Tooth Loss and Head and Neck Cancer: A Meta-Analysis of Observational Studies

Xian-Tao Zeng, Wei Luo, Wei Huang, Quan Wang, Yi Guo, Wei-Dong Leng

1 Department of Stomatology, Taihe Hospital, Wuhan University School of Public Health, Wuhan, People's Republic of China; 2 Institute of Stomatology, General Hospital of Chinese People's Liberation Army, Beijing, People's Republic of China; 3 Department of Epidemiology, School of Public Health, Wuhan University, Wuhan, People's Republic of China

Introduction

Head and neck cancer (HNC) mainly originates in the oral cavity, pharynx, and larynx. HNC accounts for 12% of all malignancies worldwide. An estimated total of 400000 cases of oral cancer and pharynx diseases, 160000 cases of laryngeal cancer, and 300000 mortality per year [1]. Therefore, finding and preventing the risk factors are important and significant research areas. In the past decades, smoking (active and passive), alcohol, genetic factors, viral infection (mostly human papillomavirus), sex, and occupational exposure have been identified as significant risk factors for HNC. Among these factors, smoking and alcohol are the most significant [2,3]. Tooth loss has been considered to influence food choice, diet, nutrition intake, and esthetics significantly [4]. A systematic review and meta-analysis provided that tooth loss is associated with the impairment of the oral health-related quality of life and the location and distribution of tooth loss significantly and independently affect the severity of the impairment [5]. Epidemiological studies has shown that age, gender, diabetes, social and geographical disparities, smoking, patients and dentists attitudes on oral health status, and alcohol are the risk factors of tooth loss [6,7,8,9].

Both HNC and tooth loss share common risk factors; moreover, given their special anatomic location, an interesting assumption was formed on whether or not an association between tooth loss and HNC existed. Zheng et al (1990) [10] first investigated the association between HNC and tooth loss, and found that tooth loss is a strong risk factor for oral cancer in both males and females. Since then, many relevant studies have been published. However, these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results. In addition, the threshold on the number of missing tooth that both these studies provided inconsistent or even contradictory results.
Methods

Eligibility Criteria

Cohort, case-control, and cross-sectional studies that evaluated the association between tooth loss and HNC and those that met the following criteria were considered eligible for inclusion: (1) full-text could be obtained; (2) clear diagnostic criteria for HNC and definition of tooth loss were reported; and (3) the adjusted and/or unadjusted hazard ratios (HRs), odds ratios (ORs), or relative risks (RRs), and the associated 95% confidence intervals (CIs), or the numbers of events that can calculate these factors, were reported. If more than one study covered the same population, only the report containing the most comprehensive information on that population was included. Two authors independently evaluated the eligibility of all the retrieved studies, and disagreements were resolved by discussion.

Search Strategy

The PubMed database was searched up to January 30, 2013 (re-searched on August 31, 2013) for published studies that tested the association between tooth loss and HNC. The search term (“head and neck cancer” OR “oral cancer” OR “oropharyngeal cancer” OR “pharyngeal cancer” OR “laryngeal cancer”) AND (“dentition” OR “tooth loss”) was used. We also reviewed the reference lists of included articles and recent reviews.

Data Extraction

Two authors independently collected and tabulated the following information of each eligible study: the first author’s surname, year of publication, study design, country of origin, sample size, number of events, age range, assessment of tooth loss and HNC, tumor site and pathologic type of HNC, crude or adjusted point estimates and relevant 95% CIs, and the covariates for the adjusted point estimates.

The design of most of the included studies was a case-control study and reported ORs. Only one study was prospective cohort and reported HR [13]. We directly considered HR as RR, and then transformed RR into OR by using the following formula [14]: \( RR = OR / \left(1 - P_0\right) + \left(P_0 \times OR\right) \), where \( P_0 \) is the incidence of the outcome of interest in the non-exposed group. The standard error (SE) of the resulting converted OR was then determined using the following formula: \( SE \log(OR) = SE \log(OR) \times \log(OR) / \log(OR) \). Given that these transformations can overestimate the variance of OR derived from RR [15], we performed a sensitivity analysis by omitting the study.

The numbers of lost tooth varied in the included studies; hence, we gathered and categorized these teeth into five categories as follows: lost 1 to 6 teeth, 6 to 15 teeth, 11+ teeth, 15+ teeth, and 20+ teeth.

Data Analysis

We computed a pooled OR and relevant 95% CI by using the Comprehensive Meta-Analysis software, version 2.2 (Biostat, Englewood, New Jersey) [16] to generate the forest plots and to assess heterogeneity of the included studies. Heterogeneity was quantified using the \( Q \) and \( I^2 \) statistics [17], and the heterogeneity was defined as low, moderate, and high based on \( I^2 \) values of 25%, 50%, and 75%, respectively [18]. When the \( I^2 \leq 25\% \), which indicates no evidence of heterogeneity, we used the fixed-effect model; otherwise, we used the random-effects model. In the presence of heterogeneity, we performed sensitivity analysis to explore the possible explanations for heterogeneity by removing each study in each turn to test the robustness of the main results or by switching the fixed and random effects models.

We used the Stata 12.0 software for the dose-response estimates based on pooled ORs and 95% CIs by each category of the number of lost teeth. Publication bias was assessed by visual inspection of the funnel plots and the Egger linear regression test [19]. In addition, we calculated the number of unpublished studies that would negate the results and the pooled OR adjusted for publication bias by using the ‘trim and fill’ method to assess the effect of possible publication bias [20].

Results

Study Selection and Characteristics

From the 82 records initially found, 10 articles involving 11 case-control studies [10,21,22,23,24,25,26,27,28,29] and one cohort study [13] were included in this meta-analysis. A detailed flow chart of the selection process is shown in Fig. 1.

From the included studies, the study of Guha et al. [27] contains two multicentric case-control studies from central Europe (including Romania, Poland, and Russia) and Latin America (including Cuba, Argentina, and Brazil), whereas the other 10 were single-center studies. All of the cases were histologically, pathologically or cytologically confirmed as HNC, and clearly defined the referenced group of tooth loss, with the major characteristics presented in Table 1. All of the studies reported adjusted the point estimates and 95% CIs. The adjusted covariates are shown in Table 2.

Tooth Loss and Risk of HNC

Three studies reported 1 to 6 teeth loss and risk of HNC. Among the three studies, one [10] showed a significantly positive association between tooth loss and the risk of HNC, the other two were negative [21,26]. Overall, no association between 1 to 6 teeth loss and HNC (OR = 1.29, 95% CI = 0.52–3.20, p = 0.59; Table 3) was observed. Substantial heterogeneity was observed (p < 0.001, \( I^2 = 83.59\% \)). Nine articles involving 10 studies [10,13,21,22,23,24,25,26,27,28] reported 6 to 15 teeth loss and risk of HNC, where obviously
heterogeneity was observed ($p<0.001$, $I^2 = 82.92\%$). The result from the random-effects model showed that 6 to 15 teeth loss could significantly increase the risk of developing HNC by 1.58 times ($OR = 1.58$, $95\% CI = 1.08–2.32$, $p = 0.02$; Table 3). All the included studies reported their result based on the random-effects model ($p<0.001$, $I^2 = 74.41\%$) of 11+ teeth loss and the risk of HNC. A significantly increased risk for developing HNC by 1.63 times was observed ($OR = 1.63$, $95\% CI = 1.23–2.14$, $p<0.001$; Table 3). All of the included studies reported 15+ teeth loss and the risk of HNC. The result of the meta-analysis showed that 15+ teeth loss could significantly increase the risk of HNC by 1.72 times ($OR = 1.72$, $95\% CI = 1.26–2.36$, $p<0.001$; Fig. 2). Substantial heterogeneity was observed ($p<0.001$, $I^2 = 76.53\%$). The pooled result of the three case-control studies [22,26,29] indicated that exposure to 20+ teeth loss could increase the risk of HNC by 1.89 times ($OR = 1.89$, $95\% CI = 1.27–2.80$, $p<0.001$; Table 3) based on the random-effects model ($p = 0.14$, $I^2 = 49.93\%$).

Fig. 3 shows the trend of the simulative dose-response effect based on the ORs and the corresponding CIs of the numbers of lost teeth, which indicated that the association between tooth loss and HNC risk may have a dose-response relationship.

### Sensitivity and Subgroups Analyses

Table 3 shows the results of the sensitivity and subgroups analyses. We switched all the random-effects models to the fixed effect models, which indicated that all the results were not substantial changed. We removed the study of Michaud et al. [13], which reported HR yielded similar results and with substantial evidence of heterogeneity. Further exclusion of any single study did not materially alter the combined OR, with a range from 1.40 ($95\% CI = 1.14–1.73$, $p<0.001$) to 1.77 ($95\% CI = 1.35–2.32$, $p<0.001$) of 11+ teeth loss, and from 1.48 ($95\% CI = 1.14–1.91$, $p<0.001$) to 1.90 ($95\% CI = 1.40–2.57$, $p<0.001$) of 15+ teeth loss (Fig. 4). The results of the subgroup analyses were varied, especially for the country of origin.

### Table 1. Characteristics of included studies in the meta-analysis.

| References  | Country     | Study design | Sample sizes (case/control) | Age (yrs) | Outcomes                          | Definition of reference group |
|-------------|-------------|--------------|-----------------------------|-----------|-----------------------------------|-------------------------------|
| Zheng 1990  | China       | Case-control | 404/404                     | 18 to 80  | Oral cavity and pharynx           | No lost tooth                 |
| Marshall 1992 | USA       | Case-control | 290/290                     | <50 to 76+| Oral cavity and pharynx           | No lost tooth                 |
| Bundgaard 1995 | Denmark   | Case-control | 161/400                     | ≤45 to >75| Oral cavity and pharynx           | Number of 15+ teeth           |
| Talamini 2000 | Italy     | Case-control | 132/148                     | 27 to 86  | Oral cavity and pharynx           | Lost ≤5 teeth                 |
| Garrote 2001 | Cuba       | Case-control | 200/200                     | <55 to ≥75| Oral cavity and pharynx           | Lost ≤5 teeth                 |
| Lissowska 2003 | Poland    | Case-control | 122/124                     | <45 to ≥75| Oral cavity and pharynx           | Lost 0 to 5 teeth             |
| Rosenquist 2005 | Sweden    | Case-control | 132/320                     | 33 to 89  | OOSCC                             | No lost tooth                 |
| Guha E 2007 | Central Europe | Case-control | 792/928                     | All ages  | HNSCC                             | Lost ≤5 teeth                 |
| Guha LA 2007 | Latin America | Case-control | 2113/1805                   | All ages  | HNSCC                             | Lost ≤5 teeth                 |
| Hiraki 2008  | Japanese   | Case-control | 429/858                     | 20 to 79  | Head and neck                     | Number of ≥21 teeth           |
| Michaud 2008 | USA        | Cohort       | 118                         | 40 to 75  | Oropharyngeal                     | Number of 23 to 32 teeth      |
| Divaris 2010 | USA        | Case-control | 1389/1396                   | 20 to 80  | OOSCC                             | Lost 0 to 5 teeth             |

OOSCC, oral and oropharyngeal squamous cell carcinoma; HNSCC, head and neck squamous cell carcinoma; Guha E 2007, the study conducted in Europe; Guha LA 2007, the study conducted in Latin-America.

doi:10.1371/journal.pone.0079074.t001

### Table 2. Adjustments in studies included in this meta-analysis.

| References | Adjustment                                                                 |
|------------|---------------------------------------------------------------------------|
| Zheng 1990 | age, gender, tobacco, alcohol, and education                              |
| Marshall 1992 | tobacco and alcohol                                                        |
| Bundgaard 1995 | tobacco and alcohol                                                        |
| Talamini 2000 | age, gender, tobacco, alcohol, and fruit and vegetable intake              |
| Garrote 2001 | gender, age, area of residence, education, tobacco, and alcohol            |
| Lissowska 2003 | tooth brushing                                                             |
| Rosenquist 2005 | tobacco and alcohol                                                        |
| Guha 2007   | age, gender, country, education, tobacco, alchoho, and all other oral health variables |
| Hiraki 2008  | age, gender, tobacco, alcohol, vegetable and fruit intake, body mass index, and regular exercise |
| Michaud 2008 | age, race, physical activity, history of diabetes, alcohol, body-mass index, geographical location, height, calcium intake, total caloric intake, red-meat intake, fruit and vegetable intake, vitamin D score, and tobacco |
| Divaris 2010 | age, gender, race, education, tobacco, alcohol, and fruit and vegetable consumption |

doi:10.1371/journal.pone.0079074.t002
Figure 2. Forest plot of 15+ teeth loss and risk of head and neck cancer, studies are pooled with random-effects model. Guha E 2007, the study conducted in Europe; Guha LA 2007, the study conducted in Latin-America. doi:10.1371/journal.pone.0079074.g002

Table 3. Results of overall and subgroups analyses of pooled ORs and 95% CIs.

| Total and subgroups | 1 to 6 teeth loss | 6 to 15 teeth loss | 11+ teeth loss | 15+ teeth loss | 20+ teeth loss |
|---------------------|-------------------|-------------------|---------------|---------------|---------------|
|                     | N | OR (95% CI) | I2 (%) | N | OR (95% CI) | I2 (%) | N | OR (95% CI) | I2 (%) | N | OR (95% CI) | I2 (%) |
| Total (REM)          | 3 | 1.29 (0.52–3.20) | 85.59 | 10 | 1.58 (1.08–2.32) | 82.92 | 11 | 1.63 (1.23–2.14) | 74.41 | 11 | 1.72 (1.26–2.36) | 76.53 | 3 | 1.89 (1.27–2.80) | 49.93 |
| Total (FEM)          | 3 | 0.89 (0.71–1.11) | 85.59 | 10 | 1.37 (1.19–1.58) | 82.92 | 11 | 1.39 (1.24–1.57) | 74.41 | 11 | 1.45 (1.27–1.65) | 76.53 | 3 | 1.75 (1.35–2.27) | 49.93 |

Study design

| Definition of reference group | 1 to 6 teeth loss | 6 to 15 teeth loss | 11+ teeth loss | 15+ teeth loss | 20+ teeth loss |
|-------------------------------|-------------------|-------------------|---------------|---------------|---------------|
| Case-control                  | 0 NA NA 9 1.65 (1.08–2.52) | 84.72 | 10 | 1.63 (1.22–2.60) | 76.86 | 10 | 1.75 (1.25–2.45) | 78.83 | NA NA NA NA |

Country origin

| Country origin | 1 to 6 teeth loss | 6 to 15 teeth loss | 11+ teeth loss | 15+ teeth loss | 20+ teeth loss |
|----------------|-------------------|-------------------|---------------|---------------|---------------|
| Asia           | 1 3.99 (1.75–9.08) | NA 1 6.53 (3.98–10.71) | 0 2 2.66 (0.58–12.21) | 94.83 | 2 2.81 (0.68–11.64) | 93.22 | 1 1.40 (1.00–1.97) | NA |
| USA            | 1 0.80 (0.38–1.70) | NA 3 1.12 (0.89–1.42) | 0 3 1.47 (0.99–2.18) | 38.19 | 2 1.26 (0.99–1.59) | 0 | 0 NA NA |
| Latin-America  | 0 NA NA 2 1.32 (1.03–1.68) | 0 2 1.75 (0.86–3.54) | 70.99 | 2 1.75 (0.86–3.54) | 70.96 | 0 NA NA |
| Europe         | 1 0.78 (0.61–1.00) | NA 4 1.34 (0.74–2.44) | 66.24 | 4 1.31 (0.68–2.54) | 75.75 | 5 1.71 (0.83–3.52) | 79.21 | 2 2.40 (1.60–3.59) | 0 |

REM, random-effects model; FEM, fixed effect model; N, number of trials; OR, odds ratio; CI, confidence interval; NA, not applicable.

doi:10.1371/journal.pone.0079074.t003
Publication Bias

Visual inspection of the funnel plot did not identify any substantial asymmetry (Fig. 5) and the Egger linear regression test also indicated no evidence of publication bias among the studies (for 6–15 teeth loss, p = 0.31; for 11+ teeth loss, p = 0.14; for 15+ teeth loss, p = 0.10). The “trim and fill” method identified any possible missing studies (Fig. 5) and the adjustment estimated OR was similar to the original estimate (OR = 1.72, 95% CI = 1.26–2.36).

Discussion

Main Findings

The association between tooth loss and HNC is still not fully understood. Our meta-analysis of the 11 case-control studies and...
one cohort study provides evidence that individuals would face increased risk of HNC by 29% for those with 1 to 6 teeth loss, 58% for 6 to 15 teeth loss, 63% for 11+ teeth loss, 72% for 15+ teeth loss, and 89% for 20+ teeth loss compared with the reference group. These results indicate that greater teeth loss is associated with an increased risk of HNC. In other words, a dose-response relationship exists between tooth loss and HNC (Fig. 3). Except for 1 to 6 teeth loss, the results all have significant statistical difference, which suggests that tooth loss is probably a significant risk factor for HNC.

Tobacco smoking and alcohol drinking are known risk factors for HNC. In our meta-analysis, all the studies adjusted smoking and alcohol, except for one case-control study published in 2003 by Lissowska et al. [25]. Several studies also adjusted age, gender, ethnicity, body mass index, education, and other oral health variables, which suggests that tooth loss is probably an independent risk factor of HNC.

All the included studies contained both males and females. The study by Zheng et al. [10] provided the respective data for males and females, and their results show that females were more vulnerable than males. Thus, regardless if the patient is male or female, tooth loss is probably a risk factor for HNC.

Sources of Heterogeneity

Substantial heterogeneity was observed among the studies of tooth loss and HNC risk, which is not surprising because of the differences in the characteristics of populations, definition of the reference and tooth loss group(s), and the adjustment for confounding factors. Our sensitivity analysis (by changing the effect models, removing the cohort study, and omitting every single study each time) and subgroup analysis (by study design, definition of reference group, and country origin) results provide evidence that country of origin and definition of reference group probably contributed to the heterogeneity.

Strengths and Limitations

The major strength of our study is that this is the first to perform meta-analysis on this topic. We searched relevant published studies via electronic and hand searching. To the best of our knowledge, we have collected all published studies that met the inclusion criteria and the publication bias test also provided no evidence of publication bias. Moreover, we performed sensitivity analysis by using three methods and subgroups analysis based on the study design, definition of the reference group, country of origin, which could improve the reliability of the results and reduce the performance bias of the meta-analysis. Third, the association of tooth loss with the risk of HNC persisted and remained without substantial change in the sensitivity analyses based on various methods. In addition, the subgroup analysis results indicate that, with accumulating evidence and enlarged sample sizes, the statistical power is enhanced to provide more precise and reliable risk estimates. Finally, our results were based on adjusted estimates, thereby making the result more credible than unadjusted ones.

However, there was an interesting finding when we re-searched the PubMed database on August 31, 2013. We found there was a similar paper by Wang RS et al [30] have been published in PLoS One on Aug 29, 2013 (http://www.ncbi.nlm.nih.gov/pubmed/23990929). Their work is perfect! However, when we compared our meta-analysis to theirs, we found there were three major differences/advantages of our meta-analysis. First, the deadline of search of theirs was March, 2013 and yielded eight case-control studies and one cross-sectional study; however, the deadline of search in our meta-analysis was January 30, 2013 and yielded 10 articles involving 11 case-control studies and one cohort study. Obviously, our search is more comprehensive. Second, we performed meta-analysis based on the number of lost tooth (Table 3); however, they pooled all studies together and ignored the influence of difference number lost tooth, which may biased the results. Third, our meta-analysis conducted a simulative dose-response effect analysis based on the number of lost tooth; this may provide more reference information than their meta-analysis.
However, our study also has some limitations. First, the definition of the reference group and tooth loss used among studies varied, and the former might be the source of heterogeneity. No international unification index of evaluating tooth loss for relevant studies is available, which caused heterogeneity, and increased the difficulty performing the meta-analysis, and even resulted in the failure of the criteria for the meta-analysis. Second, heterogeneity was detected. Although heterogeneity between studies is very common in the meta-analysis of observational studies, we did not ignore it. We performed subgroup analyses to verify the heterogeneity, but it was still observed. Third, we were unable to investigate the histopathological subtypes because only 3 studies [26,27,28] clearly reported that the type of cancer is squamous cell carcinoma, whereas others are mixed. Finally, the results are significantly inconsistent based on the subgroups analyses and the statistical power was limited because of a relatively small number of major included studies. Fourth, the examination of tooth loss and HNC has not been the primary association of interest for many studies, and as a result, adjustment for other ‘proximal’ variables such as caries, periodontitis, alcoholic mouthwash use, or reason for extractions/tooth loss is rarely/never done. Therefore, the facticity of results might be influenced by this.

Implications for Further Research

Based on the results our meta-analysis, several questions arise. First, in routine clinical work, we found the oral health of patients who undergo HNC are more severe; hence, the association of tooth loss with HNC might or might not be causal. A prospective cohort study design with enough follow-up time and adequate control for confounding factors is needed to answer this question. Second, tooth loss is not acceptable and can potentially influence future demand for treatment [31]. Thus, patients should seek treatment if they lose their teeth. Obviously, individuals in developed countries can obtain more convenient and better oral healthcare. Therefore, is there a difference between developed and developing countries because of the social economic differences? Thus, studies should perform stratified analysis based on social economics and should respectively report the results. Third, what are the exact mechanisms in which tooth loss independently increase the risk of HNC? To answer this question, we suggest that experimental studies be conducted. Fourth, is there a dose-response effect between tooth loss and HNC risk? Although our study indicated that dose-response effects exist, the numbers of lost teeth overlapped with one another. Therefore, further studies should answer this question with sequential or without repeated numbers, and they should explore the critical value numbers. Finally, could preventing or treating tooth loss decrease the risk of HNC? Well-designed clinical trials, especially randomized controlled trials, are suggested to answer this question. Finally, we suggest further relevant studies can take tooth loss as the primary interesting.

Conclusions

This meta-analysis indicates that tooth loss is probably a significant and dependent risk factor of HNC, which may have a dose-response effect. People who lost six or more teeth should pay attention to symptoms of HNC, and losing 11 teeth or 15 teeth may be the threshold.

Supporting Information

Checklist S1  PRISMA Checklist. (DOC)

Author Contributions

Conceived and designed the experiments: XTZ WDL. Performed the experiments: WL WH. Analyzed the data: XTZ YG. Contributed reagents/materials/analysis tools: YG XTZ. Wrote the paper: XTZ QW. Reviewed the manuscript: WDL YG.

References

1. Wozniak A, Snyder K, Snyder W, Florek E (2012) [Head and neck cancer—history]. Przegl Lek 69: 1079–1083.
2. Conway DI, Hashibe M, Boffetta P, consortium I, Wunsch-Filho V, et al. (2009) Enhancing epidemiologic research on head and neck cancer: ENHANCE - The international head and neck cancer epidemiology consortium. Oral Oncol 45: 743–746.
3. Mehanna H, Paleri V, West CM, Nutting C (2010) Head and neck cancer – Part 1: Epidemiology, presentation, and prevention. BMJ 341: e6484.
4. Adegoye AE, Twetman S, Christensen LB, Heitmann BL (2012) Intake of dairy calcium and tooth loss among adult Danish men and women. Nutrition 28: 779–784.
5. Gerritsen AE, Allen PF, Witter DJ, Bronkhorst EM, Creugers NH (2010) Tooth loss and oral health-related quality of life: a systematic review and meta-analysis. Health Qual Life Outcomes 8: 126.
6. Taylor GW, Manz MC, Borgnakke WS (2004) Diabetes, periodontal diseases, dental caries, and tooth loss: a review of the literature. Compend Contin Educ Dent 25: 179–184, 196–198, 190; quiz 192.
7. Matthews JC, You Z, Wadley VG, Gushman M, Howard G (2011) The association between self-reported tooth loss and cognitive function in the REasons for Geographic And Racial Differences in Stroke study: an assessment Of Observational Studies in Epidemiology (MOOSE) group. JAMA 305: 779–784.
8. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, et al. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 305: 770–772.
9. Tong V, Gao WQ, Reviewed the manuscript: WDL YG.
10. Borenstein M, Hedges L, Rothstein H (2005) Comprehensive Meta-analysis. Version 2 ed. Biostat, Englewood, New Jersey.
11. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21: 1539–1558.
12. Greenland S (2004) Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. Am J Epidemiol 160: 301–305.
13. Michaud DS, Liu Y, Meyer M, Giovannucci E, Joshipura K (2008) Periodontal disease, tooth loss, and cancer risk in male health professionals: a prospective cohort study. Lancet Oncol 9: 550–558.
14. Zhang J, Yu KF (1998) What’s the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA 280: 1690–1691.
15. Greenland S (2004) Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. Am J Epidemiol 160: 301–305.
16. Borenstein M, Hedges L, Rothstein H (2005) Comprehensive Meta-analysis. Version 2 ed. Biostat, Englewood, New Jersey.
17. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21: 1539–1558.
18. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327: 557–560.
19. Everitt B, Smith L, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 313: 629–634.
20. Duvall S, Tweedie R (2000) Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 56: 455–463.
21. Marshall JR, Graham S, Haughey BP, Shedd D, O’Shea R, et al. (1992) Smoking, alcohol, dentition and diet in the epidemiology of oral cancer. Eur J Cancer & Oral Oncol 28B: 9–15.
22. Bunnagd T, Widj J, Frydenberg M, Elborn O, Nielsen JE (1995) Case-control study of squamous cell cancer of the oral cavity in Denmark. Cancer Causes Control 6: 57–67.
23. Talamini R, Vaccarella S, Barbone F, Tavani A, La Vecchia C, et al. (2000) Oral hygiene, dentition, sexual habits and risk of oral cancer. Br J Cancer 83: 1298–1302.
24. Garrote LF, Herrero R, Reyes RM, Vaccarella S, Anta JL, et al. (2001) Risk factors for cancer of the oral cavity and oro-pharynx in Cuba. Br J Cancer 85: 46–54.
25. Lisowska J, Pilar ska A, Pilarski P, Samoelsczyk-Wasyura D, Piekarczyk J, et al. (2003) Smoking, alcohol, diet, dentition and sexual practices in the epidemiology of oral cancer in Poland. Eur J Cancer Prev 12: 25–33.
26. Rosenquist K, Wennerberg J, Schildt EB, Bladstrom A, Goran Hansson B, et al. (2005) Oral status, oral infections and some lifestyle factors as risk factors for oral and oropharyngeal squamous cell carcinoma. A population-based case-control study in southern Sweden. Acta Otolaryngol 125: 1327–1336.
27. Guha N, Belletta P, Wunsch Filho V, Eluf Neto J, Shangina O, et al. (2007) Oral health and risk of squamous cell carcinoma of the head and neck and esophagus: results of two multicentric case-control studies. Am J Epidemiol 166: 1159–1173.
28. Divaris K, Oldham AF, Smith J, Bell ME, Weisler MC, et al. (2010) Oral health and risk for head and neck squamous cell carcinoma: the Carolina Head and Neck Cancer Study. Cancer Causes Control 21: 567–575.
29. Hiraki A, Matsuo K, Suzuki T, Kawase T, Tajima K (2008) Teeth loss and risk of cancer at 14 common sites in Japanese. Cancer Epidemiol Biomarkers Prev 17: 1222–1227.
30. Wang RS, Hu XY, Gu WJ, Hu Z, Wei B (2013) Tooth loss and risk of head and neck cancer: a meta-analysis. PLoS One 8: e71122.
31. Cronin M, Meaney S, Jepson NJ, Allen PF (2009) A qualitative study of trends in patient preferences for the management of the partially dentate state. Gerodontology 26: 137–142.