Author’s response to reviews

Title: A comparison of gender-linked population cancer risks between alcohol and tobacco: how many cigarettes are there in a bottle of wine?

Authors:

THERESA HYDES (therasa@doctors.org.uk)

Robyn Burton (Robyn.Burton@phe.gov.uk)

Hazel Inskip (hmi@mrc.soton.ac.uk)

Mark Bellis (m.a.bellis@bangor.ac.uk)

Nick Sheron (nick.sheron@soton.ac.uk)

Version: 1 Date: 06 Oct 2018

Author’s response to reviews:

REVIEWER 1

Freddy Sitas, D. Phil: This is an interesting analogy attempting to create a common currency of absolute risks between smoking and alcohol consumption in the UK.

(1) I think the authors need to make it absolutely clear that they are describing increases in absolute risks in the population for cancers only and not relative risks. There is no doubt that public health campaigns for reductions in alcohol need to be better resourced and taken more seriously. But care needs to be taken in the (mis)interpretation of these results. There is a likelihood that the hazard of smoking will be trivialized. By equating the hazard of smoking to one bottle a week many (normal) people may use this as an excuse start smoking, or not to stop! Cancer deaths are a fraction of the total numbers of deaths caused by smoking and alcohol. Rough calculations: long term current smokers of 10 cigarettes a day double their risk of (overall) death. This is in no way equivalent to a bottle of wine a week - that's more equivalent to a bottle a day. See (Zaridze et al - Studies from Russia). Some commentary is needed.

Clarity is needed to ensure the authors are talking about absolute numbers attributed to each exposure (described as absolute / lifetime risks) and not the relative risk between the two
exposures. For example the abstract refers to three different terms 'the cancer risk' (that can be misinterpreted as a relative risk) attributed fractions and absolute risks. This is very confusing. The terminology needs to be made more consistent across the document. Cancer risk / absolute risk of xx related cancer / etc. High absolute risks / attributable fractions are dependent on the prevalence of the exposure and its relative risk. A statement around that (smoking: high risk & lower prevalence vs alcohol low risk & higher prevalence) needs to be added.

We thank the reviewer for making this important point, and are also keen that our message be absolutely clear and not subject to any misinterpretation. We have therefore edited any mention of “risk” to ensure it is clear we are referring to an “increase in absolute risk of cancer”, rather than relative risk and that our terminology is consistent throughout the manuscript. (p5,L23; p6,L6; p8,L19; p8,L21; p12,L8; p13,L11; p13,L14; p13,L20; p13,L23; p14,L9; p15,L7; p18,L20; p20,L16). We have also added the word ‘purely’ at the beginning of the sentence ‘in terms of cancer risk – how many cigarettes are there in a bottle of wine.’ (p8,L23).

We have added in the following two paragraphs to the discussion to further clarify our message and avoid any misinterpretation of our findings.

“We must first be absolutely clear that this study is not saying that drinking alcohol in moderation is in any way equivalent to smoking. Smoking kills up to two thirds of its users [2], and cancer is just one of the many serious health consequences. This study purely addresses cancer risk in isolation. The UK chief medical officer’s moderate drinking guideline of 14 units per week is set at a level at which there is a 1% absolute risk of mortality from alcohol [35]. Furthermore the average consumption of cigarettes by smokers is around 80 per week in the UK and 100 per week in the United States (US) [36], far greater than our cigarette equivalent for moderate drinkers.” (p14,L15-22).

“It is noteworthy that the attributable fractions and the absolute risk scores calculated here are dependent on both the prevalence of exposure to a risk factor within a population and the relative risk of that behaviour resulting in cancer. For smoking the prevalence is low (approximately 20% of individuals in the UK are daily smokers for example [52]), with a high relative risk of cancer for current smokers; whereas alcohol consumption is more common (72% of women and 83% of men consume some alcohol in countries with a high socio-demographic index [10]), but is associated with a lower relative risk of cancers overall; even for high levels of consumption [53]. Critically, our findings are not meant to detract from the substantive cancer risks associated with
smoking which remains the single largest preventable cause of cancer worldwide [54], and for which even very low levels of exposure are associated with an increased risk of cancer [46]. Furthermore, cancer deaths are a fraction of the total number of deaths caused by smoking and alcohol and this study is not a comparison of the overall mortality of smoking versus alcohol.”(p20, L1–14).

(2) A stronger statement needs to focus this message to policy makers, followed by a careful interpretation for public consumption.

Here is a suggestion how to reword the abstract.

"In contrast to our knowledge about the number of cancer deaths attributed to smoking, the number of cancer deaths attributed to alcohol is poorly understood by the public. We estimate the increase in absolute risk of cancer (number of deaths per 1000) attributed to moderate levels of alcohol, and compare these to the absolute risk of cancer attributed to low levels of smoking, creating a 'cigarette-equivalent of population cancer harm'."

We thank the reviewer for their suggestions and have re-worded the abstract accordingly. We agree that this statement more clearly describes the purpose and method of the paper for both the public and policy makers (p5, L3-8).

(3) Small comments. Figure 3, Fix spelling on y axis.

We have corrected the spelling of “lifetime” on the y axis for Figure 3.

REVIEWER 2

Sakari Bertel Alfred Suominen: This is a good study on an important topic, namely how much even moderate alcohol consumption might increase the combined risk of several cancers. The conclusion of this paper includes also an important message to the general public quite as the authors write, since increase of cancer risk by consumption of even small quantities of alcohol is
not generally very well known, contrary to what can be said about general awareness of tobacco related health risks.

I have read the manuscript carefully and have only minor comments and this applies also to the Methods chapter despite my recommendation of additional statistical review, since I am to my basic training a MD and not a statistician.

Below I give my minor comments according to the chapters of the manuscript.

(1) Abstract

I would suggest editing the sentence: 'In contrast to smoking, the cancer risk associated with alcohol is poorly understood by the public.' to 'In contrast to cancer risk associated with smoking, the corresponding risk associated with alcohol consumption is poorly understood by the public.'

We thank the reviewer for their suggestion. This section of the abstract has already been updated as per the suggestions of the first reviewer (p5,L3-8).

(2) I find the following sentence unnecessary to be included in the Abstract 'Among 1,000 individuals drinking at this level we estimate an additional ten cancers for men, 14 for women.' since this is obvious based on the previous sentence. But this is remains an editorial decision, probably the sentence is directed to the general public.

We thank the reviewer for their suggestion and have removed this sentence from the abstract (p5). This was intended for clarity for the general public, but we agree it simply repeats the results presented in the previous sentence.

(3) However, I would suggest that the final message to the general public, even if this is not the specific focus of this study, would be edited with an added note that smoking can substantially increase the alcohol related cancer risk. With this I refer to the more than additional effect that
can be found between alcohol consumption and smoking in relation to the risk of several forms of cancer. I find this important since many individuals that consume alcohol at least occasionally also smoke, at least there is a known positive correlation between these two health behaviours.

We have also added in a comment in the first paragraph of the discussion acknowledging the synergistic interaction between alcohol and tobacco for cancers of the upper aerodigestive tract in particular, and agree this is a very pertinent point given a higher incidence of smoking among social drinkers compared to alcohol abstainers. “It is also worth considering that there is a higher incidence of smoking among social drinkers compared to alcohol abstainers [39]. This is important as smoking can substantially increase the carcinogenic risk associated with alcohol consumption, particularly for cancers of the upper aerodigestive tract [25,26].” (p15,L17-21).

(4) Introduction

The Introduction is quite focused on U.K. which is understandable but could you add up some concrete numbers on health losses worldwide caused by smoking and alcohol consumption in line with what is written about the U.K.?

In response to the reviewer’s comments we have updated the introduction to include global data on the health consequences of tobacco and alcohol use.

“Tobacco use accounts for 7 million deaths per year globally with an estimated two thirds of smokers expected to die from their habit [1,2]. Smoking is responsible for 22% of cancer deaths worldwide [3].”(p7,L4-7).

“Each year approximately 3.3 million deaths occur due to the harmful use of alcohol, corresponding to 5.9% of all deaths globally [9]. Furthermore alcohol was the leading cause of death among 15-49 year olds worldwide in 2016 [10].” (p7,L19-21).
(5) Methods

The authors, quite correctly adjusted the results for the combination of alcohol and tobacco as risk for cancer. I would just like to comment that we seriously talk about alcohol consumers that have never smoked but the alcohol history of smokers is more unreliable, however, at its worst this leads only to a slight underestimation of the combined cancer risk but some smokers might previously have been heavy drinkers.

We have acknowledged this factor in the discussion: “We acknowledge however that the alcohol history of smokers is generally less accurate, and that a higher proportion of smokers may have previously been heavy drinkers. This factor may have led to a minor underestimate of the combined cancer risk.” (p18,L5-8).

(6) Results

Delete percentage in the sentence 'In non-smoking men the percentage increase in the absolute lifetime risk of cancer 21 from drinking one bottle of wine per week was 1.0%'

We have deleted the word “percentage” from this sentence. (p12,L6).

(7) Are percent marks missing in the sentence 'Consumption of ten units of alcohol per week carried an equivalent cancer risk to four cigarettes per week for men (3.5), and ten cigarettes per week for women (9.8), as breast cancer risks did not require adjustment.' for the risk estimates?

There are no percentage markers missing from this sentence as the % increases in absolute lifetime risk are described in the preceding sentence. This sentence describes the cigarette equivalent in terms of cancer risk for consuming ten units of alcohol following the sensitivity analysis. (p14,L8-11).
(8) Discussion

The authors mention the huge cost burden caused by deaths in breast cancer. I would like to add that quite many of the deaths strike rather young women and hence, also represent a huge mental burden for their families, particularly minor children. Otherwise, the Discussion is excellent and I have nothing of importance to add to it.

We agree with the reviewer that this is an important point and have included a comment on this in the discussion: “In addition breast cancer affects women at a relatively younger age compared to lung cancer [51], resulting in a significant burden for them and their families, including young children.” (p19,L20-22).

(9) Supplementary Tables

In the caption of the supplementary Table 1 'original' should probably be 'originally'

We have made this change.

(10) In the caption of the supplementary Table 3 why is thirty once written in letters and once in numbers?

We think the reviewer is referring to supplementary table 4. We have changed ‘thirty’ to ‘30’.
ADDITIONAL COMMENTS

Please note we have adjusted the breast cancer statistics presented in the discussion on page 16 as these have been updated by CRUK since the paper was submitted. (p16,L19-23).