PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Cross-sectional association between cigarette smoking and abdominal obesity among Austrian bank employees
AUTHORS	de Oliveira Fontes Gasperin, Lizia; Neuberger, Manfred; Tichy, Alexander; Moshammer, Hans

VERSION 1 - REVIEW

REVIEWER	Catherine Hankey University of Glasgow, Glasgow, UK
REVIEW RETURNED	10-Mar-2014

GENERAL COMMENTS	This work is interesting and examines the relationships between body weight and shape and reported smoking history. The work is carried out on data from the employees of a firm in Austria. A main limitation is that the majority (all?) of the findings depend on self reported measures. These are know to be mispreported, especially dietary data from the overweight. Can the authors discuss what benefit a smokelyser or other actual measurement of breath carbon monoxide may have had, given the whole study discusses the impact of smoking duration and intensity which is self reported. The work is interesting, and has some different findings to the wider literature. The role of a longer smoking duration on BMI and body shape, a majority of other workers have shown that BMI is lowered after long smoking periods. Can the authors discuss this. The anthropometric measurements made include waist to hip raio and waist height and calculated BMI. Also height to waist. Not sure why all of these data are reported. Can the authors consider the issue between waist to hip ratio and muscle mass in smokers, this has not been considered in depth. The authors state no differences in in WC, WHR or WHtR, can they speculate why, given the impact on smoking on waist to hip ratio. The novelty of the findings ought to be emphaised. I am not sure that this manuscript reports new findings, and I am keen to determine what is new to the literature. The biochemical findings are certainly already well reported

REVIEWER	Dexter Canoy Nuffield Department of Population Health University of Oxford UK
REVIEW RETURNED	02-May-2014

GENERAL COMMENTS	This is a cross-sectional study investigating the relationship between smoking and adiposity (and other metabolic risk markers) in a sample of workers. The authors found that current smokers, particularly heavy smokers, have higher weight and body mass index, as well as higher concentration of white blood cell count. Smoking may be mistakenly used as a way to regulates weight for some groups in the population. In this study, the authors argue that it is not the case as smokers have higher weight and BMI. However, the findings of this study needs to be treated with caution, both in terms of the study population as well as the analytical strategies used. The use of employees as a study population is a convenient sample to test the hypothesis that smoking may be associated with adiposity. Needless to say, there is a potential selection bias. Note that the proportion of smokers in this study differs widely to the estimates reported for the whole of Austria (page 3, first paragraph). The study sample size, contrary to what the authors claim, is small. Even using crude values, weight and BMI varied for some of the smoking categories. But the differences are not significant. I think this is mainly due to lack of power to detect small but meaningful differences. How weight and height have been measured is unclear. The methods described on page 4 is not clear. The limitations described on page 10 suggest that weight and height have been self-reported. This was not mentioned on page 4's methods section. Moreover, if weight and height have been self-reported, why not measure these? The other anthropometric measures seem to have been measured at the clinic. Measurement error plus the small sample size would have limited the statistical power of this study to detect modest differences in the outcomes across smoking categories. Data on covariates are either inadequate or inconsistently applied. Obtaining total energy intake from a single 24-hour food recall is very limited. It is unlikely to adjust appropriately for differences in energy intake across smoking groups. The authors describe of 'two indices of diet quality' in the statistical analyses, but these were not described elsewhere in the manuscript. What are these? Were these indices used as covariates in the analyses? Data on alcohol intake was not included as a covariate. It would be a major limitation if such data have not been collected as it is an important determinant of body composition and may correlate well with smoking as part of a high-risk lifestyle. More importantly, any measure of socio-economic position or education should be used as an important covariate. There are huge differences in the proportion of high and medium/low education by smoking status (in men, this is not statistically significant, but this is mainly because of lack of power.) (Please check the educational level in men – the proportion for smokers is wrong.) Age seems an important covariate that needs further exploration.

	The study involves a very wide range of ages, but BMI varies greatly with age, and most adults would have gained most weight would be in their middle ages. Smoking also had a strong age correlation. Adjusting for age without further detailed age-specific analyses is therefore inadequate. What is the age range? (Many would have retired in their mid-60s.) What is the age distribution of the employees overall? What is the age, sex, and smoking distribution? Are the current smokers in younger age groups lean? Are the current smokers in older age groups heavier? Were most of the employees younger? Understanding these distributions would reveal why we may see a different pattern of smoking-adiposity results in this group of workers as the general population. Age should also be included in the table of characteristics (Tables 1 and 2). On page 6, last paragraph – what is outcome is being compared across smoking groups? This could have been the most important outcome being investigated, yet, it is missing. The investigators reported on smoking and leukocyte count. It would be useful to compare their results with other studies that have investigated this association. Analyses for waist circumference and waist-hip ratio, as measures of relative fat distribution, without taking into account total body size is inappropriate unless accompanied by results showing total body size, such as body mass index, has been adjusted for. Further, analyses showing that over 80% of total body size (ie, body mass index) being explained by waist circumference is rather biologically implausible. I could not imagine how waist circumference could explain most of one's body mass index. I suggest that the authors just report on the correlations, not the variance. The end paragraph of the discussion section is irrelevant to the main focus of the manuscript. I suggest that these would be dropped (and report these findings in a different manuscript).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

This work is interesting and examines the relationships between body weight and shape and reported smoking history. The work is carried out on data from the employees of a firm in Austria.

A main limitation is that the majority (all?) of the findings depend on self-reported measures. These are known to be misreported, especially dietary data from the overweight. Information on smoking, diet, physical activity, and body weight were self-reported. We agree that this is a limitation of the study. For dietary data we used 24-hour recall which is deemed to be more accurate, but on an individual basis more prone to day-by-day fluctuations. In the total group on average it is deemed to give a less biased estimate. The reported data were checked by nutritional experts for plausibility before they were entered into the data base. (Thus some persons with missing data on food intake had to be accepted. The effect estimates in persons with full data did not differ from the total data set.) To our comfort the effect estimates for calories intake on anthropometric measures were plausible supporting the validity of the dietary data.

Can the authors discuss what benefit a smokelyser or other actual measurement of breath carbon monoxide may have had, given the whole study discusses the impact of smoking duration and intensity which is self-reported. This examination was done among employees of one bank institute

where all probands know each other and each other's smoking behaviour. A crass miss-classification of smoking categories is therefore less likely. The examination was set in the routine annual health check-up and was performed by the usual occupational health team of the bank that was personally acquainted with most of the people. It is plausible that smokers, especially strong smokers, tend to underestimate the number of cigarettes smoked, though. CO in exhaled air would not be a good measure of number of cigarettes smoked per day because of the short biological half-time of CO after smoking. Maybe another biomarker like cotinine would have been better suited to estimate the smoking intensity. On the other hand translating cotinine concentration (e.g. in spot urine) into number of cigarettes is not very straightforward and even had we had this information it would therefore have been less meaningful than number of cigarettes. Unfortunately data on both biomarkers were not available.

The work is interesting, and has some different findings to the wider literature.

The role of a longer smoking duration on BMI and body shape, a majority of other workers have shown that BMI is lowered after long smoking periods. Can the authors discuss this. We did not really try to study the impact of smoking duration because duration was highly correlated with age. We did discuss our findings on smoking status and smoking intensity in light of the wider literature though: "Although several studies found that smokers have lower body weight and BMI than nonsmokers,[17, 18] the results in the literature are inconclusive. Our data are in accordance with previous studies which found no significant differences between smokers and non-smokers regarding those anthropometric indices.[19, 20] (...)" Generally I feel we did discuss our finding in the light of the wider literature.

The anthropometric measurements made include waist to hip ratio and waist height and calculated BMI.

Also height to waist. Not sure why all of these data are reported. Can the authors consider the issue between waist to hip ratio and muscle mass in smokers, this has not been considered in depth. We studied the following anthropometric endpoints: weight, WC, HC, BMI, WHR, WhtR. Of these endpoints the first 3 are obviously affected by height which makes them less meaningful for the comparison between groups of people. We were primarily interested in "unhealthy" fat distribution (abdominal fat) and that is best reflected by the waist circumference (either in relation to height or to the hip circumference). WC also had the advantage of having been measured by the examination team while body weight was mostly self-reported only. On the other hand for the sake of comparability with the wider literature we also reported effect estimates on BMI. Although BMI does neither discern between lean and fat mass nor between different types of fat distribution, in our study population WC and weight (or WhtR and BMI) were highly correlated. That shows that BMI, although not being an ideal measure of body fat, is overall still meaningful. It also shows that the self-reported weight, even if there was a tendency of under-reporting among obese people, was sufficiently reliable.

The authors state no differences in in WC, WHR or WHtR, can they speculate why, given the impact on smoking on waist to hip ratio. We never said that these measures do not differ! They are indeed highly correlated with each other. They do not significantly (and in my mind also not meaningfully) differ between groups of smoking status, although former smokers tend to have more weight and larger WC. We did show an effect of smoking intensity though (not significant for all the endpoints).

The novelty of the findings ought to be emphasised. I am not sure that this manuscript reports new findings, and I am keen to determine what is new to the literature. Indeed our findings are not completely new, but still controversial due to conflicting results in the literature, as we already have pointed out, e.g. in the introduction: "Some studies reported that smoking is associated with abdominal obesity,[7] which would favour the development of metabolic syndrome, a cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus (T2DM) that includes central obesity, dyslipidaemia, hyperglycaemia, and hypertension.[8, 9] Since other studies [10] failed to find a

positive association between cigarette smoking and abdominal obesity, this issue is still controversial and remains to be elucidated."

The biochemical findings are certainly already well reported

Reviewer: 2

This is a cross-sectional study investigating the relationship between smoking and adiposity (and other metabolic risk markers) in a sample of workers. The authors found that current smokers, particularly heavy smokers, have higher weight and body mass index, as well as higher concentration of white blood cell count. Smoking may be mistakenly used as a way to regulates weight for some groups in the population. In this study, the authors argue that it is not the case as smokers have higher weight and BMI. However, the findings of this study needs to be treated with caution, both in terms of the study population as well as the analytical strategies used. We did not find that smokers generally have higher weight and BMI. On the contrary, ex-smokers had the highest BMI. But the difference was neither significant nor clinically very relevant.

The use of employees as a study population is a convenient sample to test the hypothesis that smoking may be associated with adiposity. Needless to say, there is a potential selection bias. Note that the proportion of smokers in this study differs widely to the estimates reported for the whole of Austria (page 3, first paragraph). This was not a study to investigate the smoking prevalence or weight distribution in Austria. Therefore it must not be on a representative sample of Austrians. The uniformity of the sample is rather a benefit because it makes uncontrolled confounding less likely. The higher smoking rate among our sample has 2 reasons: (1) this is a sample from the city of Vienna that does have a higher smoking rate than the total of Austria. (2) "Smoking" was defined differently in the Austrian-wide survey as it did not include "occasional" smokers. But investigating a sample with a higher percentage of smokers did really increase the power to detect an effect of smoking.

The study sample size, contrary to what the authors claim, is small. Even using crude values, weight and BMI varied for some of the smoking categories. But the differences are not significant. I think this is mainly due to lack of power to detect small but meaningful differences. The examination of roughly 1000 people is not a small undertaking! Given the uniformity of the sample (regarding job background, socio-economic status, area of living) the sample size is most probably sufficient to detect relevant effects. It is of course always a matter of debate how much a certain difference in e.g. BMI is clinically relevant. We did find practically no difference in BMI between smokers and non-smokers. Former smokers did have somewhat higher BMI but the difference was less than 1 both in men and women. And this difference was really far from any significance.

How weight and height have been measured is unclear. The method described on page 4 is not clear. The limitations described on page 10 suggest that weight and height have been self-reported. This was not mentioned on page 4's methods section. Moreover, if weight and height have been self-reported, why not measure these? The other anthropometric measures seem to have been measured at the clinic. Measurement error plus the small sample size would have limited the statistical power of this study to detect modest differences in the outcomes across smoking categories. To save space and words we did not explain the source of the weight data in detail. But as the reviewer was able to learn how weight was collected (by self-report usually), it seems we did report our methods sufficiently. This study was not done at a "clinic" but at a routine health check-up at the bank. These employees come to that check-up regularly (every 1-2 years), as it is a free service and it is done during the working time. The questionnaires regarding diet and physical activity were the extras introduced for the sake of this study together with the measurement of WC and HC. The other parameters including the laboratory examination (blood sample) were part of the routine work as were weight and height. The occupational health staff does not weigh the employees on a regular basis (only when the person is unsure about his/her weight) as this might be deemed "impolite" to the obese

ones. Unfortunately also alcohol intake was deemed “embarrassing” in the given setting and was not asked.

Data on covariates are either inadequate or inconsistently applied. Obtaining total energy intake from a single 24-hour food recall is very limited. It is unlikely to adjust appropriately for differences in energy intake across smoking groups. The authors describe of ‘two indices of diet quality’ in the statistical analyses, but these were not described elsewhere in the manuscript. What are these? Were these indices used as covariates in the analyses? The pros and cons of a single 24.hour recall have already been discussed in answer to the first reviewer. Nutritional experts rated the plausibility of the reports and eventually added a “flag” for “implausibly low” or “implausibly high”. In the final analyses various approaches were tried how to accommodate this: Leaving “implausible” data out as “missing” (and checking the impact of the reduction of sample size on the effect estimates of the other parameters) and alternatively by including these “flags” in the analysis. None of the two approaches seems optimal. Nor is a single 24-hour recall an optimal measure of calories intake. From the blood sample we had also information on nutritional parameters (vitamins and micronutrients) and these parameters were well in accordance with the reported dietary habits (not reported here). Therefore we think that the reported data on calories intake are fairly reliable. The mentioning of the two indices rather confuses the reader and since that method produced no results substantially different from the “leaving out implausible data” approach, we decided to delete this part of the text in the methods section.

Data on alcohol intake was not included as a covariate. It would be a major limitation if such data have not been collected as it is an important determinant of body composition and may correlate well with smoking as part of a high-risk lifestyle. We agree with the reviewer. This is an important limitation of the study and is now mentioned.

More importantly, any measure of socio-economic position or education should be used as an important covariate. There are huge differences in the proportion of high and medium/low education by smoking status (in men, this is not statistically significant, but this is mainly because of lack of power.) We agree and indeed we have included educational level in our analyses! (Please check the educational level in men – the proportion for smokers is wrong.) We corrected the error.

Age seems an important covariate that needs further exploration. The study involves a very wide range of ages, but BMI varies greatly with age, and most adults would have gained most weight would be in their middle ages. Smoking also had a strong age correlation. Adjusting for age without further detailed age-specific analyses is therefore inadequate. What is the age range? (Many would have retired in their mid-60s.) What is the age distribution of the employees overall? What is the age, sex, and smoking distribution? Are the current smokers in younger age groups lean? Are the current smokers in older age groups heavier? Were most of the employees younger? Understanding these distributions would reveal why we may see a different pattern of smoking-adiposity results in this group of workers as the general population. Age should also be included in the table of characteristics (Tables 1 and 2). Although we have reported age by smoking status in the “results” section of the text we now also report this information in the tables 1 and 2. Weight indeed increased with age and we now also provide additional results (electronic file, excels.xls) of the association between age and weight etc. A separate analysis of the effect of smoking on weight by age group was unfortunately not possible because of lack of study power (data not shown).

On page 6, last paragraph – what is outcome is being compared across smoking groups? This could have been the most important outcome being investigated, yet, it is missing. Does he really refer to that paragraph: “Among both men and women, no statistically significant differences were found between the three smoking groups regarding the anthropometric indices. The results did not change after excluding occasional smokers (<1 cigarette per day) from the group of smokers (data not shown).” Apart from the excluded occasional smokers (that might include recent quitters) this is simply a verbal description of tables 1 and 2! What does the reviewer not understand here?

The investigators reported on smoking and leukocyte count. It would be useful to compare their results with other studies that have investigated this association. We reduced the discussion on that part on purpose. In fact we do not find it so surprising that smoking causes inflammation. This is a rather well-known fact. Inflammation is important for the object of our study as it might serve as mediator of the effect of smoking on abdominal fat, but per se it is not a very novel finding.

Analyses for waist circumference and waist-hip ratio, as measures of relative fat distribution, without taking into account total body size is inappropriate unless accompanied by results showing total body size, such as body mass index, has been adjusted for. Further, analyses showing that over 80% of total body size (ie, body mass index) being explained by waist circumference is rather biologically implausible. I could not imagine how waist circumference could explain most of one's body mass index. I suggest that the authors just report on the correlations, not the variance. Exactly for that reason did we calculate ratios of WC to HC and to height. We never pretended that WC explains "over 80% of BMI". We did report the Pearson's correlation coefficient (which was about 80%). Therefore R^2 is about 0.64 which is a measure that shows how much of the variance of one parameter is explained by the variance of the other. Since R^2 can easily be calculated from R reporting of both values is indeed redundant and could be skipped. But we do not understand why this finding is biologically implausible!

The end paragraph of the discussion section is irrelevant to the main focus of the manuscript. I suggest that these would be dropped (and report these findings in a different manuscript). We followed the advice and dropped this paragraph: "Similarly, cigarette smoking was also self-reported, which could lead to some misclassification of smoking status. However, the reliability of self-reported smoking as a reliable tool for the assessment of smoking status has been confirmed in the literature.[40]"