs. never users or exclusive current smokers vs. exclusive former smokers), for age interval i, is the sum of the variance of each measure.

Jia's variance formula for a difference between two groups contains a covariance term. Given the way we've calculated QALY and the death rate, our values of QALY across groups are independent, and therefore, do not require the covariance term. Jia's methods estimate the death rate using dependent models, thus requiring a covariance term.

Table A3
Calculation of QALYs for exclusive current cigarette smokers.

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population		Life years remaining	QALYs (SE)
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')		
Female							
25–29 years	100,000	499,076	0.79	396,191	3,623,147	50.9	36.2 (0.040)
30–34 years	99,630	497,032	0.79	390,493	3,226,956	46.1	32.4 (0.038)
35–39 years	99,182	493,990	0.78	383,218	2,836,463	41.2	28.6 (0.036)
40–44 years	98,414	489,273	0.76	371,167	2,453,246	36.6	24.9 (0.035)
45–49 years	97,295	481,143	0.73	352,706	2,082,078	31.9	21.4 (0.033)
50–54 years	95,162	468,972	0.71	332,791	1,729,372	27.6	18.2 (0.031)

(continued on next page)

[3] Scherbov, S., Ediev, D. (2011). Significance of life table estimates for small populations: Simulation-based study of standard errors. *Demographic Research, 24*(22), 527–550. doi: https://doi.org/10.4054/DemRes.2011.24.22.

Table A3 (*continued*)

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population			
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')	Life years remaining	QALYs (SE)
55–59 years	92,427	452,325	0.68	309,543	1,396,581	23.3	15.1 (0.029)
60–64 years	88,503	427,887	0.66	283,792	1,087,038	19.3	12.3 (0.026)
65–69 years	82,652	391,748	0.67	262,548	803,246	15.5	9.7 (0.023)
70–74 years	74,048	341,827	0.65	223,795	540,698	12.0	7.3 (0.019)
75–80 years	62,683	272,606	0.61	167,136	316,903	8.7	5.1 (0.016)
81–84 years	46,359	182,393	0.58	105,522	149,767	5.9	3.2 (0.012)
85+ years	26,598	89,099	0.50	44,245	44,245	3.3	1.7 (0.007)
Male							
25–29 years	100,000	497,177	0.82	405,688	3,464,448	46.8	34.6 (0.061)
30–34 years	98,871	491,269	0.81	396,840	3,058,760	42.3	30.9 (0.059)
35–39 years	97,637	483,998	0.80	386,180	2,661,920	37.8	27.3 (0.057)
40–44 years	95,962	475,235	0.78	371,038	2,275,740	33.4	23.7 (0.055)
45–49 years	94,132	462,604	0.76	349,356	1,904,702	29.0	20.2 (0.053)
50–54 years	90,910	443,424	0.73	324,477	1,555,346	25.0	17.1 (0.050)
55–59 years	86,460	418,421	0.71	295,604	1,230,869	21.1	14.2 (0.047)
60–64 years	80,909	387,140	0.69	265,337	935,265	17.4	11.6 (0.044)
65–69 years	73,947	342,268	0.69	236,963	669,929	13.8	9.1 (0.040)
70–74 years	62,960	283,967	0.68	192,200	432,965	10.8	6.9 (0.035)
75–80 years	50,627	212,584	0.64	135,042	240,765	7.8	4.8 (0.029)
81–84 years	34,407	129,973	0.60	78,072	105,723	5.3	3.1 (0.024)
85+ years	17,583	53,307	0.52	27,651	27,651	3.0	1.6 (0.015)

Source: 1987, 1991, 1992, 1994, 1998, 2000, 2005, 2010, and 2012–2014 NHIS National Longitudinal Mortality Study, NCHS, CDC.
[a] Of 100,000 population for the first age group.
[b] Source: 2000, 2005, 2010, 2012–2017 NHIS, NCHS, CDC. SE = standard error. $T'_x = \sum_{i \geq x} L_i Q_i.$

Table A4
Calculation of QALYs for exclusive former cigarette smokers.

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population			
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')	Life years remaining	QALYs (SE)
Female							
25–29 years	100,000	499,406	0.83	416,443	4,131,700	55.7	41.3 (0.037)
30–34 years	99,762	498,091	0.83	411,263	3,715,257	50.8	37.2 (0.035)
35–39 years	99,474	496,130	0.82	404,737	3,303,994	46.0	33.2 (0.034)
40–44 years	98,978	493,080	0.80	393,793	2,899,256	41.2	29.3 (0.032)
45–49 years	98,254	488,056	0.77	377,310	2,505,463	36.5	25.5 (0.030)
50–54 years	96,968	480,677	0.75	360,338	2,128,153	31.9	21.9 (0.029)
55–59 years	95,303	470,451	0.72	340,780	1,767,816	27.4	18.5 (0.027)
60–64 years	92,878	455,142	0.70	320,088	1,427,036	23.1	15.4 (0.024)
	89,179	431,502	0.71	306,463	1,106,948	19.0	

(*continued on next page*)

Table A4 (*continued*)

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population		Life years remaining	QALYs (SE)
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')		
65–69 years							12.4 (0.021)
70–74 years	83,422	397,045	0.69	275,840	800,485	15.1	9.6 (0.019)
75–80 years	75,396	345,436	0.65	225,616	524,645	11.4	7.0 (0.016)
81–84 years	62,778	268,957	0.62	166,369	299,029	8.2	4.8 (0.013)
85+ years	44,804	247,220	0.54	132,660	132,660	5.5	3.0 (0.009)
Male							
25–29 years	100,000	498,207	0.86	426,471	4,003,322	52.0	40.0 (0.060)
30–34 years	99,283	494,445	0.85	419,198	3,576,851	47.4	36.0 (0.058)
35–39 years	98,495	489,792	0.84	410,409	3,157,653	42.7	32.1 (0.056)
40–44 years	97,421	484,151	0.82	397,379	2,747,244	38.2	28.2 (0.054)
45–49 years	96,239	476,014	0.80	378,537	2,349,865	33.6	24.4 (0.052)
50–54 years	94,166	463,560	0.77	357,767	1,971,327	29.3	20.9 (0.050)
55–59 years	91,257	447,016	0.75	333,699	1,613,560	25.2	17.7 (0.047)
60–64 years	87,549	425,772	0.73	308,858	1,279,862	21.1	14.6 (0.044)
65–69 years	82,760	394,342	0.73	288,801	971,004	17.2	11.7 (0.041)
70–74 years	74,977	351,396	0.72	251,905	682,203	13.7	9.1 (0.037)
75–80 years	65,582	293,293	0.68	198,052	430,298	10.3	6.6 (0.033)
81–84 years	51,735	214,981	0.64	137,739	232,246	7.4	4.5 (0.029)
85+ years	34,257	169,142	0.56	94,507	94,507	4.9	2.8 (0.023)

Source: 1987, 1991, 1992, 1994, 1998, 2000, 2005, 2010, and 2012–2014 NHIS National Longitudinal Mortality Study, NCHS, CDC.
[a] Of 100,000 population for the first age group.
[b] Source: 2000, 2005, 2010, 2012–2017 NHIS, NCHS, CDC. SE = standard error. $T'_x = \sum_{i\geq x} L_i Q_i$

Table A5
Calculation of QALYs for never users (5-year age groups).

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population		Life years remaining	QALYs (SE)
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')		
Female							
25–29 years	100,000	499,406	0.85	423,344	4,393,453	58.8	43.9 (0.031)
30–34 years	99,762	498,091	0.84	418,145	3,970,110	53.9	39.8 (0.029)
35–39 years	99,474	496,130	0.83	411,592	3,551,964	49.0	35.7 (0.028)
40–44 years	98,978	493,080	0.81	400,606	3,140,372	44.3	31.7 (0.027)
45–49 years	98,254	488,851	0.79	384,679	2,739,766	39.6	27.9 (0.026)
50–54 years	97,287	483,287	0.76	368,972	2,355,087	35.0	24.2 (0.025)
55–59 years	96,028	475,539	0.74	351,035	1,986,115	30.4	20.7 (0.023)
60–64 years	94,187	463,855	0.72	332,624	1,635,079	25.9	17.4 (0.021)
65–69 years	91,355	445,926	0.72	322,869	1,302,455	21.7	14.3 (0.019)
70–74 years	87,016	419,610	0.71	297,314	979,586	17.6	11.3 (0.017)
	80,828	378,880	0.67	252,694	682,272	13.8	

(*continued on next page*)

Table A5 (*continued*)

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population			
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')	Life years remaining	QALYs (SE)
75–80 years							8.4 (0.015)
81–84 years	70,724	315,065	0.63	199,243	429,578	10.4	6.1 (0.013)
85+ years	55,302	418,466	0.55	230,334	230,334	7.6	4.2 (0.01)
Male							
25–29 years	100,000	498,207	0.87	433,355	4,273,692	55.1	42.7 (0.057)
30–34 years	99,283	494,445	0.86	426,029	3,840,337	50.5	38.7 (0.055)
35–39 years	98,495	489,792	0.85	417,177	3,414,308	45.8	34.7 (0.053)
40–44 years	97,421	484,151	0.83	404,069	2,997,131	41.3	30.8 (0.052)
45–49 years	96,239	477,465	0.81	386,288	2,593,062	36.8	26.9 (0.05)
50–54 years	94,747	468,458	0.79	368,020	2,206,774	32.3	23.3 (0.048)
55–59 years	92,637	456,388	0.76	347,001	1,838,754	28.0	19.8 (0.046)
60–64 years	89,918	440,697	0.74	325,773	1,491,753	23.8	16.6 (0.044)
65–69 years	86,360	416,591	0.75	310,851	1,165,979	19.7	13.5 (0.042)
70–74 years	80,276	382,459	0.73	279,457	855,128	16.0	10.7 (0.039)
75–80 years	72,708	334,292	0.69	230,357	575,671	12.4	7.9 (0.036)
81–84 years	61,009	264,960	0.65	173,422	345,315	9.3	5.7 (0.034)
85+ years	44,975	300,216	0.57	171,892	171,892	6.7	3.8 (0.031)

Source: 1987, 1991, 1992, 1994, 1998, 2000, 2005, 2010, and 2012–2014 National Longitudinal Mortality Study, NCHS, CDC.

[a] Of 100,000 population for the first age group.

[b] Source: 2000, 2005, 2010, 2012–2017 NHIS, NCHS, CDC. SE = standard error. $T_x' = \sum_{i \geq x} L_i Q_i$

Table A6

Calculation of QALYs for exclusive current smokeless tobacco users.

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population			
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')	Life years remaining	QALYs (SE)
Male							
25–34 years	100,000	992,498	0.84	829,526	3,870,076	51.6	38.7 (0.163)
35–44 years	98,500	962,225	0.81	782,414	3,040,550	42.3	30.9 (0.147)
45–54 years	93,945	904,801	0.77	694,505	2,258,136	34.1	24.0 (0.132)
55–64 years	87,015	812,608	0.72	585,579	1,563,631	26.4	18.0 (0.116)
65–74 years	75,507	696,352	0.71	494,422	978,052	19.7	13.0 (0.098)
75–84 years	63,764	521,439	0.65	336,502	483,630	12.4	7.6 (0.077)
85+ years	40,524	270,765	0.54	147,128	147,128	6.7	3.6 (0.057)
Overall							
25–34 years	100,000	995,295	0.83	827,465	4,012,260	54.2	40.1 (0.167)
35–44 years	99,059	972,989	0.81	786,524	3,184,795	44.7	32.2 (0.151)
45–54 years	95,539	926,706	0.76	706,814	2,398,271	36.2	25.1 (0.135)
55–64 years	89,803	846,037	0.72	605,155	1,691,457	28.1	18.8 (0.118)
	79,405	744,424	0.70	524,004	1,086,302	21.2	

(continued on next page)

Table A6 (*continued*)

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population			
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')	Life years remaining	QALYs (SE)
65–74 years							13.7 (0.102)
75–84 years	69,480	583,088	0.64	372,302	562,297	13.5	8.1 (0.081)
85+ years	47,138	354,216	0.54	189,995	189,995	7.5	4.0 (0.065)

Source: 1987, 1991, 1992, 1994, 1998, 2000, 2005, 2010, and 2012–2014 NHIS U.S. National Longitudinal Mortality Study, NCHS, CDC.
[a] Of 100,000 population for the first age group.
[b] Source: 2000, 2005, 2010, 2012–2017 NHIS, NCHS, CDC. SE = standard error. $T'_x = \sum_{i \geq x} L_i Q_i$.

Table A7
Calculation of QALYs for exclusive former smokeless tobacco users.

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population			
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')	Life years remaining	QALYS (SE)
Male							
25–34 years	100,000	992,498	0.85	843,963	4,193,235	55.1	41.9 (0.124)
35–44 years	98,500	973,752	0.83	805,951	3,349,272	45.9	34.0 (0.115)
45–54 years	96,251	944,845	0.78	738,986	2,543,321	36.8	26.4 (0.104)
55–64 years	92,718	896,182	0.74	658,840	1,804,335	28.1	19.5 (0.093)
65–74 years	86,518	797,904	0.72	578,132	1,145,495	19.7	13.2 (0.077)
75–84 years	73,063	597,482	0.66	394,266	567,363	12.4	7.8 (0.061)
85+ years	46,434	310,252	0.56	173,097	173,097	6.7	3.7 (0.045)
Overall							
25–34 years	100,000	995,295	0.84	840,211	4,309,364	57.5	43.1 (0.122)
35–44 years	99,059	982,363	0.82	806,683	3,469,152	48.0	35.0 (0.112)
45–54 years	97,413	960,370	0.78	744,790	2,662,470	38.7	27.3 (0.101)
55–64 years	94,661	920,396	0.73	670,130	1,917,679	29.7	20.3 (0.089)
65–74 years	89,419	838,303	0.72	600,823	1,247,549	21.2	14.0 (0.075)
75–84 years	78,242	656,621	0.65	427,662	646,726	13.5	8.3 (0.061)
85+ years	53,082	398,886	0.55	219,064	219,064	7.5	4.1 (0.051)

Source: 1987, 1991, 1992, 1994, 1998, 2000, 2005, 2010, and 2012–2014 National Longitudinal Mortality Study, NCHS, CDC.
[a] Of 100,000 population for the first age group.
[b] Source: 2000, 2005, 2010, 2012–2017 NHIS, NCHS, CDC. SE = standard error. $T'_x = \sum_{i \geq x} L_i Q_i$.

Table A8
Calculation of QALYs for never users(10-year age groups).[a]

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population			
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')	Life years remaining	QALYs (SE)
Female							
25–34 years	100,000	997,322	0.84	841,075	4,388,790	58.7	43.9 (0.050)
35–44 years	99,464	988,580	0.82	811,295	3,547,715	49.0	35.7 (0.047)
45–54 years	98,252	971,425	0.78	752,965	2,736,420	39.5	27.9 (0.044)
55–64 years	96,033	937,178	0.73	682,409	1,983,455	30.3	20.7 (0.040)

(continued on next page)

Table A8 (*continued*)

Age	Number living at beginning of age interval[a] (l_x)	Stationary population in the age interval (L_x)	Average HRQOL of persons in the age interval[b] (Q_x)	Quality-adjusted stationary population		Life years remaining	QALYs (SE)
				In the age interval (Q_x*L_x)	In this and subsequent age intervals (T_x')		
65–74 years	91,402	862,160	0.72	618,646	1,301,046	21.6	14.2 (0.036)
75–84 years	81,030	686,270	0.65	448,045	682,400	13.7	8.4 (0.034)
85+ years	56,224	425,391	0.55	234,355	234,355	7.6	4.2 (0.034)
Male							
25–34 years	100,000	992,498	0.87	859,169	4,277,698	55.1	42.8 (0.053)
35–44 years	98,500	973,752	0.84	820,870	3,418,529	45.9	34.7 (0.050)
45–54 years	96,251	944,845	0.80	753,462	2,597,660	36.8	27.0 (0.046)
55–64 years	92,718	896,182	0.75	672,571	1,844,198	28.1	19.9 (0.042)
65–74 years	86,518	797,904	0.74	590,356	1,171,627	19.7	13.5 (0.037)
75–84 years	73,063	597,482	0.68	403,420	581,271	12.4	8.0 (0.033)
85+ years	46,434	310,252	0.57	177,850	177,850	6.7	3.8 (0.031)
Overall							
25–34 years	100,000	995,295	0.85	846,223	4,344,108	57.5	43.4 (0.049)
35–44 years	99,059	982,363	0.83	812,617	3,497,885	48.0	35.3 (0.046)
45–54 years	97,413	960,370	0.78	750,591	2,685,268	38.7	27.6 (0.043)
55–64 years	94,661	920,396	0.73	675,690	1,934,677	29.7	20.4 (0.039)
65–74 years	89,419	838,303	0.72	605,887	1,258,988	21.2	14.1 (0.035)
75–84 years	78,242	656,621	0.66	431,628	653,101	13.5	8.3 (0.033)
85+ years	53,082	398,886	0.56	221,473	221,473	7.5	4.2 (0.034)

Source: 1987, 1991, 1992, 1994, 1998, 2000, 2005, 2010, and 2012–2014 National Longitudinal Mortality Study, NCHS, CDC.

[a] Of 100,000 population for the first age group.

[b] Source: 2000, 2005, 2010, 2012–2017 NHIS, NCHS, CDC. SE = standard error. $T_x' = \sum_{i \geq x} L_i Q_i$.

References

Centers for Disease Control and Prevention, 2008. Smoking-attributable mortality, years of potential life lost, and productivity losses – United States, 2000–2004. MMWR 57 (45), 1226-122819008791.

Chaiton, M., Diemert, L., Cohen, J.E., et al., 2016. Estimating the number of quit attempts it takes to quit smoking successfully in a longitudinal cohort of smokers. BMJ Open 6, e011045. https://doi.org/10.1136/bmjopen-2016-011045.

Chiang, C.L., 1984. Statistical inference regarding life table functions. In: The life table and its applications. Robert E. Krieger Publishers, Malabar, FL.

Christensen, C.H., Rostron, B., Cosgrove, C., et al., 2018. Association of cigarette, cigar, and pipe use with mortality risk in the US population. JAMA Intern. Med. 178 (4), 469–476. https://doi.org/10.1001/jamainternmed.2017.8625.

Cromwell, J., Bartosch, W.J., Fiore, M.C., et al., 1997. Cost-effectiveness of the clinical practice recommendations in the AHCPR guideline for smoking cessation. JAMA 3; 278 (21), 1759–1766. https://doi.org/10.1001/jama.1997.03550210057039.

Danaei, G., Ding, E.L., Mozaffarian, D., et al., 2009. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. PLoS Med. 6 (4), e1000058 https://doi.org/10.1371/journal.pmed.1000058.

Doll, R., Peto, R., Wheatley, K., et al., 1994. Mortality in relation to smoking: 40 years' observations on male British doctors. BMJ 309 (6959), 901–911. https://doi.org/10.1136/bmj.309.6959.901.

Erickson, P., Wilson, R., Shannon, I., 1995. Years of healthy life. In: Healthy People 2000 Statistical Notes, 7, pp. 1–15. https://doi.org/10.1037/e583992012-001.

Feirman, S.P., Glasser, A.M., Teplitskaya, L., et al., 2016 Dec. Medical costs and quality-adjusted life years associated with smoking: a systematic review. BMC Public Health 16 (1), 1. https://doi.org/10.1186/s12889-016-3319-z.

Fenelon, A., Preston, S.H., 2012. Estimating smoking-attributable mortality in the United States. Demography. 49 (3), 797–818. https://doi.org/10.1007/s13524-012-0108-x.

Fiscella, K., Franks, P., 1996. Cost-effectiveness of the transdermal nicotine patch as an adjunct to physicians' smoking cessation counseling. JAMA. 275 (16), 1247–1251. https://doi.org/10.1001/jama.1996.03530400035035.

Fisher, M.T., Tan-Torres, S.M., Gaworski, C.L., et al., 2019a. Smokeless tobacco mortality risks: an analysis of two contemporary nationally representative longitudinal mortality studies. Harm Reduct. J. 16 (1), 1–10. https://doi.org/10.1186/s12954-019-0294-6.

Fisher, M.T., Tan-Torres, S.M., Gaworski, C.L., et al., 2019b. Smokeless tobacco mortality risks: an analysis of two contemporary nationally representative longitudinal mortality studies. Harm Reduct. J. 16, 27. https://doi.org/10.1186/s12954-019-0294-6.

Forouzanfar, M.H., Afshin, A., Alexander, L.T., et al., 2016. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the global burden of disease study 2015. Lancet. 388 (10053), 1659–1724. https://doi.org/10.1016/S0140-6736(16)31679-8.

Hatsukami, D., Zeller, M., Gupta, P., et al., 2014. Smokeless tobacco and public health: A global perspective. In: NIH publication; no. 14-7983. https://stacks.cdc.gov/view/cdc/43373 [Accessed Feb. 20, 2020].36.

Holtgrave, D.R., Wunderink, K.A., Vallone, D.M., Healton, C.G., 2009 May 1. Cost–utility analysis of the national truth® campaign to prevent youth smoking. Am. J. Prev. Med. 36 (5), 385–388. https://doi.org/10.1016/j.amepre.2009.01.020.

Javitz, H.S., Swan, G.E., Zbikowski, S.M., et al., 2004. Cost-effectiveness of different combinations of bupropion SR dose and behavioral treatment for smoking cessation: a societal perspective. Am. J. Manag. Care 10 (3), 217–226. http://www.ncbi.nlm.nih.gov/pubmed/15032259.

Jha, P., Ramasundarahettige, C., Landsman, V., et al., 2016. 21st-century hazards of smoking and benefits of cessation in the United States. N. Engl. J. Med. 368 (4), 341–350. https://doi.org/10.1056/NEJMsa1211128.

Jia, H., Zack, M.M., Thompson, W.W., 2011. State quality-adjusted life expectancy for U. S. adults from 1993 to 2008. Qual Life Res. 20 (6), 853–863. https://doi.org/10.1007/s11136-010-9826-y.

Jia, H., Zack, M.M., Thompson, W.W., et al., 2013. Quality-adjusted life expectancy (QALE) loss due to smoking in the United States. Qual. Life Res. 22 (1), 27–35. https://doi.org/10.1007/s11136-012-0118-6.

Kaplan, R.M., Anderson, J.P., Kaplan, C.M., 2007. Modeling quality-adjusted life expectancy loss resulting from tobacco use in the United States. Soc. Indic. Res. 81 (1), 51–64. https://doi.org/10.1007/s11205-006-0014-y.

Keeler, T.E., Hu, T.W., Keith, A., et al., 2002. The benefits of switching smoking cessation drugs to over-the-counter status. Health Econ. 11 (5), 389–402. https://doi.org/10.1002/hec.677.

Lim, S.S., Vos, T., Flaxman, A.D., et al., 2012. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the global burden of disease study 2010. Lancet. 380 (9859), 2224–2260. https://doi.org/10.1016/S0140-6736(12)61766-8.

Lortet-Tieulent, J., Kulhánová, I., Jacobs, E.J., et al., 2017. Cigarette smoking-attributable burden of cancer by race and ethnicity in the United States. Cancer Cause Control. 28 (9), 981–984. https://doi.org/10.1007/s10552-017-0932-9.

National Center for Health Statistics, 2018a. Survey Description, National Health Interview Survey, 2017. Hyattsville, Maryland. Avaiable at. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHIS/2017/srvydesc.pdf [Accessed Feb. 20, 2020].

National Center for Health Statistics, 2018b. National Health Interview Survey Methods: Variance Estimation Guidance, NHIS 2016-2017 Data. Hyattsville, Maryland. Avaiable at. https://www.cdc.gov/nchs/data/nhis/2016var.pdf [Accessed Feb. 20, 2020].

Nonnemaker, J., Rostron, B., Hall, P., et al., 2014. Mortality and economic costs from regular cigar use in the United States, 2010. Am. J. Public Health 104, e86–e91. https://doi.org/10.2105/AJPH.2014.301991.

Reitsma, M.B., Fullman, N., Ng, M., et al., 2017 May 13. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the global burden of disease study 2015. Lancet. 389 (10082), 1885–1906. https://doi.org/10.1016/S0140-6736(17)30819-X.

Rostron, B., 2011. Smoking-attributable mortality in the United States. Epidemiology 22 (3), 350–355. https://doi.org/10.1097/EDE.0b013e3182126729.

Rostron, B., Chang, C.M., Pechacek, T.F., 2014. Estimation of cigarette smoking-attributable morbidity in the United States. JAMA Intern. Med. 174 (12), 1922–1928. https://doi.org/10.1001/jamainternmed.2014.5219.

Russell, L.B., Gold, M.R., Siegel, J.E., et al., 1996. The role of cost-effectiveness analysis in health and medicine. Panel on cost-effectiveness in health and medicine. JAMA. 276 (14), 1172–1177. https://doi.org/10.1001/jama.1996.03540140060028.

Sanders, G.D., Neumann, P.J., Basu, A., et al., 2016. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. JAMA 316 (10), 1093–1103. https://doi.org/10.1001/jama.2016.12195.

Scherbov, S., Ediev, D., 2011. Significance of life table estimates for small populations: Simulation-based study of standard errors. Demographic Research 24 (22), 527–550. https://doi.org/10.4054/DemRes.2011.24.22.

Siddiqi, K., Husain, S., Vidyasagaran, A., et al., 2020 Dec. Global burden of disease due to smokeless tobacco consumption in adults: an updated analysis of data from 127 countries. BMC Med. 18 (1), 1–22. https://doi.org/10.1186/s12916-020-01677-9.

Siegel, J.E., Weinstein, M.C., Russell, L.B., et al., 1996. Recommendations for reporting cost-effectiveness analyses. Panel on Cost-Effectiveness in Healthand Medicine. JAMA 276 (16), 1339–1341. https://doi.org/10.1001/jama.1996.03540160061034.

Stewart, S.T., Cutler, D.M., Rosen, A.B., 2009. Forecasting the effects of obesity and smoking on U.S. life expectancy. N. Engl. J. Med. 361 (23), 2252–2260. https://doi.org/10.1056/NEJMsa0900459.

U.S. Department of Health and Human Services, 2014. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. U.S. Department of Health and Human Services.Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta [Accessed Feb. 20, 2020].

Villanti, A.C., Curry, L.E., Richardson, A., et al., 2012 Dec 1. Analysis of media campaign promoting smoking cessation suggests it was cost-effective in prompting quit attempts. Health Affair. 31 (12), 2708–2716. https://doi.org/10.1377/hlthaff.2012.0277.

Weinstein, M.C., Siegel, J.E., Gold, M.R., et al., 1996. Recommendations of the panel on cost-effectiveness in health and medicine. JAMA. 276 (15), 1253–1258. https://doi.org/10.1001/jama.1996.03540150055031.

Xu, X., Alexander Jr., R.L., Simpson, S.A., et al., 2015. A cost-effectiveness analysis of the first federally funded antismoking campaign. Am. J. Prev. Med. 48 (3), 318–325. https://doi.org/10.1016/j.amepre.2014.10.011.