

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Smoking and serum vitamin D in older Chinese people: cross-sectional analysis based on the Guangzhou Biobank Cohort Study
AUTHORS	Jiang, Chao Qiang; Chan, YH; Xu, Lin; Jin, Ya Li; Zhu, Tong; zhang, Wei Sen; Cheng, Kar Keung; Lam, Tai Hing

VERSION 1 - REVIEW

REVIEWER	<p>Mohamed Kacem Ben Fradj Department of Biochemistry, Rabta Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar, 1007 Jebbari, Tunis, Tunisia</p> <p>and</p> <p>Faculty of Sciences of Tunis, University of Tunis El Manar, Campus Universitaire, 2092, Tunis, Tunisia,</p>
REVIEW RETURNED	15-Jan-2016

GENERAL COMMENTS	<p>"Smoking and serum vitamin D in older Chinese people: Guangzhou Biobank Cohort Study" is a good paper trying to research the association between vitamin D and smoking. It is also attractive because few studies have been carried out and there no conclusive results.</p> <p>Revision required:</p> <p>a) INTRODUCTION (minor)</p> <p>1. In the introduction; background and rationale for the investigation are well explained. In contrast, I suggest some modifications:</p> <ul style="list-style-type: none"> - The authors stated "The major sources of serum vitamin D are vitamin D produced in the skin during sunlight exposure, taking vitamin D supplements and vitamin D ingested from foods" and they states "Other lifestyles that ". The authors clarify the sources of vitamin D and said other lifestyles that may influence vitamin D concentration. I suggested rewriting the sentence concerning «sources of vitamin D» and avoiding repetition (vitamin D), clarify which factors may influence vitamin D concentration as skin type, body mass index, season..... . thus, they could states "Other lifestyles that". - The authors states "with natural exposure to vitamin D". this sentences should be replaced by "without vitamin D supplementation". <p>b) Methods (minor)</p> <p>In "outcome" the authors should/may further give information about the method of vitamin D measuring, use of quality control and CV of the measuring.</p> <p>In "statistical analysis" the authors didn't mentioned if they tested the</p>
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	<p>normality of vitamin D. if yes it should be mentioned.</p> <p>c) Results (major) In table 2, concerning assessing serum vitamin D concentration by, smoking duration, amount of cigarette smoking by day, smoking status by pack years, authors choose never smoker as referent group, and this is a comparison between never smoker and different current smoker (different duration and amount of cigarette). In another part I recommend to do the analysis only in smoker and to choose the lower strata as referent group (1-9 cigarette by day; 1-39 year and by pack-years). Thus the impact of smoking in vitamin D status will be clearer.</p> <p>d) Study design (major) Why subjects weren't administered a validated food frequency questionnaire to assess VD intake. In older, endogenous vitamin D synthesis were limited (lower skin concentrations of the vitamin D precursor, 7-DHC) and dietary vitamin D could be important to affect vitamin D status. Ignoring VD intake may lead to confounding bias. It is a limitation.</p>
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REVIEWER	Yao He Institute of Geriatrics, Chinese PLA General Hospital, Beijing, China
REVIEW RETURNED	21-Jan-2016

GENERAL COMMENTS	<p>The study examined the association of smoking status with serum vitamin D in older Chinese men and found a dose-response association between them. The conclusions are presented in an appropriate fashion and are supported by the data. However, there are some recommendations to the authors and invite to improve the manuscript:</p> <ol style="list-style-type: none"> 1. Methods: Sampling - It is important to describe the sampling method also in this paper. Only the details could refer to another paper. 2. Methods: Definition-The definition of smoking (Page 7, lines 36-38) should have reference. 3. Methods: Physically activity has been involved in the regression as adjusted factors, and the method to judge the quantification of physically activity should be provided in the methods paragraph. 4. Results: The diet also have effect on serum vitamin D, did the questionnaire have the information of it? If the answer is yes, the diet should involve in the regression as adjusted factor. 5. Results: In table 2, the sum of Smoking status by pack-years (1-39 and 40+) was not 188 (number of current smokers), and the sum of Duration of quitting (years) (1-9, 10-19, 20+) was not 154 (number of former smokers), either, Why?
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REVIEWER	Robin Turner UNSW Australia
REVIEW RETURNED	08-Feb-2016

GENERAL COMMENTS	This manuscript presents a cross sectional analysis of vitamin D levels by smoking status. I have some comments outlined below.
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	<p>This analysis is based on data that is part of a larger cohort study, more detail on the sampling strategy used in the cohort is needed. Was it a simple random sample? How representative is the sample?</p> <p>The sampling appears to overlap with changes in the smoking legislation, how much influence would the indoor smoking policies introduced in 2010 (as per the introduction) have had on the data collected from 2009 to 2011?</p> <p>I would suggest replacing “generalised” with “general” linear model to describe the regression given the outcome is continuous and I assume ordinary least squares was used to fit the model.</p> <p>What diagnostics were assessed? Do the models fit well? Does the outcome variable have any skew in it? Are the regression assumptions met?</p> <p>Was linearity of variables such as age assessed?</p> <p>For the results section units should be reported for all the regression coefficients.</p> <p>For the tests of trend the categorical variables had at most 4 levels and often only 3 levels. The test for trend is essentially fitting a straight line through the categories and usually more than 3 or 4 points are needed to adequately fit a straight line and then assess departures away from linearity.</p> <p>Table 2: Some of the numbers in each category are missing</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 Mohamed Kacem Ben Fradj

Department of Biochemistry, Rabta Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar and Faculty of Sciences of Tunis, University of Tunis El Manar

Please leave your comments for the authors below

Comment: Dear authors: "Smoking and serum vitamin D in older Chinese people: Guangzhou Biobank Cohort Study" is a good paper trying to research the association between vitamin D and smoking. It is also attractive because few studies have been carried out and there no conclusive results.

RESPONSE: Thank you for your positive comments.

Comment: Revision required:

a) INTRODUCTION (minor)

1. In the introduction; background and rationale for the investigation are well explained. In contrast, I suggest some modifications:

- The authors stated "The major sources of serum vitamin D are vitamin D produced in the skin during sunlight exposure, taking vitamin D supplements and vitamin D ingested from foods" and they states "Other lifestyles that ". The authors clarify the sources of vitamin D and said other lifestyles that may influence vitamin D concentration. I suggested rewriting the sentence concerning «sources of vitamin D»

and avoiding repetition (vitamin D), clarify which factors may influence vitamin D concentration as skin type, body mass index, season..... thus, they could states "Other lifestyles that".

RESPONSE: Thanks for your comments. We have revised the sentence to "*The factors that may influence serum vitamin D concentration include skin type, body mass index, season and vitamin D ingested from foods or supplements*" in the paper.

Comment: - The authors states "with natural exposure to vitamin D". this sentences should be replaced by "without vitamin D supplementation".

RESPONSE: Thanks for your comments. We have changed the sentence in the text accordingly.

Comment: b) Methods (minor)

In "outcome" the authors should/may further give information about the method of vitamin D measuring, use of quality control and CV of the measuring.

RESPONSE: Thanks for your comments. We have added the following information into the paper: "*The serum levels of 25-hydroxyvitamin D (unit: nmol/L) were assessed using ELISA (IDS 25-Hydroxy Vitamin D EIA kit, Immunodiagnostic Systems Ltd, UK). The intra-assay CV for 25-hydroxyvitamin D ranged from 4.6% to 8.7%.and the inter-assay CV ranged from 5.3% to 6.7%.*"

Comment: In "statistical analysis" the authors didn't mentioned if they tested the normality of vitamin D. if yes it should be mentioned.

RESPONSE: Thanks for your comments. We have added the following information in the methods: "The normality for vitamin D was tested by Shapiro–Wilk normality test for normality in STATA. As we cannot reject that vitamin D was normally distributed, data analysis was based on the original scale of vitamin D."

Comment: c) Results (major)

In table 2, concerning assessing serum vitamin D concentration by, smoking duration, amount of cigarette smoking by day, smoking status by pack years, authors choose never smoker as referent group, and this is a comparison between never smoker and different current smoker (different duration and amount of cigarette). I recommend to do the analysis only in smoker and to choose the lower strata as referent group (1-9 cigarette by day; 1-39 year and by pack-years). Thus the impact of smoking in vitamin D status will be clearer.

RESPONSE: Thank you for your comments. To be consistent with our previous study (Jiang et al. JECH 2010; 64:1004-1009) and facilitate comparison with other studies from other settings, we suggest to keep never smokers as the reference group. Moreover, as the dose-response associations within current smokers (amount of cigarettes per day, duration, pack-years) were clearly presented, using lower strata as reference group might not add much information to the readers. Thus we suggest to keep the current reference group but can change if the editors strongly recommended.

Comment: d) Study design (major)

Why subjects weren't administered a validated food frequency questionnaire to assess VD intake. In older, endogenous vitamin D synthesis were limited (lower skin concentrations of the vitamin D precursor, 7-DHC) and dietary vitamin D could be important to affect vitamin D status. Ignoring VD intake may lead to confounding bias. It is a limitation.

RESPONSE: Thank you for your comments. We acknowledged that the lack of FFQ could be potential problem and have added this as one of the limitations in the text, as follows: "*Fourth, in older people, endogenous vitamin D synthesis were limited (lower skin concentrations of the vitamin D precursor, 7-Dehydrocholesterol) and dietary vitamin D could affect vitamin D status. The lack*

of detailed assessment of dietary vitamin D intake may be a concern. However, it is unlikely that dietary intake affect the smoking status per se, the underlying factors could be socioeconomic position (SEP). For example, people of lower SEP tend to smoke than those of higher SEP, and people of higher SEP tend to select foods rich in vitamin D, such as milk.[23] We have adjusted for education as a proxy of SEP in this study. Thus the potential confounding effect of dietary vitamin D intake due to SEP, if any, should not be a major concern.”

Reviewer: 2 Yao He

Institute of Geriatrics, Chinese PLA General Hospital, Beijing, China

Please leave your comments for the authors below

Comment: The study examined the association of smoking status with serum vitamin D in older Chinese men and found a dose-response association between them. The conclusions are presented in an appropriate fashion and are supported by the data. However, there are some recommendations to the authors and invite to improve the manuscript:

1. Methods: Sampling - It is important to describe the sampling method also in this paper. Only the details could refer to another paper.

RESPONSE: Thank you for your helpful comments. We have added a paragraph describing the sampling methods in Methods, as follows:

“Guangzhou Biobank Cohort Study (GBCS) is a three-way collaboration among the Guangzhou No. 12 Hospital and the Universities of Birmingham and Hong Kong. Details of the setting and subject recruitment have been described elsewhere.[10] From September 2003 to January 2008, 30,430 Guangzhou permanent residents aged 50 years or above were recruited and attended a half-day detailed assessment session which included a structured interview and a physical examination. All GBCS participants were invited to return during March 2008 to December 2012 for a follow-up examination. The methods and some results based on the follow-up data have been published elsewhere.[11 12] The GBCS received approval from the Medical Ethics Committee of the Guangzhou Medical Association, and all participants gave written informed consent.”

Comment: 2. Methods: Definition-The definition of smoking (Page 7, lines 36-38) should have reference.

RESPONSE: Thank you for your helpful comments. We have quoted our previous papers as references for the definition of smoking, as follows:

Reference 13. Jiang CQ, Lao XQ, Yin P, et al. Smoking, smoking cessation and aortic arch calcification in older Chinese: the Guangzhou Biobank Cohort Study. Atherosclerosis 2009;202(2):529-34 doi: 10.1016/j.atherosclerosis.2008.03.004[published Online First: Epub Date]].

Reference 14. Jiang CQ, Xu L, Lam TH, Lin JM, Cheng KK, Thomas GN. Smoking cessation and carotid atherosclerosis: the Guangzhou Biobank Cohort Study--CVD. Journal of epidemiology and community health 2010;64(11):1004-9 doi: 10.1136/jech.2009.092718[published Online First: Epub Date]].

Comment: 3. Methods: Physically activity has been involved in the regression as adjusted factors, and the method to judge the quantification of physically activity should be provided in the methods paragraph.

RESPONSE: Thank you for your helpful comments. We have added the methods for assessment of physical activity using International Physical Activity Questionnaire in the Methods, as follows:

“We collected detailed information of physical activity by the Chinese version of International Physical Activity Questionnaire (IPAQ). The validity and reliability of this questionnaire was assessed in 224 subjects during a 7-day interval, and the results showed adequate test-retest reliability (intra-class correlation coefficient =0.89) [13]. Subjects were asked to recall the amount of time during the past week spent on physical activity including vigorous activity such as heavy lifting, digging, aerobics or fast

bicycling, moderate activity such as carrying light loads, bicycling at a regular pace or doubles tennis, and walking. Frequency and average amount of time per day was asked. A metabolic equivalent value (MET) was assigned to each type of activity according to accepted standards (see www.ipaq.ki.se), where 1 MET is a resting metabolic rate obtained during quiet sitting. MET value is 3.3 for walking, 4 for moderate activity and 8 for vigorous activity. Subjects were classified as physically active, moderately active and inactive according to the IPAQ. Physically active was defined as having vigorous activity at least 3 days a week, achieving at least 1500 MET minutes per week or activity on 7 days of the week achieving at least 3000 MET minutes per week. Moderately active was defined as having vigorous activity at least 3 days a week, achieving 480 METs, or at least 5 days of any combination of walking, moderate or vigorous activities achieving a least 600 METs. Those who did not meet the criteria for active or moderately active were considered to be physically inactive.”

Comment: 4. Results: The diet also have effect on serum vitamin D, did the questionnaire have the information of it? If the answer is yes, the diet should involve in the regression as adjusted factor.

RESPONSE: Thanks for the comments. We acknowledged that the lack of assessment of dietary vitamin D intake via standard food frequency questionnaire could be a potential problem and have added this as one of the limitations in the text, as follows:

“Fourth, in older people, endogenous vitamin D synthesis were limited (lower skin concentrations of the vitamin D precursor, 7-Dehydrocholesterol) and dietary vitamin D could affect vitamin D status. The lack of detailed assessment of dietary vitamin D intake may be a concern. However, it is unlikely that dietary intake affect the smoking status per se, the underlying factors could be socioeconomic position (SEP). For example, people of lower SEP tend to smoke than those of higher SEP, and people of higher SEP tend to select foods rich in vitamin D, such as milk.[23] We have adjusted for education as a proxy of SEP in this study. Thus the potential confounding effect of dietary vitamin D intake due to SEP, if any, should not be a major concern.”

Comment: 5. Results: In table 2, the sum of Smoking status by pack-years (1-39 and 40+) was not 188 (number of current smokers), and the sum of Duration of quitting (years) (1-9, 10-19, 20+) was not 154 (number of former smokers), either, Why?

RESPONSE: Thank you for your checking and our apology for the confusion caused. We have added a footnote in Table 2 explaining the exclusion of subjects with missing information from the regression model, as follows:

“[†]: 8 current smoker with missing information on duration of smoking and 7 former smokers with missing information on duration of quitting were excluded from data analysis here only.”

Reviewer: 3 Robin Turner

UNSW Australia

Please leave your comments for the authors below

Comment: This manuscript presents a cross sectional analysis of vitamin D levels by smoking status. I have some comments outlined below.

Comment: This analysis is based on data that is part of a larger cohort study, more detail on the sampling strategy used in the cohort is needed. Was it a simple random sample? How representative is the sample?

RESPONSE: Thank you for your comments. We have added the following details on the sampling methods in the Methods:

“Guangzhou Biobank Cohort Study (GBCS) is a three-way collaboration among the Guangzhou No. 12 Hospital and the Universities of Birmingham and Hong Kong. Details of the setting and subject recruitment have been described elsewhere.[10] From September 2003 to January 2008, 30,430 Guangzhou permanent residents aged 50 years or above were recruited and attended a half-day detailed assessment session which included a structured interview and a physical examination. Within our

sample, the participants had fairly similar levels of chronic diseases such as diabetes and hypertension to nationally representative samples of urban Chinese.[10] All GBCS participants were invited to return during March 2008 to December 2012 for a follow-up examination. The methods and some results based on the follow-up data have been published elsewhere.[11 12] The GBCS received approval from the Medical Ethics Committee of the Guangzhou Medical Association, and all participants gave written informed consent.

The present study included 612 unselected men who returned for follow-up at the second examination from 2009 to 2011...”

Comment: The sampling appears to overlap with changes in the smoking legislation, how much influence would the indoor smoking policies introduced in 2010 (as per the introduction) have had on the data collected from 2009 to 2011?

RESPONSE: Thank you for raising this issue. As per the introduction, Guangzhou introduced the indoor smoking policy in public place (mainly in working place) in 2010, at that time all participants of our study were retired and they usually smoked at home (http://www.wpro.who.int/china/tobacco_report_20150819_en.pdf). Hence this policy would not have substantial influence on the smoking behavior change in our sample.

Comment: I would suggest replacing “generalised” with “general” linear model to describe the regression given the outcome is continuous and I assume ordinary least squares was used to fit the model.

RESPONSE: Thank you for your comments. The word “generalized” has been changed to “general” in the text.

Comment: What diagnostics were assessed? Does the outcome variable have any skew in it? Are the regression assumptions met? Was linearity of variables such as age assessed?

RESPONSE: Thank you for the questions.

(1) The outcome was vitamin D and it was measured using Enzymeimmunoassay by Uranus (AE 90) Auto Analyzer. We have added some detailed information on the measurement of vitamin D in the Methods.

(2) We have added the following information in the methods: “*The normality for vitamin D was tested by Shapiro–Wilk normality test for normality in STATA. As we cannot reject that vitamin D was normally distributed, data analysis was based on the original scale of vitamin D.*”

(3) As age was treated as a potential confounder in the analysis, we will not include the results of age and vitamin D in the main result table. We have conducted sensitivity analysis using age groups (50-59/60-69/70+ years) instead of using age as a continuous variable in the regression and the results were the same.

Comment: For the results section units should be reported for all the regression coefficients.

RESPONSE: Thanks for your comments. We have added the unit for vitamin D in the text and Table 2 accordingly.

Comment: For the tests of trend the categorical variables had at most 4 levels and often only 3 levels. The test for trend is essentially fitting a straight line through the categories and usually more than 3 or 4 points are needed to adequately fit a straight line and then assess departures away from linearity.

RESPONSE: Thank you for pointing this out. We agree that ideally more than 3/4 points are needed to test for linear trend and we only have 3 points in some measures of smoking status (smoking status, duration and pack-years). However, due to the restraint in sample size, we could not have more subgroups. We have added a limitation in the Discussion, as follows:

“Fifth, the sample size of the current study was relatively small, particularly in detailed assessment of the linearity of smoking exposure and vitamin D.”

Comment: Table 2: Some of the numbers in each category are missing

RESPONSE: Our apology for the carelessness. Thank you very much for your checking. We have added the missing numbers in Table 2 accordingly.

VERSION 2 – REVIEW

REVIEWER	Mohamed Kacem Ben Fradj Department of Biochemistry, Rabta Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar and Faculty of Sciences of Tunis, University of Tunis El Manar
REVIEW RETURNED	25-Mar-2016

GENERAL COMMENTS	<p>Dear authors, thanks for your responses to my comment, i think that the paper is better than previously. I just regretted that you ignored may unique major Comment: c) Results (major) In table 2, concerning assessing serum vitamin D concentration by, smoking duration, amount of cigarette smoking by day, smoking status by pack years, authors choose never smoker as referent group, and this is a comparison between never smoker and different current smoker (different duration and amount of cigarette). I recommend to do the analysis only in smoker and to choose the lower strata as referent group (1-9 cigarette by day; 1-39 year and by pack-years). Thus the impact of smoking in vitamin D status will be clearer.</p> <p>Your response: Thank you for your comments. To be consistent with our previous study (Jiang et al. JECH 2010; 64:1004-1009) and facilitate comparison with other studies from other settings, we suggest to keep never smokers as the reference group. New comment, i didn't said that it's not consistent</p> <p>Moreover, as the dose-response associations within current smokers (amount of cigarettes per day, duration, pack-years) were clearly presented, using lower strata as reference group might not add much information to the readers.</p> <p>New comment, as a reviewer and as a reader in my point of view it could add much information (intensity of smoking vs VD)</p> <p>Thus we suggest keeping the current reference group but can change if the editors strongly recommended. This response is specific to the editors and not the reviewer.</p> <p>I RECOMMENDED TO LET THE PREVIOUS ANALYSE AND TO ADD NEW ANALYSE. Response needed.</p>
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REVIEWER	Yao He Institute of Geriatrics, Chinese PLA General Hospital, Beijing, China
REVIEW RETURNED	23-Mar-2016

GENERAL COMMENTS	I think the authors have addressed all of the concerns raised by the reviewers and the paper now is acceptable for publication.
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1 Mohamed Kacem Ben Fradj

Department of Biochemistry, Rabta Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar and Faculty of Sciences of Tunis, University of Tunis El Manar

Please leave your comments for the authors below

Comment: Dear authors, thanks for your responses to my comment, i think that the paper is better than previously. I just regretted that you ignored may unique major Comment:

c) Results (major) In table 2, concerning assessing serum vitamin D concentration by, smoking duration, amount of cigarette smoking by day, smoking status by pack years, authors choose never smoker as referent group, and this is a comparison between never smoker and different current smoker (different duration and amount of cigarette). I recommend to do the analysis only in smoker and to choose the lower strata as referent group (1-9 cigarette by day; 1-39 year and by pack-years). Thus the impact of smoking in vitamin D status will be clearer.

New comment, as a reviewer and as a reader in my point of view it could add much information (intensity of smoking vs VD) I RECOMMENDED TO LET THE PREVIOUS ANALYSE AND TO ADD NEW ANALYSE. Response needed.

RESPONSE: Thanks again for your suggestions.

We appreciate your comments and have added the analysis accordingly. The results have been added into the Table 2 (the 3rd column of β) as well as the Results section in the text, as follows:

“Analysis in current smokers showed that, compared to smokers with the lowest intensity of exposure (1-9 cigarettes per day; 1-39 years of duration and by pack-years), those with higher levels of exposure consistently showed lower levels of vitamin D, and the result was statistically significant in those with smoking duration of 40+ years (β -6.55, 95% CI -12.09 to -1.01) (Table 2).”

Table 2. Crude and adjusted regression coefficient (β -coefficient, 95% confidence interval, CI) for serum vitamin D concentration (nmol/l) by cigarette smoking status in men

	Number	Crude β -coefficient (95% CI)	Adjusted β -coefficient (95% CI)	Adjusted β -coefficient (95% CI)
Smoking status				
Never	270	Reference (0.00)	Reference (0.00)	-
Former	154	-1.31 (-4.5 to 1.88)	-0.92 (-4.29 to 2.45)	-
Current	188	-3.53 (-6.53 to -0.53)*	-3.85 (-7.1 to -0.59)*	-
P for trend		0.02	0.02	-
Amount of cigarette smoking per day[†]				
Never	270	Reference (0.00)	Reference (0.00)	-
1-9	37	-2.88 (-8.55 to 2.8)	-3.11 (-9.05 to 2.82)	Reference (0.00)
10-19	62	-2.69 (-7.25 to 1.87)	-3.29 (-8.3 to 1.72)	-0.54 (-7.48 to 6.41)
20+	89	-4.39 (-8.34 to -0.43)**	-4.61 (-8.89 to -0.33)*	-1.98 (-8.44 to 4.48)
P for trend		0.01	0.01	0.50
Smoking duration (years)^{†‡}				
Never	270	Reference (0.00)	Reference (0.00)	-
1-39	77	-1.45 (-5.64 to 2.74)	-1.39 (-6.09 to 3.30)	Reference (0.00)
40+	103	-5.05 (-8.81 to -1.29)**	-5.39 (-9.42 to -1.35)**	-6.55 (-12.09 to -1.01)*
P for trend		0.01	0.008	-
Smoking status by pack-years[†]				
Never	270	Reference (0.00)	Reference (0.00)	-
1-39	119	-2.79 (-6.37 to 0.78)	-2.89 (-6.78 to 1.01)	Reference (0.00)
40+	61	-4.91 (-9.52 to -0.30)**	-5.58 (-10.48 to -0.67)*	-3.95 (-9.17 to 1.27)
P for trend		0.02	0.009	-
Duration of quitting (years)[‡]				
Current smokers	188	Reference (0.00)	Reference (0.00)	-
1-9	50	-1.39 (-6.11 to 3.33)	-0.70 (-5.74 to 4.34)	-
10-19	50	2.22 (-2.50 to 6.94)	3.55 (-1.57 to 8.66)	-
20+	47	5.34 (0.51 to 10.18)*	4.66 (-0.45 to 9.77)	-
P for trend		0.03	0.04	-

Adjusted coefficient: adjusting for age, education, alcohol use, physical activity, body mass index and self-reported diabetes, hypertension, cardiovascular disease and respiratory disease.

[†]: Excluding former smokers.

[‡]: 8 current smokers with missing information on duration of smoking and 7 former smokers with missing information on duration of quitting were excluded from data analysis here only.

*: P<0.05; **: P<0.01;