A systematic review of cephalometric normative data in children

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TABLE OF CONTENTS page

ABSTRACT

Background: The head and neck consist of an intricate arrangement of bones, musculature, and airways playing a pivotal role in facial aesthetics, communication, chewing, swallowing, and breathing. Understanding the characteristics of craniofacial structures as well as their growth patterns in children is essential in orthodontic diagnosis and treatment planning.

Rationale: Many separate studies report normative data on craniofacial structures in cross-sectional or longitudinal study designs. However, there is currently no systematic review compiling this information to evaluate consistency and the need for further normative data collection.

Objectives: This study aims to aggregate normative data assessing the development of craniofacial skeletal structures in children with well-balanced face and normal occlusion; and identify different cephalometric characteristics between males and females and among races.

Methods: With the help of a librarian from the McGill University library, Medline, Embase and Scopus were searched on 23 Dec 2020. Records were deduplicated in Endnote and resulted in 5,656 unique articles. Inclusion criteria were i) studies involving individuals with well-balanced face and normal occlusion, ii) subjects less than 18 years of age, iii) assessment of orofacial skeleton using a cephalometric analysis of hard tissues from 2D radiographs or 3D tomographs. In the first screening phase, 240 articles were selected based on review of titles and abstracts using Rayyan. In the second phase, 44 articles were selected after full text assessment, including 13 longitudinal studies and 31 cross-sectional studies, whose quality was appraised through a 10-point grading scale.

Results: The review shows that, from childhood to adulthood, the length of cranial base increases significantly, while cranial base angle remains constant; the upper and lower jaws move forward and downward. Growth spurt occurs earlier in females; however, the great extent of growth lasts longer in males. Generally, males have longer linear parameters than females (except for similar Wits appraisal between sexes); however, difference of angular measurements between sexes is insignificant, with exception for greater mandibular plane angle in females from the age of 15 onwards. The profile becomes straighter with age as the growth of the mandible is greater than that of the maxilla. Regarding racial comparisons, when compared to whites, Asians present a shorter cranial base, more retrusive mandible, and more clockwise rotated mandible; black populations have a more protrusive maxilla. Whites tend to exhibit a straighter profile than Asians and blacks. Gaps in the literature are discussed.

Conclusions: Here, we aggregate and synthesize knowledge from cephalometric investigations of children with a well-balanced face and normal occlusion. Our results indicate age-, sex- and race-dependent patterns in orofacial skeletal parameters. Therefore, normative data for age, sex, and race should be taken into account for diagnosis and treatment planning to better identify and serve different populations as well as for research on craniofacial morphology.

RÉSUMÉ

Contexte: La tête et le cou sont constitués d'un agencement complexe d'os, de muscles et de voies respiratoires jouant un rôle central dans l'esthétique du visage, la communication, la mastication, la déglutition et la respiration. Comprendre les caractéristiques craniofaciales ainsi que leurs modèles de croissance chez les enfants est essentiel dans le diagnostic orthodontique et la planification du traitement.

Rationale: De nombreuses études distinctes rapportent des données normatives sur les structures craniofaciales dans des études transversales ou longitudinales. Cependant, il n'existe actuellement aucune revue systématique compilant ces informations pour évaluer la cohérence et la nécessité de poursuivre la collecte de données normatives.

Objectifs: Cette étude vise à agréger les données normatives évaluant le développement des structures squelettiques craniofaciales chez les enfants ayant un visage bien équilibré et une occlusion normale ; et identifier les différentes caractéristiques céphalométriques entre les sujets masculins et féminins et entre les races.

Méthodes: La recherche a été effectuée sur les bases de données Medline, Embase et Scopus avec l'aide d'un bibliothécaire de la bibliothèque de l'Université McGill le 23 décembre 2020. Les enregistrements ont été dédupliqués dans Endnote et ont donné lieu à 5 656 articles uniques. Les critères d'inclusion étaient i) des études portant sur des individus ayant un visage bien équilibré et une occlusion normale, ii) des sujets de moins de 18 ans, iii) une évaluation du squelette orofacial à l'aide d'une analyse céphalométrique des tissus durs à partir de radiographies 2D ou de tomographes 3D. Dans la première phase de sélection, 240 articles ont été sélectionnés sur la base d'un examen des titres et des résumés à l'aide de Rayyan. Dans la deuxième phase, 44 articles ont été sélectionnés après évaluation du texte intégral, dont 13 études longitudinales et 31 études transversales, dont la qualité a été appréciée au moyen d'une échelle de notation en 10 points.

Résultats: L'examen montre que, de l'enfance à l'âge adulte, la longueur de la base crânienne augmente de manière significative, tandis que l'angle de la base crânienne reste constant ; les mâchoires supérieure et inférieure se déplacent vers l'avant et vers le bas. La poussée de croissance se produit plus tôt chez les sujets féminins; cependant, la grande étendue de la croissance dure plus longtemps chez les individus masculins jusqu'à l'âge adulte. Généralement, les sujets masculins ont des paramètres linéaires plus grands que les sujets féminins (à l'exception d'une évaluation

Wits similaire entre les sexes); cependant, la différence des mesures angulaires entre les sexes est non significative, à l'exception d'un plus grand angle du plan mandibulaire chez les femmes à partir de 15 ans. Le profil devient plus droit avec l'âge car la croissance de la mandibule est supérieure à celle du maxillaire. En ce qui concerne les comparaisons raciales, par rapport aux Blancs, les Asiatiques semblent présenter une base crânienne plus courte, une mandibule plus rétrusive et une mandibule ayant effectué une rotation de croissance dans le sens horaire; les populations noires ont un maxillaire plus protrusif. Les Blancs ont tendance à présenter un profil plus droit que les Asiatiques et les Noirs. Les lacunes dans la littérature sont discutées.

Conclusion: Ici, nous agrégeons et synthétisons les connaissances issues des investigations céphalométriques d'enfants avec un visage bien équilibré et une occlusion normale. Nos résultats indiquent des modèles dépendent de l'âge, du sexe et de la race dans les paramètres squelettiques orofaciaux. Par conséquent, les données normatives pour l'âge, le sexe et la race doivent être prises en compte pour le diagnostic et la planification du traitement afin de mieux identifier et servir différentes populations ainsi que pour la recherche sur la morphologie craniofaciale.

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Firstly, I would like to thank Dr. Elizabeth A. Zimmermann, my supervisor, who is very dedicated throughout the course of my thesis. She has created all favorable conditions for me to participate in systematic review courses; moreover, she has participated in all phases of the research as well as edited the content of the article.

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CONTRIBUTION OF AUTHORS

Tuan Khang Nguyen: Master's candidate, formulated research objectives, research questions; discussed search strategies; was one of three reviewers in screening articles for final selection; extracted data, synthesized data; presented results to Professor Elizabeth A. Zimmermann; preparation and editing of the manuscript.

Elizabeth A. Zimmermann: Assistant Professor, Faculty of Dental Medicine and Oral Health Sciences, McGill University, developed research objectives, eligibility criteria; discussed search strategies; was the second reviewer in the process of screening articles for final selection; guided the process of data extraction and synthesis; and edited the article.

Akanksha Cambala: Master student of dental sciences, was the third reviewer in screening articles for final selection.

Svelana Komarova: Professor, Faculty of Dental Medicine and Oral Health Sciences, McGill University, assisted in determining research objectives, contributed professional opinions for the steps of a systematic review, and advised on the scope of the topic.

Manuela Isabelle Hrit: Orthodontist, Faculty of Dental Medicine and Oral Health Sciences, McGill University, provided professional ideas related to orthodontics for the presentation of the results.

Genevieve Gore: Associate Librarian in the Schulich Library of Physical Sciences, Life Sciences, and Engineering at McGill University, discussed and conducted search strategies.

LIST OF TABLES AND APPENDICES:

LIST OF FIGURES:

LIST OF ABBREVIATIONS

2D: two-dimensional

3D: three-dimensional

ALFH: anterior lower facial height

ATFH: anterior total facial height

AUFH: anterior upper facial height

CBCT: cone beam computed tomography

CI: confidence interval

CT: computed tomography

e.g.: for example

EMBASE: Excerpta Medica dataBASE

FH: Frankfort horizontal plane

Fig.: Figure

i.e.: that is (id est)

MEDLINE: Medical Literature Analysis and Retrieval System Online

MeSH: Medical Subject Headings

MP: mandibular plane

NIH: National Institutes of Health (United States)

OP: occlusal plane

PA: postero- anterior

PLFH: posterior lower facial height

PP: palatal plane

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analysis

PTFH: posterior total facial height

PUFH: posterior upper facial height

SD: standard deviation

SE: standard error

1. INTRODUCTION

Understanding craniofacial growth is essential in orthodontic diagnosis and treatment planning (1). However, evidence of morphological differences between various age groups has been reported, especially in growing children (2,3). Moreover, according to Alió-Sanz et al. (4), growth prediction should be taken into account during treatment planning as it can favorably or adversely affect treatment outcomes, both short term and long term. Methods for evaluating the craniofacial growth comprise craniometry, anthropometry, serial photographs, metallic implant radiography, vital staining methods, and cephalometric x-rays (5–10). Of these, lateral cephalometry, which was invented in the 1930s, has become the most common method (10).

These days, the demand for early orthodontic treatment has been increasing as parents are more and more concerned about their children's oral health. Therefore, orthodontists must account for each stage of the child’s growth through normative data when diagnosing and planning treatment. In this way, early orthodontic treatment can be promptly and properly performed, contributing to optimal results in terms of aesthetics, function, and creation of a favorable environment for dentofacial development. Additionally, many craniofacial morphological norms depend on race and sex (11,12).

The review will gather data on standard craniofacial morphology from both longitudinal and cross-sectional studies performed on children with well-balanced face and normal occlusion, published between 1946 and December 2020, aiming to provide an overview of differences in standard craniofacial morphological characteristics among different age groups, between males and females and among races. The well-balanced face was assessed in each individual study, presumably based on local cultural norms. Longitudinal studies mainly provide information on morphological changes at different ages and cephalometric differences between males and females while cross-sectional studies compare data between sexes and among populations.

1.1 Rationale

A great number of independent cross-sectional or longitudinal studies reported normative data on craniofacial structures. However, there is currently no systematic review compiling this information to evaluate consistency and the need for further normative data collection.

1.2 Objectives

This study aims to provide an overview of studies evaluating the growth of craniofacial skeletal structures in children with well-balanced face and normal occlusion, aggregate data assessing the development of those structures, specifically the spatial relationship between the cranial base, maxilla, and mandible during growth, and identify different cephalometric characteristics between males and females and among races.

2. LITERATURE REVIEW

2.1 Introduction of the structural characteristics of craniofacial bone

2.1.1 Cranial base

Cranial base, the most inferior part of the skull, is a structure of interest to both anthropologists and orthodontists. The cranial base comprises the anterior cranial base (from point sella to nasion on cephalometric radiograph) and the posterior cranial base (from point sella to basion or articulare) (13). The anterior cranial base has been widely used as reference by orthodontists for superimposition of cephalometric radiographs to assess craniofacial growth because this structure is thought to mature in advance as compared to other orofacial structures (14,15). Anatomically, the anterior cranial base comprises the anterior component of the body and the lesser wing of the sphenoid bone, the cribriform plate of the ethmoid bone, and the orbital component of the frontal bone, connected to each other by cranial sutures, including the intersphenoid synchondrosis and the spheno-ethmoidal synchondrosis. The posterior cranial base is mainly composed of the occipital bone, spheno-occipital synchondrosis, and a small portion of the temporal bone, and the sphenoid bone.

2.1.2 Face

The face is the most anterior part of the head, comprising important structures that play a pivotal role in masticatory function, respiration, speech, facial aesthetics, and identity. The face is covered on the outside by skin; the inner structures include muscles, nerves, blood vessels, fat, and bone. The face comprises three main components: upper face, midface, and lower face (16). Of these, the midface and lower face contain the maxilla and mandible, respectively, which are skeletal structures that can change significantly during childhood and adolescence growth or due to environmental influences, such as orthodontic and orthopedic treatment (1).

2.1.2.1 Maxilla

The maxilla is the dominant structure of the middle face and has a crucial function in shaping facial architecture and supporting the viscerocranium. Structurally, the maxillary bones are the combination of two halves, the right and left halves of the maxilla, which are fused at the midline to form the intermaxillary suture. The maxilla contains the maxillary sinus connected to the middle nasal cavity and separates the nasal sinus and nasal fossa from the oral cavity (17,18).

Each half of the maxilla has a pyramid shape with the apex being the zygomatic process (19). Each half of the maxilla consists of a main bony body (containing the maxillary sinus), and four processes including the alveolar, frontal, zygomatic, and palatine processes, which help it articulate with surrounding facial skeletal structures (20,21). The frontal process is the part of the maxilla that connects superiorly to the frontal bone and medially to the nasal bone (22,23). The most lateral component of the maxillary bone is the zygomatic process, which connects laterally to the zygomatic bone. It is considered an essential structure in creating the prominence of the cheekbones and the width of the face (19,24). The site where the two halves of the maxilla fuse is called the palatine process, forming the anterior nasal floor superiorly and anterior two-thirds of the hard palate inferiorly (24). The palatine process of the maxilla connects posteriorly to the palatine bone, forming the hard palate. The alveolar process is the most inferior portion of the maxilla, forming the maxillary dental arch where the upper dentition is contained (21).

2.1.2.2 Mandible

The mandible is the only movable bone and the largest bone in the craniofacial complex. It is also the only bone that is not connected to surrounding skeletal structures via a suture (25). Instead, it links to the cranial base through the temporomandibular joint, resulting in its mobility for functions, such as mastication and speech (26). The lower jaw is composed of the mandibular corpus and two mandibular rami. The body has a horseshoe shape and is the anterior part of the mandible, anatomically bounded by two borders (superior and inferior borders) and two surfaces (external and internal surfaces). The superior border is also known as the alveolar border as it contains sockets to hold lower teeth. The inferior border forms the lower contour of the face. The external surfaces that make up the front contour of the lower jaw are characterized by the mandibular symphysis at the midline, creating the eminence of the chin. The internal surface contains the fossa to accommodate nerves and blood vessels (26). The rami form the lateral contour of the mandible on both sides and are continuous with the mandibular body forming the gonial angle (27). The condyle is the most superior component of the mandibular ramus, which articulates with the temporal bone via the articular disc, forming the temporomandibular joint.

2.2 Changes in craniofacial skeletal structure during growth

There have been a great number of publications about the growth of craniofacial skeletal structures, such as Enlow & Hans (28), Proffit et al. (1), Björk & Skieller (29), Popovich &

Thompson (30). However, in most publications, inclusion criteria of well-balanced face and normal occlusion were not mentioned.

Post-natal bone growth in the craniofacial region occurs in two ways: intramembranous ossification and endochondral ossification. Intramembranous ossification is characterized by bone formation proceeding from direct differentiation of an osteoblast from a collection or condensation of mesenchymal cells, while endochondral ossification is characterized by bone formation on a cartilage template (1).

2.2.1 Cranial base

The cranial base is initially formed as cartilage and then transforms into bone through endochondral ossification. The growth of the cranial base is attributed to areas of growing cartilage between bones, known as synchondroses (1). Essential synchondroses in the development of the base of the skull include the spheno-ethmoidal synchondrosis, intersphenoid synchondrosis and spheno-occipital synchondrosis. Structurally, synchondroses consists of a band of immature cartilage cells in the center which function in cell proliferation and a band of maturing cartilage cells at both margins, which is subsequently replaced by bone (1). The anterior cranial base grows rapidly after birth and completes its growth at approximately 7 years, while the growth of the posterior cranial base is slower and is considered to complete during puberty (31). As the growth of the anterior cranial base is considered to be complete earlier than other facial skeletal structures (14), the anterior cranial base has been used as a reference structure to evaluate the growth of other orofacial structures (1,15). However, recent studies have shown that the anterior and posterior cranial base continue to grow until early adulthood (32,33). Therefore, the growth of cranial base throughout childhood and adolescence would be considered in this review.

2.2.2 Maxilla

The maxilla grows after birth by intramembranous ossification in two ways: bone apposition at the sutures connecting the maxilla to the cranial base, and bone modeling at surfaces (1).

As the maxilla is in the midface, its growth is influenced by the growth of surrounding structures. Up to 6 years of age, the growth of the cranial base plays a key role in translating the maxilla forward because there is an attachment between the maxilla and the anterior end of the cranial base (28). From age 7 to 11, the upper jaw continues to grow by a different mechanism, its size then does not change significantly after puberty (34,35). At about 7 years of age, the maxilla grows forward and downward mainly due to structural changes at sutures. The growth of the surrounding soft tissues in midfacial region induces an inferior and anterior movement of the maxilla, resulting in enlarged sutures (1). For the width of sutures to be maintained, new bone is deposited on both sides of the sutures, resulting in the elongation of the maxilla (i.e., downward and forward growth) (28). In addition, the maxillary tuberosity located at the posterior border of the maxillary bone has a free surface on which the bone deposition occurs to create more room for the eruption of maxillary molars (i.e., forward growth). As the maxilla grows forward and downward, bone modeling (bone formation or bone resorption) at surfaces occurs simultaneously at most of the anterior surface of the maxilla by bone resorption. Overall, this modeling in resorptive regions, such as the anterior aspect of alveolar process, reduces the anterior growth of the maxilla. In contrast, growth of the palate forward and downward is enhanced with translation of the maxilla and bone modeling, which includes bone apposition at oral surface and bone resorption at nasal surface of the palate (28).

2.2.3 Mandible

Unlike the maxilla, elongation of the cranial base does not significantly affect the position of the mandible; instead, endochondral ossification and bone modeling play a more pivotal role in this event (1). In the craniofacial complex, the mandible is the structure with the greatest growth (31). During the first few years postnatally, the condyle and ramus develop significantly in the superior and posterior direction, causing anterior and inferior growth of the mandible (31). The mandibular condyle is a structure covered with cartilage, which allows bones to be created by endochondral ossification mechanism. In addition, developmental changes in the mandible in growing individuals are also significantly influenced by bone modeling (i.e., bone formation or bone resorption) on bone surfaces (1). Both endochondral ossification of the condyle and bone modeling on surfaces increase greatly the height of the ramus. In the anteroposterior direction, the position of the ramus considerably changes due to periosteal apposition at its posterior border and resorption at its anterior border, resulting in the elongation of the mandibular body, the distance from the ramus to the chin (28). In contrast to the vigorous development of the mandibular ramus, several vital staining studies showed that only slight developmental changes of the chin and mandibular body occur (1). In general, mandibular growth occurs throughout childhood and adolescence, and peaks during puberty, from the age of 13.6 to 14.5 years in males and 10 to 12 years in females (36); growth of the lower jaw is almost completed by the age of 16 for men and 14 years for women (37,38). However, there are differences in the growth timing of the mandible in the vertical, anteroposterior, and tranverse directions. Specifically, completion of mandibular growth transversely is earliest (39), while vertical growth continues until adulthood (28,29).

2.3 Cephalometric radiographs

2.3.1 Introduction of cephalometric radiographs

Cephalometry is a method formalized in the 1930s and is still routinely used to assess relationships between craniofacial bones by measuring angles and distances between landmarks on a lateral head film (10). Based on x-ray projections, there are generally three types of cephalometric radiograph, comprising postero-anterior (PA) cephalographs, lateral cephalographs, and submento-vertex (SMV) (40). Of these, PA films have often been used to evaluate craniofacial width and facial asymmetry through mediolateral measurements (10). Lateral cephalometric radiographs are essential for orthodontic diagnosis, treatment planning as well as assessment of orthodontic treatment results and monitoring of craniofacial growth (41). To create a cephalometric film, several pieces of equipment are required such as an x-ray source, an adjustable cephalostat, a film cassette, and a film cassette holder (10). The cephalostat is a device used to maintain the patient's head position, where the Frankfort plane is held parallel to the floor, through bilateral ear rods placed in the external auditory canals, which helps to create reproducibility of the film, ensuring that films taken at different times can be comparable to each other (40). In the framework of this project, we only cover the points related to lateral cephalometric radiographs.

Regarding measurement procedure on cephalometric radiographs, manual tracing is performed by identifying landmarks on matte acetate tracing paper 0.003mm of thickness; determining reference planes, lines, angles; and carrying out angular and linear measurements with a protractor and millimeter scale (42). These days, cephalometric radiographs are usually analyzed digitally.

A number of cephalometric analyses or parameters have been developed, for example by Down, Steiner, or McNamara. In the following sections, the essential cephalometric measurements are presented. The identification of references planes (section 2.3.2, Fig. 1) is an essential step in cephalometric tracing. Additionally, there are a number of parameters defined by linear distances and angles that describe the position and size of the cranial base (section 2.3.3.1, Fig. 2), maxilla (section 2.3.3.2, Fig. 3), mandible (section 2.3.3.3, Fig. 4), maxillomandibular relationship (section 2.3.3.4, Fig. 5) and vertical measurements (section 2.3.3.5, Fig. 6, 7).

2.3.2 Cephalometric reference planes (Fig. 1)

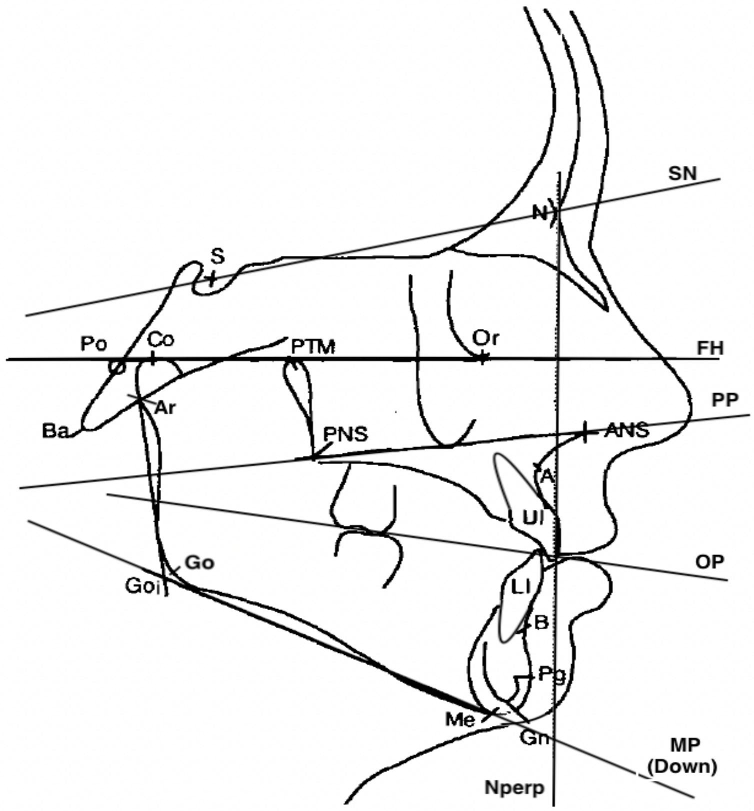


Figure 1: Cephalometric landmarks and reference planes. Adapted from Ursi et al., 1993 (3).

SN: S–N plane, this plane represents the anterior cranial base and is formed by connecting point sella (S) to point nasion (N).

FH: Frankfort horizontal plane, this plane extends from point porion (Po, superior point of the external auditory meatus) to point orbitale (Or, lowest point of the orbit) (10).

PP: Palatal plane, this plane is formed by connecting ANS (anterior nasal spine) to PNS (posterior nasal spine) and is used to measure the vertical tilt of the maxilla.

OP: Occlusal plane, this plane is formed by bisecting the incisors and the most posterior distal cusps in occlusion.

MP: Mandibular plane, there are 3 different definitions of mandibular plane:

1. Formed by connecting points Go (gonion) and Gn (gnathion) (Steiner's analysis) (43).
2. Formed by connecting points Go (gonion) and Me (menton).
3. Formed by a line at the lower border of the mandible tangent to the gonial angle and point menton (Down's analysis) (44).

Nperp: Nasion perpendicular, Line starting at Nasion and perpendicular to FH (44).

2.3.3 Cephalometric measurements and their significance

2.3.3.1 Cranial base

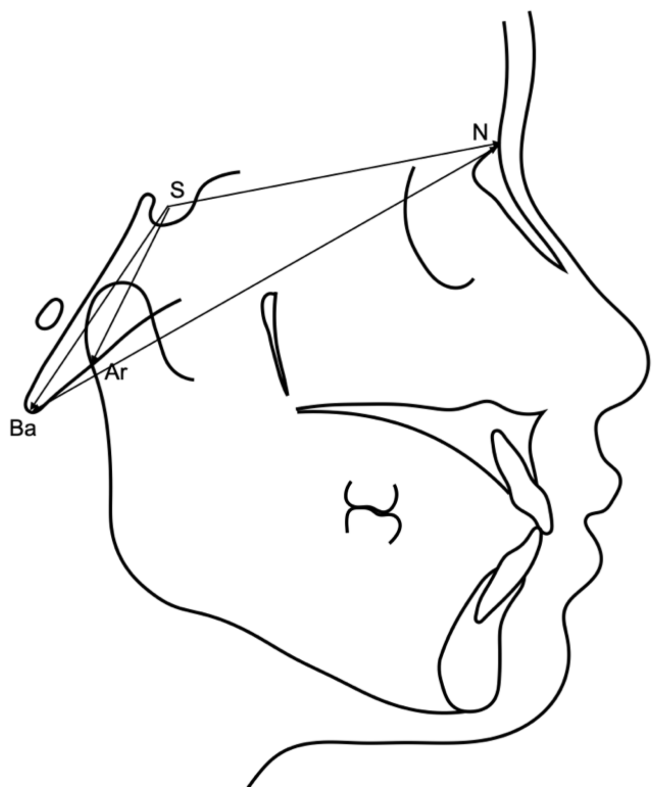


Figure 2: Cephalometric parameters for cranial base.

N-Ba: linear distance from nasion to basion, total cranial base length.

S-N: linear distance from sella to nasion, anterior cranial base length.

S-Ba: linear distance from sella to basion, posterior cranial base length.

NSBa, NSAr: nasion-sella-basion angle, nasion-sella-articulare angle, respectively, cranial base angle, representing cranial base flexure.

2.3.3.2 Maxilla

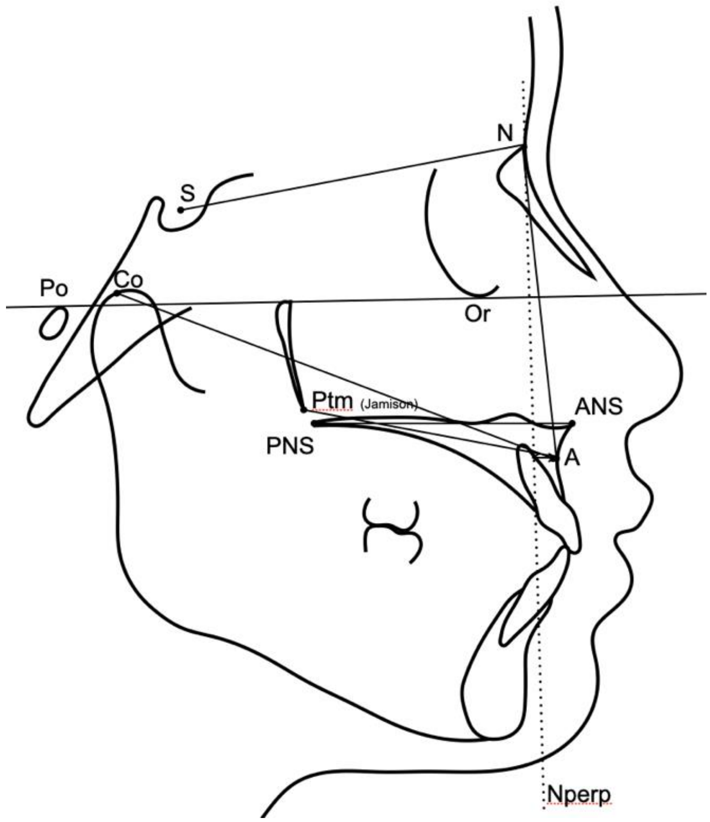


Figure 3: Cephalometric parameters for maxilla and point Ptm in Jamison et al., 1982 (45).

SNA: angle formed by sella-nasion-point A, representing relative antero-posterior position of maxilla in relation to cranial base.

- Norm: 82^0 (Steiner's analysis) (43).
- Greater SNA than norm: protruded maxilla in relation to cranial base.
- Smaller SNA than norm: retruded maxilla in relation to cranial base.

A-Nperp: linear distance from point A to nasion perpendicular, which is a perpendicular line to Frankfort plane from nasion, representing antero-posterior position of maxilla in relation to cranial base. Mean value of A-Nperp is positive if position of point A is anterior relative to nasion perpendicular line; mean value of A-Nperp is negative if position of point A is posterior relative to nasion perpendicular line.

- Norm: 0 – 1mm (McNamara's analysis) (46).
- Greater A-Nperp than norm: protruded maxilla in relation to cranial base.
- Smaller A-Nperp than norm: retruded maxilla in relation to cranial base.

A-Ptm: maxillary length, linear distance from point A to pterygoid point (Ptm), described in Jamison et al. (45) (Fig. 2), which is different from the usual Ptm (described by Ricketts (47) and illustrated in Fig. 1).

A-PNS: linear distance from point A to point PNS, maxillary length.

ANS-PNS: linear distance from anterior nasal spine to posterior nasal spine, length of the palate.

Co-A: linear distance from condylion (Co) to point A, effective midfacial length (46).

2.3.3.3 Mandible

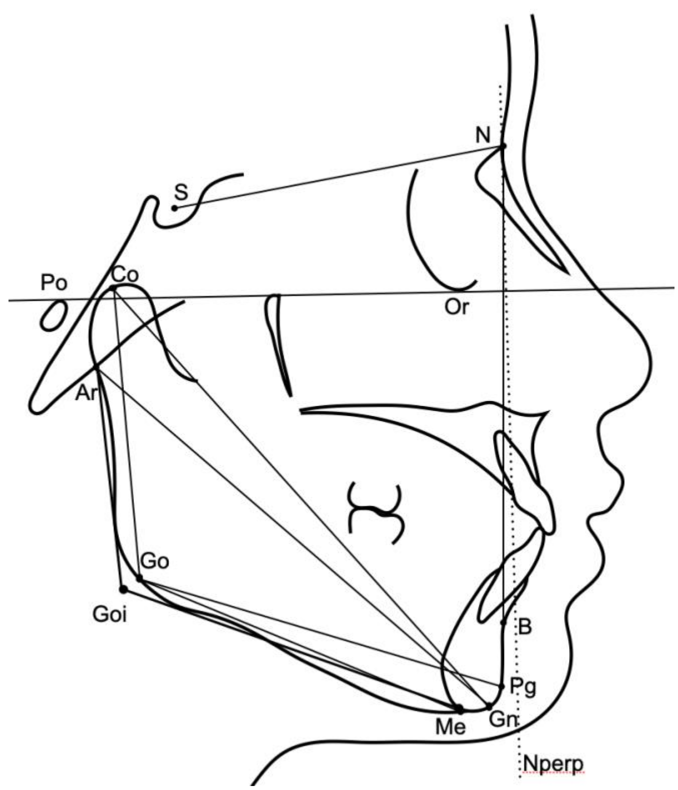


Figure 4: Cephalometric parameters for mandible and point Goi (gonial intersection).

SNB: angle formed by sella-nasion-point B, relative antero-posterior position of mandible in relation to cranial base.

- Norm: 80^0 (Steiner's analysis) (43).
- Greater SNB than norm: protruded mandible in relation to cranial base.
- Smaller SNB than norm: retruded mandible in relation to cranial base.

SNPg (or SNPog), SNGn, SNMe: angle formed by sella-nasion-pogonion, sella-nasion-gnathion, sella-nasion-menton angle, respectively, relative antero-posterior position of mandible in relation to cranial base.

Pg-Nperp: linear distance from pogonion to nasion perpendicular, which is a perpendicular line to Frankfort plane from nasion, representing antero-posterior position of the chin in relation to cranial base. Mean value of Pg-Nperp is positive if position of pogonion is anterior relative to nasion perpendicular line; mean value of Pg-Nperp is negative if position of pogonion is posterior relative to nasion perpendicular line.

- Norm: -4 – 0mm (McNamara's analysis) (46).
- Greater Pg-Nperp than norm: protruded chin in relation to cranial base.
- Smaller Pg-Nperp than norm: retruded chin in relation to cranial base.

Facial angle (FH/NPg): angle formed by intersection of facial plane (nasion-pogonion) and FH plane, representing relative antero-posterior positioning of the chin in relation to upper face.

- Norm: $87.8^0 \pm 3.57^0$ (Down's analysis) (44).
- Greater Pg-Nperp than norm: protrusive chin in relation to upper face.
- Smaller Pg-Nperp than norm: retrusive chin in relation to upper face.

Ar-Pg, Ar-Gn: length of the mandible.

Go-Pg (or Goi-Pg), Go-Gn, Go-Me (or Goi-Me): length of the mandibular body. In several studies, point Go was replaced by point Goi, gonial intersection, which is intersection of Down's mandibular plane and tangent of mandibular ramus (Fig. 4).

Co-Go: linear distance from condylion to gonion, height of the mandibular ramus.

Co-Gn: linear distance from condylion to gnathion, effective mandibular length (46).

2.3.3.4 Maxillomandibular relationship

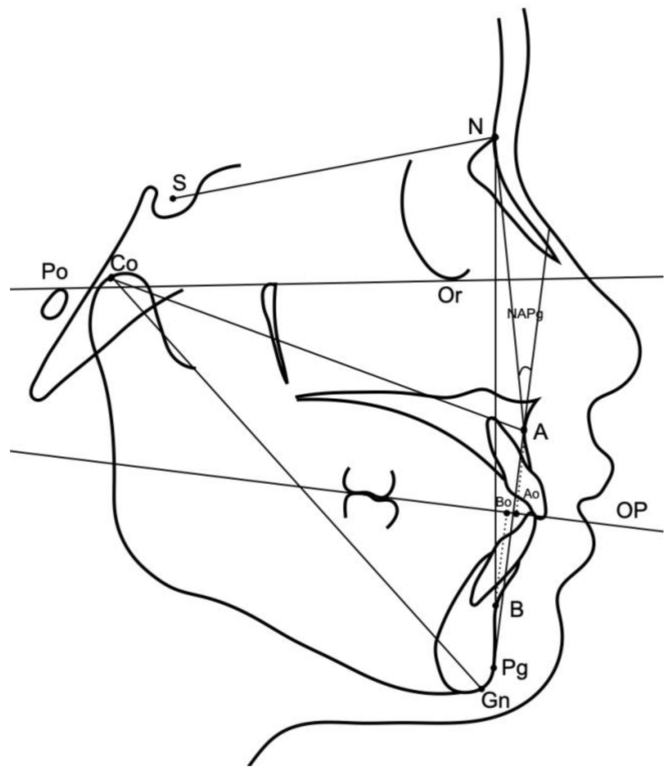


Figure 5: Cephalometric parameters for maxillomandibular relationship.

ANB: angle formed by point A-nasion-point B, antero-posterior relationship between maxilla and mandible.

- Norm (skeletal class I): 2^0 (Steiner's analysis) (43).
- Greater ANB than norm: skeletal class II.
- Smaller ANB than norm: skeletal class III.

NAPg: angle formed by nasion-point A-pogonion, facial convexity (44).

- Norm: $0^0 \pm 5.09^0$ (Down's analysis) (44).
- Greater NAPg than norm: convex profile.
- Smaller NAPg than norm: concave profile.

Wits appraisal: AoBo, linear distance from point Ao to point Bo (Ao, Bo are the projection of point A, B, respectively, on the occlusal plane) (Fig. 5). Mean value of AoBo is positive if position of Ao is anterior relative to Bo; mean value of AoBo is negative if position of Ao is posterior relative to Bo (48).

- Norm (skeletal class I): -1.17 ± 1.9mm (for male), -0.1 ± 1.77mm (for female) (48).
- Greater AoBo than norm: skelatal class II.
- Smaller AoBo than norm: skelatal class III.

Mx-Md: maxilomandibular difference, the difference of Co-Gn minus Co-A, relationship between maxilla and mandible (46).

2.3.3.5 Vertical measurements

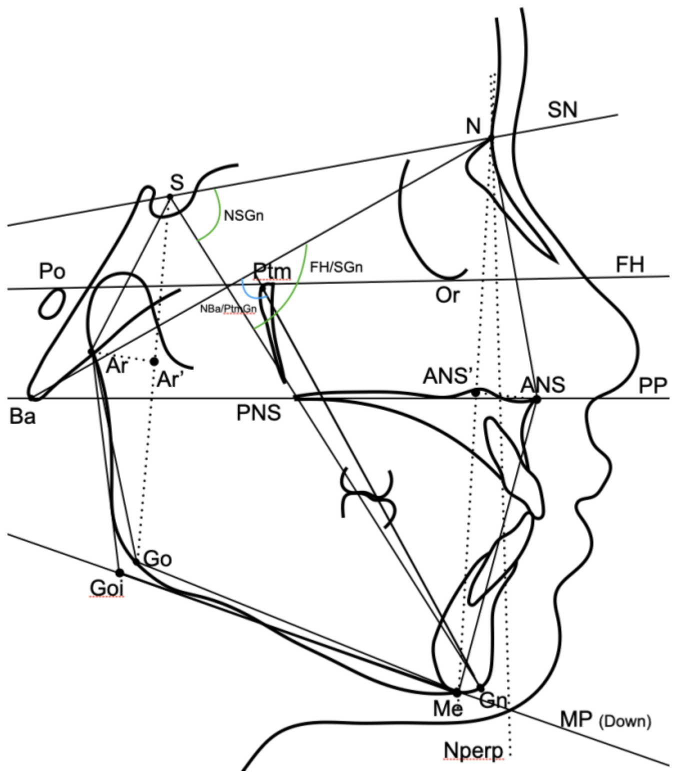


Figure 6: Vertical parameters.

AUFH: anterior upper facial height, N-ANS, linear distance from nasion to anterior nasal spine, or N-ANS' (ANS' is projection of ANS on N-Me plane).

ALFH: anterior lower facial height, ANS-Me, linear distance from anterior nasal spine to menton, or ANS'-Me (ANS' is projection of ANS on N-Me plane).

ATFH: anterior total facial height, N-Me, linear distance from nasion to menton.

PUFH: posterior upper facial height, S-Ar, linear distance from point sella to articulare, or S-Ar' (Ar' is projection of Ar on S-Go plane).

PLFH: posterior lower facial height, Ar-Go, linear distance from articulare to gonion, or Ar'-Go (Ar' is projection of Ar on S-Go plane).

PTFH: posterior total facial height, S-Go, linear distance from point sella to gonion.

AUFH/ATFH: the ratio of anterior upper facial height and anterior total facial height.

ALFH/ATFH: the ratio of anterior lower facial height and anterior total facial height.

PUFH/PTFH: the ratio of posterior upper facial height and posterior total facial height.

PLFH/PTFH: the ratio of posterior lower facial height and posterior total facial height.

PTFH/ATFH: the ratio of posterior total facial height and anterior total facial height.

PUFH/AUFH: the ratio of posterior upper facial height and anterior upper facial height.

PLFH/ALFH: the ratio of posterior lower facial height and anterior lower facial height.

Moreover, perpendicular line to Frankfort plane or perpendicular line to ANS-PNS can be used in several studies as reference planes for measuring vertical dimensions (Fig. 7). Furthermore, in some articles, point Me and Go can be replaced by Gn and Goi, respectively, to establish vertical parameters.

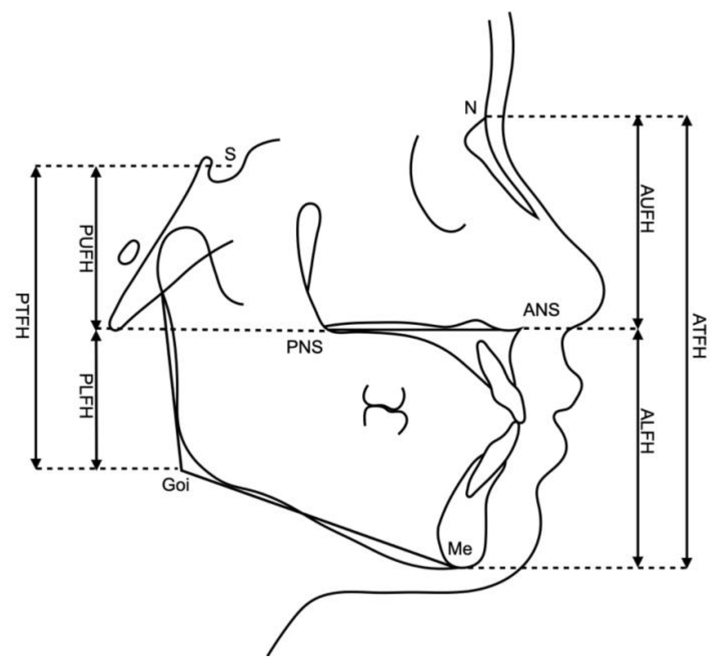


Figure 7: Perpendicular line of ANS-PNS used as reference for measuring facial height. Adapted from Chang et al., 1993 (49).

SN/FH: angle formed by intersection of S-N plane and FH plane, representing the tilt of the anterior cranial base relative to FH plane.

SN/PP or FH/PP: angle formed by intersection of S-N plane or FH plane, respectively, and palatal plane; representing the tilt of palatal plane.

SN/MP or FH/MP: mandibular plane angle, angle formed by intersection of S-N plane or FH plane, respectively, and mandibular plane; increased in hyperdivergent facial pattern and decreased in hypodivergent facial pattern.

NSGn or FH/SGn: angle formed by intersection of S-N plane or FH plane, respectively, and sella-gnathion; representing the growth pattern of the mandible.

- Great angle: representing vertical growth of mandible.
- Small angle: representing horizontal growth of mandible.

NBa/PtmGn: facial axis angle, angle formed by intersection of nasion-basion plane and facial axis (pterygoid point-gnathion); representing the growth pattern of the mandible (47).

- Great angle ($>90^0$): representing horizontal growth of mandible.
- Small angle ($<90^0$): representing vertical growth of mandible.

Mandibular gonial angle: increased in hyperdivergent facial pattern and decreased in hypodivergent facial pattern.

3. METHODS

3.1 Protocol and registration

A protocol for this systematic review was not registered. PRISMA 2009 checklist was followed, see Appendix 4 (50).

3.2 Eligibility criteria

Studies were included if they reported measurements of craniofacial hard tissues from 2D radiographs or 3D tomography techniques reporting data as mean ± standard deviation (SD) or standard error (SE). Studies were included if the measurements were performed on children and adolescents (age less than or equal to 18 years) with a well-balanced face and normal occlusion, which focuses the patient selection criteria for normative purposes and to reduce variability. Terms indicating well-balanced face included those referring to balanced or harmonious facial profile, good facial proportions, no craniofacial malformations, or no asymmetry. The well-balanced face was assessed in each individual study, presumably based on local cultural norms. Terms indicating normal occlusion included class I molar, canine and incisor relationship, normal overjet, normal overbite, mild or no tooth crowding or spacing, or adequate space in dental arches. Included studies comprise both longitudinal and cross-sectional articles. Studies were excluded if they included treatment groups (e.g., orthodontics, tooth extraction, implants, maxillofacial surgery), cohorts with malocclusion, cohorts with underlying disease, disorder or syndrome, studies involving animals or case studies.

3.3 Information sources and search strategy

A search strategy based on the study objectives was translated into search protocols for Medline, Embase and Scopus with the help of a librarian from McGill University. Searches on the three databases were performed on 23 Dec 2020, using both medical subject heading (MeSH) and text words. Keywords are **“**cephalometry” or “cone beam”, “craniofacial” or “maxilla” or “mandible”, “children”, “norm” or “standard”, and NOT “disease”. The search strategy is given in Table 1 and the full searches for each database are given in Appendices 1-3. Records were deduplicated in Endnote (according to McGill library methods).

TABLE 1. Search strategy	
Search group	Medical subject heading or key word
1	Cephalometry/ OR exp Cone-Beam Computed Tomography OR (cephalogra* or cephalometr* or cone beam).mp
2	exp infant/ OR exp child/ OR adolescent/ OR exp pediatrics/ OR (child* or pediatric* or paediatric* or prematur* or preterm* or perinat* or neonat* or neo nat* or newborn* or new born* or infan* or baby* or babies or toddler* or boy* or girl* or kid$1 or school* or juvenil* or underage* or under age* or teen* or minor$1 or youth$1 or adolescen* or pubescen* or puberty).mp. OR (neonat* or infan* or child* or adolescen* or pediatric* or paediatric*).mp,jw.
3	st.fs. or reference standards/ or reference values/ OR (standard* or norm* or longitudinal).mp.
4	exp dentistry/ or exp jaw/ or exp tooth diseases/ or (alveolar* or craniofacial or "cranio facial" or dental or dentist* or dento* or mandib* or maxill* or jaw* or malocclusion* or occlusion* or orthodontic* or tooth or teeth).mp. or (craniofacial or dental or dentist* or dento* or orofacial or orthodontic*).jw.
5	(exp infections/ or exp neoplasms/ or exp musculoskeletal diseases/ or exp digestive system diseases/ or ankyloglossia/ or exp jaw diseases/ or exp mouth diseases/ or exp pharyngeal diseases/ or exp stomatognathic system abnormalities/ or exp temporomandibular joint disorders/ or exp respiratory tract diseases/ or exp otorhinolaryngologic diseases/ or exp nervous system diseases/ or exp eye diseases/ or exp cardiovascular diseases/ or exp "hemic and lymphatic diseases"/ or exp "congenital, hereditary, and neonatal diseases and abnormalities"/ or exp "skin and connective tissue diseases"/ or exp "nutritional and metabolic diseases"/ or exp endocrine system diseases/ or immune system diseases/ or exp "disorders of environmental origin"/ or exp "pathological conditions, signs and symptoms"/ or exp chemically-induced disorders/ or exp "wounds and injuries"/) not exp tooth diseases/

6	1 AND 2 AND 3 AND 4
7	6 NOT 5

Table 1: Search strategy

3.4 Study selection

At least two out of three reviewers (EZ, TKN, AC) (blinded to the other reviewer's assessment) assessed inclusion or exclusion of articles based on eligibility criteria. Disagreements were settled through discussion. In the first screening phase, titles and abstracts were viewed using Rayyan and the articles were assessed based on the inclusion/exclusion criteria. In the second screening phase, two reviewers (EZ, TKN) assessed the full text of the articles for eligibility.

3.5 Data extraction process and data items

From the included studies, the key study parameters were extracted from each study and stored in a Microsoft Excel spreadsheet. The following parameters about the study were extracted: study design (longitudinal, cross-sectional), geographical location of study, cephalometric measurements, measurement technique (2D radiograph, CBCT), and key results. The following parameters were extracted concerning the study population: sample size, age groups, sex, race, ethnicity. Race and ethnicity were classified based on the National Institutes of Health (NIH) racial and ethnic categories (NOT-OD-15-089) (51).

3.6 Risk of bias in individual studies

The quality of the included articles for the review was appraised with the 10-point grading system shown in Table 2. The quality appraisal is based on the 'Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies' developped by the NIH (52) and the checklist published by Afrand et al. (32). Bias evaluation was performed by one reviewer (TKN); then, was presented and discussed with another reviewer (EZ).

Quality Criteria	Satisfactory (1)	Not Satisfactory (0)
Q1. Was the research question or objective in this paper clearly stated?		
Q2. Was the study population clearly specified and defined?		
Q3. Were selection criteria clearly described and adequate?		
Q4. Was follow-up length clearly described for longitudinal studies? Were the age groups in the sample clearly described for the cross-sectional study?		
Q5. Was a sample size justification, power description, or variance and effect estimates provided?		
Q6. Was the measurement method clearly defined and appropriate?		
Q7. Is the statistical analysis appropriate to answer the research question?		
Q8. Was validity of cephalometric x-rays described?		
Q9. Was reliability of cephalometric tracings described?		
Q10. Were outcome data presented with exact P value, SD, SE or CI?		

Table 2: List of questions for quality appraisal

3.7 Data synthesis and statistical methods

The cephalometric parameters are continuous variables, reported as mean ± standard deviation or standard error. Comparing the difference in mean and variance through statistical analyses, such as student t-test and analysis of variance, performed in each study, yielded specific results. From these results, qualitative data synthesis was performed to produce knowledge aggregation about changes during growth and intra-, inter-races comparisons. Inconsistency of reference landmarks, reference planes, and magnification of cephalometric films in several studies may contribute to risk of bias across studies.

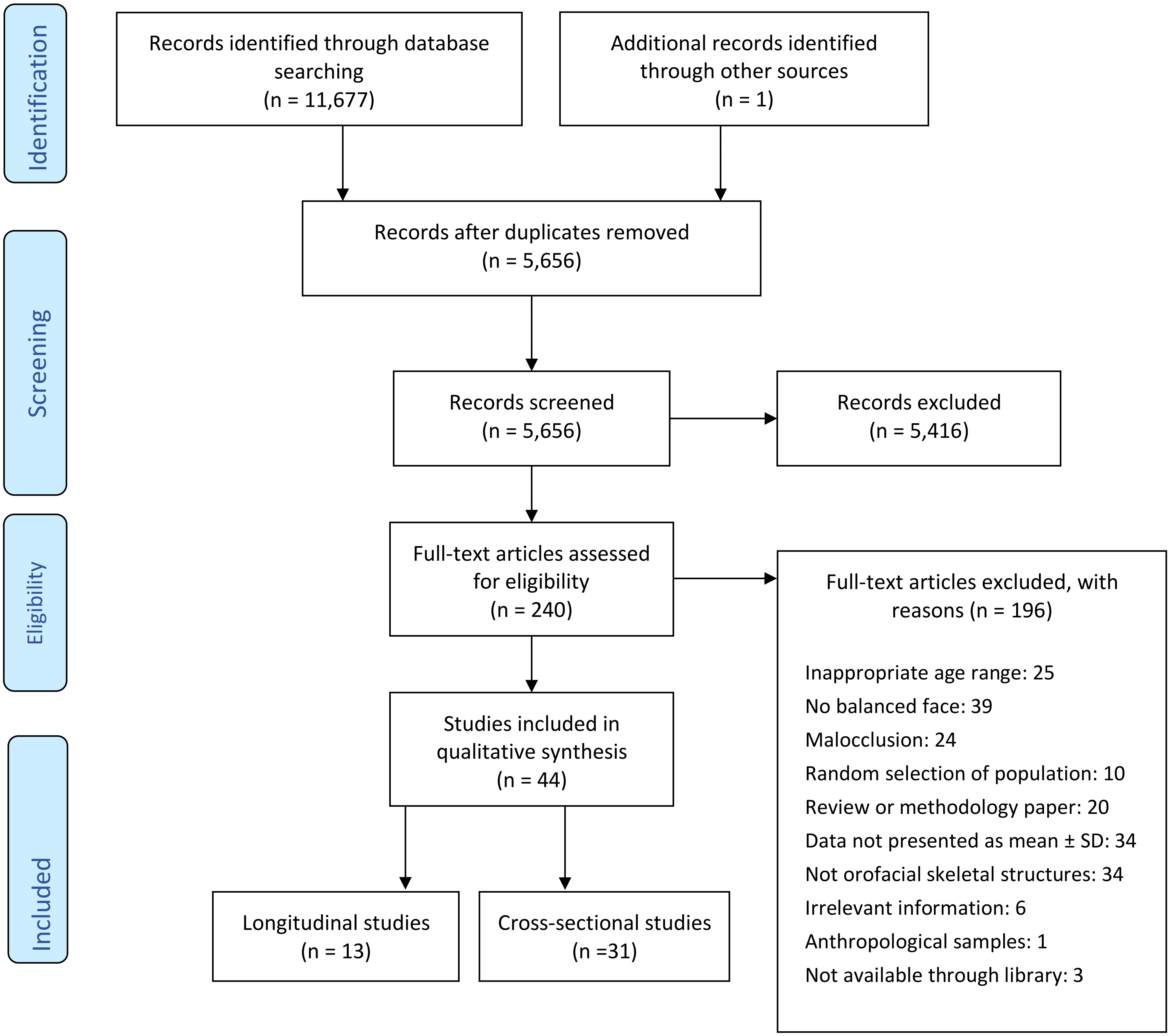
4. RESULTS

4.1 Study selection

Embase returned 3,128 articles. Medline found 3,171 records. Scopus found 5,378 records. Besides, 1 additional article was identified through other source. Records were deduplicated in Endnote and resulted in 5,656 unique articles (Fig. 8).

At least two reviewers (blinded to the other reviewer's assessment) assessed inclusion or exclusion of articles based on eligibility criteria. Disagreements were settled through discussion. In the first screening phase, 240 articles were selected based on review of titles and abstracts by using Rayyan with the inclusion/exclusion criteria. In the second phase, the full articles were assessed, resulting in 44 articles for the final selection, including 13 longitudinal studies and 31 cross-sectional studies, whose quality was appraised. Finally, data were extracted and knowledge was synthesized.

Figure 8: Flow diagram for final selection (PRISMA 2009 Flow Diagram)



4.2 Study characteristics

The final selection for the systematic review comprises 44 articles published between 1954 and 2020. Of these, 43 articles are published in English language and 1 is published in Mandarin (53). Normative data are stratified by race: 21 studies investigate white populations, 10 black populations, 9 Asian populations, 1 Hispanic or Latino, and 3 mixed-race. All studies include both males and females, except for Sobreira et al., 2011 (54), whose sample solely consists of female subjects. In all 44 included studies, measurements were made on lateral cephalometric radiographs; there are no articles in the final selection using cone-beam CT for measurements (Table 3a, 3b).

Study	Sample size and sex	Age at measurement timepoints	Race (Location)	Orthodontic measurements		Results	Validity/Reliability
Jamison et al. (1982) (45)	20 M, 15 F	Biannually from: 8- 12 y Annually from: 12- 17 y	White (Iowa, USA)	Maxilla	A-Ptm (Ptm- Jamison) [1]	A-Ptm significantly increased from 8-17 y, by 7.5 mm for M and 5.1 mm for F; change in M> in F.	Subject's head positioned in cephalostat and oriented to Frankfort horizontal plane./ All measures performed by two independent investigators.
					SNA	SNA increased significantly by 1.7° in M, insignificantly by 0.4° in F.	
				Mx-Md	ANB NAPg	ANB insignificantly decreased 0.6° for M and 1° for F from 8-17 y. NAPg insignificantly decreased 3.8° for M and 3.6° for F from 8-17 y. Changes in ANB, NAPg for both sexes were not significantly different.	
Bishara et al. (1984) (2)	20 M, 15 F	Biannually from: 4.5- 12 y Annually from: 12- 17 y Final set at 25.5 y GP I: 5- 10 y GP II: 10- 15 y GP III: 15- 25.5 y	White (Iowa, USA)	Maxilla	A-PNS	A-PNS: changes in GP II≈ GP I> GP III for M, changes in GP I> GP II> GP III for F.	Subject's head positioned in cephalostat and oriented to Frankfort horizontal plane./ Two investigators independently measured each parameter on each cephalogram twice.
					SNA	SNA: greatest increase by 1.4° occurred in M in GP II; the total change of SNA for F was solely 0.4°.	
				Mandible	Ar-Pg	Ar-Pg: changes in GP II≈ GP I> GP III for M (change significantly less in GP III but still accounted for 26% of the total change); changes in GP I> GP II> GP III for F.	
					SNB, SNPg	SNB, SNPg: the difference of increase in 3 growth periods was insignificant in M. The least amount of increase occurred in GP III in F.	
				Mx-Md	ANB NAPg	ANB, NAPg: decreased mostly in GP I, GP III for M, and the most was in GP III. ANB, NAPg decreased in GP I, GP II for F.	
				Vertical parameters	N-ANS', N-Me, N-ANS'/N-Me [2] ArGo, S-Go ArGo/S-Go S-Go/N-Me SN/MP	N-ANS', N-Me increased the most in GP I, the least in GP III in both sexes. N-ANS'/N-Me increased mostly in GP I in both sexes. Ar-Go, S-Go: no significant difference in 3 GP in M; but in F, the greatest increase was in GP I. Ar-Go/S-Go decreased in GP I and increased in GP II, GP III in both sexes. S-Go/N-Me, SN/MP changed the most in M, and the least in F during GP III.	
					NSGn	NSGn: insignificantly changed in the 3 growth periods for both sexes.	
Ursi et al. (1993) (3)	16 M, 16 F	Measures at 6, 9, 12, 14, 16, 18 y	White (Ohio, USA)	Cranial base	S-N S-Ba NSBa	S-N: M> F at all ages, especially at 16, 18 y (p<.001). S-Ba: M> F at 16, 18 y. NSBa: no significant difference between sexes.	NA/ Each lateral cephalometric radiograph traced by one investigator and checked for accuracy by a second.
				Maxilla	SNA, A-Nperp Co-A	SNA, A-Nperp: no significant differences between M and F. Co-A: M> F at 9, 14, 16, 18 y; especially at 16, 18 y (p<.001).	
				Mandible	SNB, Pg-Nperp Co-Gn	SNB, Pg-Nperp: no significant differences between M and F, except at 14 y, M< F in SNB; Co-Gn: M> F at 16, 18 y.	

				Vertical parameters	N-ANS, ANS-Me FH/MP (Go-Me) NBa/PtmGn	N-ANS: M> F at 14, 16, 18 y; ANS-Me: M> F at 16, 18 y. FH/MP: no significant difference between M and F. NBa/PtmGn: M< F at 14 y.	
Higley et al. (1954) (55) Broadbent et al. (1975) (56)			97% White (Iowa, USA) White (Ohio, USA)	Studies reported normative cephalometric data without any statistic test or interpretation of results.			
el-Batouti et al. (1994) (57)	35 M, 39 F	Measures at 6, 9, 12, 15, 18 y	White (Oslo, Norway)	Cranial base	NSBa	NSBa: no significant difference between M and F from 6- 18 y.	Subject's head positioned in cephalostat and oriented to Frankfort horizontal plane./ A replicate measurement trial was performed on 20 randomly selected cephalograms at each age.
				Maxilla	SNA	SNA: M> F at 9, 12, 15, 18; M≈ F at 6 y. SNA increased more in M than F from 6- 18 y. The greatest increase occurred between 9- 15 y.	
				Mandible	SNB	SNB: M> F at 18; M≈ F at 6, 9, 12, 15 y. SNB increased in both sexes from 6-18 y (increase in M> in F).	
				Mx-Md	ANB, NAPg	ANB, NAPg: M> F at 15; M≈ F at 6, 9, 12, 18 y.	
				Vertical parameters	N-ANS ⊥FH, ANS-Me ⊥FH, N-ANS /ANS-Me (⊥FH) [3] S-Go ⊥FH [3] SN/FH, SN/PP SN/MP (Go-Me)	N-ANS ⊥FH: M> F at 18; M≈ F at 6, 9, 12, 15 y. N-ANS /ANS-Me (⊥FH): M< F at 6, 9, 12; M≈ F at 15, 18 y. ANS-Me ⊥FH, S-Go ⊥FH: M> F at all ages. N-Me ⊥FH, S-Go ⊥FH: increase in M> in F. SN/FH: M≈ F, SN/PP: M< F at all ages. SN/MP: M≈ F at 6, 9, 12, 15 y; M< F at 18 y; SN/MP decreased from 6- 18 y in both sexes.	
el-Batouti et al. (1995) (58)	Norwegian: 35 M, 39 F Iowan: 20 M, 15 F	Measures at 6, 9, 12, 15, 18 y	White (Oslo, Norway) Comparison to White (Iowa, USA)	Maxilla	SNA	Norwegian had a relatively larger SNA than Iowan, especially in M at 12, 15, 18 y.	Subject's head positioned in cephalostat and oriented to Frankfort horizontal plane./ Landmarks on each cephalogram identified by one investigator and checked by another.
				Mandible	SNB, SNPg, FH/NPg	Norwegian had a greater mandibular protrusion than the Iowan (larger SNB, SNPg, FH/NPg).	
				Mx-Md	ANB, NAPg, Wits	ANB, NAPg, Wits: insignificant difference between Norwegian and Iowan.	
				Vertical parameters	N-ANS', N-Me, N-ANS'/N-Me [2], Ar'-Go, S-Go, Ar'-Go/S-Go [4], S-Go/N-Me, SN/MP, FH/MP NSGn, FH/SGn	N-ANS', N-Me, N-ANS'/N-Me, Ar'-Go: insignificant difference between Norwegian and Iowan. S-Go, S-Go/N-Me: Norwegian< Iowan; Ar'-Go/S-Go: Norwegian> Iowan. SN/MP, FH/MP: insignificant difference between Norwegian and Iowan. NSGn: Norwegian F< Iowan F; FH/SGn: Norwegian< Iowan.	
	Group Umeå: 55 M, 67 F	Group Umeå: Measures in 3 age groups at i) 7 and 10 y, ii) 10	White (Umeå and Enköping, Sweden)	Cranial base	S-N NSAr NSBa	S-N increased with age; an increase of 1-1.5mm was even observed from 16- 19 y. In M, one-third of the total increase was noted between 13-16 y. NSAr was stable in both sexes from the primary until the adult period. NSBa decreased around 4° during the observation period.	Cephalograms taken in maximal intercuspal position with head fixed in cephalostat./ 10 cephalograms

Thilander et al. (2005) (59)	Group Enköping: 20 M, 27 F	and 13 y, iii) 13, 16, 19 and 31 y Group Enköping: Measures at 5, 7, 10 and 13 y		Maxilla	SNA	SNA remained constant.	digitized by one author and then compared with the filed data digitized by two other authors.
				Mandible	Ar-Pg, Goi-Me [5] SNB, SNPg	The length of the mandible (Ar-Pg, Goi-Me) increased until the young adult period and increase in M> in F. A growth acceleration was noticed between 13- 16 y in M. SNB, SNPg increased continuously during the observation period.	
				Mx-Md	ANB NAPg	ANB decreased during growth. Facial convexity (NAPg) changed from slight convexity to straight.	
				Vertical parameters	N-ANS', N-Me, S-Goi ANS'-Me [2,5] ANS'-Me/ N-Me Ar–Goi N-Me/ S-Goi SN/PP, SN/MP (Down), MP/PP	In M, growth acceleration in N-ANS', N-Me, S-Goi was noted between 13-16 y. ANS'-Me increased the most between 13- 16 y for both sexes. ANS'-Me/ N-Me was constant during the follow-up (55%). Posterior lower facial height (Ar–Goi) increased the most from 13-16 y in M. N-Me/ S-Goi decreased continuously (about 16%), coinciding with an upward rotation of the mandible. Only small variations in SN/PP could be seen in both sexes. A continuous decrease in SN/MP, MP/PP with age in both sexes.	
Stahl de Castrillon et al. (2013) (60)	16 M, 16 F	Yearly measures from 6- 17 y (except at the age of 14)	White (Rostock, Germany)	Cranial base	NSBa, NSAr S-N, S-Ba, S-Ar	NSBa, NSAr: M≈ F, remained constant in both sexes. The length of cranial base (S-N, S-Ba, S-Ar) increased in both sexes. S-N: M> F at 6, 16, 17; S-Ba: M> F at 6 y.	Cephalograms taken in natural head position./ 10 randomly chosen subjects retraced.
				Maxilla	SNA, A-Nperp Co-A, ANS-PNS	SNA, A-Nperp: increased with age in M, remained constant in F. Co-A: M> F at 6, 16, 17; ANS-PNS: M> F at 16 y.	
				Mandible	SNB, SNPg, Pg-Nperp Co-Gn, Ar-Gn, Go-Me, Co-Go	SNB, SNPg, Pg-Nperp became larger with age in both sexes. Mandibular length increased with age. Co-Gn: M> F at 6, 7, 15, 16, 17 y; Ar-Gn: M> F at 6, 15, 16, 17 y; Go-Me: M> F at 15, 17 y; Co-Go: M> F at 17 y.	
				Mx-Md	ANB Wits	ANB, Wits: M≈ F at all ages. ANB became smaller with age, Wits value remained constant in both sexes.	
				Vertical parameters	SN/PP, SN/MP (Down), PP/MP, ArGoMe N-Me, ANS-Me, S-Go	SN/PP remained constant; SN/MP, MP/PP and ArGoMe became smaller in both sexes: counter-clockwise rotation of mandible with age. N-Me: M> F at 15, 16, 17; ANS-Me: M> F at 15, 17; S-Go: M> F at 17 y.	
Alió-Sanz et al. (2011) (4)	22 M, 16 F	Sample divided into 3 groups Group GI: 8- 11 y Group GII: 12- 14 y Group GIII: 15- 18 y	White (Madrid, Spain)	Maxilla	Co-A ANS-PNS SNA point A	Co-A increased progressively, means at GIII> GII> GI. The biggest differences were found between GI and GII; increase in M> in F. ANS-PNS: means at GI< GII≈ GIII; increased the most in the prepubescent group. Co-A, ANS-PNS: M> F. SNA increased insignificantly from GI to GIII. The advance of the point A is greater in F than M.	NA/ All cephalograms traced by two researchers.

		Annual measures for 6 years		Vertical parameters	point ANS point PNS N-ANS SN/PP	point ANS: moved downward in GI≈ GII≈ GIII. point PNS: moved downward in GIII< GII, GI. From GI to GII, PNS move downward more than ANS. N-ANS: mean at GI< GII≈ GIII; the greatest vertical growth of the maxilla was noted in the prepubescent group. SN/PP: M< F.	
Hamamci et al. (2013) (61)	22 M, 16 F	Measures at 9, 14, 18 y	White (Diyarbakir, Turkey)	Maxilla	SNA A-Nperp Co-A	SNA significantly increased by 2.28° in F and 1.07° in M between 9- 18 y. SNA significantly increased from 9- 14 in F, from 14- 18 y in M. A-Nperp significantly increased in F from 9- 14 and 14-18 y, in M from 9- 14 y. Co-A significantly increased in both sexes between 9 and 14, 14 and 18 y. Co-A increased 13.2 mm in F and 10.71 mm in M from 9- 18 y.	Subject's head positioned in cephalostat and oriented to Frankfort horizontal plane./ NA
				Mandible	SNB Pg-Nperp Co-Gn	SNB, Pg-Nperp, Co-Gn significantly increased in both sexes from 9- 14, 14- 18 y. SNB increased by 3.2° for F, 2.24° for M from 9- 18 y. Pg-Nperp increased by 6.03 mm for F and 4.71 mm for M from 9- 18 y. Co-Gn increased by 18.7 mm in F and 19.9 mm in M from 9- 18 y.	
				Mx-Md	ANB Mx-Md difference	ANB decreased significantly from 9- 14 in F, 14- 18 y in M. ANB decreased by 0.92° in F, 1.35° in M from 9- 18 y. Maxillomandibular difference increased significantly from 9- 14, 14- 18 y in M, F.	
				Vertical parameters	ANS-Me SN/MP (Go-Me) NBa/PtmGn	ANS-Me increased significantly from 9- 14, 14- 18 y in both sexes. ANS-Me increased by 10.64 mm in F, 10.42 mm in M. SN/MP decreased significantly from 9- 14 y in F, from 9- 14 and 14- 18 y in M. The total decrease was 1.35° in F, 1.42° in M. NBa/PtmGn changed insignificantly in both sexes.	
Jiménez et al. (2020) (62)	Baseline: 19 M, 30 F Follow-up: 10 M, 23 F	Annually from 6- 24 y	Mixed race - White and American Indian (Medellin, Colombia)	Cranial base	S-N	S-N: M≈F from 6- 14 y, M> F from 16- 24 y. S-N: F had a constant acceleration from 8- 16 y, after that growth rate slowed down. M had a significant acceleration of growth between 14- 16 y, which decreased after 20 y.	NA/ One researcher performed measurements on the same radiographs after 2-weeks; two observers performed measurements in 15 blinded radiographs.
				Maxilla	Co-A	Co-A: M≈F from 6- 14 y, M> F from 16- 24 y. Growth of Co-A plateaued from 8- 14 y in both sexes. M had a pubertal peak in Co-A between 14- 16 y, while growth in F decreased after 14 y.	
				Mandible	Co-Gn	Co-Gn: M≈F from 6- 14 y, M> F from 16- 24 y. Similar to Co-A, growth of Co-Gn plateaued from 8- 14 y. Males had a pubertal peak in Co-Gn between 14- 16 y, while growth in F decreased after 14 y.	

				Vertical parameters	N-Me ANS-Me S-Goi [5] SN/MP (Down)	N-Me: M> F from 16- 24 y; F had a constant acceleration from 8- 14 y, after that growth rate slowed down; significant pubertal spurt occurred between 14- 16 y in M. ANS-Me: M> F from 16- 24 y; the growth spurt was between 12- 14 in F, and 14- 16 y in M. S-Goi: M> F from 16- 24 y; the growth spurt was between 10- 12 in F, and 14- 16 y in M. SN/MP decreased with age, no difference between 2 sexes.	
Chuang (2020) (63)	24 M, 24 F	Biennially at 8, 10, 12 y	Asian - Mongolian ancestry (Kaohsiung, Taiwan)	Cranial base	S-N, S-Ba, N-Ba, S-Ar	S-N, S-Ba, N-Ba: M≈ F; increased significantly from 8- 10, 10- 12 y in both sexes. S-Ar: M> F at 8, 12 y; increased significantly from 8- 10, 10- 12 y in both sexes.	Subject's head positioned in cephalostat and oriented to Frankfort horizontal plane./ All points traced and digitized twice.
				Maxilla	NSBa SNA ANS-PNS	NSBa: M≈ F; remained constant from 8- 12 y. SNA, ANS-PNS: M≈ F at 8, 10, 12 y; SNA insignificantly changed in both sexes, only a small increase from 10- 12 y in M. ANS-PNS increased significantly from 10- 12 y in both sexes.	
				Mandible	SNB, SNMe, SNGn Go-Gn, Ar-Gn, Ar-Go	SNB, SNMe, SNGn: M< F; increased insignificantly from 8- 12 y in both sexes. Go-Gn: M≈ F; increased significantly from 8- 10, 10- 12 y; Ar-Go: M≈ F; increased significantly from 10- 12 y; Ar-Gn: M< F at 12 y; increased significantly from 8- 10, 10- 12 y.	
				Mx-Md	ANB, NAPg	ANB, NAPg: M≈ F at 8, 10 y; M< F at 12 y (due to earlier growth of mandible in girls). ANB, NAPg decreased significantly from 8- 12 y.	
				Vertical parameters	SN/MP (Go-Me), FH/MP, PP/MP, ArGoMe	SN/MP, FH/MP, PP/MP, ArGoMe: M≈ F; decreased insignificantly from 8- 12 y.	

Table 3a: Summary of characteristics of included longitudinal studies

Study	Sample size and sex	Age at measurement timepoints	Race (Location)	Orthodontic measurements		Results	Validity/Reliability
Bishara & Fernandez (1985) (11)	North Mexican: 36 M, 45 F Iowan: 20 M, 15 F	North Mexican: M: 12.76 y (11-14.16 y) F: 13 y (11.08-14 y) Iowan: 12- 14 y	Hispanic/Latinx (Chihuahua, Mexico) Comparison to White (Iowa, USA)	Maxilla	SNA	No significant differences between 13 y North Mexican M and 13 y Iowan M were found. 13 y North Mexican F had greater SNB, SNPg, Ar-Go/S-Go (%) than 13 y Iowan F. 13 y North Mexican M had significantly larger N-ANS', N-Me, and S-Go than F. 13 y Iowan M had significantly larger N-ANS', N-Me, Ar-Go, and S-Go than F.	Subject's head positioned in cephalostat and oriented to Frankfort horizontal plane./ Intra- and inter-reliability allowable at 0.5° for angular measurements and 0.5 mm for linear measurements.
				Mandible	SNB, SNPg, FH/NPg		
				Mx-Md	ANB, NAPg, Wits		
				Vertical parameters	N-ANS', N-Me, N-ANS'/N-Me [2], Ar-Go, S-Go, Ar-Go/S-Go, S-Go/N-Me; SN/MP, FH/MP, FH/SGn, NSGn		
Bishara et al. (1990) (12)	Egyptian: 39 M, 51 F Iowan: 33 M, 22 F	12- 14 y Egyptian: 12.5± 0.6 y Iowan: 13± 0.9 (M), ± 0.8 y (F)	White (Alexandria, Egypt) Compared to White (Iowa, USA)	Cranial base	NSAr, NSBa, N-Ba, S-Ba, S-N	13 y Iowan M had greater S-N and Ar'-Go, S-Go than Egyptian M. Egyptian F had greater S-Ba, N-Ba, NAPg, Wits, N-ANS' than Iowan F. Iowan M had greater N-Ba, S-Ba, S-N and N-ANS', Ar'-Go, S-Go than Iowan F. 13 y Egyptian M had larger N-Ba, S-N and smaller NSGn than Egyptian F.	NA/ Intra- and inter-reliability allowable at 0.25° for angular measurements and 0.2 mm for linear measurements.
				Maxilla	SNA		
				Mandible	SNB, SNPg, FH/NPg		
				Mx-Md	ANB, NAPg, Wits		
				Vertical parameters	N-ANS', N-Me, N-ANS'/N-Me, Ar'-Go, S-Go, Ar'-Go/S-Go [2, 4], S-Go/N-Me; SN/MP, FH/MP, FH/SGn, NSGn		
El-Batran et al. (2008) (64)	61 M, 34 F	7.5- 9.5 y (mean: 8.5 y)	White (Giza, Egypt)	Cranial base	NSBa, N-Ba, S-Ba, S-N	8.5 y Egyptian M had larger ANS-Gn, SN/MP, and ArGoiMe than Egyptian F.	NA/ Intra- and inter-reliability allowable at 0.5° for angular measurements and 0.2 mm for linear measurements.
				Maxilla	SNA, ANS-PNS		
				Mandible	SNB, Go-Me		
				Mx-Md	ANB, NAPg		
				Vertical parameters	N-Gn, N-ANS, ANS-Gn; SN/FH, SN/PP, SN/MP (Down), ArGoiMe [5]		
Thilander et al. (1982) (65)	27 M, 36 F	10 y 9 m	White (Sweden)	Cranial base	NSAr, NSBa, S-N, S-Ar	11 y Norwegian children had smaller S-N, ANS-PNS than Swedish children.	NA/ NA.
				Maxilla	SNA, ANS-PNS		
				Mandible	SNB, SNPg, Ar-Goi, Goi-Pg [5], FH/NPg		
				Mx-Md	ANB, NAPg		

				Vertical parameters	N-ANS, N-Me; SN/FH, SN/PP, SN/MP (Down), FH/PP, FH/MP, PP/MP, ArGoiMe [5]		
Humerfelt (1970) (66)	36 M, 20 F	10-12 y M: 10 y 9m (10 y- 11 y 11m) F: 10 y 8m (10 y- 11 y 5m)	White (Oslo, Norway)	Cranial base Maxilla Mandible Mx-Md Vertical parameters	NSAr, NSBa, S-N, S-Ar SNA, ANS-PNS SNB, SNPg, Ar-Goi, Goi-Pg [5] ANB, NAPg N-ANS, N-Me; SN/PP, SN/MP (Down), PP/MP, ArGoiMe [5]	No significant differences between sexes for angular measurements were found. 11 y Norwegian M had greater linear measurements than F.	NA/ All measurements were controlled a second time.
Obloj et al. (2008) (67)	39 M, 34 F	9.25- 11.22 y (10.37± 0.52 y)	White (Wegrow County, Poland)	Cranial base Maxilla Mandible Mx-Md Vertical parameters	NSBa, S-N SNA, A-Nperp, Co-A SNB, Pg-Nperp, Co-Gn ANB, Wits N-Me, N-ANS, ANS-Me, S-Go, S-Go/N-Me, SN/MP, NBa/PtmGn, ArGoiMe [5]	10 y Polish M had greater S-N, N-Me, ANS-Me, S-Go and smaller SNA, A-Nperp, Pg-Nperp, NBa/PtmGn than F.	Cephalograms taken in maximal intercuspal position with head fixed in cephalostat./ Measurement errors calculated.
Kilic et al. (2010) (68)	33 M, 83 F	11-16 y M: 13.65 ± 1.47 y F: 13.42 ± 1.13 y	White (Erzurum, Turkey)	Maxilla Mandible Mx-Md Vertical parameters	A-Nperp, CoA Pg-Nperp, Co-Gn Mx-Md diff ANS-Me, FH/MP (GoMe), NBa/PtmGn	14 y Turkish M had greater Co-A, Co-Gn, ANS-Me than Turkish F. Compared to 14 y white Americans in Broadbent's study, Turkish had shorter Co-A; Turkish F had shorter Co-Gn than American F. Compared to white adults reported by McNamara, Turkish had significantly larger FH/MP and smaller NBa/PtmGn, more retruded mandible (Pg-Nperp); Turkish F had significantly smaller A-Nperp.	All radiographs taken with Frankfort plane parallel to the floor./ 15 random radiographs remeasured by the same examiner after 2 weeks.
Hassan (2005) (69)	29 M, 33 F	9- 12 y	White (western Saudi Arabia)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB, FH/NPg ANB, NAPg ANS-Me; FH/MP (Down), SN/MP (Down), FH/SGn	No significant differences between Saudis children M and F. Compared to Saudis adults, 9- 12 y Saudis children had a significantly greater NAPg, smaller ANS-Me; ANB angle in children was insignificantly greater than in adults.	NA/ A second tracing was prepared for every 10 tracings.
Hamdan & Rock (2001) (70)	33 M, 32 F	14–17 y (15.5± 0.5)	White (Amman, Jordan)	Maxilla Mandible Mx-Md	SNA SNB ANB	Compared to British adult, 15.5 y Jordanian had similar SNA, SNB, ANB; and smaller PP/MP.	Lateral cephalograms taken in natural head position./

				Vertical parameters	PP/MP		25 films digitized twice at 3–4 weeks apart.
Gleis et al. (1990) (71)	18 M, 22 F	mean: 13.5 y M: 12- 16.5 y F: 11- 14 y	White (Israel)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB, Pg-NB, FH/NPg ANB, NAPg SN/GoGn, FH/MP (Down), FH/PP, FH/SGn	No significant differences between 13.5 y Israeli M and F were noted, except for FH/SGn: M> F. Compared to white North American adult, 13,5 y Israeli has a convex profile, a retrusive mandible, a steep mandibular plane (increased NAPg, ANB, SN/GoGn; decreased SNB).	Radiographs taken in standard position./ Tracings completed and verified by two orthodontists, independently.
Aleksic et al. (2012) (72)	36 M, 42 F	mean: 9± 0.35 y M: 9± 0,17 y F: 9± 0,43 y	White (Pančevo and Belgrade, Serbia)	Cranial base Maxilla Mandible Vertical parameters	S-N SNA SNB N-Me, S-Goi, S-Goi/N-Me; SN/PP, SN/MP (Down), ArGoiMe [5]	9 y Serbian M had larger S-N, N-Me, SN/MP; smaller S-Goi/N-Me, SNA, SNB than F. No significant differences between 2 sexes were noted in S-Goi, SN/PP, ArGoiMe.	All radiographs taken with Frankfort plane parallel to the floor./ Errors of measurements calculated based on Cronbah alpha coefficient.
Huang et al. (1998) (73)	White American: 32 M, 35 F African American: 39 M, 30 F	Young: 6- 12 y Old: 12- 18 y	White (Alabama, USA) Black (Alabama, USA)	Maxilla Mandible Mx-Md	SNA SNB ANB, Wits	Compared to white children, African American children had greater SNA, SNB, ANB, and similar Wits. No significant differences were found between M and F.	NA./ Intra- reliability allowable at 0.5°, 0.4 mm for angular and linear measurements.
Alexander & Hitchcock (1978) (74)	50 children	8 y-13 y (10.18± 1.38)	Black (Alabama, USA)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB, SNPg ANB SN/MP (Down), NSGn	10 y Negro American children had greater SNA, ANB, SN/MP than 10 y white Southern Americans; and similar SNB, SNPg, NSGn.	NA/ 50 films traced independently by two reviewers.
Barter et al. (1995) (75)	50 M, 54 F	M: 14 y 1m (11y 4m- 16y 1m) F: 13 y 6m (11 y 4m- 16 y 9m)	Black - Sotho-Tswana peoples (central district of Botswana)	Cranial base Maxilla Mandible Mx-Md Vertical parameters	S-N SNA, Co-A SNB, FH/NPg, Co-Gn, Go-Gn ANB, Wits N-ANS, ANS-Me; SN/PP, SN/GoGn, ArGoGn, NSGn	14 y South-African M had smaller SN/PP than F.	Each subject kept their teeth in centric occlusion, for each exposure./ 10% of radiographs, chosen at random, were checked and measured by a second operator.
Ajayi (2005) (76)	66 M, 34 F	11- 13 y (12.6± 0.6 y)	Black - Igbo ethnic group (Enugu, Nigeria)	Maxilla Mandible Mx-Md	SNA SNB ANB	No significant differences in SNA, SNB, ANB, FH/MP between 11-13 y Nigerian Igbo M and F.	Subject's head oriented to FH plane./ 25 randomly selected

				Vertical parameters	FH/MP (Go-Me)		radiographs retraced 1 month later.
Folaranmi & Isiekwe (2013) (77)	40 M, 60 F	12.2 y (12- 15 y)	Black (Benin City, Nigeria)	Vertical parameters	N-ANS, ANS-Me, N-Me, ANS-Me/N-Me	No significant differences in vertical parameters between 12 y Nigerian M and F.	Subject's head oriented to FH plane./ NA.
Beugre et al. (2007) (78)	Ivorians: 26 M, 27 F Senegalese: 25 M/25 F Chadians: 31 M, 31 F	Ivorians: 9.5- 17 y Senegalese: 12- 16 y Chadians: 12- 16 y	Black (Abidjan, Ivory Coast) Black (Dakar, Senegal) Black (Ndjamena, Chad)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB, SNPg ANB, Wits S-Go, N-Me, S-Go/ N-Me; FH/MP, SN/MP (Go-Gn), SN/PP	Sagitally, skeletal measurements were quite similar between Senegalese and Ivorian; Chadian had greater SNA, SNB, SNPg than Ivorian and Senegalese. No significant differences in ANB among 3 African populations. Vertically, Senegalese showed the most significant hyperdivergence in facial height (FH/MP, SN/MP, S-Go, N-Me).	Cephalograms taken in natural head position./ 20 cephalograms randomly selected and retraced by same examiner 2 weeks.
Kapila (1989) (79)	28 M, 28 F	11.30 y (9- 15 y) M: 11.5 y F: 10.85 y	Black – Kikuyu descent (Nairobi, Kenya)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB ANB FH/MP (Go-Gn)	11 y Kikuyu F had larger SNB than M. In compared to black American, Kikuyu had larger FH/MP. In compared to white, Kikuyu had larger SNA, ANB, FH/MP.	NA./ Radiographs traced twice.
Sobreira et al. (2011) (54)	70 Brazilian F, 35 White, 35 Black	8- 10 y (22 at 8 y, 18 at 9 y, 30 at 10 y)	Black (Brazil), White (Brazil)	Vertical parameters	ANS-Me/N-Me, S-Go/N-Me, Ar-Go/S-Go, Ar-Go/ANS-Me	Vertical parameters in Afro-Brazilian F≈ white Brazilian F in 8-10 y children. The facial proportions remained constant from 8- 10 y in both races.	NA/ All tracings performed twice.
de Freitas et al. (2010) (80)	White: 25 M, 25 F Black: 28 M, 28 F	White: 13.17± 1.07 y (11.40- 14.90 y) Black: 13.24±0.56yrs (12.08- 14.33 y)	Black (São Paolo, Brazil), White (São Paolo, Brazil)	Maxilla Mandible Mx-Md Vertical parameters	SNA, A-Nperp SNB, Co-Gn, Pg-Nperp, Pg-NB ANB, NAPg, Wits FH/MP (Go-Me), SN/GoGn	13 y black Brazilian had greater SNA, A-Nperp, SNB, Pg-Nperp, ANB, NAPg; and smaller Co-Gn, Pg-NB, FH/MP, SN/GoGn than white Brazilian. No difference in Wits between black and white Brazilian.	NA/ 30 random cephalograms retraced and re-measured by same examiner after 1 month.
de Freitas et al. (2007) (81)	Group 1: 74 Whites M: 37, F: 37 Group 2: 56 Blacks M: 28, F: 28	White: 13.71± 0.84 y (11.91- 14.91 y)/ Black: 13.86± 0.92 y (12.08- 15.75 y)	Black (São Paolo, Brazil), White (São Paolo, Brazil)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB ANB N-Me, N-ANS', ANS'-Me, N-ANS'/N-Me, ANS'-Me/N-Me, S-Go, S-Ar', Ar'-Go, S-Ar'/S-Go, Ar'-Go/S-Go [2, 4]	14 y black Brazilian had greater SNA, SNB, ANB, ANS'-Me/N-Me; and smaller N-ANS', N-ANS'/N-Me than white Brazilian. Black M had significantly greater S-Go, N-ANS', S-Ar', S-Ar'/S-Go; and smaller Ar'-Go/S-Go than Black F. White M had significantly greater S-Ar', S-Ar'/S-Go and smaller Ar'-Go/S-Go than White F.	NA/ 40 randomly selected cephalograms retraced and remeasured by same examiner.

Janson et al. (2011) (82)	White: 40 (M: 20, F: 20) Afro-Caucasian: 40 (M: 20, F: 20)	White: 13.02 y (11.89± 15.03 y) Afro-Caucasian: 13.02 y (12± 14.30 y)	White (São Paolo, Brazil) Mixed – Black and White (São Paolo, Brazil)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB ANB N-Me, N-ANS', ANS'-Me, S-Go, S-Ar', Ar'-Go [2, 4]	13 y Afro-Caucasian Brazilian had greater SNA, S-Ar'; and smaller N-ANS', Ar'-Go than Caucasian Brazilian; and similar SNB, ANB, ANS'-Me, N-Me, S-Go. Caucasian Brazilian: M≈ F. Afro-Caucasian Brazilian: M> F in SNB, S-Go, S-Ar'; M≈ F in SNA, ANB, N-Me, N-ANS', ANS'-Me, Ar'-Go.	Lateral cephalograms obtained in centric occlusion with lips at rest.
Vieira et al. (2014) (83)	15 M, 15 F	14 y (11.91-16.61 y)	Mixed – White and Asian (Bauru, Brazil)	Vertical parameters	N-Me, N-ANS', ANS'-Me, N-ANS'/N-Me, ANS'-Me/N-Me, S-Go, S-Ar', Ar'-Go, S-Ar'/S-Go, Ar'-Go/S-Go [2, 4]	14 y Japanese-Brazilian M had greater N-Me, ANS'-Me, S-Go, S-Ar' than F.	NA/ 50% of sample retraced by same examiner a month after.
Singh Rathore et al. (2012) (84)	50 M, 50 F	11- 13 y	Asian (Mewar, India)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB ANB SN/MP (GoGn)	11- 13 y Mewari children had greater ANB; and smaller SNB than white adults.	Cephalograms taken in natural head position./ Each landmark and point rechecked.
Anuradha et al. (1991) (85)	30 M, 30 F	4- 5 y	Asian (Punjab, India)	Maxilla Mandible Mx-Md Vertical parameters	SNA SNB ANB SN/ MP (GoGn)	The difference between sexes in 4-5 y North Indian was insignificant. Compared to white adults, Indian children had smaller SNA, SNB; and larger ANB.	NA/ Each measurement repeated a week later.
Singh et al. (2019) (86)	110 M, 110 F	11- 13 y	Asian (Lingayat population, Northern India)	Mandible Mx-Md Vertical parameters	FH-NPg NAPg FH/MP (Down)	The craniofacial form of Lingayat children is similar to Chinese children. 11- 13 y Lingayat M had more convex facial profile (larger NAPg) than the F.	Cephalograms taken in natural head position./ Forty cephalograms retraced by same operator.
Moldez et al. (2006) (87)	78 M, 79 F	Group GI: 7 y; Group GII: 9.5 y; Group GIII: 14 y; Group GIV: 22 y	Asian (Manila, Philippines)	Cranial base Maxilla Mandible Mx-Md Vertical parameters	S-N SNA SNB, Co-Gn, Co-Go, FH/NPg ANB, NAPg N-Me, N-ANS, ANS-Me; FH/PP, SN/FH, SN/PP, SN/MP (Go-Me), FH/SGn	Filipino M> F in S-N, N-Me, N-ANS, Co-Go, Co-Gn at GI, GIII, GIV. Filipino M> F in ANS-Me at GIII, GIV. In GII, no significant differences between sexes were noted for linear measurements. There were no significant differences in angular parameters between sexes in GI, GII, GIII. In GIV, M had larger SNB, SN/FH, and smaller SN/PP, SN/MP.	Cephalograms taken in natural head position./ 10 randomly selected cases retraced and remeasured.

Zhao et al. (2013) (88)	32 Chinese and 32 White (16 M, 16 F in each group)	Chinese: 12 y 11m- 13 y 1 m/ White: 13 y	Asian (Peking, China) Compared to White (Broadbent -Bolton)	Cranial base Maxilla Mandible Mx-Md Vertical parameters	S-N, S-Ba, NSAr SNA, ANS-PNS SNB, SNPg, FH/NPg Go-Pg, Ar-Go ANB, NAPg N-ANS, ANS-Me, N-Me; FH/MP (Go-Gn), SN/MP, PP/MP, FH/SGn	Compared to 13 y White, 13 y Chinese subjects presented a smaller cranial base (smaller S-N, Ar-N), shorter palate (PNS-ANS), shorter mandibular length (smaller Go-Pg), retruded mandible (smaller FH/NPg, SNPg), greater FH/SGn, SN/GoGn, greater NSAr, and more convex profile (NAPg); and similar N-ANS, ANS-Me, N-Me, and Ar-Go. 13 y White: M≈ F. 13 y Chinese: M> F in N-ANS.	NA/ Another investigator verified the anatomic outlines and landmark identification.
Gu et al. (2011) (89)	Southern Chinese: 70 M, 60 F/ Northern Chinese: 50 M, 50 F/ White: 43 M, 43 F	Southern Chinese M: 12.4± 0.6, F: 12.5± 0.4 y/ Northern Chinese M: 12.8± 1.8, F: 12.4± 1.2 y/ White: 12 y	Northern Chinese (Beijing), Southern Chinese (Hong Kong), White (British origin in Hong Kong)/ China	Maxilla Mandible Mx-Md Vertical parameters	A-Nperp, Co-A Pg-Nperp, Co-Gn Mx-Md diff FH/MP (GoMe), ANS-Me	12.5 y White had a greater Co-A than Southern Chinese, but less than Northern Chinese. White had the shortest vertical facial dimension in 3 groups. White and Southern Chinese had similar Pg-Nperp, Co-Gn, ANS-Me, whereas significantly increased Co-Gn, FH/MP, ANS-Me, and decreased Pg-Nperp were found in Northern Chinese.	Cephalograms taken in natural head position./ Cephalograms re-digitised and independently re-measured on 2 separate occasions 2 months apart.
Pan et al. (1996) (53)	25 M, 32 F	12 y	Asian (Shanghai, China)	Maxilla Mandible Vertical parameters	A-Nperp, Co-A Pg-Nperp, Co-Gn ANS-Me	M had greater Co-A, A-Nperp than F. No significant differences between sexes in Co-Gn, Pg-Nperp, ANS-Me.	NA/ NA.
Chang et al. (1993) (49)	Children: 40 M, 40 F Young adult: 40 M, 40 F	11 y 1m- 12 y 8m/ young adult	Asian - Chinese (Taiwan)	Cranial base Maxilla Mandible	S-N, S-Ar, NSAr Co-A Co-Gn Ar-Goi, Goi-Pg [5]	S-N, S-Ar: M> F; significantly increased from 11 y child to young adult. NSAr: M≈ F, remained constant with age. Co-A: M≈ F in 11 y child, M> F in adult; increased significantly with age in either sex. Co-Gn: M> F ($p< 0.05$) in 11 y child, M> F ($p< 0.001$) in young adult; increased significantly with age in either sex. Ar-Goi, Goi-Pg: M≈ F in 11 y child, M> F in young adult; increased significantly with age in both sexes.	NA./ All cephalograms traced by one investigator and checked by another.

Vertical parameters	ATFH, AUFH, ALFH, PTFH, PUFH, PLFH, AUFH/ATFH, ALFH/ATFH, AUFH/ALFH, PUFH/AUFH, PLFH/ALFH, PTFH/ATFH [6]	M> F: in ATFH, ALFH in child & adult; and AUFH, PTFH, PUFH, PLFH only in adult. M< F: in PLFH/ALFH, PTFH/ATFH in child; but became M> F in young adult. M≈ F: in AUFH/ATFH, ALFH/ATFH, AUFH/ALFH, PUFH/AUFH in child& adult. These parameters remained constant during growth. Significant increases of ATFH, ALFH, AUFH, PTFH, PUFH, PLFH, PLFH/ALFH, PTFH/ATFH with age were noted, except for PTFH/ATFH in F.
	SN/FH, SN/PP, FH/PP, SN/MP (Down), FH/MP, PP/MP	M≈ F: in SN/FH, SN/PP, FH/PP in child& adult. These parameters remained constant during growth. M> F: in SN/MP, FH/MP, PP/MP in child; but became M< F in young adult. These parameters decreased significantly only in M.

Table 3b: Summary of characteristics of included cross-sectional studies

Legends:

NA: not available

M: male/ F: female

y: year/ m: month

≈: no significant difference

Mx: maxilla/ Md: mandible/ Mx-Md: maxillomandibular relationship/ Mx-Md diff: maxillomandibular difference

GP: growth period

FH: Frankfort horizontal plane

PP: palatal plane

MP: mandibular plane

1: point Ptm in measurement of maxillary length (A-Ptm), described in Jamison's study (45)

2: point ANS', projection of point ANS on N-Me plane

3: ⊥FH, perpendicular line to Frankfort plane was used as reference plane to measure facial height

4: point Ar', projection of point Ar on S-Go plane

5: point Goi, gonial intersection, intersection of mandibular plane (Down) and tangent of mandibular ramus

6: perpendicular line to palatal plane was used as reference plane to measure facial height

4.3 Risk of bias within studies

The quality appraisal of final selection was performed through a following 10-point grading system, related to clarity and appropriateness of research question or objective (Q1), study population (Q2), selection criteria (Q3), age groups (Q4), sample size (Q5), measurement method (Q6), statistic analysis (Q7), as well as description of validity of cephalometric radiograph (Q8), reliability of cephalometric tracings (Q9), outcome data with exact P value, SD, SE or CI (Q10). The above criteria were applied to all selected articles, which yielded the following scores for each article (Table 4).

Study	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Total score**
Jamison et al. (1982) (45)	1	1	1	1	0	1	1	1	1	1	*9*
Bishara et al. (1984) (2)	1	1	1	1	0	1	1	1	1	1	*9*
Ursi et al. (1993) (3)	1	1	1	1	0	1	1	0	1	1	*8*
el-Batouti et al. (1994) (57)	1	1	1	1	0	1	1	1	1	1	*9*
el-Batouli et al. (1995) (58)	1	1	1	1	0	1	1	1	1	1	*9*
Thilander et al. (2005) (59)	1	1	1	1	0	1	0	1	1	1	*8*
Stahl de Castrillon et al. (2013) (60)	1	1	1	1	0	1	1	1	1	1	*9*
Alió-Sanz et al. (2011) (4)	1	1	1	1	0	1	1	0	1	1	*8*
Hamamci et al. (2013) (61)	1	1	1	1	0	1	1	1	0	1	*8*
Jiménez et al. (2020) **(62)**	1	1	1	1	0	1	1	0	1	1	*8*
Chuang (2020) (63)	1	1	1	1	0	1	1	0	1	1	*8*
Bishara & Fernandez (1985) (11)	1	1	1	1	0	1	1	1	1	1	*9*
Bishara et al. (1990) (12)	1	1	1	1	0	1	1	0	1	1	*8*
El-Batran et al. (2008) (64)	1	1	1	1	0	1	1	0	1	1	*8*
Thilander et al. (1982) (65)	1	1	1	1	0	1	1	0	0	1	*7*
Humerfelt (1970) (66)	1	1	1	1	0	1	1	0	1	1	*8*
Obloj et al. (2008) (67)	1	1	1	1	0	1	1	1	1	1	*9*
Kilic et al. (2010) (68)	1	1	1	1	0	1	1	1	1	1	*9*
Hassan (2005) (69)	1	1	1	1	0	1	1	0	1	1	*8*
Hamdan & Rock (2001) (70)	1	1	1	1	0	1	1	1	1	1	*9*
Gleis et al. (1990) (71)	1	1	1	1	0	1	1	1	1	1	*9*
Aleksic et al. (2012) (72)	1	1	1	1	0	1	1	1	1	1	*9*
Huang et al. (1998) (73)	1	1	1	0	0	1	1	0	1	1	*7*
Alexander & Hitchcock (1978) (74)	1	0	1	1	0	1	1	0	1	1	*7*
Barter et al. (1995) (75)	1	1	1	1	0	1	1	1	1	1	*9*
Ajayi (2005) (76)	1	1	1	1	0	1	1	1	1	1	*9*

Folaranmi & Isiekwe, 2013 (77)	1	1	1	1	0	1	1	1	0	1	*8*
Beugre et al. (2007) (78)	1	1	1	1	0	1	1	1	1	1	*9*
Kapila (1989) (79)	1	1	1	1	0	1	1	0	1	1	*8*
Sobreira et al. (2011) (54)	1	1	1	1	0	1	1	0	1	1	*8*
de Freitas et al. (2010) (80)	1	1	1	1	0	1	1	0	1	1	*8*
de Freitas et al. (2007) (81)	1	1	1	1	0	1	1	1	1	1	*9*
Janson et al. (2011) (82)	1	1	1	1	0	1	1	1	1	1	*9*
Vieira et al. (2014) (83)	1	1	1	1	0	1	1	0	1	1	*8*
Singh Rathore et al. (2012) (84)	1	1	1	1	0	1	1	1	1	1	*9*
Anuradha et al. (1991) (85)	1	1	1	1	0	1	1	0	1	1	*8*
Singh et al. (2019) (86)	1	1	1	1	1	1	1	1	1	1	*10*
Moldez et al. (2006) (87)	1	1	1	1	0	1	1	1	1	1	*9*
Zhao et al. (2013) (88)	1	1	1	1	0	1	1	0	1	1	*8*
Gu et al. (2011) (89)	1	1	1	1	0	1	1	1	1	1	*9*
Pan et al. (1996) (53)	1	1	1	1	0	1	1	0	0	1	*7*
Chang et al. (1993) (49)	1	1	1	1	0	1	1	0	1	1	*8*

Table 4: Results of quality appraisal for each study in final selection

Based on the scores for each article from the table, it can be seen that the quality of the included articles ranges from pretty good to excellent. However, all included studies had a similar weakness, which was not to justify or calculate sample size, except for the article conducted by Singh et al. (2019) (86). It is the only study that has achieved the maximum score from the quality appraisal; however, only a small number of cephalometric parameters were measured in the study.

4.4 Synthesis of results:

Final selection comprises 13 longitudinal and 31 cross-sectional aticles. Within the longitudinal articles, normative data are analyzed in terms of differences between age groups and sexes; the only exceptions are el-Batouti et al. (1995) (58), which compares cephalometric measurements between different populations (i.e., individuals from Norway and Iowa, USA) and two studies solely reporting normative data without hypothesis testing. All longitudinal studies investigate white populations, except for one study investigating longitudinal changes in an Asian population and one in a mixed-race population. Within the cross-sectional studies, the aim of the normative data is to provide information on differences between males and females as well as among races. However, there are three articles in the cross-sectional group, including Moldez et al. (2006) (87), Chang et al. (1993) (49) and Sobreira et al. (2011) (54), which describe different craniofacial characteristics in various age groups as well as between sexes or among races. Therefore, there are a total of 13 articles, including 10 longitudinal and 3 cross-sectional, providing information about the craniofacial structural changes during growth, as well as sexual dimorphism in different age groups. Based on those data, the timing of growth of skeletal structures in each age group can be interpreted for either males or females. Furthermore, there are a total of 32 articles, including 1 longitudinal and 31 cross-sectional studies, showing differences in normative cephalometric data in various populations, and/ or differences between males and females in a specific population.

For further knowledge aggregation, the cephalometric measurements are grouped into five categories: cranial base, maxilla, mandible, relationship between maxilla and mandible, and vertical parameters. Not all studies report all cephalometric measurements.

4.4.1 Cranial base

The parameters used to assess cranial base structures from lateral cephalometric radiographs consist of length of anterior cranial base (S-N), length of posterior cranial base (S-Ba or S-Ar), total length of cranial base (N-Ba), and cranial base angle (NSBa or NSAr).

4.4.1.1 Changes during growth

In terms of sex-related differences in cranial base length, most articles showed a longer S-N in males than females (3,60,62,87), except for one article (63) reporting an insignificant difference in S-N between the sexes. Stahl de Castrillon et al. (60) recorded a longer S-N in males at 6, 16, and 17 years old throughout the period of 6-17 years. Ursi et al. (3) found that S-N in males was larger than in females at all ages, while Jiménez et al. (62) only found a significant difference between males and females from the age of 16 onwards. It seems that females have a constant acceleration of S-N from 8 to 16 years of age, followed by a decrease in growth rate, while males have an acceleration of growth between 14 and 16 years of age, which decreases after 20 years of age (62). In support, Thilander et al. (59) found an increase in S-N by 11.3 mm in females and 12.9 mm in males between 5- 31 years, and by 1- 1.5 mm between adolescence and young adulthood; one-third of the total increase was noted between 13-16 years, especially in males. In other studies, a significant increase in S-N was also observed in both sexes from 8-12 years (63), from 6-18 years (62) and from 11 years old to young adult (49). Ursi et al. (3) and Stahl de Castrillon et al. (60) showed trends in growth of S-N from childhood to adulthood; however, increases in S-N with growth were not statistically tested.

Similar to the anterior cranial base, the posterior cranial base (S-Ba) grows in length in both males and females from 6-17 years (without statistical tests) (60); and from 8-12 years (with statistical tests) (63). Regarding sexual dimorphism, S-Ba in males was greater than in females at 6 years (60), and from the age of 16 onwards (3). In contrast, no significant differences in S-Ba between males and females were observed from 8- 12 years (63).

Means of cranial base angle (NSBa) were not significantly different between sexes (3,57,60,63). Thilander et al. (59) observed that NSBa decreased slightly during period of growth (no statistical analysis), while Stahl de Castrillon et al. (60) and Chuang (63) showed the NSBa remained constant with age. There is a consensus that NSAr was stable in both sexes from the primary until the adult period (49,59,60).

4.4.1.2 Intra-/inter-racial comparisons

Nine studies compared cranial base parameters in different populations to mainly white populations. Similar to the longitudinal studies, the S-N length is typically greater in boys than girls. Greater S-N was observed in 8.5-year-old Iowan and Norwegian boys (12), 11-year-old Norwegian boys (66), 10-year-old Polish boys (67), 9-year-old Serbian boys (72), Filipino boys (7 and 14 years) (87), and 11-year-old Chinese boys (49) than girls. However, a number of studies showed an insignificant difference in S-N between sexes in 14-year-old South-African (75), 9.5-year-old Filipino (87), and 13-year-old Chinese children (88).

Regarding the length of posterior cranial base, S-Ba was greater in 8.5-year-old Iowan boys than girls (12); however, no sexual dimorphism was reported in 8.5-year-old Norwegian (12) and 13-year-old Chinese children (88).

No significant differences between sexes for angular measurements (NSAr, NSBa) were observed in 8.5-year-old Iowan and Norwegian (12) and 11-year-old Norwegian children (66). Between sexes, Obloj et al. (67) also showed a similar NSBa in Polish children at 10 years; while Zhao et al. (88) and Chang et al. (49) noted a similar NSAr in 13-year-old and 10-year-old Chinese children, respectively.

Comparing cranial base parameters in different populations, 11-year-old Norwegian children had smaller S-N than Swedish children but similar NSAr, NSBa, and S-Ar (65). In girls, 13-year-old Egyptian girls had longer N-Ba and S-Ba than Iowan girls but similar NSAr, NSBa, and S-N (12). In boys, 13-year-old Egyptian boys had longer S-N than Iowan boys with similar NSAr, NSBa, N-Ba, and S-Ba (12). 13-year-old Chinese subjects presented a shorter cranial base (S-N, Ar-N) and greater NSAr than 13-year-old Whites (88).

In summary, the cranial base lengthens during growth from childhood to adulthood, while the cranial base angle remains constant. The anterior cranial base tends to be longer in males than in females, especially at the age of 16 onwards, while no sexual dimorphism is seen in the cranial base angle. Chinese children appear to present a shorter cranial base and greater cranial base angle than white children.

4.4.2 Maxilla

The maxillary position and length can be assessed with lateral cephalometry. SNA and distance from point A to Nasion perpendicular (A-Nperp) are measurements describing the position of the maxilla relative to the cranial base. To describe maxillary size and midfacial length, three measures are commonly used: A-Ptm, A-PNS (maxillary length), ANS-PNS (palate length), and Co-A (effective midfacial length).

4.4.2.1 Changes during growth

The position of the maxilla relative to cranial base (SNA, A-Nperp) was found to be insignificantly different between sexes in 4 articles (3,4,63,87). Ursi et al. (3), measuring white Americans at 6, 9, 12, 14, 16, 18 years of age, showed insignificant differences in SNA and A-Nperp between males and females. Similarly, Alió-Sanz et al. (4) revealed insignificant differences in the mean value of SNA between males and females from 8-18 years of age. In Asian populations, Chuang (63) and Moldez et al. (87) measuring SNA in Taiwanese children at 8, 10, and 12 years, and in Filipinos at the age of 7, 9.5, 14, and 22 years, respectively, also noted that no sexual dimorphism was observed. However, el-Batouti et al. (57), comparing value of SNA in white Norwegians between the sexes at the age of 6, 9, 12, 15, 18 years, concluded males had insignificant greater SNA at 6 years of age, but significantly larger SNA at 9, 12, 15, 18 years.

Most articles showed an augmentation of SNA in males is greater than in females during childhood and adolescence (2,45,57,60), while Hamamci et al. (61) stated the opposite trend. Jamison et al. (45) reported a significant increase of SNA by 1.7^0 in males between 8-17 years, but insignificant changes in females (by only 0.4^0). Similarly, Stahl de Castrillon et al. (60) observed that SNA and A-Nperp increased by 1.1^0 and 0.7 mm, respectively, from 6-17 years in males, while remained constant in females (no statistical test for age-related changes). In support, Bishara et al. (2) revealed that the greatest increase of SNA by 1.4° occurred in males from 10- 15 years; while the total change of SNA in females was solely 0.4° from childhood to adulthood. Additionally, el-Batouli et al. (57) observed SNA increased more in males than females from 6-18 years; the greatest increase was between 9- 15 years of age. In contrast, Hamamci et al. (61) noticed that SNA, A-Nperp significantly increased by 2.28^0 and 1.25 mm, respectively, in females and 1.07^0 and 1 mm, respectively, in males between 9-18 years. The significant increases in SNA were observed from 9-14 years in females and from 14-18 years in males. A-Nperp significantly increased from 9-14 years and from 14-18 years in females, but solely from 9-14 years in males. Moreover, there are 3 articles noting insignificant increases in SNA with age (4,59,63). Thilander et al. (59) observed that SNA remained constant from childhood to adulthood. Chuang (63), assessing growth in the period of 8-12 years of age, observed that the changes of SNA were not considerable in either boys or girls, with only an insignificant increase from 10-12 in boys being noticed. Alió-Sanz et al. (4) also concluded that SNA did not significantly increase from pre-pubescent to post-pubescent in either sex; but the advance of point A was significantly greater in females.

Linear midfacial dimensions were reported to be greater in males than females in most articles. Alió -Sanz et al. (4) found greater ANS-PNS and Co-A in males than females between 8-18 years of age. Similarly, Ursi et al. (3) observed that males had insignificantly greater Co-A than females at the age of 6 years, and significantly longer Co-A at 9, 14, 16, and 18 years. Stahl de Castrillon et al. (60) showed a greater Co-A at 6, 16, and 17 years as well as a longer ANS-PNS at 16 years in males than females during the period of 6-17 years; however, Chuang (63) observed a similar ANS-PNS between Taiwanese males and females from 8- 12 years. Chang et al. (49) noticed that Co-A was similar between sexes at 11 years of age, but significantly greater in male adult than female adult. In support, Jiménez et al. (62) noted that Co-A was similar between males and females from 6-14 years. He observed a constant growth of Co-A from 6- 14 years in both sexes; then, males had a pubertal peak between 14- 16 years, while growth decreased after 14 years in females, which resulted in a greater Co-A in males compared to females from the age of 16 onwards. An increase of the effective midfacial length (Co-A) from childhood to adulthood was also reported in 3 other articles (4,61,62). Hamamci et al. (61) showed that Co-A increased significantly in both females and males between 9 and 14 and from 14 and 18 years.

Maxillary length significantly increased with age (2,4,45,63). Chuang (63) showed a significant increase of palate length (ANS-PNS) from 8- 12 years in both sexes. Similarly, Alió-Sanz et al. (4) observed that the length of ANS-PNS increased with age, and the most increase occurred between the age of 8- 11 years; moreover, during growth, point ANS and PNS moved downward 0.71 ± 0.47 and 0.84 ± 0.61 mm, respectively, for females, and 1.21 ± 0.69 and 1.18 ± 0.51 mm, respectively, for males. In addition, two studies (2,45) reported a significant increase of maxillary length from childhood to adulthood, where maxillary length increased the most from 10- 15 years in males and from 5- 10 years in females (2). Similarly, Chuang (63) demonstrated a significant increase of ANS-PNS from 8-12 years in both sexes.

4.4.2.2 Intra-/inter-racial comparisons

In terms of comparisons between boys and girls in different populations, four studies investigated differences in maxilla. In 10-year-old Polish children, girls had greater SNA and A-Nperp than boys, which means the maxilla was more protruded in girls (67). Similar to the results in longitudinal studies, boys generally have greater maxillary length than girls: in 11-year-old Norwegian children, boys had longer ANS-PNS than girls (66); in 14-year-old Turkish children, males had greater Co-A than females (68). According to Pan et al. (53), 12-year-old Chinese males had greater Co-A and A-Nperp than females.

Within white populations, there are differences in maxillary parameters. El-Batouti et al. (58) observed Norwegian children to have a significantly larger SNA than American children and shorter palate length (ANS-PNS) than Swedish children (65). Compared to white Americans, Turkish children had a shorter Co-A and more retruded maxilla (smaller A-Nperp) (68).

Compared to white Americans, African Americans and Kikuyu (Kenyan) children had greater mean value of SNA (73,74,79). Similarly, de Freitas et al. (81) and Janson et al. (82) showed that 13-year-old black Brazilians and Afro-Caucasian Brazilians, respectively, had greater

SNA than white Brazilians. De Freitas et al. (81) also observed that black Brazilian children presented greater A-Nperp than white Brazilian children.

Two studies explored maxillary values in Asian populations. Maxilla in Northern Indian children at 4-5 years of age appears to be retruded (smaller SNA) in comparison to white American adults (85). Compared to 13-year-old white Americans, Chinese children presented a shorter palate (PNS-ANS) (88).

In summary, the length of the maxilla increases during childhood and adolescence. The maxilla moves forward and downward with respect to cranial base with increased SNA, A-Nperp, especially in males, and downward movement of ANS-PNS during growth. The greatest periods of growth seem to correspond with puberty; thus, growth of the maxilla appears to reach a peak earlier in females than males. There is a consensus albeit from a limited number of studies that black populations have a more protrusive maxilla (greater SNA, A-Nperp) than white populations; however, more research, especially longitudinal studies on diverse populations, are warranted. Most articles showed insignificant difference in SNA between males and females, while greater Co-A was noted in males. Although there is still controversy among studies about the difference in the extent of maxillary growth in the two sexes, greater augmentation of SNA in males was agreed by most studies.

4.4.3 Mandible

To assess the position of mandible relative to the cranial base, several parameters have been defined such as SNB, SNPg, SNGn, SNMe, FH/NPg, and the distance from point pogonion to nasion perpendicular (Pg-Nperp). Of these, SNB, SNPg and Pg-Nperp are commonly used. A number of other measures are commonly utilized to evaluate size of the mandible: Ar-Pg, Ar-Gn, Go-Me, Go-Gn (mandibular length), Co-Go (mandibular ramus height), and Co-Gn (effective mandibular length).

4.4.3.1 Changes during growth

Sex-related differences in position of the mandible are inconclusive. Two articles found more protrusive mandible in females than males (3,63). Specifically, Ursi et al. (3) observed trends toward higher values of SNB, Pg-Nperp in females at the age of 6, 9, 12, 14, 16, and 18 years, which were only significant at 14 years for SNB. Chuang (63) found that SNB in Taiwanese females was significantly greater than males from 8-12 years old. In contrast, Moldez et al. (87) observed males and females at the age of 7, 9.5, 14, and 22 years and only found significant differences at 22 years of age, when females have significantly smaller SNB than males. Additionally, Stahl de Castrillon et al. (60) concluded that females had more retrusive mandible, but only significantly at the age of 17 years.

Significant anterior growth of the mandible with respect to the anterior cranial base was observed in most articles (2,57,59–61). In more detail, Thilander et al. (59) stated that SNB and SNPg increased continuously from childhood to adulthood; the mean of SNB increased from 77^0 to 81^0 between 5- 31 years. Significant increases in SNB and Pg-Nperp in both sexes from 9 to 14 years and from 14 to 18 years of age were also noticed by Hamamci et al. (61); SNB and Pg-Nperp increased by 3.2^0 and 6.03 mm for females, by 2.24^0 and 4.71 mm for males from 9- 18 years of age. Stahl de Castrillon et al. (60) showed that SNB, SNPg and Pg-Nperp became larger with age from the age of 6 to 17 years in both sexes; however, no statistical tests were performed. Similarly, el-Batouti et al. (57) concluded that SNB increased in both males and females from the age of 6 to 18 years (no statistics performed); the increase in males was greater than females. Bishara et al. (2) noted that mandible moved forward relative to cranial base from childhood to adulthood (SNB increased by 3.6^0 in males and 1.8^0 in females); the difference of increase in SNB, SNPog in 3 growth periods (5- 10, 10- 15, 15- 25.5 years of age) was not significant in males, whereas the smallest change from 15- 25.5 years was observed in females. However, there was only one article conducted by Chuang (63) that reported an insignificant increase in SNB, SNMe, and SNGn throughout the period of evaluation from 8- 12 years of age in both sexes.

Mandibular length Ar-Gn was found to be greater in males at the age of 6 and from 15-17 years (60). Males had significantly larger Ar-Gn at 6, 15, 16, and 17 years; Go-Me at 15 and 17 years of age (63); however, Chuang (63) showed that Ar-Gn in females was greater than in males at the age of 12 years.

The length of the mandible (Ar-Pg) increased from childhood until young adulthood and more in males than females; a growth acceleration was recorded between 13- 16 years in males (59); specifically, from 5- 31 years of age, the total increase of Ar-Pg was 27.9 mm in females and 33.1 mm in males. Chuang (63), conducting research on children between 8 and 12 years old, concluded that Go-Gn and Ar-Gn increased significantly from 8-10 and 10-12 years; while Ar-Go considerably lengthened from 10-12 years. Bishara et al. (2) compared mandibular length (Ar-Pg) during 3 growth periods: GP I (5-10 years), GP II (10-15 years) and GP III (15-25.5). Ar-Pg increased the most in GP II in males; however, substantial growth also occurred during the other growth periods. In males, the increase of Ar-Pg in GP III accounted for 26% of the total change (by 8.4 mm), which was the least compared with that in GP I, GP II. In females, the changes in the three growth periods were significantly different; Ar-Pg increased the most in GP I (by 10 mm) and the least in GP III (by 2.2 mm).

Only two studies measured mandibular height Co-Go, with conflicting results. Filipino males had significantly greater Co-Go at 7, 14, and 22 years of age than females (87). However, Stahl de Castrillon et al. (60) only found a larger mandibular ramus height Co-Go in males at 17 years throughout the period of evaluation from 6- 17 years of age.

Four studies measured effective mandibular length Co-Gn, with some conflicting results. In two studies, males were observed to have a longer Co-Gn than females from the age of 16 onwards (3,62). Jiménez et al. (62) explained that growth of Co-Gn plateaued from 8 to 14 years of age; males then had a pubertal peak in Co-Gn between 14 and 16 years of age, while growth velocity in females decreased after 14 years. Meanwhile, Hamamci et al. (61) showed significant increase of Co-Gn in both sexes from 9-14 and 14-18 years of age. Filipino males had significantly greater Co-Gn at 7, 14, and 22 years of age than females (87).

4.4.3.2 Intra-/inter-racial comparisons

Sexual dimorphism in various races was mentioned in eight articles. Sex-related differences in mandibular position varied. There were no sex-related differences in mandibular position relative to cranial base in 4-5 year old North Indian (SNB) (85), 8.5-year-old Egyptian (SNB) (64) and 11-year-old Norwegian children (SNB, SNPg) (66). However, greater mandibular protrusion was observed in females in 11-year-old Kenyan (SNB) (79) and 10-year-old Polish children (Pg-Nperp) (67). In contrast, Aleksic et al. (72) observed that 9-year-old Serbian boys had larger SNB than girls. Regarding effective mandibular length, Kilic et al. (68) noted that 14-year-old Turkish males had greater Co-Gn than Turkish females, which is similar to Moldez's study (87). Larger mandibular size (Ar-Goi, Goi-Pg) in males than females was noticed in 11-year-old Norwegian by Humerfelt (66).

Within white populations, Norwegian group had a relatively greater mandibular protrusion than the Iowan group (SNB, SNPog, FH/NPg) (58). No significant differences in mandibular position (SNB, SNPog, FH/NPg) and size (Ar-Goi, Goi-Pg) between 11-year-old Norwegian and 11-year-old Swedish children were found (65). According to Kilic et al. (68), 14-year-old Turkish girls had significantly shorter Co-Gn than 14-year-old white American girls; and 14-year-old Turkish had a more retruded mandible (smaller Pg-Nperp) than white adults. No significant differences between 15.5-year-old Jordanian and British adult were found for SNB (70). In comparison to white North American adults, 13.5-year-old Israeli children had a retrusive mandible (smaller SNB) (71). No significant differences between 13-year-old North Mexican and Iowan boys were found, while 13-year-old North Mexican girls had greater SNB and SNPog than Iowan girls (11).

In North American populations, one study found African American children to have greater mean values of SNB than white American children (73), while Alexander & Hitchcock (74) did not find any significant differences between 10-year-old African Americans and 10-year-old white Americans in SNB and SNPg. Three articles published in Brazil described the similarities and differences among races in this country. Specifically, 13-year-old black Brazilians had a more protruded mandible (SNB, Pg-Nperp) (80) and a smaller effective mandibular length (Co-Gn) than 13-year-old white Brazilians; and 14-year-old black Brazilians had greater SNB than 14-year-old white Brazilians (81). Another study compared mixed-race 13-year-old Afro-Caucasian Brazilians to Caucasian Brazilians and found not significant difference in SNB (82).

There are four articles comparing white and Asian populations, in which two are Chinese and two are Indian populations. In comparison to 13-year-old white subjects, 13-year-old Chinese presented a shorter mandibular body length (Go-Pg) and retruded mandible (FH/NPg, SNPg) (88). Additionally, 12-year-old white and Southern Chinese had similar Co-Gn, Pg-Nperp, whereas significantly increased Co-Gn and decreased Pg-Nperp were observed in Northern Chinese (89). A retruded mandible (smaller SNB) was observed in 11-13 and 4-5 years old North Indian children (84,85) compared to white adults.

In summary, many studies agree that anterior growth of the mandible with respect to cranial base (increased SNB, SNPg, Pg-Nperp) occurs throughout childhood and adolescence. Similarly, there is consensus that the mandibular length increases significantly from childhood to young adulthood. Males present a significantly greater increase of mandibular length in comparison to females at middle and late adolescence, resulting in a significantly longer mandible in males at that age. From these studies, sexual dimorphism is not conclusive in young children. It appears that Asian populations present a more retrusive mandible (decreased SNB, SNPg, FH/NPg) than white subjects. Differences in mandibular position between males and females, as well as between black and white populations are conflicting among studies.

4.4.4 Maxillomandibular relationship

Relationship between maxilla and mandible is assessed through ANB, NAPg (facial convexity), AoBo (Wits appraisal), and maxillomandibular difference (Mx-Md difference) (Co-Gn minus Co-A).

4.4.4.1 Changes during growth

A number of articles observed that parameters assessing the maxillomandibular relationship were not significantly different between males and females from childhood to adulthood (60,87). However, one article by Chuang (63) noted that ANB and NAPg were significantly larger in boys at 12 years, and insignificantly different between boys and girls at 8 and 10 years. These differences at 12 years may result from earlier growth of the mandible in girls.

There is a consensus among included longitudinal studies that ANB decreased during growth (2,45,59–61,63); and facial convexity (NAPg) became straighter in adult from slight convexity in childhood (2,45,59,63). In support, Hamamci et al. (61) revealed a significant decrease of ANB and significant increase of maxillo-mandibular difference from 9-14 years and from 14-18 years in both sexes (ANB decreased by 0.92^0 in females and 1.35^0 in males from 9- 18 years of age). According to Bishara et al. (2), for males, a decrease in ANB and NAPg occurred in either growth period I (5-10 years), growth period II (10-15 years), or growth period III (15-25.5 years). The decrease for males was the least in growth period II, and more than one third of the total change of ANB and NAPg happened in growth period III; for females, ANB, NAPg only decreased in growth period I and II. Jamison et al. (45) noticed an insignificant decrease of ANB by 0.6° for males and 1° for females as well as an insignificant decrease of NAPg by 3.8° for males and 3.6° for females from 8-17 years. These decreases in ANB and NAPg indicate a relatively increased prominence of the mandibular base with respect to the maxillary base. He also noted that changes in ANB and NAPg for males and females were not significantly different. Similarly, Thilander et al. (59) showed trends towards a decrease in ANB and NAPg from childhood to adulthood; however, it was not statistically tested. Specifically, ANB decreased from 5^0 in young children to 2^0 in 16-year-old individuals, to 1.7^0 in female adults and 1.3^0 in male adults. Wits appraisal value was reported to be constant from 6 to 17 years old in both sexes (60).

4.4.4.2 Intra-/inter-racial comparisons

Cross-sectional studies comparing the maxillomandibular relationship in different specific age groups showed no significant differences in ANB between males and females in 11 articles on white, black and Asian populations. In more detail, no significant difference in ANB between males and females was observed in 13-year-old children from North Mexico and Iowa (11), 8.5-year-old Egyptian children (64), 11-year-old Norwegian (66), 10-year-old Polish (67), 14-year-old Turkish (68), 13.5-year-old Israeli children (71), white and African American children from Alabama (73), 14-year-old South-African children (75), 13-year-old Nigerian Igbo children (76), 11-year-old Kikuyu children (Kenyan), 4-5 year old North Indian (85), and Filipino children at 7, 9.5, 14 and 22 years of age (87).

With regard to facial convexity (NAPg), most studies revealed insignificant differences between white male and female children from 8.5 to 14 years (11,64–68) as well as Filipinos from childhood to adulthood (87). However, there was one exception from Singh et al. (86) concluding that 11-13 year-old Lingayat (Indian) boys had a more convex facial profile than the girls.

The difference in Wits appraisal was also insignificant between sexes in white populations, including 13-year-old North Mexican, 13-year-old Iowan (11), and 10-year-old Polish children (67).

There was only one article describing the sexual distinction in Mx-Md difference (68). No significant difference between 14-year-old Turkish males and females was observed (68).

Comparing Mx-Md difference among races showed either similarities or differences. Within white population, no significant differences in maxillomandibular relationship were observed between 13-year-old North Mexican and Iowan populations (11), between 13-year-old Egyptian and Iowan boys (12), between 11-year-old Norwegian and 11-year-old Swedish children (65), between 15.5-year-old Jordanian children and British adults (70), and between 14-year-old Turkish and 14-year-old white American children (68). However, 13-year-old Egyptian girls had significantly greater facial convexity (NAPg) and Wits appraisal (AoBo) than 13-year-old Iowan girls (12). In addition, 13.5-year-old Israeli presented a more convex profile with increased NAPg and ANB when compared to white North American adults (71).

African Americans had greater ANB and similar AoBo, when compared to white Americans (73). Similarly, two studies (74,79) showed greater value of ANB in 10-year-old African American children and in 11-year-old Kenyan, respectively, than white southern American children. Within African populations, no significant difference in ANB in children among three African populations, including Ivorians, Senegalese, Chadians was observed (78). Two articles about Brazilian populations showed that in 13-year-old and 14-year-old children, black Brazilians had greater ANB and NAPg than white Brazilians (80,81). However, no significant differences in Wits appraisal between 13-year-old black and white Brazilians (80) and between African American and white American children (73) were found.

Comparing to Asian populations, white adults had smaller ANB than North Indian children at the age of 11-13 years (84) and 4-5 years (85). Similarly, 13-year-old Chinese had more convex profile (NAPg) than 13-year-old white Americans (88); 12.5-year-old Chinese had greater Mx-Md difference than 12.5-year-old white Americans (89).

In short, a straighter profile emerges with growth, characterized by decreased ANB and NAPg with age, while Wits appraisal remains stable throughout the period of growth. There are insignificant differences in ANB, NAPg, or Wits appraisal between males and females in any races. It seems that white subjects have straighter profile (smaller ANB, NAPg) when compared to Asians and Africans.

4.4.5 Vertical parameters

Cephalometric radiographs have been used to assess facial height as well as facial divergence through linear vertical measurements, the ratio between linear vertical measurements and angular vertical measurements.

Linear vertical parameters comprise anterior total facial height (ATFH, N-Me), anterior upper facial height (AUFH, N-ANS), anterior lower facial height (ALFH, ANS-Me), posterior total facial height (PTFH, S-Go), posterior upper facial height (PUFH, S-Ar), posterior lower facial height (PLFH, Ar-Go).

The ratio between linear vertical parameters includes the ratio of anterior upper facial height and anterior total facial height (AUFH/ATFH, N-ANS/N-Me), the ratio of anterior lower facial height and anterior total facial height (ALFH/ATFH, ANS-Me/N-Me), the ratio of posterior upper facial height and posterior total facial height (PUFH/PTFH, S-Ar/S-Go), the ratio of posterior lower facial height and posterior total facial height (PLFH/PTFH, Ar-Go/S-Go), the ratio of posterior total facial height and anterior total facial height (PTFH/ATFH, S-Go/N-Me), the ratio of posterior upper facial height and anterior upper facial height (PUFH/AUFH, S-Ar/N-ANS), the ratio of posterior lower facial height and anterior lower facial height (PLFH/ALFH, Ar-Go/ANS-Me).

In a number of studies, instead of directly measuring the distance between 2 reference points, N-Me was used as a reference plane for vertical measurement; point ANS or/ and Ar were replaced by point ANS' or/ and Ar', respectively (2,11,12,81–83). ANS' and Ar' are projection of ANS and Ar, respectively, on N-Me plane. Moreover, in the final selected articles, there is one study using the line perpendicular to Frankfort plane (57); one study using the line perpendicular to ANS-PNS (49) as reference planes for measuring vertical dimensions; and one study using point Gn, instead of point Me, to measure anterior facial height (64).

Angular vertical parameters consist of angles between reference planes (SN/FH, SN/PP, SN/MP, FH/PP, FH/MP, PP/MP) and other angles including NSGn, FH/SGn, NBa/PtmGn, and gonial angle. There are three variations of mandibular plane presented in the included studies, including Go-Gn (Steiner) (43), Go-Me, and a line at the lower border of the mandible tangent to gonial angle and point menton (Down) (44). Furthermore, point Go was replaced by Goi (gonial intersection) in several studies (49,59,64–66,72). Inconsistency of landmarks and reference planes among studies can be a potential source of risk of bias across studies in the systematic review.

4.4.5.1 Changes during growth

Mean of anterior facial height (ATFH, AUFH, ALFH) was reported significantly greater in males in most articles. Males presented a greater ATFH than females at the age of 15 onwards (60), 16 onwards (62) and at 7, 14, 22 years (87). Regarding AUFH, Ursi et al. (3) and Moldez et al. (87) observed a greater value of AUFH in males from 14-18 years, and at 7, 14, and 22 years, respectively, while el-Batouli et al. (57) measuring on children from 6- 18 years concluded males had a greater AUFH than females solely at 18 years. In addition, ALFH was longer in males at the age 16 and 18 (3), at 15 and 17 years (60), at 11 years and young adult (49), and from 6- 18 years (57).

There are two longitudinal articles reporting a greater PTFH in males at the age of 16 onwards (62) and at 17 years (60).

Regarding the ratio between linear vertical measurements, el-Batouti et al. (57) noticed that AUFH/ALFH is similar between sexes from 6- 12 years; and significantly smaller in males than females from 15- 18 years. This means, in comparison to females, males had a greater elongation of ALFH than AUFH in older children. However, a cross-sectional study conducted by Chang et al. (49), comparing 11-year-old children to young adults, showed that no significant differences between sexes were observed in either AUFH/ALFH or AUFH/ATFH, ALFH/ATFH, PUFH/AUFH in both 11-year-old children and young adults. He also noticed that males had greater vertical parameters than females in ATFH and ALFH in both 11-year-old children and young adults; but solely AUFH, PTFH, PUFH, PLFH in young adults. Interestingly, PLFH/ALFH, PTFH/ATFH in males were smaller than females in children, but became greater in young adults, that means posterior facial height increased more in males than in females. Comparing mean values between children and young adults also showed that significant increases of ATFH, ALFH, AUFH, PTFH, PUFH, PLFH, PLFH/ALFH, PTFH/ATFH with age were noted, except for PTFH/ATFH in females.

On the other hand, it would be more adequate to rely on longitudinal studies to assess growth. Most of longitudinal reported a significant increase in linear vertical parameters during growth (2,4,57,59,61,62).

Regarding timing of growth, Alió-Sanz et al. (4), conducting research on children aged 8-18 years, noted a greater increase of AUFH from 8-11 years, when compared to 12- 14 years and 15- 18 years of age. Similarly, Bishara et al. (2) concluded that AUFH, ATFH increased the most between 5- 10 years of age, the least after 15 years; the ratio AUFH/ ATFH increased mostly from 5- 10 in both sexes; PLFH, PTFH constantly increased from chidhood to adulthood in males, while more significantly increased during 5- 10 years than 10- 15 and 15- 25.5 years of age in females; the ratio PLFH/ PTFH decreased from 5- 10 years and increased from 10- 15 years and 15- 25.5 years of age in both sexes, which means that the increase of posterior facial height was attributed to vertical growth of upper posterior segment at early age, of lower posterior component at later age. However, Thilander et al. (59) revealed that ALFH increased the most between 13- 16 years for both sexes, while growth acceleration in AUFH, ATFH, PTFH, PLFH was noted between 13- 16 years of age in males; the ratio ALFH /ATFH remained constant during growth (around 55%); the ratio ATFH/ PTFH continuously decreased (approximately 16%), resulting an upward and forward rotation of the mandible. Recently, Jiménez et al. (62) described females had a constant acceleration of ATFH from 8- 14 years of age, after that growth rate slowed down, while significant pubertal spurt was between 14- 16 years in males; similarly, growth spurt of ALFH, PTFH occured between 12- 14 years in females, and 14- 16 years of age in males. According to Bishara et al. (2), the ratio PTFH/ATFH increased the most in males, and the least in females after 15 years of age, resulting in a greater counterclockwise rotation of the mandible in males at this age.

Most of studies showed similar angular vertical parameters between males and females. In more detail, no sexual dimorphism was found in FH/MP from 6- 18 years (3); SN/FH from 6- 18, SN/MP from 6- 15 years (57); SN/MP from childhood to adulthood (62); SN/FH, SN/PP, SN/MP at 7, 9.5, 14 years old children (87). Similarly, Chuang (63) revealed insignificant differences between sexes in SN/MP, FH/MP, PP/MP, and gonial angle throughout the period of study from 8- 12 years of age. Regarding SN/PP, there are 2 studies (4,57) showed a significantly smaller SN/PP in males than females from young child to 18 years of age.

It is agreed that SN/MP decreased during growth, and this change lasted longer in males (2,57,61). Indeed, Hamamci et al. (61) noted a significant decrease of SN/MP from 9- 14 years of age in females, from 9- 14 and 14- 18 years in males (SN/MP decreased by 1.35^0 in females and 1.42^0 in males from 9- 18 years of age). Bishara et al. (2) similarly concluded that SN/MP changed the most in males, while the least in females after 15 years of age. Similarly, el-Batouli et al. (57) found that SN/MP significantly decreased from 6- 18 years in both sexes; SN/MP was similar between males and females from 6- 15 years, became smaller in males at 18 years of age, resulting from a greater decrease of SN/MP in males from 15- 18 years of age. In support, Thilander et al. (59) and Stahl de Castrillon et al. (60) noticed a continuous decrease in SN/MP, MP/PP, gonial angle and a stable SN/PP from childhood to adulthood in both sexes. A significant decrease of SN/MP (by 3.1^0 for females and 7.1^0 for males, in average) from 6- 24 years of age was also observed by Jiménez et al (62). Other angular measurements including NSGn, NBa/PtmGn remained constant from childhood to adulhood (2,61).

4.4.5.2 Intra-/inter-racial comparisons

In cross-sectional group, difference of anterior facial height between males and females is incontistent among articles. Males generally exhibited a greater AUFH than females within white, black and Asian populations: 11-year-old Norwegian (66), 13-year-old North Mexican (11), 13-year-old Iowan (11,12), 14-year-old black Brazilian (81), 14-year-old South African (75), 12-year-old Nigerian (77), and 13-year-old Chinese children (88). However, no significant difference in AUFH was found in 8.5-year-old Egyptian (64), 10-year-old Polish (67), 13-year-old Afro-Caucasian Brazilian, 13 and 14-year-old white Brazilian (81,82), and 14-year-old Japanese-Brazilian children (83).

Regarding ALFH, males presented a longer ALFH in 10-year-old Polish (67), 14-year-old Turkish (68), and 14-year-old Japanese-Brazilian children (83). In contrast, a similar ALFH between males and females was found in 8.5-year-old Egyptian (64), 9- 12 year-old Saudis (69), 14-year-old black and white Brazilian (81), 13-year-old Afro-Caucasian Brazilian (82), 12-year-old Nigerian (77), 14-year-old South African (75), and 12-year-old Chinese children (53).

For ATFH, males had a significantly greater value than females in 13-year-old North Mexican, 13-year-old Iowan (11), 11-year-old Norwegian (66), 10-year-old Polish (67), 9-year-old Serbian (72), and 14-year-old Japanese-Brazilian children (83). However, the difference of ATFH was considered insignificant in 8.5-year-old Egyptian (64), 14-year-old black and white Brazilian (81), 13-year-old white and Afro-Caucasian Brazilian (82), and 12-year-old Nigerian children (77).

Posterior upper facial height (PUFH) was assessed in a small number of studies because S-Ar is also considered posterior cranial base, presented in category of cranial base structure. In this section, evaluation of PUFH is only assessed through S-Ar’, in which, Ar’ is projection of Ar on S-Go plane. PUFH was greater in males than females in 14-year-old black and white Brazilian (81), 13-year-old Afro-Caucasian Brazilian (82), and 14-year-old Japanese-Brazilian children (83); however, a similar mean value was found in 13-year-old white Brazilian children (82).

Most of studies concluded that no significant differences of PLFH between sexes were observed in 13-year-old North Mexican (11), and 13- 14 year-old Brazilian children (81–83). However, a greater PLFH in males than females was observed in 13-year-old Iowan children (11,12).

A majority of studies showed a greater PTFH in males for 13-year-old North Mexican, 13-year-old Iowan (11,12), 10-year-old Polish (67), 9-year-old Serbian (72), 14-year-old black and white Brazilian (81), 13-year-old Afro-Caucasian Brazilian (82), and 14-year-old Japanese-Brazilian children (83). However, the difference was insignificant in 13-year-old white Brazilian children (82).

Data for the ratio between vertical facial dimension is pretty focused. In white populations, almost all articles stated that no sexual dimorphism was observed in AUFH/ATFH, PLFH/PTFH, PTFH/ATFH in 13-year-old North Mexican, 13-year-old Iowan (11,12); in AUFH/ATFH, ALFH/ATFH in 14-year-old Black and White Brazilian (81), in PUFH/PTFH, PLFH/PTFH in 14-year-old Japanese-Brazilian (83), in ALFH/ATFH in 12-year-old Nigerian (77). However, according to de Freitas et al. (81), 14-year-old black and white Brazilian males had greater PUFH/PTFH and smaller PLFH/PTFH than females. Aleksic et al. (72) showed that smaller PTFH/ATFH was seen in 9-year-old Serbian males.

At a very young age 4-5 years old, no significant difference in SN/MP between sexes was found in North Indian children (85). However, males had a significantly larger SN/MP than females in 8.5-year-old Egyptian (64) and 9-year-old Serbian children (72). In older children, sex-related differences were not significant: 14-year-old South-African (75), 13.5-year-old Israeli (71), 13-year-old Iowan (12), 11-year-old Norwegian (66), 10-year-old Polish (67), 9- 12 year-old Saudis (69), 11- 13 year-old Mewari (North Indian) (84), and 13-year-old Chinese children (88). Similarly, no sexual dimorphism in FH/MP was noted in 14-year-old Turkish (68), 13.5-year-old Israeli (71), 9- 12 year-old Saudis (69), 12-year-old Nigerian (76), 11-year-old Kenyan (79), 11-13 year-old Lingayat (Indian) (86), and 13-year-old Chinese children (88). Gonial angle was greater in males than females in 8.5-year-old Egyptian (64), was similar between sexes in 14-year-old South-African (75), 11-year-old Norwegian (66), 10-year-old Polish (67), 9-year-old Serbian (72), 13-year-old Chinese (88). Thus, there is a general consensus towards no sex-related differences in the mandibular plane angle, expect perhaps around the age of 10- 14 years.

Regarding the tilt of the palatal plane , there were no significant sex-related differences in SN/PP in most articles on 11- 13 year-old white children (64,66,72). However, a smaller SN/PP and FH/PP was observed in 14-year-old South-African males (75) and 13.5-year-old Israeli males (71), respectively.

For other angular measurements, the differences between male and female children were insignificant, including SN/FH in 8.5-year-old Egyptian (64), PP/MP in 11-year-old Norwegian (66), FH/MP, FH/SGn, NSGn in 13-year-old Iowan (12), FH/SGn in 9- 12 year-old Saudis (69), NSGn in 14-year-old South-African (75), NBa/PtmGn in 14-year-old Turkish (68), PP/MP, FH/SGn in 13-year-old Chinese (88); except for smaller NBa/PtmGn in 10-year-old Polish boys (67), and greater FH/SGn in 13.5-year-old Israeli boys (71).

Several morphological differences in vertical parameters were observed among white and Asian populations. In comparison to white children, Chinese children presented a clockwise rotated mandible with greater FH/MP at 12.5 years (89) and greater SN/MP, FH/SGn at 13 years of age (88). However, no significant differences between 13-year-old Chinese and 13-year-old white were noticed in AUFH, ALFH, ATFH, PLFH (88).

Little consensus is formed from studies comparing black and white populations. 10-year-old African American children had a greater SN/MP than 10-year-old white Southern American (74); 11-year-old Kenyan presented larger FH/MP than black American and white children (79). However, within the Brazilian populations, 13-year-old Afro-Caucasian Brazilian had a greater PUFH, smaller AUFH and PLFH than Caucasian Brazilian children, and similar APFH, ATFH, PTFH (82); in contrast, no significant differences in AUFH/ATFH, PTFH/ATFH, PLFH/PTFH, and PLFH/ALFH were observed in 8- 10 year-old black and white Brazilian children (54); de Freitas et al. (80,81) showed that 14-year-old black Brazilian presented smaller AUFH, AUFH/ATFH, larger ALFH/ATFH than white Brazilian children. Also, 13-year-old black Brazilian had smaller FH/MP, SN/MP than white Brazilian children, which is opposite to conclusion from Alexander & Hitchcock and Kapila (74,79).

In summary, the linear vertical parameters increase with age in both sexes. Most angular vertical parameters remain constant; one exception is counterclockwise rotation of mandibular plane from childhood to adulthood, which is greater in males than females. In general, males present greater linear measurements and similar angular parameters when compared to females, except for smaller mandibular plane angle observed in males after the age of 15 years. In comparison to white population, Chinese children present with a clockwise rotated mandible.

5. DISCUSSION

5.1 Craniofacial characteristics

The systematic review has aggregated information from independent studies and has yielded a number of general results about i) the growth of craniofacial bone during childhood and adolescence by comparing normative cephalometric data in children of different ages, ii) sexual dimorphism pertaining to differences in mean values of parameters at specific ages as well as the difference of the extent and timing of growth, and iii) the difference of craniofacial morphology in children among races.

Regarding cranial base, its length increases during growth from childhood to adulthood, while cranial base angle remains stable. Males present a longer anterior cranial base than females, especially at the age of 16 onwards, resulting from more significant growth in males than females at this age. For cranial base angle, the difference between male and female is insignificant throughout the period of growth. With regard to racial characteristics, Asian children seem to present a shorter cranial base and larger cranial base angle when compared to white children. This result about growth of anterior cranial base (S-N) is consistent with that from a systematic review investigating changes in anterior cranial base during growth conducted by Afrand et al. (32), whose inclusion criteria do not include well-balanced face and normal occlusion. Afrand et al. noted that point sella moves backward and downward and nasion moves forward until adulthood, which induce a continuous increase of length of the anterior cranial base. Although S-N plane was introduced as a stable structure for cephalometric superimposition by several authors (1,15), it is recommended that it should not be used as a reference plane for superimposition. Instead, the cribriform plate and presphenoid regions may be used for this purpose because of their structural stability after the age of 7 years (32). The elongation of the posterior cranial base S-Ba until adulthood was also reported in another systematic review about the growth of the posterior cranial base carried out by Currie et al. (33). In this study, both point S and Ba move downward and backward with age; however, the amount of change of point Ba is greater, leading to an increase of S-Ba. Regarding cranial base angle, the result of the literature review coincides with a recent longitudinal article published in 2017 (90), which showed that cranial base angle NSBa remains constant from the age of 6- 18 years in either class I subjects with normal occlusion or class II division 2 occlusion subjects (based on Angle’s occlusal classification).

With regard to maxilla, the review shows the elongation as well as downward and forward growth of the maxilla. This is noticed through the increases of mean values of the measurements: SNA (2,45,57,60,61), A-Nperp (60,61), A-Ptm or A-PNS (2,45), ANS-PNS (4,63), Co-A (4,61,62). Moreover, according to Alió-Sanz et al. (4), point A moves forward, point ANS and PNS move downward during growth. The results correspond to Enlow's and Proffit's description (1,28) of the growth of the nasomaxillary complex. According to Enlow and Proffit (1,28), maxillary growth is mainly attributed to two mechanisms, including growth as a consequence of cranial base's growth and growth at the nasomaxillary sutures. The elongation of the cranial base induces the forward displacement of the maxilla because of the attachment between them. On the other hand, growth of the soft tissues in midfacial region leads to the forward, downward translation of the maxilla (due to the anatomic direction of sutures) and the expansion of sutures in nasomaxillary region, new bone then formed at both sides of the sutures, resulting in the forward and downward growth of the maxilla. Moreover, bone apposition occurs in the posterior surface of the maxillary tuberosity, contributing to the elongation of the maxilla. Additionally, bone modeling processes in the palate, including bone removal at the nasal side and bone apposition at the oral side, induce downward growth of the palate. The review's result on the earlier growth of the maxilla in females is consistent to that of a longitudinal study published in 2014 by Nahhas et al. (91). Nahhas et al. stated that the increase of maxillary length (A-PNS) begins at approximately 7 years old in females and around 8 years in males, peaks between 10- 12 years in girls and 12- 14 years in boys, ceases at around 16 years in females and nearly 20 years of age in males. Regarding racial comparisons, black populations present a more protrusive maxilla than white populations, but it is not clear whether this results from greater growth rates or differences in the timing of growth.

This systematic review shows that the mandible grows forward from childhood to adulthood (2,57,59–61) and lengthens with age (2,61–63), which coincides with previous publications (1,28). Enlow & Hans (28) stated that mandibular condyle and ramus grow significantly in childhood in superior and posterior direction, inducing a forward and downward translation of the mandible. Furthermore, according to Proffit et al. (1), bone modeling occurs at the ramus, including bone apposition at posterior surface and bone resorption at anterior surface, leading to an increased distance from the ramus to the chin, which means elongation of the mandible. According to this review, decreased velocity of mandibular growth occurs earlier in females when compared to males, which was also reported in a number of articles (37,91). In those studies, Costello et al. (37) stated that growth of the mandible is nearly completed at the age of 14 in females and 16 years in males, while Nahhas et al. (91) concluded that the increase of mandibular length (Ar-Me) starts at around 7.2 years of age in females and about 8.4 years in males, peaks between 9.4- 12.4 years in girls and 12.2- 14.7 years in boys, ends at around 17 years in females and nearly 20 years of age in males. Both articles found that peak velocity and cessation of mandibular growth happen at the earlier age in females, which is consistent with our review. However, our result showed that mandible continues to grow after 16 years of age in males contributing to a greater mean value of mandibular length in males than females, which is different from Costello's conclusion. In comparison to white populations, it seems that Asians have more retrusive mandible.

Regarding maxillomandibular relationship, there is high consensus among included studies about the stability of Wits appraisal, the decrease of ANB and NAPg during childhood and adolescence, as well as insignificant differences of those measurements between males and females. ANB equals SNA minus SNB; therefore, the decrease of ANB can be interpreted based on the information about the changes of SNA and SNB during orofacial growth. Both SNA and SNB increase with age; thus, the decrease of ANB is attributed to that the growth of the mandible is greater than that of the maxilla. This is corresponding to statement from Burr & Allen (31); it is stated that, in the craniofacial complex, the mandible is structure presenting the greatest growth. One included longitudinal study in the review (2) noted the extent of decrease in ANB during growth is different in the 3 age groups (between 5- 10 years, between 10- 15 years, and after 15 years of age) and between males and females. In males, ANB decreased mostly between 5- 10 years, and after 15 years of age; the decrease was the least between 10- 15 years; more than one third of the total change of ANB occured after 15 years old. Meanwhile, in females, ANB solely decreased between 5- 10 and 10- 15 years of age. This can be because both maxilla and mandible grows significantly in males between 10- 15 years, resulting in an insignificant decrease of ANB in this period. However, after 15 years old, in males, the maxilla grew forward less than the mandible, contributing to significant decrease of ANB; in females, it has been known by literature that the growth of maxilla and mandible considerably decelerates after the age of 15 years (37,38), resulting in a relatively stable ANB in females after 15 years of age. For racial differences, Asians or Africans appear to have a more convex profile with larger ANB, NAPg than white subjects, which may be attributed to a more protrusive maxilla in black populations and a more retrusive mandible in Asians in comparison to white populations.

This review reports a significant increase in facial height with age in both sexes. This is because both maxilla and mandible move forward and downward during growth (1,28). According to Lowrey & Watson (92), midface and lower face account for a low proportion of the head in children; however, this proportion considerably increases during growth. Regarding growth differences in vertical parameters, posterior facial height lengthens more than anterior facial height during growth in either sex, resulting in a continuous decrease of the mandibular plane angle and increase of the ratio PTFH/ATFH; leading to a counterclockwise rotation of the mandible. This is consitent with the results from a study conducted by Björk & Skieller (29). Moreover, there is consensus among studies that decrease of mandibular plane angle is significantly greater in males than females at the age of 15 onwards (2,57,61), contributing to smaller mandibular plane angle in males in comparison to females at this period. The counterclockwise rotation of the mandible has also been reported in the literature (93,94). Interestingly, in 2018, Hardin et al. (93), conducting a study synthesizing data from six longitudinal articles of human growth, found that change of mandibular plane angle with age is significantly different among individuals with different facial types (hyperdivergent, well-balanced, hypodivergent). Specifically, in individuals with hyperdivergent face, the change of mandibular plane angle was insignificant; a slight increase was even recorded in females. In contrast, a severe decrease of this angle was observed in those with hypodivergent face, and a moderate decrease was reported in subjects with well-balanced face from childhood to young adult. In the study, the decrease of mandibular plane angle was also found to be greater in males than females. In 2020, Hardin et al. (94) carried out another longitudinal study and showed similar trends. Regarding racial comparisons, Chinese children appear to exhibit a more clockwise rotated mandible than white subjects, which corresponds to a more retrusive mandible being seen in Chinese population in this review.

Generally, inter-racial differences in cephalometric parameters may come from various craniofacial morphological characteristics among races; however, this can be attributed to different cultural standards, personal opinions for well-balanced face, and even Eurocentric influence (95). For example, white cultures may have historically considered that a harmonious profile should be straight or slightly convex, while black cultures may have a tendency to accept a more convex profile as a balanced face (96). However, several studies, in which both black and white populations are assessed by the same examiners (80,81), showed that different morphological features between the two populations can be observed through a number of cephalometric measurements. In general, this knowledge of cephalometric norms in different populations can aid in better understanding the healthcare needs of these populations and to better serve them.

5.2 Limitations

Our systematic review has several limitations. Firstly, sample size in all included studies was not calculated or justified, except for Singh's article (86). This study has achieved the highest score from the quality appraisal; however, it only examined a small number of cephalometric measurements. Secondly, there are several factors contributing to risk of bias across studies in the systematic review: a few landmarks and reference planes used are inconsistent among studies, standardization of cephalometric radiographs can be difficult (different magnification of cephalometric films among studies). A bias could also be the term well-balanced face. This was assessed in each study by the investigators. Presumably this quality is based on the local cultural norms; however, it could also be influenced by Eurocentric standards. Thirdly, we are aware that clinicians' interest is to be offered a set of normative values and standard deviations for different age, sexes, and races, which could be a basis for orthodontic diagnosis and treatment planning. However, in a systematic review, pooled means and standard deviations for each age groups, males and females, and different populations cannot be computed. Instead, a meta-analysis should be conducted to provide that information.

5.3 Knowledge gaps

There are few studies investigating longitudinal growth in children with a well-balanced face and normal occlusion other than white populations. In more detail, the included articles for this systematic review solely comprise one longitudinal study in Asians, no longitudinal study for black populations, and two cross-sectional studies in Asians comparing differences in various age groups; therefore more cephalometric research on Asian and black populations is necessary for comprehensive knowledge about differences in craniofacial growth among races. Furthermore, data were not available for other racial and ethnic categories identified by the NIH, such as American Indian or Alaska Native and Native Hawaiian or other Pacific Islander. It is not clear why more diverse populations have not been investigated but it could be due to reasons such as a lack of attention to racial minorities in health research, and/or taboos attached to race.

Few statistics have been done on growth, not clear if these studies are adequately powered or whether there is no difference.

All included studies used chronological age to assess growth; however, according to Proffit et al. (1), growth onset and spurt occur at different chronological age in different female individuals. Specifically, the early-maturing girl has already passed the peak of the growth spurt at the age of 11 years, where the late-maturing girl has not even entered the rapid grow phase. Instead, Tanner stage or classification of cervical vertebral maturation is recommended to be used in growth evaluation for females. Therefore, more study using Tanner stage or classification of cervical vertebral maturation for categorizing growth periods should be conducted in the future.

In all included studies, 2D lateral cephalometric analyses were performed. Although it is undeniable that traditional 2D cephalometric radiographs have served as a essential tool in dental practice and craniofacial research, 3D reconstructed cephalometry exhibit several benefits. For instance, image magnification and distortion can be prevented with the 3D imaging technique (97). Moreover, a number of studies showed that 3D cephalometry can provide an accurate assessment of craniofacial anatomy (98–101); therefore, it should be used more frequenly in research on craniofacial morphology.

5.4 Implications

This study aggregates cephalometric data in children with well-balanced face and normal occlusion; therefore, it can be an important database for orthodontic diagnosis and treatment planning as well as for future studies on craniofacial developmental abnormalities in children. The review found that there are a great number of differences in craniofacial skeletal characteristics between sexes pertaining to mean value of parameters and growth timing, as well as among races. Therefore, the results of the review can be used as a basis for early detection and early intervention for craniofacial skeletal discrapancies. For example, orthopedic treatment for skeletal discrapancies between upper and lower jaws should be performed earlier in females to obtain optimal outcomes; and determining the timing for orthopedic intervention in girls should be investigated to determine whether Tanner stage or chronologic age more accurately reflect the timing of orofacial growth, to optimize orthopedic intervention in girls. In contrast, orthopedic treatment for boys can be carried out later than for girls to reduce treatment time and still achieve treatment goals. It is necessary because a prolonged treatment can negatively affect patient cooperation, which has been known as the key in successful orthopedic treatment (1).

This review identifies differences in normative data of cephalometric measurements among different races, which should be known to better treat orthodontically specific individuals in various populations.

Additionally, our study will highlight gaps in the published studies of craniofacial morphology. More research on populations other than white populations, research using Tanner stage or classification of cervical vertebral maturation for categorizing growth period, and research with 3D imaging are required.

6. CONCLUSION

In conclusion, this review shows that both the cranial base, maxilla, and mandible lengthen throughout childhood and adolescence. The growth of maxilla and mandible is in forward and downward direction in both sexes and reaches a peak earlier in females; however, the great extent of growth lasts longer in males. Males appear to present a greater mean values of linear parameters than females, except for similar Wits appraisal between two sexes; no significant difference between sexes is observed in angular measurements, except for smaller mandibular plane angle (counterclockwise rotation of the mandible) in males from the age of 15 onwards. During growth period, the mandible grows more than the maxilla, resulting a straighter profile in young adult from a convex profile in children. With regard to racial differences, as comparison to white populations, Asians seem to exhibit a shorter cranial base, more retrusive mandible, more convex profile, and more clockwise rotated mandible; black populations have a more protrusive maxilla, and more convex profile. Therefore, age, sex, and race should be taken into account for diagnosis and treatment planning as well as for research on craniofacial morphology.

7. REFERENCES

1. Proffit WR, Fields HW, Larson B, Sarver DM. Contemporary Orthodontics - E-Book. [Internet]. Philadelphia: Mosby; 2018 [cited 2022 Feb 16]. Available from: http://www.vlebooks.com/vleweb/product/openreader?id=none&isbn=9780323543880

2. Bishara SE, Peterson LC, Bishara EC. Changes in facial dimensions and relationships between the ages of 5 and 25 years. Am J Orthod. 1984 Mar 1;85(3):238–52.

3. Ursi WJ, Trotman CA, McNamara JA, Behrents RG. Sexual dimorphism in normal craniofacial growth. Angle Orthod. 1993;63(1):47–56.

4. Alió-Sanz J, Iglesias-Conde C, Pernía J-L, Iglesias-Linares A, Mendoza-Mendoza A, Solano-Reina E. Retrospective study of maxilla growth in a Spanish population sample. Med Oral Patol Oral Cirugia Bucal. 2011 Mar 1;16(2):e271-277.

5. Finlay LM. Craniometry and cephalometry: a history prior to the advent of radiography. Angle Orthod. 1980 Oct;50(4):312–21.

6. Brons S, van Beusichem ME, Bronkhorst EM, Draaisma J, Bergé SJ, Maal TJ, et al. Methods to quantify soft-tissue based facial growth and treatment outcomes in children: a systematic review. PloS One. 2012;7(8):e41898.

7. Björk A. The use of metallic implants in the study of facial growth in children: method and application. Am J Phys Anthropol. 1968 Sep;29(2):243–54.

8. Sarnat BG. Some methods of assessing postnatal craniofaciodental growth: a retrospective of personal research. Cleft Palate-Craniofacial J Off Publ Am Cleft Palate-Craniofacial Assoc. 1997 Mar;34(2):159–72.

9. Baccetti T, Franchi L, McNamara JA. Thin-plate spline analysis of treatment effects of rapid maxillary expansion and face mask therapy in early Class III malocclusions. Eur J Orthod. 1999 Jun;21(3):275–81.

10. Jacobson A, Jacobson RL. Radiographic cephalometry: from basics to 3-D imaging [Internet]. Chicago: Quintessence Pub.; 2006 [cited 2022 Feb 16]. Available from: https://search.ebscohost.com/login.aspx?direct=true&scope=site&db=nlebk&db=nlabk&AN=887123

11. Bishara SE, Fernandez AG. Cephalometric comparisons of the dentofacial relationships of two adolescent populations from Iowa and northern Mexico. Am J Orthod. 1985 Oct;88(4):314–22.

12. Bishara SE, Abdalla EM, Hoppens BJ. Cephalometric comparisons of dentofacial parameters between Egyptian and North American adolescents. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 1990 May;97(5):413–21.

13. Thiesen G, Pletsch G, Zastrow MD, Valle CVM do, Valle-Corotti KM do, Patel MP, et al. Comparative analysis of the anterior and posterior length and deflection angle of the cranial base, in individuals with facial Pattern I, II and III. Dent Press J Orthod. 2013 Feb;18:69–75.

14. Bastir M, Rosas A, O’higgins P. Craniofacial levels and the morphological maturation of the human skull. J Anat. 2006 Nov;209(5):637–54.

15. Ghafari J, Engel FE, Laster LL. Cephalometric superimposition on the cranial base: A review and a comparison of four methods. Am J Orthod Dentofacial Orthop. 1987 May 1;91(5):403–13.

16. Nguyen JD, Duong H. Anatomy, Head and Neck, Face. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Feb 16]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK551530/

17. Dalgorf D, Higgins K. Reconstruction of the midface and maxilla. Curr Opin Otolaryngol Head Neck Surg. 2008 Aug;16(4):303–11.

18. Kühnel TS, Reichert TE. Trauma of the midface. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2015 Dec 22;14:Doc06.

19. Okay DJ, Genden E, Buchbinder D, Urken M. Prosthodontic guidelines for surgical reconstruction of the maxilla: a classification system of defects. J Prosthet Dent. 2001 Oct;86(4):352–63.

20. Saffar JL, Lasfargues JJ, Cherruau M. Alveolar bone and the alveolar process: the socket that is never stable. Periodontol 2000. 1997 Feb;13:76–90.

21. Soriano RM, M Das J. Anatomy, Head and Neck, Maxilla. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Feb 16]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK538527/

22. Danesh-Sani SA, Loomer PM, Wallace SS. A comprehensive clinical review of maxillary sinus floor elevation: anatomy, techniques, biomaterials and complications. Br J Oral Maxillofac Surg. 2016 Sep;54(7):724–30.

23. Ogle OE, Weinstock RJ, Friedman E. Surgical anatomy of the nasal cavity and paranasal sinuses. Oral Maxillofac Surg Clin N Am. 2012 May;24(2):155–66, vii.

24. Sadrameli M, Mupparapu M. Oral and Maxillofacial Anatomy. Radiol Clin North Am. 2018 Jan;56(1):13–29.

25. White TD, Black MT, Folkens PA. Human osteology [Internet]. Amsterdam; Boston: Elsevier/Academic Press; 2012 [cited 2022 Feb 16]. Available from: http://site.ebrary.com/id/10446604

26. Breeland G, Aktar A, Patel BC. Anatomy, Head and Neck, Mandible. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Feb 16]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK532292/

27. Norton NS, Netter FH. Netter's head and neck anatomy for dentistry [Internet]. Philadelphia, PA: Elsevier/Saunders; 2012 [cited 2022 Feb 16]. Available from: http://www.clinicalkey.com/dura/browse/bookChapter/3-s2.0-C20110041741

28. Enlow DH, Hans MG. Essentials of facial growth. Ann Arbor, MI: Distributed by Needham Press; 2008.

29. Björk A, Skieller V. Normal and abnormal growth of the mandible. A synthesis of longitudinal cephalometric implant studies over a period of 25 years. Eur J Orthod. 1983 Feb;5(1):1–46.

30. Popovich F, Thompson GW. Craniofacial templates for orthodontic case analysis. Am J Orthod. 1977 Apr;71(4):406–20.

31. Burr DB, Allen MR. Basic and applied bone biology [Internet]. 2014 [cited 2022 Feb 16]. Available from: http://site.ebrary.com/id/10720312

32. Afrand M, Ling CP, Khosrotehrani S, Flores-Mir C, Lagravère-Vich MO. Anterior cranial-base time-related changes: A systematic review. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 2014 Jul;146(1):21-32.e6.

33. Currie K, Sawchuk D, Saltaji H, Oh H, Flores-Mir C, Lagravere M. Posterior cranial base natural growth and development: A systematic review. Angle Orthod. 2017 Nov;87(6):897–910.

34. Brahim JS. Dental implants in children. Oral Maxillofac Surg Clin N Am. 2005 Nov;17(4):375–81.

35. Glowacki J, Christoph K. Gender Differences in the Growing, Abnormal, and Aging Jaw. Dent Clin North Am. 2013 Apr;57(2):263–80.

36. Suri S, Prasad C, Tompson B, Lou W. Longitudinal comparison of skeletal age determined by the Greulich and Pyle method and chronologic age in normally growing children, and

clinical interpretations for orthodontics. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 2013 Jan;143(1):50–60.

37. Costello BJ, Rivera RD, Shand J, Mooney M. Growth and development considerations for craniomaxillofacial surgery. Oral Maxillofac Surg Clin N Am. 2012 Aug;24(3):377–96.

38. Liu Y-P, Behrents RG, Buschang PH. Mandibular growth, remodeling, and maturation during infancy and early childhood. Angle Orthod. 2010 Jan;80(1):97–105.

39. Albert AM, Payne AL, Brady SM, Wrighte C. Craniofacial Changes in Children-Birth to Late Adolescence. ARC J Forensic Sci. 2019;4(1):1–19.

40. Rozylo-Kalinowska I. Cephalometric Radiograph in Dentistry/Oral Health. In: Rozylo-Kalinowska I, editor. Imaging Techniques in Dental Radiology: Acquisition, Anatomic Analysis and Interpretation of Radiographic Images [Internet]. Cham: Springer International Publishing; 2020 [cited 2022 Feb 16]. p. 57–64. Available from: https://doi.org/10.1007/978-3-030-41372-9_5

41. Steiner C. The use of cephalometrics as an aid to planning and assessing orthodontic treatment. 1960;

42. Hlongwa P. Cephalometric analysis: manual tracing of a lateral cephalogram. South Afr Dent J. 2019 Aug 1;74.

43. Steiner CC. Cephalometrics for you and me. Am J Orthod. 1953 Oct 1;39(10):729–55.

44. Downs WB. Variations in facial relationships; their significance in treatment and prognosis. Am J Orthod. 1948 Oct;34(10):812–40.

45. Jamison JE, Bishara SE, Peterson LC, DeKock WH, Kremenak CR. Longitudinal changes in the maxilla and the maxillary-mandibular relationship between 8 and 17 years of age. Am J Orthod. 1982 Sep;82(3):217–30.

46. McNamara JA. A method of cephalometric evaluation. Am J Orthod. 1984 Dec 1;86(6):449–69.

47. Ricketts RM. The wisdom of the bioprogressive philosophy. Semin Orthod. 1998 Dec 1;4(4):201–9.

48. Jacobson A. The “Wits” appraisal of jaw disharmony. Am J Orthod. 1975 Feb;67(2):125–38.

49. Chang HP, Kinoshita Z, Kawamoto T. A study of the growth changes in facial configuration. Eur J Orthod. 1993 Dec;15(6):493–501.

50. prisma checklist 2009 word - Google Search [Internet]. [cited 2022 Feb 8]. Available from: https://www.google.com/search?q=prisma+checklist+2009+word&client=firefox-b-d&sxsrf=APq-WBtb2ENFPm2IW37Oc4V95zxyGB6gog%3A1644369363863&ei=0xUDYraYNOaZptQP1dSm4AU&oq=prisma+2009+word&gs_lcp=Cgdnd3Mtd2l6EAEYATIGCAAQBxAeMgYIABAHEB4yBAgAEB46BwgAEEcQsAM6BwgjELACECdKBAhBGABKBAhGGABQmQZYshRgkS1oAXABeAGAAcABiAHxCpIBAzcuNpgBAKABAcgBCMABAQ&sclient=gws-wiz

51. NOT-OD-15-089: Racial and Ethnic Categories and Definitions for NIH Diversity Programs and for Other Reporting Purposes [Internet]. [cited 2022 Feb 16]. Available from: https://grants.nih.gov/grants/guide/notice-files/not-od-15-089.html

52. Study Quality Assessment Tools | NHLBI, NIH [Internet]. [cited 2022 Feb 17]. Available from: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

53. Pan XG, Liu HH, Cao HJ. [McNamara cephalometric analysis for Shanghai adolescents and adults]. Shanghai Kou Qiang Yi Xue Shanghai J Stomatol. 1996 Dec;5(4):195–7.

54. Sobreira CR, Vilani GNL, Siqueira VCV de. Comparative study of facial proportions between Afro Brazilian and White Brazilian children from 8 to 10 years of age. Dent Press J Orthod. 2011 Apr;16:85–93.

55. Higley LB. Cephalometric standards for children 4 to 8 years of age. Am J Orthod. 1954 Jan 1;40(1):51–9.

56. Broadbent BH, Broadbent BH, Golden WH. Bolton standards of dentofacial developmental growth. Saint Louis: Mosby; 1975.

57. el-Batouti A, Ogaard B, Bishara SE. Longitudinal cephalometric standards for Norwegians between the ages of 6 and 18 years. Eur J Orthod. 1994 Dec;16(6):501–9.

58. el-Batouti A, Bishara S, Ogaard B, Jakobsen J. Dentofacial changes in Norwegian and Iowan populations between 6 and 18 years of age. Eur J Orthod. 1995 Jun;17(3):241–9.

59. Thilander B, Persson M, Adolfsson U. Roentgen-cephalometric standards for a Swedish population. A longitudinal study between the ages of 5 and 31 years. Eur J Orthod. 2005 Aug;27(4):370–89.

60. Stahl de Castrillon F, Baccetti T, Franchi L, Grabowski R, Klink-Heckmann U, McNamara JA. Lateral cephalometric standards of Germans with normal occlusion from 6 to 17 years of age. J Orofac Orthop Fortschritte Kieferorthopadie OrganOfficial J Dtsch Ges Kieferorthopadie. 2013 May;74(3):236–56.

61. Hamamci N, Başaran, Kiralp. Longitudinal Study of Untreated Skeletal Class I Subject's Growth and Development with Mc Namara Cephalometric Analysis: Biotechnology & Biotechnological Equipment: Vol 20, No 3 [Internet]. 2013 [cited 2022 Feb 4]. Available from: https://www.tandfonline.com/doi/abs/10.1080/13102818.2006.10817398

62. Jiménez I, Villegas L, Salazar-Uribe JC, Álvarez LG. Facial growth changes in a Colombian Mestizo population: An 18-year follow-up longitudinal study using linear mixed models. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 2020 Mar;157(3):365–76.

63. Chuang SY. Craniofacial growth changes of Mongolian children with normal occlusion from 8 to 12 years. Kaohsiung J Med Sci. 2000 Aug;16(8):400–13.

64. El-Batran M, Soliman N, El-Wakil K. The relationship between cranial base and maxillo-facial morphology in Egyptian children. Homo Int Z Vgl Forsch Am Menschen. 2008;59(4):287–300.

65. Thilander B, Persson M, Skagius S. Roentgencephalometric standards for the facial skeleton and soft tissue profile of Swedish children and young adults. II. Comparisons with earlier Scandinavian normative data. Swed Dent J Suppl. 1982;15:219–28.

66. Humerfelt A. A roentgenographic cephalometric investigation of Norwegian children with normal occlusion. Scand J Dent Res. 1970;78(2):117–43.

67. Obloj B, Fudalej P, Dudkiewicz Z. Cephalometric standards for Polish 10-year-olds with normal occlusion. Angle Orthod. 2008 Mar;78(2):262–9.

68. Kilic N, Catal G, Oktay H. McNamara norms for Turkish adolescents with balanced faces and normal occlusion. Aust Orthod J. 2010 May;26(1):33–7.

69. Hassan AH. Cephalometric norms for the Saudi children living in the western region of Saudi Arabia: a research report. Head Face Med. 2005 Aug 24;1:5.

70. Hamdan AM, Rock WP. Cephalometric norms in an Arabic population. J Orthod. 2001 Dec;28(4):297–300.

71. Gleis R, Brezniak N, Lieberman M. Israeli cephalometric standards compared to Downs and Steiner analyses. Angle Orthod. 1990;60(1):35–40; discussion 41.

72. Aleksic E, Lalic M, Milic J, Gajic M, Stankovic Z, Jevremovic D, et al. Cephalometric standards for 9 year-old Serbian children with neutroocclusion. Acta Stomatol Naissi. 2012 Jan 1;28:1155–63.

73. Huang WJ, Taylor RW, Dasanayake AP. Determining cephalometric norms for Caucasians and African Americans in Birmingham. Angle Orthod. 1998 Dec;68(6):503–11; discussion 512.

74. Alexander TL, Hitchcock HP. Cephalometric standards for American Negro children. Am J Orthod. 1978 Sep;74(3):298–304.

75. Barter MA, Evans WG, Smit GL, Becker PJ. Cephalometric analysis of a Sotho-Tswana group. J Dent Assoc South Afr Tydskr Van Tandheelkd Ver Van Suid-Afr. 1995 Nov;50(11):539–44.

76. Ajayi EO. Cephalometric norms of Nigerian children. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 2005 Nov;128(5):653–6.

77. Folaranmi N, Isiekwe M. Anterior face height values in a nigerian population. Ann Med Health Sci Res. 2013 Oct;3(4):583–7.

78. Beugre JB, Sonan NK, Beugre-Kouassi AM, Djaha F. Comparative cephalometric study of three different ethnic groups of black Africa with normal occlusion. Odonto-Stomatol Trop Trop Dent J. 2007 Mar;30(117):34–44.

79. Kapila S. Selected cephalometric angular norms in Kikuyu children. Angle Orthod. 1989;59(2):139–44.

80. de Freitas LMA, de Freitas KMS, Pinzan A, Janson G, de Freitas MR. A comparison of skeletal, dentoalveolar and soft tissue characteristics in white and black Brazilian subjects. J Appl Oral Sci Rev FOB. 2010 Apr;18(2):135–42.

81. de Freitas LMA, Pinzan A, Janson G, Freitas KMS, de Freitas MR, Henriques JFC. Facial height comparison in young white and black Brazilian subjects with normal occlusion. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 2007 Jun;131(6):706.e1-6.

82. Janson G, Quaglio CL, Pinzan A, Franco EJ, de Freitas MR. Craniofacial characteristics of Caucasian and Afro-Caucasian Brazilian subjects with normal occlusion. J Appl Oral Sci Rev FOB. 2011 Apr;19(2):118–24.

83. Vieira FP, Pinzan A, Janson G, Fernandes TMF, Sathler RC, Henriques RP. Facial height in Japanese-Brazilian descendants with normal occlusion. Dent Press J Orthod. 2014;19(5):54–66.

84. Singh Rathore A, Dhar V, Arora R, Diwanji A. Cephalometric Norms for Mewari Children using Steiner's Analysis. Int J Clin Pediatr Dent. 2012 Sep;5(3):173–7.

85. Anuradha null, Taneja JR, Chopra SL, Gupta A. Steiner's norms for North Indian pre-school children. J Indian Soc Pedod Prev Dent. 1991 Mar;8(1):36–7.

86. Singh I, Kumar KK, Raj P, Babu RH, Pithani N, Thekiya AH. Cephalometric Evaluation of Natural Head Position in Lingayat Population of Karnataka. J Pharm Bioallied Sci. 2019 Feb;11(Suppl 1):S59–66.

87. Moldez MA, Sato K, Sugawara J, Mitani H. Linear and angular filipino cephalometric norms according to age and sex. Angle Orthod. 2006 Sep;76(5):800–5.

88. Zhao X-G, Hans MG, Palomo JM, Lin J-X. Comparison of Chinese and white Bolton standards at age 13. Angle Orthod. 2013 Sep;83(5):809–16.

89. Gu Y, Hagg U, Wu J, Yeung S. Differences in dentofacial characteristics between southern versus northern Chinese adolescents. Aust Orthod J. 2011 Nov;27(2):155–61.

90. Barbosa LAG, Araujo E, Behrents RG, Buschang PH. Longitudinal cephalometric growth of untreated subjects with Class II Division 2 malocclusion. Am J Orthod Dentofacial Orthop. 2017 May 1;151(5):914–20.

91. Nahhas RW, Valiathan M, Sherwood RJ. Variation in Timing, Duration, Intensity, and Direction of Adolescent Growth in the Mandible, Maxilla, and Cranial Base: the Fels Longitudinal Study. Anat Rec Hoboken NJ 2007. 2014 Jul;297(7):1195–207.

92. Lowrey GH, Watson EH. Growth and development of children. Chicago: Year Book Medical Publishers; 1973.

93. Hardin AM, Knigge RP, Oh H, Duren DL, Valiathan M, McNulty KP, et al. Growth-related change in the mandibular plane angle with clinical implications. 2018 [cited 2022 Feb 23]; Available from: https://mospace.umsystem.edu/xmlui/handle/10355/66591

94. Hardin AM, Valiathan M, Oh H, Knigge RP, McNulty KP, Leary EV, et al. Clinical implications of age-related change of the mandibular plane angle. Orthod Craniofac Res. 2020 Feb;23(1):50–8.

95. Marchiori GE, Sodré LO, da Cunha TCR, Torres FC, Rosário HD, Paranhos LR. Pleasantness of facial profile and its correlation with soft tissue cephalometric parameters: Perception of orthodontists and lay people. Eur J Dent. 2015;9(3):352–5.

96. Turley PK. Evolution of esthetic considerations in orthodontics. Am J Orthod Dentofacial Orthop. 2015 Sep 1;148(3):374–9.

97. Swennen G, Schutyser F, Hausamen J-E. Three-dimensional Cephalometry: A Color Atlas And Manual [PDF] [1926kk1cc440] [Internet]. [cited 2022 Feb 24]. Available from: https://vdoc.pub/documents/three-dimensional-cephalometry-a-color-atlas-and-manual-1926kk1cc440

98. Gribel BF, Gribel MN, Frazäo DC, McNamara JA, Manzi FR. Accuracy and reliability of craniometric measurements on lateral cephalometry and 3D measurements on CBCT scans. Angle Orthod. 2011 Jan;81(1):26–35.

99. Pinheiro M, Ma X, Fagan MJ, McIntyre GT, Lin P, Sivamurthy G, et al. A 3D cephalometric protocol for the accurate quantification of the craniofacial symmetry and facial growth. J Biol Eng. 2019 May 17;13(1):42.

100. Zamora N, Llamas J-M, Cibrián R, Gandia J-L, Paredes V. A study on the reproducibility of cephalometric landmarks when undertaking a three-dimensional (3D) cephalometric analysis. Med Oral Patol Oral Cirugia Bucal. 2012 Jul 1;17(4):e678-688.

101. Li N, Hu B, Mi F, Song J. Preliminary evaluation of cone beam computed tomography in three-dimensional cephalometry for clinical application. Exp Ther Med. 2017 May;13(5):2451–5.

Appendix 1

Database: Ovid MEDLINE(R) ALL <1946 to December 22, 2020>

Search Strategy:

1 Cephalometry/ (26965)

2 exp Cone-Beam Computed Tomography/ (10624)

3 (cephalogra* or cephalometr* or cone beam).mp. (44833)

4 1 or 2 or 3 (44833)

5 exp infant/ or exp child/ or adolescent/ or exp pediatrics/ (3626010)

6 (child* or pediatric* or paediatric* or prematur* or preterm* or perinat* or neonat* or neo nat* or newborn* or new born* or infan* or baby* or babies or toddler* or boy* or girl* or kid$1 or school* or juvenil* or underage* or under age* or teen* or minor$1 or youth$1 or adolescen* or pubescen* or puberty).mp. (4918655)

7 (neonat* or infan* or child* or adolescen* or pediatric* or paediatric*).mp,jw. (4358821)

8 5 or 6 or 7 (4992481)

9 st.fs. or reference standards/ or reference values/ (910952)

10 (standard* or norm* or longitudinal).mp. (4144493)

11 9 or 10 (4228620)

12 exp dentistry/ or exp jaw/ or exp tooth diseases/ (524501)

13 (alveolar* or craniofacial or "cranio facial" or dental or dentist* or dento* or mandib* or maxill* or jaw* or malocclusion* or occlusion* or orthodontic* or tooth or teeth).mp. (1017043)

14 (craniofacial or dental or dentist* or dento* or orofacial or orthodontic*).jw. (344495)

15 or/12-14 (1110305)

16 4 and 8 and 11 and 15 (4502)

17 (exp infections/ or exp neoplasms/ or exp musculoskeletal diseases/ or exp digestive system diseases/ or ankyloglossia/ or exp jaw diseases/ or exp mouth diseases/ or exp pharyngeal diseases/ or exp stomatognathic system abnormalities/ or exp temporomandibular joint disorders/ or exp

respiratory tract diseases/ or exp otorhinolaryngologic diseases/ or exp nervous system diseases/ or exp eye diseases/ or exp cardiovascular diseases/ or exp "hemic and lymphatic diseases"/ or exp "congenital, hereditary, and neonatal diseases and abnormalities"/ or exp "skin and connective tissue diseases"/ or exp "nutritional and metabolic diseases"/ or exp endocrine system diseases/ or immune system diseases/ or exp "disorders of environmental origin"/ or exp "pathological conditions, signs and symptoms"/ or exp chemically-induced disorders/ or exp "wounds and injuries"/) not exp tooth diseases/ (14467104)

18 16 not 17 (3171)

Appendix 2

Database: Embase Classic+Embase <1947 to 2020 December 21>

Search Strategy:

1 Cephalometry/ (24023)

2 Cone Beam Computed Tomography/ or Cone Beam Computed Tomography Scanner/ (20004)

3 (cephalogra* or cephalometr* or cone beam).mp. (49296)

4 1 or 2 or 3 (49296)

5 exp juvenile/ or pediatrics/ (4056380)

6 (child* or pediatric* or paediatric* or prematur* or preterm* or perinat* or neonat* or neo nat* or newborn* or new born* or infan* or baby* or babies or toddler* or boy* or girl* or kid$1 or school* or juvenil* or underage* or under age* or teen* or minor$1 or youth$1 or adolescen* or pubescen* or puberty).mp. (5676501)

7 (neonat* or infan* or child* or adolescen* or pediatric* or paediatric*).mp,jw. (4771848)

8 5 or 6 or 7 (5839400)

9 standard/ or reference value/ or normal value/ (491886)

10 (standard* or norm* or longitudinal).mp. (6102849)

11 9 or 10 (6142754)

12 exp dentistry/ or exp jaw/ or exp tooth disease/ (359654)

13 (alveolar* or craniofacial or "cranio facial" or dental or dentist* or dento* or mandib* or maxill* or jaw* or malocclusion* or occlusion* or orthodontic* or tooth or teeth).mp. (1258407)

14 (craniofacial or dental or dentist* or dento* or orofacial or orthodontic*).jw. (329755)

15 or/12-14 (1358544)

16 4 and 8 and 11 and 15 (4217)

17 exp diseases/ not (exp tooth disease/ or exp jaw disease/) (24740841)

18 16 not 17 (3128)

Appendix 3

Scopus

Search run on December 23, 2020

5378 records

(TITLE-ABS-KEY (cephalogra* OR cephalometr* OR "cone beam")) AND ((TITLE-ABS-KEY (child* OR pediatric* OR paediatric* OR prematur* OR preterm* OR perinat* OR neonat* OR "neo nat*" OR newborn* OR "new born*" OR infan* OR baby* OR babies OR toddler* OR boy* OR girl* OR kid OR school* OR juvenil* OR underage* OR "under age*" OR teen* OR minor OR youth OR adolescen* OR pubescen* OR puberty OR "to 18 years" OR "to 18 yrs") OR SRCTITLE (neonat* OR infan* OR child* OR adolescen* OR pediatric* OR paediatric*))) AND (TITLE-ABS-KEY (standard* OR reference* OR norm* OR longitudinal)) AND ((TITLE-ABS-KEY (*alveolar* OR craniofacial OR "cranio facial" OR dental OR dentist* OR dento* OR mandib* OR maxill* OR jaw* OR *occlusion* OR orthodontic* OR tooth OR teeth) OR SRCTITLE (craniofacial OR dental OR dentist* OR dento* OR orofacial OR orthodontic*)))

Appendix 4: PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	5-6
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	15
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	15-16
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	31
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	31
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	31
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	33
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	33
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	33

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	33-34
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	35
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	35
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	35
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	36 Fig. 8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	38-51
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	52-53
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 3a, 3b
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	53-71
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	72-76
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	76

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	77-79
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA

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