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The accuracy of non-radiographic mixed dentition predictive methods used for the diagnosis of space discrepancies in orthodontic patients in the mixed dentition phase in Africa: A systematic review of diagnostic test accuracy

Dr Sarika Brijlall

Student number: 3312728

Correspondence**: sarikabrijlall@gmail.com**

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Supervisor: Professor Angela Harris
Co-supervisor: Dr Faheema Kimmie-Dhansay
Co-supervisor: Dr Deon Joubert

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Principal author: Sarika Brijlall
Correspondence: Sarika Brijlall; sarikabrijlall@gmail.com
Co-authors: Professor Angela Harris, Dr Faheema Kimmie-Dhansay, Dr Deon Joubert

Abstract

The accuracy of non-radiographic mixed dentition predictive methods used for the diagnosis of space discrepancies in orthodontic patients in the mixed dentition phase in Africa: a Systematic Review of Diagnostic Test Accuracy

S Brijlall

MSc Dent Thesis, Department of Orthodontics, Faculty of Dentistry, University of Western Cape

Background

Orthodontic space analysis is a critical component into informing diagnosis and leading to targeted interceptive treatment planning in the mixed dentition stage of tooth development. Accurate and reliable space analysis methods - radiographic and non-radiographic - are beneficial for the early detection of imbalances between the mesiodistal diameter of unerupted permanent teeth and its alveolar bone support, which can contribute significantly in preventing severe malocclusions. Due to the ease and simplicity in its application, the non-radiographic mixed dentition space analysis methods; Moyers, and Tanaka and Johnston; were widely recommended. However, due to these space analysis methods derived from data of a Caucasian European population in the early 1970s, the external validation question, with dubious applicability of these methods in other populations, has been questioned. This has prompted researchers to seek newer, more context-specified prediction tables and equations for specific sample population groups.

Objectives

To determine the diagnostic test accuracy of mixed dentition space analysis index tests for the prediction of unerupted permanent canines and premolars in the maxillary and mandibular arches for studies conducted in Africa.

Search methods

The research team undertook a search of the following databases: African Index Medicus (AIM) (inception to August 2021); PUBMED) (inception to August 2021); Sabinet African Journals) (inception to August 2021); Wiley (inception to August 2021); Scopus (inception to August 2021); EbscoHost (academic search complete, cinahl, dentistry and oral sciences) (inception to August 2021); ScienceDirect (inception to August 2021). Investigators studied the included studies' reference lists and published diagnostic test accuracy studies.

Selection criteria

Research included diagnostic test accuracy study designs that compared, either independently or combined, one or more index tests (non-radiographic mixed dentition space analysis methods) with a reference standard. This included cross-sectional studies that evaluated the diagnostic accuracy of single index tests and studies that directly compared two or more index tests. Additionally, in vivo studies were eligible for inclusion.

Data collection and analysis

The principal investigator and the co-investigator extracted independently and in duplicate using standardised data extraction and quality extraction form based on the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) specific to the review context. The estimates of the diagnostic accuracy test from primary studies were not expressed as sensitivity or specificity but rather with mean differences and standard deviations with 95% confidence

intervals (CI) for each dataset (1). Therefore, the data variability of the sensitivity and specificity of each included study was unable to be displayed on coupled forest plots. As a result of the substantial diversity in characteristics of the included studies, coupled with the paucity of data for each index test, a meta-analysis was not appropriate in this review.

Main Results

The study included 11 cross-sectional diagnostic test accuracy studies. Of these, none reported a pre-specified diagnostic threshold or presented data in a standard 2 x 2 format. Given the small number of studies, incomplete reporting of the outcomes data within the existing studies and the substantial diversity of characteristics of the included studies, the comparative accuracy of the different index tests were unable to be formally evaluated and considered in this review. The pooling of poor quality data may produce misleading evidence with limited credibility for the index tests investigated; consequently, a meta-analysis was not considered appropriate in this review. Using QUADAS-2, all eleven studies were judged to be at an overall high risk of bias and of having unclear applicability concerns (within patient selection and index test domains). Reasons included bias in the selection process, an absence of positivity thresholds, inadequate information on the sequence of testing and information bias due to the index test being interpreted with knowledge of the reference standards.

A critical appraisal was completed and studies were presented in a descriptive review format, as they are likely to provide useful information for the purpose of future research, with more clinical relevance to space analysis methods in the mixed dentition stages.

Authors conclusions

Due to the paucity of the evidence base, high levels of bias and applicability concerns in the methodological quality and the multitude of limitations for its clinical application, the accuracy and reliability of non-radiographic diagnostic tests of the studies included in this review cannot be established. Based on the presented evidence, researchers cannot make recommendations on the use of these index tests in clinical practice, and subsequently encourage future research

into the use of radiographic methods in establishing a more accurate diagnosis of space discrepancies.

Declaration

I declare that *The accuracy of non-radiographic mixed dentition predictive methods used for the diagnosis of space discrepancies in orthodontic patients in the mixed dentition phase in Africa: a systematic review of diagnostic test accuracy* is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by the references.

Full name: Sarika Brijlall

Signature: 

November 2021

List of Abbreviations

nRMDSA ..... non Radiographic Mixed dentition Space Analysis
LCPM ..... Lower Canine and Premolar
UCPM ..... Upper Canine and Premolar
MD ..... Mesiodistal
CPM ..... Canine and Premolar
AAaF ..... Abdhul Azm and Fouda
TaJ ..... Tanaka and Johnston
SaW ..... Schirmer and Wiltshire
CBCT ..... Cone Beam Computed Tomography
TSALD ..... Tooth Size Arch Length Discrepancy
AIM ..... African Index Medicus
PRISMA ..... Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ETD ..... Electronic Thesis and Dissertation
QUADAS-2 ..... Quality Assessment of Diagnostic Accuracy Studies 2
CI ..... Confidence Intervals
LI ..... Lower Incisors
DTA ..... Diagnostic Test Accuracy
SROC ..... Summary Receiver Operating Characteristics
mTaJ ..... modified Tanaka and Johnston

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Table 1. Summary of findings of systematic review for nRMDSA DTA studies in Africa

Question	**What is the diagnostic accuracy of mixed-dentition space analysis index tests for the prediction of unerupted permanent canines and premolars in the maxillary and mandibular arch in African countries.**
Population	Children or adults between the age group 13-23 years, with fully erupted permanent teeth. Patients had to be free from interproximal caries, no previous orthodontic treatment, no attrition or congenital defects. Mild rotations and crowding were accepted. Studies included both male and female, and no ethnic exclusions. However, included studies were restricted within Africa.
Index Test	Non-radiographic mixed dentition space analysis predictive methods (nRMDSA). Included studies investigated and reported on the accuracy of traditionally space analysis methods applied - Tanaka and Johnston Equations and Moyers Probability tables - as well as 3 novel methods - Schirmer and Wilshire, a modified Tanaka and Johnston method by Khan and Seedat and Abdhul Azm and Fouda Novel method.
Target condition	Mesiodistal dimensions of unerupted canines and premolars in the maxillary and mandibular arches.
Reference standard	High quality study models of the mandibular and maxillary arches
Study design	Cross-sectional diagnostic test accuracy (DTA) studies
Action	The diagnosis of space discrepancies can provide opportunities for targeted early interceptive treatments that aim to prevent severe malocclusion. This can be accomplished by creating or maintaining dental arch space to accommodate the unerupted permanent teeth.
Diagnostic stage	Aimed at general dental practitioners and specialist orthodontists assessing space analyses of orthodontics patients in the mixed dentition phase
Quantity of evidence	The review included 11 studies within South Africa, Nigeria, Uganda, Senegal, Egypt, Sudan and Libya; evaluating 2573 participants.
Findings	
	No of studies Participants Interpretation

Tanaka and Johnston equation (Table 3)	8	2352	4 of the 8 included studies reported and provided descriptive statistical data; the mean differences, *p*—values and CI (95%). Each included study reported on statistically significant results found in the mean differences in the index test and reference standard, reporting the Tanaka and Johnston index test inappropriate for use in the respective populations. Studies had recommended newly derived index tests that were population specific.
Moyers Prediction tables (Table 4 and 5)	6	1092	4 of the 6 included studies investigated and reported on the mean differences in the various Moyers probability percentiles for males and females. Statistically significant results were reported in 4 studies, with $p<0.005$ for the UCPM and LCPM in males and females. The index test was unsuitable for use in the respective populations, and new diagnostic index tests were proposed in each study.
Schirmer and Wiltshire prediction tables (Table 6)	1	100	The study reported no statistically significant results in the mean differences for the UCPM ($p=0.1748$) and LCPM ($p=0.2990$) in males and females respectively at the 75th percentile for a Black South African population.
Modified Tanaka and Johnston equation (Table 6)	1	100	The study reported no statistically significant results in the mean differences for the UCPM ($p=0.1848$) and LCPM ($p=0.3776$) in females. This method was recommended for the Black South African population
Abdhul Azm and Fouda novel method (Table 7)	1	21	The study reported no statistically significant results in the mean differences for the UCPM and LCPM in females, recommending the use of this index test for the Egyptian female population.
Quality of studies	Using QUADAS-2, researchers judged the 11 included studies to be an overall high risk of bias. Reasons included possible bias in the selection and random selection of participants with 8 studies judged as unclear. A high risk of bias was observed in the index test domain due the lack of pre-specified diagnostic thresholds and information bias. There was an element of information bias from the lack of methodological sequence at which the research had been conducted, with no blinding from reference standards for interpretation. There was a high risk of bias in the reference standard domain due to results interpreted with knowledge of the index test . There was an unclear risk of bias in the flow and timing domain, with concerns about the lack of time intervals in between testing. However, one reference standard was used in all studies, and all participants were included in the analyses.		

Applicability of evidence to the review question	Patient selection was judged as an unclear concern in studies, as studies reported on the mean differences and the statically significant results of the entire sample populations, instead of individual patients data. It was impossible to assess the sensitivity and specificity of the data. Lack of pre-specified diagnostic thresholds for the index test was an area of concern for applicability. There was a low concern in the use of study models as the reference standard, as this provides static data that can be reproduced and cross-referenced.

Given the small number of studies and the large heterogeneity in the clinical and methodological characteristics of the studies, researchers were unable to pool the results of the study. Consequently, a formal evaluation of the comparative accuracy of tests was not conducted. *CI*, Confidence Intervals; *QUADAS-2,* Quality assessment of Diagnostic Accuracy Studies 2; *UCPM*, Upper Canine and Premolar; *LCPM,* Lower Canine and Premolar.

1 Literature Review

1.1 Background

Orthodontic treatment aims to achieve a functionally and aesthetically satisfactory occlusion. Early orthodontic treatment refers to orthodontic interventions carried out before the eruption of permanent dentition (excluding third molars) is complete. Numerous factors influence the commencement of orthodontic interventions: the patients' maturation level, classification and severity of malocclusion, mechanotherapy, duration of treatment, retentive mechanisms and patients' compliance. Desired treatment outcomes become compromised by these significant factors (1).

Mixed dentition treatment goals focus on skeletal correction rather than dental correction. The early mixed dentition stage transitions into the early permanent dentition stage between 6 to 12 years. The recommended management of localized malocclusion of neuromuscular etiology (digit sucking habits; functional shifts of the lower jaw from a narrow palate) is with removable or fixed orthodontic appliances at the early mixed dentition stage. Due to the adolescent growth spurt, it is recommended that malocclusions of skeletal (jaw prognathism or increase in anterior facial height) or dentoalveolar etiology (class II molar relation, deep bite, crowding) are managed at a late mixed dentition or early permanent definition stage with treatment options including fixed and removable functional appliances. Due to the plasticity of hard tissue and adaptability of soft tissues, growth of facial and dentoalveolar structures assists in achieving a desired orthodontic result.

To achieve optimal results at the mixed dentition stage of development, an accurate and reliable diagnostic tool for the estimation of the unerupted canines and premolars is critical to the success of a treatment plan. Diagnostic tools assist in providing clinical data of the mesiodistal dimensions of teeth and its associated bone support (2–6).

There are four main approaches to determine the mesiodistal dimensions of the unerupted canines and premolars:

I. The direct measurement of unerupted teeth from radiographs (7).
II. Analysis based on mean values of the canines and permanent premolars using established tables of average tooth sizes (8,9).
III. The use of regression equations based on high linear correlations that relate the mesiodistal widths of erupted permanent lower incisors to the unerupted permanent canines and premolars (10–13).
IV. A combination of the non-radiographic methods from erupted teeth and radiographic analysis of the unerupted teeth (7).

Current trends in the literature recommend using a combination of high-quality radiographic imaging and non-radiographic diagnostic aids. There is no doubt that cone beam computed tomography (CBCT) and 2D radiographic imaging are valuable diagnostic tools. The radiographic diagnostic power of CBCT boasts the highest accuracy and positive predictive value and is thus currently considered the gold standard. Consequently, CBCT can be considered a reliable reference standard for the mesiodistal dimensions of teeth. Potential drawbacks with the use of CBCT are its dependence on well-maintained infrastructure and up to-date-software. Radiation exposure has always been a concern, and its risks versus the benefits need to be clinically justified. However, researchers are cognizant of the limited access to high-quality radiographic equipment in many developing countries.

As an effect of economic and resource constraints, researchers developed non-radiographic predictive methods to assist in the diagnosis of space discrepancies in the mixed dentition stage (7).

There are numerous non-radiographic mixed dentition space analysis methods to estimate the dimensions of the unerupted permanent canines and premolars. The Moyers analysis (8) was published in 1971, followed by the Tanaka and Johnston method (13) in 1974. Both methods were derived from a Northern European population.

The Moyers prediction method was derived by Robert Moyers in 1971, who developed probability tables to predict canines and premolars using a sample of Northern European Caucasian subjects in Michigan, USA. In his study, Moyers had measured the sum of the mesiodistal widths of lower incisors using callipers. Measurements were correlated to the

dimensions of the permanent canines and premolars, and regression analysis was used to derive prediction tables (8).

The Moyers probability tables are still widely referenced and applied around the world. This can be attributed to the advantages of a system that has minimum systemic errors. It can be applied to both the mandible and maxilla without radiographs and can easily be applied to dental casts or directly to the mouth. Moyers claimed that at a 75% level, it overestimated the dimensions of the erupting teeth. It was seen as a favourable outcome eliminating the possibility of crowding the dentition (8,14). Moyers left little clarity with his sample population selection criteria and recognised the potential limitations of his methods. The Moyers method did not consider cumulative factors, such as bodily rotations of teeth or tipping of the incisors, information vital for a comprehensive treatment plan (5).

In contrast, Tanaka *et al.* (1974) formulated a constant representing the maxillary and mandibular arches to estimate tooth widths. The predictive method can be applied to both males and females without radiographs. The derived linear equations are $y = a + bx$, where x is the mesiodistal width of the lower incisors, b= 0.5, and a= 11 for the maxilla and 10.5 for the mandible (13). Researchers noted that a drawback in this method was a significant variation in the mesiodistal dimension of teeth by ethnicity. Nevertheless, it proved simpler to remember and easier to implement (2,8,10,13).

The Moyers and Tanaka and Johnston methods were popularised by Ackerman and Profit, who outlined its many advantages and simplicity (15). Although there were no known limitations regarding ethnicity initially, many studies have reported numerous disciplinary inaccuracies of space analysis when applied to diverse ethnic populations (2,8,10,13). Consequently, newly derived methods aligned its applicability to specific ethnic and population groups, especially in non-Caucasian populations. These included the Hixon and Oldfathers method, Staley Kerber's method, Schirmer and Wiltshire Methods and many more (14,16,17).

Studies in North America by Hixon *et al.*(1956), and Staley *et al.*(1980), developed mixed dentition predictive tools. These tools were not popularised due to concerns regarding the methodological approach in the development of these methods - such as an under-represented sample population - which may have resulted in the cautious application of this method. Other

reasons that may have contributed to the failure of its widespread use are the complexity of depending on radiographs, probability tables and the dimensions of the permanent mandibular incisors (17,18).

Altherr *et al.*(2007) had investigated the ethnic and gender influences using the Tanaka and Johnston method (TaJ) on a sample of white and black participants in North Carolina. The study had reported that the TaJ method was inaccurate for the participants. Researchers had developed four new linear regression formulae from the data to predict the mesiodistal dimensions of the unerupted teeth (19).

Similarly, Bishara *et al.*(1989) conducted a cross-sectional study amongst three different populations from Mexico, Egypt, and the United States, to establish if tooth size variation occurred amongst different genders and ethnicity. Researchers have reported significant differences (21). Egyptian and Mexican tooth dimensions were similar to Iowa participants. The study had under-reported the choice of the confidence intervals or parameters utilised. An unrepresentative sample size per population group can result in clinically misleading and unreliable data (21).
In a different study, the same authors' investigated the Boston University Method with the Tanaka and Johnston method (20). The study reported that both index tests investigated had significant differences and identified confounding factors that may have affected the determination of these permanent successor teeth. The authors recommended radiographic space analysis methods independent of the tooth-development stage, providing greater accuracy than non-radiographic methods (16,17,19–21).

In South America, researchers also reported differences when comparing mixed dentition predictive tools. The primary study comparisons reported were between the TaJ method and the Moyers Probability tables. Researchers reported on gender and ethnic variations. Chilean, Northern Brazilian and Columbian researchers reported on the inconsistencies in the non-radiographic methods investigated and highlighted an underestimation in predicting the tooth dimensions. New or adjusted methods were recommended. Melgaço *et al.*(2007) had formulated new regression equations in Brazil to predict the permanent canines and premolars. Researchers had proposed a simplified equation, utilizing the sum of the mesiodistal

dimensions of the permanent mandibular incisors and mandibular permanent first molars bilaterally, multiplied by a constant value (22–25).

Numerous studies from countries in Asia have investigated and reported on the validity of the Moyers and Tanaka and Johnston space analysis predictive methods (26-30). The assumption that tooth dimensions vary amongst ethnic groups prompted researchers to investigate and report on participants from pre-specified ethnicities. The researchers had conducted interviews with probing questions on the participants' lineage to ensure multi-ethnic participants were excluded from the sample population. This unorthodox survey method to confirm the participant's lineage has come under intense scrutiny due to its racial connotations. Nevertheless, the investigated index tests were reported to be invalid for Pacific Asian populations, with new regression equations developed by the researchers.
Researchers in Malaysia had derived a method that utilised the permanent mandibular incisors and the mandibular molars to predict permanent mandibular and maxillary canines and premolars (28). All these studies recommended further investigation on the new probability methods to assess its validity and applicability (26–30).

In the Middle-Eastern countries in Asia, researchers investigated and reported inaccuracies in Moyers and TaJ index tests for the prediction of the unerupted teeth in the Arab, Syrian, Jordanian and Kurdish populations. Researchers had also developed new regression equations to predict the dimensions of the permanent canines and premolars.
Nourallah *et al.*(2002) reported high correlations between the mesiodistal widths of the first mandibular incisors and the mandibular first molars. This sparked the development of new regression equations using reference teeth (31–37).

Kakkar *et al.* (2019), Baheti *et al.* (2016), Durgekar *et al.* (2009), Akhtar *et al.*(2020), Bherwani *et al.* (2011), Ramesh *et al.* (2014), Srivastava *et al.*(2013) reported significant inaccuracies in the TaJ and the Moyers probability methods in Indian and Pakistan. All the studies recommended that new regression formulas be developed for these populations (38–45).

In Africa, similar studies were also reported in the different countries to determine the most appropriate methods that can be applied for the prediction of permanent canines and premolars.

Studies in Egypt have investigated and reported on the TaJ, and the Abdhul- Azm and Fouda index tests (46). The Abdul-Azm and Fouda novel method was developed in 1989 and reported high correlations of the maxillary canine and premolar dimensions and the buccolingual widths of the first permanent molar. Fouda had claimed the method was 75% reliable on a sample size of 22 participants (46).

Refai *et al.*(2012) reported the TaJ methods invalid for the Egyptian population and created four prediction equations in relation to the first molar. They reported a high correlation between the first permanent molar and the combined mesiodistal widths of the permanent canine and premolars (46–48).

Ajayi (2014) reported the TaJ method to underestimate the mesiodistal widths of the canines and premolars in a Nigerian population. The Moyers Probability tables were applicable at the 75% and 85% percentile levels. However, the researcher proposed a new regression equation for the Nigerian population and recommended further research be conducted to determine its validity (49).

Similarly, Senegal, Sudanese and Libyan studies investigated the Moyers and TaJ predictive methods, reporting limited utility to the sample populations (50-52). The authors had formulated new predictive methods, encouraging further investigations of each of the new methods in different populations to assess the reliability and applicability (50–52).

In South Africa, four independent studies were investigated and reported on the accuracy of different mixed dentition space analysis index tests. Researchers reported statistically significant results, which had led to modifications and developments of new tables and formulae (3,12,14,53).

The first study, conducted by Van der Merwe *et al.* (1991), had applied the Moyers predictive method to a group of Caucasian subjects in the Western Cape, South Africa (2). The authors had reported significant mean differences and developed new data tables for the population group studied (53). Even though this research has been cited in many global studies, its clinical application is minimal to non-existent in South Africa. The study was conducted three decades ago with limited credibility, resulting in this index test being obsolete (2,53).

Wiltshire and Schirmer (14), in 1997, had similarly conducted research to compare the Moyers probability tables to a South African Black population. The Moyers method had significantly underestimated the mesiodistal tooth dimensions at all the percentile levels except at the 75th, 85th and 95th percentile levels for Black females. Researchers derived new tables for the Black South African population and recommended further testing its applicability and reliability (14).

Khan *et al*. (2007) investigated the applicability of the Tanaka and Johnston prediction method on a sample of Black South Africans (12). The study reported the TaJ method to be applicable to Black South African females but invalid for males. The researchers derived a new formula for the South African Black male population.

Moyers probability tables and the TaJ equations are the foundation of many studies of non-radiographic mixed dentition space analysis methods. There is a global trend to investigate, report and formulate new predictive index tests based on regression analysis of the data.

The diagnostic test accuracy studies of non-radiographic mixed dentition space analysis methods from various studies are presented in Table 2 and illustrated in Figure 1.

This study systematically reviews space analysis index tests to determine the mesiodistal dimensions of the unerupted premolars and canines for studies conducted in African countries.

Table 2. Summary of DTA studies of mixed dentition space analysis methods in various studies.

Article	Year	Country	Population	Number of participants (n)	Index Test	Results	New Method derived (Y/N)
Moyers (8)	1971	Michigan	Northern European	Unspecified no (♂ and ♀)	-	Moyers Probability tables ♀ and ♂	N/A
Tanaka and Johnston (13)	1974		Northern European	506 (♂ and ♀)	-	Tanaka and Johnston equation ♀ and ♂	N/A
Hixon *et al.* (16)	1958	USA, Iowa	North-west European	41 (15♂ 26♀)	-	Hixon and Oldfathers method ♀ and ♂	N/A
Altherr et al. (19)	2007	USA, North Carolina	Black and White	120 (60♂ 60♀)	TaJ	*White ♂ and Black ♀ U and L **White ♀ overestimation U and L **Black ♂ underestimation L	Y
Bishara *et al.* (21)	1989	USA, Iowa	Egyptian (E) Mexican (M) White (W)	57 (35♂ 22♀) 60 (26♂ 34♀) 55 (33♂ 22♀)	MD tooth dimension comparison	** Tooth-size ♂ > ♀ E, M, W **Tooth-size ♂ E > M+W **Tooth-size ♀ E > M+W	N
Bishara *et al.* (20)	1998	USA, Iowa	North-west European	55 (33♂ 22♀)	TaJ method Boston University method (BU)	**TaJ: overestimated ♀ and ♂ U and L **BU: underestimation ♀ and ♂ U and L	N
Melgaço *et al.* (54)	2007	Brazil	White Brazilian	500 (250♂ 250♀)	Novel method	*♀ and ♂ U and L	Y

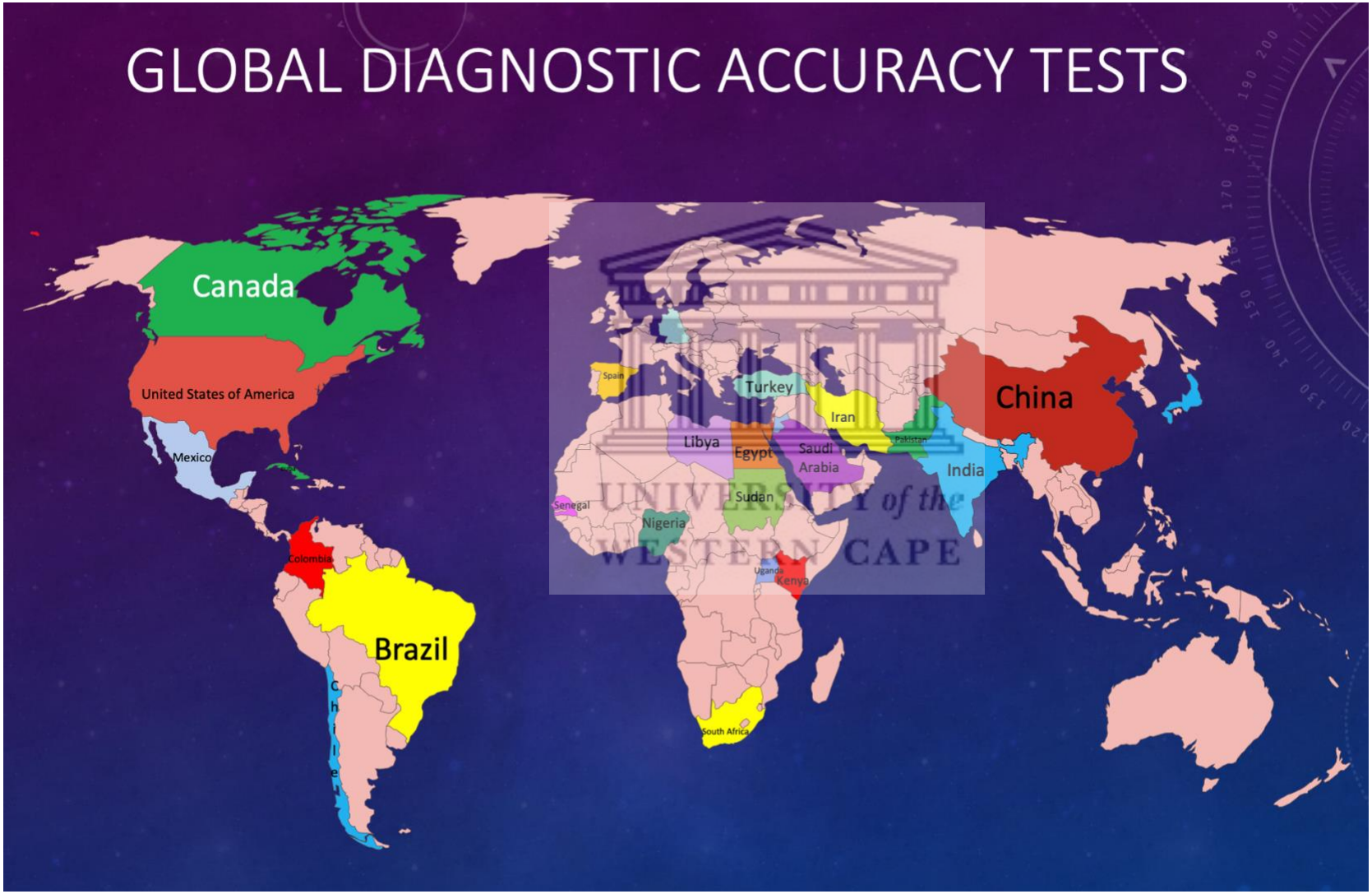
Botero *et al.* (25)	2014	South America, Columbia	Columbian	56 (♂ and ♀)	Moyers Tanaka and Johnston	**Moyers 85% underestimation ♀ and ♂ U **Moyers & TaJ overestimated ♀ and ♂ L **TaJ overestimation ♀ and ♂ U	N
Galdino *et al.* (24)	2019	Brazil	North-Eastern Brazil	100 (33♂ 22♀)	Moyers	* Moyers 75% ♀ and ♂ U and L	N
Sherpa *et al.* (27)	2015	China	Han North Eastern China	130 (65♂ 65♀)	Moyers TaJ	*TaJ ♂ U *Moyers 75% U and 85% L ♂ *Moyers 75% U ♀	Y
Lee-Chan *et al.* (55)	1998	USA	Asia-Pacific-American	201 (♂ and ♀)	TaJ	**TaJ: overestimation and underestimation ♀ and ♂ U and L	Y
Nourallah *et al.* (35)	2013	India	North Indian	200 (100♂ 100♀)	Moyers	** Moyers ♀ and ♂ U and L	Y
Fouda *et al.* (46)	2019	Egypt	Egyptian	21 ♀	Abdhul- Azm and Fouda	* ♀ U and L	N
Refai *et al.* (56)	2012	Egypt	Egyptian	1000 (500♂ 500♀)	TaJ	**TaJ: overestimation ♀ and ♂ U and L	Y
Alzubir *et al.* (52)	2016	Sudan	Sudanese	250 (132♂ 118♀)	TaJ	**TaJ: overestimation ♀ and ♂ U and L	Y
Ajayi *et al.* (49)	2014	Nigeria	Nigerian	54 (33♂ 21♀)	TaJ Moyers	**TaJ: ↑ underestimation ♀ and ♂ U and L *Moyers 75% U ♀ and ♂ *Moyers 85% L ♂	Y
Bugaighis *et al.* (50)	2013	Libya	Libyan	343 (169♂ 174♀)	TaJ Moyers	** TaJ ♀ and ♂ U and L ** Moyers ♀ and ♂ U and L	Y

Buwembo *et al.* (57)	2012	Uganda	Ugandan	220 (85♂ 135♀)	Moyers TaJ	*Moyers 65% and 75% ♀ and 75% ♂ L *Moyers 75% and 95% and 75% U ♀ ** TaJ ♀ and ♂ U and L	N
Khan *et al.* (12)	2007	South Africa	Black South African	110 (55♂ 55♀)	TaJ	*TaJ ♀ U and L **TaJ underestimated ♂ U and L	Y
Diagne *et al.* (58)	2003	Senegal	Senegalese	50 (25♂ 25♀)	TaJ Moyers	**TaJ overestimated ♂ and ♀ U and L **Moyers 50% overestimated U ♀ and ♂ **Moyers 50% underestimated L ♀ and ♂	Y
Schirmer *et al.* (59)	1997	South African	Black South African	100 (50♂ 50♀)	Moyers	*Moyers 85% and 95% U ♀	Y
Sethusa *et al.* (3)	2018	South African	Black South African	100 (50♂ 50♀)	Modified TaJ SaW	**mTaJ overestimated ♂ U **mTaJ overestimated ♀ L **SaW underestimated ♀ U **SaW overestimated ♀ L	N

Summary of non-radiographic mixed-dentition space analysis DTA studies for the prediction of unerupted CPM in various countries.

* = Highest correlation results between the actual and predicted values from the index test. **= Statistically significant result (P<0.05).♀ = Female; ♂ = Male; *U* = Upper arch; *L* = Lower arch; *TaJ,* Tanaka and Johnston; *mTaJ,* Modified Tanaka and Johnston; *SaW*, Schirmer and Wiltshire; N/A, not applicable.

Figure 1. Diagnostic test accuracy studies for non-radiographic mixed dentition space analysis methods conducted in various countries



1.2 Target Condition being diagnosed

Space analysis or tooth-size-arch length discrepancy (TSALD) can be described as the difference in the basal space available in the dental arch and the space required to accommodate the mesiodistal dimensions of teeth. Space analysis, diagnostic cephalometric radiographs and profile analysis play a pivotal role in orthodontic treatment planning (60).

The transition from primary dentition to permanent dentition is a complex phenomenon. The exfoliation of primary teeth, the eruption of permanent teeth and the establishment of dental occlusion occurs independently yet in a pre-orchestrated sequence. The growth and maturation of craniofacial structures and neuromuscular systems contribute to this process. The disturbance to any or all these processes may influence the developing occlusion and cause an imbalance in the dental harmony of teeth and its supporting structures, commonly referred to as malocclusion. Malocclusions can present as space discrepancies, deep overbite, midline deviation, excessive overjet, anterior crossbite, mal-alignment and open-bite (61).

Space discrepancies can occur due to the early loss of primary teeth, detrimental habits, dental diseases such as caries, abnormal tooth morphology or hereditary influence on the clinical appearance of teeth (62).

In the mixed dentition space analysis, assessing the mesiodistal dimensions of the unerupted permanent canines and premolars is critical in diagnosing space discrepancies. The leeway space and incisor liability also contribute to the arch perimeter in space analyses.

The assessment of the severity of the mixed dentition space analysis traditionally uses radiographic and non-radiographic methods. Radiographic methods include cephalometric radiographs, panoramic x-ray and CBCT. The Moyers (8) and TaJ methods are amongst the most popular non-radiographic mixed dentition space analysis methods (13). Well-established clinical diagnostic thresholds can judge the severity of the space discrepancies to ensure that radiographic and non-radiographic index tests provide both clinically and statistically significant results, as suggested by Altherr *et al.* (19).

1.3 Treatment of space discrepancies

Appropriate orthodontic interventions to manage space discrepancies can be initiated at different stages of tooth maturation. Some patients benefit from early orthodontic interventions, while others benefit from treatment at a later stage. A comprehensive orthodontic examination must be performed to identify the orthodontic treatment needs of the patient and the best possible timing. A treatment approach is also dependent on various factors, such as patient compliance, the severity of the malocclusion and the duration of the proposed treatment.

Studies have identified benefits in early and late orthodontic interventions. Orthodontic interventions include fixed and removable orthodontics appliances, dependent on the etiology and the treatment objectives. However, sound clinical judgement is encouraged to weigh out the risk and benefits for each case (61,63).

Orthodontic management of detrimental habits, such as digit sucking, occurs at the early mixed dentition stages (5-9 years). Treatment options include fixed or removable orthodontic appliances, such as tongue-gate appliances.

Space regaining treatment options, such as up-righting, molar distalization and de-rotation of teeth, ideally occur at the mixed dentition stage (9-12 years). Treatment options include fixed and removable orthodontic appliances, expansion devices, headgears, and functional appliances.

A comprehensive orthodontic treatment plan is essential for alignment correction at the late mixed dentition or early permanent dentition stages. Figure 2 outlines possible treatment options for patients at the different stages of tooth maturation (36,64–66).

Figure 2. Orthodontic treatment option guidelines for space discrepancies (58)

Chronological age	5.5 yrs.- 9.5 yrs.	9 yrs. - 12 yrs.	11 yrs. - 14 yrs.	15+
Dental stage	Early mixed dentition	Mixed dentition	Late mixed dentition	Permanent dentition
Dentition (Dental Maturation varies +/-2 yrs.)	Upper and lower first molars Upper and lower incisors c/d/e in all quadrants	Lower canines Lower premolars Upper first bicuspids Upper c and e	Upper canines Upper second bicuspids Upper and lower second molars	No baby teeth
Etiology	Neuromuscular etiology (i.e. functional shift of lower jaw due to narrow maxilla, non-nutritive digit sucking habit)	Skeletal etiology (i.e. jaw prognathism, increased anterior facial height) Dentoalveolar (i.e. CL II molar relation, deep bite, dental crowding)	Skeletal etiology (i.e. jaw prognathism, increased anterior facial height) Dentoalveolar (i.e. CL II molar relation, deep bite, dental crowding)	Skeletal etiology (i.e. jaw prognathism, increased anterior facial height) Dentoalveolar (i.e. CL II molar relation, deep bite, dental crowding)
Orthodontic treatment	Early orthodontic treatment	Early orthodontic treatment +/- Growth modification	Comprehensive orthodontic treatment	Comprehensive orthodontic treatment
Treatment objective	Eliminate jaw shift Eliminate traumatic occlusion Eliminate habit Providing a favourable environment for adult teeth to erupt	Eliminate or reduce skeletal dysplasia Increase available arch space for erupting teeth	Compensate skeletal dysplasia Align and level upper and lower teeth	Compensate skeletal dysplasia Or Eliminate skeletal dysplasia (jaw surgery) Align and level upper and lower teeth
Treatment mechanics	Fixed or removable orthodontic appliances	Fixed or removable orthodontic appliances + Headgear + Rapid palatal expander + Functional appliances	Braces on the upper and lower teeth. + Clear Aligners	Braces on the upper and lower teeth + Clear Aligners +/- jaw surgery

1.4 Index Test(s)

This review assesses the non-radiographic mixed dentition space analysis methods, focusing on studies conducted in countries within Africa. Upon reviewing the included diagnostic test accuracy studies, Moyers and Tanaka and Johnston methods were identified as conventional methods for predicting the unerupted permanent CPM. The non-radiographic mixed dentition space analysis methods assessed in this review include:

- Moyers probability tables
- TaJ equation

Moyers probability tables (8) was developed by Robert Moyers in 1971 from a Northern European Caucasian population. Due to its simplistic method, it was adopted by many

practitioners around the globe. The method was suitable for use without the need for radiographs and provided a predictive measurement for both the mandible and the maxilla. The method had required only the measurement of the mesiodistal widths of the mandibular central and lateral incisors. At the 75% accuracy level, it produced the desired outcome to overestimate the permanent canine and premolar values in the mandible and maxilla.

Tanaka *et al.* (13) developed a linear equation in 1974, with a Northern European Caucasian population. The method can be applied to males and females, and its application did not require radiographs. Ethnic limitations in the TaJ method were reported by many authors investigating its utility in different populations. Nevertheless, it proved simple to remember and easy to implement (2,8,10,13).

The linear equation derived was in the form y = a + bx, , were x is the mesiodistal width of the lower incisors, b= 0.5, and a= 11 for the maxilla and 10.5 for the mandible respectively:

- Maxillary canines and premolars = 11mm +0.5x
- Mandibular canines and premolars = 10.5mm + 0.5x;

Diagnostic test accuracy studies of the Moyers and Tanaka and Johnston methods reported inaccuracies in numerous studies conducted in different African population groups.

As a result, researchers developed and recommended population-specific index tests, which were independently investigated for applicability in the intended population (12,15,67).

These novel non-radiographic mixed dentition space analysis methods were also assessed in this review:

- Schirmer and Wiltshire tables (9)
- Modified Tanaka and Johnston method by Khan and Seedat (12)
- Abdhul Azm and Fouda method (46)

1.5 Clinical Pathway

A comprehensive orthodontic examination has five intertwined phases: clinical examination, radiographic examination, study model analysis, diagnosis and treatment plan. Upon completion of a clinical examination, patients are classified according to the dental maturation stage, i.e. primary, mixed or permanent dentition (Keystone A).

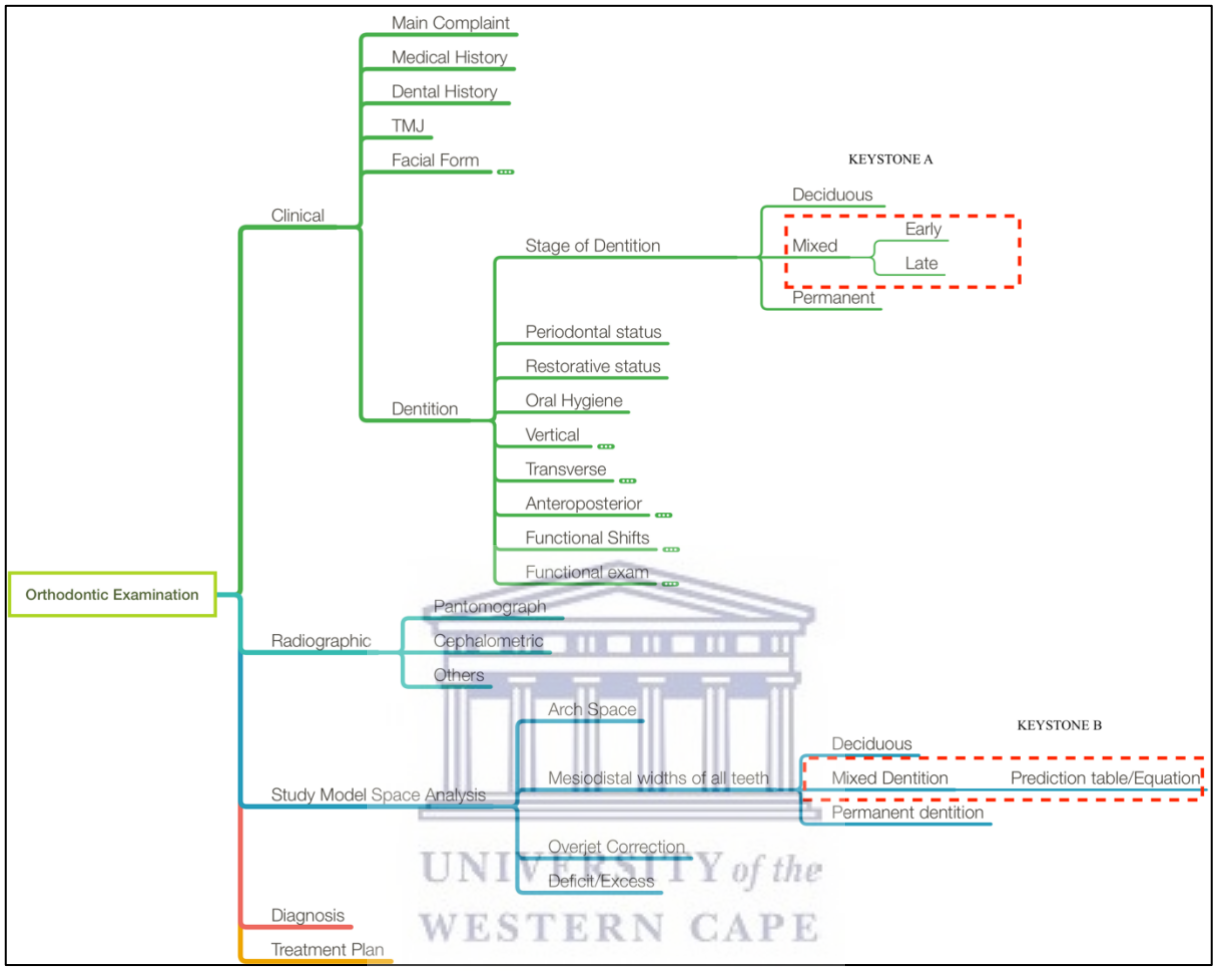
Space analysis is required for all patients in the mixed dentition stage to determine the TSALD. Radiographic and non-radiographic index tests provide estimated mesiodistal widths of the unerupted permanent canines and premolars. Since space analysis is a dynamic process for detecting space discrepancies, index test results alone cannot determine the future care of orthodontic treatments. A comprehensive space analysis must consider the Bolten discrepancies, arch length, overjet, rotations and leeway space to inform on a final diagnosis and develop an orthodontic treatment plan aligned to the patient's orthodontic needs, expectations and risk factors (68).

Figure 1 presents the critical elements of an orthodontic examination. This review aims to map a coherent landscape of non-radiographic mixed dentition space analysis methods, zooming in on specific African regions and making informed pronouncements on the methods.

1.6 Prior Tests

Patients requiring space-analysis in the mixed dentition stage routinely complete a comprehensive medical and dental history, clinical and radiographic examination prior to any diagnostic index tests. This process ensures the diagnosis and management of other dental-related conditions, such as congenitally missing teeth, impactions, translocation of teeth or grossly carious teeth, are addressed prior to orthodontic interventions.

Figure 3. Clinical Pathway for Orthodontic Treatment planning. Keystone A and B indicating the stages of mixed dentition and mixed dentition space analysis treatment pathway



1.7 Role of Index Tests

The purpose of the index test in the mixed dentition space analysis can be used as an adjunct to detect and diagnose space discrepancies. In clinical practice, conventional oral and radiographic examinations will always be undertaken as part of the clinical examination. As such, it is unlikely that a non-radiographic index test would be used as a complete replacement for the diagnosis of space discrepancies. Space analysis index tests, with a pre-defined diagnostic threshold to determine the severity of space discrepancy (positive test result of the index test), can supplement the clinical and radiographic findings in formulating a treatment approach to produce a desired clinical outcome (38,69,70).

1.8 Alternative Tests

Alternate tests include:

- Comprehensive visual or visual-tactile clinical examination of teeth to identify the risk factors to suggest a potential space discrepancy. These can include, but are not limited to, bodily movements of teeth, early loss of deciduous teeth, interproximal caries, crowding of teeth and detrimental habits.
- Radiographic methods: Direct measurements of the mesiodistal widths from periapical radiographs or a 45° Cephalometric radiograph (71–73).
- Cone-beam Computed tomography (CBCT) (74) provides three-dimensional images, which has displayed great potential with highly accurate results compared to conventional radiographic methods (7,60,75).

2 Research design and methodology

2.1 Rational

Buwembo *et al.* (76) conducted a meta-analysis in 2004 and reported on seven studies that met the inclusion criteria for the meta-analysis. The review was restricted to studies that included only the Moyers method. Due to the significant variations in the correlation coefficients reported, it was concluded that the Moyers method could not be universally applied.

Luu *et al.* (77) completed an extensive review to determine the validity and reliability of the mixed dentition space analysis methods, reporting on positively correlated validity and high interrater reliability. Concerns were demonstrated on the clinical significance of the data in practice and the efficiency in using mesiodistal space analysis methods compared to radiographic methods. Correlatively, two reviews, conducted by Sidra *et al.* (78) and Galvão *et al.* (5), reported on inaccuracies found with Moyers method and cautioned its application for space analysis for various ethnic populations.

The diagnostic test accuracy (DTA) review aimed to provide a panoptic perspective on the non-radiographic space analysis methods reported in different countries within Africa. The review expanded its search strategy to capture all relevant studies, which assessed the body of evidence using QUADAS-2 (79) to facilitate producing evidence-based summaries and results. This review also aimed to encourage researchers to look beyond the disciplinary stereotypes for DTA studies in the dentistry field and consequently develop improved protocols for DTA research to make informed pronouncements on space analysis methods.

To our knowledge, this is the first diagnostic test accuracy systematic review to report on non-radiographic space analysis methods on African studies.

2.2 Objective

To determine the diagnostic accuracy of non-radiographic mixed dentition space analysis index tests to predict the unerupted permanent canines and premolars in the maxillary and mandibular arch in the mixed dentition phases used in Africa.

Investigators had aimed to evaluate the comparative accuracy of the Moyers and Tanaka and Johnston space analysis methods and three novel methods for DTA studies conducted in Africa.

The specific research question addressed in this systematic review is:

- What is the diagnostic test accuracy of non-radiographic mixed dentition space analysis index tests compared to an appropriate reference standard for African populations?

2.3 Criteria for considering studies for this review

2.3.1 Types of Studies

The included diagnostic test accuracy study designs were:

- Studies with a single-set inclusion criterion that validated and compared non-radiographic mixed dentition space analysis methods to a reference standard. Studies that directly compared two or more index tests were included.
- Studies that evaluated the diagnostic test accuracy on a single index test to a reference standard.
- Studies that evaluated the diagnostic accuracy of two or more index tests to a reference standard.

2.3.2 Participants

Studies that had recruited participants with all permanent fully erupted teeth, up to the permanent first molar present, in the oral cavity were considered in this review. The participants had no prior orthodontic treatment, no apparent loss of tooth structure from dental caries, interproximal wear, or congenital defects and minor malocclusions. This would have ensured accurate measurements of tooth dimensions. Participants' age categories ranged from 13-23 years. There were no ethnic restrictions or gender exclusions.

Studies were restricted to a geographic location. Only DTA studies conducted in Africa were considered in this review.

2.3.3 Index Tests

Non-radiographic mixed dentition space analysis methods (nRMDSA) were assessed to predict the unerupted permanent canines and premolars (CPM). The conventional index tests, Moyers and TaJ, were conducted on the study models of participants that were included in the selection criteria. Three novel index tests, derived for specific population groups in South Africa and

Egypt, were also assessed in the DTA review. All the included studies reported correlation statistic results. However, the included studies failed to adequality report data to enable the construction of 2 x 2 contingency tables. They had not described the diagnostic threshold needed to measure clinical significance or diagnostic performance. Researchers made a critical appraisal and presented studies as a descriptive review to provide helpful information for future research, yielding clinically relevant space analysis methods in the mixed dentition stages.

2.3.4 Target Condition

Prediction of mesiodistal dimensions of unerupted canines and premolars in the mandible and maxilla for space analysis in the mixed dentition phase. These measurements are essential to diagnose imbalances between the mesiodistal dimensions of permanent canines and premolars with the available space in the arch.

Dental malocclusion occurs due to space discrepancies and the dental arch and hard tissue disharmony. The lack of mesiodistal arch space to accommodate the permanent canines and premolars in the mixed dentition stage can lead to crowding and severe dental malocclusion (24,80,81).

2.3.5 Reference Standards

Several reference standards can be used in primary diagnostic test accuracy studies for mixed dentition space analysis. The only way of achieving a true diagnostic accuracy of the mesiodistal dimensions of the unerupted permanent canine and premolars is to prospectively evaluate the participants once the teeth erupt into the oral cavity. This approach is, however, an impractical study design.

CBCT is considered an excellent and reliable reference standard; however, the increased radiation risks do not justify exposing the patient solely for research purposes (7).

Participants were selected with all permanent teeth, including the permanent first molar, with minimal dental interventions and “normal” occlusion. Study models from dental impressions

of the maxillary and mandibular arches from each participant provided static data of the mesiodistal dimensions of the permanent canines and premolars. The sum of the mesiodistal widths of the permanent mandibular incisors was recorded and applied to the index test.

Investigators had hoped to compare the results of different reference standards being utilized. However, all the included studies reported dental study models as the reference standard of choice and appropriate for this DTA study.

2.4 Search Methods for the Identification of studies

2.4.1 Electronic searches

The research team had developed the search strategy and conducted all searches to August 21, 2021. There were no language limitations applied to the searches.

An electronic search was conducted for primary and ongoing studies in the following databases:

- African Index Medicus (AIM) (inception to August 2021) (Appendix 2)
- PUBMED (inception to August 2021) (Appendix 3)
- Sabinet African Journals (inception to August 2021) (Appendix 4)
- Wiley (inception to August 2021) (Appendix 5)
- Scopus (inception to August 2021) (Appendix 6)
- EbscoHost (academic search complete, cinahl, dentistry and oral sciences) (inception to August 2021) (Appendix 7)
- ScienceDirect (inception to August 2021) (Appendix 8)

2.4.2 Searching other resources

Investigators had searched the reference list of included studies and previously published systematic reviews not identified in the electronic searches. Studies previously conducted for academic fulfilment and appeared on the South African Nationally Electronic Thesis and Dissertation (ETD) portal were excluded.

2.5 Data collection and analysis

2.5.1 Selection of Studies

The principal investigator and co-investigator independently screened both the titles and abstracts of the selected studies and retrieved full-text articles for those regarded to be relevant and for studies that could not be judged on the title and abstract alone. Any disagreements were settled on thorough discussion and were necessary, consultation with a third co-supervisor of the review. The study selection process was reported on an adapted PRISMA flow chart (82).

2.5.2 Data extraction and management

The principal researcher completed the data extraction on included full-text articles into a data collection tool developed using Microsoft Excel (Microsoft Inc). The co-supervisor verified all the studies for general characteristic information and outcome data. Any disagreements were resolved by consensus and through discussion with co-supervisors of review.

Data was extracted under the following: study methods, population, interventions, comparisons, outcomes, and conclusions. These are elaborated below (83,84):

Publication Details:

Authors, year of publication, year of research, language, publication status, Country of recruited population.

Characteristics of the Study:

Study design, reference standard, methodology, sample size, reliability methods, source of funding and academic institution affiliations.

Characteristics of the population:

Age, gender, ethnicity, previous dental or orthodontic management, samples directly from participants or duplication of the oral cavity in a dental cast, information regarding representatives of the included populations.

Index Test:

Non-radiographic mixed dentition space analysis method (nRMDSA).

Study Results:

Investigators intended to report on the true positive, true negative, false positive, false negative, equivocal results and QUADAS-2 items (Appendix 1).

2.5.3 Assessment of methodological quality

Methodological quality refers to the risk of bias resulting from the design and conduct of the study. The quality of a diagnostic test accuracy study is determined by its design, the research methods by which the study sample was recruited, the conduct of tests involved, blinding in interpreting results, and the comprehensiveness of the study report (1,85).

The principal investigator and co-investigator critically appraised the included studies using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) instrument to assess the risk of bias of the included primary studies over the four domains of patient selection, index tests, reference standard and flow and timing tailored for this review (1,79,82,86,87). 'Review specific' descriptions of how the QUADAS-2 items were contextualised and implemented are detailed in the accompanying checklist (Appendix 1).

An assessment for the 'Risk of bias' judgement (high, low, unclear) was made for each domain for each study. If the answers to all signalling questions within the domain were judged "yes", the domain was judged to be at low risk of bias. If any signalling question were judged as "no", the domain was judged to be at high risk of bias. Similarly, if any signalling questions were judged as "unclear", indicating an unclear risk of bias, the domain was judged to be at unclear risk of bias. Concerns regarding applicability were then completed for participation selection, index tests and reference standard domains. Responses to the risk of bias and applicability judgements are presented in the Characteristics of included studies tables and summarised graphically (Figure 5 and Figure 5).

The elements in consideration of each domain are detailed below:

Domain 1: Participant selection

All studies should have fully reported the methods used to select the participants. Ideally, a randomised, consecutive sampling would be used, and the procedure explicitly reported. It was deemed acceptable for studies to focus on patients in the adolescent aged category 13 -23 years. Inappropriate exclusions may have led to an over or underestimation of the tests' ability to detect space discrepancies, thus affecting the study's internal validity. It was also acceptable for studies to report on single or multiple index tests. The severity of space discrepancies and their prevalence should have been clearly reported, as this information is of potential utility in the assessment for the applicability of the index tests to a broader population.

Domain 2: Index Tests

The prediction of the MD widths of the unerupted CPM (index test) should have ideally been conducted prior to recording the MD dimensions of the permanent CPM from the study models (reference standard). This testing sequence (index test followed by reference standard) ensures that the index test results are not influenced by the reference standard results, eliminating potential information bias.

To further minimise bias, separate examiners should have been utilized to record the index test and reference standard.

A clinical diagnostic threshold to determine positive and negative space discrepancy results should also be pre-specified.

Domain 3: Reference Standard/Tests

The focus of this section was to determine the potential bias introduced by the conduction and interpretation of the reference standard tests. While reference testing can be conducted by the same examiner of the index tests, a second examiner to conduct the reference testing to reduce information bias is advised. All reference standards should ideally be completed without knowledge of the index test results. Inter-reliability methods should be explicitly reported to ensure reproducible and reliable results. Ideally, participants within a study should receive the

same reference test. If a study allocated participants to different reference standards, reasons for this differential allocation should be explicitly reported.

Domain 4: Flow and Timing

This section aimed to determine the risk of bias attributed to the index test and reference standard testing sequence. Lengthy-time delays can alter the dimensions of the tooth morphology or its supportive alveolar ridge, which can impact space analysis results.
Superior quality study models of the dentition stored appropriately will ensure that no change of the tooth morphology would be experienced. All observations should have received both the index test and reference standard.

The principal investigator and co-investigator discussed each appraisal domain of the review's included studies. Discussions of what constituted an acceptable review were made to allocate a positive appraisal compared to a negative or unclear response.

2.5.4 Statistical analysis and data synthesis

Data tables were used to present the descriptive statistics of each included study. The Characteristics of included studies tables detail the patient sample, study design, mixed dentition space analysis, index test technique and the descriptive statistic at which space accuracy was reported. Researchers extracted the mean differences, confidence intervals (CI) (95%), and *p*-values for all included studies. The risk of bias results in each domain of the QUADAS-2 assessment of individual studies are presented graphically (1).

The threshold of interest is determined by the predicted values from the index tests and the actual tooth measurements of the permanent CPM from the reference standard. The included studies did not pre-specify positive diagnostic thresholds for the index tests. It was impossible to produce diagnostic test accuracy estimates as sensitivity and specificity with 95% CI for each study and index test. Investigators were unable to display the variability of the sensitivity and specificity of each included study on coupled forest plots and present the results on summary receiver operating characteristics (SROC) plots (88).

For the primary analysis, investigators had intended to undertake a meta-analysis to combine the results of the studies for each index test. However, the substantial diversity of characteristics of the studies and the paucity of data for each index test meant a meta-analysis was not appropriate in this review.

2.5.5 Investigation of Heterogeneity

Heterogeneity exists when the estimates of test accuracy vary between studies more than would be expected from within sampling error alone. Investigators had planned to undertake a meta-regression analysis to explore the possible sources of heterogeneity by a formal model comparison using a likelihood ratio Chi^2 statistic. Subgroup analysis can also be used to detect heterogeneity.

Due to the diversity of the clinical and methodological characteristics of the included studies, the planned investigations of heterogeneity could not be assessed (88).

2.5.6 Sensitivity analyses

Investigators planned a sensitivity analysis to assess the impact of the methodological quality on the results of a meta-analysis. Had there been a sufficient number of studies that investigated the same index test, the impact of the study quality could have been produced on a summary table to assess the sensitivity and specificity of the results.

In this review, investigators were unable to undertake sensitivity analysis due to the paucity of the studies evaluating each space analysis method (index test).

2.5.7 Assessment of reporting bias

Methods currently available to assess reporting or publication bias for diagnostic test accuracy studies are not well established and may lead to uncertainty and misleading results from funnel plots. Consequently, the investigators had opted against testing for reporting bias (89).

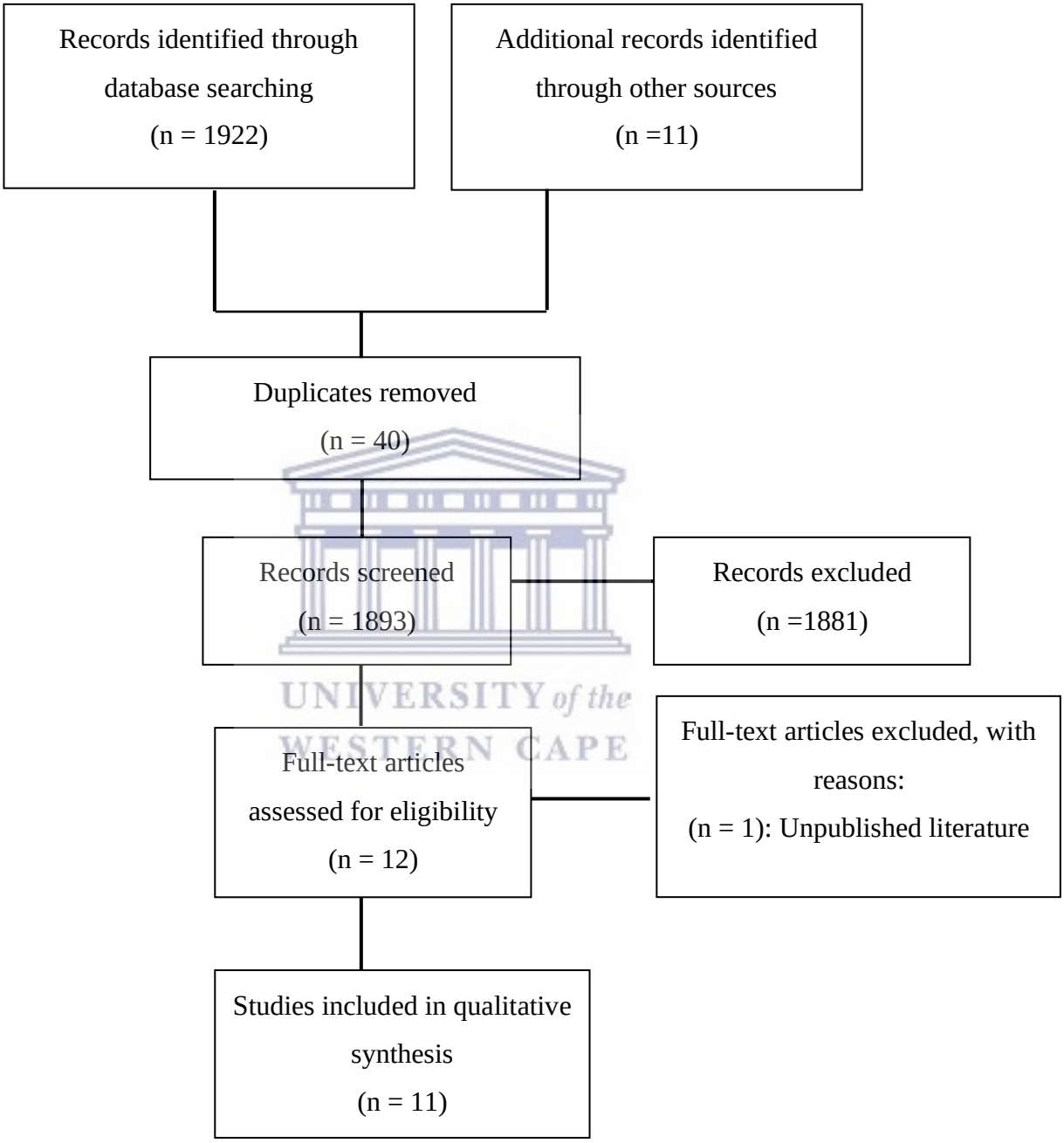
3 Results

3.1 Results of the search

The literature search identified 1922 references for the space analysis index tests from the following databases: African Index Medicus (AIM)(n = 12), PubMed (n = 971), Sabinet African Journals (n = 20), Wiley (n = 207), Scopus (n = 3), EbscoHost (academic search complete, cinahl, dentistry and oral sciences)(n = 692), Science Direct (n = 18). A further 11 references were identified through reference list citation searching.

The PRISMA flow diagram on the search process is presented in Figure 4. Titles were screened to exclude duplicates (n = 40), and a further 1881 references were eliminated based on the titles and abstracts as they did not address the research question or did not meet the eligibility criteria. The full-text articles of 12 references were retrieved and assessed for its eligibility. Ultimately, 11 studies were eligible and provided data for this review, and 1 study was excluded due to it being unpublished research.

Figure 4. PRISMA flow diagram: Results of the search for studies evaluating the diagnostic accuracy of non-radiographic mixed dentition space-analysis methods in Africa.



Eleven cross-sectional diagnostic test accuracy studies published between 1997 and 2019 were eligible for inclusion. The included studies spanned seven African countries; the majority had been carried out in South Africa (3 studies) and Egypt (3 studies), followed by 1 study each in Sudan, Libya, Senegal, Uganda, and Nigeria. Forty-five percent (5/11) of the studies performed the tests on participants in schools, 45% (5/11) on participants from academic dental institutions, and 9,09% (1/11) on participants from a clinical dental practice (3,12,14,46,49,50,52,56,57,90,91). All participants were in adolescence to ensure that all the permanent teeth had fully erupted up to the first permanent molar.

The five index tests assessed in the included studies were non-radiographic space analysis methods for the prediction of the unerupted canines and premolars. Eight studies reported on the TaJ DTA methods (12,49–52,56,57,92), six reported on Moyers probability tables (49,50,57–59,92), and two studies reported on three novel nRMDSA methods (3,46). The majority of studies assessed two index tests on a single sample population (3,49–51,57,92), with only five studies assessing a single index test on its sample population (12,46,52,56,59). Of the included studies, bilateral symmetry of teeth from the maxillary quadrants 1 and 2, and mandibular quadrants 3 and 4 were assessed in eight of the eleven studies (12,46,49,50,52,56,58,90), and gender comparisons were analysed in nine of the eleven studies (3,9,12,49,50,52,57,58,90).

Ten included studies reported the index tests being investigated to have either overestimated or underestimated the values for the unerupted permanent CPM and were considered invalid for its study populations (3,9,12,49,50,52,56–58,90). Fouda *et al.*(46), who evaluated a novel approach, was the only study that reported valid index test results for that sample population (46). As a result of these findings, eight of the eleven included studies had developed and proposed new equations or tables to predict the unerupted CPM (9,12,49–52,56,90,93).

The included studies reported on the comparative correlation rather than on diagnostic estimate accuracy. None of the included studies had reported on the diagnostic estimates of the data with pre-specified diagnostic thresholds. Investigators were unable to extract true-positive, false-positive, true-negative or false-negative results, therefore unable to construct 2 x 2 tables. This highlighted the critical issue of incomplete reporting of data outcomes and the paucity in the evidence base (3,9,12,46,49–52,56,57).

Investigators critically appraised and presented studies as a descriptive review, as the results and information reported are beneficial for future research to produce clinically relevant outcomes for space analysis methods.

One article was excluded from this review because it is an academic study to fulfil a higher degree academic thesis. Unpublished DTA studies were explicitly excluded from this review (94).

3.2 Methodological quality of included studies

The individual methodological quality assessment of the included studies are summarised in Figure 5 and Table 16 and illustrated in Figure 5. There were no studies judged at low risk of bias across all domains. All studies were judged as a low concern of applicability for patient selection domains, index test and reference standard domains.

Figure 5. QUADAS-2 risk of bias and applicability concerns graph including review authors' judgements about each domain presented as percentages across included studies.

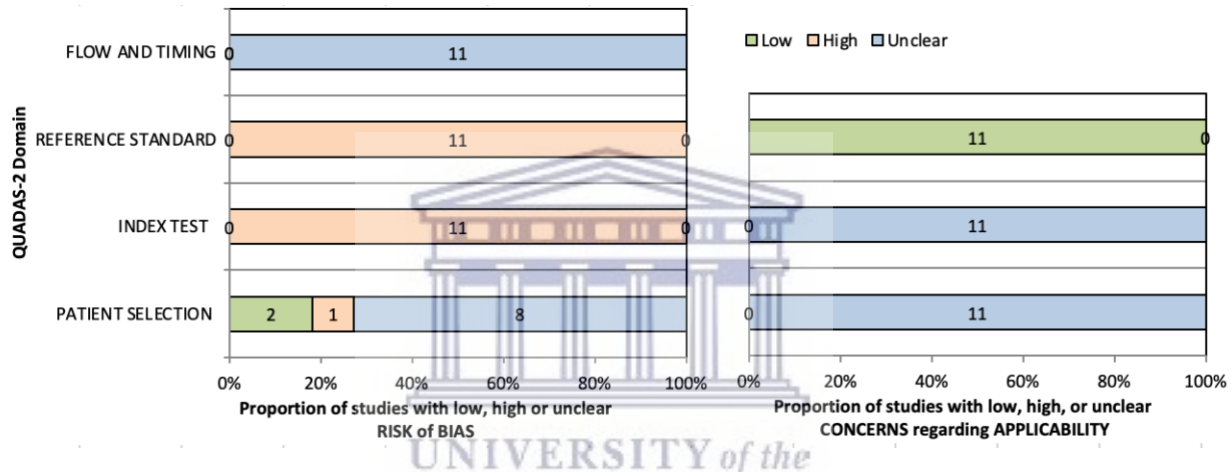


Figure 6. Risk of bias and applicability concerns summary: review investigators' judgements about each domain for each included study.

Study	Reference	RISK OF BIAS				APPLICABILITY CONCERNS		
		PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Study 1	Fouda 2019	☹	☹	☹	?	?	?	☺
Study 2	Refai 2012	?	☹	☹	?	?	?	☺
Study 3	Alzubir 2016	?	☹	☹	?	?	?	☺
Study 4	Ajayi 2014	?	☹	☹	?	?	?	☺
Study 5	Bugaighis 2013	☺	☹	☹	?	?	?	☺
Study 6	Buwembo 2012	☺	☹	☹	?	?	?	☺
Study 7	Khan 2007	?	☹	☹	?	?	?	☺
Study 8	Diagne 2003	?	☹	☹	?	?	?	☺
Study 9	Schirmer 1997	?	☹	☹	?	?	?	☺
Study 10	Sethusa 2018	?	☹	☹	?	?	?	☺
Study 11	Hammad 2010	?	☹	☹	?	?	?	☺

☺ Low Risk ☹ High Risk ? Unclear Risk

Patient selection domains were judged to be at low risk of bias in two out of the eleven studies (18.18%) (50,57). These studies had clearly stated the random selection of participants. Investigators had judged the remaining eight studies (72.72%) to be at unclear risk of bias as patient recruitment information was incompletely reported (3,12,49,52,56,59,91,92). The remaining one study (9.09%) was judged at high risk of bias due to the recruitment of participants from within a private dental clinic, with incomplete reporting of the random selection of participants (46).

All the included studies were judged as unclear concerns for applicability (100%) for the patient selection domain. The studies had statistically reported on the mean differences found in the data of the sample population instead of assessing the diagnostic estimates per participant.

The overall judgement of the index test domain was at high risk of bias in all the included studies. The diagnostic threshold to determine the index test positive or negative was not pre-specified. One study (59) had failed to provide sufficient details and a reference for the diagnostic threshold vaguely mentioned in the literature. Therefore, it was judged at an unclear risk of bias in the index test domain. Blinding of investigators was not reported, with one included study reported having had two investigators who independently measured the reference standard (9). Therefore, it was implied that the index test results were interpreted with knowledge of the reference standards on single or multiple index test studies (3,12,14,46,49–52,56,57,92). To minimise bias, a clear protocol on the testing sequence on the study design should be outlined in DTA studies.

The index test domain was judged as an unclear concern for applicability in all the included studies. None of the studies had indicated a pre-specified diagnostic threshold for the index tests investigated. However, there were detailed descriptions of the application of each index test in the included studies, which could be replicated for future studies.

The reference standard domain was judged at a high risk of bias in all included studies. As part of the risk of bias assessment, all the included studies had failed to report on blinding from index test results and had also not reported on the sequence at which investigations were carried out. Diagnostic study models of the dentition were the reference standard of choice in all the included studies. It was an appropriate reference standard that presented the fully erupted permanent CPM data in the maxillary and mandibular arches.

All studies were judged at low concern for applicability for the reference standard domain.

The flow and timing domain was deemed an unclear risk of bias in all the included studies (3,12,46,49–52,56,57,59,92). The included studies had failed to report timing between index test and reference standards investigations explicitly. There was no information reported on the safe storage, accurate indexing and accessibility of the study models.

3.3 Findings of the review

Given the small number of studies, incomplete reporting of the outcomes data, and the substantial diversity of characteristics of the included studies, investigators were unable to formally evaluate the comparative accuracy of the different index tests considered in the review. The pooling of poor quality data may produce misleading evidence with limited credibility for the investigated index tests; hence a meta-analysis was not considered appropriate in this review.

A critical appraisal was completed, and studies were presented in a descriptive review format. They are likely to provide useful information for future research, with more clinical relevance to space analysis methods in the mixed dentition stages.

3.3.1 Non-radiographic mixed dentition index test

Eight studies measured the TaJ index test (12,49–52,56,57,92). Five studies also evaluated the Moyers probability index test to the reference standard (48–51,57). Moyers probability index test was validated independently in 1 study (14). Three novel index tests were validated in 2 studies, Abdhul Azm and Fouda, Schirmer and Wiltshire and Modified Tanaka and Johnston equation (3,46).

All the included studies failed to include a pre-specified diagnostic threshold to determine the clinical significance of the results, i.e., the difference between the dimensions of the unerupted permanent teeth and its predictive value, which indicates an excess of tooth material to be accommodated in the available arch space. One study vaguely indicated a clinically significant

threshold of approximately 1mm. However, no further details or references to validate this information was included in the research methodology (14).

Statistically significant mean differences (*p*-values) between the index test and the reference standard were reported to assess diagnostic accuracy. However, only six of the included studies presented summation data tables on these differences in its literature (46,48,50,52,57,59). The researchers of the remaining five included studies had failed to provide sufficient data and summation tables in its literature to establish certainty in the results reported.
A study that investigated the novel Abdhul Azm and Fouda method concluded it was an appropriate diagnostic predictor in the Egyptian population in Angles Class I cases. (46).

Ten of the included studies reported at least one or both index tests assessed to be inaccurate for its sample populations. Eight of the studies recommended using newly derived methods to determine the MD widths of the unerupted CPM (12,14,48–52,56).

Figure 7 Non-radiographic mixed-dentition index tests investigated by researchers of the included studies. Three studies reported on Tanaka and Johnston (TaJ) equations exclusively, on reported on Moyers predictive tables, five had reported on both the TaJ and Moyers. Two studies reported on novel methods.

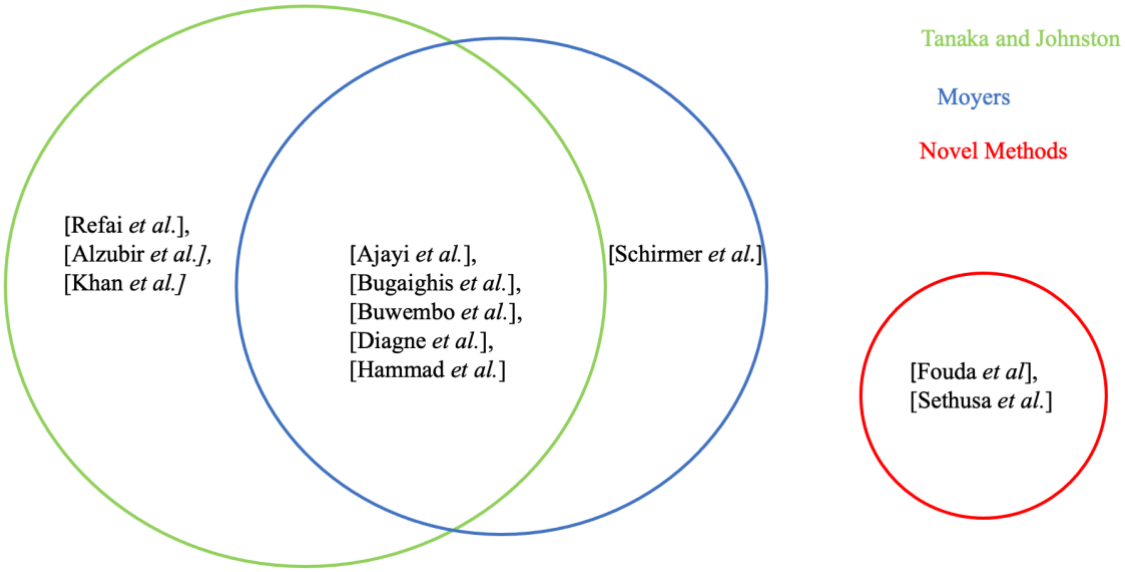


Table 3. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Tanaka and Johnston equation (1974) of the whole sample in the included studies.

Study	Country	Sex	Sample (n)	Arch	Mean Difference	Standard deviation (mm)	*p* value	CI (95%)
Alzubir 2016	Sudan	M+F	250	UCPM	0.44*	-	<0.001	-
				LCPM	0.39*	-	<0.001	-
						-		-
Bugaighis 2013	Libya	M	169	UCPM	0.8*	-	-	-0.93 to -0.66
				LCPM	0.67*	-	-	-0.80 to -0.55
		F	174	UCPM	0.97*	-	-	-0.92 to -0.66
				LCPM	0.68*	-	-	-0.79 to -0.55
		M+F	343	UCPM	0.8*	-	-	-0.89 to -0.70
				LCPM	0.67*	-	-	-0.76 to -0.59
Buwembo 2012	Uganda	M	85	UCPM	-0.85*	0.1	-	-0.91 to -0.78
				LCPM	-0.53*	0.22	-	-0.67 to -0.38
		F	135	UCPM	-0.98*	0.12	-	-1.06 to -0.90
				LCPM	-0.8*	0.33	-	-1.02 to -0.59
		M+F	220	UCPM	0.75*	0.11	-	0.66 to 0.81
				LCPM	-0.8*	0.25	-	-0.86 to -0.53

Study	Country	Sex	Sample (n)	Arch	Mean Difference	Standard deviation (mm)	*p* value	CI (95%)
Hammad 2010	Egypt	M	180	UCPM	0.8398*	0.839	-	0.779 to 0.899
				LCPM	0.680*	0.68	-	0.616 to 0.743
		F	145	UCPM	1.393*	0.51	-	1.310 to 1.477
				LCPM	1.507*	0.431	-	1.436 to 1.577
Refai 2012	Egypt	M+F	1000	UCPM	-	-	-	-
				LCPM	-	-	-	-
Ajayi 2014	Nigeria	M+F	54	LI	-	-	-	-
				UCPM	-	-	-	-
				LCPM	-	-	-	-
Khan 2007	South Africa	M+F	110	UCPM	-	-	-	-
				LCPM	-	-	-	-
Diagne 2003	Senegal	M+F	50	UCPM	-	-	-	-
				LCPM	-	-	-	-

Summary of Tanaka and Johnston index tests conducted in Africa from 2000- 2014. Missing values (-) indicate paucity of data from the included studies. Where possible, CI (95%) and *p*-values were reported. Investigators were unable to formally evaluate the comparative accuracy of tests due to heterogeneity in the clinical and methodological characteristics of the studies. Statistically significant results $p<0.001$. *Indicates statistically significant results reported. *M*, Male; *F*, Female; *UCPM,* Upper canine and premolar; *LCPM,* Lower canine and premolar; *LI,* Lower Incisor; *CI,* Confidence Intervals.

3.3.1.1 Tanaka and Johnston (Table 3)

Three studies (12,52,56) exclusively investigated the TaJ equations and reported on the statistically significant discrepancies (p<0.001) identified. One study by Alzubir *et al.* (52) reported a statistically significant mean difference of 0.44mm and 0.39mm for the upper canine and premolars (UCPM) and the lower canine and premolars (LCPM), respectively, for a combined sample population of males and females.

A study by Refai *et al.* (56) investigated and reported on the upper and lower limits of agreement from the UCPM and LCPM ranging from [-1.263mm–3.563mm] and [-1.203mm–3.128mm] respectively for the combined males and females sample population.

Khan *et al.* (12) provided limited data to substantiate the index test validity results reported for the female Black South African population. However, new proposed population-specific index tests were derived for Black South African males from regression analysis of the collated data.

Table 4. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Moyers probability tables of the male sample in the included studies.

Study	Country	*Number (n)*	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
Bugaighis 2013	Libya	n = 169					
		Maxilla (UCPM)	35	0.107*	0.111	0.88	- 0.02 to 0.25
			50	0.0001	-0.235	0.88	-0.37 to -0.10
			75	<0.0001	-0.89	0.88	-1.02 to 0.75
		Mandible (LCPM)	35	0.0001	0.228	0.84	0.10 to 0.36
			50	<0.0001	-0.472	0.84	0.60 to -0.35
			75	<0.0001	-0.872	0.84	0.99 to -0.75
Buwembo 2012	Uganda	n = 85					
		Maxilla (UCPM)	5	<0.0001	-1.61	0.08	-1.66 to -1.56
			15	<0.0001	-1.06	0.07	-1.14 to -1.04
			25	<0.0001	-0.79	0.07	-0.84 to -0.74
			35	<0.0001	-0.54	0.09	-0.59 to -0.48

Study	Country	*Number (n)*	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
			50	<0.0001	-0.2	0.06	-0.25 to -0.16
			65	0.001	0.11	0.08	0.06 to 0.16
			75	0.451*	-0.13	5.73	-4.96 to 2.36
			85	<0.0001	0.67	0.1	0.60 to 0.16
			95	<0.0001	1.2	0.1	1.14 to 1.27
		Mandible (LCPM)	5	<0.0001	2.32	0.29	2.13 to 2.51
			15	<0.0001	1.61	0.3	1.42 to 1.8
			25	<0.0001	1.16	0.28	0.98 to 1.34
			35	<0.0001	0.81	0.3	0.62 to 1.01
			50	0.002	0.37	0	0.17 to 0.57
			65	0.388*	-0.08	0.32	-0.28 to 0.12
			75	0.001	-0.43	0.34	-0.65 to -0.21
			85	<0.0001	-0.86	0.33	-1.06 to -0.64
			95	<0.0001	-1.6	0.36	-1.84 to -1.37
Schirmer 1997	South Africa	n = 50					
		Maxilla (UCPM)	5	0.0002	2.55		
			15	0.0002	2.13		

Study	Country	*Number (n)*	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
			25	0.0002	1.89		
			35	0.0002	1.68		
			50	0.0002	1.42		
			65	0.0002	1.15		
			75	0.0002	0.95		
			85	0.0002	0.7		
			95	0.0002	0.29		
		Mandible (LCPM)	5	0.0002	3.45		
			15	0.0002	2.86		
			25	0.0002	2.49		
			35	0.0002	2.2		
			50	0.0002	1.82		
			65	0.0002	1.43		
			75	0.0002	1.15		
			85	0.0002	0.79		
			95	0.002	0.16		
Hammad 2010	Egypt	n = 180					

Study	Country	*Number (n)*	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
		Maxilla (UCPM)	35		-0.526	-0.394	-0.584 to -0.468
			50		-0.19	0.4	-0.248 to -0.131
			75		0.438	0.746	0.329 to 0.548
		Mandible (LCPM)	35		-0.553	0.419	-0.735 to -0.611
			50		-0.231	0.413	-0.292 to -0.170
			75		0.533	0.411	0.493 to 0.614

UCPM, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*,number; *CI*, Confidence Intervals; statistically significance ($p<0.001$).

Table 5. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Moyers probability tables of the whole female sample in the included studies.

Study	Country	Number (n)	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
Bugaighis 2013	Libya	n = 174					
		Maxilla (UCPM)	35	0.036	0.14	0.89	0.01 to 0.27
			50	0.002	-0.21	0.89	-0.34 to -0.08
			70	<0.0001	-0.86	0.89	-0.99 to -0.73
		Mandible (LCPM)	35	<0.0001	0.26	0.85	0.13 to 0.39
			50	<0.0001	-0.44	0.85	-0.57 to -0.31
			70	<0.0001	-0.84	0.85	-0.94 to -0.71
Buwembo 2012	Uganda	n = 135					
		Maxilla (UCPM)	5	<0.001	-2.47	0.47	-2.77 to -2.17
			15	<0.001	-1.81	0.48	-2.12 to -1.51
			25	<0.001	-1.44	0.49	-1.75 to -1.12
			35	<0.001	-1.14	0.49	-1.45 to -0.82
			50	<0.001	-0.74	0.49	-1.05 to -0.42

Study	Country	Number (n)	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
			65	0.044	-0.33	0.5	-0.65 to -0.01
			75	0.865*	-0.02	0.49	-0.34 to 0.29
			85	0.041	0.34	0.51	0.01 to 0.66
			95	0.702*	-0.67	5.94	-4.45 to 3.10
		Mandible (LCPM)	5	<0.001	-2.66	0.28	-2.84 to -2.48
			15	<0.001	-1.93	0.28	-2.11 to -1.75
			25	<0.001	-1.5	0.27	-2.67 to -1.32
			35	<0.001	-1.15	0.28	-1.33 to -0.97
			50	<0.001	-0.7	0.29	-0.87 to -0.50
			65	0.027	-0.22	0.29	-0.40 to -0.02
			75	0.195*	0.13	0.31	-0.07 to 0.32
			85	<0.001	0.55	0.3	0.35 to 0.74
			95	<0.001	1.28	0.31	1.08 to 1.48
Schirmer 1997	South Africa	n = 50					
		Maxilla (UCPM)	5	0.0002	2.48		
			15	0.0002	1.94		
			25	0.0002	1.65		
			35	0.0002	1.4		

Study	Country	Number (n)	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
			50	0.0002	1.12		
			65	0.0010	0.75		
			75	0.0107	0.52		
			85	0.2263*	0.22		
			95	0.0947	-0.3		
		Mandible (LCPM)	5	0.0002	2.94		
			15	0.0002	2.33		
			25	0.0002	1.98		
			35	0.0002	1.69		
			50	0.0002	1.31		
			65	0.0002	0.92		
			75	0.0002	0.64		
			85	0.0002	0.28		
			95	0.0002	-0.32		
Hammad 2010	Egypt	n= 145					
		Maxilla (UCPM)	35		0.497	0.496	-0.579 to 0.416
			50		-0.095	0.494	-0.176 to -0.014
			75		0.486	1.591	0.225 to 0.747

Study	Country	Number (n)	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
		Mandible (LCPM)	35		-0.459	0.328	0.512 to -0.405
			50		0.058	0.315	-0.046 to -0.057
			75		0.824	0.305	0.774 to 0.874

UCPM, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*,number; *CI*, Confidence Intervals; statistically significance (p<0.001).

3.3.1.2 Moyers Index test (Table 4 and Table 5)

Schirmer and Wiltshire (14) investigated and reported on the Moyers DTA for a South African black population. The study reported statistically significant differences (p<0.001) found in the mean differences between the index test and the reference standard at each percentile for the UCPM and LCPM for males and females, except at the 85th percentile level (p = 0.2263) for UCPM in females. Consequently, researchers had derived and recommended new tables for Black South Africans for nRMDSA.

3.3.1.3 Tanaka and Johnston and Moyers Index Tests (Table 3, Table 4 and Table 5)

Five studies investigated both the TaJ and Moyers index tests (48–50,57,58) and reported the comparative mean differences between the index test and reference standards for nRMDSA.

Three (48,50,57) of the studies that investigated the TaJ index test reported statistically significant mean differences for the UCPM and the LCPM ranging from [-0.85mm–0.839mm] and [-0.53mm–0.680mm] respectively for males. In females, studies reported statistically significant mean differences for the UCPM and the LCPM ranging from [-0.98mm–1.393mm] and [-0.8mm–1.507mm] respectively.
The two (50,57) remaining studies reported statistically significant mean differences for the UCPM and LCPM ranging from [0.75mm–0.8mm] and [-0.8mm–0.67mm] respectively for the combined sample of males and females.

Bugaighis *et al.* (50), Buwembo *et al.* (57) and Hammad *et al.* (48) investigated the Moyers index tests and reported on the mean differences at each percentile between the index test and the reference standard in both the maxilla (UCPM) and the mandible (LCPM) for males and females.

The study by Bugaighis *et al.* (50) reported no statistically significant discrepancies in the mean differences (p=0.107) between the index test and the reference standard at the 35th percentile

for the UCPM in males. Researchers had derived new index test methods from the regression analysis of the data better suited for the Libyan population.

Buwembo *et al.* (57) reported no statistically significant discrepancies in the mean differences between the index test and the reference standard at the 75th (p=0.451) and 65th (p=0.388) percentile levels for the UCPM and LCPM, respectively for males. In the female population, there were no statistically significant discrepancies in the mean differences between the index test and the reference standard at the 75th (p=0.865) and 95th (p=0.702) percentile levels for the UCPM, and at the 75th (p=0.195) percentile level for the LCPM respectively. Researchers had concluded that the Moyers index test had provided sufficient diagnostic accuracy at the above-mentioned percentile levels for the Ugandan population.

The study by Hammad *et al.* (48) reported no statistically significant discrepancies in the mean differences [0.058mm] between the index test and the reference standard at the 50th percentile for the LCPM in females. Newly formulated tables for the nRMDSA for an Egyptian population were derived and recommended.

Two studies by Ajayi *et al.* (49) and Diagne *et al.* (58) provided limited data in its DTA study to appraise the statistical findings and results critically; However, both the studies had developed new nRMDSA methods for Nigerian and Senegalese populations.

Table 6. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Modified Tanaka and Johnston and Schirmer and Wiltshire predictive methods of the male and female samples.

						Index test 1. Modified Tanaka and Johnston			**Index test 2. Schirmer and Wiltshire**		
Study	Country	Sex	Sample (n)	Arch	Actual MD widths (mm)	Mean (mm)	Standard deviation (mm)	P value	Mean (mm)	Standard deviation (mm)	P value
Sethusa 2018	South Africa	M	50								
				UCPM	47.20	48.37	2.11	0.0001	47.64	0.88	0.1748*
				LCPM	47.28	48.61	2.28	0.0001	48.12	1.04	0.0198
		F	50								
				UCPM	45.60	45.95	1.32	0.1848*	44.92	1.33	0.0114
				LCPM	45.21	44.95	1.32	0.3776*	44.89	1.28	0.2990*

M, Male; *F*, Female; *UCPM*, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*, number; *, statistically significance (p<0.001)

Table 7. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Abdhul Azm and Fouda predictive methods in the whole female sample.

Study	Country	Quadrant	Sample (n)	Arch	P value	Mean Difference
Fouda 2019	Egypt		n= 21			
		1 and 4 (RHS)		UCPM	0.026	-0.63
				LCPM	0.176	-0.16
		2 and 3 (LHS)		UCPM	0.493	0.27
				LCPM	0.805	-0.06

RHS, Right hand side*; LHS,* Left hand side*; M,* Male; *F,* Female; *UCPM,* Upper canine and premolar; *LCPM,* Lower canine and premolar; *n*,number; statistically significance (p<0.05)

3.3.1.4 Novel Index Tests (Table 6 and Table 7)

Two studies (3,46) investigated and reported on three novel predictive methods, the Schirmer and Wiltshire index test, Modified Tanaka and Johnston equation and the Abdhul Azm and Fouda method for a South African and Egyptian population, respectively.

The Abdhul Azm and Fouda index test (46) investigated by Fouda reported a statistically significant mean difference (p=0.026) for the right UCPM. The author had recommended the index test diagnostic accuracy for nRMDSA for an Egyptian female population (Table 7).

Sethusa *et al.* (3) investigated and reported on the two novel DTA index tests, the Schirmer and Wiltshire index test by Schirmer *et al.* (9) and the Modified Tanaka and Johnston index test developed by Khan *et al.* (12) for a Black South African population. The authors' investigation of the Schirmer and Wiltshire (9) index test had reported no statistically significant discrepancies in the mean differences, between the index test and the reference standard, for the UCPM (p=0.1748) for males and LCPM (p=0.2990) for females. The investigation of the Modified Tanaka and Johnston index test (12) had reported no statistically significant discrepancies found in the mean differences, between the index test and the reference standard, for the UCPM (p=0.1848) and LCPM (p=0.3776) for the female participants. Based on these results, the authors recommended using the Modified Tanaka and Johnston index test over the Schirmer and Wiltshire index test for a Black South African population (Table 6).

Due to the insufficient and incomplete reporting on important outcome data, coupled with the diversity in clinical and methodological characteristics, researchers were unable to undertake the planned investigations of heterogeneity and sensitivity analysis.

4 Discussions

4.1 Summary of results

This review aims to report on the diagnostic accuracy of non-radiographic mixed dentition space analysis methods to predict the unerupted permanent canines and premolars for patients in the African continent. The included studies evaluated the index test of 4 non-radiographic space analysis methods: TaJ, Moyers probability tables, Schirmer and Wiltshire tables, Modified Tanaka and Johnston and the Abdhul Azm and Fouda methods (Figure 7).

- Three studies investigated the TaJ index test.
- One study investigated the Moyers index test
- Five studies investigated both the TaJ and Moyers index tests
- Two studies investigated three novel index tests: the modified Tanaka and Johnston method, Schirmer and Wiltshire table and the Abdhul Azm and Fouda method

Evaluating diagnostic test accuracy requires, at the very least, knowledge of the sensitivity and specificity. The sensitivity and specificity are measures defined conditional on the disease status. These measures are computed as proportions of the number of diseased and non-diseased, respectively. The sensitivity of a test is defined as the probability that the index test will be positive in a disease case. The specificity of a test is defined as the probability that the index test results will be negative in a non-diseased case. Performing a meta-analysis allows a trade-off between sensitivity and specificity between studies that vary in the diagnostic threshold value used to define test positives and test negatives (85).

Of the 11 studies included, none reported a pre-specified threshold to determine a positive test. Additionally, outcome data were incompletely reported in all the included studies. Consequently, the investigators could not present this data on standard 2 x 2 tables rendering it impractical to perform diagnostic accuracy sensitivity and specificity analysis.

Due to the limitations of poorly reported data outcomes, diversity in the clinical and methodological characteristics and a high or unclear risk of bias judgements in methodological quality assessments of the included studies, a meta-analysis was not considered an option in this review. This would only serve to compound and produce erroneous results, which may be inappropriately interpreted as having the credibility to inform clinical practice. Researchers were, therefore, unable to formally evaluate the comparative accuracy of the various index tests considered in this review.

A critical appraisal was completed, and the included studies were presented in a descriptive review format, as they are likely to provide useful information for future research, with more clinical relevance to space analysis methods in the mixed dentition stages.

4.2 Results compared to other reviews

Buwembo *et al.* (2) carried out a meta-analysis of seven studies, reporting the comparative mean differences found with the Moyers index test investigated in seven different population groups. A pooled diagnostic estimate from a few studies reported that the Moyers method had, indeed, population variations and recommended the development of new nRMDSA index tests for each population to ensure more accurate estimates for the prediction of the unerupted CPM. However, this recommendation is impractical, as it will only serve to promote similar studies that lack the methodological discipline of high-quality DTA research, creating a bombardment of index tests with little clarity and precision for the prediction of the permanent CPM. From a medical and dental global approach initiative, this will not make a meaningful or impactful contribution that addresses the clinical relevance of a diagnostic test accuracy tool to diagnose space discrepancies. The study lacked the methodological rigour when critically appraising the articles and failed to report heterogeneity and sensitivity; essential components to any high-quality DTA systematic review, as recommended in the Cochrane Handbook for Systematic Reviews of Diagnostics Test Accuracy (85)

Sidra *et al.* (78) conducted a descriptive literature review on an unspecified number of studies that investigated non-radiographic and radiographic predictive methods for space analysis. The study reported on the utility of the first mandibular permanent molar, in addition to the four lower incisors, in increasing the predictive accuracy of index tests to determine the MD widths of the permanent CPM. However, the study lacked significant methodological quality assessment information, clinical thresholds, and summation data from included studies to support the conclusions and recommendations.

Galvão *et al.* (5) conducted a systematic review reporting on the Moyers index test, in accordance with the Cochrane Handbook for Systematic reviews of interventions. Although the study had a well-designed search strategy, it lacked critical elements of a Cochrane Systematic Review of Diagnostic Test Accuracy. The inclusion and exclusion criteria were vague and ambiguous, leaving room for error of judgements in the selection process. The study did not conduct methodological quality assessments of the included studies. In a tabular form, the authors had reported the outcomes found in each study, indicating either an overestimation or underestimation at the different percentile levels of the index test. There was a reporting

error in the Schirmer and Wiltshire study; the sample population is South African, not American. Due to the high degree of variability reported in individual results of the included studies, the authors had recommended new tables be formulated for specific populations or an alternative method be explored.

Luu *et al.* (95) reviewed studies that reported non-radiographic and radiographic approaches for mixed dentition space analysis, investigating the validity and the reliability of index tests in 39 studies, assessing the means differences, the measure of error and the correlation of the data. The study vaguely highlighted a clinical significance threshold of 0.6mm in the review, which unfortunately, lacked empirical evidence. The researchers refrained from performing a meta-analysis due to the uncertainty of the clinical implications of the space analysis index tests reported in the included studies. Radiographic approaches to estimate the MD widths of the CPM were recommended.

All studies had statistically reported the mean differences of the index test associated with the reference standard. Investigators recommend using a bivariate meta-analysis on studies that report pre-specified diagnostic thresholds, as suggested in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (85). This method is statistically more rigorous and directly accounts for the within- and between-study variability in sensitivity and specificity, ensuring methodological compliance of impeccable research standards.

4.3 Strengths and Weaknesses of the review

The strengths of this systematic review, as guided by the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (85), are the completion of multiple and comprehensive electronic literature searches and a rigorous application of the methodology to ensure that screening, the inclusion criteria and the data extraction were performed in duplicate by a multiple disciplinary team of clinicians. Unlike most diagnostic test accuracy systematic reviews, investigators did not restrict the inclusion criteria to studies presenting data in a standard 2 x 2 format. This highlights the issue of incompleteness in reporting the outcome data in primary DTA studies for space analysis. A precise and reproducible method was utilised for the application of the methodological decisions.

This is the second diagnostic test accuracy systematic review to report non-radiographic mixed dentition space analysis index tests for unerupted permanent canines and premolars for studies conducted in Africa. Despite the extensive search conducted, a relatively low number of included studies suggests this is a poorly researched field. The geographic limitation imposed in the inclusion criteria resulted in several potentially eligible studies being excluded, raising concerns on the utility of the results reported.

The inclusion criteria focused on published articles of non-radiographic mixed dentition space analysis methods. Investigators anticipated difficulty retrieving full-text articles of unpublished studies to determine the potential eligibility for this review. Additionally, making judgements on methodological quality based on the abstracts alone proved challenging. However, this exclusion of unpublished data could potentially eliminate valuable information on the index tests of nRMDSA methods and contribute to a high risk of publication bias.

The principal and co-investigator screened all the titles and abstracts independently, with a third independent investigator acting as a mediator in the event of disagreements. Full-text articles that were deemed relevant based on the title and the abstract were retrieved and analysed, and a precise and reproducible process for methodological decision making was followed.

A judgement of high risk of bias was allocated to the domain of index test and reference standards for all the included studies, in accordance with the QUADAS-2 assessment tool. Moreover, the studies displayed a high risk of information bias, attributable mainly to a lack of blinding and unclear methodological sequence descriptions.

Another drawback of this review is the incomplete presentation of outcome data in the included studies. Unlike many DTA studies, the included studies reported statistically significant mean differences between the index test and the reference standards instead of diagnostic accuracy data. None of the studies reviewed had established a pre-specified diagnostic test threshold for space discrepancy. This placed concern on the clinical significance of the results of the aforementioned tests. No feedback was received after contacting the relevant authors to access raw data, which could have aided in reanalysing diagnostic accuracy data.

Given the small number of included studies, clinical and methodological characteristics and heterogeneity in the data in the included studies, pooling of the results to perform a meta-analysis was not appropriate.

4.4 Strengths and weaknesses of the included studies

A significant weakness of this review was the high risk of bias index test and reference standard domains and an unclear risk of bias in the patient selection and flow and timing domains. There is considerable between-study variation in the reporting of 1) index test investigated; 2) patient selection age; 3) ethnicity 4) population; 5) reporting of inter-reliability methods; 6) a number of investigators per study; 7) Blinding; 8) descriptive statistical approach; 9) reporting of bilateral symmetry of teeth; 10) reporting on gender differences 10) Confidence intervals (95%). Due to the diversity in the nature of the included studies and the characteristics of the participants, it was not appropriate to pool the data. The failure to provide summary estimates of the sensitivity and specificity in contrast to previous systematic reviews could be regarded as a limitation instead of a weakness of the review.

The QUADAS-2 assessment of the included studies highlighted the extent of quality concerns in the existing literature. Studies that reported on the same index test displayed considerable between-study heterogeneity; they reported different confidence intervals and an unspecified diagnostic thresholds for investigated index tests.

The included studies displayed an overall patient spectrum bias due to the sample population being different from the spectrum of patients for whom the index test was indicated in clinical practice.

Participants recruited into the studies had a similar inclusion criterion: participants were age (12-23 years), all permanent teeth up to the permanent molars in both the maxilla and mandible present in the oral cavity and the absence of interproximal caries and tooth defects. The majority of the included studies had failed to explicitly explain the sampling methods to ensure a representative sample population, which followed an unbiased randomised selection process. Only two of the included studies described the methods used in patient recruitment to ensure randomization and were judged at low risk of bias in the patient selection domain (50,57).

An overall high source of bias was the sequence at which the reference standard was conducted. Studies had avoided differential bias by using study models as the reference standard of choice, which ensured that patient data recorded remained static to allow reproducibility and reliability

assessments to be conducted. However, sufficient information on the storage and indexing of the reference standards were not stated in the included studies.

Data collection from the reference standard was measured manually with digital callipers calibrated to 0.01mm. There were limitations identified in the methodology, as there was no formal training provided to investigators and no specified time delays between the data collection to prevent errors due to fatigue.

There was a concern of information bias in the reference standard data. Only three studies (14,56,92) reported having two investigators, with the remainder of the studies having a single investigator for both the reference standard and index tests, with no blinding from the reported results. It can be assumed that the data was interpreted with knowledge of the index test results in all the included studies. Blinding was not explicitly stated, nor the interpretation sequence of the index test and reference test. This knowledge could have influenced the interpretations of the results and reported an overestimation of the accuracy.

Inter-reliability methods, which demonstrated the consistency in the reference standard measurements, were conducted in all the included studies. Two studies had conducted reliability assessments in 100% of the sample population (14,91). Concerns were identified with the low percentage of participants (average of 15%) included in reliability assessment in the remaining studies, resulting in incorrect assumptions of high levels of agreement in the study results. Two studies had reported having two investigators for the intra-reliability testing (14,92). The remainder of the included studies had only one investigator. Two of these studies reported on blinding from the results to ensure credibility and minimise the risk of observational bias (3,57). Six studies had ensured an average two week time interval between the reliability measurements to ensure credible correlation results (48–50,52,56,57). Inter-rater reliability was assessed infrequently, with only five included studies reporting on it. The entire sample population was verified using the intended reference standard. This precluded the risk of selection bias in the studies.

The index test domain was also deemed high risk of bias. The index tests were interpreted with knowledge of the reference standards (information bias) and outlining no clear sequence in the testing methods. Empirical evidence suggests that information bias increases sensitivity in

diagnostic and index test reviews. Therefore there must be a degree of blinding between index tests being conducted.

There were concerns noted in the inferential statistical approach in all included primary studies. Studies compared the mean differences, ranges and standard deviations (SD) between the index tests and reference standards. The statistical approach used in all the primary studies had reported on the degree of association, not on comparative data agreements. Highly correlated results do not imply close agreement. It is impossible to determine estimates' true accuracy and precision with a descriptive statistical approach. Drawing conclusions based on correlation can result in misleading and inappropriate conclusions with limited credibility and clinical significance.

The sensitivity and specificity of data are essential indicators of test accuracy and determine the diagnostic tool's appropriateness. Preliminary studies had failed to provide pre-defined thresholds to determine the presence of excess tooth material. The data was presented in a format that did not permit the construction of standard 2 x 2 tables to determine the sensitivity, specificity, positive and negative predictive values and the positive and negative likelihood ratios.

4.5 Applicability of findings to the review questions

Concerns regarding patient selection arose from the inclusion criteria to ensure patients were of a specific lineage. It is considered unethical to clinically classify a patient's native origin based on their aesthetic appearance, accent, language preference or intrusive probing questions into family history. However, the use of genetic investigations can guide these assumptions. Due to limitations of ethnicity and nationality inclusion criteria in the included studies, it can be assumed that the diagnostic test accuracies investigated will report findings that have poor clinical relevance and applicability in the global medical research field of orthodontics.

Another primary concern was that the patient data was presented in a format that reported on the entire statistic (sample) by assessing the association between the index test and reference standard, using comparative and correlation inferential statistical approaches. The researchers had concluded results for the parameter (population) based on the levels of association. Impeccably high research standards for DTA studies that analyse individual patient sensitivity and specificity data with a pre-defined diagnostic threshold are critical in providing valuable research and results.

There was an unclear level of concern of applicability for the index test domain in all studies. There were five non-radiographic diagnostic tests investigated across the different studies. All of the included studies had failed to report a pre-specified diagnostic threshold for the index tests investigated. The results from the studies had reported on statistically significant mean differences and the association between the index tests and reference standard on collated data of the sample. This approach in determining diagnostic test accuracy can lead to crucial unaccounted information, with conclusions and recommendations that lack credibility and clinical relevance.

The concern for the applicability of the reference standards was judged as low in all the studies. Studies models utilized ensured reproducibility and provided an unwavering reference standard measurement.

5 Conclusion

This paper conducted a review of a legion of studies by various authors into the development of a non-invasive diagnostic tool for the prediction of the unerupted canines and premolars in the mixed dentition phase to be utilised by general dental practitioners and orthodontic specialists. However, researchers reported statistically significant results of the estimations from index tests that unfortunately display limited clinical significance within the field.

A significant academic finding is the presentation of a vague understanding and lack of empirical data on the definition of clinical diagnostic thresholds to determine a positive or negative result in space analysis methods. Furthermore, the use of estimates leaves a substantial quantity of factors, such as genetics and clinical variations, widely unaccounted for. Future diagnostic test accuracy studies must provide scientifically defensive methods and rigorous methodology to ensure impeccable research standards, create and promote development and growth, and add clinical mass in the academic field of Orthodontics.

Progressively revised and refined stringent tests of this premise are critical to ensure no further misinterpretations and assumptions drawn from future studies regarding non-radiographic diagnostic tests for the unerupted canines and premolars. With science and technology advancements in medicine, we will have the ability to predict these values with greater accuracy and clinical significance, than the assumed estimate from quondam methods.

5.1 Implications for practice

This systematic review was undertaken to provide results directly applicable to the general dental practitioners and orthodontic specialists for the management of orthodontic patients in the mixed dentition phase. Clinicians require an efficient and practical evidence-based diagnostic tool that establishes the most accurate assessment of space availability to formulate a treatment plan. These space analysis methods form a crucial part of the clinical approach to establishing an accurate diagnosis, which is applicable to undergraduate and postgraduate orthodontic teaching. Additionally, reliable space analysis methods save time, money and ensure patient satisfaction.

It is essential to highlight the impracticalities and limitations to the representation of diverse ethnic and nationality populations that resonate within the research outcomes present in over 90% of the included studies. The general connotation to develop – either by tables or equations – contemporary and innovative non-radiographic predictive methods for specific nationalities and ethnicities will ultimately lead to multiple index tests with limited utility and of negligible value to the broad perspective of orthodontic research. This demonstrates a lack of understanding in the research being conducted, inhibiting its objective of a global impact on clinical relevance in the field.

Additionally, it is of critical importance to define the clinically significant diagnostic threshold for the unerupted permanent canines and premolars to assist in the diagnosis and treatment planning. This will ensure that positive, negative, false-positive or false-negative results can be detected for index tests, radiographic or non-radiographic. Upon critically reviewing the included articles, it is encouraged that clinicians critically appraise and identify high-quality research before adopting recommendations into their clinical practice.

The paucity of the evidence base resulted in high levels of bias and applicability concerns in the methodological quality and a multitude of limitations for its clinical application. Therefore, the accuracy and reliability of non-radiographic diagnostic tests of the included studies in this review cannot be established. Based on the presented evidence, investigators cannot make recommendations on the use of these non-radiographic index tests in clinical practice and

encourage future research into the use of radiographic methods in establishing a more accurate diagnosis of space discrepancies.

5.2 Implications for research

As a consequence of the small number of studies, the significant clinical and methodological differences and the substandard quality of the included studies, a meta-analysis was not appropriate. Additional diagnostic test accuracy studies addressing these concerns is imperative to the future of research into this field.

In response to the methodological limitations highlighted in the review, authors who wish to conduct future research investigating the diagnostic accuracy of non-radiographic mixed dentition analysis methods should take heed to report on a diagnostic threshold. Data extracted must be presented to enable a cross-tabulation of the index test and reference standard to allow the construction of standard 2 x 2 tables to accurately identify true-positive, false-positive, false-negative and true-negative results.

An essential outcome from this review is the overall poor quality of reporting diagnostic test accuracy studies in this field. Future studies must strive to demonstrate the highest quality of methodological rigour by applying the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (85). This will produce results that can be recommended in clinical approaches and encourage further research.

The QUADAS methodological assessment of the included studies identified several weaknesses in the study design that can impede an objective evaluation of findings. The sampling method of participants using consecutive or random sampling to minimise the risk of bias is an essential consideration for future studies. The sample size should be predefined via a power calculation to ensure a representative selection. Studies require a clear statement of the methodological sequence of the diagnostic test accuracy study. Index tests should be undertaken by trained investigators and ensure that results have a level of blinding to minimise the risk of information bias. Future studies are recommended to conduct inter-reliability and intra-reliability testing more frequently to reduce the risk of bias in the data collection.

It is crucial to consider the diagnostic threshold for a positive test. Future studies should consider radiographs as a reference standard to acquire a patient spectrum similar to that for which the index tests are intended. Flow and timing of the diagnostic test accuracy study should

be clearly stated to ensure that the reference standard is undertaken within a short time frame after the index test.

A recurrent theme found in the included studies to develop new methods for specific ethnic and population groups. It can only be assumed that this linear recurrence will only lead to further poorly designed DTA studies, with more assumptions and equations developed. Eventually, there will be an abundant amount of equations based on geographic and ethnic origins that will lack utility.

The investigators recommend research aimed to explore radiographic methods for the mixed dentition space analysis. Specific opportunities for further research identified by this review include the following.

1. Establish a pre-defined diagnostic clinical threshold of clinical significance to determine a positive result for space analysis in the mixed dentition.
2. Establishing and recommending a universally applied radiographic diagnostic approach with pre-specified clinical threshold and meticulous methodology to ensure reproducibility. This will eliminate limitations based on ethnicities, gender and nationalities
3. Develop a diagnostic algorithm utilising imaging techniques for the diagnosis of space discrepancies.
4. Future high-quality research on non-radiographic mixed dentition space analysis methods. Meticulous methodological execution guided by Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (85) will ensure high-quality research to report on high-quality results.

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Characteristics of included studies

Study 1 Fouda 2019

Study Characteristics	
Aims	To determine the validity of predicting the combined widths of permanent canines and bicuspids from the bucco-lingual widths of the first permanent molars according to Abdul- Azm and Fouda method in Angle class I case
Patient Sampling	Sampling Technique: Not Specified/ Convenience Series Sample Size: 22 Females No details on determination of the sample size Included characteristics: • All permanent teeth up present (excluding 8s) • Angles Class 1 • No Caries, no interproximal restorations, no missing teeth, no fractured teeth, no tooth wear. • 14-16 years old
Patient Characteristics and Setting	Age: 14-16 years old Sex : Female Ethnicity: Egyptian

	Country: Egypt Setting: Authors private practice
Index Test	Test examined: Abdhul Azm and Fouda Maxillary = (1st Permanent Molar Buccal-Lingual Width x 2) – 1 Mandible = (1st Permanent Molar Buccal-lingual width x 2 Category of test: Non Radiographic Diagnostic Test Index test not fully detailed to be replicated. Unclear on reference teeth and location (mandible or maxilla) Sequence of test: Reference Standard measurements prior to index tests. Examiner training and calibration: • 1 examiner • Tool : Digital Calliper- calibrated to the nearest 0.01mm • No prior training • Measured proximal surfaces of bicuspids and canines • Measured Buccolingual surface of the first permanent molar No test threshold mentioned for positive or negative test.
Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference Standard prior to index test No blinding Teeth: Mesiodistal (MD) dimensions of first permanent molars, bicuspids and canines Examiner training and calibration • One investigator

	• No prior training • 1 examiner • No blinding Intra-reliability test only • 5 casts remeasured • No randomization • No blinding from initial data Target Condition: Space Analysis to determine if there are any discrepancies due to imbalance of MD dimensions of permanent bicuspids and canines with space available in the arch.
Flow and Timing	All participants had both reference and index tests No exclusions noted form initial sample set No intervals or interventions between index test and reference standards No interval between intra-reliability tests.
Analysis	Descriptive Statistics using the mean, range, median, standard deviation. Compared actual and predicted values: Paired t-test; 0.5% statistically significant level
Results	Cross tabulation between index test and reference standards mean and median values Paired t test- Upper right only statically significant 75% accuracy in the index test- unclear how arrived

*No scatter plots or precision test (confidence interval) data mentioned or available

Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		High Risk	
Are there concern that the included participants or teeth do not match the review question?			Unclear concern
DOMAIN 2: INDEX TEST(S)			
Was the index test result interpreted without knowledge of the results of the reference standard?	No		

Was the diagnostic threshold at which the test was considered positive pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High Risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear concern
DOMAIN 3: REFERENCE STANDARD			
Is the reference standard likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern

DOMAIN 4 : FLOW AND TIMING		
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear	
Did all participants receive the same reference standard?	Yes	
Were all participants included in the analysis?	Yes	
Could the patient flow introduced bias?		Unclear risk

Study 2 Refai 2012

Study Characteristics	
Aims	• Assess applicability of Tanaka and Johnston analysis amongst group of Egyptians • Predict relationship between the first permanent molar mesiodistal width, and those of the relative bicuspid and cuspid teeth.
Patient Sampling	Design: Cohort Cross sectional Sampling Technique: Unclear; some randomization 5 different cities Sample Size: 1000 Male: 500 Female: 500 No details on determination of the sample size Included characteristics: • All permanent teeth up present (excluding 8s) • No Caries, no interproximal restorations, no missing teeth, no fractured teeth, no tooth wear, no artificial crowns. • 12-16 years old • No previous Orthodontic treatment Exclusion: • Subjects not originating from the area were excluded. • Detailed history of patient's parents to determine origin

Patient Characteristics and Setting	Age: 12-16 years old Sex : Male (500) and Female (500) Ethnicity: Egyptian Country: Egypt Setting: Schools across 5 different governorates in Egypt; Great Cairo, Alexandria, and three Upper Egypt governorates.
Index Test	Test examined: 1. Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference Standard measurements prior to index tests. Examiner training and calibration: • 2 examiners • Means were calculated • Dental Casts scanned into specially designed software • 1:1 scan image magnification • No mention of prior training or who had scanned records in

	• Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s No test threshold mentioned for positive or negative test to determine specificity and sensitivity. New equations based on regression analysis from the actual values of sample population. **1.** Modified Tanaka and Johnston- modified with smaller constants Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 10 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 9.5 New Equations derived Mx= 0.39 (M-D width of mandibular 31,32,41,42) + 12.25 Md = 0.419 (M-D width of mandibular 31,32,41,42) + 11.333 New equation derived using MD width of 1st permanent molar – developed from relation between first permanent molar and 3s',4s',5s. Persons correlation coefficient Upper teeth: Y = 0.158 X + 7.21 Lower teeth: Y = 0.26 X + 5.58. Y is MD width of first permanent molar and X is combined widths of cuspid and bicuspid
Target condition and reference standard(s)	Category: Dental Alginate impressions were taken. Study model casts poured in dental stone, digitally scanned and analysed. Sequence of test: Reference Standard results prior to index test No blinding

	Teeth: All mesiodistal dimensions calculated from the anatomic mesial and distal contact points. Examiner training and calibration: • 2 examiners • Dental Casts scanned into specially designed software • Mesiodistal widths calculated on computer software • 1:1 scan image magnification • No mention of prior training or who had scanned records in • Measured anatomic mesial and distal contact of all teeth. Intra-reliability accuracy test: • 10 models were remeasured twice • 1 week interval Inter-reliability accuracy: • Second operator • Remeasure 10 models twice • Mean measurements compared to each other Target Condition: Prediction of Mesiodistal (MD) dimensions of unerupted canines and premolar. Important for space analysis to determine if there are any discrepancies due to imbalance of MD dimensions of permanent bicuspids and canines with space available in the arch.
Flow and Timing	All participants had both reference and index tests

	No intervals or interventions between index test and reference standards One week intervals in the reliability tests, to remeasure 10 study models twice. No mention of method of choosing these models. No exclusions noted form initial sample set
Analysis	Data tabulated and analysed using SPSS program version 17 Descriptive Statistics: Mean , Standard deviation and standard error values calculated. One way ANOVA test (analysis of variance) – no statistical difference between Right and left teeth MD widths. Pearson's Correlation Coefficient – measure the relation Concordant correlation coefficient (CCC) – measure the equality Coefficient of determination (R^2) – Trend line 95% Confidence level of CCC Cross tabulation between index test and reference standard mean and median values, CCC 3 separate analysis for each index test (Traditional, Modified and New)
Results	Bilateral symmetry (left and right MD widths of teeth) Tanaka and Johnston not reliable- overestimated New equation more reliable, however not satisfy all the demands – however the new equations were evaluated on the same sample population it was derived from. Results will inadvertently correlate. High risk of bias Direct relationship between first molar and premolars and canines.

Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?			Unclear concern
DOMAIN 2: INDEX TEST(ALL TESTS)			
Was the index test result interpreted without knowledge of the results of the reference standard?	No		

Was the diagnostic threshold at which the test was considered positive pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High Risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear concern
DOMAIN 3: REFERENCE STANDARD			
Is the reference standard likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern

DOMAIN 4 : FLOW AND TIMING	
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear
Did all participants receive the same reference standard?	Yes
Were all participants included in the analysis?	Yes
Could the patient flow introduced bias?	Unclear risk

Study 3 Alzubir 2016

Study Characteristics	
Aims	1. Assess applicability of Tanaka and Johnston analysis for the prediction of the unerupted Canines and premolars in a Sundanese Sample 2. Develop new prediction equations for Sudanese population
Patient Sampling	Design: Descriptive cross-sectional study Sampling Technique: Simple random techniques (unclear) 2 Schools selected after reviewing other schools in Khartoum state Sample Size: 610 : Male= 285 Female= 325 Final sample based on inclusion criteria: 250 Male = 132 Female: 118 Included characteristics: • Sudanese Natives • All permanent teeth up present (excluding 8s) • No Caries, no interproximal restorations, no missing teeth, no fractured teeth, no tooth wear, no dental anomalies. • Class 1 Molar, canine and incisor relationship • Overbite and overjet <3mm • Mild crowding or spacing <2mm • 13-19 years old • No previous Orthodontic treatment

Patient Characteristics and Setting	Age: 13-19 years old Sex : Male (132) and Female (118) Ethnicity: Sudanese Country: Sudan Setting: 2 High schools
Index Test	Test examined: Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests. Examiner training and calibration: • 1 examiner • Dental Casts, quality checked, coded and stored. • Teeth measurements directly from dental casts • Digital Calliper to the nearest 0.01mm • Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s No test threshold mentioned for positive or negative test. 6 new index tests subsequent from the sample population regression analysis of actual values.

	• Males
	  ○ Maxilla: Y = 11.66 + 0.46X
	  ○ Mandible: Y= 10.78 + 0.48X
	• Females
	  ○ Maxilla: Y= 9.67 + 0.53X
	  ○ Mandible: Y= 8.67 + 0.55X
	• Combined
	  ○ Maxilla: Y= 9.94 + 0.53X
	  ○ Mandible: Y = 8.91 + 0.55X

Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference Standard results prior to index test No blinding from index test results mentioned Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars Examiner training and calibration: • 1 examiners / principal examiner • Dental Casts measured with digital calliper to the nearest 0.01mm • No mention of prior training Intra-reliability accuracy test: • Same investigator • 56 models • One month interval • Dalberg formular to assess error of measurement applied • No Statistical significance noted Inter-reliability accuracy:

	• None Target Condition: Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.
Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards One month intervals in the reliability tests, to remeasure 56 study models. Exclusions from the initial sample set due to inclusion criteria
Analysis	Data tabulated and analysed using SPSS program version 17 Descriptive Statistics: Mean , Standard deviation, range and standard error values calculated. Two tailed paired t-test – To assess bilateral symmetry. Pearson's Correlation Coefficient – measure the correlation between groups of teeth Independent t-tests- Compare actual and predictive values 95% Confidence level
Results	Mesiodistal widths of premolars and canines larger in males than females Bilateral symmetry

	Tanaka and Johnston: • Significant results between predicted and actual values (p<0.001) • Predicted values higher than actual values for maxilla. • Overestimation of the mesiodistal widths of the CPM • Not reliable 6 new equations : Paired t-test – no significance between new equations prediction and actual value. New equation more reliable, however not satisfy all the demands Direct relationship between first molar and premolar and canine.		
Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		

Could the selection of participants have introduced bias?	Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?		Unclear concern
DOMAIN 2: INDEX TEST(ALL TESTS)		
Was the index test result interpreted without knowledge of the results of the reference standard?	No	
Was the diagnostic threshold at which the test was considered positive pre-specified?	No	
Could the conduct or interpretation of the index test have introduced bias?	High Risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear concern
DOMAIN 3: REFERENCE STANDARD		

Is the reference standard likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern
DOMAIN 4 : FLOW AND TIMING			
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear		

Did all participants receive the same reference standard?	Yes
Were all participants included in the analysis?	Yes
Could the patient flow introduced bias?	Unclear risk

Study 4 Ajayi 2014

Study Characteristics	
Aims	1. Evaluate the applicability of Moyers and Tanaka and Johnston mixed Dentition space analysis for the prediction of the unerupted Canines and premolars in a Nigerian population 2. Develop new probability tables and regression equations for Nigerian population
Patient Sampling	Design: Descriptive cross sectional study Sampling Technique: Not Specified Samples collected from the Dental School at the University of Benin. Sample Size: 54 : Male= 33 Female= 21 Included characteristics: • Native Nigerians • Fully erupted permanent teeth up until first molar to molar present (excluding 8s) • No Caries, no interproximal restorations, no missing teeth, no fractured teeth, no tooth wear, no dental anomalies. • Mean Age: 26.6 +-2.1 years
Patient Characteristics and Setting	Age: 26.6 (mean age) Sex : Male (33) and Female (21) Ethnicity: Nigerian

	Country: Nigeria Setting: School of Dentistry, University of Benin, Benin City
Index Test	Test examined: 1) Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 2) Moyers Probability tables 5th to 95th Percentile confidence levels Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests. Examiner training and calibration: • 1 examiner • Dental Casts • Teeth measurements directly from dental casts • Each tooth measured twice, threshold of 0.2mm threshold to ensure consistency. • Digital Calliper to the nearest 0.1mm • Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s No test threshold mentioned for positive or negative test.

Secondary Analysis

New index tests from the sample population by regression analysis of actual values.

1) New Probability table for Nigerian

Male (5%- 95%)

Females (5-95%)

Combined (5%- 95%)

2) New Regression Equation

Male:

Mandible: Y = 9.53 + 0.54x

Maxilla: Y = 10.98 + 0.49x

Female

Mandible Y = 12.75 + 0.39x

Maxilla: Y = 12.95 + 0.40x

Combined Male and Female

Mandible: Y = 10.27 + 0.51x

Maxillary: Y = 11.49 + 0.47x

Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference Standard results prior to index test No blinding from index test results mentioned Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars Examiner training and calibration: • 1 examiners / principal examiner • Dental Casts measured with digital calliper to the nearest 0.01mm • All teeth measure twice • No mention of prior training Intra-reliability accuracy test: • Same investigator • 20 models • 2 week month interval • No Statistical significance noted Inter-reliability accuracy: • None Target Condition:

	Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.
Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards Two week intervals in the reliability tests, to remeasure 20 study models.
Analysis	Data tabulated and analysed using SPSS program version 17 Descriptive Statistics: Mean , Standard deviation, range and standard error values calculated. Paired t-test – To assess bilateral Independent t-test – To determine any gender statistical differences. Wilcoxon signed rank test – To compare the predicted values obtained with Moyers at the 5^{th} to 95^{th} percentiles confidence levels. Unclear if Tanaka and Johnston was evaluated in a similar manner Statistical significance at $p<0.05$
Results	Gender: No statistical significant differences Bilateral symmetry noted; No statistical significance differences. Moyers probability results:

- Significant differences noted between the actual and predicted values (P<0.01)
- Underestimation. <23mm MD Lower incisor dimensions
- Over-estimation: >24mm MD Lower incisor dimensions
- Inadequate to be used

Tanaka and Johnston:

- Significant results between predicted and actual values
- Underestimation of the mesiodistal widths of the CPM
- Inadequate for use in population

New Probability tables and regression equations developed for a Nigerian population

- Advised further testing on larger population groups.

Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			

Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Yes	
Could the selection of participants have introduced bias?	Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?		Unclear concern
DOMAIN 2: INDEX TEST(ALL TESTS)		
Was the index test result interpreted without knowledge of the results of the reference standard?	No	
Was the diagnostic threshold at which the test was considered positive pre-specified?	No	

Could the conduct or interpretation of the index test have introduced bias?		High Risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear concern

DOMAIN 3: REFERENCE STANDARD

Is the reference standard likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern

DOMAIN 4 : FLOW AND TIMING		
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear	
Did all participants receive the same reference standard?	Yes	
Were all participants included in the analysis?	Yes	
Could the patient flow introduced bias?		Unclear risk

Study 5 Bugaighis 2013

Study Characteristics	
Aims	1. Evaluate the applicability of Moyers and Tanaka and Johnston mixed dentition space analysis for the prediction of the unerupted canines and premolars in a Libyan population 2. Develop new probability tables and regression equations for Libyan population
Patient Sampling	Design: Observational cross-sectional prospective study • Incorrect description – it is not a prospective study Sampling Technique: Randomly selected Samples collected from 4 intermediate level schools in each of the 5 different geographical regions (central, north, south, east and west) Every 5th child selected from class list Initial Sample size: 900 (452 Males and 447 females) Sample Size: 343 (Male: 169 , Females 174) Included characteristics: • Native Libyans, minimum of 2 previous generations (parents and grandparents) • Fully erupted permanent teeth up until first molar to molar present (excluding 8s) • No Caries, no restorations, no hypodontia, no fractured teeth, no tooth wear, no craniofacial anomalies. • Age: 12-17 years

Patient Characteristics and Setting	Age: 12-17 years Sex : Male (169) and Female (174) Ethnicity: Libyan Country: Libya Setting: 4 intermediate level schools per region (20 schools) randomly selected.
Index Test	Test examined: 1) Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 2) Moyers Probability tables 35%, 50% and 75% probability levels Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests. No test threshold mentioned for positive or negative test. Examiner training and calibration: • 1 examiner • Dental Casts • Teeth measurements directly from dental casts • Digital Calliper to the nearest 0.01mm

- Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s

Secondary Analysis

New index tests from the sample population by regression analysis of actual values.

New Regression Equation from current study

Male:

Maxilla: Y = 9.63 + 0.53(x)

Mandible: Y = 9.29 + 0.52 (x)

Female

Maxilla Y = 11.71 + 0.43(x)

Mandible: Y = 11.84 + 0.41 (x)

Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference standard results prior to index test No blinding from index test results mentioned Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars Examiner training and calibration: • 1 examiners / principal examiner • Dental Casts measured with digital vernier calliper to the accuracy of 0.01mm

	• No mention of prior training Intra-reliability accuracy test: • Same investigator • 30 models remeasured • 2 week interval • No Statistical significance noted • Excellent levels of reproducibility Inter-reliability accuracy: • None Target Condition: Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.
Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards Two week intervals in the inta-reliability tests, to remeasure 30 study models.
Analysis	Data tabulated and analysed using SPSS program version 17 Descriptive Statistics:

	Mean , Standard deviation, range and standard error values calculated. Paired t-test – To assess bilateral symmetry Independent t-test – To determine any gender statistical differences. Paired student t-test – To compare the mean values of measured and predicted mesiodistal widths of buccal segments, according to Tanaka and Johnston equations and Moyers tables at the 35%, 50%, and 75% percentiles confidence levels. Statistical significance level set at P<0.05
Results	Gender: No statistical significant differences Bilateral symmetry noted; No statistical significance differences. Tanaka and Johnston: • Significant results between predicted and actual values • All the differences were statistically significant (p<0.001) • Overestimation of the mesiodistal widths of the CPM • Inadequate for use in population Moyers tables • Statistically significant results at 35%, 50% and 75% levels for both males and females except at a 35% level for males *p*=0.107

- Underestimation of results

New Probability regression equations developed for a Libyan population

- No statistical significant differences observed from present data..

Recommendations:

1. Prediction equations developed more suitable for Libyan population
2. Clinical discrepancy tooth size disparity of 1.5mm - 2mm , which is set as a threshold of clinical significance was not evidence based. Further studies recommended.

Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		

Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		Low Risk	
Are there concern that the included participants or teeth do not match the review question?			Unclear concern
DOMAIN 2: INDEX TEST (ALL TESTS)			
Was the index test result interpreted without knowledge of the results of the reference standard?	No		
Was the diagnostic threshold at which the test was considered positive pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High Risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear concern
DOMAIN 3: REFERENCE STANDARD			

Is the reference standard likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern
DOMAIN 4 : FLOW AND TIMING			
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear		
Did all participants receive the same reference standard?	Yes		
Were all participants included in the analysis?	Yes		
Could the patient flow introduced bias?		Unclear risk	

Study 6 Buwembo 2012

Study Characteristics	
Aims	1. Evaluate the applicability of Moyers and Tanaka and Johnston mixed dentition space analysis for the prediction of the unerupted canines and premolars in a Ugandan population 2. Develop new probability tables or regression equations for Ugandan population
Patient Sampling	Design: Cross-sectional study Sampling Technique: Random Samples collected from 5 randomly selected secondary level schools in a 6km radius from the Makerere University College of Health Sciences Every 5th child selected from class list Initial Sample size: 232 Sample Size: 220 (Male: 85 , Females 135) Included characteristics: • Native Ugandan of African descent • Fully erupted permanent teeth up until first molar to molar present (excluding 8s) • No Caries, no restorations, no hypodontia, no fractured teeth, no tooth wear, no craniofacial anomalies, no orthodontic history, • Age: 12-17 years
Patient Characteristics and Setting	Age: 12-17 years Sex : Male (85) and Female (135) Ethnicity: Ugandan

	Country: Uganda Setting: 5 secondary level schools 6km radius from the Makerere University College of Health Sciences
Index Test	Test examined: 1) Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 2) Moyers Probability tables Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests. No test threshold mentioned for positive or negative test. Examiner training and calibration: • 1 examiner • Dental Casts • Teeth measurements directly from dental casts • Digital Calliper to the nearest 0.01mm • Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s

Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference standard results prior to index test No blinding from index test results mentioned Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars Examiner training and calibration: • 1 examiners / principal examiner • Dental Casts measured with digital vernier calliper to the accuracy of 0.01mm • No mention of prior training Intra-reliability accuracy test: • Same investigator • Blinding • 22 models remeasured (10%) • Every 10th study cast • 1 week interval • Intraclass correlation coefficients showed excellent levels, ensuring reproducibility. Inter-reliability accuracy: • None Target Condition: Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.

Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards Blind intra-reliability tests at one week intervals of 22 study models.
Analysis	Data tabulated and analysed using SPSS program version 17 Descriptive Statistics: Mean , Standard deviation, range and standard error values calculated. Student t-test – To determine any gender statistical differences, to compare the mean values of actual and predicted mesiodistal widths of buccal segments from Tanaka and Johnston equations and Moyers tables. Statistical significance level set at $P<0.05$
Results	Gender: Male values significantly greater than females. Tanaka and Johnston: • Significant results between predicted and actual values • All the differences were statistically significant ($p<0.001$) • Overestimation of the mesiodistal widths of the CPM • Inadequate for use in Ugandan population Moyers tables

- No statistically significant results in Mandibular arch at 65th and 75th percentile level for Males and females respectively.
- No statistical significant results in maxillary arch at 75th percentile level for males and 75th and 95th percentile level for females.

Recommendations:

- Moyers probability tables can accurately be used in a Ugandan population

Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		Low Risk	

Are there concern that the included participants or teeth do not match the review question?	Unclear concern
DOMAIN 2: INDEX TEST(ALL TESTS)	
Was the index test result interpreted without knowledge of the results of the reference standard?	No
Was the diagnostic threshold at which the test was considered positive pre-specified?	No
Could the conduct or interpretation of the index test have introduced bias?	High Risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
DOMAIN 3: REFERENCE STANDARD	
Is the reference standard likely to correctly classify the target condition?	Yes

Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern
DOMAIN 4 : FLOW AND TIMING			
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear		
Did all participants receive the same reference standard?	Yes		
Were all participants included in the analysis?	Yes		
Could the patient flow introduced bias?		Unclear risk	

Study 7 Khan 2007

Study Characteristics	
Aims	1. Evaluate the applicability of Tanaka and Johnston mixed dentition space analysis for the prediction of the unerupted canines and premolars in a Black South African population 2. Develop new regression equations for Black South African population
Patient Sampling	Design: Cross-sectional study / Not specified Sampling Technique: Unclear / Not specified Samples collected were pre-treated orthodontic study casts from the Orthodontic department's patient records at the University of Limpopo, Medunsa. Initial Sample size: 110 Sample Size: 110 (Male: 55 , Females 55) Included characteristics: • Black South African- no further stratification to determine homogenous ethnic sample. • Angle Class 1 molar relation with fully erupted permanent teeth up until first molar to molar present (excluding 8s) • Study casts and teeth must be free of voids, defects, visible fractures, excess plaster and abnormality in shape, No interproximal caries or restorations • Age: 21 years and younger.
Patient Characteristics and Setting	Age: 21 years and younger Sex : Male (55) and Female (55) Ethnicity: Black South African

	Country: South Africa Setting: Pre-treated study models from Orthodontic patient records at the Orthodontic Department at the University of Limpopo, Medunsa
Index Test	Test examined: Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests. No test threshold mentioned for positive or negative test. Examiner training and calibration: • Unclear on number of examiners • Dental Casts • Teeth measurements directly from dental casts • Digital Calliper to the nearest 0.01mm • Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s
Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference standard results prior to index test No blinding from index test results mentioned

Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars

Examiner training and calibration:

- Unclear on number of examiners
- Dental Casts measured with digital vernier calliper to the accuracy of 0.01mm
- No mention of prior training

Intra-reliability accuracy test:

- Unclear on the examiner numbers or different examiner
- No Blinding mentioned
- 22 models remeasured (20%)
- Randomization noted, lack of details
- No intervals between intra-reliability tests and reference standards.
- Student t-test to ensure reliability in data.

Inter-reliability accuracy:

- 22 (20%) randomly selected and measured.
- Lack of information on randomization technique
- No blinding mentioned
- Unclear on primary or secondary examiner
- No interval noted
- Student t-test to ensure correlation and reliability

Target Condition:

	Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.
Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards intra-reliability and Inter-reliability tests conducted on 20% of population/ Unclear on timing or intervals.
Analysis	Data tabulated and analysed using SPSS program version 17 Descriptive Statistics: Mean , Standard deviation calculated. Student t-test – To determine any gender statistical differences, to compare the mean values of actual and predicted mesiodistal widths of buccal segments from Tanaka and Johnston equation. Statistical significance level set at $P<0.05$
Results	Gender: Male values significantly greater than females. Tanaka and Johnston: • Significant results between predicted and actual values in Males mandibular and maxillary values. • No significant results between actual and predicted values in female mandible and maxilla. • Overestimation of the mesiodistal widths of the CPM • Inadequate for use in male South African population

	Recommendations: New equation for Black South African males • Maxillary canines and premolars per quadrant = 8.31mm + 0.62x • Mandibular canines and premolars per quadrant = 7.15 mm + 0.67x		
Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?			Unclear concern
DOMAIN 2: INDEX TEST(ALL TESTS)			

Was the index test result interpreted without knowledge of the results of the reference standard?	No	
Was the diagnostic threshold at which the test was considered positive pre-specified?	No	
Could the conduct or interpretation of the index test have introduced bias?		High Risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear concern
DOMAIN 3: REFERENCE STANDARD		
Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index test?	No	

Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk
Does the target condition as defined by the reference standard match the review question?		Low Concern
DOMAIN 4 : FLOW AND TIMING		
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear	
Did all participants receive the same reference standard?	Yes	
Were all participants included in the analysis?	Yes	
Could the patient flow introduced bias?		Unclear risk

Study 8 Diagne 2003

Study Characteristics	
Aims	1. To produce odontometric data for a Senegalese population sample, 2. To derive coefficients of correlation between the combined mesiodistal widths of the permanent mandibular incisors and the canine and first and second premolar of a maxillary or mandibular quadrant 3. To test the reliability of both the Moyers and the Tanaka and Johnston methods in a Senegalese group 4. To develop new probability tables for Senegalese children
Patient Sampling	Design: Cross-sectional study / Not specified Sampling Technique: Selection process was not specified to ensure a random selection technique Samples collected Dental students from the department of dentistry Initial Sample size: 50 Sample Size: 110 (Male: 25 , Females 25) Included characteristics: • Native Senegalese - no further stratification to determine homogenous ethnic sample. • Angle Class 1 molar relation with fully erupted permanent teeth up until first molar to molar present (excluding 8s) • No Caries, no restorations, no hypodontia, no fractured teeth, no tooth wear, no craniofacial anomalies, no orthodontic history Age: 21 years and younger. • Mean age: 23.76 years

Patient Characteristics and Setting	Mean age: 23.76 years Sex : Male (25) and Female (25) Ethnicity: Native Senegalese Country: Senegal Setting: Dental student from the Department of Dentistry, University Cheikh Anta Diop, Dakar, Senegal.
Index Test	Test examined: 1) Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 2) Moyers Probability tables 50th Percentile level Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests. Examiner training and calibration: • One investigator for both index and reference standard measurements • Teeth measurements directly from dental casts • Digital Calliper to the nearest 0.01mm • Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s

Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference standard results prior to index test No blinding from index test results mentioned Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars Examiner training and calibration: • Single investigator on number of examiners • Dental Casts measured with digital vernier calliper to the accuracy of 0.1mm • No mention of prior training Intra-reliability accuracy test: • Same investigator • No Blinding mentioned • All teeth measured twice • No randomization noted • No intervals between intra-reliability tests and reference standards. • Predetermined threshold of 0.2mm to ensure intra-reliability. Inter-reliability accuracy: • No Inter-reliability assessment conducted • Target Condition: Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.

Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards intra-reliability tests conducted by measuring all teeth twice. No time intervals between measurements.
Analysis	Data tabulated and analysed Descriptive Statistics: Mean , Standard deviation calculated. Student t-test – To determine any gender statistical differences Correlation coefficient and regression equations to assess relationship between sum of mandibular incisors and canines and premolars. Correlation coefficients were used to compare the mean values of actual and predicted mesiodistal widths with Tanaka and Johnston equation and Moyers probability table (50%) Statistical significance level not mentioned
Results	Gender: Male values significantly greater than females. Tanaka and Johnston: • Significant results between predicted and actual values • Overestimation of the mesiodistal widths of the canine and premolars (CPM) • Inadequate for use in Senegalese population

Moyers

- Underestimation at the 50th percentile level
- Not suitable for use in population group

Recommendations:

New prediction tables for Senegalese children (males and females)

Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?			Unclear concern

DOMAIN 2: INDEX TEST (ALL TESTS)	
Was the index test result interpreted without knowledge of the results of the reference standard?	No
Was the diagnostic threshold at which the test was considered positive pre-specified?	No
Could the conduct or interpretation of the index test have introduced bias?	High Risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear concern
DOMAIN 3: REFERENCE STANDARD	
Is the reference standard likely to correctly classify the target condition?	Yes

Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern
DOMAIN 4 : FLOW AND TIMING			
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear		
Did all participants receive the same reference standard?	Yes		
Were all participants included in the analysis?	Yes		
Could the patient flow introduced bias?		Unclear risk	

Study 9 Schirmer 1997

Study Characteristics	
Aims	1. Determine the applicability of the Moyers probability tables for use on Black patients in South Africa. 2. Formulate new tables for the prediction of unerupted canines and premolars.
Patient Sampling	Design: Cross-sectional study / Not specified Sampling Technique: Unclear on random selection process of participants / Not specified Samples collected were pre-treated orthodontic study casts from a major university orthodontic clinic. Initial Sample size: 100 Sample Size: 100 (Male: 50 , Females 50) Included characteristics: • Black South African- no further stratification to determine homogenous ethnic sample. • Angle Class 1 molar relation with fully erupted permanent teeth up until first molar to molar present (excluding 8s) • Study casts and teeth must be free of voids, defects, visible fractures, excess plaster and abnormality in shape, No obvious loss of interproximal tooth material due to caries or restorations • Age: Male: 13-20 years Female: 13-19 years
Patient Characteristics and Setting	Age: 13-20 years Sex : Male (50) and Female (50) Ethnicity: Black South African

	Country: South Africa Setting: Pre-treated study models from Orthodontic patient records at the Orthodontic Department at a major university.
Index Test	Test examined: Moyers Probability Table 5^{th} – 95^{th} Percentile confidence level Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests No index test positive threshold of significance noted. Examiner training and calibration: • Two investigators measured teeth manually and independently • Teeth measurements directly from dental casts • Digital Calliper to the nearest 0.01mm • Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s
Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference standard results prior to index test No blinding from index test results mentioned Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars

	Examiner training and calibration: • Two investigators measured teeth manually and independently • Dental Casts measured with digital vernier calliper to the accuracy of 0.01mm • No mention of prior training Intra-reliability accuracy test: • Unclear • Stated in methods however not substantiated • Two investigators measured all models . Inter-reliability accuracy: • Two investigators measured teeth independently • Lack of information on randomization technique • Measurements were compared with a reliability threshold of 0.2mm • No Blinding mentioned. • No intervals between inter-reliability tests and reference standards Target Condition: Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.
Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards

	intra-reliability test method was unclear Inter-reliability tests had no time intervals.
Analysis	Descriptive Statistics: Mean values calculated from the sum of groups of teeth, the four mandibular incisors and mandibular and maxillary canines and premolars. Used a correlation test to determine relationship from mean values. No bilateral or gender comparisons conducted . Wilcoxon singed rank test used to statistically compare the actual and predicted values from Moyers probability tables. Statistical significance level not stated however graphically, significance shown at $P<0.05$ No clinical significance threshold set/stated. Proposed new tables analysed on same sample size derived from. Definite bias.
Results	Moyers Significant results between predicted and actual values in all percentile levels except in Maxilla in females at the 75^{th} , 85^{th} and 95^{th} percentile. • Maxillary posterior teeth underestimated by 0.223mm per quadrant in Black females with Moyers. Recommendations: New tables for Black South African males and females more appropriate to population

	Further studies on larger sample groups, with greater ethnic diversity, to establish prediction error and formulate more accurate and applicable data.			
Methodological Quality				
ITEM		Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION				
Was a consecutive or random sample of patients enrolled?		Unclear		
Was a case-control design avoided?		Yes		
Did the study avoid inappropriate exclusions?		Yes		
Could the selection of participants have introduced bias?			Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?				Unclear concern
DOMAIN 2: INDEX TEST (ALL TESTS)				

Was the index test result interpreted without knowledge of the results of the reference standard?	No	
Was the diagnostic threshold at which the test was considered positive pre-specified?	Unclear	
Could the conduct or interpretation of the index test have introduced bias?	High Risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear concern

DOMAIN 3: REFERENCE STANDARD

Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index test?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?	High Risk	

Does the target condition as defined by the reference standard match the review question?	Low Concern
DOMAIN 4 : FLOW AND TIMING	
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear
Did all participants receive the same reference standard?	Yes
Were all participants included in the analysis?	Yes
Could the patient flow introduced bias?	Unclear risk

Study 10 Sethusa 2018

Study Characteristics	
Aims	Determine whether the modified Tanaka and Johnston method by Khan *et al.*, or the Schirmer and Wiltshire method was more accurate in the prediction of the mesiodistal widths of unerupted canines and premolars in Black South African patients.
Patient Sampling	Design: Cross-sectional survey Sampling Technique: Random selection of participants, used Epi 7 at 95% confidence level and 5% confidence limits, frequency of 8%. Samples collected were pre-treated orthodontic study casts from the Department of Orthodontics at the Sefako University, Medunsa Oral Health Centre. Initial Sample size: 813 Sample Size: 100 (Male: 50 , Females 50) Included characteristics: • Black South African- no further stratification to determine homogenous ethnic sample. • Angle Class 1 molar relation with fully erupted permanent teeth up until first molar to molar present (excluding 8s) • Study casts and teeth must be free of voids, defects, visible fractures, excess plaster and abnormality in shape, No obvious loss of interproximal tooth material due to caries or restorations • Age: 17-21

Patient Characteristics and Setting	Age: 17-21 years Sex : Male (50) and Female (50) Ethnicity: Black South African Country: South Africa Setting: Pre-treated study models from Orthodontic patient records at the Orthodontic Department at the Medunsa Oral Health Centre
Index Test	Test examined: 1) Modified Tanaka and Johnston (Khan and Seedat) Males: Maxillary canines and premolars per quadrant = 8.31mm + 0.62(M-D width of mandibular 31,32,41,42) Mandibular canines and premolars per quadrant = 7.15 mm + 0.67(M-D width of mandibular 31,32,41,42) Females: (Not stated in Article) Maxillary canines and premolars per quadrant = 0.5 (M-D width of mandibular 31,32,41,42) + 11 Mandibular canines and premolars per quadrant = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 2) Schirmer and Wiltshire Tables Category of test: Non Radiographic Diagnostic Test Sequence of test: Reference standard measurements prior to index tests

	No index test positive threshold of significance noted. Examiner training and calibration: 3) One principal investigator measured teeth manually 4) Teeth measurements directly from dental casts 5) Digital Calliper to the nearest 0.5mm 6) Measured anatomic mesial and distal contacts in 31,32,41,42 to be used in equations to predict 3s,4s,5s 7) Data tool collection sheet not clear or mentioned
Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference standard results prior to index test No blinding from index test results mentioned Teeth: All mesiodistal anatomic contact points of mandibular and maxillary canine and premolars Examiner training and calibration: • One investigator measured teeth manually • Dental Casts measured with digital vernier calliper to the accuracy of 0.5mm • No mention of prior training Intra-reliability accuracy test: • 10% sample remeasured • Blinded • Reliability threshold not mentioned • Correlation test conducted • No intervals between measurements

	. Inter-reliability accuracy: • Second investigator measured 10 % teeth independently • No reliability threshold mentioned • Blinded. • No intervals between inter-reliability tests and reference standards • Correlation test conducted Target Condition: Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.
Flow and Timing	All participants had both reference and index tests No intervals or interventions between index test and reference standards intra-reliability test and inter-reliability tests time intervals unclear.
Analysis	Descriptive Statistics: Mean values calculated from the sum of groups of teeth, the four mandibular incisors and mandibular and maxillary canines and premolars. Used a correlation test to determine relationship from mean values. Gender comparisons conducted .

	Student t test used to statistically compare the actual and predicted values for each index test. No clinical significance threshold set/stated.
Results	Modified Tanaka and Johnston (MTJ) • Significant results between predicted and actual values in Mandibular and Maxillary arch in Males with an overestimation • Females measurements showed no statistical significance and was comparatively accurate Schirmer and Wiltshire(SaW) • Males: Maxillary measurements showed **no** statistical significance Mandible showed statistical significant results and an overestimation • Females: Maxilla statistically significant results with an underestimation Mandible: **No** statistical significant results. Limitations: No Bolton's analysis Conclusion: MTJ more accurate than SaW Recommendations: New equations and tables of data be developed based on a adequately powered study with a representative sample

	* Sample calculation mentioned		
Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?			Unclear concern
DOMAIN 2: INDEX TEST (ALL TESTS)			
Was the index test result interpreted without knowledge of the results of the reference standard?	No		

Was the diagnostic threshold at which the test was considered positive pre-specified?	No		
Could the conduct or interpretation of the index test have introduced bias?		High Risk	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?			Unclear concern
DOMAIN 3: REFERENCE STANDARD			
Is the reference standard likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index test?	No		
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk	
Does the target condition as defined by the reference standard match the review question?			Low Concern

DOMAIN 4 : FLOW AND TIMING	
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear
Did all participants receive the same reference standard?	Yes
Were all participants included in the analysis?	Yes
Could the patient flow introduced bias?	Unclear risk

Study 11 Hammad 2010

Study Characteristics	
Aims	1. Determine the applicability of the Tanaka and Johnston and Moyers method of prediction in an Egyptian population 2. Develop new prediction methods
Patient Sampling	Design: Cross-sectional study / Not specified Sampling Technique: Unclear on random selection of participants/ unspecified Samples collected from 10 schools in Mansoura city, Dakahlia. Initial Sample size: 400 Sample Size: 325 (Male:180, Females 145) Included characteristics: • Native Egyptian- no further stratification to determine homogenous ethnic sample. • Angle Class 1 molar relation with fully erupted permanent teeth up until first molar to molar present (excluding 8s) • No Crowding, spacing and rotations on teeth • No proximal caries, no restorative treatments except class 1 restoration, no missing teeth, no supernumerary teeth • No previous orthodontics treatment • Study impressions of maxilla and mandible • Age: 13-16 years

Patient Characteristics and Setting	Age: 13-16 years Sex : Male (180) and Female (145) Ethnicity: Egyptian Country: Egypt Setting: School children, from ten schools in Mansoura city. Initial selection at the schools. No randomization technique detailed.
Index Test	Test examined: 1) Moyers Probability Table 35^{th} , 50^{th} , 75^{th} Percentile confidence level 2) Tanaka and Johnston Mx= 0.5 (M-D width of mandibular 31,32,41,42) + 11 Md = 0.5 (M-D width of mandibular 31,32,41,42) + 10.5 Category of test: Non Radiographic Diagnostic Test Sequence of test: No description or details explicitly noted. Assumption Reference standard measurements prior to index tests No index test positive threshold of significance noted. No mention of data storage Examiner training and calibration: • Two investigators measured teeth manually at two week intervals.

	• 5 pairs measured per day per examiner from dental casts • Digital Calliper to the nearest 0.01mm • Measured anatomic mesial and distal contacts in 31,32,41,42 (independent variable) to be used in equations to predict 3s,4s,5s, and to derive new regression models.
Target condition and reference standard(s)	Category: Study mode casts Sequence of test: Reference standard results prior to index test (assumption) / not specified on order of study No blinding from index test results mentioned Teeth: Mesiodistal buccal segments mandibular and maxillary canine and premolars Examiner training and calibration: • Two investigators measured teeth manually. • Dental Casts measured with digital vernier calliper to the accuracy of 0.01mm • No mention of prior training Intra-reliability accuracy test: • Prior to study, 20 randomly selected models • Measured twice at two week intervals • Error analysis no statistical significant differences • Correlation at 0.95, indicative that no random error. Inter-reliability accuracy: • Prior to study, 20 randomly selected models • Measured twice at two week intervals

	• Error analysis no statistical significant differences • Correlation at 0.95, indicative that no random error. • No Blinding mentioned. Target Condition: Prediction of mesiodistal dimensions of unerupted canines and premolar in the mandible and maxilla for space analysis in the mixed dentition phase. This is important to determine imbalances between in mesiodistal dimensions of permanent bicuspids and canines with the available space in the arch.
Flow and Timing	All participants had both reference and index tests Two investigators measured 5 pairs of models at two week intervals, not specific of this was independently conducted. No intervals or interventions between index test and reference standards No Blinding from index tests and reference standards Unclear sequence applied to determine the index test and reference test results.
Analysis	Descriptive Statistics: Mean values calculated from the sum of groups of teeth, the four mandibular incisors and mandibular and maxillary canines and premolars. Used a correlation test to determine relationship from mean values. Student t-tests to determine if there are gender and bilateral symmetry discrepancies.

	Paired t-test to statistically compare the actual and predicted values from Moyers probability tables and Tanaka and Johnston. Statistical significance level at P<0.05 No clinical significance threshold set/stated to determine test positive or negative. Proposed new tables analysed on same sample size derived from. Definite bias.
Results	Moyers Significant results between predicted and actual values in all percentile levels at the 35th and 75th probability levels. • No statistically significant results for females at the 50th percentile level. Tanaka and Johnston: • Significant results between predicted and actual values in males and females Recommendations: New tables for Egyptian population Males: Maxilla Y= 14.26+ 0.32(x) Mandible. Y= 10.52+ 0.47(x) Females: Maxilla Y= 12.83 + 0.37(x) Mandible Y= 11.20+ 0.40(x)

Further studies on samples with racial and ethnic differences to confirm its applicability and consistency

Methodological Quality			
ITEM	Author's Judgement	Risk of bias	Applicability concerns
DOMAIN 1: PATIENT SELECTION			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
Could the selection of participants have introduced bias?		Unclear Risk	
Are there concern that the included participants or teeth do not match the review question?			Unclear concern
DOMAIN 2: INDEX TEST (ALL TESTS)			

Was the index test result interpreted without knowledge of the results of the reference standard?	No	
Was the diagnostic threshold at which the test was considered positive pre-specified?	No	
Could the conduct or interpretation of the index test have introduced bias?		High Risk
Are there concerns that the index test, its conduct, or interpretation differ from the review question?		Unclear concern

DOMAIN 3: REFERENCE STANDARD

Is the reference standard likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index test?	No	
Could the reference standard, its conduct, or its interpretation have introduced bias?		High Risk

Does the target condition as defined by the reference standard match the review question?	Low Concern
DOMAIN 4 : FLOW AND TIMING	
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Unclear
Did all participants receive the same reference standard?	Yes
Were all participants included in the analysis?	Yes
Could the patient flow introduced bias?	Unclear risk

Characteristics of excluded studies

Study	Reason for exclusion
Ngesa 2004	Unpublished literature

Data

Presented below are all the data for all the tests entered in this review:

Table 8. Summation of mesiodistal widths of mandibular lower incisors and maxillary and mandibular canines and premolar segments from the included studies.

Study	Country	Index Test	Sex	Sample (n)	Arch	Mean (mm)	Median (mm)	Range (mm)	SD (mm)	SEM
Ahmed Maher Fouda *et al.*	Egypt	Abdhul Azm and Fouda	F	21						
2019			Right		UCPM	22.22	22	20.5–24.80	1.11	
					LCPM	21.34	21.2	20.20–22.80	0.81	
			Left		UCPM	21.54	21.5	20.40–23.10	0.77	
					LCPM	21.57	21.5	20–24.10	0.96	
Refai *et al.*	Egyptian	Tanaka and Johnston	M	500						
2012			F	500						
			M + F	1000	UCPM					
					LCPM					

Study	Country	Index Test	Sex	Sample (n)	Arch	Mean (mm)	Median (mm)	Range (mm)	SD (mm)	SEM
Alzubir *et al.*	Sudan	Tanaka and Johnston	M	118	LI	22.82		19.25–28.12	1.41	
2016					UCPM	22.21		19.15–24.84	1.05	
					LCPM	21.79		18.48–23.99	1.11	
			F	132	LI	22.28		18.72–26.54	1.51	
					UCPM	21.48		18.48–24.34	1.18	
					LCPM	21		18.01–23.77	1.15	
			M+F	250	LI	22.53		18.72–28.12	1.49	
					UCPM	21.83		18.48–24.84	1.17	
					LCPM	21.38		18.01–23.99	1.19	
Ajayi *et al.*	Nigerian	Tanaka and Johnston	M	33	LI	23.54		19.66–26.10	1.5	
2014		Moyers			UCPM	22.59		20.72–25.62	1.04	
					LCPM	22.34		20.51 -24.42	1.09	
			F	21	LI	23.43		19.76–24.90	1.2	
					UCPM	22.41		19.95–24.42	0.16	
					LCPM	21.85		19.80–23.70	0.93	
			M+F	54	LI	23.5		19.66–26.10	1.38	
					UCPM	22.52		19.95–25.62	1.08	
					LCPM	22.15		19.80–24.42	1.05	
Bugaighis *et al.*	Libyan	Tanaka and Johnston	M	169	LI	23		19.34–27.12	1.46	

Study	Country	Index Test	Sex	Sample (n)	Arch	Mean (mm)	Median (mm)	Range (mm)	SD (mm)	SEM
2013		Moyers			UCPM	21.7		18.66–24.59	1.17	
					LCPM	21.33		18.55–24.44	1.13	
			F	174	LI	22.67		19.04–25.70	1.4	
					UCPM	21.55		18.56–24.43	1.06	
					LCPM	21.16		18.78–23.88	0.99	
			M+F	343	LI					
					UCPM	21.62			1.12	
					LCPM	21.24			1.06	
Buwembo *et al.*	Ugandan	Tanaka and Johnston	M	85	LI	21.53			2.49	0.27
2012		Moyers			UCPM	21.05			1.76	0.191
					LCPM	20.62			1.94	0.21
			F	135	LI	20.99			2.34	0.202
					UCPM	20.53			0.14	0.14
					LCPM	19.99			0.163	0.163
			M+F	220	LI	21.2			2.41	0.163
					UCPM	20.73			1.75	0.118
					LCPM	21.24			1.93	0.13
Khan *et al.*	South African	Tanaka and Johnston	M	55	LI	24.23			1.72	
					UCPM	23.27			1.43	

Study	Country	Index Test	Sex	Sample (n)	Arch	Mean (mm)	Median (mm)	Range (mm)	SD (mm)	SEM
2007					LCPM	23.34			1.41	
			F	55	LI	23.32			1.34	
					UCPM	22.32			1.01	
					LCPM	22.1			1.03	
Diagne *et al.*	Senegalese	Tanaka and Johnston	M	25	LI	23.71		21.8–26.1	1.25	
2003		Moyers			UCPM	22.6		20.6–25.5	1.22	
					LCPM	22.7		20.7–25.8	1.01	
			F	25	LI	22.86		21.2–25.0	1.12	
					UCPM	21.64		20.6–23.8	0.99	
					LCPM	21.87		20.0–23.7	0.77	
			M+F	50	LI	23.28		21.2–26.1	1.25	
					UCPM	22.27		20.6–25.5	0.97	
					LCPM	22.12		20.0–25.8	1.19	
Schirmer *et al.*	South African	Moyers	M	50	LI	23.92			1.9	
1997					UCPM	23.45			1.37	
					LCPM	23.22			1.11	
			F	50	LI	23.66			1.59	
					UCPM	22.2			1.24	
					LCPM	22.28			1.28	

Study	Country	Index Test	Sex	Sample (n)	Arch	Mean (mm)	Median (mm)	Range (mm)	SD (mm)	SEM
Sethusa *et al.*	South African	Khan & Seedat	M	50	LI					
2018		SaW			UCPM	47.2			2.65	
					LCPM	47.28			2.86	
			F	50	LI					
					UCPM	45.6			2.3	
					LCPM	45.21			2.44	
Hammad *et al.*	Egyptian	Tanaka and Johnston	M	180	LI	22.98		20.00 –25.50	1.19	0.09
2010		Moyers			UCPM	21.63		20.05–23.05	0.48	0.04
					LCPM	21.29		20.05–22.75	0.62	0.05
			F	145	LI	21.25		19.20–23.50	1.07	0.09
					UCPM	20.23		18.10–22.00	0.62	0.05
					LCPM	19.63		18.55–20.85	0.48	0.04
			M+F	325						

UCPM, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*,number; *CI*, Confidence Intervals; *SD*, Standard Deviation; *M*, Males; *F*, Females; *SEM*, Standard error of mean; statistically significance (p<0.001).

Table 9. Data tables by index test for nRMDSA of studies within Africa

Test	No of studies	Participants
Tanaka and Johnston equation	8	2352
Moyers Prediction tables	6	1092
Schirmer and Wiltshire prediction tables	1	100
Modified Tanaka and Johnston equation	1	100
Abdhul Azm and Fouda novel method	1	21

Table 10. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Tanaka and Johnston equation (1974) of the whole sample in the included studies.

Study	Country	Sex	Sample (n)	Arch	Mean Difference	Standard deviation (mm)	*p* value	CI (95%)
Alzubir 2016	Sudanese	M+F	250	UCPM	0.44*	-	<0.001	-
				LCPM	0.39*	-	<0.001	-
Bugaighis 2013	Libyan	M	169	UCPM	0.8*	-	-	-0.93 to -0.66
				LCPM	0.67*	-	-	-0.80 to -0.55
		F	174	UCPM	0.97*	-	-	-0.92 to -0.66
				LCPM	0.68*	-	-	-0.79 to -0.55
		M+F	343	UCPM	0.8*	-	-	-0.89 to -0.70
				LCPM	0.67*	-	-	-0.76 to -0.59
Buwembo 2012	Ugandan	M	85	UCPM	-0.85*	0.1	-	-0.91 to -0.78
				LCPM	-0.53*	0.22	-	-0.67 to -0.38
		F	135	UCPM	-0.98*	0.12	-	-1.06 to -0.90
				LCPM	-0.8*	0.33	-	-1.02 to -0.59
		M+F	220	UCPM	0.75*	0.11	-	0.66 to 0.81
				LCPM	-0.8*	0.25	-	-0.86 to -0.53
Hammad 2010	Egyptian	M	180	UCPM	0.8398*	0.839	-	0.779 to 0.899

Study	Country	Sex	Sample (n)	Arch	Mean Difference	Standard deviation (mm)	*p* value	CI (95%)
				LCPM	0.680*	0.68	-	0.616 to 0.743
		F	145	UCPM	1.393*	0.51	-	1.310 to 1.477
				LCPM	1.507*	0.431	-	1.436 to 1.577
Refai 2012	Egyptian	M+F	1000	UCPM	-	-	-	-
				LCPM	-	-	-	-
Ajayi 2014	Nigerian	M+F	54	UCPM	-	-	-	-
				LCPM	-	-	-	-
Khan 2007	South African Black	M+F	110	UCPM	-	-	-	-
				LCPM	-	-	-	-
Diagne 2003	Senegalese	M+F	50	UCPM	-	-	-	-
				LCPM	-	-	-	-

Table 8 showing the summary of Tanaka and Johnston index used in Africa from 2000- 2014. Missing values (-) indicate paucity of data from the selected studies. Where possible, CI (95%) and *p*-values were reported. Given the small number of studies and the large heterogeneity in the clinical and methodological characteristics of the studies investigators were unable to pool results of the study. Consequently, a formal evaluation of the comparative accuracy of tests was not conducted. Statistically significant results $p<0.001$. *Indicates statistically significant results reported. *M*, Male; *F*, Female; *UCPM,* Upper canine and premolar; *LCPM,* Lower canine and premolar; *LI,* Lower Incisor; *CI,* Confidence Intervals.

Table 11. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Moyers probability tables of the whole male sample in the included studies.

Study	Country	Male	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
Bugaighis 2013	Libyan	n = 169					
		Maxilla (UCPM)	35	0.107	0.111	0.88	- 0.02 to 0.25
			50	0.0001	-0.235	0.88	-0.37 to -0.10
			75	<0.0001	-0.89	0.88	-1.02 to 0.75
		Mandible (LCPM)	35	0.0001	0.228	0.84	0.10 to 0.36
			50	<0.0001	-0.472	0.84	0.60 to -0.35
			75	<0.0001	-0.872	0.84	0.99 to -0.75
Buwembo 2012	Ugandan	n = 85					
		Maxilla (UCPM)	5	<0.0001	-1.61	0.08	-1.66 to -1.56
			15	<0.0001	-1.06	0.07	-1.14 to -1.04
			25	<0.0001	-0.79	0.07	-0.84 to -0.74
			35	<0.0001	-0.54	0.09	-0.59 to -0.48

Study	Country	Male	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
			50	<0.0001	-0.2	0.06	-0.25 to -0.16
			65	0.001	0.11	0.08	0.06 to 0.16
			75	0.451	-0.13	5.73	-4.96 to 2.36
			85	<0.0001	0.67	0.1	0.60 to 0.16
			95	<0.0001	1.2	0.1	1.14 to 1.27
		Mandible (LCPM)	5	<0.0001	2.32	0.29	2.13 to 2.51
			15	<0.0001	1.61	0.3	1.42 to 1.8
			25	<0.0001	1.16	0.28	0.98 to 1.34
			35	<0.0001	0.81	0.3	0.62 to 1.01
			50	0.002	0.37	0	0.17 to 0.57
			65	0.388	-0.08	0.32	-0.28 to 0.12
			75	0.001	-0.43	0.34	-0.65 to -0.21
			85	<0.0001	-0.86	0.33	-1.06 to -0.64
			95	<0.0001	-1.6	0.36	-1.84 to -1.37
Schirmer 1997	South African	n = 50					
		Maxilla (UCPM)	5	0.0002	2.55		
			15	0.0002	2.13		

Study	Country	Male	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
			25	0.0002	1.89		
			35	0.0002	1.68		
			50	0.0002	1.42		
			65	0.0002	1.15		
			75	0.0002	0.95		
			85	0.0002	0.7		
			95	0.0002	0.29		
		Mandible (LCPM)	5	0.0002	3.45		
			15	0.0002	2.86		
			25	0.0002	2.49		
			35	0.0002	2.2		
			50	0.0002	1.82		
			65	0.0002	1.43		
			75	0.0002	1.15		
			85	0.0002	0.79		
			95	0.002	0.16		
Hammad 2010	Egyptian	n = 180					

Study	Country	Male	Percentile	*p* value	Mean Difference	Standard deviation (mm)	CI (95%)
		Maxilla (UCPM)	35		-0.526	-0.394	-0.584 to -0.468
			50		-0.19	0.4	-0.248 to -0.131
			75		0.438	0.746	0.329 to 0.548
		Mandible (LCPM)	35		-0.553	0.419	-0.735 to -0.611
			50		-0.231	0.413	-0.292 to -0.170
			75		0.533	0.411	0.493 to 0.614

UCPM, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*,number; *CI*, Confidence Intervals; statistically significance ($p<0.001$).

Table 12. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Moyers probability tables of the whole female sample in the included studies**.**

Study	Country	Female	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
Bugaighis 2013	Libyan	n = 174					
		Maxilla (UCPM)	35	0.036	0.14	0.89	0.01 to 0.27
			50	0.002	-0.21	0.89	-0.34 to -0.08
			70	<0.0001	-0.86	0.89	-0.99 to -0.73
		Mandible (LCPM)	35	<0.0001	0.26	0.85	0.13 to 0.39
			50	<0.0001	-0.44	0.85	-0.57 to -0.31
			70	<0.0001	-0.84	0.85	-0.94 to -0.71
Buwembo 2012	Ugandan	n = 135					
		Maxilla (UCPM)	5	<0.001	-2.47	0.47	-2.77 to -2.17
			15	<0.001	-1.81	0.48	-2.12 to -1.51
			25	<0.001	-1.44	0.49	-1.75 to -1.12
			35	<0.001	-1.14	0.49	-1.45 to -0.82
			50	<0.001	-0.74	0.49	-1.05 to -0.42

Study	Country	Female	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
			65	0.044	-0.33	0.5	-0.65 to -0.01
			75	0.865	-0.02	0.49	-0.34 to 0.29
			85	0.041	0.34	0.51	0.01 to 0.66
			95	0.702	-0.67	5.94	-4.45 to 3.10
		Mandible (LCPM)	5	<0.001	-2.66	0.28	-2.84 to -2.48
			15	<0.001	-1.93	0.28	-2.11 to -1.75
			25	<0.001	-1.5	0.27	-2.67 to -1.32
			35	<0.001	-1.15	0.28	-1.33 to -0.97
			50	<0.001	-0.7	0.29	-0.87 to -0.50
			65	0.027	-0.22	0.29	-0.40 to -0.02
			75	0.195	0.13	0.31	-0.07 to 0.32
			85	<0.001	0.55	0.3	0.35 to 0.74
			95	<0.001	1.28	0.31	1.08 to 1.48
Schirmer 1997	South African	n = 50					
		Maxilla (UCPM)	5	0.0002	2.48		
			15	0.0002	1.94		
			25	0.0002	1.65		
			35	0.0002	1.4		

Study	Country	Female	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
			50	0.0002	1.12		
			65	0.0010	0.75		
			75	0.0107	0.52		
			85	0.2263	0.22		
			95	0.0947	-0.3		
		Mandible (LCPM)	5	0.0002	2.94		
			15	0.0002	2.33		
			25	0.0002	1.98		
			35	0.0002	1.69		
			50	0.0002	1.31		
			65	0.0002	0.92		
			75	0.0002	0.64		
			85	0.0002	0.28		
			95	0.0002	-0.32		
Hammad 2010	Egyptian	n= 145					
		Maxilla (UCPM)	35		0.497	0.496	-0.579 to 0.416
			50		-0.095	0.494	-0.176 to -0.014
			75		0.486	1.591	0.225 to 0.747

Study	Country	Female	Percentile	P value	Mean Difference	Standard deviation (mm)	CI (95%)
		Mandible (LCPM)	35		-0.459	0.328	0.512 to -0.405
			50		0.058	0.315	-0.046 to -0.057
			75		0.824	0.305	0.774 to 0.874

UCPM, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*,number; *CI*, Confidence Intervals; statistically significance (p<0.001).

Table 13. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Modified Tanaka and Johnston and Schirmer and Wiltshire predictive methods of the male and female samples**.**

					Index test 1. Modified Tanaka and Johnston			**Index test 2. Schirmer and Wiltshire**		
Study	Country	Sex	Sample (n)	Arch	Mean (mm)	Standard deviation (mm)	*p* value	Mean (mm)	Standard deviation (mm)	*p* value
Sethusa 2018	South Africa	M	50							
				UCPM	48.37	2.11	0.0001	47.64	0.88	0.1748
				LCPM	48.61	2.28	0.0001	48.12	1.04	0.0198
		F	50							
				UCPM	45.95	1.32	0.1848	44.92	1.33	0.0114
				LCPM	44.95	1.32	0.3776	44.89	1.28	0.2990

M, Male; *F*, Female; *UCPM*, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*,number; statistically significance ($p<0.001$)

Table 14. The differences between the mean values (mm) of the actual MD widths of the CPM, and the predicted values using Abdhul Azm and Fouda predictive methods in the whole sample.

Study	Country	Sex	Sample (n)	Arch	P value	Mean Difference
Ahmed Maher Fouda *et al.*	Egypt	Female	n= 21			
2019		Right		UCPM	0.026	-0.63
				LCPM	0.176	-0.16
		Left		UCPM	0.493	0.27
				LCPM	0.805	-0.06

UCPM, Upper canine and premolar; *LCPM*, Lower canine and premolar; *n*,number; statistically significance (p<0.05)

Additional tables

Non-radiographic mixed dentition space analysis methods

Table 15. Non-radiographic mixed dentition space analysis methods

Test/ Year/ Population	Characteristics	Other information	Intended use in clinical pathway
Tanaka and Johnston (1974) **Northern European Population**	Maxillary(Mx) CPM = 11 + 0.5(x) Mandibular (Md) CPM = 10.5 + 0.5(x)	Advantages: Ease of use, minimal invasion, no radiographs required, little to no clinical training or expertise required. Can be used for males and females. Disadvantages: Uncertainty in reliability to detect the space discrepancies, in different ethnic and populations. No diagnostic threshold determined.	Non-radiographic space analysis in the treatment of patients in the mixed dentition phase. It is indicated to determine the mesiodistal width of the unerupted permanent canines and premolars in the mandible and maxilla, to diagnoses and
Moyers (1973; 1988) **Northern European Population**	Prediction tables for males and females at different percentile levels (Appendix 9)	Advantages: Easy to use, no radiographs required, minimal clinical training Disadvantages: Uncertainty in reliability to detect the space discrepancies, in different ethnicities and populations. No diagnostic threshold determined.	

Schirmer and Wiltshire (1997) **South African Blacks**	Prediction tables for males and females at different percentile levels (Appendix 10)	Advantages: Ease of use, no radiographs required, minimal clinical training Disadvantages: Uncertainty in reliability to detect the space discrepancies, in other ethnicities and populations. No diagnostic threshold determined.	potential space discrepancies
Modified Tanaka and Johnston (2007) **South African Blacks**	Males : Mx CPM= 8.31mm + 0.62(x) Md CPM= 7.15mm + 0.67(x) Females: Mx CPM = 11 + 0.5(x) Md CPM = 10.5 + 0.5(x)	Advantages: Easy to use, no radiographs required, minimal clinical training Disadvantages: Uncertainty in reliability to detect the space discrepancies, in other ethnicities and populations. No diagnostic threshold determined.	
Abdhul Azm and Fouda (1989) **Egyptian**	Mx CPM=(Buccolingual (BL) width of 1st Molar x 2)-(1) Md CPM= BL width of 1st Molar x 2	Advantages: Easy to use, no radiographs required, minimal clinical training Disadvantages: Uncertainty in reliability to detect the space discrepancies, in other ethnicities and populations. No diagnostic threshold determined. Only	

Mx, Maxillary; *Md*, Mandibular; *BL*, Buccolingual; *CPM*, Canine and Premolar, *x*= mesiodistal width of lower incisors(mm)

QUADAS-2 Risk of bias summary table

Table 16. Risk of bias summary table

	Domain 1. Patient selection					Domain 2. Index Test 1				
	Was a consecutive or random sample of patients enrolled?	Was a case-control design avoided?	Did the study avoid inappropriate exclusions	Risk of bias	Index test	Was the index test result interpreted without knowledge of the results of the reference standard?	Was the diagnostic threshold at which the test was considered positive pre-specified?	If multiple index tests were tested, were each threshold or index test interpreted without prior knowledge of the results of the others?	Risk of bias
Study 1. Fouda 2019	NO	YES	YES	HIGH	AAaF	NO	NO	N/A	HIGH
Study 2. Refai 2012	UNCLEAR	YES	YES	UNCLEAR	TaJ	NO	NO	N/A	HIGH
Study 3. Alzubir 2016	UNCLEAR	YES	YES	UNCLEAR	TaJ	NO	NO	N/A	HIGH
Study 4. Ajayi 2014	UNCLEAR	YES	YES	UNCLEAR	TaJ	NO	NO	NO	HIGH
Study 5. Bugaighis 2013	YES	YES	YES	LOW	TaJ	NO	NO	NO	HIGH
Study 6. Buwembo 2012	YES	YES	YES	LOW	TaJ	NO	NO	NO	HIGH
Study 7. Khan 2007	UNCLEAR	YES	YES	UNCLEAR	TaJ	NO	NO	N/A	HIGH
Study 8. Diagne 2003	UNCLEAR	YES	YES	UNCLEAR	TaJ	NO	NO	NO	HIGH
Study 9. Schirmer 1997	UNCLEAR	YES	YES	UNCLEAR	Moyers	NO	UNCLEAR	N/A	HIGH
Study 10. Sethusa 2018	UNCLEAR	YES	YES	UNCLEAR	SaW	NO	NO	NO	HIGH
Study 11. Hammad 2010	UNCLEAR	YES	YES	UNCLEAR	TaJ	NO	NO	NO	HIGH

AAF, Abdhul Azm and Fouda; *TaJ*, Tanaka and Johnston; *SaW*, Schirmer and Wiltshire.

	Domain 2. Index Test 2				
	index test	Was the index test result interpreted without knowledge of the results of the reference standard?	Was the diagnostic threshold at which the test was considered positive pre-specified?	If multiple index tests were tested, were each threshold or index test interpreted without prior knowledge of the results of the others?	Risk of bias
Study .1 Fouda 2019					
Study 2. Refai 2012					
Study 3. Alzubir 2016					
Study 4. Ajayi 2014	Moyers	NO	NO	NO	HIGH
Study 5. Bugaighis 2013	Moyers	NO	NO	NO	HIGH
Study 6. Buwembo 2012	Moyers	NO	NO	NO	HIGH
Study 7. Khan 2007	-				
Study 8. Diagne 2003	Moyers	NO	NO	NO	HIGH
Study 9. Schirmer 1997					
Study 10. Sethusa 2018	Khan & Seedat Modified TaJ	NO	NO	NO	HIGH
Study 11. Hammad 2010	Moyers	NO	NO	NO	HIGH

	Domain 3. Reference standard			Domain 4. Flow and Timing			
	Is the reference standard likely to correctly classify the target condition?	Were the reference standard results interpreted without knowledge of the results of the index test?	Risk of bias	Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	Did all participants receive the same reference standard?	Were all participants included in the analysis?	Risk of bias
Study 1. Fouda 2019	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 2. Refai 2012	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 3. Alzubir 2016	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 4. Ajayi 2014	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 5. Bugaighis 2013	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 6 Buwembo 2012	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 7. Khan 2007	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 8. Diagne 2003	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 9 Schirmer 1997	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 10. Sethusa 2018	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR
Study 11. Hammad 2010	YES	NO	HIGH	UNCLEAR	YES	YES	UNCLEAR

Table 17. Concerns on applicability summary table

	Patient selection		Index Test(s)					Reference standard	
	Do the included participants have no apparent or suspected space discrepancies such as severe crowding or congenitally missing teeth?	Did the study report data of per-patient rather than on per tooth or quadrant of teeth ?	Where the study impressions obtained casted in Hard Dental stone to ensure reproducibility and reliability tests?	Concern	Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Was the test interpretation carried out by an experienced examiner?	Concern	Does the target condition as defined by the reference standard match the review question	Concern
Study 1. Fouda 2019	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 2. Refai 2012	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 3. Alzubir 2016	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 4. Ajayi 2014	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 5. Bugaighis 2013	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 6. Buwembo 2012	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 7. Khan 2007	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 8. Diagne 2003	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low

Study 9. Schirmer 1997	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 10. Sethusa 2018	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	Low
Study 11. Hammad 2010	Yes	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Low

Appendices

Appendix 1. QUADAS-2 tool

ITEM	RESPONSE (DELETE AS REQUIRED)
DOMAIN 1 : PATIENT SELECTION **Risk of bias**	
1. Was a consecutive or random sample of patients enrolled?	**Yes -** Where participants selected consecutively or allocated to the study via a randomisation process? **No –** If studies described another method of sampling **Unclear –** if participants sampling not clear
2. Was a case-control design avoided?	**Yes –** if case-control design clearly not used **No –** if study describes a case-control sampling of participants with particular diagnosis **Unclear –** if not clearly described

3. Did the study avoid inappropriate exclusions?	**Yes -** if the study indicates the included patients were “relatively normal occlusion”, lack of caries, all permanent teeth present and no previous orthodontic treatment of interproximal fillings/ wear ? **No -** If participants included had missing teeth, interproximal wear, advanced caries, severe malocclusion, major crowding and rotations **Unclear -** if not clearly reported
Could the selection of participants have introduced bias?	
If answers to all of questions 1) and 2) and 3) was 'yes'	Risk is low
If answers to any of questions 1) and 2) and 3) was 'no'	Risk is high
If answers to any of questions 1) and 2) and 3) was unclear	Risk us unclear
Concerns regarding applicability	
1. Do the included participants have no apparent or suspected space discrepancies such as severe crowding or congenitally missing teeth?	**Yes** – if a group of participants or teeth has been included which is no apparently space discrepancies or indicative of severe malocclusion. **No** – if a group of participants or teeth has been included which is suspected of severe malocclusion

	Unclear – if insufficient details are provided to determine the dental malocclusion of participants or alignment teeth
2. Did the study report data of per-patient rather than on per tooth or quadrant of teeth ?	**Yes** – if the analysis was reported on per tooth or quadrant of teeth **No** – if the analysis was reported on a per-patient basis **Unclear** - if it is not possible to assess whether data are presented on a per-patient or per-tooth/per quadrant basis
3. Were the study impressions obtained casted in Hard Dental stone to ensure reproducibility and reliability tests?	**Yes** – if the study impressions were casted in dental hard plaster **No –** if the study impressions were not casted **Unclear** – if it was not possible to assess the method of study model technique
Is there concern that the included participants or teeth do not match the review question?	
If answers to all of questions 1) and 2) and 3) was 'yes'	Concern is low
If answers to any of questions 1) and 2) and 3) was 'no'	Concern is high
If answers to any of questions 1) and 2) and 3) was unclear	Concern is unclear

DOMAIN 2: INDEX TEST(S) **Risk of bias** **If more than one index test was used, please complete for each test.**	
1. Was the index test result interpreted without knowledge of the results of the reference standard?	**Yes** – if the index test described is always conducted and interpreted prior to the reference standard result, or for retrospective studies interpreted without prior knowledge of the reference standard **No –** if index test described as interpreted in knowledge of reference standard result **Unclear –** if index test blinding is not described
2. Was the diagnostic threshold at which the test was considered positive pre-specified?	**Yes** – if threshold was pre-specified (i.e. prior to analysing the study results) **No** – if threshold was not pre-specified **Unclear** – if not possible to tell whether or not diagnostic threshold was pre-specified
3. If multiple index tests were tested, where each threshold or index test interpreted without prior knowledge of the results of the others?	**Yes** – if thresholds or index tests were selected retrospectively and each was interpreted by a different clinician or interpreter **No** – if study states reported by same interpreter

	Unclear - if no mention of number of interpreter for each threshold or if pre-specification of threshold not reported **N/A** - multiple diagnostic index tests not tested.
Could the conduct or interpretation of the index test have introduced bias?	
If answers to all of questions 1) and 2) and 3) was 'yes'	Risk is low
If answers to any of questions 1) and 2) and 3) was 'no'	Risk is high
If answers to any of questions 1) and 2) and 3) was unclear	Risk us unclear
Concerns regarding applicability	
1) Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	**Yes** – if the criteria for detection or diagnosis of the target disorder were reported in sufficient detail to allow replication **No** – if the criteria for detection or diagnosis of the target disorder were not reported in sufficient detail to allow replication **Unclear** - if some but not sufficient information on criteria for diagnosis to allow replication were provided

2) Was the test interpretation carried out by an experienced examiner?	Yes – if the test clearly reported that the test was interpreted by an experienced examiner No – if the test was not interpreted by an experienced examiner Unclear – if the experience of the examiner(s) was not reported in sufficient detail to judge or if examiners described as 'Expert' with no further detail given
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	
If answers to all of questions 1) and 2) was 'yes'	Concern is low
If answers to any of questions 1) and 2 was 'no'	Concern is high
If answers to any of questions 1) and 2) was unclear	Concern is unclear

DOMAIN 3: REFERENCE STANDARD

Risk of bias

1) Is the reference standard likely to correctly classify the target condition?	**Yes** – if all concerned teeth (permanent canines and premolars per quadrant) had the mesiodistal dimensions measured and recorded as a reference standard. **No** – if a final diagnosis for any participant or tooth was reached without mesiodistal dimension reference standards **Unclear** – if the method of final diagnosis was not reported
2) Were the reference standard results interpreted without knowledge of the results of the index test?	**Yes** – if the reference standard examiner was described as blinded to the index test result **No** – if the reference standard examiner was described as having knowledge of the index test result **Unclear** – if blinded reference standard interpretation was not clearly reported
Could the reference standard, its conduct, or its interpretation have introduced bias?	
If answers to all of questions 1) and 2) was 'yes'	Risk is low
If answers to any of questions 1) and 2)) was 'no'	Risk is high
If answers to any of questions 1) and 2) was unclear	Risk us unclear

Concerns regarding applicability	
Does the target condition as defined by the reference standard match the review question**?**	**Yes -** same target condition of space discrepancy of disease positive used, or teeth can be disaggregated and re- grouped according to review definition **No** – Target condition differ from the review questions and teeth cannot be disaggregated. **Unclear** - definition of target condition not clearly reported
DOMAIN 4 : FLOW AND TIMING **Risk of bias**	
Was there an appropriate interval between index test and reference standard (in vivo studies less than 3 months, in vitro no limit but must be stored appropriately)?	**Yes** - if study reports index and reference standard had a suitable interval or storage method **No** - if study reports greater than 3-month interval between index and reference standard or inappropriate storage of index data and study models prior to reference standard **Unclear** - if study does not report interval or storage methods between index and reference standard
Did all participants receive the same reference standard?	**Yes** - if all participants underwent the same reference standard

	No - if patients received different reference standard **Unclear** - if not clearly reported
Were all participants included in the analysis?	**Yes** - if all participants were included in the analysis **No** - if some participants were excluded from the analysis **Unclear** - if not clearly reported
If answers to all of questions 1) and 2) and 3) was 'yes'	Risk is low
If answers to any of questions 1) and 2) and 3) was 'no'	Risk is high
If answers to any of questions 1) and 2) and 3) was unclear	Risk us unclear

Appendix 2. African Index Medicus (AIM) search strategy

1. Prediction OR "Mixed dentition" OR Analysis OR Comparison OR Validation OR Reliability OR Applicability OR Moyers OR "Tanaka and Johnstone" OR "Schirmer and Wiltshire" OR "Predictive methods" OR "Probability tables" OR "Mixed dentition analysis" OR "Mixed dentition prediction" OR "Regression equations" OR "Predictive equations"
2. Unerupted OR Space Or Canines OR Premolars OR "Permanent teeth" OR sizes OR "Space analysis" OR "Space discrepancies" OR "Mixed dentition" OR "Tooth width predictions" OR "Unerupted canines" OR "Unerupted premolars" OR "Mesiodistal widths"
3. Children OR "Mixed dentition" OR Orthodontic OR Patients OR School
4. Africa[tw]

Appendix 3. PUBMED search strategy

((((("Africa"[MeSH] OR Africa*[tw] OR Algeria[tw] OR Angola[tw] OR Benin[tw] OR Botswana[tw] OR "Burkina Faso"[tw] OR Burundi[tw] OR Cameroon[tw] OR "Canary Islands"[tw] OR "Cape Verde"[tw] OR "Central African Republic"[tw] OR Chad[tw] OR Comoros[tw] OR Congo[tw] OR "Democratic Republic of Congo"[tw] OR Djibouti[tw] OR Egypt[tw] OR "Equatorial Guinea"[tw] OR Eritrea[tw] OR Ethiopia[tw] OR Gabon[tw] OR Gambia[tw] OR Ghana[tw] OR Guinea[tw] OR "Guinea Bissau"[tw] OR "Ivory Coast"[tw] OR "Cote d'Ivoire"[tw] OR Jamahiriya[tw] OR Kenya[tw] OR Lesotho[tw] OR Liberia[tw] OR Libya[tw] OR Libya[tw] OR Madagascar[tw] OR Malawi[tw] OR Mali[tw] OR Mauritania[tw] OR Mauritius[tw] OR Morocco[tw] OR Mozambique[tw] OR Mozambique[tw] OR Namibia[tw] OR Niger[tw] OR Nigeria[tw] OR Principe[tw] OR Reunion[tw] OR Rwanda[tw] OR "Sao Tome"[tw] OR Senegal[tw] OR Seychelles[tw] OR "Sierra Leone"[tw] OR Somalia[tw] OR "South Africa"[tw] OR "St Helena"[tw] OR Sudan[tw] OR Swaziland[tw] OR Tanzania[tw] OR Togo[tw] OR Tunisia[tw] OR Uganda[tw] OR "Western Sahara"[tw] OR Zaire[tw] OR Zambia[tw] OR Zimbabwe[tw] OR "Central Africa"[tw] OR "Central African"[tw] OR "West Africa"[tw] OR "West African"[tw] OR "Western Africa"[tw] OR "Western

African"[tw] OR "East Africa"[tw] OR "East African"[tw] OR "Eastern Africa"[tw] OR "Eastern African"[tw] OR "North Africa"[tw] OR "North African"[tw] OR "Northern Africa"[tw] OR "Northern African"[tw] OR "South African"[tw] OR "Southern Africa"[tw] OR "Southern African"[tw] OR "sub Saharan Africa"[tw] OR "sub Saharan African"[tw] OR "sub-Saharan Africa"[tw] OR "subSaharan African"[tw]) NOT ("guinea pig"[tw] OR "guinea pigs"[tw] OR "aspergillus Niger"[tw])) AND ((Children OR "Mixed dentition" OR Orthodontic OR Patients OR School[MeSH Terms]) OR (Children[Title/Abstract] OR "Mixed dentition"[Title/Abstract] OR Orthodontic[Title/Abstract] OR Patients[Title/Abstract] OR School[Title/Abstract]))) AND ((Unerupted OR Space Or Canines OR Premolars OR "Permanent teeth"[Title/Abstract] OR sizes OR "Space analysis"[Title/Abstract] OR "Space discrepancies"[Title/Abstract] OR "Mixed dentition"[Title/Abstract] OR "Tooth width predictions"[Title/Abstract] OR "Unerupted canines"[Title/Abstract] OR "Unerupted premolars"[Title/Abstract] OR "Mesiodistal widths"[Title/Abstract]) OR (Unerupted OR Space Or Canines OR Premolars OR "Permanent teeth" OR sizes OR "Space analysis" OR "Space discrepancies" OR "Mixed dentition" OR "Tooth width predictions" OR "Unerupted canines" OR "Unerupted premolars" OR "Mesiodistal widths"[MeSH Terms]))) AND ((Prediction OR Mixed dentition OR Analysis OR Comparison OR Validation OR Reliability OR Applicability OR Moyers OR "Tanaka and Johnstone"[Title/Abstract] OR "Schirmer and Wiltshire"[Title/Abstract] OR "Predictive methods"[Title/Abstract] OR "Probability tables"[Title/Abstract] OR "Mixed dentition analysis"[Title/Abstract] OR "Mixed dentition prediction"[Title/Abstract] OR "Regression equations"[Title/Abstract] OR "Predictive equations"[Title/Abstract]) OR (Prediction OR Mixed dentition OR Analysis OR Comparison OR Validation OR Reliability OR Applicability OR Moyers OR "Tanaka and Johnstone" OR "Schirmer and Wiltshire" OR "Predictive methods" OR "Probability tables" OR "Mixed dentition analysis" OR "Mixed dentition prediction" OR "Regression equations" OR "Predictive equations"[MeSH Terms]))

Appendix 4. Sabinet African Journals search strategy

1. Prediction OR "Mixed dentition" OR Analysis OR Comparison OR Validation OR Reliability OR Applicability OR Moyers OR "Tanaka and Johnstone" OR "Schirmer and Wiltshire" OR "Predictive methods" OR "Probability tables" OR "Mixed dentition analysis" OR "Mixed dentition prediction" OR "Regression equations" OR "Predictive equations"
2. Unerupted OR Space Or Canines OR Premolars OR "Permanent teeth" OR sizes OR "Space analysis" OR "Space discrepancies" OR "Mixed dentition" OR "Tooth width predictions" OR "Unerupted canines" OR "Unerupted premolars" OR "Mesiodistal widths"
3. Children OR "Mixed dentition" OR Orthodontic OR Patients OR School
4. Africa[tw]

Appendix 5. Wiley online library search strategy

1. Prediction OR "Mixed dentition" OR Analysis OR Comparison OR Validation OR Reliability OR Applicability OR Moyers OR "Tanaka and Johnstone" OR "Schirmer and Wiltshire" OR "Predictive methods" OR "Probability tables" OR "Mixed dentition analysis" OR "Mixed dentition prediction" OR "Regression equations" OR "Predictive equations"
2. Unerupted OR Space Or Canines OR Premolars OR "Permanent teeth" OR sizes OR "Space analysis" OR "Space discrepancies" OR "Mixed dentition" OR "Tooth width predictions" OR "Unerupted canines" OR "Unerupted premolars" OR "Mesiodistal widths"
3. Children OR "Mixed dentition" OR Orthodontic OR Patients OR School
4. Africa[tw]
5. Dentistry [filter]

Appendix 6. Scopus search strategy

"SPACE analysis" AND AFRICA and "MIXED DENTITION"

Appendix 7. EbscoHost search strategy

"SPACE analysis" AND AFRICA and "MIXED DENTITION"

Appendix 8. Science Direct search strategy

SPACE analysis" AND AFRICA and "MIXED DENTITION"

Appendix 9. Moyers prediction tables (1988) (8)

Probability Tables for Predicting the Sizes of Unerupted Cuspids and Bicuspids*

A, Mandibular Bicuspids and Cuspids

21/12 = (%)	19.5	20.0	20.5	21.0	21.5	22.0	22.5	23.0	23.5	24.0	24.5	25.0	25.5
MALES													
95	21.6	21.8	22.0	22.2	22.4	22.6	22.8	23.0	23.2	23.5	23.7	23.9	24.2
85	20.8	21.0	21.2	21.4	21.6	21.9	22.1	22.3	22.5	22.7	23.0	23.2	23.4
75	20.4	20.6	20.8	21.0	21.2	21.4	21.6	21.9	22.1	22.3	22.5	22.8	23.0
65	20.0	20.2	20.4	20.6	20.9	21.1	21.3	21.5	21.8	22.0	22.2	22.4	22.7
50	19.5	19.7	20.0	20.2	20.4	20.6	20.9	21.1	21.3	21.5	21.7	22.0	22.2
35	19.0	19.3	19.5	19.7	20.0	20.2	20.4	20.67	20.9	21.1	21.3	21.5	21.7
25	18.7	18.9	19.1	19.4	19.6	19.8	20.1	20.3	20.5	20.7	21.0	21.2	21.4
15	18.2	18.5	18.7	18.9	19.2	19.4	19.6	19.9	20.1	20.3	20.5	20.7	20.9
5	17.5	17.7	18.0	18.2	18.5	18.7	18.9	19.2	19.4	19.6	19.8	20.0	20.2
FEMALES													
95	20.8	21.0	21.2	21.5	21.7	22.0	22.2	22.5	22.7	23.0	23.3	23.6	23.9
85	20.0	20.3	20.5	20.7	21.0	21.2	21.5	21.8	22.0	22.3	22.6	22.8	23.1
75	19.6	19.8	20.1	20.3	20.6	20.8	21.1	21.3	21.6	2.9	22.1	22.4	22.7
65	19.2	19.5	19.7	20.0	20.2	20.5	20.7	21.0	21.3	21.5	21.8	22.1	22.3
50	18.7	19.0	19.2	19.5	19.8	20.0	20.3	20.5	20.8	21.1	21.3	21.6	21.8
35	18.2	18.5	18.8	19.0	19.3	19.6	19.8	20.1	20.3	20.6	20.9	21.1	21.4
25	17.9	18.1	18.4	18.7	19.0	19.2	19.5	19.7	20.0	20.3	20.5	20.8	21.0
15	17.4	17.7	18.0	18.3	18.5	18.8	19.1	19.3	19.6	19.8	20.1	20.3	20.6
5	16.7	17.0	17.2	17.5	17.8	18.1	18.3	18.6	128,9	19.1	19.3	19.6	19.8

B, Maxillary Bicuspids and Cuspids

21/12 = (%)	19.5	20.0	20.5	21.0	21.5	22.0	22.5	23.0	23.5	24.0	24.5	25.0	25.5
MALES													
95	21.2	21.4	21.6	21.9	22.1	22.3	22.6	22.8	23.1	23.4	23.6	23.9	24.1
85	20.6	20.9	21.1	21.3	21.6	21.8	22.1	22.3	22.6	22.8	23.1	23.3	23.6
75	20.3	20.5	20.8	21.0	21.3	21.5	21.8	22.0	22.3	22.5	22.8	23.0	23.3
65	20.0	20.3	20.5	20.8	21.0	21.3	21.5	21.8	22.0	22.3	22.5	22.8	23.0
50	19.7	19.9	20.2	20.4	20.7	20.9	21.2	21.5	21.7	22.0	22.2	22.5	22.7
35	19.3	19.6	19.9	20.1	20.4	20.6	20.9	21.1	21.4	21.6	21.9	22.1	22.4
25	19.1	19.3	19.6	19.9	20.1	20.4	20.6	20.9	21.1	21.4	21.6	21.9	22.1
15	18.8	19.0	19.3	19.6	19.8	20.1	20.3	20.6	20.8	21.1	21.3	21.6	21.8
5	18.2	18.5	18.8	19.0	19.3	19.6	19.8	20.1	20.3	20.6	20.8	21.0	21.3
FEMALES													
95	21.4	21.6	21.7	21.8	21.9	22.0	22.2	22.3	22.5	22.6	22.8	22.9	23.1
85	20.8	20.9	21.0	21.1	21.3	21.4	21.5	21.7	21.8	22.0	22.1	22.3	22.4
75	20.4	20.5	20.6	20.8	20.9	21.0	21.2	21.3	21.5	21.6	21.8	21.9	22.1
65	20.1	20.2	20.3	20.5	20.6	20.7	20.9	21.0	21.2	21.3	21.4	21.6	21.7
50	19.6	19.8	19.9	230.1	20.2	20.3	20.5	20.6	20.8	20.9	21.0	21.2	21.3
35	19.2	19.4	19.5	19.7	19.8	19.9	20.1	20.2	20.4	20.5	20.6	20.8	20.9
25	18.9	19.1	19.2	19.4	19.5	19.6	19.8	19.9	20.1	20.2	20.3	20.5	20.6
15	18.5	18.7	18.8	19.0	19.1	19.3	19.4	19.6	19.7	19.8	20.0	20.1	20.2
5	17.8	18.0	18.2	18.3	18.5	18.6	18.8	18.9	19.1	19.2	19.3	19.4	19.5

*Measure and obtain the mesial distal widths of the four permanent mandibular incisors and find that value in the horizontal row of the appropriate male or female table. Reading downward in the appropriate vertical column obtain the values for expected width of the cuspids and premolars corresponding to the level of probability you wish to choose. Ordinarily I use the 75% of probability rather than the mean of 50% since although the values distribute normally toward crowding and spacing, crowding is a much more serious clinical problem and the 75% predictive values thus protects the clinician on the safe side. Note that the mandibular incisors are used for the prediction of both the mandibular and maxillary cuspid and bicuspid widths.

Appendix 10. Schirmer and Wiltshire Probability Table (9)

Table IV. New proposed probability tables for black subjects of African descent for predicting the mesiodistal widths of unerupted mandibular canines and premolars

Σ 21 | 12	19.5	20.0	20.5	21.0	21.5	22.0	22.5	23.0	23.5	24.0	24.5	25.0	25.5
Males													
95	21.6	21.8	22.0	22.3	22.5	22.7	22.9	23.2	23.4	23.7	24.0	24.3	24.6
85	21.4	21.6	21.9	22.1	22.3	22.6	22.8	23.1	23.4	23.6	23.9	24.2	24.5
75	21.3	21.5	21.8	22.0	22.3	22.5	22.8	23.0	23.3	23.6	23.9	24.1	24.4
65	21.2	21.4	21.7	21.9	22.2	22.5	22.7	23.0	23.3	23.5	23.8	24.1	24.4
50	21.0	21.3	21.6	21.9	22.1	22.4	22.7	22.9	23.2	23.5	23.8	24.0	24.3
35	20.9	21.2	21.5	21.8	22.0	22.3	22.6	22.9	23.2	23.4	23.7	24.0	24.3
25	20.8	21.1	21.4	21.7	22.0	22.3	22.6	22.9	23.1	23.4	23.7	23.9	24.2
15	20.7	21.0	21.3	21.6	21.9	22.2	22.5	22.8	23.1	23.4	23.6	23.9	24.1
5	20.5	20.8	21.1	21.5	21.8	22.1	22.4	22.7	23.0	23.3	23.5	23.8	24.0
Females													
95	20.6	20.8	21.0	21.2	21.4	21.6	21.9	22.1	22.3	22.6	22.9	23.2	23.6
85	20.3	20.6	20.8	21.0	21.3	21.5	21.8	22.0	22.3	22.5	22.8	23.1	23.4
75	20.2	20.5	20.7	20.9	21.2	21.4	21.7	22.0	22.2	22.5	22.8	23.1	23.4
65	20.1	20.4	20.6	20.9	21.1	21.4	21.6	21.9	22.2	22.5	22.7	23.0	23.3
50	20.0	20.2	20.5	20.8	21.0	21.3	21.6	21.9	22.1	22.4	22.7	22.9	23.2
35	19.8	20.1	20.4	20.7	21.0	21.2	21.5	21.8	22.1	22.4	22.6	22.9	23.1
25	19.7	20.0	20.3	20.6	20.9	21.2	21.5	21.8	22.0	22.3	22.6	22.8	23.1
15	19.6	19.9	20.2	20.5	20.8	21.1	21.4	21.7	22.0	22.3	22.5	22.8	23.0
5	19.3	19.7	20.0	20.4	20.7	21.0	21.3	21.6	21.9	22.2	22.4	22.7	22.9

Percentile (%)

Table V. New proposed probability tables for black subjects of African descent for predicting the mesiodistal widths of unerupted maxillary canines and premolars

Σ 21 | 12	19.5	20.0	20.5	21.0	21.5	22.0	22.5	23.0	23.5	24.0	24.5	25.0	25.5
Males													
95	21.7	21.9	22.1	22.3	22.4	22.6	22.8	23.1	23.3	23.5	23.8	24.0	24.3
85	21.5	21.7	21.9	22.1	22.3	22.5	22.8	23.0	23.2	23.4	23.7	23.9	24.2
75	21.4	21.6	21.8	22.1	22.3	22.5	22.7	22.9	23.2	23.4	23.6	23.9	24.1
65	21.3	21.5	21.8	22.0	22.2	22.4	22.7	22.9	23.1	23.4	23.6	23.8	24.1
50	21.2	21.4	21.7	21.9	22.1	22.4	22.6	22.9	23.1	23.3	23.6	23.8	24.0
35	21.1	21.3	21.6	21.8	22.1	22.3	22.6	22.8	23.0	23.3	23.5	23.7	24.0
25	21.0	21.3	21.5	21.8	22.0	22.3	22.5	22.8	23.0	23.3	23.5	23.7	23.9
15	20.9	21.2	21.4	21.7	22.0	22.2	22.5	22.7	23.0	23.2	23.4	23.7	23.9
5	20.7	21.0	21.3	21.6	21.9	22.1	22.4	22.7	22.9	23.1	23.4	23.6	23.8
Females													
95	20.4	20.6	20.8	21.1	21.3	21.6	21.8	22.1	22.4	22.7	23.0	23.4	23.7
85	20.1	20.4	20.7	20.9	21.2	21.5	21.7	22.0	22.3	22.6	22.9	23.3	23.6
75	20.0	20.3	20.6	20.8	21.1	21.4	21.7	22.0	22.3	22.6	22.9	23.2	23.5
65	19.9	20.2	20.5	20.8	21.0	21.3	21.6	21.9	22.2	22.5	22.8	23.1	23.5
50	19.8	20.1	20.4	20.7	21.0	21.3	21.6	21.9	22.2	22.5	22.8	23.1	23.4
35	19.6	19.9	20.2	20.6	20.9	21.2	21.5	21.8	22.1	22.4	22.7	23.0	23.3
25	19.5	19.8	20.2	20.5	20.8	21.1	21.5	21.8	22.1	22.4	22.7	23.0	23.2
15	19.4	19.7	20.0	20.4	20.7	21.1	21.4	21.7	22.0	22.3	22.6	22.9	23.2
5	19.1	19.5	19.9	20.2	20.6	20.9	21.3	21.6	22.0	22.3	22.5	22.8	23.1

Percentile (%)

Appendix 11. BMREC Approval Letter

UNIVERSITY of the WESTERN CAPE

50 YEARS of hope, action & knowledge

3 November 2021

Dr S Brijlal and Dr D Joubert
Orthodontics
Faculty of Dentistry

Ethics Reference Number: BM21/6/8

Project Title: Validity and reliability of mixed-dentition space analysis methods in Africa: A systematic review and meta-analysis.

Approval Period: **23 July 2021 – 23 July 2024**

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project and the requested amendment to the project.

Any further amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report annually by 30 November for the duration of the project.

For permission to conduct research using student and/or staff data or to distribute research surveys/questionnaires please apply via:
https://sites.google.com/uwc.ac.za/permissionresearch/home

The permission letter must then be submitted to BMREC for record keeping purposes.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

NHREC Registration Number: BMREC-130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

Ethical considerations

Permission will need to be obtained to undertake this research Biomedical Research Ethics Committee at the University of the Western Cape

All information obtained during this research remains strictly confidential and data that may be reported in law or scientific journals will not include any information which identifies the participants in this study.

Data / information will be published anonymously. No information will be disclosed to any third party without written permission.

Contribution of authors

All review authors collaborated in the conception of the review purpose and design.

Drafting the protocol: Sarika Brijlall

Developing the search strategy: Sarika Brijlall and Faheema Kimmie-Dhansay

Screening of papers against eligible criteria: Sarika Brijlall (SB) and Deon Joubert (DJ)

Moderators at all stages: Faheema Kimmie-Dhansay (FKD) and Angela Harris (AH)

Appraising the quality of the articles: Sarika Brijlall and Deon Joubert

Developing the data extraction tool: Sarika Brijlall

Extracting data for the review: Sarika Brijlall

Analysis of the data: Sarika Brijlall and Faheema Kimmie-Dhansay

Drafting of the review: Sarika Brijlall

FKD provided comments and edited the draft.

Declaration of interest

Sarika Brijlall: Masters Student in Dentistry; Orthodontics (Part time).

Angela Harris: Head of Department; Orthodontic Department, University of Western Cape

Deon Joubert: Junior Lecturer; Orthodontic Department, University of Western Cape

Faheema Kimmie-Dhansay: Academic Research and Innovation; Statistician, University of Western Cape.

Differences between protocol and review

The principal investigator had changed the title of the article from “Validity and Reliability of mixed dentition space analysis methods in Africa: A Systematic Review” to “The accuracy of non-radiographic mixed dentition predictive methods used for the diagnosis of space discrepancies in orthodontic patients in the mixed dentition phase in Africa: A systematic review of diagnostic test accuracy”.

Researchers were not able to investigate and report on the initial objectives to determine the diagnostic test accuracy of non-radiographic mixed dentition space analysis methods used in Africa and determine the validity and reliability due to the lack of data presented in the included studies and the lack of a diagnostic threshold to determine clinical significance.

Researchers were unable to perform a meta-analysis due to the small number of included studies, clinical and methodological characteristics, and heterogeneity in the data. The index test performed in the included studies could not be judged against a predetermined diagnostic criteria, to determine sensitivity and specificity. These metrics of tests performance are helpful and an informative way to summarize diagnostic data.

Researchers did not perform sensitivity analysis and the assessment of heterogeneity due to insufficient data.

Sources of support

Internal Sources

- The University of Western Cape Oral Health Centre and the Biomedical Research and Ethics Council.
- Research and Innovation Department: University of Western Cape for the funding of publications in a recognized journal.

External Sources

- Prospero for the registration of the Protocol
- Cochrane Handbook for Systematic Reviews of Diagnostic test accuracy (version 1 and 2)

Index terms

Medical Subject Headings (MeSH)

Mixed dentition; Moyers; Tanaka and Johnstone; Schirmer and Wiltshire; Predictive methods; Probability tables; Mixed dentition analysis; Mixed dentition prediction; Regression equations; Predictive equations; Space analysis; Mixed dentition; Mesiodistal widths; Africa

MeSH check words

Children; canines; premolars; unerupted; prediction; dentition