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SYSTEMATIC REVIEW

# Periodontal outcomes of children and adolescents with attention deficit hyperactivity disorder: a systematic review and meta-analysis

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## Abstract

**Background** This systematic review and meta-analysis aimed to answer the following question: Are children and adolescents with attention deficit hyperactivity disorder (ADHD) more likely to have gingival or periodontal disease-related outcomes than their non-ADHD peers?

**Methods** Searches were conducted in the following databases: Embase, Scopus, Web of Science, and PubMed. Google Scholar and OpenGrey were also verified. Observational studies were included in which children and adolescents with ADHD were compared with their healthy peers in terms of gingival and/or periodontal endpoints. Bias appraisal was performed using the Joann Briggs tool for case–control and cross-sectional studies. Meta-analysis was performed using R language. Results are reported as mean difference (MD) and odds ratio (OR). Statistical analyses were performed in RStudio.

**Results** A total of 149 records were identified in the searches. Seven studies were included. The meta-analysis showed that children and adolescents with ADHD had a higher mean gingival bleeding index (percentage) than their non-ADHD peers (MD = 11.25; CI = 0.08–22.41; $I^2$ = 73%). There was no difference between groups for plaque index (MD = 4.87; CI = −2.56 to 12.30; $I^2$ = 63%) and gingivitis (OR = 1.42; CI = 0.22–9.21; $I^2$ = 76%). Regarding the assessment of risk of bias, the major issue found in the articles was the absence of analyses for the control of confounding factors.

**Conclusion** Children and adolescents with ADHD had more gingival bleeding than their non-ADHD peers, but no difference regarding plaque or gingivitis was detected between groups.

**Clinical registration** CRD42021258404.

**Keywords** Adolescent · Attention deficit hyperactivity disorder · Child · Oral health · Periodontal disease

## Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition characterised by a high degree of inattentiveness and hyperactivity behaviour (Posner et al. 2020). This condition initially develops in childhood and affects about 5% of children worldwide. In 50% of individuals diagnosed with ADHD, this condition persists into adulthood (Spencer et al. 2007). Manifestations related to ADHD can overwhelm the ability of affected individuals to develop social skills, to engage in school activities and to hold a job (Gallo and Posner 2016; Sayal et al. 2017). In addition, a substantial economic impact associated with ADHD has been reported. On average, cost estimates per person/year range from US$831.38 to 20,538.00. In the United States, the economic burden of ADHD ranges from US$356 million to 20.27 billion (Chhibber et al. 2021).

Evidence supports the presence of a link between oral health status and ADHD (Ertugrul et al. 2018). For instance, the occurrence of caries is increased in these children due to poor hygiene and augmented consumption of sugary foods (Drumond et al. 2022; Kohlboeck et al. 2013). Moreover, these individuals receive a multimodal approach that may

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include the use of psychostimulant medications, primarily methylphenidate and amphetamines (Posner et al. 2020), which in turn can also impact oral health status (Hasan and Ciancio 2004).

Periodontitis, a disease of the tissue surrounding the tooth structure, and gingival diseases are outcomes that can impact the oral health of children and adolescents and that are strongly associated with impaired levels of oral health-related quality of life in young individuals (Bekes et al. 2021; Moghaddam et al. 2020). Epidemiological assessment of periodontal outcomes is a challenge. Normally, the exams are performed through the evaluation of visible plaque, gingival bleeding and, in more severe cases, by probing of periodontal pockets and measurements of clinical attachment (Ainamo and Bay 1975; Peres et al. 2019). Periodontal outcomes of children and adolescents with ADHD have been assessed in previous studies (Blomqvist et al. 2011; Chau et al. 2017). However, a systematic summary of the evidence about this issue with assessment of bias has not been carried out so far.

Systematic compilation of data is useful to practitioners as a guideline and can be helpful during the decision-making process and for the implementation of coherent health care policies aimed at addressing oral health conditions in a particular population (Faggion 2013). In addition, it is worthwhile to assess morbidity and outcomes related to periodontal manifestations in individuals with a specific condition (Hanisch et al. 2019). Thus, the purpose of this systematic review and meta-analysis was to assess evidence about the periodontal outcomes of children and adolescents with ADHD in studies in which children and adolescents without ADHD were also evaluated.

## Materials and methods

### Registration and protocol

This systematic review and meta-analysis was reported based on guidelines proposed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020) (Page et al. 2021). A protocol registration was performed in the PROSPERO (International Prospective Register of Systematic Reviews, University of York, England) database and the following identification number was obtained: CRD42021258404.

### Eligibility criteria

Observational studies (longitudinal, cross-sectional and case–control studies) in which children and adolescents with ADHD were compared with their non-ADHD peers in terms of periodontal outcomes were eligible. Children and adolescents were defined as subjects under 19 years of age (World Health Organization 2006). Studies without a control group were excluded, nor were meeting/conferences abstracts, editorials, or qualitative studies considered. No language or publication date restrictions were imposed. The following PECO framework was considered to assemble this study:

P (Population): children and adolescents;
E (Exposure): ADHD;
C (Comparison): no ADHD;
O (Outcome): primary outcomes: periodontitis, gingivitis, and gingival bleeding index; secondary outcomes: bleeding on probing, probing depth, dental plaque, and clinical attachment level.

### Information sources and search strategies

Electronic searches were performed on PubMed (National Library of Medicine), Embase (Elsevier), Web of Science (Clarivate Analytics), and Scopus (Elsevier) from databases' inception date to July 2021. An update was performed on May 2022. Studies retrieved from these databases were entered into EndNote (Clarivate Analytics, Toronto, Canada) for the deduplication and record screening process. A Google Scholar search and a grey literature search using OpenGrey were also performed. For these two databases, reference screening was limited to the first 300 hits for each (Haddaway et al. 2015). If necessary, contact would have been made with the authors. A search strategy was set up considering keywords related to children, adolescents, ADHD, and periodontal outcomes. Boolean operators ("AND" and "OR") were used to link the keywords. The search strategy was initially tailored for PubMed and was adapted according to the individual settings of each database. All the search strategies used are described in Supplementary File 1.

### Study selection

After excluding duplicates, the selection of studies was performed in two phases. In the first phase, titles and abstracts were screened by two independent reviewers (V.Z.D. and A.A.A.). Titles and abstracts that apparently met the established inclusion criteria were selected for a second phase conducted by the same reviewers. In this second phase, the full text of the references selected in the first phase were read. References that fulfilled the eligibility criteria were included in the qualitative and/or quantitative synthesis. In cases of disagreement between authors, a third author (L.G.A.) was consulted and the disagreements were resolved.

### Data extraction

Data extraction of the studies selected in the screening process was performed by two reviewers (V.Z.D. and L.G.A.). The former performed the extraction and the latter double-checked the data retrieved from the full text of the included studies. Disagreements were resolved in a discussion between review authors. The following data were retrieved from the studies: last name of the first author, year of publication, sample size and setting, evaluation methods of exposure (ADHD) and outcomes (periodontal outcomes), as well as results comparing children and adolescents with ADHD and without ADHD.

### Narrative synthesis of the results

A narrative synthesis of the results regarding the comparison of periodontal outcomes between children and adolescents with ADHD and those without ADHD was provided. For continuous outcomes, the mean difference (MD) between groups, the Pooled Standard Deviation (Pooled SD), and the Cohen's *d* effect size (ES) were calculated (Cohen 1988). For the determination of the Pooled SD, the following formula was used:

$$\text{Pooled SD} = \sqrt{\frac{(\text{SD}_{\text{ADHD}})^2 + (\text{SD}_{\text{Control}})^2}{2}}.$$

For the calculation of Cohen's *d* ES, the following formula was applied:

$$\text{Cohen's } d \text{ ES} = \frac{\text{Mean}_{\text{ADHD}} - \text{Mean}_{\text{Control}}}{\text{SD}_{\text{pooled}}}.$$

For dichotomous outcomes, the odds ratio (OR) and the 95% confidence intervals (95% CI) were determined. For the calculation of the OR and the CI, data were arranged in contingency tables ($2 \times 2$) on MedCalc software (Ostend, Belgium, 2020).

### Risk of bias of individuals studies

Risk of bias was assessed by the same review authors who performed the data extraction according to the criteria summarised in the Critical Appraisal Tool checklist (Moola et al. 2020) developed by the Joanna Briggs Institute from The University of Adelaide, Australia. The bias assessment tool has 10 items and is based on five main topics, as follows: case and control matching (assessed by the first, second, and third items); exposure-related items that evaluate whether the exposure had been assessed with a standard tool in the same way for cases and controls and whether the exposure period had been enough (assessed by the fourth, fifth, and ninth items); controlling and strategies to deal with confounding factors (assessed by the sixth and seventh items); outcome-related criteria assessing whether the outcome had been evaluated in a standard and reliable way (assessed by the eighth item); and the statistical methods used in the studies were evaluated in in terms of correct deployment of data analysis (assessed by the tenth item).

### Quantitative synthesis of results

The observational studies included were grouped into meta-analyses taking into account methodological homogeneity. The k indicated the number of studies aggregated in each meta-analysis. Data retrieved from the studies were entered into a spreadsheet and imported into RStudio software (RStudio, Boston, USA). Meta-analyses were obtained using the R programming language (R Core Team, Vienna, Austria), applying the *meta* package for R (Balduzzi et al. 2019). Continuous data meta-analyses were performed considering the mean and standard deviation of the groups and the meta-analysis results are reported as MD and 95% CI. Meta-analyses of dichotomous outcomes were performed considering the number of events and the total number of cases or controls evaluated, and the results are reported as OR and CI.

A random-effects model was fitted in all meta-analyses, assuming that estimated true effects across studies were different due to the differences between samples (e.g. methods to assess exposure, educational level, income, potential and non-assessed oral habits, socioeconomic level, and human development index of the country where the study was carried out). The restricted maximum-likelihood estimator was implemented for all meta-analytic models (Viechtbauer 2005). $I^2$ was used to estimate the variability of inconsistency between studies, $\tau^2$ (tau-square) was used to evaluate the variance between the studies, and the absolute measure of heterogeneity was evaluated using $H^2$ (Hardy and Thompson 1998; Higgins and Thompson 2002; Higgins et al. 2003; Knapp et al. 2006). Heterogeneity metrics were reported with their respective 95% uncertainty intervals (95% UI). Drapery plots displayed the confidence interval for each study incorporated into the meta-analyses (Balduzzi et al. 2019).

### Sensitivity analysis

Sensitivity analysis was performed in the light of the assessment of the risk of bias of individual studies.

### Assessment of strength of evidence

Strength of evidence was appraised using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. In GRADE, study design, number of studies included in the meta-analysis, risk of bias, inconsistency, indirectness, imprecision, and publication bias were evaluated. The strength of the evidence can be very low, low, moderated, or high (Guyatt et al. 2011).

## Results

### Study selection

A total of 568 records were obtained through searches in electronic databases. One-hundred and forty-nine records were identified as duplicates and excluded. In the first phase, 353 studies were evaluated. In the second phase, the full texts of 11 studies were assessed. After the screening process, seven studies (Begnini et al. 2019; Bimstein et al. 2008; Blomqvist et al. 2007; Blomqvist et al. 2011; Chau et al. 2017; Ehlers et al. 2019; Pinar-Erdem et al. 2018) met the eligibility criteria and were included in the qualitative and/or quantitative synthesis. A summary of the screening process is presented in Fig. 1. Supplementary File 2 summarises the reasons why the four studies were excluded in the second phase of the selection process.

### General characteristics of the studies

All studies included in this systematic review and meta-analysis were cross sectional and had a control group. Among the seven studies included (Bimstein et al. 2008; Blomqvist et al. 2007; Blomqvist et al. 2011; Chau et al. 2017; Ehlers et al. 2019; Pinar-Erdem et al. 2018), a retrospective analysis of data was performed in one (Blomqvist et al. 2007). The publication date of the included studies ranged from 2007 (Blomqvist et al. 2011) to 2019 (Begnini et al. 2019; Ehlers et al. 2019) and all studies were originally published in English. The studies were conducted in Brazil (Begnini et al. 2019), the United States (Bimstein et al. 2008), Sweden (Blomqvist et al. 2007, 2011), China (Chau et al. 2017), Germany (Ehlers et al. 2019), and Turkey (Pinar-Erdem et al. 2018).

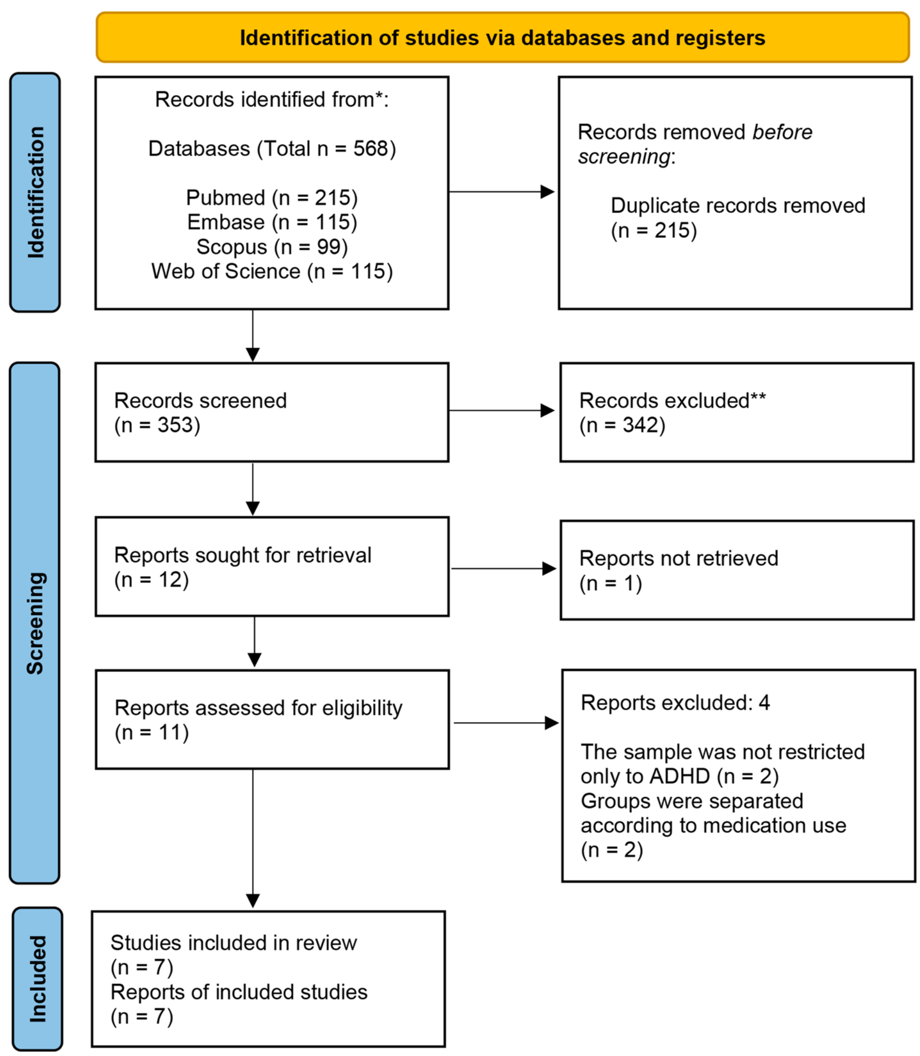



**Fig. 1** PRISMA flowchart of the selection process of the systematic review and meta-analysis

### Sample characteristics

A total of 698 children and adolescents were evaluated; of these, 252 with ADHD and 446 without ADHD. The sample size of studies ranged from 58 (Pinar-Erdem et al. 2018) to 152 participants (Bimstein et al. 2008). The age of the individuals ranged from 6 (Pinar-Erdem et al. 2018) to 17 years (Blomqvist et al. 2011). Participants in the ADHD group were recruited from university dental clinics (Bimstein et al. 2008), regular schools or schools for people with special needs (Blomqvist et al. 2007, 2011), from a university psychiatric department (Chau et al. 2017), from care facilities (Ehlers et al. 2019), and from children's and adolescents' psychiatric clinics (Pinar-Erdem et al. 2018). Individuals without ADHD were recruited in the same setting where individuals in the ADHD group were recruited (Begnini et al. 2019; Blomqvist et al. 2007; Blomqvist et al. 2011; Chau et al. 2017; Ehlers et al. 2019). In one study, information regarding the source of the control group was unavailable (Pinar-Erdem et al. 2018) and in another study, information about the setting where data collection took place was unavailable (Begnini et al. 2019).

### Exposure assessment

The exposure assessment was performed according to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders—4th edition) manual in four studies (Blomqvist et al. 2007; Blomqvist et al. 2011; Chau et al. 2017; Ehlers et al. 2019). In one study, the DSM-V was employed (Pinar-Erdem et al. 2018) and in one study, information on exposure assessment was not provided (Begnini et al. 2019). In one study, exposure data were obtained retrospectively by analysing information described in dental charts (Bimstein et al. 2008).

### Outcome assessment

In one study, histories of gingival bleeding, plaque, gingival inflammation, and calculus were assessed as dichotomous (presence/absence) outcomes (Bimstein et al. 2008). In four studies, the percentage of bleeding sites (Gingival Bleeding Index [GBI%]) was evaluated (Begnini et al. 2019; Blomqvist et al. 2007, 2011; Chau et al. 2017). Percent visible plaque index (Visual Plaque Index [VPI%]) (Chau et al. 2017; Begnini et al. 2019), percent visual approximal plaque (Approximal Plaque Index [API%]) (Ehlers et al. 2019), a score of plaque index (PI) (Pinar-Erdem et al. 2018), and gingivitis as a dichotomous outcome (Ehlers et al. 2019) were assessed as well. Sulcus bleeding index and probing pocket depth were also evaluated in one study (Pinar-Erdem et al. 2018). Six studies conducted outcome assessment with a clinical examination performed by a single and calibrated examiner (Begnini et al. 2019; Blomqvist et al. 2007; Blomqvist et al. 2011; Chau et al. 2017; Ehlers et al. 2019; Pinar-Erdem et al. 2018). In one study, outcome assessment was retrospective, based on analysis of data available in dental charts (Bimstein et al. 2008).

### Dichotomous data for the evaluation of the association between periodontal outcomes and ADHD

#### History of gingival bleeding, dental plaque, gingival inflammation, calculus, and gingivitis

In one study (Bimstein et al. 2008), a history of gingival bleeding was greater among children with ADHD compared with children without ADHD (OR 3.46; 95% CI [1.13, 10.60]; $p < 0.05$). No difference between groups was observed for plaque (OR 0.78; 95% CI [0.15, 4.05]; $p > 0.05$), gingival inflammation (OR 1.45; 95% CI [0.35, 5.86]; $p > 0.05$), or calculus (OR 3.15; 95% CI [0.64, 15.48]; $p > 0.05$). In one study (Ehlers et al. 2019), no difference was observed between groups regarding gingivitis (OR 0.52; 95% CI [0.12, 2.20]; $p > 0.05$).

#### Continuous data for the evaluation of the association between periodontal outcomes and ADHD

**GBI%, VPI% and API%** In three studies—Begnini et al. (2019) (MD = 3.43; pooled SD = 9.08; Cohen's $d$ ES = 0.37), Blomqvist et al. (2011) (MD = 19.0; pooled SD = 32.38; Cohen's $d$ ES = 0.58) and Chau et al. (2017) (MD = 16.3; pooled SD = 24.56; Cohen's $d$ ES = 0.66)—children and adolescents with ADHD had higher GBI% than their non-ADHD peers ($p < 0.05$), whereas in a previous study by Blomqvist et al. (2007) (MD = − 1.1; pooled SD = 5.86; Cohen's $d$ ES = 0.18) no significant difference in GBI% was observed between groups ($p > 0.05$). In one study (Chau et al. 2017), no difference in VPI% (MD = 2.80; pooled SD = 16.56; Cohen's $d$ ES = 0.16) was observed between children and adolescents with and without ADHD ($p > 0.05$). In one study (Begnini et al. 2019), children and adolescents in the ADHD group had a higher VPI% (MD = 12.3; pooled SD = 20.61; Cohen's $d$ ES = 0.59) than their non-ADHD peers ($p < 0.05$). In one study (Ehlers et al. 2019), no significant difference in API% (MD = − 0.2; pooled SD = 16.55; Cohen's $d$ ES = 0.01) was observed between children and adolescents with ADHD and their non-ADHD peers ($p > 0.05$).

**PI score** In one study (Pinar-Erdem et al. 2018), children and adolescents with ADHD had a significantly lower PI score than children and adolescents without ADHD (OR 0.34; 95% CI [0.16, 0.72]; $p < 0.05$).

**Sulcus bleeding index** In one study (Pinar-Erdem et al. 2018), no significant difference in sulcus bleeding index (MD = 1.08; pooled SD = 4.36; Cohen's $d$ ES = 0.24) was observed between children and adolescents with and without ADHD ($p > 0.05$).

**Probing pocket depth** In one study (Pinar-Erdem et al. 2018), no significant difference in probing pocket depth (MD = −0.03; pooled SD = 0.32; Cohen's $d$ ES = 0.09) was observed between children and adolescents with ADHD and their peers without ADHD ($p > 0.05$). Data extracted from the included studies are shown in Supplementary File 3.

**Risk of bias within-studies** All included studies achieved low risk of bias for group comparison regarding presence and absence of exposure, exposure period, and appropriate statistical tools. Two studies (Begnini et al. 2019; Bimstein et al. 2008) had high risk of bias for cases and corresponding controls and an unclear risk of bias for the criteria used for participant identification. For exposure assessment, risk of bias was low in four studies (Blomqvist et al. 2007, 2011; Ehlers et al. 2019; Pinar-Erdem et al. 2018), unclear in two (Begnini et al. 2019; Bimstein et al. 2008), and high in one (Chau et al. 2017). One study (Begnini et al. 2019) had a high risk of bias for the identification of confounding factors. For equality in the measurement of exposure for case and controls, risk of bias was low in three studies (Blomqvist et al. 2007, 2011; Begnini et al. 2019), high in three (Chau et al. 2017; Ehlers et al. 2019; Pinar-Erdem et al. 2018), and unclear in one (Bimstein et al. 2008). All studies had a high risk of bias for strategies used to deal with confounding factors. Supplementary File 4 summarises the results of risk of bias assessment. The bar graph displayed in Supplementary File 5 presents the results of bias assessment.

**Results of meta-analyses** Meta-analyses were assembled considering methodological homogeneity across the studies. Three meta-analyses were conducted for the comparison of GBI%, plaque index (VPI% and API%), and gingivitis between children and adolescents with and without ADHD. In the meta-analyses assessing GBI%, data from three studies (Begnini et al. 2019; Blomqvist et al. 2011; Chau et al. 2017) were merged ($k = 3$). This meta-analysis revealed that children and adolescents with ADHD had a higher mean GBI% than children and adolescents of the control group (MD = 11.25; 95% CI [0.08, 22.41]). The results of the metrics of heterogeneity showed $I^2 = 73\%$ (95% UI [9.3%, 92.0%]), $\tau^2 = 59.3$ (95% UI [0.076, > 593.55]), and $H^2 = 3.6$ (95% UI [1.10, 12.46]) (Fig. 2). A drapery plot disaggregating the confidence interval of each study incorporated into the meta-analysis was also built (Supplementary File 6).

In the meta-analysis of plaque index, data from three studies (Begnini et al. 2019; Blomqvist et al. 2011; Chau et al. 2017) were combined ($k = 3$). This meta-analysis showed no significant difference regarding plaque index between children and adolescents with ADHD and their non-ADHD peers (MD = 4.87; 95% CI [−2.56 to 12.29]). The results of the metrics of heterogeneity demonstrated $I^2 = 62.5\%$ (95% UI [0.0%, 89.3%]), $\tau^2 = 59.3$ (95% UI [0.00, > 267.76]), and $H^2 = 2.65$ (95% UI [1.00, 12.46]) (Fig. 3). A drapery plot disaggregating the confidence interval of each study incorporated into the meta-analysis was also built (Supplementary File 7).

In the meta-analyses for the assessment of gingivitis, data from two studies (Bimstein et al. 2008; Blomqvist et al. 2007) were aggregated ($k = 2$). This meta-analysis revealed no significant difference in gingivitis between children and adolescents with and without ADHD (OR 1.42; 95% CI [0.22–9.21]). The results of the metrics of heterogeneity showed $I^2 = 75.8\%$ (95% UI [0.0%; 94.5%]), $\tau^2 = 1.34$, and

**Fig. 2** Forest plot showing the comparison of Gingival Bleeding Index (GBI%) between children with attention deficit hyperactivity disorder (ADHD) and their non-ADHD peers

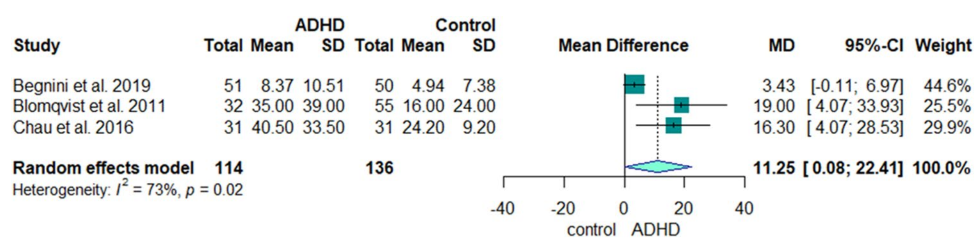
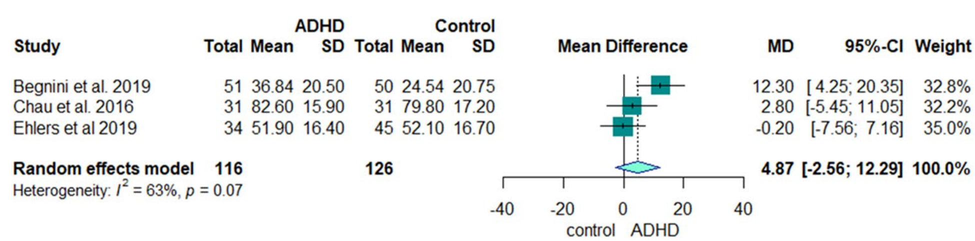



**Fig. 3** Forest plot showing the comparison of plaque index (Visual Plaque Index [VPI%] and Approximal Plaque Index [API%]) between children with attention deficit hyperactivity disorder (ADHD) and their non-ADHD peers



$H^2 = 4.12$ (95% UI [1.10, 18.23]) (Fig. 4). A drapery plot disaggregating the confidence interval of each study incorporated into the meta-analysis was also built (Supplementary File 8).

The script used to perform the meta-analyses is available in Supplementary File 9. The datasets used to conduct the meta-analyses are provided in Supplementary File 10.

**Sensitivity analysis** In the meta-analyses of GBI% and Plaque Index, sensitivity analyses were performed. In both sensitivity analyses, the study of Begnini et al. (2019) was removed due to the flaws exhibited in the risk of bias assessment. For GBI% and Plaque Index, the results remained. Children and adolescents with ADHD had a higher mean GBI% than children and adolescents of the control group (MD = 17.38; 95% CI [7.92, 26.84]) (Fig. 5). No significant difference regarding plaque index between children and adolescents with ADHD and their non-ADHD peers was observed (MD = 1.13; 95% CI [−4.36, 6.62]) (Fig. 6). In the two-sensitivity analyses, $I^2 = 0\%$, $\tau^2 = 0$ and $H^2 = 1.00$.

**Strength of evidence** The three meta-analyses exhibited issues related to risk of bias, inconsistency, indirectness, and imprecision. The strength of evidence was very low (Supplementary File 11).

**Additional information** Two reports (Blomqvist et al. 2007, 2011) shared the same sample. In the first, participants were assessed at age 13. In the second, the participants were 17 years old. Both reports were included in the narrative synthesis. However, for the quantitative synthesis, the unit of analysis was the study and not the publication. Therefore, in the quantitative synthesis, data from only one report were pooled.

We did not build funnel plots to evaluate publication bias because the number of studies whose data were aggregated into each meta-analysis was only three. Studies in which high effect sizes are provided are more likely to be published than studies showcasing lower effect sizes. Therefore, unpublished studies or studies that we were unable to retrieve in the searches might have had non-significant results (Borenstein et al. 2021) for the comparison of periodontal outcomes between ADHD and non-ADHD individuals. This trend might have the potential to nullify the effect of the meta-analysis regarding GBI%.

## Discussion

A plethora of periodontal outcomes can affect children and adolescents. In several cases, these conditions are related to biofilm. Others are associated with systemic factors,

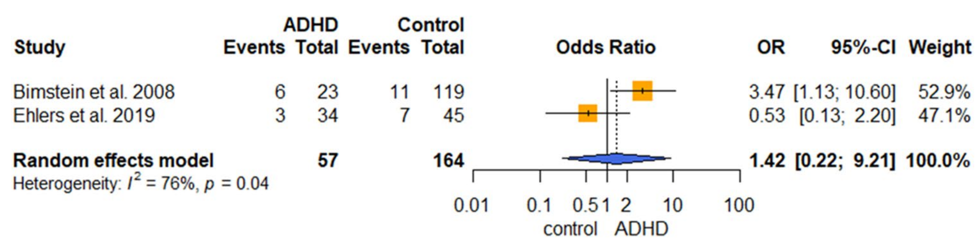



**Fig. 4** Forest plot showing the comparison of gingivitis between children with attention deficit hyperactivity disorder (ADHD) and their non-ADHD peers

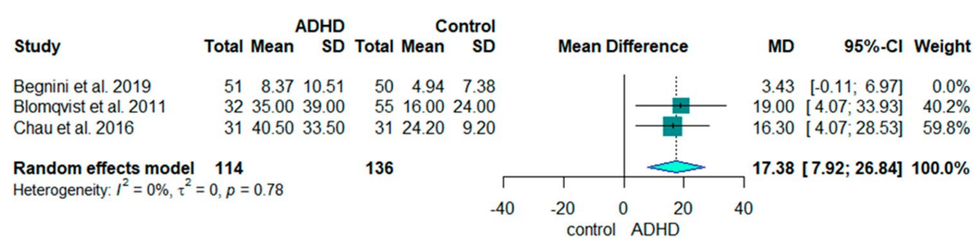



**Fig. 5** Forest plot showing the sensitivity analysis comparing the Gingival Bleeding Index (GBI%) between children with attention deficit hyperactivity disorder (ADHD) and their non-ADHD peers

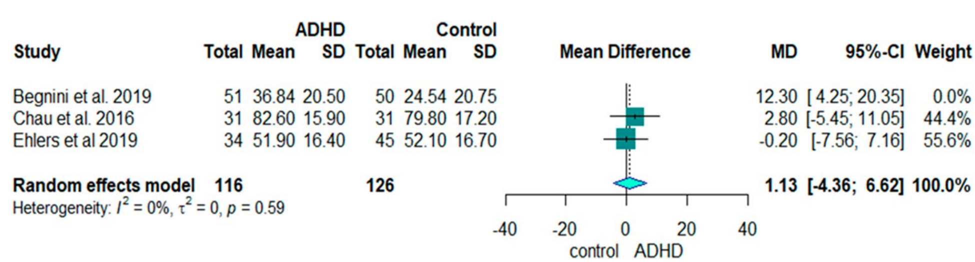



**Fig. 6** Forest plot showing the sensitivity analysis comparing the plaque index (Visual Plaque Index [VPI%] and Approximal Plaque Index [API%]) between children with attention deficit hyperactivity disorder (ADHD) and their non-ADHD peers

infections, and trauma (Albandar and Tinoco 2002). The use of some drug classes can also lead to the development of pathological processes that affect periodontal tissues (Hatahira et al. 2017). Findings from a meta-analysis demonstrated that children and adolescents with ADHD had a higher GBI% compared to their non-AHDH peers; however, no difference was observed between groups in the plaque index meta-analysis. Conversely, there is no strong evidence that individuals with ADHD have physiological changes that affect their oral cavity. However, these individuals tend to use medication that may cause changes in periodontal tissues, as observed in the study by Hasan and Ciancio (2004), which assessed the effects of amphetamines used in the management of ADHD symptoms on children's periodontal health. The results of the cited study revealed that children with ADHD were more likely to develop gingival inflammation and swelling that those without ADHD. Furthermore, these authors did not observe any difference in plaque levels between groups (Hasan and Ciancio 2004). These findings are in line with the results of the present systematic review and meta-analysis.

Norepinephrine–dopamine reuptake inhibitors are commonly used in the treatment of ADHD. The mechanism of action of this class of drugs is very similar to the mechanism of action of psychostimulants (e.g. bupropion), which is widely employed in the treatment of ADHD (Sharma and Couture 2014). Friedlander et al. (2007) evaluated the impact that these medications may have on the oral cavity of individuals with ADHD and concluded that gingivitis is an adverse effect related to the use of bupropion. Nevertheless, the body of knowledge showing the correlation between medication intake and periodontal health in these individuals is still poor. A study by Kohlboeck et al. (2013) assessed oral-related outcomes and oral hygiene in individuals with ADHD and observed that information about medication intake was provided in less than 10% of the individuals evaluated in the study, making it impossible to reach a more assertive conclusion in this regard.

Herein, a meta-analysis with dichotomous data assessing gingivitis showed no difference between individuals with ADHD and those without ADHD. This finding was a counterpoint to the results of the meta-analysis of GBI%. However, it is important to emphasise that the dichotomous assessment of gingival status does not portray the severity of gingival disease since this measure simply records the presence or absence of the disease and is not based on the number or percentage of affected sites, in contrast to the evaluation of bleeding on probing, which consists of evaluating bleeding on each of the four dental surfaces (Axelsson and Lindhe 1978; Barbano and Clemmer 1974). The logic of this line of reasoning led to the conclusion that both groups had similar results for gingivitis; however, children and adolescents with ADHD appear to have more severe levels of gingival bleeding.

Several factors such as age, oral hygiene, socioeconomical status, access to dental treatment, geographic location, and ethnicity are associated with periodontal outcomes in children and adolescents. These aspects are of particular relevance for the epidemiological evaluation of periodontal outcomes (Pinar-Erdem et al. 2018). In observational studies, strategies for dealing with confounders are crucial to understanding causality and associations between variables (Gianicolo et al. 2020). Regression analyses can be employed to control for these factors (Grimes and Schulz 2002). However, none of the included studies adopted strategies to deal with potential confounding factors associated with periodontal outcomes, a fact representing a limitation of the present systematic review and meta-analysis. In this regard, studies that implement statistical procedures to manage these confounders are needed to fully clarify the relationship between ADHD and periodontal outcomes. Longitudinal studies evaluating the influence of medications on the oral health of individuals with ADHD are also highly encouraged since the medications used in the management of ADHD appear to have implications for the oral health of individuals with this condition (Friedlander et al. 2007; Hasan and Ciancio 2004).

The results of this systematic review and meta-analysis should be appraised with caution due to the shortcomings presented by the primary studies. The most remarkable limitation concerns the lack of controlling for potential confounding factors and the design of the primary studies. All studies were cross-sectional and only $p$ values were used to report the results; thus, a causal relation between periodontal outcomes and ADHD could not be inferred (Wang and Cheng 2020). Regarding the lack of controlling for the confounding variables in primary studies, failure to control for these factors can lead to a misinterpretation of the real result regarding the association of ADHD and periodontal outcomes (Jager et al. 2008). It is also important to highlight that the results of the present systematic review and meta-analysis derive from a small number of primary studies carried out in different settings, with different samples and adopting different methods of assessment of exposure (ADHD). Another point that should be addressed concerns the intake of medication. In the studies included, the burden of medication intake by children and adolescents with ADHD and its impact on these individuals' oral health were not evaluated (Hasan and Ciancio 2004). Finally, quantitative synthesis revealed a high degree of heterogeneity and statistical inconsistency that could affect the plausibility of the clinical results (Higgins and Thompson 2002).

When compared to individuals without ADHD, children and adolescents with this special condition do not show very severe changes in tooth supporting tissues. However, some periodontal outcomes such as gingival bleeding might take place with greater intensity in young individuals with ADHD. The role of paediatric dentists and health practitioners in preventive guidance is of fundamental importance in establishing the oral health of these individuals. During appointments, tailored instructions should be given to parents and caregivers (Charles 2010; Sujlana and Dang 2013). In the counselling of guardians of children and adolescents with ADHD, information on the possible periodontal repercussions of the medications taken by young people should be highlighted (Hasan and Ciancio 2004). Among the many common features of ADHD, the literature reports poor motor coordination (Friedlander et al. 2007; Gallo and Posner 2016) that may be associated with ineffective toothbrushing. However, instructions regarding the importance of oral hygiene practices coming from the oral health provider might have contributed to encouraging parents and caregivers to assist their sons/daughters during toothbrushing. The support during oral hygiene practices may have been a major determinant of the similar levels of dental plaque between children with and without ADHD (Chau et al. 2017) observed in this systematic review and meta-analysis, reinforcing the relevance of communication between the paediatric dentist or any other health professional and the parents of individuals with ADHD in the maintenance of the oral health of the young individual. Systematic reviews and meta-analyses of observational studies may be also helpful in policy-making, allowing decision-makers to evaluate the magnitude of a particular health issue in a specific population, providing support for the identification of adequate strategies to manage those issues and of barriers that might be on the way during the process of implementation of policies that meet the needs of people (Lavis 2009).

## Conclusion

This systematic review and meta-analysis provides useful information regarding periodontal-related outcomes in children and adolescents with ADHD. The summarised evidence suggests that the periodontal health of children and adolescents with ADHD should be brought to the attention of paediatric dentists and health practitioners. Additionally, counselling and anticipatory guidance from paediatric dentists and the medical team are important in instructing parents about the repercussions of controlled medication on the oral health of this specific population.

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## Declarations

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