PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The Costs of Smoking and Secondhand Smoke Exposure in Taiwan: A Prevalence-Based Annual Cost Approach
AUTHORS	Sung, Hai-Yen; Chang, Li-Chuan; Wen, Yu-Wen; Tsai, Yi-Wen

VERSION 1 - REVIEW

REVIEWER	Chi Pang Wen NHRI, Taiwan
REVIEW RETURNED	11-Apr-2014

GENERAL COMMENTS	This study lacks novelty and significant or interesting findings, more appropriate for domestic consumption than for international audience. 1) SAM and health care costs have been published by many countries, with CDC offering a computer software to calculate. Each country had published SAM and health care costs figures, but they would not be interesting to international audience. 2) Even in Taiwan, both of these subjects have been published. The authors did not comment on the differences of results from earlier publication. 3) The authors claimed that they used newer but lower smoking rate in calculating SAM, which accounted for a smaller SAM than before. There are some technical issues here. People are getting older and should have more deaths (absolute number) than previously, not less. There is a debate as to the age structure when the relative risks were derived, and the age structure when smoking prevalence was calculated. There is some merit with the suggestion for the use of smoking prevalence of 10 years earlier to calculate SAM and not the most recent one. 3) Health care cost as an absolute number is too bland to readers.

REVIEWER	Qiang Li Boehringer Ingelheim International Trading (Shanghai) Co., Ltd.
REVIEW RETURNED	22-Apr-2014

GENERAL COMMENTS	This paper estimated the cost of smoking and SHS in Taiwan. The authors estimated that smoking causes 14332 deaths among males and 1172 deaths among females in Taiwan in 2010. My major concern is that the authors may underestimated the death toll because of the limitation of their methods. Although the authors mentioned the possibility of underestimation in the discussion, the issue is not fully addressed.

	This paper estimated the costs of smoking and secondhand smoke exposure in Taiwan. The authors used the ASBS data and the NHI data to quantify the cost of smoking and SHS exposure, including the direct cost of healthcare expenditure, indirect cost of mortality and morbidity. The paper is well written and the methods are appropriate. Overall, this paper has important policy implications, not only for Taiwan but also for other countries/regions in Asia. I have the following concerns/questions: 1. The authors may underestimate the cost of smoking and SHS in Taiwan, especially for SHS exposure. Although the authors mentioned this point in the discussion part, there may be more reasons for the underestimate. First, only 19 diseases were included in the analyses. Second, the SHS exposure rate was obtained by combining the exposure at home and at workplaces. Exposure in public places was not included in the analysis, although it is well known that the exposure rate in public places in Taiwan may be low. Third, according to data from China and other countries, exposure to SHS may result in severe disease burden in children, and this is not included in the analysis (the authors talked about this in the discussion). Fourth, the authors only calculated the direct cost of healthcare expenditures. Some expenses, such as transportation, was not included in the analysis. These should be fully discussed in the discussion. 2. For SHS exposure, why do you consider 6 diseases but only 3 causes of death? Is it possible that this become another reason for the underestimates for SHS? 3. Since you derived the RR of disease-specific death for former smokers using an interpolation approach, you should be cautious in discussing the results in table 3, given the possibility that inaccurate estimate may occur. For example, patients with respiratory disease may be more likely to quit smoking compared to patients with liver cancer, which may bias the results for each specific disease. 4. When calculating the RRF for each disease specific death, the authors calculated the attributable risk first (RRAf-1, RRAc-1, RRc-1), and then calculated the attributable risk for former smokers (RRf-1). Why didn't you calculate the RRf directly from RRAf, RRAc, RRc? My understanding is that the results should be the same. Minor points: 1. Page 5, line 1, shouldn't it be indoor public places instead of indoor places? 2. Page 5, last sentence, which year was Yang et al's study? 3. Page 26, the authors mentioned, "tobacco control programs are costly". Are there any figures for how much the 2009 Act cost in Taiwan? If there is a figure, then readers can compare the cost and the benefit.

REVIEWER	Kai-Wen Cheng Institute of Health Policy and Management, National Taiwan University, Taiwan
REVIEW RETURNED	25-Apr-2014

GENERAL COMMENTS	1. The unclear dollar unit. This study should mention in the beginning which unit of dollars was used, and keep the unit consistent throughout the paper. 2. Need more citations. One page 4, lines 42-48. “During 1960s and 1970s, …..and 8-12% for women.” This sentence needs citation. One page 4, lines 48-51. “In 1987, Taiwan’s cigarette……and a 13% jump in youth smoking within three years.” This sentence needs citation. 3. Page 4-5, “As a consequence, the government launched a series of tobacco control initiatives such as……through which indoor places became partially smoke-free [4]” and “In 2002, the government levied tobacco taxes of NT$5 per pack and started the Outpatient Smoking Cessation Services. [5]” The citations [4] and [5] are empirical articles and they seem not appropriate citations for the descriptions for tobacco control policies. Government reports may be better citations for those descriptions. 4. The measure for secondhand smoke exposure may be problematic and needs clarification. This study identified the respondent exposed to SHS if one answered that someone smoked in front of him/her last week at home or at workplace. I have a concern about whether it is a good measure for SHS exposure, especially because the author could not differentiate their SHS exposure levels. If it turns out that a majority of the people exposed to SHS are only occasionally exposed which may lead to the effect on reduced SHS overestimated. Authors may need to clarify this point in the limitation section.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Chi Pang Wen
Comments to the Author

This study lacks novelty and significant or interesting findings, more appropriate for domestic consumption than for international audience.

1. SAM and health care costs have been published by many countries, with CDC offering a computer software to calculate. Each country had published SAM and health care costs figures, but they would not be interesting to international audience.

Response: SAM and health care costs research has been developed and applied well. The significance of this study is to relate the estimated monetary values of SAM and smoking-attributed health care costs to policy interventions. In Table 5 of this paper, we compared the estimated SAM and smoking-attributed costs in 2010 (the year immediately following Taiwan’s 2009 Act of multi-pronged tobacco control policy intervention) with the corresponding estimates in 2008 (the year before the 2009 Act intervention) and showed that the total economic costs of smoking would be

6.4% higher (US$1,777 million vs. US$1,670 million) if the 2009 Act intervention was not implemented. These results provide important empirical evidence to the international audience including policymakers in other countries to realize the economic benefit of reducing smoking and SHS exposure.

2. Even in Taiwan, both of these subjects have been published. The authors did not comment on the differences of results from earlier publication.

Response: There is one previous study done by Yang and Fann et al. (2005) which also used a prevalence-based approach to estimate the SAM and smoking-attributable medical costs in Taiwan. We have re-written the 2nd paragraph of page 26 to provide detailed comparisons between our results and their results.

3. The authors claimed that they used newer but lower smoking rate in calculating SAM, which accounted for a smaller SAM than before. There are some technical issues here. People are getting older and should have more deaths (absolute number) than previously, not less. There is a debate as to the age structure when the relative risks were derived, and the age structure when smoking prevalence was calculated. There is some merit with the suggestion for the use of smoking prevalence of 10 years earlier to calculate SAM and not the most recent one.

Response: As stated in the 2nd paragraph of page 26, “Yang and Fann et al. (2005) estimated that active smoking caused 233,223 years of potential life lost (YPLLs) and US$467 million (after converting into 2010 constant dollars) in excess healthcare costs for 2001. Our corresponding estimates for 2010 are 265,198 years and US$742 million. Our 2010 estimates are larger than the 2001 estimates. We have provided several explanations about this and clarified that the total number of deaths from the 19 smoking-related diseases increased from 77,953 to 75,003 deaths between 2001 and 2010.

After pondering over the question of whether using smoking prevalence in current year or using smoking prevalence of 10 years earlier, we decide it is more reasonable to choose the former way because this study is based on prevalence-based annual cost approach. By definition, the smoking-attributable fraction for year t is originated from the ratio of the excess costs for smokers in year t divided by the total costs for all adults (including smokers and nonsmokers) in year t. Therefore, it depends on the composition of current smokers and nonsmokers in year t, which is captured by the smoking prevalence rate in year t. However, as the reviewers pointed out, the age structure when the relative risks were derived from earlier studies for earlier years is different from the age structure when the risks of death or disease need to be compared between smokers and nonsmokers in year t. We have addressed this limitation in greater detail in page 29, 1st paragraph.

4. Health care cost as an absolute number is too bland to readers.

Response: The absolute number of smoking-attributable costs may not be easy for international readers to comprehend its economic implication. Therefore, in Table 5, we present these costs in terms of the percentage of national healthcare expenditures and the percentage of GDP so that they can be used for meaningful policy interpretation and cross-country comparison.

Reviewer: 2
Reviewer Name: Qiang Li
Comments to the Author

This paper estimated the cost of smoking and SHS in Taiwan. The authors estimated that smoking causes 14332 deaths among males and 1172 deaths among females in Taiwan in 2010. My major concern is that the authors may underestimated the death toll because of the limitation of their methods. Although the authors mentioned the possibility of underestimation in the discussion, the issue is not fully addressed.

Response: We have added detailed discussion to fully address the issue of underestimation in the manuscript as shown in pages 25-26

This paper estimated the costs of smoking and secondhand smoke exposure in Taiwan. The authors used the ASBS data and the NHI data to quantify the cost of smoking and SHS exposure, including the direct cost of healthcare expenditure, indirect cost of mortality and morbidity. The paper is well written and the methods are appropriate. Overall, this paper has important policy implications, not only for Taiwan but also for other countries/regions in Asia. I have the following concerns/questions:

1. The authors may underestimate the cost of smoking and SHS in Taiwan, especially for SHS exposure. Although the authors mentioned this point in the discussion part, there may be more reasons for the underestimate. First, only 19 diseases were included in the analyses. Second, the SHS exposure rate was obtained by combining the exposure at home and at workplaces. Exposure in public places was not included in the analysis, although it is well known that the exposure rate in public places in Taiwan may be low. Third, according to data from China and other countries, exposure to SHS may result in severe disease burden in children, and this is not included in the analysis (the authors talked about this in the discussion). Fourth, the authors only calculated the direct cost of healthcare expenditures. Some expenses, such as transportation, was not included in the analysis. These should be fully discussed in the discussion.

Response: We would like to thank the reviewer to point out the need to discuss whether and why this study may underestimate the true cost of smoking and SHS exposure. We have added detailed discussion to fully address the issue of underestimation in the revised manuscript as shown in pages 25-26

2. For SHS exposure, why do you consider 6 diseases but only 3 causes of death? Is it possible that this become another reason for the underestimates for SHS?

Response: We identified the 6 SHS-associated diseases (lung cancer, ischemic heart disease, cerebravascular disease, COPD, asthma, and breast cancer) and 3 SHS-associated causes of death (lung cancer, ischemic heart disease, and cerebravascular disease) according to the 2005 California Environmental Protection Agency Report and a World Health Organization Report.

In a recently published study which estimated the costs of SHS exposure in California [Max, Sung, and Shi; 2013], they included 4 SHS-associated diseases (asthma, lung cancer, ischaemic heart disease, and breast cancer) and 3 SHS-associated causes of death (ischaemic heart disease, lung cancer, and asthma) for adults. Their selection was based on the 2005 California Environmental Protection Agency Report and the 2006 U.S. Surgeon General's Report. Notice that the number of SHS-associated diseases is also more than the number of SHS-associated causes of death in their study. However, they included asthma in the 3 SHS-associated causes of death while we did not. Based on their study, we have revised our analysis by adding asthma as a SHS-associated cause of death as well. As a result, our estimates for smoking and SHS attributable deaths and economic costs have increased slightly as shown in the revised manuscript.

REFERENCE

Max W, Sung HY, Shi Y. The cost of secondhand smoke exposure at home in California. Tob Control Published Online First: 19 April 2013 doi: 101136/tobaccocontrol-2012-050852 2014:tobaccocontrol-2013-051253.

3. Since you derived the RR of disease-specific death for former smokers using an interpolation approach, you should be cautious in discussing the results in table 3, given the possibility that inaccurate estimate may occur. For example, patients with respiratory disease may be more likely to quit smoking compared to patients with liver cancer, which may bias the results for each specific disease.

Response: We thank for reviewer's suggestion, and have added a discussion about the implication of using this approach (see page 28, 2nd paragraph). In that paragraph, we stated:

"To test the validity of this, we applied this approach to the widely cited American RR data which consist of disease-specific and all-cause RRs for current and former smokers and are available in the internet-based SAMMEC software.[24] We found that our derived RRs for former smokers follow a consistent pattern with the actual RRs for former smokers across diseases,"

The table below shows the results of the comparison between actual RRs and our estimated RRs using the RRs for Americans according to the data reported in the SAMMEC system.

Table. Relative risk for current and former smokers among male adults aged 35+, based on 6-year (1982-1988) follow-up of American Cancer Society's Cancer Prevention Study II (CPS-II), United States

RRC and RRF published in the 2014 U.S. Surgeon General's Report Ratio = (RRF−1) / (RRC−1)
RRF estimated from Eq. (1a)

Current Smoker	Former Smoker	Former Smokers
Specific disease:		
• Lung cancer	23.26	8.70 0.3459 10.63
• Esophagus cancer	6.76	4.46 0.6007 3.49
• Stomach cancer	1.96	1.47 0.4896 1.42
• Ischemic heart disease (age 35-64)	2.80	1.64 0.3556 1.78
• Ischemic heart disease (age 65+)	1.51	1.21 0.4118 1.22
• Cerebrovascular disease (age 35-64)	3.27	1.04 0.0176 1.98
• Cerebrovascular disease (age 65+)	1.63	1.04 0.0635 1.27
• Chronic airway obstruction	10.58	6.80 0.6054 5.14
• Bronchitis, emphysema	17.10	15.64 0.9093 7.97
• Influenza, pneumonia	1.75	1.36 0.4800 1.32
• All Causes	2.34	1.58 0.4238

Ratio = (RRAF−1) / (RRAC−1)=(1.58 – 1) / (2.34 – 1) = 0.4328

4. When calculating the RRF for each disease specific death, the authors calculated the attributable risk first (RRAf-1, RRAc-1, RRc-1), and then calculated the attributable risk for former smokers (RRf-1). Why didn't you calculate the RRf directly from RRAf, RRAc, RRc? My understanding is that the results should be the same.

Response: We calculated the RR of a disease specific cause of death for former smokers (denoted by RRF) using the following formula:

RRF = (RRC − 1) x (RRAF − 1) / (RRAC − 1) + 1 (Eq. 1a)

where
(RRC − 1)= the excess risk of a disease specific cause of death for current smokers over never smokers,
(RRAF − 1)= the excess risk of all causes of death for former smokers over never smokers,
(RRAC − 1)= the excess risk of all causes of death for current smokers over never smokers.

This equation can be rewritten as:

(RRF − 1) / (RRC − 1) = (RRAF − 1) / (RRAC − 1) (Eq. 1b)

The left-hand side of Equation (1b) denotes the ratio of "the disease-specific excess risk for former smokers" to "the disease-specific excess risk for current smokers". The right-hand side of Equation (1b) denotes the ratio of "the all-cause excess risk for former smokers" to "the all-cause excess risk

for current smokers". Therefore, our calculation of RRF is based on the assumption that these two ratios are equal. We have described this assumption in the revised manuscript (see page 11, the 1st paragraph).

If we understood this comments correctly, the reviewer asked why we did not use the following formula to calculate the RRF.

RRF = (RRC) x (RRAF) / (RRAC) (Eq. 2a)

where
RRC= the relative risk of a disease specific cause of death for current smokers over never smokers,
RRAF= the relative risk of all causes of death for former smokers over never smokers,
RRAC= the relative risk of all causes of death for current smokers over never smokers.

Equation (2a) can be rewritten as:

(RRF) / (RRC) = (RRAF) / (RRAC) (Eq. 2b)

The left-hand side of Equation (2b) denotes the ratio of "the disease-specific relative risk for former smokers" to "the disease-specific relative risk for current smokers". The right-hand side of Equation (2b) denotes the ratio of "the all-cause relative risk for former smokers" to "the all-cause relative risk for current smokers".

Given the huge body of scientific evidence that smokers have a greater risk of mortality compared with never smokers, the relative risk for smokers (regardless of current or former) should be greater than 1. Also, given the evidence from many studies showing that smokers who stop smoking reduce their risk of developing and dying from tobacco-related illnesses, the relative risk for former smokers should be smaller than the relative risk for current smokers. Therefore, the following relationships should hold true.

(RRF) / (RRC) > (RRF − 1) / (RRC − 1) (Eq. 3a)

(RRAF) / (RRAC) > (RRAF − 1) / (RRAC − 1) (Eq. 3b)

Given these relationships, the results estimated from Equation (1a) would be different from the results estimated from Equation (2a).

We decided to choose the approach as shown in Equation (1a) for two reasons. First, the disease-specific RRF estimated from Equation (1a) is guaranteed to be greater than 1, while it is not necessarily true if using Equation (2a). Second, we compared the RRF results derived from these two approaches by using the published U.S. relative risks of mortality for current smokers and former smokers among males aged 55-64 [See the 2014 U.S. Surgeon General's Report, Table 12.6]. As shown in the following table, from Equation (1a), the estimated RRF values (column 4) are greater than 1 for every disease and they are pretty close to the actual RRs (column 3). On the other hand, from Equation (2a), the estimated RRF values (column 5) contains a value smaller than 1 for "other cancers" and they look almost 2-fold as large as the actual RRs for two disease groups.

Table. Relative risks for current and former smokers for male adults aged 55-64, United States
RRC and RRF published in the 2014 U.S. Surgeon General's Report RRF estimated from Eq. (1a) RRF estimated from Eq. (2a)
Current Smoker Former Smoker Former Smokers Former Smokers
Specific disease:
• Lung cancer 19.03 4.57 5.30 9.42
• Other cancers 1.86 1.31 1.21 0.92
• Ischemic heart disease 2.99 1.52 1.47 1.48
• Other cardiovascular disease 2.51 1.51 1.36 1.24
• Influenza, pneumonia, Chronic obstructive pulmonary disease 15.17 3.98 4.38 7.51

All Causes 2.97 1.47
(RRAF − 1) / (RRAC − 1)=(1.47 – 1) / (2.97 – 1) = 0.2386
(RRAF) / (RRAC) =(1.47) / (2.97) = 0.4949

Minor points:

1. Page 5, line 1, shouldn't it be indoor public places instead of indoor places?

Response: We have changed "indoor places" to indoor workplaces and public places" as shown on page 5, line 4.

2. Page 5, last sentence, which year was Yang et al's study?

Response: We have clarified this point by adding "in 2001" on page 5, line 57.

3. Page 26, the authors mentioned, "tobacco control programs are costly". Are there any figures for how much the 2009 Act cost in Taiwan? If there is a figure, then readers can compare the cost and the benefit.

Response: We appreciate this very helpful suggestion, and have incorporated the reviewer's suggestion into the first three sentences of the 2nd paragraph on Page 27:

"Tobacco control programs are costly. In 2009, the government of Taiwan spent US$15.7million US dollars (or NT$520 million based on the 2009 exchange rate of NT$33.049 against US$1) on tobacco control programs.[30]"

Reviewer: 3
Reviewer Name: Kai-Wen Cheng
Comments to the Author

1. The unclear dollar unit. This study should mention in the beginning which unit of dollars was used, and keep the unit consistent throughout the paper.

Response: We have fixed the unclear dollar unit problem by expressing all the dollars either in NT$ (i.e., New Taiwan Dollar) or US$ throughout this paper.

2. Need more citations. One page 4, lines 42-48. "During 1960s and 1970s, …..and 8-12% for women." This sentence needs citation. One page 4, lines 48-51. "In 1987, Taiwan's cigarette……and a 13% jump in youth smoking within three years." This sentence needs citation.

Response: We have added a citation for these two sentences as shown on page 4, line 48 & 51.

3. Page 4-5, "As a consequence, the government launched a series of tobacco control initiatives such as……through which indoor places became partially smoke-free [4]" and "In 2002, the government levied tobacco taxes of NT$5 per pack and started the Outpatient Smoking Cessation Services. [5]" The citations [4] and [5] are empirical articles and they seem not appropriate citations for the descriptions for tobacco control policies. Government reports may be better citations for those descriptions.

Response: On page 5, we have changed the citation in these two places by citing reference [5], which is a government report "2012 Taiwan Tobacco Control Annual Report".

4. The measure for secondhand smoke exposure may be problematic and needs clarification. This study identified the respondent exposed to SHS if one answered that someone smoked in front of him/her last week at home or at workplace. I have a concern about whether it is a good measure for SHS exposure, especially because the author could not differentiate their SHS exposure levels. If it turns out that a majority of the people exposed to SHS are only occasionally exposed which may lead to the effect on reduced SHS overestimated. Authors may need to clarify this point in the limitation section.

Response: To address the issues related to the measurement for SHS exposure, we have added the following sentences in the Discussion section (see pages 25, lines 45-57):

"… we measured SHS exposure based on self-reported exposure in the home and workplace during the last week, but did not consider exposure that may have occurred in other public places or at an earlier time. It has been shown that self-reported SHS exposure greatly underestimates actual exposure assessed by the biomarker such as cotinine level.[29] Therefore, our estimated SHS-attributable costs are most likely to be underestimated."

VERSION 2 – REVIEW

REVIEWER	Kai-Wen Cheng Institute of Health Policy and Management, National Taiwan University
REVIEW RETURNED	16-Jun-2014

GENERAL COMMENTS	The authors have answered all my questions, and incorporated my comments in the paper.