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PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<u>see an example</u>) 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)	The association of dental plaque with cancer mortality in
	Sweden. A longitudinal study.
AUTHORS	Birgitta Söder, Maha Yakob, Jukka H. Meurman, Leif C. Andersson
	and Per-Östen Söder

VERSION 1 - REVIEW

REVIEWER	Leif Jansson DDS, PhD Department of Periodontology at Skanstull Stockholm County Council Sweden
REVIEW RETURNED	I have no conflicts of interests 12/03/2012

THE STUDY	In table 2, also individuals with periodontitis were included. It's not clear why these subjects were included since they were not included in the study population according to material and methods. In results, the following sentence: "Of the total 3273 participants in the original cohort, 6.2% had died; 3.2% of the women and 5.9% of the men (p<0.01)" raises the following question: if 6.2% of the whole sample had died, how can it be possible that the figures for both sexes was lower than 6.2%? Should not 6.2% be the mean value of 3.2 and 5.9?
	In results, the sentence "Demographic data and risk factors at the baseline examination" risk factors is not an adequate description of the independent variables. It should be changed to "risk predictor" or "risk indicator". The cofounding variable "life style" might be an explanation of the significant correlation between plaque and mortality. I miss this part in the discussion section.

REVIEWER	Søren Jepsen
	Professor and Chair
	Dept. of Periodontology, Operative and Preventive Dentistry
	University of Bonn
	Germany
REVIEW RETURNED	09/04/2012

THE STUDY	Participants, methods:
	Table 2: the n of subjects is different from the 1390 described in the
	manuscript - please clarify
	Have there been repeated oral examsin 1996, 1998, 2000, 2001,
	2003, 2009 or only one in 1985?

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How many examiners had been involved to measure the plaque index - how were they calibrated?

Table 3: since all 1390 subjects had been free of periodontal disease - how could the authors adjust for periodontal disease, missing molars in subjects with periodontitis?

Abstract:

Objective should read: "..... associate with premature death from cancer." Move the "chronic infection - carcinogenesis paradigm" to a different sentence or to the conclusion.

Conclusion should read: ".....was associated with increased cancer mortality" instead "...appeared to pose an increased cancer-mortality risk:"

VERSION 1 – AUTHOR RESPONSE

Reviewer: Leif Jansson DDS, PhD Department of Periodontology at Skanstull Stockholm County Council Sweden

In table 2, also individuals with periodontitis were included. It's not clear why these subjects were included since they were not included in the study population according to material and methods. Answer:

By mistake during submission wrong table 2 was included in the manuscript. The correct table 2 is now included in the revised manuscript; and yes, the study population did not include periodontitis patients.

In results, the following sentence: "Of the total 3273 participants in the original cohort, 6.2% had died; 3.2% of the women and 5.9% of the men (p<0.01)" raises the following question: if 6.2% of the whole sample had died, how can it be possible that the figures for both sexes was lower than 6.2%? Should not 6.2% be the mean value of 3.2 and 5.9?

Answer:

Yes, a miscalculation was made and now the sentence is changed to read: "Of the total 3273 participants in the original cohort, 6.21 % had died; 2.3% of the women and 3.9% of the men, respectively (p<0.001)."

In results, the sentence "Demographic data and risk factors at the baseline examination..." risk factors is not an adequate description of the independent variables. It should be changed to "risk predictor" or "risk indicator".

Answer:

The sentence "Demographic data and risk factors at the baseline examination... are now changed to: "Demographic data and risk indicators at the baseline examination"

The cofounding variable "life style" might be an explanation of the significant correlation between plaque and mortality. I miss this part in the discussion section.

Answer

The statistical analysis was performed with adjustments for several demographic variables and established risk markers for mortality, such as education, pack-years of smoking, frequency of dental visits, income level, and socioeconomic status. All these are makers for lifestyle. Therefore none of

these variables confounded the association observed between the age, male gender, the amount of dental plaque, and premature death.

Reviewer: Søren Jepsen, Professor and Chair

Dept. of Periodontology, Operative and Preventive Dentistry

University of Bonn, Germany

Participants, methods:

Table 2: the n of subjects is different from the 1390 described in the manuscript - please clarify

Answer:

By mistake during submission wrong table 2 was included in the manuscript. The correct table 2 is now included in the revised manuscript; and yes, the study population did not include periodontitis patients.

Have there been repeated oral examsin 1996, 1998, 2000, 2001, 2003, 2009 or only one in 1985?

Answer:

Only the clinical examination in 1985 was included in present study.

How many examiners had been involved to measure the plaque index - how were they calibrated? Answer:

In 1985 six periodontists performed the examination. The pre-study calibration included six sessions of common registrations of the parameters used.

Table 3: since all 1390 subjects had been free of periodontal disease - how could the authors adjust for periodontal disease, missing molars in subjects with periodontitis?

Answer:

Thank you for that observation. In the section Statistical analysis the correct variables included in are described. The heading for table 3 is now changed as follows to avoid confusion: "The results of multiple logistic regression analysis of the relationship between death as a dependent variable and several independent variables (age, gender, dental visits, dental plaque, calculus, education, income, socioeconomic status, pack-years of smoking)."

Abstract:

Objective should read: "..... associate with premature death from cancer."

Answer

The sentence is now changed in the revised version as follows: "To study whether the amount of dental plaque, which indicates poor oral hygiene and is potential source of oral infections, associates with premature death from cancer."

Conclusion should read: "....was associated with increased cancer mortality" instead "...appeared to pose an increased cancer-mortality risk:"

Answer:

Conclusion is now changed in the revised version as follows:

"Our study hypothesis was confirmed by showing that poor oral hygiene, as reflected in the amount of dental plaque, was associated with increased cancer mortalit

VERSION 2 – REVIEW

REVIEWER	Leif Jansson
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	DDS, PhD Department of Periodontology at Skanstull Stockholm County Council
	Sweden
REVIEW RETURNED	19/04/2012

The reviewer completed the checklist but made no further comments.