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# Alcohol consumption is associated with periodontitis. A systematic review and meta-analysis of observational studies

Shaju Jacob Pulikkotil,[1] Sonia Nath,[2] Muthukumaraswamy,[3] Lalli Dharamarajan,[4] Kweh Ting Jing[5] and Rathna Devi Vaithilingam.[6]

*[1]Division of Clinical Dentistry, School of Dentistry, International Medical University, Kuala Lumpur, Malaysia; [2]Department of Periodontology, Kusum Devi Sunderlal Dugar Jain Dental College and Hospital, Kolkata, India; [3]Department of Periodontology, Tamil Nadu Government Dental College, Chennai, India; [4]Masters in Molecular Medicine, School of Post graduate studies, International Medical University, Kuala Lumpur, Malaysia; [5]Dental Officer, Klinik Pergigian Jitra, Ministry of Health, Malaysia; [6]Department of Restorative Dentistry, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia.*

***Objective:*** To determine whether alcohol consumption is associated with the risk of periodontitis. ***Basic Research Design:*** Systematic review and meta-analysis of observational studies performed using the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines. ***Method:*** PubMed and Scopus were searched for eligible articles published in English from inception till November 2018. The quality of studies was assessed by the Newcastle Ottawa Scale. Pooled odds ratios (OR) and 95% confidence intervals (CI) were calculated for the risk of periodontitis associated with highest versus lowest/non-alcohol in a random effects meta-analysis model. Heterogeneity and sensitivity were investigated in meta regression analysis. A funnel plot was used to assess publication bias. ***Results:*** Twenty-nine observational studies were included. One study with two separate datasets was considered as two separate studies for analysis. Alcohol consumption was significantly associated with the presence of periodontitis (OR = 1.26, 95% CI= 1.11-1.41). Significant heterogeneity (I2=71%) was present in the overall analysis, primarily attributable to sampling cross-sectional studies (I2=76.6%). A funnel plot and Egger tests (p=0.0001) suggested the presence of publication bias. ***Conclusion:*** Alcohol consumption was associated with increased occurrence of periodontitis and should be considered as a parameter in periodontal risk assessment. Publication bias should be explored in future studies.

**Keywords:** *Alcohol consumption, meta-analysis, risk factor, periodontitis, systematic review*

## Introduction

The World Health Organization (2011) sees alcohol consumption as the world's third largest risk factor for disease and disability and the greatest risk among middle-income countries. Consumption of alcohol influences the immune system with a broad range of detrimental effects. High consumption of alcoholic beverages can cause cardiovascular disease, obesity, stroke, cancer, suicide and accidents and death (Rocco *et al*., 2014; WHO, 2011; Xi *et al*., 2017). Alcohol consumption may affect the oral cavity and the upper digestive tract leading to morphologic, metabolic and functional changes (Riedel *et al.,* 2005).

Periodontitis is a chronic inflammatory disease associated with a dysbiotic bacterial biofilm in a susceptible host leading to progressive loss of teeth supporting structures (Caton *et al.*, 2018). Several risk factors have been associated with its development and progression such as composition of the subgingival bacterial plaque, tobacco use, diabetes mellitus, obesity, male gender, socioeconomic status, psychological factors, HIV infection and alcohol consumption (Van Dyke & Sheilesh, 2005).

Increased periodontal breakdown and tooth loss have been reported in people with severe alcoholism (Hornecker *et al*., 2003). Long-term excessive alcohol use is reported to affect bone metabolism and may play an important role in extensive bone loss (de Souza *et al*., 2006; Porto *et al*., 2012. Samnieng et al. (2013) reported that regular use of alcohol was significantly associated with lower salivary flow, fewer teeth and functional tooth units and higher oral malodour and periodontal disease. Some studies have suggested that the relationship between periodontitis and alcohol consumption is confounded by poor oral hygiene (Hornecker *et al*., 2003; Park *et al*., 2014; Pitiphat *et al*., 2003).

The effect of alcohol use on periodontal disease is still being investigated, with the findings of recent studies still inconclusive (Amaral *et al*., 2009; Gay *et al*., 2018; Wang *et al*., 2016). Some long-term studies have shown positive associations between alcohol consumption and periodontitis (Nishida *et al*., 2008; 2010; Pitiphat *et al*., 2003; Wagner *et al*., 2017) while Okamoto et al. (2006) did not find such a link. A systematic review by Amaral et al. (2009) including five longitudinal and 11 cross sectional studies concluded that alcohol consumption can be considered as a risk indicator for periodontitis. Another meta-analysis using data from 18 observational studies also supported the link between alcohol consumption and periodontitis (Wang *et al*., 2016). The difference in results between various studies may be attributed partly to differences in assessment and definition of periodontal disease, confounding factors, small sample size, and variations in the frequency and the amount of alcohol consumed (Wagner *et al*., 2017).

Correspondence to: Sonia Nath, Department of Periodontology, Kusum Devi Sunderlal Dugar Jain Dental College and Hospital, India. Email: sonianath_12@yahoo.co.in

The present systematic review and meta-analysis was conducted to update the evidence on the association between alcohol consumption and the presence/occurrence of periodontitis in the light of studies reported since the earlier reviews on this topic. The research question was aligned to the PECOS model: What is the level of association (O) between alcohol consumption (E) compared to no or low alcohol consumption (C) and periodontitis in adults (P) from observational studies (S)?

## Materials and Methods

The reporting of this systematic review and meta-analyses followed the Preferred Reporting Items for systematic review and Meta-Analyses (PRISMA) guidelines.

### *Literature search and strategy*

A literature search performed on the PubMed and Scopus databases for eligible studies from inception to 30th November 2018 used the following search terms ((Alcohol OR Ethanol)) AND (periodontitis OR "periodontal disease") as free-text terms. This strategy was found to include relevant studies identified in an earlier review (Wang *et al*., 2016). The reference list of all the eligible studies, systematic reviews, and narrative reviews were also searched for eligible studies.

### *Study selection*

The criteria for inclusion were observational studies published in the English language as original research on the association between alcohol consumption and periodontitis that had calculated relative risk (RR) or odds ratios (OR) with 95% confidence intervals (CI) for alcohol consumption adjusted for other confounders by study design or multivariate analysis. Case reports, case series and ecological studies were excluded. All the studies identified through the initial search were screened by two independent reviewers (SJ, SN) based on their titles and abstracts. Full text assessment of the studies screened positive was also done independently by the two reviewers. Any disagreements were resolved by consensus or by arbitration by the third reviewer (MK).

### *Data extraction*

Relevant data were extracted independently from the source papers to a bespoke form that recorded: (1), Study characteristics: name of the first author, publication year, country of study, number of participants, study design, population, sampling methods and sample size; (2), Participant characteristics: mean age at baseline, sex, definition and prevalence of periodontitis and the factors adjusted for; (3), Exposure and comparator details: definition of alcohol consumption and alcohol reference group; (4), Outcome measures: multivariate adjusted risk estimates and 95% CI for highest versus lowest/non-alcohol consumption.

### *Quality Assessment*

Included studies were assessed for quality using the Newcastle-Ottawa Scale (NOS) (Stang, 2010) checklist (cohort and case control studies) independently by two reviewers (SJ, SN). The NOS scale is commonly employed to assess the quality of observational studies. A star system was used to score in three domains: selection of groups, comparability of groups and exposure/outcome measurement. Different criteria were used for cross-sectional and longitudinal studies.

### *Statistical Analysis*

Analysis was performed with STATA (version 15.0, StataCorp, College Station, TX, USA). Meta-analyses using DerSimonian and Laird's random-effects model were used to estimate summary measures of the association between alcohol consumption and periodontitis. Sensitivity meta-analysis excluded low quality studies and subgroup analysis considered characteristics that could affect any apparent association between alcohol consumption and periodontitis including: study design (cross sectional vs. longitudinal), population (country), sex (both, males or females), sampling (probabilistic vs. non-probabilistic), reference alcohol group (no consumption or low consumption), age range of population (<40 years or >40 years), periodontitis prevalence based on a median cut-off (<30 or >30%), total participants in the study based on a median cut-off (<800, >800). Further meta regression considered the number of cases (people with periodontitis) and total participants in the study to evaluate their effect in explanation of the heterogeneity and the association in influencing the overall outcome. Publication bias was assessed in the Egger test and visually through a funnel plot.

## Results

The initial search identified 1568 unique studies of which 1526 were excluded after screening by title and abstract. The full texts of 42 articles were assessed for eligibility of which 10 were excluded due to absence of any estimates on the association (Amaral *et al*., 2008; Enberg *et al*., 2001; Harris *et al*., 1996; Jansson, 2008; Khocht *et al*. 2003; Lages *et al*., 2015; Novacek *et al*., 1995; O'Sullivan, 2012; Ogawa *et al*., 2002; Wickholm *et al*., 2003) and one older study had same data as the follow-up report (Park *et al*., 2014) (Figure 1).

A total of 29 reports were finally selected for systematic review and meta-analysis (Table 1). One study presented data for males and females that could be included in the analysis independently (Kongstad *et al*., 2008), making 30 datasets. Twenty-three reports described cross sectional studies and six longitudinal. Follow up in the longitudinal studies ranged from 2-12 years. The studies originated from 11 different countries and participants' ages ranged from 13 to 96 years. Most sources had studied urban populations and had used multi-stage complex sampling. Two reports (Antoniazzi *et al*., 2016; Tanner *et al*., 2015) described *a priori* sample size calculations. In all cases, data on alcohol use were collected in interviews or questionnaires, which was computer assisted in one study (Gay *et al*., 2018).

Many different criteria were used to define the presence of periodontitis and the prevalence of periodontitis ranged between 19% to 81% across studies. Nineteen reports did not specify the prevalence of periodontitis in their samples. The criteria for defining alcohol consumption also differed between studies, ranging from 'more than once a week', 'heavy drinking' or relating to chronicity. Reference values were often 'no or mild consumption of alcohol'.

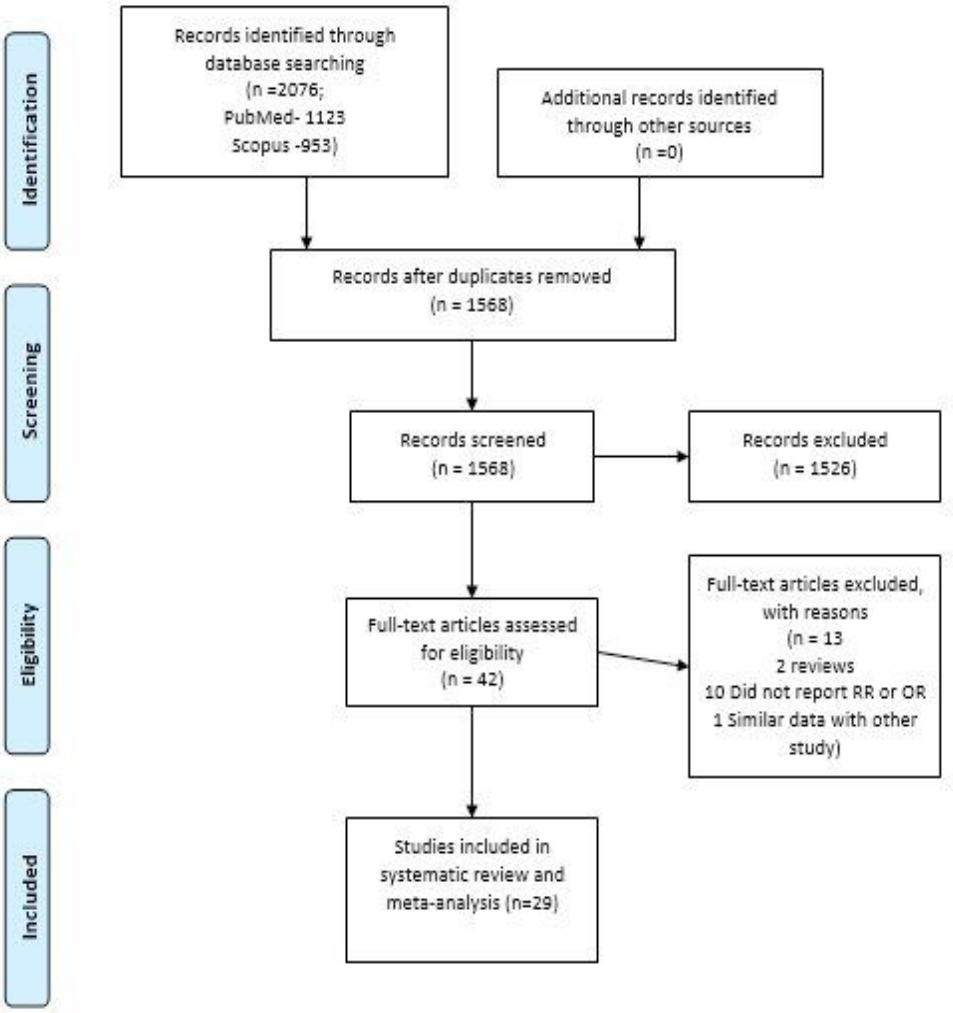


*Figure 1. Prisma Flow chart*

Five sources reported no association, one reported a negative association and the remainder identified positive associations between alcohol consumption and the presence of periodontitis (Figure 2).

Using the NOS scale to score study quality, 12 of the 23 cross sectional scored ≥ 6 stars, as did all the longitudinal studies (Supplementary tables, available at https://studentimuedu-my.sharepoint.com/:w:/g/personal/shaju_jacob_imu_edu_my/Ef2vdkRr7SBKi1lTYGC_VL0BM5NGr5xY5tDQq4Iwkwh4jg?e=k0XcZD).

The pooled OR estimates and 95% confidence intervals for the overall, subgroup and sensitivity meta-analyses is presented in Table 2. Alcohol consumption was associated with greater prevalence or occurrence of periodontitis (OR =1.26, 95% CI=1.11-1.41) (Figure 2). The relationship between alcohol use and the presence of periodontitis persisted in subgroup analyses for study design, sampling technique, participant age and the prevalence of periodontitis in the total sample. The relationship also persisted in reports where data for men and women had been aggregated and where it was reported males only. Subgroup analysis for women (two studies) did not find a relationship. Subgroup analyses by country yielded varying results. The one study in China provided the highest risk estimate, while aggregated data from the eight Japanese studies did not relate alcohol consumption to the presence of periodontitis. (Supplementary figure 1a-1g; Full results available at https://studentimuedu-my.sharepoint.com/:w:/g/personal/shaju_jacob_imu_edu_my/EQm8tpUO4RRCuYX-eC-PUH5UBd-J4MhYP9of5x5Fmw4kldA?e=DykqeI).

Studies where the reference group was defined as persons who consumed less alcohol than the cases did not associate alcohol with the presence of periodontitis, whereas studies where the reference group consumed no alcohol did find an association.

### *Meta-regression analysis*

Meta regression analysis did not reveal sample size or the number of cases of periodontitis to be associated with heterogeneity (Supplementary Figure 2a-2b; https://studentimuedu-my.sharepoint.com/:w:/g/personal/shaju_jacob_imu_edu_my/EQm8tpUO4RRCuYXeC-PUH5UBd-J4MhYP9of5x5Fmw4kldA?e=DykqeI).

### *Sensitivity analysis*

Meta-analysis after excluding low-quality studies i.e. cross-sectional studies scoring fewer than 5 or 6 stars (OR 1.03; 95% CI 0.88-1.19 and OR 1.12; 95% CI 0.98-1.25 respectively) rendered the pooled OR non-significant. No sensitivity analysis was done for longitudinal studies as all studies scored more than 6 stars in quality assessment. No studies exerted an increased influence in the overall effect size in leave-one-out analysis (Supplementary Figures 3a-3b, available at https://studentimuedu-my.sharepoint.com/:w:/g/personal/shaju_jacob_imu_edu_my/EQm8tpUO4RRCuYX-eC-PUH5UBd-J4MhYP9of5x5Fmw4kldA?e=DykqeI).

**Table 1.** Characteristics of 29 included studies

| *Author Year Country* | *Design* | *Sample M/F No. cases periodontitis* | *Sampling* | *Alcohol reference Group* | *Alcohol definition* | *Age* | *Factors adjusted for* | *Diagnostic criteria for periodontitis* | *OR, CI* |
|---|---|---|---|---|---|---|---|---|---|
| Gay 2018 USA | LS | 7062 3509/3553 3884 | Probability | <1 drink/ week | 8+ drinks/ week | 30+ | Age, gender, race/ethnicity, education level, income-to-poverty ratio, cigarette use, overall oral health & HbA1c | ≥2 interproximal sites with CAL ≥6 mm & ≥1 with PD ≥5 mm | 1.9, 1.2-3 |
| Suwama 2018 Japan | LS | 438 236/202 368 | Probability | Non-drinker | ≥40 g for men, ≥20 g for women | 73 | Number of existing teeth, smoking, use of interdental brushes | CPI score 4 | 2.44, 1.03-5.78 |
| Kongstad 2017 Denmark | CS | 3665 1425/2240 337 | Probability | No alcohol | Alcohol consumption | 18-96 | Age, sex, smoking status, T2DM, ISCED, physical activity, BMI, WC, body fat, triglyceride, total cholesterol, CRP | ≥2 interproximal sites with CAL ≥6 mm & ≥1 with PD ≥5 mm | 1, 0.99-1.01 |
| Wagner 2017 Brazil | CS | 502 209/293 302 | Probability | Non drinker | > 1 glass/ day | 18-65 | Age, sex, smoking, socioeconomic status, & body mass index | mean CAL > 1.5 mm | 1.3, 1.07-1.58 |
| Akpata 2016 Nigeria | CS | 500 240/260 185 | Probability | Less than 600 ml of alcohol a day | Chronic alcohol consumption | >50 | Age, gender, education, income, previous dental visit & history of medical illness | ≥2 interproximal sites with CAL ≥6 mm & ≥1 with PD ≥5 mm | 1.17, 0.59-2.33 |
| Antoniazzi 2016 Brazil | CS | 212 158/54 168 | Non-probabilistic | Less than once/week | Once or more/week | 13-46 | Sex, age, skin colour, schooling in years, household income, tobacco use | At least three sites with CAL >4mm &2+ sites with PD >3 mm | 2.24, 1.03-4.90 |
| Lee 2016 South Korea | CS | 18448 NA 5165 | Probability | Alcohol drinking <6.8 GY | Long term drinking ≥ 6.8 GY | >19 | Sex, age, education level, household income, marital status, recent dental visit, use of oral hygiene device, the number of decayed, missing or filled permanent teeth, frequency smoking | CPI 3 | 1.22, 0.96-1.56 |
| Hach 2015 Denmark | LS/CS data of 168 volunteers | 168 77/91 43 | Probability | 0–3 units/ week for women, 0–7 units for men | >7 units/week for women, >14 units for men | >65 | Age, gender, smoking, number of teeth & dental plaque | ≥3 teeth with CAL ≥4 mm | 2.24, 0.58-8.58 |
| Susin 2015 Brazil | CS | 1115 513/602 318 | Probability | No alcohol | > 1 glass/ day | 18-65 | Age, gender, race, socioeconomic status, dental care, body mass index, diabetes & smoking | Individuals with ≥ 30% teeth with periodontal attachment loss ≥ 5 mm | 1.48, 0.88-2.48 |

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...table 1 continued

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Tanner<br>2015<br>Finland | CS | 8539<br>8539/0<br>5633 | NA | No alcohol or <once/ month | > once/week | NA | Teeth brushing, father's & mother's education, own education, smoking & last visit to dental care | CPI score ≥ 2 | 0.98 (0.76-1.26) |
| Kim<br>2014<br>South Korea | CS | 5291<br>2409/2882<br>1671 | Probability | Non-alcohol use | Harmful alcohol use defined as total AUDIT score of 8 or higher | >19 | Age, gender, household income, education level, daily frequency of brushing, use of floss or interdental brush, current smoker, active caries, diabetes mellites, obesity | CPI 3 | 1.15, 0.96-1.38 |
| Costa<br>2013<br>Brazil | CS | 705<br>341/364<br>92 | Non-probabilistic | No/ occasional alcohol | Alcohol use defined as total AUDIT score of 8 or higher | 35-65 | Smoking, sex, age, family income, educational level, co-habitation status, BMI, last dental visit, diabetes | Mean CAL ≥3mm | 1.94, 1.39-2.72 |
| Wu<br>2013<br>China | CS | 754<br>0/754<br>639 | NA | Never drinker/ former drinker | ≥1 drinks/ weeks | 20-29 | Age | Two or more sites with CAL≥3 mm | 2.44, 2.02-3.87 |
| Lages<br>2015<br>Brazil | CS | 542<br>292/250<br>134 | Non-probabilistic | No/occasional alcohol | Alcohol dependence | 35-55 | Gender, age, family income, education level, co-habitation status, dental visit, BMI, diabetes, smoking | ≥4 teeth with one or more sites with PD ≥4 mm and CAL ≥3 mm at the same site. | 4.72, 2.73-7.92 |
| Okamoto<br>2006<br>Japan | LS | 1332<br>1332/0<br>592 | NA | Non-drinker | >20g alcohol /day | 30-59 | Age, alcohol consumption | CPI score 3 or 4 | 0.74, 0.34-1.64 |
| Nishida<br>2010<br>Japan | CS | 183<br>164/19<br>78 | NA | <33g alcohol /day | ≥33 g alcohol /day | 18-63 | Age, gender, smoking habit | Mean CAL ≥3mm | 4.28, 1.2-15.3 |
| Kongstad<br>2008<br>Denmark | CS | 817<br>0/817<br>NA | NA | <1drinks/ week | 21+ drinks/week for women | 20-95 | Age, smoking, education level income, body mass index, physical activity, diabetes, number of teeth, plaque scores | CAL ≥3mm | 0.82 (0.37-1.82) |
| Kongstad<br>2008<br>Denmark | CS | 704<br>704/0<br>NA | NA | 1-13 drinks/ week | 35+ drinks/week for men | 20-95 | Age, smoking, education level income, body mass index, physical activity, diabetes, number of teeth, plaque scores | CAL ≥3mm | 0.34 (0.15-0.79) |
| Nishida<br>2008<br>Japan | LS | 200<br>179/21<br>99 | NA | < every day | Every day | 18-62 | Age, gender, physical exercise, smoking habit, sleep, eating breakfast, nutritional balance, working hours, subjective mental stress | 1+ teeth with an increase ≥2.0mm in CAL and PD for 2 years | 2.03, 1.05-3.93 |

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...table 1 continued

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Minaya-Sanchez 2007<br>Mexico | CS | 161<br>161/0<br>74 | Non-probabilistic | Never drinker | Current/ former drinker<br>Current drinker ≥1 drink/week for 6m. | >20 | Age, schooling, number of teeth, marital status, dental care in previous month, tooth brushing frequency, tobacco use, use of antibiotics in past 6 months, presence of dental plaque, presence of calculus, presence of suppuration, presence of gingivitis | CAL ≥ 4 mm in at least one site | 0.60, 0.25-1.46 |
| Torrungruang 2005<br>Thailand | CS | 2005<br>1492/513<br>548 | Non-probabilistic | Non-drinker | Current drinker ≥12 drinks in 1 year | 50-74 | Age, gender, education level, income, plaque score, smoking status, diabetes mellitus, BMI, WC | CAL ≥4.0 mm | 2.30, 1.70-3.20 |
| Ojima 2006<br>Japan | LS | 4828<br>1896/2932<br>554 | Probability | Never drinker | Current drinker | >40 | Smoking, gender, age, BMI, vitamin C, vitamin E | CPI score = 4 | 1, 0.76-1.33 |
| Bouchard 2006<br>France | CS | 2132<br>1044/1088<br>421 | Probability | occasional intake | Non-drinker /regular drinker | 35-64 | Age, gender, BMI, WBC | CAL >5 mm | 1.60, 1.20-2.20 |
| Shimazaki 2005<br>Japan | CS | 961<br>378/583<br>90 | Probability | no alcohol consumption | heavy drinking ≥30 g/day | 40-79 | Amount of smoking, glucose tolerance, age, sex, number of teeth, mean plaque index | PD ≥4 mm | 2.5, 1.1-5.7 |
| Nishida 2004<br>Japan | CS | 372<br>290/82<br>206 | NA | < 33 g/day | ≥ 33 g alcohol /day | 20-59 | Age, gender, BMI, smoking status, frequency of tooth brushing | PD ≥3.5 mm | 5.36, 1.39-20.77 |
| Tezal 2004<br>US | CS | 12723<br>6007/ 6716<br>3478 | Probability | no alcohol | 20 drinks/week | >20 | Age, gender, race, education, income, smoking, diet, diabetes, number of remaining teeth, gingival bleeding | CAL > 1.5 mm | 1.67, 1.25-2.23 |
| Pitiphat 2003<br>US | CS | 39461<br>39461/0<br>2125 | Probability | 0 g/day | ≥30 g alcohol /day | 40-75 | Diabetes, BMI, physical activity, calories time period, & caloric intake | NA | 1.27, 1.08-1.49 |
| Tezal 2001<br>US | CS | 1371<br>661/710<br>156 | Probability | No alcohol | 10 drinks/ week | 25-74 | Age, gender, race, education, income, smoking, diabetes mellitus, dental plaque. | CAL > 4mm | 1.44, 1.04-2.22 |
| Shizukuishi 1998<br>Japan | CS | 310<br>252/58<br>70 | Non-probabilistic | Not everyday | Everyday | 20-59 | Age, gender, physical exercise, smoking habit, sleeping hours, eating breakfast, smoking, working hours, mental stress | Miller's modified CPI score >25th percentile | 1.8, 1.1-3.1 |
| Sakki 1995<br>Finland | CS | 527<br>266/261<br>121 | NA | 0 drinks/2 weeks | 7 or more drinks /2 weeks | 55 | Dietary habits, tobacco, smoking habits, tooth brushing frequency. | PPD ≥ 3 mm | 2.52, 1.40-4.54 |

NA: Not available; OR: Odds ratio; CI: Confidence interval; M: Male; F: Female; CAL: Clinical attachment level; PD: Probing depth; CPI: Community Periodontal Index; BMI: Body Mass Index; CRP: C-reactive Protein; WC: Waist Circumference; ISCED: International Standard Classification of Education; T2DM: Type 2 diabetes mellitus; CDC: Centre of Disease Control; AAP: American Association of Periodontology; GY: Glass Year; CAGE: cut down, annoyed, guilty, eye-opener; AUDIT: alcohol use disorders identification test.
# dependent on the case definition of periodontitis.

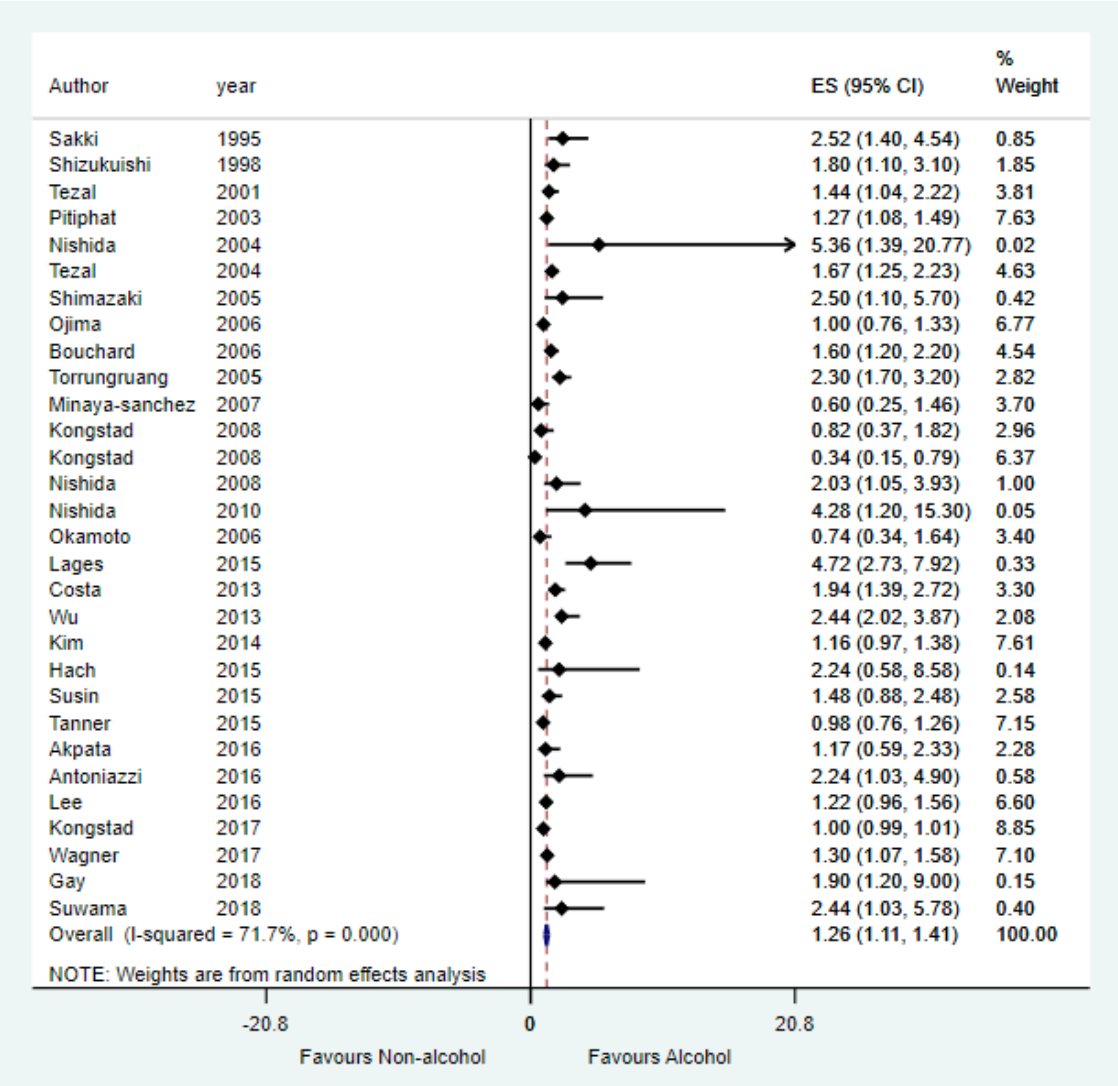


*Figure 2. Forest plot synthesising results from 30 datasets of the association between alcohol use and the presence of periodontitis*

### *Publication bias*

The funnel plot and Egger's test (p=0.001) suggested significant publication bias and is provided as supplementary (Figures 4 and 5 accessible at https://studentimuedu-my.sharepoint.com/:w:/g/personal/shaju_jacob_imu_edu_my/EQm8tpUO4RRCuYXeC-PUH5UBdJ4MhYP9of5x5Fmw4kldA?e=DykqeI).

## Discussion

Alcohol is a risk factor common to several chronic diseases. Our review updated evidence on the association between alcohol use and the presence of periodontitis from observational studies that had controlled for other risk factors. As well as elucidating the relationship between alcohol use and the presence of periodontitis, the additional studies included in this update allowed investigation of heterogeneity through subgroup and sensitivity analysis. Analysis of 29 reports involving 30 datasets and 117,239 participants associated alcohol consumption with periodontitis. The association consistent across populations around the world, except for studies in Japan. A dose-response relationship could not be calculated due to the varying thresholds for alcohol consumption in the reports.

Our findings are compatible with previous systematic reviews. Amaral et al. (2009) included 16 studies, 12 related to alcohol consumption and 4 to alcohol dependence. Seven studies of alcohol consumption and all four studies on alcohol dependence reported positive associations between alcohol intake and periodontitis. Wang and colleagues (2016) included 18 studies with 90,147 participants. Our review supplemented the studies reported by Wang et al. (2016) with another 11 reports.

Subgroup analyses suggested that the relationship was consistent across study designs, population groups and underlying levels of periodontitis. Differences between countries may be attributable to different underlying levels of alcohol consumption and periodontitis and to the different diagnostic thresholds used in the source studies. Genetic variation among populations may also explain differences in effects of alcohol and organ health (Matsushita and Higuchi, 2017). Similarly, whilst males had higher risk for periodontitis than females, a WHO report (2005) identified different consumption patterns between males and females and differing effects of alcohol consumption.

**Table 2.** Summary of meta-analysis of all included studies and subgroup analyses.

| *Groups and subgroups* | | *No of datasets* | *Odds ratio* | *95% Confidence Interval* | *I2 %* |
|---|---|---|---|---|---|
| All studies | | 30 | 1.26 | 1.11-1.41 | 71.7 |
| Design | Cross-sectional | 20 | 1.32 | 1.12-1.52 | 76.6 |
| | Longitudinal | 10 | 1.21 | 1.06-1.35 | 3.4 |
| Country | Nigeria | 1 | 1.74 | 0.30-2.04 | |
| | Brazil | 5 | 1.741 | 1.15-2.33 | 60.5 |
| | Denmark | 4 | 0.746 | 0.25-1.24 | 82.3 |
| | South Korea | 2 | 1.178 | 1.01-1.35 | 0 |
| | Japan | 8 | 1.245 | 0.81-1.68 | 24.6 |
| | United States | 4 | 1.341 | 1.16-1.52 | 0 |
| | Thailand | 1 | 2.300 | 1.55-3.05 | |
| | Mexico | 1 | 0.600 | -0.010-1.20 | |
| | China | 1 | 2.440 | 1.52-3.37 | |
| | France | 1 | 1.600 | 1.10-2.10 | |
| | Finland | 2 | 1.547 | 0.09-3.00 | 72.3 |
| Sex | Both | 23 | 1.43 | 1.24-1.63 | 67.5 |
| | Males | 5 | 1.26 | 1.11-1.41 | 71.7 |
| | Females | 2 | 1.60 | 0.02-3.19 | 86.3 |
| Sampling | Probabilistic | 16 | 1.20 | 1.08-1.33 | 58.4 |
| | Non-probabilistic | 6 | 1.92 | 1.11-2.73 | 76.2 |
| | Others | 8 | 1.36 | 0.64-2.08 | 75.7 |
| Alcohol reference | Less consumption | 17 | 1.31 | 0.91-1.66 | 69.9 |
| | No consumption | 13 | 1.30 | 1.12-1.49 | 75.6 |
| Age range | >40 | 21 | 1.45 | 1.08-1.83 | 54.5 |
| | <40 | 9 | 1.26 | 1.06-1.46 | 74.1 |
| Periodontitis prevalence | >30 | 6 | 1.80 | 1.13-2.47 | 72.3 |
| | <30 | 5 | 1.57 | 1.17-1.97 | 47.8% |
| | Others (not specified) | 19 | 1.10 | 0.93-1.27 | 66.9% |
| Total participants | >800 | 15 | 1.21 | 1.06-1.35 | 66.1 |
| | <800 | 15 | 1.63 | 1.14-2.13 | 76.4 |

The stricter reference case definition of 'no alcohol consumption' was associated with the presence of periodontitis, unlike the more relaxed definition of less than the cases. This laxer definition may have permitted false positives into the reference category, leading to dilution of risk estimates (Radoï and Luce, 2013).

Heterogeneity was expected due to the variety in the pooled studies in terms of population, study design and case definitions (Munafò and Flint, 2004). The included studies spanned the five major continents and recruited participants with varying ages. By contrast, reports from the US, South Korea and Japan showed low heterogeneity. Minimal heterogeneity was observed among the longitudinal studies. There was considerable variation in the case definitions for alcohol and periodontitis. Subgroup analysis identified possible sources of heterogeneity. Variation by gender, sampling strategy, reference definition for alcohol consumption, age (>40 or <40 years), prevalence of periodontitis (<30 or >30%) and sample size (<800 or >800) did not affect the degree of heterogeneity to a major extent. Sub-group meta-analysis was not able to identify whether differences in heterogeneity has any statistical significance. Meta-regression for the effect of continuous variables did not identify relationships between the number of participants or the prevalence of periodontitis and heterogeneity (Thompson & Higgins, 2002). The sources of heterogeneity identified in subgroup and sensitivity meta-analysis points future investigators to variables that may confound the relationship between alcohol consumption and periodontitis.

Sensitivity analysis excluding low-quality studies among the cross-sectional studies showed non-significant association of alcohol consumption to periodontitis. This result could not be compared with earlier reviews that did not use quality assessment but gains importance due to the effect on reliability. Leave-one-out analysis was used to identify if any studies had a greater influence on the overall results. No single study swayed the results of these pooled analyses, validating the accuracy of our results.

The strong possibility of publication bias highlights an important issue on the possible preference of authors and journals to submit and publish studies with positive findings (Gadde *et al*., 2018). However, the large samples in many published studies suggest that publication bias would not have affected the accuracy of the effect estimates (Egger *et al*., 1997).

As is always the case, this study has limitations arising from the source studies and the review process. The primary studies varied in their definitions of periodontitis and alcohol, creating heterogeneity. This is reflected further in the large range of prevalence estimates across the selected studies. One consequence of this methodological heterogeneity was that strict inclusion criteria for exposure and outcome could not be adopted for this review. However, the weighting of each study in meta-analysis according to its strength strengthens the results of the review. The heterogeneity also prevented analysis of a possible dose response effect between alcohol consumption and periodontitis.

## Conclusion

Alcohol consumption is associated with the presence of periodontitis despite inconsistent case definitions for periodontitis and alcohol consumption. Alcohol consumption is a common risk factor for various chronic diseases and the positive association revealed in this review is in addition to the role of alcohol in oral carcinogenesis (Kumar *et al*., 2016). Dental clinicians and public health specialists should advise their patients and the public to avoid alcohol consumption. These findings suggest that future studies are required in this area with proper sampling methods, consistent and valid definitions for periodontitis and alcohol consumption and longer follow-up. The risk of publication bias should encourage authors and journals to publish study reports with neutral or negative findings.

### *Conflict Of Interest*

None

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