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# Craniofacial growth studies in orthodontic research – lessons, considerations and controversies

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The distinguishing features of Class I, Class II and Class III craniofacial growth have been subjects of orthodontic research since the middle of the 20th century. However, the moral and practical issues related to studying craniofacial growth in modern times have presented unresolved challenges to researchers. While previous longitudinal growth investigations are typically based on historical data sets, the cephalometric growth studies of contemporary populations must now rely on cross-sectional data. Furthermore, clinical orthodontic research has faced similar ethical challenges in which therapeutic outcomes are analysed using historical control data. These limitations, amongst others, have obscured the conclusions that can be drawn from both types of studies. This article begins with a review of the defining characteristics of Class I, Class II and Class III growth and then explores the limitations of growth studies and the use of historical control groups in orthodontic research. (Aust Orthod J 2018; 34: 61-69)

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## Introduction

The orthodontic profession has had a long-standing interest in the growth pattern of different facial types.<sup>1</sup> This has been driven by a desire to understand the aetiology of malocclusions and to improve therapy. Understanding growth differences between individuals is important, not only for diagnosis but also for understanding treatment effects and relapse. Despite its many limitations,<sup>2</sup> lateral cephalometry has been the traditional tool to study the growth of the face and jaws. The moral and practical challenges of gathering observational growth data using cephalograms has been partly overcome by using historical data as well as cross-sectional studies. Historical growth data is also used to construct control groups for orthodontic research in which concurrent controls may not be feasible on ethical grounds.

The present literature review firstly examines how untreated Class I, Class II/1, Class II/2 and Class III

individuals grow with reference to the distinguishing features identified in growth studies. A second part of the review considers key methodological issues underlying growth research and the problems arising from historical growth data when used as a control comparison.

## *Class I*

Early anatomists noted that pre- and postnatal development occurred in a 'wave adopting a head to tail direction',<sup>3</sup> giving rise to the concept of a 'cephalocaudal gradient'. In childhood, the relative maturity of the maxilla in relation to the mandible gives rise to a profile convexity that can make it difficult to differentiate a Class I from a Class II growth pattern.<sup>4</sup>

The growth of the maxilla is closely related to the maturation of the cranial base (and brain),<sup>5-9</sup> and from approximately six years of age until adulthood

the maxilla has a small but steady rate of growth.<sup>10</sup> Longitudinal studies show that during puberty and adolescence the horizontal growth of the mandible exceeds that of the maxilla by about twofold in Class I individuals.<sup>5,6,11</sup> This 'differential horizontal growth', in combination with a tendency in most individuals for forward (clockwise) mandibular rotation,<sup>12-14</sup> results in a characteristic profile straightening as Class I children mature.<sup>5,7,8,15</sup> Cross-sectional data reflect this change by a decline in the proportion of Class II individuals in the population from childhood through adolescence.<sup>16</sup>

Facial growth in the transverse dimension is less well documented than growth in the anteroposterior and vertical dimensions.<sup>17</sup> Transverse growth of the mandible and maxilla is closely related to the maturation of the cranial base due to their common articulation.<sup>18</sup> Consequently, about 80% of transverse facial growth is completed by the age of six years.<sup>11,19</sup> Thereafter, there is a slow decline in the rate of transverse growth of both jaws.<sup>20</sup> Interestingly, however, mandibular width increases more than maxillary width during adolescence,<sup>20,21</sup> which could help preserve occlusal contacts as the mandible undergoes differential horizontal growth.

The pattern of vertical development is established early and persists throughout life.<sup>5,7,22</sup> During childhood and adolescence, the total vertical growth of the face exceeds both transverse and sagittal growth.<sup>9,11</sup> Vertical facial growth largely reflects maxillary descent from the cranial base,<sup>5</sup> as well as vertical alveolar development.<sup>23</sup> Implant studies demonstrate that rotations of both the maxilla and mandible take place, but these are mostly masked by remodelling.<sup>13,24</sup> According to the servosystem theory of facial growth, maxillary descent also promotes mandibular growth by creating occlusal interferences that cause postural adaptation and stimulate growth.<sup>25</sup>

Maxillary vertical growth must be matched by vertical growth of the mandible, otherwise backward (counterclockwise) rotation will redirect mandibular length gain vertically, rather than horizontally, and create a retrognathic profile.<sup>8</sup> In this respect, it has been estimated that 1 mm of vertical mandibular growth can counteract 1 mm of horizontal length increase.<sup>26</sup> Therefore, hyperdivergent individuals require more growth in mandibular length than hypodivergent faces for a Class I relationship to eventuate.<sup>7,27</sup>

Due to the variable thickness of the soft tissues, the

relationship between skeletal growth and profile change is rarely linear.<sup>28</sup> A relatively large growth of the nose during and after adolescence is well documented<sup>22,29</sup> and longitudinal data suggest that lip thickness peaks around mid-adolescence,<sup>15,30</sup> whilst lip length continues to increase<sup>7,15</sup> into adulthood. A recently-published investigation using consecutive laser scans found that, whilst soft tissue growth was generally constant before and during puberty, mid-facial height had a greater increase pre-puberty and chin projection increased more during puberty.<sup>31</sup>

### *Class II division 1*

A key difference between a Class I and Class II/1 growth pattern is that the 'normal' profile convexity seen in childhood persists or worsens in Class II/1 during puberty, whereas in Class I individuals it straightens.<sup>5,32</sup> Although the malocclusion pattern in the mixed dentition is generally stable with age,<sup>10,33</sup> it has been found that some individuals initially classified as Class II in childhood can experience 'catch-up' growth to become Class I during puberty.<sup>34,35</sup> Similarly, some Class I children may become Class II.<sup>34</sup> However, the transformation of Class II to Class I via adolescent growth has been questioned<sup>33</sup> and it is possible that such observations reflect the early difficulty of differentiating milder cases of Class II from Class I growers.

There has been historical debate regarding whether maxillary protrusion<sup>36-38</sup> or mandibular retrusion<sup>4,9,39-41</sup> is the most common cause of the Class II/1 pattern. It has been proposed that mandibular deficiency is more prevalent since the mandible matures later than the maxilla and, consequently, is more susceptible to adverse environmental influences.<sup>4</sup> The majority of the literature using longitudinal rather than cross-sectional data points to a lack of mandibular growth as the predominant cause of Class II/1.<sup>4,33-35,41,42</sup> It is also possible that a Class II/1 pattern might develop in an individual in whom mandibular length increase is normal but the mandible is either retropositioned<sup>9,43</sup> or hyperdivergent.<sup>8,44,45</sup>

A vertical growth pattern may predispose to a Class II/1 by redirecting mandibular growth more downward and backward.<sup>8</sup> Indeed, some studies have noted an increased gonial angle<sup>46</sup> or an overall increased vertical growth tendency in Class II/1 individuals.<sup>41,45,47</sup> Similarly, a more obtuse cranial base angle may

predispose the mandible to a more retrognathic position, and some studies have implicated this in the development of a Class II/1.<sup>34,42,48</sup> Alternative studies, however, have not been able to show any differences in cranial base flexure<sup>33,41,49</sup> or glenoid fossa position of a Class II/1 compared with a Class I pattern.<sup>50</sup>

In the transverse dimension, there is a propensity for a Class II/1 to be characterised by maxillary constriction.<sup>45,50-52</sup> This observation has led researchers to implicate maxillary constriction as an aetiological factor in the development of a Class II/1 as the mandible assumes a more posterior position to optimise occlusal contact.<sup>50</sup>

### ***Class II division 2***

There has been considerable and ongoing debate regarding the diagnostic criteria related to a Class II/2.<sup>53,54</sup> Angle originally described a Class II/2 as molar distocclusion in combination with incisor retroclination.<sup>55</sup> Whilst the latter part of this definition seems agreed upon, the other characteristics of this malocclusion are varied and consensus about the growth pattern and morphology of a Class II/2 is lacking.<sup>56</sup> Furthermore, nearly all of the Class II/2 growth research has been cross-sectional in design and few longitudinal investigations exist.<sup>9,57</sup>

The discrepancies between the findings of various studies on Class II/2 growth have been well recognised.<sup>56</sup> The only common finding of the cited Class II/2 investigations appears to be upper incisor retroclination. This is not surprising since this represents the common inclusion criterion of subjects participating in these studies. It has been proposed that hypo-occlusion of the posterior segments causes excessive resting upper lip pressure against the upper incisors resulting in their retroclination.<sup>58</sup> The resulting influence of the upper incisor on the position of the mandible has been the subject of ongoing debate,<sup>59</sup> with some suggesting that the mandible is forced into a posterior position from upper incisor retroclination,<sup>60</sup> while others dispute this hypothesis.<sup>59,61</sup> Another perspective is that a deep overbite in a Class II/2 restrains the mandibular dentition from growing forward with the basal bone.<sup>54,56</sup>

Individuals who are Class II/2 do not show the characteristic upper arch constriction observed in a Class II/1.<sup>52,62-64</sup> The majority of growth studies suggest that a Class II/2 is characterised by a

normal maxilla<sup>9,65-67</sup> and variable mandibular size.<sup>9,57</sup> Alternative studies have shown a tendency for a small<sup>53,65,67</sup> and/or retropositioned mandible<sup>64,66,67</sup> whilst others report that mandibular size and position is comparable with Class I individuals.<sup>57,65</sup> Notably, Lux et al. found in their comparison of Class II/I and Class II/2 malocclusions that differences in mandibular size depended upon which geometric plane of reference was used for the cephalometric measurements.<sup>32</sup>

There is a tendency for a decreased lower anterior face height in Class II/2,<sup>9,57,64</sup> although this is not a universal finding.<sup>53,66,67</sup> The few published longitudinal studies have shown a vertical deficiency that is evident in childhood and the production of smaller increments of vertical growth throughout adolescence.<sup>9,57</sup> These studies<sup>9,57</sup> have also demonstrated a more acute gonial angle, which also agrees with reported cross-sectional data,<sup>9,65,68</sup> as well as studies showing a pronounced forward mandibular rotation.<sup>14,49,54</sup> Consequently, characteristic profile features of a Class II/2 include a well-defined chin<sup>64,65</sup> and putting of the lips with a tendency towards lower lip eversion.<sup>56</sup>

In light of these findings, authors have proposed that the Class II/2 is a distinct entity characterised by a skeletal pattern somewhere between a Class I and Class II/1, and a tendency toward hypodivergence.<sup>54,64,65</sup> Others have suggested that incisor inclination is the only feature that distinguishes a Class II/2 from a Class I,<sup>66,67</sup> or a Class II/1.<sup>53</sup>

### ***Class III***

Longitudinal growth studies of Class III individuals have traditionally been lacking due to the relatively low incidence of this occlusion in Caucasian populations and the propensity to treat Class III patients early. As for Class II/2, the majority of Class III growth studies have been cross-sectional in design and require inferences from population averages.

Although there has been a historical trend to make a Class III malocclusion synonymous with mandibular prognathism,<sup>69</sup> a deficient, or retropositioned, maxilla may also be the cause.<sup>70,71</sup> Similar to a Class II/1, cranial base morphology has been implicated in the Class III phenotype. Shorter anterior cranial base lengths have been associated with midface deficiency and an acute cranial base angle.<sup>70,72</sup> A more anteriorly placed glenoid fossa<sup>33,73,74</sup> has been associated with

mandibular prognathism. Whilst these distinctions are important from the point of view of appreciating the possible aetiology of a Class III malocclusion, the distinction between length versus a positional discrepancy seems to have little bearing on therapeutic considerations in true skeletal Class III cases.

Longitudinal<sup>75</sup> and cross-sectional data<sup>69,74,76-78</sup> show that a Class III skeletal pattern is established early in life, although the sagittal differences between Class I and Class III may not be distinct in facial patterns with vertical excess.<sup>78</sup> The growth pattern of a Class I and Class III is not dissimilar, in the sense that the maxillary position tends to maintain a stable position over time,<sup>69,72,77,79</sup> regardless of whether it is classified as 'normal'<sup>72</sup> or 'retrusive',<sup>75-77</sup> and mandibular growth accounts for a worsening of profile concavity.<sup>71,72,80-83</sup> When present, maxillary hypoplasia appears to be multidimensional, since transverse<sup>75</sup> and vertical deficiencies have also been reported in Class III individuals.<sup>69,76,77</sup>

While the mandibular growth peak in Class III subjects occurs around the same time as Class I individuals, it is typically longer in duration and more intense.<sup>77,79</sup> Rapid mandibular growth has been observed well into Cervical Stage 6, with gains in length of over 6 mm per year for males and 4 mm for females during this time.<sup>72,77</sup> Although these observations are limited by their cross-sectional nature, a longer and more intense mandibular growth spurt in Class III cases is consonant with clinical experience.

A tendency toward a more vertical growth pattern in Class III individuals has also been reported,<sup>69,71,75-77,83</sup> although, in some cases, a vertical growth pattern may effectively mask a prognathic mandible.<sup>83</sup> Similarly, incisor angulations may also mask the skeletal disharmony in Class III cases.<sup>84</sup>

### ***Methodological limitations of growth research***

The above discussion has presented key findings reported in the literature, which distinguish the growth patterns of different facial types. Studies have not always agreed on where these differences lay, and the possible reasons for this are important to consider.

One major cause for discrepancies is the comparison of cross-sectional and longitudinal data. It has been shown that longitudinal and cross-sectional analysis of the same population leads to different conclusions.<sup>44</sup>

Cross-sectional studies involve comparing different individuals at different stages during growth by using averages. Whilst this methodology makes it easier to evaluate a larger sample size, interpretation is confined to inferences between growth stages and only tends to detect significant changes.<sup>44</sup> Alternatively, longitudinal data allows a clearer examination of the growth trajectory since data are gathered on the same individuals. However, ethical issues surrounding radiation exposure means that longitudinal studies are now largely confined to historical populations, who are mostly Caucasian and may not be representative of contemporary populations (discussed below).

Recent research has also suggested that many growth studies may have been underpowered. This was highlighted by Yoon and Chung, who calculated that a sample size of between 79 and 143 individuals was required for their longitudinal growth study. Unfortunately, this was a size beyond the number of subjects available to the authors, and is significantly larger than sample sizes in previously-published studies.<sup>85</sup>

Growth research has also suffered from a general trend of relying on dental inclusion criteria to provide a sample for analysis. The assumption that a malocclusion is representative of an underlying skeletal base dates back to Edward Angle.<sup>86</sup> Although lateral cephalometry has subsequently shown that this is not always true,<sup>87</sup> a considerable amount of growth research has continued on this assumption. For example, a Class II/1 malocclusion may not necessarily have a skeletal component,<sup>51</sup> and the number of dental Class II patients who also have a skeletal Class II has been estimated to be around 75%.<sup>4</sup> Similarly, the Class III malocclusion has at least three distinct skeletal subtypes<sup>69</sup> that can all present with a reverse overjet. A reverse overjet may also arise from a functional shift (pseudo-Class III), in which case the underlying skeletal base could be Class I, II or III (Figure 1). Therefore, using overjet as an inclusion criterion in either a Class II/1 or a Class III growth study makes it difficult to draw meaningful conclusions, since it is difficult to be certain of the skeletal patterns under examination. A similar criticism has been made of randomised controlled trials (RCT) of Class II treatment.<sup>88</sup> A summary of the limitations of growth research is presented in Table I.



Figure 1. Each of the patients shown above have a reverse overjet of 3 mm but different growth patterns.

Table 1. Limitations of growth research.

Study Aspect	Description
Inclusion criteria	Dental versus skeletal discrepancies
	Phenotypic variation within the same malocclusion category
	Variations in vertical growth pattern
	Chronological versus skeletal age
	Ethnic variations
	Exclusion of severe cases
Study design	Secular trends
	Cross-sectional versus longitudinal data
	Varying observation periods
	Insufficient sample size
Data analysis	Cephalometric tracing error
	Variation in cephalometric analyses

### ***The use of historical controls in orthodontic research***

Historical facial growth studies have also found application in the creation of historical control groups (HCG) in orthodontic research. A control group in medical research provides a standard against which a therapy can be evaluated.<sup>89</sup> Whilst this is ideally achieved through a prospective and randomised

allocation of subjects to either the control or intervention,<sup>90</sup> ethical and practical constraints (e.g., radiation exposure and the withholding of treatment) have meant that this is not often possible in the modern context. In the past few years HCG data have become freely available online via the Craniofacial Growth Legacy Collection of the American Association of Orthodontists Foundation (AAOF).<sup>91</sup>

The use of HCG in medicine has been mooted for almost half a century.<sup>92</sup> Although there has been a modest increase in orthodontic randomised controlled trials in recent times,<sup>93</sup> the use of HCG in orthodontics is still relatively common.<sup>94</sup> As the profession shifts towards an 'evidence-based' paradigm, there has been a natural interest in evaluating treatment outcomes,<sup>95</sup> which may account for the continued popularity of the HCG in orthodontic research.

For a control group to be valid, it must be comparable with the intervention group with respect to all prognostic factors.<sup>96</sup> Therefore, the relevant prognostic factors of facial growth include maturation stage, gender and ethnicity, as well as the vertical and sagittal skeletal pattern. Nevertheless, studies using HCG have not always matched ethnicity,<sup>97</sup> or they have used the occlusion as an indicator of the skeletal pattern,<sup>98,99</sup> or chronological age as an indicator of maturity.<sup>100</sup> Furthermore, even if it was feasible to

match control and intervention groups for all relevant growth variables, the problem of secular changes would remain. Craniofacial morphology appears to be more prone to secular trends than the other bones in the body.<sup>101,102</sup> Antoun et al. recently measured the cephalometric records of 138 adolescents from multiple growth collections over three generations in the AAOF Legacy Collection, and found a general increase in the size of the maxilla and cranial base with a concomitant reduction of the ANB angle.<sup>103</sup> Although no significant trends in mandibular length were detected, other research has pointed to a tendency towards a longer and narrower mandible noted in the first half of the twentieth century,<sup>104</sup> and an earlier onset of peak mandibular growth.<sup>102</sup>

An additional requirement for control group validity is a random selection of all the potentially available patients.<sup>96</sup> Although it is speculative to consider whether historical participants were a random selection of their contemporaries, within the study design eligible subjects should ideally be chosen in a random fashion from a database. Unfortunately, however, studies generally do not specify how the HCG was constructed beyond the inclusion criteria and name of the database(s) used. No doubt this reflects the limited availability of suitably matched controls. However, it does open the process to a selection bias that is difficult to quantify.

A final consideration is that the magnitude of the observed effects in orthodontic research is typically small. In general, the lesser the treatment effect observed, the greater the potential influence of bias on the outcome of the study.<sup>105</sup> Orthodontic research often hinges upon observations that are a few millimetres or degrees, which may not be much larger than the potential measurement error. Hence, if inherent biases existed in the control group, the outcomes of interest may be particularly vulnerable to the effects of these biases.

In view of these limitations, it is not surprising that Papageorgiou et al. have recently shown that HCG in orthodontic research does indeed bias results.<sup>94</sup> Unlike the effect of HCG in medicine<sup>106</sup> however, the direction of the bias is towards a lesser treatment effect. Notably, the HCG studies included in Papageorgiou's meta-analysis were typically well matched for key factors, such as skeletal base and ethnicity.<sup>107-116</sup> Furthermore, the negative bias introduced by the HCG was found to exist even when a retrospective study design

was used, which itself tends to bias results in favour of therapy.<sup>117</sup> Whilst the reason for the negative direction of this effect remains unclear, these results suggest that readers should be cautious in how they interpret the findings of research using HCG.

## Conclusion

The present review has provided a summary of the characteristic features of Class I, Class II/1, Class II/2 and Class III growth as presented in the literature, and has considered some of the limitations associated with growth research in orthodontics. Although it is possible to create a general picture of the differences in the respective growth patterns, methodological and practical limitations associated with growth research have, at times, led to contradictory findings that make it difficult to obtain a detailed understanding and draw firm conclusions. Additionally, recent evidence has cast doubt on the validity of HCGs in orthodontic research generally, and so the conclusions drawn from such studies need to be viewed accordingly.

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