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## **Coordinatore: Prof. Sandro Rengo**

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# Craniofacial growth rates of individuals of different centuries: a case-control study

RELATORE

CANDIDATO

Chiar.ma Prof. Rosa Valletta

Dott. Stefano Martina

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#### Abstract

OBJECTIVE: The aim of the study is to describe secular changes in mandibular growth comparing a historical group of non-treated subjects from AAOF legacy, used as control group in many cross-sectional studies on craniofacial skeletal growth, with a contemporary group of similar subjects.

MATERIALS AND METHODS: The subjects group of historical controls from Bolton-Brush Growth Collection were matched for sex, age and race with subjects from a contemporary control group. Two examiners performed all of the cephalometric measurements at  $T_0$  and  $T_1$  (12 months later) according to Pancherz's method using Dolphin Imaging 11.0 software. Data were analysed by conventional descriptive statistics.

RESULTS: The mandibular increment in contemporary group is significantly higher than in the historical group (p=0.03). The dental values are also statistically higher in contemporary group, whilst for the other values there is not a significant increase.

DISCUSSION: The results confirm the secular trends in craniofacial growth already described by other authors using anthropometry and cephalometric analysis. Add to this, there are some limitations in using the historical controls, resulting from difficulty to make a diagnosis of skeletal class II having only cephalometric data.

CONCLUSIONS: An increased growth trend in contemporary subjects compared with historical controls is confirmed. The clinical trials using as controls individuals from historical collection could not have validity. There is need for further research to verify secular trends of growth on larger samples.

#### Introduction

One of the most controversial topic in orthodontics is still the treatment approach to Class II patients. The source of these controversies is related both to the field of diagnosis and, as a consequence, to the field of treatment strategy.

The most common and used diagnostic tool, the cephalometric analysis, whatever the used method, presents an insufficient reliability in assessing upper and lower jaw sagittal position and relationship. As an example the popular values of Steiner analysis, SNA and SNB angles have been largely re-evaluated, because of Nasion position changes; these changes can influence the amount of the SNA, SNB, and ANB angles, making impossible to determine the type of skeletal imbalance in Class II patients (1). For the same reason Ricketts cephalometric analysis fails in assessing sagittal discrepancy. Jacobson proposed the so called Wits Appraisal in order to eliminate the use of point Nasion, but the variability of occlusal plan inclination could influence even more the assessment of anteroposterior jaw relationship (2,3).

As matter of fact, the more common outcome of cephalometric analysis of Class II patients is a diagnosis of upper jaw protrusion. On the contrary the majority of patients diagnosed as dental and skeletal Class II, according to studies performed by many authors (4-6), present a mandibular retrusion rather than an upper maxilla protrusion.

The treatment strategy in patients with mandibular retrusion should be the correction of dental and jaw sagittal relationships by advancing the mandible (7,8) rather than by distalizing the upper jaw and/or dentition. As matter of fact this treatment approach should also improve the impaired facial profile (9,10).

In growing patients, this objective may be obtained by the use of functional appliances that posture the mandible forward and thus stimulate supplementary mandibular growth (11-14).

Then our focus inevitably shifts on mandibular growth. Our knowledge of mandibular growth patterns mostly derives from cephalometric radiography studies.

The radiographic cephalometrics were introduced in 30's by Hofrath in Germany and Broadbent in the United States provided both a research and a clinical tool for the study of malocclusion and underlying skeletal disproportions. The original purpose of cephalometrics was research on growth patterns in the craniofacial complex (15).

For this reason, since the early 30's it was possible to monitor the craniofacial growth through cephalograms repeated at regular intervals of time, producing accurate longitudinal data. Much of the current picture of craniofacial growth is based on cephalometric studies.

In some of the major universities of US and Canada there are a number of longitudinal collections of x-ray images and other physical records of craniofacial development of growing children with malocclusions who did not receive orthodontic treatment. The longitudinal records were acquired during a historically brief window in time roughly between 1930 and 1985. Yet well before the end of the 20th century the continued gathering of such information from untreated children was precluded by the recognition of the possibility of deleterious effects from the excessive use of ionizing radiation for diagnostic purposes. Clearly longitudinal studies of this kind can never be repeated (16).

It is well known that the best scientific evidence should be provided by a systematic review of randomized clinical trials (17).

A recent literature review of these studies with the objective of evaluating the quality of RCT abstracts with reference to the CONSORT guidelines (18) in 4 leading orthodontic journals showed that the quality is suboptimal. In particular there's a lack of information on randomization procedures, allocation concealment, blinding, reporting of results and methods of data analysis (19).

On the other side there is a spread opinion that RCT are too costly and eventually not able to provide crucial evidence in this field of research (20).

As a consequence, several clinical trials designed to investigate the efficacy of growth modification appliances used and still use historical controls from large-scale growth studies of the past century instead of randomized concurrent controls (21-29).

The results of these clinical trials testing the efficacy of functional appliances are not consistent and it could be partly explained by the inclusion of historical controls in the studies and by the encouragement of *post-hoc* deductions (20).

In fact, the size of the human body has undergone considerable change as a result of secular trends (30); from the 30s to today, the overall mean values of height and weight in children increased (31). Consistently with findings, several recent investigations identified notable secular change in tooth size (32-34), malocclusion severity (35) and in cranial size and morphology over the last century (36,37). Jantz and Jantz argued that these changes have resulted from primarily environmental factors. During the last century, nutritional quality has increased, medical care has improved and physical activity has decreased, allowing the body more time and more favorable conditions for growth (38). Indeed, secular trends in craniofacial growth determined a significant mandibular length increase of Caucasians over a 50-year time span; more specifically, the mandible seems to have become longer, while the height and breadth of its *corpus* became progressive smaller (39).

All these data seem to make questionable the use of historical controls for comparisons with contemporary patients (40).

The purpose of this study was to describe secular changes that might have occurred in the mandibular growth pattern in two cohorts of contemporary and historical controls of Class II subjects. The null hypothesis is that there is no significant difference between the two groups, thus the values of mandibular growth increment reported in cross-sectionals studies with historical controls could be validated.

#### **Materials and methods**

The study is designed as a retrospective case control study.

The designed groups were two:

- The contemporary group with patients screened by two specialists in orthodontics (RM and RT) at the Department of Oral Sciences, Section of Orthodontics, University of Naples Federico II, Italy, between April 2006 and June 2007. The patients were considered eligible when they presented a full class II molar relationships, overjet>6 mm, an age range of 9-14 years for boys and of 8-12 years for girls and an informed consent form signed by the parents.

- The historical group with subjects collected from the Bolton-Brush Growth Collection of AAO legacy online database (<u>http://www.aaoflegacy-collection.org</u>) and matched for age (±1), sex and race with the contemporary group.

The following conditions were considered as further exclusion criteria: cervical vertebral maturation stage (CVMS) <2 or >3 (41), Sella-Nasion to mandibular plane (Me-Go) angle  $\geq$  normal value plus a standard deviation (42), periodontal diseases, orofacial inflammatory conditions, tooth agenesis, congenital syndromes, and previous orthodontic treatment.

The objective of the cephalometric analysis was to assess the dentoalveolar, sagittal, and vertical changes of the participants. Lateral standardized cephalograms in the intercuspal position were obtained. The cephalograms were taken in centric relation at the start ( $T_0$ ) and at the end of control period (12 months,  $T_1$ ).

The cephalometric landmarks, lines, and measurements were:

#### Landmarks:

ANS (anterior nasal spine), the tip of the anterior nasal spine;

Ba (basion), the midsagit- tal point of the anterior margin of the foramen magnum;

Co (condyle), most superoposterior point on the curvature of the condylar head; where there was a double projection to two points, the midpoint was used;

ii (incision inferius), incisal tip of the most prominent mandibular central incisor;

is (incision superius), incisal tip of the most prominent maxillary central incisor;

mi (molar inferius), distal contact point of the mandibular permanent first molar determined by a tangent perpendicular to the occlusal line (OL) - where there was a double projection to two points, the midpoint was used;

ms (molar superius), distal contact point of the maxillary permanent first molar determined by a tangent perpendicular to the OL - where there was a double projection to two points, the midpoint was used;

Pg (pogonion), most anterior point on the bony chin determined by a tangent perpendicular to the OL;

Ss (subspinale), deepest point on the anterior contour of the maxillary alveolar projection;

Sella (S), center of the hypophyseal fossa;

N (Nasion), most anterior point of the junction of the nasal and frontal bone (frontonasal suture);

Or (Orbitale), lowest point of the inferior margin of the orbit;

Po (Porion), most superior point on the anatomical external auditory meatus;

Go (Gonion), midpoint of the curvature at the angle of the mandible;

Me (Menton), most inferior point of the mandibular symphysis;

PNS (posterior nasal spine): the tip of the posterior nasal spine;

T (T point), most superior point of the anterior wall of the sella turcica at the junction with the tuberculum sella.

Two examiners performed all of the cephalometric measurements using Dolphin

Imaging 11.0 software (Chatsworth, CA, USA).

The reference points and lines used are:

Reference lines:

FH (Frankfurt horizontal), line connecting the P point to the Or point;

MP (mandibular plane), line connecting the Me point to the Go point;

SN (sella nasion line), line through S and N;

OL (occlusal line), line through the is point and the distobuccal cusp of the maxillary permanent first molar;

OLp (occlusal line perpendicular), line perpendicular to the OL through the T;

PP (palatal plane), line connecting ANS and PNS.

Linear distances/skeletal landmarks:

Ss/OLp, position of the maxillary base;.

Pg/OLp, position of the mandibular base;

Co/OLp, position of the condylar head;

Pg/OLp + Co/OLp, sagittal mandibular length.

Linear distances/dental landmarks:

is/OLp, position of the maxillary central incisor;

ii/OLp, position of the mandibular central incisor;

ms/OLp, position of the maxillary permanent first molar;

mi/OLp, position of the mandibular permanent first molar

following Pancherz's method (43).

Variables for dental changes within the maxilla and within the mandible were

calculated as follows:

is/OLp minus Ss/OLp, change in position of the maxillary central incisor within the maxilla.

Ii/OLp minus Pg/OLp, change in position of the mandibular central incisor within the mandible.

Ms/OLp minus Ss/OLp, change in position of the maxillary permanent first molar within the maxilla.

Mi/OLp minus Pg/OLp, change in position of the mandibular permanent first molar within the mandible.

For all of the linear measurements, the OL and the OLp of the initial radiograph were used as a reference grid. The grid was then transferred from the  $T_0$  to the  $T_1$  radiograph by superimposing on the Nasion–T point line, with the T point as the registering point. All of the measurements were made parallel to the OL. Differences in  $T_1$ – $T_0$  linear measurements were recorded according to Pancherz's method (43).



The examiner had been extensively trained in electronic cephalometric analysis and was blinded to the patients' name and allocation. The dates of the radiographs were also concealed from the examiner during the measurements.  $T_0$  and  $T_1$ radiographs were randomly submitted to the examiner. The cervical stage was determined on the  $T_0$  cephalogram by the same examiner according to the cervical vertebral maturation (CVM) method for the assessment of skeletal growth (41).

For the cephalograms of historical group, the scale of the image was provided by AAO Legacy. In the Bolton-Brush Growth Collection scaled measurements can be determined with four *fiducials*, reference marks embedded in the digital images, usually one at each corner. The cephalograms had a magnification of 6%, thus we considered that in the calculation of cephalometric values.

Data were analysed by conventional descriptive statistics. Absolute cephalometric changes were converted to relative changes over a 15-month period. A Shapiro-Wilk test to evaluate if the samples are normally distributed was performed. Between-group differences will be compared by means of parametric unpaired samples t-test and non-parametric statistic Mann-Whitney U test. Intra-group differences will be compared by means of parametric paired t-test of non-parametric statistic Wilcoxon signed-rank test. If the analysed variables had a Gaussian distribution we considered the p-value of parametric tests, if the distribution was asymmetric we considered the p-value of non-parametric tests.

The primary outcome was sagittal mandibular length (Pg/OLp + Co/OLp) changes. Secondary outcomes was dental relationship changes, changes in the position of the upper maxilla, and changes in divergence of the jaws.

A single operator who was blinded to patient allocation (i.e. the allocation was masked to him in the dataset) performed the statistical analyses. Statistical significance was set at p<0.05. All of the analyses were performed with commercial software (SPSS version 20.0, SPSS IBM, New York, NY).

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#### Results

Of the 110 individuals screened in our Department, 30 individuals were allocated to contemporary group; 7 individuals were lost to follow up.

Of the 23 subjects collected for the historical group, 3 were excluded for scaled measurements discrepancies between cephalograms in  $T_0$  and  $T_1$ , thus we had to exclude the 3 matched subjects of contemporary group.

The final sample comprised 20 subjects (12 boys, 8 girls, mean age $\pm$ SD = 10.4 $\pm$ 1.31) in the contemporary group and 20 subjects (12 boys, 8 girls, mean age $\pm$ SD = 10.3 $\pm$ 1.34) in the historical group.

Skeletal and dental measurements at  $T_0$  and  $T_1$  and their relative changes over time are reported in Table 1.

The mean values in skeletal and dental linear measurements are higher in the contemporary group compared with the historical. In particular, in either groups there is a significant mandibular increment between  $T_0$  and  $T_1$  (p<0.001), but the increase of mandibular length (Pg/OLp + Co/OLp) in the contemporary group are significantly higher than in the historical group (p=0.03). As regards the maxillary protrusion (A/ OLp) there is no significative difference between the increases of A-point growth in the historical and the contemporary group, though there is a major trend of growth in the second one. The positions of maxillary (is/OLp) and mandibular (ii/OLp) incisors are significantly different in the two groups (p<0.01), as well as maxillary (ms/OLp) and mandibular (mi/OLp) molars (p=0.006, p=0.01).

There are no significant differences in the angular values of mandibular divergence (SN-MP, MP-FH, PP-MP) between the two groups.

It was performed a *post-hoc* power analysis using as the main variable "mandibular increment" obtaining as result  $\beta = 44\%$ .

Measurement	Group H n=20 Group C n=20	$T_0$ (mean $\pm$ SD)	$T_{I}$ (mean ± SD)	$T_{I}-T_{0}$ (mean ± SD) -15 months -	T-Test unpaired data P between groups	Mann- a Whitney Test P between groups
Mandibular base (Pg/OI n)	н	70 2 + 4 7	71 7 + 6 4***	20 + 22		
	C	$68.8 \pm 6.0$	$71.8 \pm 4.1^{***}$	$3.5 \pm 1.6$	0.014	0.003
Condylar head (Co/OLp)	Н	$11.2 \pm 1.8$	$11.4\pm2.0$	$0.2 \pm 1.2$	0.604	0.(2)
	С	$14.9 \pm 3.5$	$14.8 \pm 3.5$	$-0.3 \pm 1.7$	0.604	0.626
Mandibular length (Pg/OLp + Co/OLp)	Н	$81.4 \pm 4.8$	$83.2 \pm 4.3^{***}$	$2.2 \pm 2.0$		
	С	83.7 ± 5.2	86.6 ± 6.2***	$3.5 \pm 2.4$	0.066	0.030
Mandibular heigth (Co – Go)	Н	$45.4 \pm 3.4$	$47.8 \pm 2.8^{***}$	$2.7 \pm 2.3$		0.465
	С	$49.8 \pm 4.2$	$51.5 \pm 4.9^{**}$	2.2 ± 3.1	0.587	0.465
Mandibular length (Co – Pg)	н	94 9 + 4 7	97 2 + 4 3***	29+27		
Multiloului longui (ee 19)	C	$99.6 \pm 5.1$	$102.8 \pm 5.8^{***}$	$3.9 \pm 2.7$	0.238	0.152
Maxillary protrusion (A/OLp)	Н	$67.2 \pm 4.0$	$68.7 \pm 3.8^{***}$	$1.8 \pm 1.7$		
	С	$69.1\pm3.0$	$71.2 \pm 4.7$ ***	$2.7\pm2.6$	0.203	0.387
Maxillary incisor (is/OLp)	Н	$73.9\pm4.8$	75.1 ± 4.6**	$1.4 \pm 1.9$	0.002	0.001
	С	77.0 ± 5.5	80.0 ± 6.2***	$3.7 \pm 2.4$	0.002	0.001
Mandibular incisor (ii/OLp)	Н	$68.8 \pm 4.7$	$69.8 \pm 4.2^{*}$	$1.3 \pm 2.2$		
	С	69.7 ± 5.5	$72.3 \pm 6.1^{***}$	$3.2 \pm 2.3$	0.009	0.002
Maxillary molar (ms/Olp)	Н	$33.4 \pm 3.7$	$34.7 \pm 3.7^{***}$	$1.6 \pm 1.3$		
	С	35.1 ± 4.3	$37.6 \pm 4.7^{***}$	2.9 ± 1.5	0.006	0.006
				10 - 10		
Mandibular molar (mi/OLp)	H C	$32.7 \pm 3.7$ $33.0 \pm 4.6$	$34.2 \pm 3.6$	$1.9 \pm 1.8$ 2.8 + 1.2	0.084	0.014
	e	55.0 - 4.0	55.5 ± 5.2	$2.0 \pm 1.2$		
SN-MP (°)	Н	30.4 ± 3.8	$30.4 \pm 4.1$	$0.3 \pm 2.3$		
	С	$30.0\pm5.7$	$30.1 \pm 4.9$	$0.4 \pm 2.6$	0.991	0.903
MP-FH (°)	Н	$22.5\pm3.7$	$22.6 \pm 3.3$	$0.3 \pm 2.3$		
	С	22.6 ± 4.7	$22.2 \pm 4.4$	$-0.3 \pm 2.3$	0.638	0.387
				A		
PP-MP (°)	H C	$27.9 \pm 3.5$ $25.7 \pm 5.1$	$27.7 \pm 3.4$ $25.1 \pm 5.3$	$0.2 \pm 2.9$ -0.9 ± 2.5	0.38	0.482
	-					

# Table 1. Cephalometric measurements before $(T_0)$ and at the end $(T_1)$ of observation periods.

Descriptive statistics for the variables examined and intra-group and between-group (Historical vs. Contemporary) statistical comparisons. Absolute cephalometric changes (T1-T0) are converted to relative changes over a 15-month period (see statistical methods). Linear measurements are in mm. Significance level was set at p < 0.05.

Bold type: statistically significant.

The stars indicate the statistical significance intra-group:

\* = p < 0.05 \*\* = p < 0.01 \*\*\* = p < 0.001

#### Discussion

The aim of this study was to evaluate retrospectively the craniofacial growth changes between individuals from a historical control group and contemporary controls.

The Bolton-Brush Growth Collection was chosen among available collections of AAOF legacy because comprises the world's most extensive source of longitudinal human growth data (44). As all the subjects included were from the 30's, we were able to compare two groups with an interval of eighty years.

We have to underline that the subjects of AAO legacy growth collections are classified according to Angle's occlusal molar relationship. But Class II molar relationships may be not necessarily the consequence or the sign of a Class II skeletal pattern (45). Moreover, we have already underlined that most cephalometric data do not allow to obtain a specific diagnosis of Class II skeletal component.

On the otherside the contemporary group was selected as a group of subjects with skeletal Class II due to mandibular retrusion. An aesthetic evaluation of the profile was used, performing the so called Fränkel maneuver (46,47). The patients were asked to posture the mandible forward until a class I molar relationship was achieved. Subjects that worsen their profile during the Fränkel maneuver were supposed to advance the mandible to reach a protruded upper jaw determining, as a consequence, a bimaxillary protrusion. Subjects that improved their profile during the Fränkel maneuver are supposed to advance the mandible to reach a normal positioned upper jaw. That means that the forward posture of the mandible during the Fränkel maneuver normalized the position of an originally retruded mandible. A study performed in our department proved that Fränkel maneuver is reproducible and is not influenced by the level of clinical experience since substantial inter-observer and intra-observer agreement were found.

According to this including criterium the contemporary group should be considered a skeletal Class II subjects group with mandibular retrusion.

The comparison between groups (Table 1) confirms the growth trends already highlighted by other authors using anthropometry (36-38). In fact, skeletal mean dimensions were higher in the contemporary group. In particular the mandible length (Pg/OLp + Co/OLp) was greater both at  $T_0$  and at T1. It is also remarkable that the growth increment in the studied interval (12 months) was significantly higher (p=0.03) in the contemporary group compared to the historical one. We have also to remind that Stahl et al. showed that skeletal Class II subjects present an average mandibular growth reduced if compared with Class I subjects (48) and we have already mentioned that the contemporary group included only skeletal Class II subjects while the historical one is selected by the molar relationship.

Although many studies on secular trends in craniofacial morphology have been published, almost all of them used anthropometric and craniometric measurements (36-39) (49,50). Therefore there is a lack of studies that analize cephalometric values. A research of the University of Otago, that will be soon published on the European Journal of Orthodontics, matched several historical controls from different AAOF legacy collection of different decades of last century. The results showed that secular trends do affect cephalometric values in a direction consistent with our data.

According to the data of present research it seems possible that the internal validity of clinical trials that used historical control groups to evaluate treatment effects in contemporary patients should be carefully re-evaluated. It is possible that discrepancy in findings between RCTs and CCTs (51) is partly due to the effects of secular trends in historical control samples.

More research is certainly needed to confirm these conclusions. First of all, a more indepth study is required recruiting larger samples to increase the statistical power. Jointly a wider analysis should be carried out including other collection from AAOF legacy in the study to verify the same growth trends.

### Conclusion

An increased growth trend in contemporary subjects compared with historical controls is confirmed.

Within the limitations of the present study, it can be concluded that the clinical trials using as controls individuals from historical collection could not have validity.

There is need for further research to verify secular trends of growth on larger samples.

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#### References

1.Pancherz H, Sack B. A critical analysis of the SNA, SNB and ANB angles in assessing orthodontic treatments. Fortschr Kieferorthop.1990; 51: 309-317.

2.Martina R, Bucci E, Gagliardi M, Laino A. Relation between the value of the Wits Appraisal and the inclination of the occlusal plane]. Minerva Stomatol. 1982; 31: 385-389.

3.Del Santo M Jr. Influence of occlusal plane inclination on ANB and Wits assessments of anteroposterior jaw relationships. Am J Orthod Dentofacial Orthop. 2006; 129: 641-648.

4.McNamara JA Jr. Components of class II malocclusion in children 8-10 years of age. Angle Orthod 1981; 51: 177–202.

5.McNamara JA Jr, Peterson JE Jr, Alexander RG. Three-dimensional diagnosis and management of Class II malocclusion in the mixed dentition. Semin Orthod. 1996; 2: 114-137.

6.Ngan PW, Byczek E, Scheick J. Longitudinal evaluation of growth changes in Class II division 1 subjects. Semin Orthod. 1997; 3: 222-231.

7.Cozza P, Baccetti T, Franchi L, De Toffol L, McNamara JA Jr. Mandibular changes produced by functional appliances in Class II malocclusion: a systematic review. Am J Orthod Dentofacial Orthop. 2006; 129: 599. e1-12.

8.Tadic N, Woods M. Contemporary Class II orthodontic and orthopaedic treatment: a review. Aust Dent J. 2007; 52: 168-174.

9.Shaw WC. The influence of children's dentofacial appearance on their social attractiveness as judge by peers and lay adults. Am J Orthod 1981; 79: 65: 399-415.

10.Quintão C, Helena I, Brunharo VP, Menezes RC, Almeida MA. Soft tissue facial profile changes following functional appliance therapy. Eur J Orthod. 2006; 28: 35-41.

11.McNamara JA Jr. On the possibilities of stimulating mandibular growth. In: Graber LW, ed. Orthodontics: State of the art, essence of the science. St Louis: Mosby, 1986.

12.Petrovic AG, Stutzmann JJ, Lavergne JM. Mechanisms of craniofacial growth and modus operandi of functional appliances: A cell-level and cybernetic approach to orthodontic decision making. In: Carlson DS, ed. Craniofacial growth theory and orthodontic treatment. Monograph 23: Craniofacial growth series. Ann Arbor: The University of Michigan, 1990: 13-70.

13.Collett AR. Current concepts on functional appliances and mandibular growth stimulation. Aust Dent J. 2000; 45: 173-178.

14.Martina R, Cioffi I, Galeotti R, Tagliaferri R, Cimino R, Michelotti A, Farella M, Paduano S. Efficacy of the Sander bite-jumping appliance in growing patients with mandibular retrusion: a randomized controlled trial. Orthod Craniofac Res. 2013 May; 16(2): 116-126.

15.Proffit WR, Fields HW, Sarver DM. Contemporary Orthodontics 4th Edition. Mosby-Elsevier;2007.

16.AAOF Project History. aaolegacycollection.org ; 2010.

17.Pocock SJ. Clinical Trials – A Practical Approach. Chichester: John Wiley & Sons Ltd; 1996.

18.Turpin DL. CONSORT and QUOROM guidelines for reporting randomized clinical trials and systematic reviews. Am J Orthod Dentofacial Orthop 2005; 128: 681-685.

19.Fleming PS, Buckley N, Seehra J, Polychronopoulou A, Pandis N. Reporting quality of abstracts of randomized controlled trials published in leading orthodontic journal from 2006 to 2011. Am J Orthod Dentofac 2012; 142: 451-458.

20.Meikle MC. Guest editorial: what do prospective randomized clinical trials tell us about the treatment of class II malocclusions? A personal viewpoint. Eur J Orthod. 2005; 27: 105-114.

21.Baccetti T, Franchi L, Stahl F. Comparison of 2 comprehensive class II treatment protocols including the bonded Herbst and headgear appliances: a double-blind study of consecutively treated patients at puberty. Am J Orthod Dentofac 2009; 135: 698-699.

22.Baccetti T, Franchi L, Toth LR, McNamara JA. Treatment timing for Twin-block therapy. Am J Orthod Dentofac 2000; 118: 159-170.

23.Faltin K Jr, Faltin RM, Baccetti T, Franchi L, Ghiozzi B, McNamara JA Jr. Long-term effectiveness and treatment timing for Bionator therapy. Angle Orthodontist 2003; 73: 221-230.

24.Flores-Mir C, Barnett G, Higgins DW, Heo G, Major PW. Short-term skeletal and dental effects of the Xbow appliance as measured on lateral cephalograms. Am J Orthod Dentofac 2009; 136: 822-832.

25.Toth LR, McNamara JA. Treatment effects produced by the Twin-block appliance and the FR-2 appliance of Fränkel compared with an untreated class II sample. Am J Orthod Dentofac 1999; 116: 597-609.

26.Mills CM, McCulloch KJ. Posttreatment changes after succesful correction of class II malocclusion with the Twin block appliance. Am J Orthod Dentofac 2000; 118: 286-295.

27.Franchi L, Baccetti T, McNamara JA, Jr. Treatment and posttreatment effects of acrylic splint Herbst appliance therapy. Am J Orthod Dentofac 1999; 115: 429-438.

28.Freeman DC, McNamara JA, Baccetti T, Franchi L, Fränkel C. Long-term treatment effects of the FR-2 appliance of Fränkel. Am J Orthod Dentofac 2009; 135: 570 e1-e6.

29.McNamara JA, Howe RP, Dischinger TG. A comparison of the Herbst and Fränkel appliances in the treatment of class II malocclusion. Am J Orthod Dentofac 1990; 98: 134-144.

30.Cole TJ. Secular trends in growth. Proceedings of the Nutrition Society 2000; 59: 317-324.

31.Karklina H1, Krumina D, Ebela I, Valeinis J, Knipse G. A cross sectional research on the height, weight and body mass index of children aged 5-6 years in Latvia and its secular changes during the last century. Cent Eur J Public Health. 2013 Mar; 21(1): 3-7.

32.Ebeling CF, Ingervall B, Hedegard B, Lewin T. Secular changes in tooth size in Swedish men. Acta Odontologica Scandinavica 1973; 31: 141-147.

33.Harris EF, Potter RH, Lin J. Secular trend in tooth size in urban Chinese assessed from two-generation family data. American Journal of Physical Anthropology 2001; 115: 312-318.

34.Suzuki N. Generational differences in size and morphology of tooth crowns in the young modern Japanese. Anthropological Science 1993; 101: 405-429.

35.Weiland FJ, Jonke E, Bantleon HP. Secular trends in malocclusion in Austrian men. Eur J Orthod 1997; 19: 355-359.

36.Jantz RL. Cranial change in Americans: 1850–1975. J For Sci 2001; 46:784–787.

37.Jonke E, Prossinger H, Bookstein F, Schaefer K, Bernhard M, Freudenthaler J. Secular trends in the facial skull from the 19th century to the present, analyzed with geometric morphometrics. Am J Orthod Dentofacial Orthoped 2007; 132:63–70.

38.Jantz RL, Jantz LM. Secular change in craniofacial morphology. Am J Hum Biol 2000; 12: 327–338.

39.Martin DC, Danforth ME. An analysis of secular change in the human mandible over the last century. Am J Hum Biol 2009; 21: 704-706.

40.Tulloch JFC, Medland W, Turcay OC. Methods used to evaluate growth modification in class II malocclusion. Am J Orthod Dentofac 1990; 98: 340-347.

41.Baccetti T, Franchi L, McNamara JA Jr. An improved version of the cervical vertebral maturation (CVM) method for the assessment of mandibular growth. Angle Orthod 2002; 72: 316-323.

42.Riolo ML, Moyers RE, McNamara JA Jr, Hunter WS. An Atlas of Craniofacial Growth. Craniofacial Growth Series #2. Ann Arbor, Mich: Center for Human Growth and Development, University of Michigan; 1974.

43.Pancherz H. The mechanism of Class II correction in Herbst appliance treatment: a cephalometric investigation. Am J Orthod 1982; 82: 104–13.

44. Bolton-Brush Growth Study Center. dental.case.edu/boltonbrush; 2010.

45.Darendeliler MA. Validity of randomized clinical trials in evaluating the outcome of Class II treatment. Semin Orthod 2006; 12: 67-69.

46. Frầnkel R, Frầnkel C. Orofacial orthopedics with the function regulator. Basel: Karger; 1989.

47.Illing HM, Morris DO, Lee RT. A prospective evaluation of Bass, Bionator and Twin Block appliances. Part I–The hard tissues. Eur J Orthod 1998; 20: 501–16.

48.Stahl F, Baccetti T, Franchi L, McNamara JA Jr. Longitudinal growth changes in untreated subjects with Class II Division 1 malocclusion. Am J Orthod Dentofacial Orthop. 2008 Jul; 134(1): 125-37.

49.Hayashi K, Saitoh S, Mizoguchi I. Morphological analysis of the skeletal remains of Japanese females from the Ikenohata-Shichikencho site. Eur J Orthod 2012; 34, 575-581.

50.Ingervall B, Lewin T, Hedegard B. Secular changes in the morphology of the skull in Swedish men. Acta Odontologica Scandinavica 1972; 30, 539-554.

51.Cozza P, Baccetti T, Franchi L, De Toffol L, McNamara JA Jr. Mandibular changes produced by functional appliances in class II malocclusion: a systematic review. Am J Orthod Dentofac 2006; 129, 599: e1-e12.