PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Obstructive Lung Disease and Edentulism in the Atherosclerosis Risk in Communities(ARIC) Study
AUTHORS	Offenbacher, Steven ; Beck, James; Barros, Silvana; Suruki, Robert; Loewy, Zvi

VERSION 1 - REVIEW

REVIEWER	Caterina Bucca Associate professor of Respiratory Medicine Department of Clinical Pathophysiology University of Torino Italy No competing interest
REVIEW RETURNED	08-Aug-2012

THE STUDY	Thew methods are not appropriate to the research question. There is no sense in grouping no COPD patientswith GOLD 0 patients. The former are healthy, while the second ones are diseased. Their disease originates, probably, from the same factors which produced more severe disease in other patients. The diagnosis of restrictive (AND NOT RESTRICTED!!!) lung disease should be based on measurement of total lung capacity. These "restrictive" patients should be excluded from the analysis since they are a small group and are confounders and not relevant to the aim of the study. There is a confusion of terms: Restricted is wrong and should be replaced with restrictive Lung obstruction should be replaced with airway obstruction
RESULTS & CONCLUSIONS	The results are seriously flawed by the wrong grouping of the patients

REVIEWER	Francesco D'Aiuto HEFCE Clinical Senior Lecturer/Hon Consultant Periodontology Unit UCL Eastman Dental Institute London, UK Conflict of interests= none
REVIEW RETURNED	27-Aug-2012

GENERAL COMMENTS	A number of hypotheses have been tested by authors using the ARIC cohort. I agree with authors that report on the association between oral health and COPD are few and lack of proper pulmonary function values, statistical analyses and experimental design and it is commendable that authors have performed a comprehensive analysis of this large and well characterized cohort.

	A number of comments are listed below with the aim of improving further this already well written manuscript. The aims/hypotheses could be included in the introduction section. Authors refers to the study as a case-control, however I would argue that based on the ARIC design and selection variables….at the end they are still left with a cross-sectional analysis. Indeed despite dividing the whole population in two groups (edentulous and dentate) the choice of controls (dentate subjects) is based purely on the presence or absence of teeth. I would argue that perhaps this is the limitation of the analysis as although in the statistical analyses some of the covariates are reported not to be statistically significant (i.e. age) do represent the most important biological confounders of these association (both with COPD and edentulism). I would have therefore named this a nested-case control study if selection criteria also included age- smoking- matched controls dentate to the cases (edentulous). Please amend design as cross-sectional All analyses are well described and provide sufficient evidence for a mild but statistically significant association. I would include however further subgroup analyses in the never smokers category for all outcomes as to confirm the reported odds ratios. A number of tables/figure could be improved. Flow chart does not depict clearly the final number of individuals included into the analyses. Table 1 descriptive is hard to follow as formatted and not needed and could just be included into the text. Table 2 and following= whenever dichotomous variables are reported please only use one category (i.e. edentulous, males). Table 6 data could be included into table 2 (which would become the first and most descriptive table) whereas the additional information on the GOLD zero categories could be included in the text. Discussion, first statement, please rephrase significant as statistically significant as well as throughout the manuscript.

VERSION 1 – AUTHOR RESPONSE

Response to reviewer 1:
1) We appreciate the importance in using preferred terminology. We had originally used the term 'restrictive' disease but changed it to match the terminology in the Mannino (2006) paper that we reference. However, we have changed it back to 'restrictive' as Dr. Bucca has recommended..
2) We appreciate the reviewers point regarding our combining of the GOLD 0 group with the no COPD group to form our reference group. However, this is an area of much debate. In the 2006 update of the GOLD guidelines, "GOLD 0" was removed and remains excluded from the current GOLD guidelines. There are studies, though limited, that suggest that these patients with symptoms but normal lung function (GOLD 0) do experience a greater impairment of quality of life compared to normal healthy subjects but there are also studies that suggest the contrary. We can certainly rerun the analysis by removing GOLD stage 0 from the reference group or treat them as a distinct disease category, or remove them from the analysis completely, given that they do not fit neatly into either the diseased or non-diseased groups. Having said that, if we leave them in the reference group as we prefer, we can argue that it would introduce a bias towards the null, since inclusion of GOLD 0 patients would render the two groups being compared more similar... AND in spite of that bias, we were still able to observe a significant association between edentulism and prior COPD. Thus, our inclusion and grouping these two groups of individuals is a more conservative approach. If we were to omit this group we would increase the observed effect of edentulism, not decrease the association. Our preference would be to take the more conservative approach and keep the analyses as described.

Response to reviewer 2:
1) We appreciate the suggestion that we include hypotheses in the introduction. We have added the sentence “We hypothesized that edentulism would be associated with a diagnosis of COPD and display a higher prevalence with more spirometry categories of COPD.”
2) The reviewer argues that the study is better described as cross-sectional rather than case-control. We debated this point as well, and can agree with this suggestion. We have modified the text to reflect cross-sectional.
3) The reviewer points out that “A number of tables/figure could be improved”
a. The flow chart in Figure 1 has been redesigned to address the reviewers’ suggestion.
b. We feel that Table 1 is highly informative to understand the subject flow shown in Figure 1. We would prefer to include it as a Table which is clearer and uses fewer words than a narrative.
c. The reviewer suggests that “Table 2 and following= whenever dichotomous variables are reported please only use one category (i.e. edentulous, males)”. We feel this is a style and clarity issue. Non-dentists might not easily recognize edentulous/dentate are dichotomous pairings. We also feel that we should include all cells of data and respectfully ask that we keep these tables as formatted.
d. Again, this is a style issue and would argue that Table 6 does not have the same column headings as Table 2. In addition, discussing the data in Table 6 prior to presenting the Tables 3-5 would impair the flow of the results and discussion. We do not agree with this suggestion and request to leave the Tables 2 and 6 as original.
e. The reviewer correctly indicated that we needed to clarify that “significant” should be replaced with “statistically significant” throughout the text. We have made those revisions.

Response to reviewer #2 :

1. The second reviewer is pointing out the very same issue that we struggled with in designing and writing up this study. The sequence of the data collection makes it difficult to articulate accurately and correctly. After re-reading the manuscript, we agree that it might be better to simply describe it as a cross-sectional study as recommended by this reviewer. It might help the reader discern more easily the exposure and outcome.
2. The point regarding the effects among never-smokers is an excellent idea. We ran those analyses and report it in the discussion, rather than in a separate table. The following text has been added “………”
3. We feel that the suggestions regarding the tables and flow are excellent suggestions.

2. I think the suggestions that he makes regarding the tables and flow chart are good.

VERSION 2 – REVIEW

REVIEWER	Caterina Bucca Professor of Respiratory Medicine Department of Clinical Pathophysiology University of Turin, Italy I declare the absence of any competing interest.
REVIEW RETURNED	30-Oct-2012

THE STUDY	There are no further questions about the work.
REPORTING & ETHICS	I could not trace research ethics in the present manuscript. However, I found in other ARIC studies the sentence that institutional review boards at participating institutions approved the study and informed consent was obtained from all subjects.