A Systematic Review and Meta-analysis on Bolton's ratios: Normal occlusion and Malocclusion

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Abstract

Introduction: The purposes of this study were to seek for overall ratio (OR) and anterior ratio (AR) patients data in normal occlusion and Angle's malocclusion studies, and to assess if such results support Bolton's standards as general references.

Methods: Pubmed, Medline, CENTRAL and Scholar databases were searched up to February 2018 (CRD42018088438). Gray literature was explored through OpenGray. Non-randomized clinical studies, published in English and assessing Bolton's OR and AR in normal occlusion and Angle's malocclusion groups (Class I, Class II, Class II division 1, Class 2 division 2, Class III) patients were included. OR and AR means and standard deviations (SD) were collected. Potential covariates (study design, publication year, country where the study was conducted, number of cases, gender, mesiodistal measurement method, and calibration method) were also extracted. The National Health Heart Lung, and Blood Institute's Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies was used to assess each included studies quality. Pairwise Random-Effects and Multilevel Bayesian Network Meta-Analyses were used to synthesize available data.

Results: Fifty-two observational studies were included (8872 participants; male/females 2674/3272; 16 studies lacked gender information). For normal occlusion, global pooled estimates for OR and AR means were 91.74% (95% CI: 91.37-92.10) and 78.24% (95% CI: 77.85-78.63), respectively. We could identify on Angle's Class III patients meaningful OR and AR mean deviations from normal occlusion (0.89, 95% credible interval [CrI], 0.66-1.12, and 0.66, 95% CrI, 0.38-0.94, respectively), while on Class I patients we found a meaningful mean deviation from normal occlusion only for OR (0.25, 95% CrI, 0.03-0.47). Concerning gender impact, male patients presented higher OR (0.30, 95% CI 0.00-0.59) and AR (0.41, 95% CI 0.00-0.83) mean values than females in Class I.

Conclusions: The results show that global pooled OR and AR mean values for normal occlusion patients are slightly above Bolton's original values. Class I, for OR mean values, and Class III, for both OR and AR, are proportionally larger than normal occlusion patients. Gender had almost no impact on teeth mesiodistal proportion.

Keywords: Tooth size; Tooth size discrepancy; Bolton ratios; Meta-analysis; Systematic review

Introduction

As once mentioned, an appropriate balance of mesiodistal tooth widths between maxillary and mandibular arches allows for a proper interdigitation, overbite, and overjet in a normal occlusion, with the best possible esthetic and function (1). Currently, the extent of mesiodistal movement roots clinical practice from conventional treatment to orthodontic aligners concept and has allured clinical interest, particularly in anteroposterior malocclusions correction (2,3).

The concept of a proportional balance between the mesiodistal sums of maxillary and mandibular teeth may have had its origins in the geometric theories of dental articulation previously proposed. In 1899, Bonwill (4) attempted to develop a geometric theory of occlusion, stating that "Nature left to herself, always brings proposition… the proportions of upper teeth to the lower teeth are as exact as any". This nature theory was pervasive in early orthodontics and was seen in the strict non-extraction period started by Edward Angle. Firmly, the mesiodistal widths of teeth were initially investigated by Black (5). Historically, Young (6) was the first to devote attention to intermaxillary tooth width ratio in occlusion, and, thereafter, Gilpatric (7) found that the upper arch was 8 to 12 millimeters wider than the lower arch. Over the years, to account and aware this proportion, several methods have been proposed to assess interarch tooth size relationship (1,8–11), but Bolton's ratios have become widely applied in orthodontics' research.

In this regards, the overall ratio (OR) is the percentage obtained by summing the widths of the 12 mandibular teeth divided by the sum of the widths of the 12 maxillary teeth. Also, the anterior ratio (AR) is the percentage obtained by summing the widths of the six mandibular anterior teeth divided by the sum of the widths of the six maxillary anterior teeth (1,11). In average, OR were of 91.3% (± 1.91) and AR were of 77.2% (± 1.65), respectively, and these promptly became standard values in the diagnosis and guidance of orthodontic treatments.

Over time, Bolton's analysis have proved to be clinically useful in extreme teeth size discrepancies. However, without neglecting his valuable contribution, its methodology and conclusions should be carefully evaluated. First, these studies had a potential selection bias since the population was not specified, particularly concerning races, ethnicities, and gender. Second, although the author has stated that his ratios were based on 55 cases "where excellent occlusions existed", 44 models were from patients who have undergone orthodontic treatment, and only 11 were untreated (1).

According to literature, teeth size variation is ethnic- and gender-related (5,12–16) pointing out an anthropological significance with genetic underpinnings (17,18). For this reason, the application of Bolton analyses and the proposed standard values for a harmonious dentition might not be valid for other populations. Therefore, this population-based variation has became a subject of interest for many researchers, which led to the attempt to establish normative standards for different racial groups (12,14,19–21).

Another relevant question is the relationship between the tooth size discrepancy for both OR and AR and the various types of Angle's malocclusion. Although several investigators have emphasized the relationship between Bolton ratios discrepancy and malocclusions in multiple populations (14,22–26), there is no consensus about its correlation with the different types of malocclusions classified by Angle.

Objectives

No study has investigated, in an evidence-based manner, normative values for mesiodistal proportions from systematically researched worldwide data in normal occlusion and Angle's malocclusions. For that reason, the primary aim of this systematic review was to synthesize global estimates for normal occlusion OR and AR mean values, and to compare such values with those proposed by Bolton, to address the following focused question: are current standards globally appropriate? Secondly, we intended to obtain OR and AR global pooled estimates for each type of Angle's malocclusion and compare them against the obtained values for normal occlusion under a multilevel bayesian network meta-analysis model.

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Materials and Methods

Protocol and registration

The protocol for this systematic review was made a priori, agreed upon by all authors and registered in PROSPERO (ID Number: CRD42018088438). This systematic review was conducted according to the Cochrane Handbook (27) and reported according to the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (28) (Supplement Table S1) and its extension for abstracts (29).

There were involved two researchers from the Orthodontics Department, Clinical Research Unit, CiiEM, [Instituto Universitário Egas Moniz]: VM and AD; and three researchers from the Clinical Research Unit, CiiEM, [Instituto Universitário Egas Moniz]: JB, PM and JJM.

Eligibility criteria

Studies were eligible for inclusion based on the following criteria:

1. Observational studies (randomized and non-randomized study cohort/longitudinal study, cross-sectional study).
2. English language studies.
3. human study population.
4. determined Bolton's analysis with normal occlusion, and/or Angle's Class I, Class II, Class II division 1, Class II division 2 and/or Class III, in patients without previous orthodontic treatment.
5. dental casts or digital models with all permanent teeth from the maxillary and mandibular right first molar to the left first molar completely erupted, without tooth deformities, mesiodistal restorations, caries or abrasion that could affect the teeth's mesiodistal diameter.
6. The study measured the largest mesiodistal teeth dimension to the nearest 0.01 mm, through digital caliper or software.

Narrative reviews, case reports, and case series studies were excluded from review.

Search strategy

A systematic search was conducted and updated in February 2018, covering the following electronic databases: Pubmed, Medline, CENTRAL and Scholar. The strategy used for the electronic search was the following: ["Bolton ratio"OR"tooth size discrepancy"OR"Bolton discrepancy"OR"tooth-size ratios"OR"tooth-size measurement"OR"Bolton analysis"].

No limitations were applied regarding publication year. The reference lists of included articles and relevant reviews were manually searched. Gray literature was searched using the latter strategy in OpenGray. Authors were contacted when necessary for additional data or clarifications.

Assessment of Validity

The eligibility of each study was assessed independently by two investigators (VM and JB), who screened the titles and/or abstracts of retrieved studies. Inclusion was dependent on the following eligibility criteria: randomized or non-randomized trials with OR and/or AR data. Final selection of studies was performed by three authors independently (JB, VM, PM), and verified by a fourth and fifth authors (JJM, AD), by reviewing the full text based on inclusion criteria above. Discussion resolved any disagreements. Non-full papers, such as conference abstracts and letters to editors, were excluded.

Data extraction

Data were extracted to a predefined table. We used information about: the first author's name, study design, publication year, country and continent where the study was conducted, number of cases and participants, gender, tooth width measurement method, OR and AR (mean and standard deviation). Type of occlusion was classified into normal occlusion, Angle's Class I, Class II (division 1 and division 2) or Class III. Populations were categorized into continental groups: African, American, Asia (including Japanese populations based in Hawaii), European, and Oceania. We extracted Bolton OR, AR means and standard deviations, for both gender, in all selected studies population samples. Concerning additional data/clarifications, we tried to contact corresponding authors (on 23rd of February 2018).

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Quality assessment and Risk of Bias in Included Studies

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies statement proposed by National Heart, Lung, and Blood Institute (NIHLBI) was used to appraise study quality (from https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). The checklist was adapted since criteria 7, 8, 10 and 13 did not apply. The reviewers (VM, JB) determined a global quality score for each article. Each methodologic quality criterion was assigned a point, to a total maximum of 10 achievable points. Studies reaching 9 or 10 points were arbitrarily considered of high quality, studies with 7 or 8 points were classified as medium quality, and studies with 6 points or less considered of low methodologic quality. To be included, articles had to be at least of medium quality. Furthermore, data extracted from selected studies were screened for precision inconsistencies, to prevent an unbalanced contribution of some studies data in the meta-analysis.

Summary Measures & Synthesis of Results

The objective of synthesis of the normal occlusion OR and AR mean values was accomplished by pairwise random effects meta-analysis using OpenMetaAnalyst (2016) [26] software. Quantity I^2 was measured to account for the degree of dispersion of Bolton ratios mean estimates, and the overall homogeneity statistical significance was calculated through the $\chi 2$ test [22]. Funnel plots were used to visualize and quantify meta-analysis publication bias, respectively, if appropriate [28–33] All tests were two-tailed with alpha set at 0.05 except for homogeneity test whose significance level cutoff was considered to be 0.10 due to the low power of the $\chi 2$ test with a limited amount of studies. Unpaired z-test was used to compare our normal occlusion mean results with Bolton original values, with significance level set at 5%.

In a number of articles [22,38–46], Class II division 1 and division 2 summary statistics were published separately, and it was necessary to calculate the combined mean ($\bar{x}_{12}$) and standard deviation (σ_{12}) for the overall Class II through the following formulas:

$$\bar{x}_{12} = \frac{N_1 \cdot \bar{x}_1 + N_2 \cdot \bar{x}_2}{N_1 + N_2}$$

$$\sigma_{12} = \sqrt{\frac{\left(N_1 - 1\right) \cdot \sigma_1^2 + \left(N_2 - 1\right) \cdot \sigma_2^2 + \frac{N_1 \cdot N_2}{N_1 + N_2} \cdot \left(\bar{x}_1^2 + \bar{x}_2^2 - 2\bar{x}_1\bar{x}_2\right)}{N_1 + N_2 - 1}}$$

Similarly, in McSwiney [41] and Nie [47] studies, it was published data for surgical and non-surgical in Class III, and we used the aforementioned formula to combine the mean and standard deviation.

To fulfill the second objective, we were required to estimate OR and AR global mean of Angle's malocclusion types (Class I, Class II, Class II division 1, Class II division 2 and Class III) and compare each them against the normal occlusion global mean value. Due to the complexity of the distribution of the extracted data across the selected reports, we aimed to address such issue globally under a multilevel Bayesian Network Meta-Analysis (Bayesian NMA) model. Therefore, we went through Rstan, a R package that inter-connects R and STAN languages making easy the design and handling of such complex model. Thus, we fitted a model with continuous outcome data, given as the randomly distributed differences between the occlusion classes means (including the normal occlusion class), with normally distributed likelihood and identity as link function. We sourced the initial mean and variance for AR and OR normal occlusion values from the Pairwise Meta-Analysis (Pairwise MA). Furthermore, for every study reporting mean values for several different OR and AR occlusion classes, it was necessary to account for the correlation between the classes differences, when the same class is used, within the same study, as baseline for difference of means determination. Therefore, we modeled all of the classes differences (across all of the studies) using a single multivariate normal distribution with a vector as mean and with a covariance matrix. Some of the covariances were zero, since classes differences sourced from different studies are not correlated. On the other hand,t the covariances for the differences sharing the same reference class within the same study were set to the variance of the shared reference class (for instance the normal occlusion class), as this was the within study "shared" variance. Sampling from the posterior

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distribution was performed by running three Hamiltonian Monte Carlo chains of 100,000 iterations each, after a warmup of 40,000. The function returned fit statistics that included adjusted estimates and associated credibility intervals (CrI; 2.5 to 97.5 percentiles) for all mean values of malocclusion classes and malocclusion classes mean differences to normal occlusion. We performed both random effects and fixed effects bayesian approaches and lately selected the fixed-effects variant results because was the one with the lowest Deviance Information Criteria (DIC).

RESULTS

Study Selection

The initial electronic database search resulted in a total of 2700 articles, leaving 2533 articles after the removal of duplicates. No additional relevant articles were identified following a hand search of reference lists. Following title and abstract screening, 178 studies were selected for full-text evaluation. After full-text eligibility assessment, 119 studies were excluded (Supplement Table S2). Five studies were excluded for presenting low quality and high risk of bias (in the Risk of bias across studies section). Two articles only reported data for Class I malocclusion, preventing its inclusion in the Bayesian Network Meta-Analysis. At last, fifty-two studies were included in this review (Figure 1).

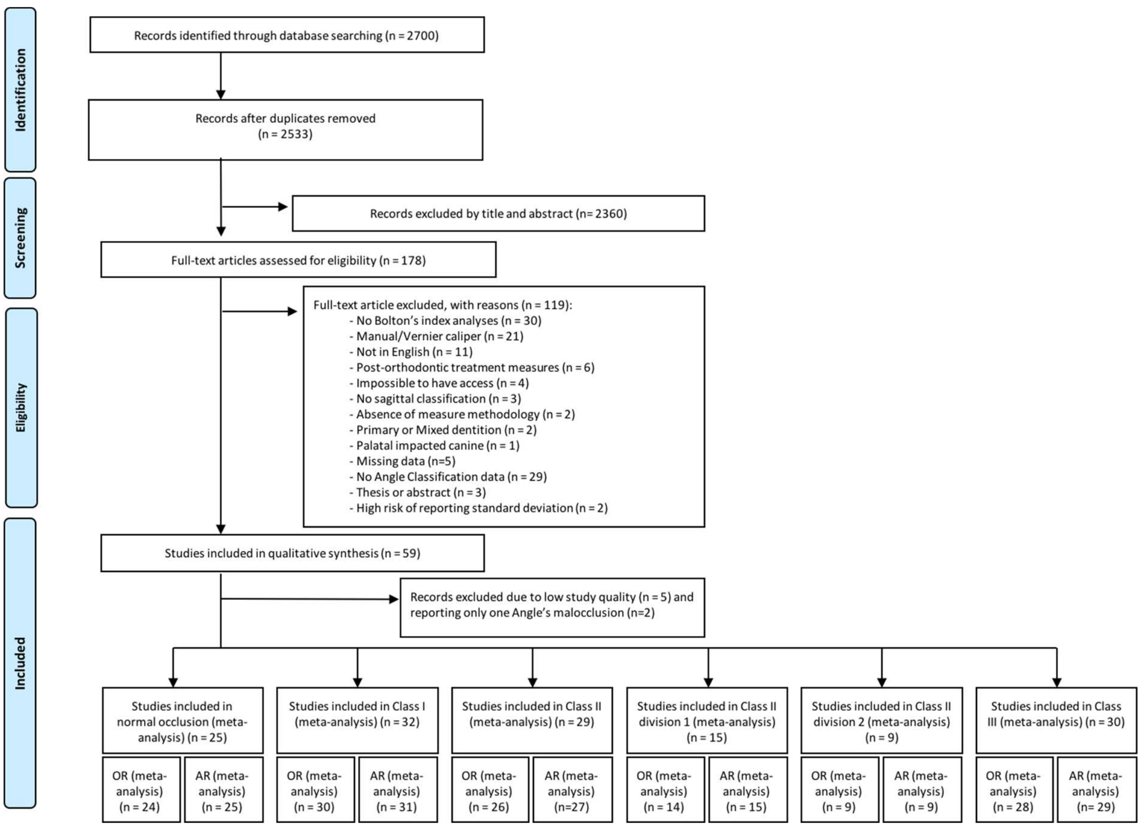

Figure 1: Flowchart of the study selection process.

Study Characteristics

Setting

Table 1 summarizes the characteristics of the included studies. Globally, the analysis included 8872 participants (2614 men and 3272 women). However, sixteen studies (25,26,30–43) lacked gender information (2986 participants). Additionally, two multicentre study (12,34) included samples from 2 and 3 different countries and from different continents and, consequently, they were counted as three samples, although in Lavelle (12) the author did not specify the African country preventing it from being analyzed in meta-regression.

Table 1 and Figure 2 shows that only one study with normal occlusion subjects (12) was published in the 70', and thereafter was a lack of published reports for almost 30 years. Additionally, the first author that investigated the Bolton ratios in Angle's malocclusion groups was Crosby at 1989 (39), more than 30 years after Bolton's article (1). After 1999 larger datasets were published on different continents. Fifty-two cross-sectional studies from four different continents, namely Africa (12,30,34,36,44–46), Asia (12,24,25,31,32,34,35,37,38,40–42,47–58), South America (26,33,39,59–66), and Europe (12,22,43,67–74) were included in the qualitative synthesis. Lavelle's (12) and Al-Duliamy's (34) were multicentric studies that comprised European, Asian, and African subjects, and Asian and African participants, respectively. Notably, no study was performed in Oceania nor North America. Due to the inadequacy of continent representation, continent subgroup analysis was not conceivable to perform.

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Table 1: Baseline characteristics for studies included in pairwise meta-analysis and Bayesian network meta-analysis.

Study (Year) (Country) (City)	Continent	Subjects (N)	Female / Male	Method	Total OR (SD)	Total AR (SD)	Female / Male OR (SD)	Female / Male AR (SD)	Included in Pairwise Meta-analysis	Included in Bayesian network meta-analysis
				Normal occlusion						
Machado et al. (2018) (Portugal) (Almada)	Europe	29	10 / 19	Digital caliper (0,01 mm)	92.1 (2.2)	78.4 (3.5)	91.7 (2.2) / 92.9 (2.1)	77.9 (3.1) / 79.3 (4.1)	Yes	Yes
Patel et al. (2017) (India) (Pune)	Asia	50	25 / 25	Digital caliper (0,01 mm)	92.73 (2.69)	80.8 (2.86)	91.92 (3.4) / 93.55 (1.36)	80.34 (3.27) / 80.6 (2.45)	Yes	No
Sakoda et al. (2016) (Brazil) (São Paulo)	America	90	45 / 45	Digital caliper (0,01 mm)	91.63 (1.95)	77.57 (2.45)	91.35 (1.87) / 91.91 (2.04)	77.3 (2.28) / 77.85 (2.64)	Yes	No
Shahid et al. (2016) (Pakistan) (different states)	Asia	128	64 / 64	Digital caliper (0,01 mm)	92.8 (2.79)	79.25 (3.81)	93.1 (2.4) / 92.5 (3.1)	79.5 (3.6) / 79 (4.4)	Yes	No
Lombardo et al. (2016) (USA) (New York)	Europe	56	22 / 34	Intraoral Scanner (3shape)	91.56 (2)	77.65 (2.46)	91.55 (2) / 91.57 (2)	77.88 (2) / 77.3 (3)	Yes	No
Chugh et al. (2015) (India) (Lucknow)	Asia	50	25 / 25	Digital caliper (0,01 mm)	91.88 (1.99)	79.64 (2.61)	91.8 (2.34) / 91.96 (1.63)	79.16 (2.23) / 80.12 (1.73)	Yes	Yes
Bugaighis et al. (2015) (Libya) (Benghazi)	Africa	15	NS	Digital caliper (0,01 mm)	90.24 (1.89)	76.88 (2.42)	NS	NS	Yes	Yes
Ismail et al. (2015) (Sudan) (Khartoum)	Africa	55	25 / 30	Digital caliper (0,1 mm)	91.47 (2.83)	77.46 (3.16)	91.25 (2.94) / 91.73 (2.9)	77.22 (3.43) / 77.73 (2.82)	Yes	Yes
Hashim et al. (2015) (Sudan) (Khartoum)	Africa	60	30 / 30	Digital caliper (0,01 mm)	90.8 (3.5)	76.9 (3.6)	90.6 (3.1) / 91 (3.9)	77 (3.7) / 76.9 (3.6)	Yes	No
Ricci et al. (2013) (Brazil) (São Paulo)	America	35	NS	Digital caliper (0,01 mm)	90.38 (1.58)	77.49 (2.2)	90.36 (1.7) / 90.44 (1.2)	77.73 (2.39) / 76.68 (1.19)	Yes	Yes
Celikoglu et al. (2013) (Turkey) (Karadeniz Ereğli)	Europe	26	14 / 12	CBCT	90.69 (2.21)	77.58 (2.71)	NS	NS	Yes	No
Jóias et al. (2011) (Brazil) (São Paulo)	America	35	8 / 27	Digital caliper (0,01 mm)	NS	77.48 (2.22)	NS	77.61 (2.45) / 77.05 (1.1)	Yes	No
Fernandes et al. (2011) (Brazil) (Bauru)	America	140	70 / 70	Digital caliper (0,01 mm)	91.32 (1.98)	77 (2.71)	90.87 (1.94) / 91.77 (1.96)	76.54 (2.79) / 77.46 (2.61)	Yes	No
Manopatanakul et al. (2011) (Thailand) (Bangkok)	Asia	37	NS	Digital caliper (0,01 mm)	91.66 (1.74)	77.09 (2.18)	NS	NS	Yes	No
Lee et al. (2011) (South Korea)	Asia	307	188 / 119	Digital caliper (0,01 mm)	90.42 (1.94)	77.54 (2.54)	90.3 (2) / 90.5 (1.9)	77.6 (2.6) / 77.5 (2.5)	Yes	No

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Oktay et al. (2010) (Turkey) (Erzurum)	Europe	100	61 / 39	RMI 550 3D (0,01 mm)	92.1 (1.95)	79.28 (2.53)	91.63 (2.04) / 92.39 (1.84)	79.17 (2.65) / 79.35 (2.47)	Yes	Yes
Jóias et al. (2010) (Brazil) (São Paulo)	America	35	8 / 27	Intraoral Scanner (3shape)	91.58 (2.2)	78.66 (2.72)	NS	NS	Yes	No
Freire et al. (2007) (Brazil) (Rio de Janeiro)	America	30	15 / 15	Digital caliper (0,01 mm)	91.46 (1.63)	77.83 (2.19)	NS	NS	Yes	No
Endo et al. (2007) (Japan) (Niigata)	Asia	60	30 / 30	Digital caliper (0,01 mm)	91.6 (2.11)	78.39 (2.18)	91.69 (2.35) / 91.51 (1.88)	78.57 (2.19) / 78.21 (2.18)	Yes	No
Ciger et al. (2006) (Turkey) (Hacettepe)	Europe	125	55 / 70	Digital caliper (0,01 mm)	91.95 (2.2)	77.95 (2.35)	91.82 (1.99) / 91.97 (1.65)	78.43 (2.41) / 78.62 (2.24)	Yes	Yes
Carreiro et al. (2005) (Brazil) (Paraná)	America	41	20 / 21	Microscribe 3DX	91.76 (2.51)	78.24 (3.4)	NS	NS	Yes	Yes
Uysal et al. (2005) (Turkey) (Konya)	Europe	150	72 / 78	Digital caliper (0,01 mm)	91.9 (3.21)	78.56 (3.23)	91.73 (2.26) / 89.83 (2.33)	78.33 (2.42) / 78.18 (2.82)	Yes	Yes
Alkofide et al. (2002) (Saudi Arabia) (Jeddah)	Asia	60	NS	Digital caliper (0,01 mm)	93.58 (2.12)	78.86 (2.55)	92.36 (2.37) / 92.12 (1.67)	78.79 (3.19) / 78.75 (2.27)	Yes	Yes
Nie et al. (1999) (China) (Beijing)	Asia	60	30 / 30	Software	93.27 (2.48)	81.52 (2.82)	93.11 (2.64) / 93.44 (2.35)	81.1 (2.27) / 81.95 (2.28)	Yes	Yes
	Europe	40	20 / 20	Digital caliper (0,1 mm)	91.25 (2)	77.15 (1.6)	90.8 (1.85) / 91.7 (2.04)	77.5 (1.62) / 76.8 (1.49)	Yes	No
Lavelle et al. (1972)	Africa	40	20 / 20	Digital caliper (0,1 mm)	93.2 (2.11)	79 (2.02)	92.9 (1.78) / 93.5 (2.35)	78.6 (1.89) / 79.4 (2.06)	Yes	No
	Asia	40	20 / 20	Digital caliper (0,1 mm)	92.75 (1.53)	78.45 (1.55)	92.1 (1.55) / 92.6 (2.47)	78.2 (1.38) / 78.7 (1.66)	Yes	No
				Class I						
Machado et al. (2018) (Portugal) (Almada)	Europe	50	29 / 21	Digital caliper (0,01 mm)	92.90 (2.70)	79.30 (4.00)	93.4 (2.30) / 92.50 (2.90)	79.60 (2.90) / 79.00 (4.60)	-	Yes
Saritha et al. (2017) (India) (Telangana)	Asia	168	110 / 58	Digital caliper (0,01 mm)	92.38 (1.86)	79.37 (2.98)	92.39 (1.95) / 92.38 (1.82)	79.49 (2.37) / 79.30 (3.27)	-	Yes
Mahmoud et al. (2017) (Sudan) (Khartoum)	Asia	52	NS	Digital caliper (0,05 mm)	91.37 (2.98)	78.44 (2.91)	NS	NS	-	Yes
Elsheikhi et al. (2017) (Libya) (Benghazi)	Africa	20	10 / 10	Digital caliper (0,01 mm)	89.91 (1.79)	74.42 (2.06)	NS	NS	-	Yes
Cançado et al. (2016) (Brazil) (Dourados)	America	321	NS	Digital caliper (0,01 mm)	91.61 (2.04)	78.37 (2.68)	NS	NS	-	Yes
Al-Duliamy Iraq et al. (2016) (Iraq) (Baghdad)	Asia	70	NS	Digital caliper (0,01 mm)	91.23 (2.20)	78.72 (4.53)	NS	NS	-	Yes
Al-Duliamy Egypt et al. (2016) (Egypt)	Africa	70	NS	Digital caliper (0,01 mm)	91.63 (2.58)	78.85 (2.79)	NS	NS	-	Yes

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Chugh et al. (2015) (India) (Lucknow)	Asia	50	25 / 25	Digital caliper (0,01 mm)	93.06 (2.28)	79.6 (3.02)	93.35 (2.31) / 92.79 (2.28)	80.17 (3.13) / 79.09 (2.92)	-	Yes
Shastri et al. (2015) (India (North)) (Lucknow)	Asia	40	NS	Digital caliper	91.73 (3.6)	76.89 (4.16)	NS	NS	-	Yes
Bughaighis et al. (2015) (Libya) (Benghazi)	Africa	220	NS	Digital caliper (0,01 mm)	91.55 (2.4)	78.29 (2.53)	NS	NS	-	Yes
Ismail et al. (2015) (Sudan) (Khartoum)	Africa	49	26 / 23	Digital caliper (0,1 mm)	91.47 (2.83)	77.46 (3.16)	91.51 (3.27) / 91.39 (2.54)	77.00 (4.65) / 76.55 (3.34)	-	Yes
Maurya et al. (2015) (India) (Madhya Pradesh)	Asia	60	30 / 30	Digital caliper (0,01 mm)	92.38 (2.51)	80.13 (3.48)	93.03 (2.34) / 91.72 (2.58)	80.86 (3.28) / 79.40 (3.64)	-	Yes
Zerouaoui et al. (2014) (Morocco) (Rabat)	Africa	30	NS	Digital caliper	91.37 (2.05)	77.93 (2.60)	NS	NS	-	Yes
Jindal et al. (2013) (India) (Punjab)	Asia	300	150 / 150	Digital caliper (0,01 mm)	92.75 (3.15)	79.82 (3.85)	93.93 (3.34) / 91.58 (2.44)	80.87 (43135) / 78.77 (3.38)	-	Yes
Asma et al. (2013) (Malaysia) (Selangor)	Asia	50	NS	Digital caliper (0,01 mm)	NS	78.83 (4.06)	NS	NS	-	Yes
Ricci et al. (2013) (Brazil) (São Paulo)	America	35	NS	Digital caliper (0,01 mm)	91.19 (2.70)	78.16 (2.87)	91.25 (3.24) / 91.17 (2.58)	78.66 (3.64) / 78.01 (2.66)	-	Yes
Ali Hyder et al. (2012) (Bangladesh) (Dhaka)	Asia	40	20 / 20	Digital caliper (0,01 mm)	90.40 (2.69)	77.70 (2.81)	89.82 (3.06) / 91.06 (2.18)	77.92 (2.80) / 77.49 (2.87)	-	Yes
Kansal et al. (2012) (India) (Karnataka)	Asia	231	NS	Digital caliper (0,01 mm)	91.80 (3.30)	79.20 (3.80)	NS	NS	-	Yes
O'Mahony et al. (2011) (Ireland) (Cork)	Europe	60	30 / 30	OrhoAnalyzer (Software)	92.30 (2.20)	79.00 (43376)	92.4 (2.20) / 92.10 (2.20)	78.40 (2.90) / 79.60 (3.20)	-	Yes
Vela et al. (2011) (USA) (Texas)	America	207	110 / 97	Digital caliper (0,01 mm)	NS	78.97 (2.29)	NS	79.12 (1.99) / 78.84 (2.49)	-	No
Endo et al. (2010) (Japan) (Niigata)	Asia	66	33 / 33	Digital caliper (0,01 mm)	91.10 (2.20)	NS	91.18 (2.27) / 91.01 (2.17)	NS	-	Yes
Oktay et al. (2010) (Turkey) (Erzurum)	Europe	100	65 / 35	RMI 550 3D (0,01 mm)	92.27 (2.16)	78.61 (2.80)	92.33 (1.88) / 92.24 (2.32)	78.66 (2.41) / 78.58 (3.01)	-	Yes
Strujić et al. (2009) (Croatia) (Zagreb)	Europe	110	68 / 42	Digital caliper (0,01 mm)	91.81 (1.99)	78.25 (2.58)	NS	NS	-	Yes
Endo et al. (2009) (Japan) (Niigata)	Asia	101	59 / 42	Digital caliper (0,01 mm)	91.15 (2.14)	77.84 (2.46)	91.14 (2.33) / 91.15 (1.99)	77.97 (2.55) / 77.74 (2.39)	-	Yes
Endo et al. (2008) (Japan) (Niigata)	Asia	60	30 / 30	Digital caliper (0,01 mm)	91.01 (1.91)	77.48 (2.17)	91.14 (2.09) / 90.88 (2.20)	77.63 (1.82) / 77.33 (2.49)	-	Yes
Al Sulaimani et al. (2006) (Saudi Arabia) (Jeddah)	Asia	98	62 / 36	Ortho-l software	93.90 (4.07)	81.11 (5.07)	NS	NS	-	Yes
Ciger et al. (2006) (Turkey) (Hacettepe)	Europe	125	70 / 55	Digital caliper (0,01 mm)	91.95 (2.20)	77.95 (2.35)	91.97 (1.65) / 91.82 (1.99)	78.62 (2.24) / 78.43 (2.41)	-	Yes

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Carreiro et al. (2005) (Brazil) (Panamá)	America	44	22 / 22	Microscribe 3DX	92.13 (2.08)	77.13 (3.15)	NS	NS	-	Yes
Uysal et al. (2005) (Turkey) (Konya)	Europe	156	150 / 6	Digital caliper (0,01 mm)	91.90 (3.21)	78.56 (3.23)	91.65 (3.51) / 91.57 (2.98)	78.18 (3.31) / 78.44 (3.18)	-	Yes
Laino et al. (2004) (Italy) (Campania)	Europe	57	31 / 26	Digital caliper (0,01 mm)	91.72 (2.20)	78.12 (2.41)	NS	NS	-	Yes
Araújo et al. (2003) (Brazil) (Belo Horizonte)	America	100	58 / 42	Digital caliper (0,01 mm)	NS	78.18 (2.85)	NS	NS	-	Yes
Alkofide et al. (2002) (Saudi Arabia) (Jeddah)	Asia	60	30 / 30	Digital caliper (0,01 mm)	92.24 (2.04)	78.77 (2.74)	92.12 (1.67) / 92.36 (2.37)	78.75 (2.27) / 78.79 (3.19)	-	Yes
Ta et al. (2001) (Hong Kong) (Sheung Wan)	Asia	50	25 / 25	Digital caliper (0,01 mm)	90.65 (1.19)	77.55 (1.80)	91.10 (1.00) / 90.20 (1.20)	77.60 (1.80) / 77.50 (1.80)	-	Yes
Nie et al. (1999) (China) (Beijing)	Asia	60	30 / 30	Software (0,01 mm)	93.27 (2.48)	81.52 (2.82)	93.62 (2.42) / 93.41 (2.53)	81.87 (2.51) / 81.25 (2.87)	-	Yes
Crosby et al. (1989) (USA) (Texas)	America	30	NS	Digital caliper (0,01 mm)	91.30 (2.40)	77.2 (2.70)	NS	NS	-	Yes
				Class II						
Machado et al. (2018) (Portugal) (Almada)	Europe	51	36 / 15	Digital caliper (0,01 mm)	91.51 (2.69)	78.6 (3.59)	91.49 (2.11) / 91.57 (3.01)	77.96 (3.58) / 78.93 (3.64)	-	Yes
Saritha et al. (2017) (India) (Telangana)	Asia	103	70 / 33	Digital caliper (0,01 mm)	92.296 (1.997)	78.642 (2.868)	92.14 (1.9) / 92.37 (2.05)	78.21 (2.56) / 78.84 (2.99)	-	Yes
Mahmoud et al. (2017) (Sudan) (Khartoum)	Asia	44	NS	Digital caliper (0,05 mm)	90.85 (2.64)	78.14 (4.35)	NS	NS	-	Yes
Cançado et al. (2016) (Brazil) (Dourados)	America	324	NS	Digital caliper (0,01 mm)	91.46 (2.06)	78.31 (2.39)	NS	NS	-	Yes
Al-Duliamy Iraq et al. (2016) (Iraq) (Baghdad)	Asia	40	NS	Digital caliper (0,01 mm)	91.54 (2.66)	79.05 (2.64)	NS	NS	-	Yes
Al-Duliamy Egypt et al. (2016) (Egypt) (Cairo)	Africa	40	NS	Digital caliper (0,01 mm)	89.14 (5.13)	78.46 (3.97)	NS	NS	-	Yes
Shastri et al. (2015) (India (North)) (Lucknow)	Asia	50	NS	Digital caliper	90.77 (2.13)	81.1 (5.01)	NS	NS	-	Yes
Bughaighis et al. (2015) (Libya) (Benghazi)	Africa	85	NS	Digital caliper (0,01 mm)	91.5 (2.43)	78.1 (2.73)	NS	NS	-	Yes
Ismail et al. (2015) (Sudan) (Khartoum)	Africa	59	27 / 22	Digital caliper (0,1 mm)	92.05 (3.11)	77.45 (4.8)	92.22 (3.84) / 91.92 (2.35)	77.17 (6.05) / 77.68 (3.44)	-	Yes
Maurya et al. (2015) (India) (Madhya Pradesh)	Asia	60	30 / 30	Digital caliper (0,01 mm)	91.69 (2.4)	79.06 (2.56)	91.67 (1.92) / 91.7 (2.87)	77.98 (1.95) / 80.14 (2.7)	-	Yes
Zerouaoui et al. (2014) (Morocco)	Africa	30	NS	Digital caliper	92.597 (2.41398)	79.5975 (2.94213)	NS	NS	-	Yes

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(Rabat)										
McSwiney et al. (2014) (Ireland) (Dublin)	Europe	60	30 / 30	Software (0,01 mm)	90.2 (2.27)	76.5 (2.77)	89.9 (2.31) / 90.5 (2.24)	76.5 (2.87) / 76.55 (2.7)	-	Yes
Asma et al. (2013) (Malaysia) (Selangor)	Asia	100	NS	Digital caliper (0,01 mm)	NS	79.54 (4.37)	NS	NS	-	Yes
Ali Hyder et al. (2012) (Bangladesh) (Dhaka)	Asia	40	20 / 20	Digital caliper (0,01 mm)	90.9 (2.79)	78.5 (3.93)	91.31 (2.25) / 90.56 (3.25)	78.7 (3.88) / 78.37 (4.08)	-	Yes
Kansal et al. (2012) (India) (Karnataka)	Asia	254	NS	Digital caliper (0,01 mm)	91.52 (3.37)	79.1 (3.94)	NS	NS	-	Yes
O'Mahony et al. (2011) (Ireland) (Cork)	Europe	120	60 / 60	OrhoAnalyzer (Software)	92.2 (2.19)	79.4 (3.36)	92.3 (2.31) / 92.05 (2.03)	79.5 (3.56) / 79.35 (3.2)	-	Yes
Endo et al. (2010) (Japan) (Niigata)	Asia	66	33 / 33	Digital caliper (0,01 mm)	91.38 (1.88)	NS	91.48 (1.91) / 91.28 (1.87)	NS	-	Yes
Oktay et al. (2010) (Turkey) (Erzurum)	Europe	200	124 / 76	RMI 550 3D (0,01 mm)	92.06 (2.16)	78.67 (2.53)	92.32 (2.1) / 91.9 (2.18)	78.43 (2.46) / 78.48 (2.58)	-	Yes
Strujić et al. (2009) (Croatia) (Zagreb)	Europe	109	60 / 49	Digital caliper (0,01 mm)	91.14 (2.14)	77.73 (2.42)	NS	NS	-	Yes
Endo et al. (2009) (Japan) (Niigata)	Asia	78	42 / 36	Digital caliper (0,01 mm)	91.57 (2.34)	77.68 (2.38)	91.47 (1.91) / 91.66 (2.65)	78.22 (2.25) / 78.07 (2.41)	-	Yes
Endo et al. (2008) (Japan) (Niigata)	Asia	60	30 / 30	Digital caliper (0,01 mm)	91.3 (1.94)	77.93 (2.25)	91.43 (1.98) / 91.17 (1.91)	77.92 (2.26) / 77.93 (2.29)	-	Yes
Al Sulaimani et al. (2006) (Saudi Arabia) (Jeddah)	Asia	52	34 / 18	Ortho-l software	93.06 (3.65)	81.88 (4.31)	NS	NS	-	Yes
Uysal et al. (2005) (Turkey) (Konya)	Europe	191	105 / 86	Digital caliper (0,01 mm)	91.27 (3.35)	78.59 (3.48)	NS	NS	-	Yes
Laino et al. (2004) (Italy) (Campania)	Europe	24	18 / 6	Digital caliper (0,01 mm)	91.24 (1.85)	78.04 (2.35)	NS	NS	-	Yes
Araújo et al. (2003) (Brazil) (Belo Horizonte)	America	100	48 / 52	Digital caliper (0,01 mm)	NS	78.16 (2.21)	NS	NS	-	Yes
Alkofide et al. (2002) (Saudi Arabia) (Jeddah)	Asia	60	60 / 60	Digital caliper (0,01 mm)	92.8 (2.2)	78.7 (2.45)	92.5 (2.17) / 93.1 (2.23)	78.56 (2.73) / 78.84 (2.17)	-	Yes
Ta et al. (2001) (Hong Kong) (Sheung Wan)	Asia	30	15 / 15	Digital caliper (0,01 mm)	91.4 (1.69)	77.75 (1.56)	91.4 (1.8) / 90.4 (0.7)	77.8 (1.7) / 77.7 (1.4)	-	Yes
Nie et al. (1999) (China) (Beijing)	Asia	120	60 / 60	Software (0,01 mm)	92.06 (2.5)	80.79 (3.19)	92.1 (2.66) / 92.02 (2.33)	80.69 (3.72) / 80.89 (2.54)	-	Yes
Crosby et al. (1989) (USA) (Texas)	America	79	NS	Digital caliper (0,01 mm)	91.5 (2.56)	77.51 (3.9)	NS	NS	-	Yes
				Class II - Division 1						
Machado et al. (2018) (Portugal) (Almada)	Europe	23	16 / 7	Digital caliper (0,01 mm)	91.4 (2.8)	78.6 (3.8)	90.5 (1.8) / 91.9 (3.1)	77.3 (3.3) / 79.2 (4)	-	Yes

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Mahmoud et al. (2017) (Sudan) (Khartoum)	Asia	41	NS	Digital caliper (0,01 mm)	90.73 (2.63)	78.11 (4.49)	NS	NS	-	Yes
Elsheikhi et al. (2017) (Libya) (Benghazi)	Africa	20	10 / 10	Digital caliper (0,01 mm)	91.38 (3.06)	76.29 (3.02)	NS	NS	-	Yes
Chugh et al. (2015) (India) (Lucknow)	Asia	40	20 / 20	Digital caliper (0,01 mm)	91.53 (2.49)	78.96 (3.56)	92.24 (2.43) / 90.83 (2.41)	79.95 (2.78) / 77.97 (3.66)	-	Yes
Bughaighis et al. (2015) (Libya) (Benghazi)	Africa	73	NS	Digital caliper (0,01 mm)	91.49 (2.58)	78.08 (2.8)	NS	NS	-	Yes
Asma et al. (2013) (Malaysia) (Selangor)	Asia	50	NS	Digital caliper (0,01 mm)	NS	78.75 (3.85)	NS	NS	-	Yes
Ricci et al. (2013) (Brazil) (São Paulo)	America	35	NS	Digital caliper (0,01 mm)	90.67 (2.4)	77.29 (2.51)	90.37 (2.35) / 90.76 (2.45)	77.27 (2.08) / 77.3 (2.65)	-	Yes
Kansal et al. (2012) (India) (Karnataka)	Asia	237	NS	Digital caliper (0,01 mm)	91.5 (3.4)	79.1 (4)	NS	NS	-	Yes
O'Mahony et al. (2011) (Ireland) (Cork)	Europe	60	30 / 30	OrhoAnalyzer (Software)	91.8 (2.1)	78.6 (3.5)	91.8 (2.4) / 91.8 (1.8)	77.9 (3.6) / 79.3 (3.3)	-	Yes
Oktay et al. (2010) (Turkey) (Erzurum)	Europe	100	61 / 39	RMI 550 3D (0,01 mm)	91.86 (2.07)	78.35 (2.34)	92.22 (2.05) / 91.64 (2.07)	78.1 (2.17) / 78.58 (2.46)	-	Yes
Ciger et al. (2006) (Turkey) (Hacettepe)	Europe	71	40 / 31	Digital caliper (0,01 mm)	90.83 (3.9)	78.04 (2.57)	90.54 (3.4) / 91.05 (4.24)	77.94 (2.46) / 78.11 (2.65)	-	Yes
Carreiro et al. (2005) (Brazil) (Panamá)	America	54	26 / 28	Microscrrib 3DX	92.24 (2.56)	79.79 (4.24)	NS	NS	-	Yes
Uysal et al. (2005) (Turkey) (Konya)	Europe	157	82 / 75	Digital caliper (0,01 mm)	91.12 (3.34)	78.5 (43162)	91.19 (2.53) / 91.07 (3.96)	78.68 (3.06) / 78.33 (2.42)	-	Yes
Nie et al. (1999) (China) (Beijing)	Asia	60	30 / 30	Software (0,01mm)	92.16 (2.5)	80.56 (3.24)	92.11 (2.61) / 92.21 (2.39)	80.31 (3.87) / 80.8 (2.42)	-	Yes
Crosby et al. (1989) (USA) (Texas)	America	30	NS	Digital caliper (0,01 mm)	91.7 (2.3)	78.2 (3.1)	NS	NS	-	Yes
				Class II - Division 2						
Machado et al. (2018) (Portugal) (Almada)	Europe	28	20 / 8	Softwares (0,01 mm)	91.6 (2.6)	78.6 (3.4)	92.3 (2) / 91.3 (2.9)	78.5 (3.7) / 78.7 (3.3)	-	Yes
Mahmoud et al. (2017) (Sudan) (Khartoum)	Asia	3	NS	Softwares (0,01 mm)	92.42 (2.17)	78.57 (1.53)	NS	NS	-	Yes
Bughaighis et al. (2015) (Libya) (Benghazi)	Africa	12	NS	Softwares (0,01 mm)	91.56 (1.21)	78.2 (2.29)	NS	NS	-	Yes
Asma et al. (2013) (Malaysia) (Selangor)	Asia	50	NS	Softwares (0,01 mm)	NS	80.33 (4.71)	NS	NS	-	Yes
Kansal et al. (2012) (India) (Karnataka)	Asia	17	NS	Softwares (0,01 mm)	91.8 (2.9)	79.1 (3)	NS	NS	-	Yes
O'Mahony et al. (2011) (Ireland) (Cork)	Europe	60	30 / 30	OrhoAnalyzer (Software)	92.6 (2.2)	80.2 (3)	92.8 (2.1) / 92.3 (2.2)	81.1 (2.7) / 79.4 (3.1)	-	Yes

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Oktay et al. (2010) (Turkey) (Erzurum)	Europe	100	63 / 37	RMI 550 3D (0,01 mm)	92.26 (2.22)	78.98 (2.67)	92.42 (2.15) / 92.16 (2.26)	78.76 (2.67) / 78.38 (2.69)	-	Yes
Uysal et al. (2005) (Turkey) (Konya)	Europe	34	23 / 11	Softwares (0,01 mm)	91.94 (3.34)	79 (4.23)	90.81 (2.27) / 89.81 (4.65)	79.63 (3.35) / 78.7 (4.64)	-	Yes
Nie et al. (1999) (China) (Beijing)	Asia	60	30 / 30	Software (0,01 mm)	91.95 (2.47)	81.02 (43376)	92.09 (2.7) / 91.82 (2.26)	81.07 (3.52) / 80.97 (2.66)	-	Yes
Crosby et al. (1989) (USA) (Texas)	America	29	NS	Softwares (0,01 mm)	91.5 (3.1)	76.8 (5.3)	NS	NS	-	Yes
				Class III						
Machado et al. (2018) (Portugal) (Almada)	Europe	38	25 / 13	Softwares (0,01 mm)	92 (2)	78 (2.9)	91.8 (1.6) / 92.1 (2.3)	78 (2.9) / 78.1 (2.9)	-	Yes
Saritha et al. (2017) (India) (Telangana)	Asia	40	21 / 19	Softwares (0,01 mm)	92.967 (1.546)	79.72 (2.52)	92.99 (1.75) / 92.94 (1.38)	79.92 (3.06) / 79.54 (1.97)	-	Yes
Mahmoud et al. (2017) (Sudan) (Khartoum)	Asia	11	NS	Softwares (0,01 mm)	91.38 (2.04)	78.37 (3.16)	NS	NS	-	Yes
Elsheikhi et al. (2017) (Libya) (Benghazi)	Africa	20	10 / 10	Softwares (0,01 mm)	92.05 (2.96)	76.65 (4.09)	NS	NS	-	Yes
Cançado et al. (2016) (Brazil) (Dourados)	America	66	NS	Softwares (0,01 mm)	91.22 (2.07)	77.9 (2.85)	NS	NS	-	Yes
Al-Duliamy et al. (2016) (Iraq) (Baghdad)	Asia	10	NS	Softwares (0,01 mm)	91.82 (2.24)	78.8 (2.15)	NS	NS	-	Yes
Al-Duliamy et al. (2016) (Egypt) (Cairo)	Africa	10	NS	Softwares (0,01 mm)	90.65 (3.71)	78.65 (4.2)	NS	NS	-	Yes
Chugh et al. (2015) (India) (Lucknow)	Asia	30	NS	Softwares (0,01 mm)	94.05 (2.01)	81.23 (3.11)	94.48 (1.83) / 93.47 (2.11)	81.96 (3.17) / 80.49 (2.98)	-	Yes
Shastri et al. (2015) (India (North)) (Lucknow)	Asia	20	NS	Softwares (0,01 mm)	91.33 (2.32)	77.51 (5.64)	NS	NS	-	Yes
Bughaighis et al. (2015) (Libya) (Benghazi)	Africa	13	NS	Softwares (0,01 mm)	90.97 (2.93)	77.48 (3.51)	NS	NS	-	Yes
Ismail et al. (2015) (Sudan) (Khartoum)	Africa	43	27 / 16	Softwares (0,01 mm)	92.6 (3.01)	77.71 (4.2)	93.58 (2.71) / 92.02 (3.03)	78.01 (4.12) / 77.53 (4.24)	-	Yes
Maurya et al. (2015) (India) (Madhya Pradesh)	Asia	24	12 / 12	Softwares (0,01 mm)	94.72 (1.13)	84.49 (1.33)	95.51 (0.72) / 93.93 (0.88)	85.56 (0.93) / 84.33 (1.57)	-	Yes
Zerouaoui et al. (2014) (Morocco) (Rabat)	Africa	30	NS	Softwares (0,01 mm)	92.075 (2.2062)	78.2358 (2.85751)	NS	NS	-	Yes
McSwiney et al. (2014) (Ireland) (Dublin)	Europe	60	NS	Softwares (0,01 mm)	92.25 (2.31)	78.35 (2.42)	92.3 (2.27) / 92.2 (2.41)	78.15 (2.37) / 78.55 (2.58)	-	Yes
Asma et al. (2013) (Malaysia) (Selangor)	Asia	50	NS	Softwares (0,01 mm)	NS	79.09 (2.82)	NS	NS	-	Yes

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Ali Hyder et al. (2012) (Bangladesh) (Dhaka)	Asia	40	20 / 20	Digital caliper (0,01 mm)	91.4 (2.58)	78.5 (3.15)	91.58 (2.62) / 91.28 (2.6)	78.7 (3.28) / 78.43 (3.09)	-	Yes
Kansal et al. (2012) (India) (Karnataka)	Asia	24	NS	Digital caliper (0,01 mm)	91.8 (3.1)	78.9 (5.3)	NS	NS	-	Yes
O'Mahony et al. (2011) (Ireland) (Cork)	Europe	60	30 / 30	OrhoAnalyzer (Software)	92.8 (2.2)	79.9 (3.1)	92.7 (2.2) / 92.9 (2.1)	80.3 (3) / 79.6 (3.2)	-	Yes
Endo et al. (2010) (Japan) (Niigata)	Asia	66	33 / 33	Digital caliper (0,01 mm)	91.56 (1.89)	NS	91.27 (1.56) / 91.85 (2.16)	() / ()	-	Yes
Oktay et al. (2010) (Turkey) (Erzurum)	Europe	100	58 / 42	RMI 550 3D (0,01 mm)	92.87 (1.92)	79.3 (2.94)	92.81 (2.05) / 92.92 (1.83)	79.39 (3.13) / 79.24 (2.83)	-	Yes
Strujić et al. (2009) (Croatia) (Zagreb)	Europe	81	45 / 36	Digital caliper (0,01 mm)	92.08 (1.82)	78.23 (2.82)	NS	NS	-	Yes
Endo et al. (2009) (Japan) (Niigata)	Asia	71	35 / 36	Digital caliper (0,01 mm)	91.54 (1.86)	77.84 (2.16)	91.28 (1.53) / 91.81 (2.12)	77.39 (1.93) / 78.31 (2.29)	-	Yes
Endo et al. (2008) (Japan) (Niigata)	Asia	60	30 / 30	Digital caliper (0,01 mm)	91.65 (1.86)	77.87 (2.18)	91.46 (1.46) / 91.83 (2.2)	77.54 (1.92) / 78.2 (2.4)	-	Yes
Carreiro et al. (2005) (Brazil) (Panamá)	America	46	23 / 23	Microscribe 3DX	92.3 (2.69)	79.54 (4.46)	() / ()	() / ()	-	Yes
Uysal et al. (2005) (Turkey) (Konya)	Europe	113	55 / 58	Digital caliper (0,01 mm)	91.69 (3.66)	78.83 (3.46)	92,34 (3,67) / 91,01 (3,56)	79,59 (3,67) / 78,03 (3,06)	-	Yes
Al Sulaimani et al. (2006) (Saudi Arabia) (Jeddah)	Asia	10	2 / 8	Ortho-l software	96.3 (1.45)	80.58 (3.74)	NS	NS	-	Yes
Laino et al. (2004) (Italy) (Campania)	Europe	13	6 / 7	Digital caliper (0,01 mm)	90.94 (2.26)	78.19 (2.27)	NS	NS	-	Yes
Araújo et al. (2003) (Brazil) (Belo Horizonte)	America	100	49 / 51	Digital caliper (0,01 mm)	NS	79.03 (2.35)	NS	NS	-	Yes
Alkofide et al. (2002) (Saudi Arabia) (Jeddah)	Asia	60	60 / 60	Digital caliper (0,01 mm)	92.71 (2.12)	78.5 (2.53)	93.2 (2.15) / 92.21 (2.02)	79.66 (2.52) / 77.34 (1.98)	-	Yes
Ta et al. (2001) (Hong Kong) (Sheung Wan)	Asia	30	15 / 15	Digital caliper (0,01 mm)	91.45 (1.8)	79.43 (2.55)	91.2 (2.1) / 91.7 (1.4)	77.9 (3.1) / 79.2 (1.8)	-	Yes
Nie et al. (1999) (China) (Beijing)	Asia	120	60 / 60	Software (0,01 mm)	95.6 (2.62)	82.74 (2.76)	95.68 (2.78) / 95.52 (2.44)	82.6 (2.94) / 82.88 (2.56)	-	Yes

AR – Anterior Ratio; OR – Overall Ratio; CBCT – cone-beam computerized tomography; NS – Not Stated; SD – Standard Deviation.

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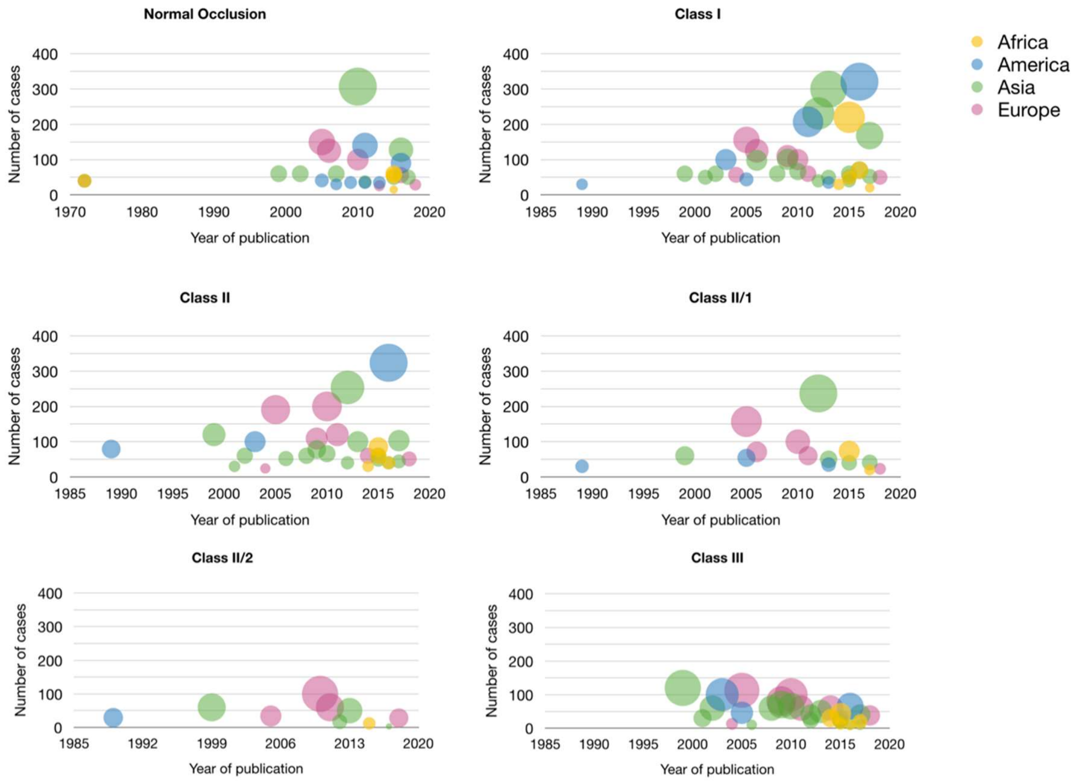

Figure 2: Datasets by year and population group by normal occlusion and Angle's malocclusion groups. Area of the circle is proportional to sample size.

Risk of bias across studies

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies statement proposed by the NIHLBI score in the final sample of articles ranged from 6 to 8 out of 10 (as shown in supplement Table S3). Among the included studies, no study presented high quality. Moreover, forty-seven articles presented medium quality, of which eleven articles presented 8 points (30,33,37,43,44,48,52,53,58,67,75), and thirty-six articles presented 7 points (12,22,25,26,31,34–36,38,39,42,45–51,54–57,59–65,67,68,70–72,76). Five were of low quality (77–81) and, consequently, were excluded.

Moreover, two articles were excluded (82,83) due to abnormal standard deviation (SD) values (10 and 100 times lower than the mean value of standard deviation presented in the remaining studies, respectively). These unusual SD values frame narrow confidence intervals gaining unreasonable weight in the meta-analysis. We unsuccessfully tried to contact the authors, and therefore, we decided for the exclusion of these, pondering the likely negative consequences for the veracity of the results.

More specifically, only seven studies reported the setting, locations and relevant dates of cast models (37,38,49,52,53,58,67), and seven determined the sample size (30,33,43,44,48,58,75). Strategies to minimize the potential sources of bias were not clearly described in most articles. Nine fail to explain how they evaluated intra- and/or inter-examiner errors or random error determination (38,49,77,79–84).

Findings from Meta-analysis

Pairwise MA findings for Normal occlusion

In normal occlusion group, the assessment of OR and AR was sourced from 24 and 25 studies, respectively (Figure 3 and 4). All those twenty-five studies provided data for AR assessment, while one study (61) had no data regarding OR. Global pooled results suggest an OR mean of 91.74% (95% CI: 91.37-92.10) and an AR mean of 78.24% (95% CI: 77.85-78.63). Globally, in both synthesis heterogeneity was high (I^2=92.59% and I^2=90.99% in OR and AR, respectively).

Next, we looked for gender differences on OR and AR at global level through gender mean difference meta-analysis. Only Class I presented a gender impact with male patients having higher OR (0.30, 95% CI 0.00-0.59) and AR (0.41, 95% CI 0.00-0.83) mean values than females (Supplement Table S4).

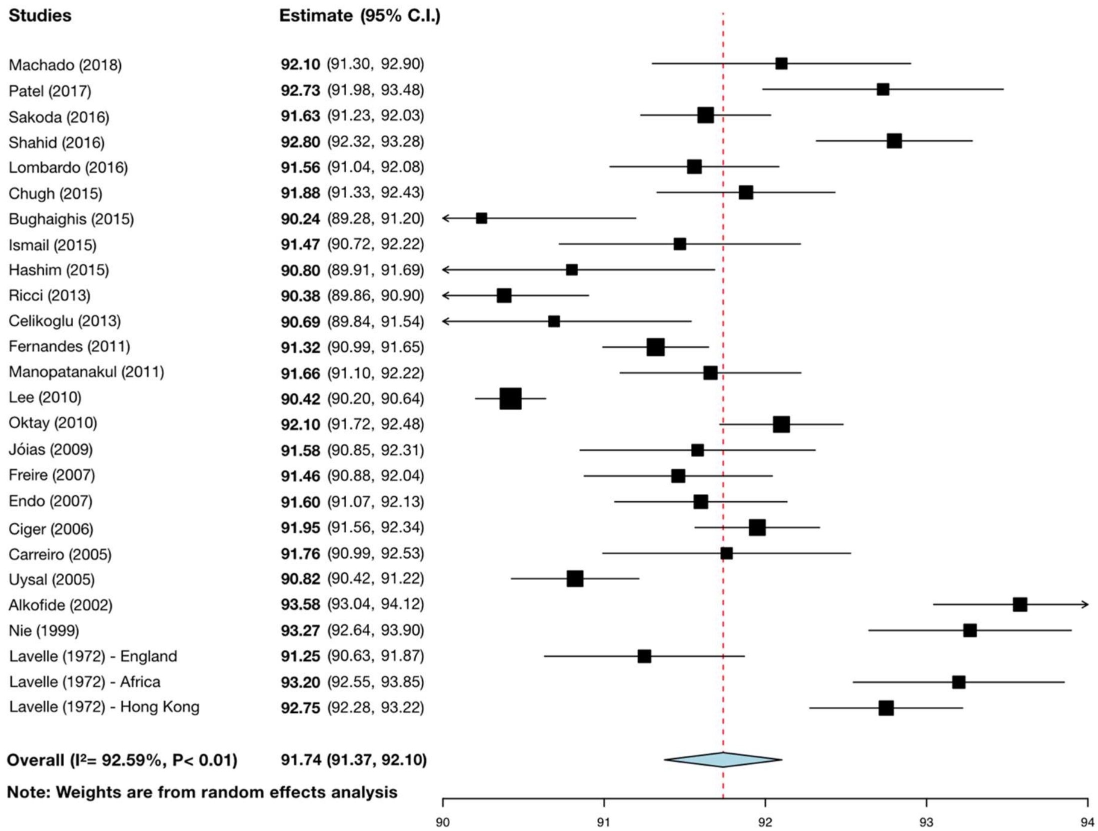

Figure 3: Forest plot of studies with OR mean values for normal occlusion patients. Mean effect size estimates have been calculated with 95% confidence intervals and are shown in the figure. Area of squares represents sample size, continuous horizontal lines and diamonds width represents 95% confidence interval. Blue diamond center and the vertical red dotted line point to the overall pooled estimate.

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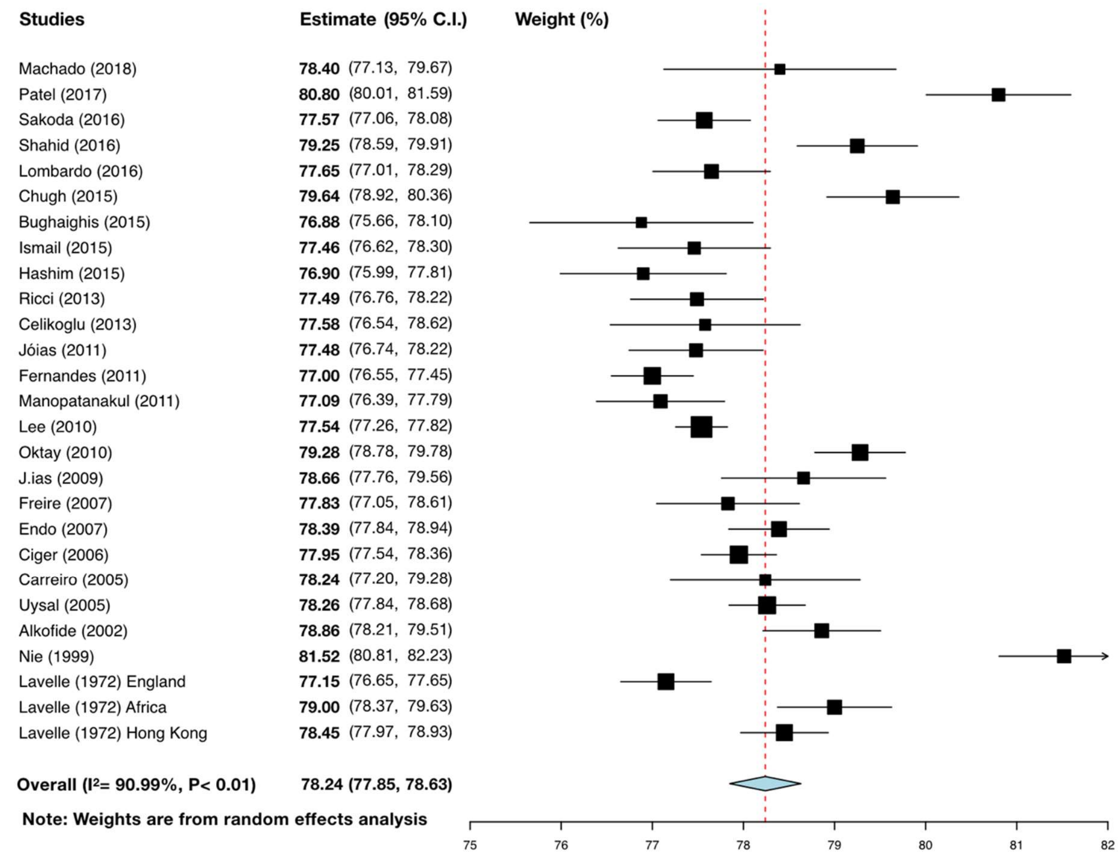

Figure 4: Forest plot of studies with AR mean values for normal occlusion patients. Mean effect size estimates have been calculated with 95% confidence intervals and are shown in the figure. Area of squares represents sample size, continuous horizontal lines and diamonds width represents 95% confidence interval. Blue diamond center and the vertical red dotted line point to the overall pooled estimate.

Pairwise MA Normal Occlusion vs. Bolton's original values

Direct comparison of the PMA pooled estimates for AR and OR normal occlusion mean values with Bolton's original values, through Z-test, revealed no significant differences, however, the statistical power for both analysis were extremely low, 5.8% and 5.7%, respectively (Table 2).

Table 2: Comparison of Pairwise MA of normal occlusion with Bolton's original values.

	AR					OR				
	N	**Mean (%)**	**SD (%)**	***P (Z-test)***	***Statistical Power***	**N**	**Mean (%)**	**SD (%)**	***P (Z-test)***	***Statistical Power***
PMA Normal occlusion	1894	78.24	8.7	0.527	5.8%	1859	91.74	8.0	0.806	5.7%
Bolton's Original Values	55	77.20	1.65			55	91.3	1.91		

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Bayesian Network meta-analysis findings for Angle's malocclusions groups

The difference in mean change for normal occlusion (baseline) compared with different Angle's malocclusion groups is presented in table 3, and can be seen as a measure of the average effort required to treat each represented malocclusion towards a proportional occlusion. In studies with no normal occlusion data, the comparison with the different types of Angle's malocclusions was not possible. Thus, we adopted a bayesian network meta-analysis approach to pool all available direct and indirect comparisons between normal occlusion versus Angle's Class I, Class II, Class II division 1, Class II division 2 and Class III values. The network fit statistic outcome included mean values for each Angle's malocclusions and the estimated normal versus malocclusion difference of means, with the degree of certainty of such differences reported as credibility intervals (CrI) (Table 3).

Table 3: Results of pairwise meta analysis of normal occlusion and Bayesian NMA of Angle's malocclusion groups.

	AR					OR				
Pairwise MA	**N**	**Mean**	**Lower CI**	**Upper CI**	**I^2**	**N**	**Mean**	**LowerCI**	**UpperCI**	**I^2**
Normal occlusion	1894	78.24	77.85	78.63	90.99	1859	91.74	91.37	92.10	92.59
Bayesian NMA	**N**	**Mean**	**Lower CrI**	**Upper CrI**		**N**	**Mean**	**LowerCrI**	**UpperCrI**	
Normal occlusion (network adjusted)	720	78.24	61.12	95.25		720	91.75	76.21	107.37	
Class I	2767	78.17	61.03	95.30		2683	91.75	76.51	107.62	
Class II	2429	78.12	61.02	95.18		2563	91.99	76.25	107.40	
Class II / div 1	1001	78.06	60.99	95.12		1051	91.813	76.06	107.11	
Class II / div 2	343	78.49	61.47	95.43		343	91.57	76.38	107.33	
Class III	1393	78.92	61.93	95.99		1409	91.812	77.21	108.20	

N, total sample size; Mean; CI, confidence interval; CrI, credibility interval; CI/CrI boundaries and I^2 in %

The mean change from normal occlusion for AR means Class I, Class II, Class II division 1 and Class II division 2 was -0.03 (95% CrI, -0.29 to 0.23), -0.10 (95% CrI, -0.37 to 0.16), -0.16 (95% CrI, -0.45 to 0.14) and 0.25 (95% CrI, -0.14 to 0.64), respectively, but in all, the 95% CrI included zero. A similar trend was also observed for OR means when we compared the means of Class II, Class II division 1 and Class II division 2 with normal occlusion (Table 4).

In contrast, we found a meaningful difference between Angle's Class III versus normal occlusion both for OR and AR means (0.89, 95% CrI, 0.66 to 1.12, and 0.66, 95% CrI, 0.38 to 0.94, respectively), and for Class I (0.25, 95% CrI, 0.03 to 0.47) against normal occlusion AR means, since the null difference is not within the credibility region (Table 4).

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Table 4: Results of Bayesian Network Meta-Analysis for Angle's malocclusion groups.

Difference to Normal Occlusion (%)	AR				OR			
Bayesian NMA	**N**	**Mean**	**Lower CrI**	**Upper CrI**	**N**	**Mean**	**Lower CrI**	**Upper CrI**
Class I	2767	-0.03	-0.29	0.23	2683	**0.25**	**0.03**	**0.47**
Class II	2429	-0.10	-0.37	0.16	2563	0.06	-0.17	0.25
Class II / div 1	1001	-0.16	-0.45	0.14	1051	-0.16	-0.41	0.09
Class II / div 2	343	0.25	-0.14	0.64	343	0.08	-0.23	0.40
Class III	1393	**0.66**	**0.38**	**0.94**	1409	**0.89**	**0.66**	**1.12**

Baseline normal occlusion is the covariate in the adjusted network meta-analysis.
N, total sample size; CrI, credibility interval; Mean and CrIs boundaries in %. Bold means that the null difference in not within the credibility interval.

Additional analyses

Funnel plots revealed no evidence of publication bias (Supplement Figure S5).

Discussion

Summary of Main Findings

To the best of our knowledge, this is the first systematic review that attempted to estimate global OR and AR values in patients with normal occlusion and Angle's malocclusion. Despite the apparent gap in observational studies about normal occlusion between 1972 and 1998, the last 20 years have been of increased interest (Figure 2). Our results in normal occlusion patients demonstrated that, globally, the OR mean was 91.7% (95% CI: 91.4-92.1) and AR mean was 78.2% (95% CI: 77.9-78.6), while the values proposed by Bolton (1) were respectively smaller.

In fact, pooled PMA normal occlusion estimates were not significantly different from Bolton's values, however this direct comparison, though necessary, is quite unfair and disproportionate as shown by the extraordinarily low statistical power. Also, the computed standard deviations from meta-analytical pooled estimates revealed very discrepant and elevated values when compared with Bolton's ones, and we believe that these direct comparisons are biased since it is not adequate to compare so unequal samples.

It is important to remark that we have not made world subgroups based on the continent since the studies are not fully representative of the continent as a whole. There is a lack of studies in North America and Oceania continent. Similarly, the African continent is portrayed only by Libya, Egypt, Morocco and Sudan, the European continent is represented mainly by Turkey and Ireland investigations, the Asia continent is mostly represented by studies from India, and the American continent only had two study from North America and the remaining studies are from Brazil. Despite this restriction, future research should address race and genetic backgrounds to weigh their influence on the mesiodistal proportions since in this study it was not possible to perform due to the lack of such data. Still, globalization and miscegenation strongly support the concept of non-static proportions and the necessity for continued research. Further, gender and geographic location, in general, are not factors that influence dental width proportions.

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Regarding the relation between normal occlusion and Angle malocclusions, in general, our results determined no significant difference in the tooth size discrepancy existed for the OR and AR between normal occlusion and different malocclusion groups, except for the Class III malocclusion both in AR and OR, and Class I malocclusion only for OR. Under these circumstances, the results indicate that the discrepancy of intermaxillary tooth size may be one of the important factors in the cause of malocclusions, especially in Angle's Class III.

The results also suggest that these OR and AR differences for normal occlusion in Angle's Class I and III may be explained by upper or/and lower discrepancy. For both Angle's Class I and III difference for normal occlusion, a possible clinical explanation for this discrepancy may be due to smaller mesiodistal maxillary tooth sizes or/and greater mesiodistal mandibular widths.

Quality of the Evidence and Potential Biases in the Review Process

All studies included in meta-analysis presented overall medium quality, according to our pre-defined quality assessment and risk of bias. However, there are important matters that need to be pointed. A hypothetical limitation would be the fact that this systematic review only contains observational studies. However, except for restorative or traumatic reasons, teeth mesiodistal width remains prospectively unchanged. Therefore, RCTs, prospective or retrospective studies on this thematic, unless as the result of a secondary observation, would be inappropriate.

On the other hand, we have to emphasize that most studies lack sample size calculation and are non-representative of the population, but rather from an academic setting. Besides, too many studies show a lack of information on calibration method or the number of examiners. These items are extremely important to minimize selection bias and strengthen the generalization of results, and its absence weakens the results of this systematic review. Additionally, no study has reported the existence of blinding examiners, since presumably the researchers themselves were involved in teeth measurements and Angle's evaluation. This potential bias should be considered in future research.

Significantly, the heterogeneity revealed by our meta-analysis refers, conceptually, to the variation in study outcomes between studies. This variation per se could flag some worrisome, however, we need to carefully assess this discrepancy, contrary to common meta-analysis. In our opinion, these results cannot be concluded as a high methodological variability rather than a high variableness of mesiodistal width proportions among the populations.

Regarding methodology, most studies took teeth measurements from plaster models. Only one investigation used intraoral 3-dimensional (3D) scanne(68), another used CBCT (75), three studies have digitized plaster models and subsequently performed the measurements (22,57,60), and also three used an electronic measuring device (52,64,70). Although in the past, calliper measurement in plaster models was the gold standard, nowadays the study of models with virtual 3D technology have higher reliability and accuracy (85–88) and should be used as the first choice for diagnosis and treatment planning in Orthodontics, specifically to determine the width of the teeth. Additionally, study models produced by CBCT are far from being perfect for replacing digital models. Hence, in the future, with proper improvement, CBCT will ensure a multiplicity of analyzes from a single record (89). Furthermore, it is imperative that, in addition to the mesiodistal width, the labio-lingual and inclination data should be evaluated since they may also present great variability in populations. Thus, it is more desirable a 3D orthodontic diagnosis and treatment plan rather than a 2D assessment.

Conclusions

The results of this systematic review show that global pooled OR and AR mean values for normal occlusion patients are slightly above Bolton's original values. Class I, for OR mean values, and Class III, for both OR and AR, are proportionally larger than normal occlusion patients. Gender had no impact on teeth mesiodistal proportion.

Implications for Clinical Practice and Research

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Despite being one of several measures used in orthodontic planning, the results of this systematic review suggest that Bolton's original values may be slightly underestimated as OR and AR global standard original. The use of inadequate standard measures for the dental proportion of each population can lead to diagnostic errors and could influence the patient's treatment outcome. Also, despite these AR and OR mean values were originally developed only for tooth width reduction (through interproximal stripping or extraction), several patients with mesiodistal disproportionality, mainly due to microdontia or agenesis in one or more teeth, require post-orthodontic rehabilitation treatments. Thus, in the future is imperative to establish normative data for different malocclusions and their impact proportion management during orthodontic treatment.

As a result, in the future, there is a clear need for further studies with more stringent methodologies with regard to sample size calculation, more representative population samples, explicit calibration methods to reduce risk bias, fostering the use of digital systems, and greater focus on the race of the population being studied combined with genetic background analysis of the patients. In addition, the question arises of the importance of orthodontic consensus to those who must establish normative data, since the results of this study point to a difference from the original Bolton's values. Still, the evolution of our species by the miscegenation due to globalization makes pressing the need for the continuous research on the human proportions, and, in this case, on the mesiodistal teeth proportion, since, apparently, these are not immutable.

In the forthcoming investigations, we believe it will be substantial to investigate the pre-orthodontic patient, in order to seek the ideal post-orthodontic position of each tooth. In this way, we will be able to know which tooth or teeth need mesiodistal intervention, so that we can achieve a normal occlusion with proper mesiodistal proportion respecting the Andrew's six keys.

Conflict of interest
Nothing to declare.

List of abbreviations
OR: overall ratio; AR anterior ratio; NIHLBI: National Heart, Lung, and Blood Institute; CBCT: cone beam computed tomography; 3D: 3-dimensional; 2D: 2-dimensional; PMA: pairwise meta-analysis; NMA: network meta analysis; RCT: randomized controlled trial; CI: confidence interval; SD: standard deviation; CrI: credibility intervals.

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