

Comparison of statural height growth velocity at different CVM stages.

Title

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Contribution

- Study design: JEH, SW, SH, GB
- Conduct and data collection: SH
- Data analysis: SH, GB
- Interpretation of data: SH, GB, JEH
- Drafting of the paper: SH
- Critical revision of the paper: SH, JEH

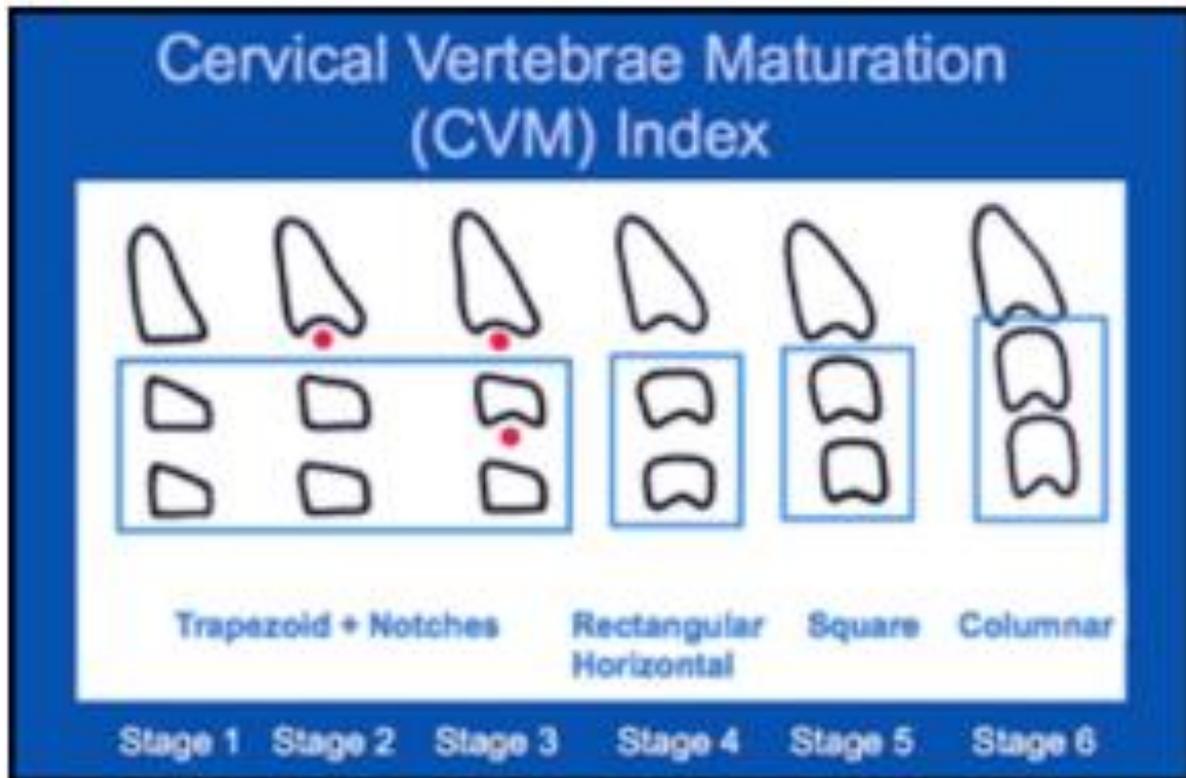
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Highlights

- CVM method is valid for identifying peak pubertal rate of growth in statural height.
- The peak rate of growth statural height occurred at CVM Stage 3 in boys and girls.
- At CVM Stage 3, girls were significantly older than the boys.
- Using a lateral cephalogram, the CVM method can be used to assess growth potential.

Graphic abstract



Abstract

Introduction: Knowledge of a patient's stage of growth and development plays a vital role in diagnosis, treatment planning, result and stability of a patient's outcome. CVM predicts the stage of growth and development, but its validity has only been investigated retrospectively, using historic samples. The objective was to prospectively assess if a correlation exists between CVM stage and statural height growth velocity.

Methods: Participants were aged between 8-18 years and of either gender. Standing height was measured every 6 weeks with participants barefoot and in natural head position. CVM stage was assessed from lateral cephalograms taken at the start of treatment. Intra- and inter-observer reliability of CVM staging and statural height measurements were assessed using Cohen's weighted kappa, percentage agreement, intra-class correlation coefficient, and Bland and Altman plots respectively. ANOVA was used to test for statistically significant differences between growth velocities at the CVM stages.

Results: 108 participants were included for analysis. The peak in statural height growth velocity occurred at CVM stage 3 ($p=0.001$). There was a statistically significant difference in the mean annualised growth velocity between all CVM stages except between CVM stages 2 and 4. Females underwent their peak pubertal growth spurt an average of 1.2 years earlier than males.

Conclusions: This study suggests that there is a significant relationship between CVM stage and statural height velocity.

Introduction

Knowledge regarding the timing and extent of growth for orthodontic patients is essential in order to manage them optimally and successfully, particularly in patients with skeletal discrepancies.¹ Such knowledge plays a vital role in the diagnosis, treatment planning, result and overall stability of the patients' outcome.¹ Depending on the stage of development and growth velocity expected for a patient, different treatment modalities may be considered more appropriate than others.²⁻⁵ For orthodontists, it therefore is crucial to be able to assess the growth potential of a patient and in cases where orthognathic surgery and/or implants are required, to know when growth has ceased (See Figure I).

Numerous methods have been investigated to identify the stage of growth and development and predict both the timing and potential of this growth.⁷⁻¹⁸ These include chronological age, dental age,⁷⁻⁹ menarche and voice changes,^{10, 11} standing height,^{12, 13} skeletal maturation of the hand and wrist,^{7, 8, 11, 14} and cervical vertebral maturation (CVM).¹⁵⁻¹⁸

None of these methods have demonstrated a strong enough correlation to growth with the exception of skeletal age of hand wrist radiographs and cervical vertebral maturation.^{5, 7, 19-24} The principle of using skeletal maturity, in order to determine the most appropriate time to carry out orthodontic treatment, has varied in popularity but has always required additional radiation exposure and additional skills for the orthodontist to interpret the hand wrist radiographs.²⁵ As a result, alternatives to hand wrist radiographs were sought using investigations which were more common place in orthodontics and more familiar to the orthodontist to facilitate interpretation.²⁶

Cervical Vertebrae Maturation (CVM) is an alternative method to hand wrist radiographs that has been shown to be reliable^{19, 20, 27-30} and does not require the use of additional radiation for patients undergoing orthodontic treatment.²⁰ The CVM index¹⁵ assesses the shape of the cervical vertebrae visible on a standard lateral cephalogram and uses this approach to predict the stage of growth and development of the patient.

Whilst many studies have looked into the validity of this index,^{15-17, 19, 24, 31-37} all have used historical samples, and have been retrospective. Methodological flaws, as well as sampling issues, means that the validity of the CVM method is yet to be shown in a contemporary population sample in a prospective manner.

For the CVM method to be of use clinically today, it must not only be reliable but it also must be valid with respect to its predictability of growth in a contemporary sample. The aim of this study was therefore to address the concerns raised in previous research²⁰ and to determine the validity of the cervical vertebral maturation stage as a predictor for growth using an appropriately sized, contemporaneous sample of children and adolescents, in a prospective manner. The objective of this study was to assess if a correlation exists between Cervical Vertebral Maturation (CVM) Stage and statural height growth velocity. Phase II of this study will assess the relationship between CVM stage and facial (mandibular growth).

Method

Routine orthodontic clinical records were collected from all patients as per departmental protocol and for use in treatment planning. These records included taking the patient's initial standing height and obtaining a lateral cephalogram radiograph together with intra- and extra-oral photographs as well as other radiographs as indicated clinically. Following this, patients started orthodontic treatment, as appropriate, to correct their malocclusion. Routine care was provided as per the consultants' treatment plan. Interim and final records were obtained as clinically necessary. In addition to this routinely acquired information, the clinicians undertaking the patients' treatment took a measurement of standing height at each visit and recorded it in the clinical records.

Participant Selection: Participants taken on for orthodontic treatment at XXXX, in the academic years 2012/13 and 2013/14 were eligible to participate in this study. At their first appointment, routine history, examination and special investigations were undertaken after which the patient and their parent/guardian were informed about the study and invited to participate if they fulfilled the inclusion criteria.

Participants were included if they:

- Were age 18 years or younger,
- Were of either gender, male or female
- Had not received previous orthodontic treatment,
- Had given informed consent/assent to participate in the study.

Patients diagnosed with any congenital clefts of the lip and/or palate, or known or suspected craniofacial syndromes or growth related conditions, were excluded.

Standing height: Standing height was measured with the patients barefoot, feet together with their heels against the wall and in natural head position (Frankfort plane parallel with the floor), using a wall mounted height measure, at every visit. Taking the standing height at each visit (every 6-weeks) was the only intervention that was in addition to routine clinical practice. It was carried out in a designated area by the treating clinician and recorded on a data sheet in the patients' notes. The height was measured at the same time of the day on each occasion. An annualised growth rate was calculated in order to allow comparison of growth rates over the same time period. This was also because there were small fluctuations in the growth velocity throughout the year, so an average growth velocity per year was calculated.

Cephalometric assessment: Lateral cephalograms (which included the cervical vertebrae) were taken at the start of treatment for diagnostic and treatment planning purposes. The lateral cephalograms were staged for maturation using the CVM index described and developed by Bacceti et al.¹⁵

Sample Size: For analysis, patients were grouped into 4 categories, CVM stages 1-2, 3, 4 and 5-6. To detect differences between these groups, of the magnitude observed in Franchi et al.²⁰ with 80% power at the 5% significance level, 17 patients per group would be needed, or a total sample size of 68.

Statistics: Intra- and inter-observer reliability of CVM staging was assessed using Cohen's weighted kappa (Kw) and percentage agreement (% agree). Intra-class correlation coefficient (ICC) and Bland and Altman plots were used to assess the reliability of the statural height measurements. ANOVA was used to test for statistically significant differences between the statural height velocities at different CVM stages.

Ethics and Regulatory Approvals: The study was conducted in compliance with the principles of the Declaration of Helsinki (1996). Ethical approval was granted from the Research Ethics Committee, reference number 13/XX/0408, protocol number XXX000751. This was granted on 30th October 2013.

Reliability and Calibration: YY was calibrated in the assessment of CVM stage, to ZZ who had been calibrated in a previous study.²⁷ The first CVM assessment was undertaken on a randomised set of images of full cephalograms by both assessors independently and in duplicate. The second assessment was undertaken 4 weeks later on the same set of images of full cephalograms that was presented in a different randomised order. In order to assess the impact of being able to see the dentition on the CVM assessment, the same set of images of cephalograms with the dentition masked and presented in a different randomised order, was assessed by both assessors one year later.

Results

Reliability and Calibration: The intra-observer reliability of CVM index was characterized as “almost perfect” agreement (Kw = 1; % agree = 100%). Inter-examiner reliability of CVM index also was characterized as “almost perfect” agreement (Full cephs Kw = 0.96, % agree = 99.3%; Masked cephs Kw = 0.83; % agree = 97.4%). Intra- and Inter-observer reliability for statural height measurements were ‘characterized as “excellent” (ICC: 0.98-0.99). Intra-observer reliability of cephalometric measurements was ‘characterized as “good” (ICC: 0.85-0.93).

The total number of patients recruited into the study was 185. However, due to various shortcomings in the data collection, which are discussed in the ‘Limitations of the Study’ section, the final sample size that could be used in the data analysis was 108. This is demonstrated in Figure II, which shows the flow of patients through the study.

The mean age at the start of treatment in the final sample (n=108) was 13.9 years (SD=1.7 years) and ranged from 10.16 years to 18.56 years. In order for the sample size in each group to be sufficient to provide adequate power to detect a statistically significant difference if one existed, data from those patients at CVM stages 1 and 2 and CVM stages 5 and 6 were combined. Those in CVM stages 3 and 4 were left separate because these stages are of particular interest for the purpose of this research.

The mean annualized growth velocity in statural height was calculated for each patient; the peak in statural height growth velocity occurred at CVM stage 3 (p=0.001).

Table I shows the mean annualized growth velocity (MAGV) in centimetres per year (cm y^{-1}) in each CVM group. There was an increase in the MAGV from CVM stage 2 to CVM stage 3 by almost 5 cm y^{-1} . The MAGV then dropped by 4.3 cm y^{-1} at CVM stage 4 relative to CVM stage 3. At CVM stage 5/6, the MAGV dropped by a further 3.5 cm y^{-1} to 1.5 cm y^{-1} MAGV. This pattern would support the idea that standing height velocity is greatest at CVM stage 3 and has dropped significantly by stage 5/6.

The trend in MAGV through the CVM stages is displayed in Figure III. This demonstrates the increase in MAGV that occurs at CVM stage 3. The growth velocity then decreased from CVM stage 3 to CVM stage 4, and further reduced going into CVM stage 5 and 6. There were 2 outliers in the CVM stage 3 group who showed a particularly high growth velocity. There were also 3 outliers at CVM group 5 and 6, which suggests that there were a few individuals who displayed some late growth.

When assessing the MAGV split between genders (Table II), the same pattern was seen as described above, with the MAGV highest at CVM stage 3 and decelerating towards CVM stage 5. However, growth velocities in males generally were higher than in females, and their peak growth velocity was 10.4 cm y^{-1} (95%CI: 7.68, 13.30) MAGV compared to only 7.5 cm y^{-1} (95%CI: 4.83, 10.26) MAGV for females; but this difference was not statistically significant in our sample ($p=0.36$).

Table III displays the mean age of males and females at CVM stage 3. The mean age of females at CVM stage 3 was 12.4 (SD 1.4) years whereas for males it was 13.6 (SD 0.9) years. This confirms previous research reporting that females reach puberty prior to males, and the difference was significant [-1.20 years (95%CI -2.12, -0.28)].²⁰

ANOVA was used to test for statistically significant differences in the MAGV between the different CVM stages. The null hypothesis, stating that there was no difference between the 4 groups, therefore was rejected, as the differences were statistically significant ($p=0.0001$). Table IV demonstrates where there was a statistically significant difference between two CVM stages.

Discussion

Growth is such a fundamental concept in orthodontics that it is not uncommon for the decision regarding timing or even modality of treatment to be influenced by the stage of growth and development of the patients.

The CVM index provides a tool that is easy to apply, readily available to orthodontists through the acquisition of routine radiographs and has been shown to be reliable.²⁷ Previous research carried out on the CVM method has focussed on its inter- and intra-observer agreement^{27,38} and on determining the correlation between the CVM index and the hand-wrist radiograph index.^{16, 19, 39}

It is of little use considering the validity of the CVM method, without considering its reliability, as a method that shows poor reproducibility will be limited in its usefulness regardless of its validity. Whilst many studies report CVM staging to be reliable, there are studies that report poor or varying levels of reliability.^{30,38,40} The main study that reports poor reliability of CVM staging, is that by Gabriel et al.³⁸ However, in Gabriel et al., the training, provided to the orthodontists, was limited and consisted of only a hard copy hand out meaning that the method was, essentially, self-taught. The training provided to the observers in the current study was through a combination of a handout, an interactive PowerPoint® presentation, a group discussion and a calibration exercise looking at reference lateral cephalograms to allow the assessors to become familiar with the subtleties of this method, prior to undertaking the main study.²⁷ Furthermore, in a reliability calibration exercise, the intra-observer reliability of XX was found to be “almost perfect”, according to the most widely used scale for the interpretation of weighted kappa (Landis and Koch). Thus we consider the method by which the assessments in the current study were made, was deemed reliable robust.

In contrast to the number of studies considering reliability of the CVM staging method, research validating the relationship between CVM and growth, both in standing height and mandibular growth, is sparse. Despite the index having been shown to be valid, the existing research has been retrospective and has used historic samples from growth studies.^{16, 20, 41} The results of the current research study have confirmed the findings of previous retrospective research based on historic samples.

When comparing the results of the current study to the research that has been done previously on this topic, the pattern of statural height growth velocity was similar to what Franchi et al.²⁰ found in their research, as shown in Figure III. They also reported a statistically significant increase in MAGV from CVM stage 2 to 3 and a significant reduction from CVM stage 3 to 4 and again from CVM stage 4 to 5.

Some fundamental differences in the methodologies of the studies, however, mean it is equivocal whether a direct comparison can be made. Firstly, Franchi et al.²⁰ had only 24 subjects in their study, so it is questionable as to whether their sample size was powered sufficiently to draw any robust conclusions. There was no power calculation mentioned in the article, and the reason for choosing the sample size was not discussed. In addition, their data

were more longitudinal in nature, whereas the results of this study were more cross-sectional in nature looking at patients over a CVM stage over a 1-year period.

The sample used by Franchi et al.²⁰ was selected from the University of Michigan Elementary and Secondary School Growth Study (UMGS). These untreated subjects were enrolled at the school from the mid 1930s to the late 1960s. The importance of conducting research on a contemporary population, in order to give us a more accurate idea of how much growth can be expected in patients at each CVM stage, needs to be considered.

Figure IV suggests that the peak growth velocity in the current sample is slightly higher than the figure reported in the Franchi study.²⁰ However, it is surprising that the growth velocity at CVM Stages 1, 2, 5 and 6 was higher in the Franchi et al.²⁰ study than in the current sample. It is difficult to say for certain why this was observed, but again these findings may be a reflection of the small sample sizes in each CVM group or perhaps to differences in the populations measured with respect to time lag and socio-economic group or ethnic mix. In order to provide more robust data, a much larger sample size, especially of patients in CVM stages 1 and 2 and 5 and 6, would be required, a possible topic of future research.

Mitani and Sato (1992) investigated growth of the mandible, in relation to cervical vertebral maturation and standing height.⁴² They showed a consistent strong correlation between statural height and cervical vertebrae maturation; however, they presented their results in terms of chronological age rather than stage of cervical maturation stage— thus a direct comparison is not possible.

Mellion et al., looked at facial growth and its relationship to maturity indicators, and in contrast to the findings of this study, reported vertebral stages to be the worst predictors of growth.⁴³ However, this study was based on subjects from the Bolton-Brush Growth study, thus being a historic population sample. Although the authors of the study used the San Roman method in an attempt to improve reliability, this approach is different from the CVM staging method used by other authors. The difference in approaches to the application of the CVM method may account for the difference in results.

CVM Stage and Age

The results of the current study showed that females reach their peak growth spurt at an earlier age than males. The average age of females at CVM stage 3 was 12.4 years (range 10.6-13.6 years, 95%CI 11.46; 13.36) whereas the average age of males at CVM stage 3 was 13.6 years (range 11.8-14.5 years, 95%CI 13.06; 14.09). These observations support previous

research, which reports that females tend to have their peak in growth spurt prior to males.^{13, 40, 44} Franchi et al.²⁰ reported that at CVM stage 3, the chronological age for females ranged from 8 years 6 months to 11 years 5 months, whereas for the males it ranged from 10 years to 14 years. Thus, the authors argue that the differences in these age ranges demonstrate why chronological age cannot be used as a parameter for the appraisal of individual skeletal maturation and for the determination of treatment timing.

Recently, Beit et al.⁴⁵ suggested that CVM staging was no better at predicting the peak in growth than chronological age. However, their sample was taken from a growth study in carried out in 1981 and the study was retrospective. Furthermore, these data suggest that there was no significant difference in the ages between CVM stages 1-2, 3 and 4. This contrasts with mean annualized growth velocity, where a very significant difference was found between the different CVM stages. The findings of the current prospective study would therefore suggest that CVM is much more valid as a predictor of growth than chronological age.

Ethical Approval

Ethical approval took approximately one year to obtain which delayed the start of data collection and reduced the duration of the study. Due to the restricted time period over which the research could be carried out, the delay in obtaining ethical approval meant that the data collection could only run for 1 year.

Loss to Follow up

In total, 77 patients had to be excluded from the final analysis, due to height measurements not being taken appropriately. These reasons included patients who only had one height recorded, cases where the first height was not recorded within 6 months of the lateral cephalogram being taken, patients included who were not within the age range specified in the inclusion criteria and cases where the second, third and fourth vertebrae were not all present on the lateral cephalogram. This was a substantial loss and their inclusion would have significantly increased the power of the study. Despite this, significant differences were found so the study was adequately powered.

Sample

The sample was taken from the patients being taken on for treatment from the orthodontic treatment waiting list. This only included patients who had been assessed and deemed appropriate for treatment under the NHS and within a hospital department. This limitation may reduce the generalisability of the results, but as all patients were enrolled regardless of gender, skeletal classification or dental anomalies, any bias should have been reduced.

Methodological Limitations

When initially staging the lateral cephalograms for CVM, the patient's dentition was not masked. Consequently, the authors accept that knowledge of the dentition stage could have had an unintended bias in CVM staging. However, the lateral cephalograms were assessed blind to the height measurements and in clinical practice, orthodontists will be in full knowledge of the patients physical attributes when making assessments of CVM stage. As a post-hoc assessment, the lateral cephalograms were reassessed and the reliability of using masked cephalograms was the same as for full cephalograms (95% agreement).

The findings of this study demonstrate a strong correlation between CVM stage and statural height velocity. Consequently, an important question that this raises, particularly in clinical orthodontics, is the relationship of statural height with jaw growth. There is scarce evidence in the literature demonstrating an association between statural height and dentofacial growth.

Mitani and Sato²⁴ made a good attempt when they explored a possible relationship of mandibular growth compared to numerous clinical variables including standing height. However, they concluded that there was a large range of variability between the different variables and that mandibular growth showed the most variation, thus this association remains inconclusive.²⁴ Following on from the current study, we are investigating the relationship between CVM stage and mandibular growth velocity.

Further Research

Phase II of this study will assess the relationship between CVM stage and facial (mandibular growth). The impact of being able to see the dentition, when assessing the CVM stage from a cephalogram, has been assessed in a follow-on study from Rainey et al.²⁷

Implications for Clinical Practice

- This method of assessment of CVM stage provides clinicians with information for assessing the timing of the peak in statural height growth velocity for patients being considered for growth modification and the cessation of growth for those being considered for orthognathic surgery and/or implants. It therefore has the potential for obviating the need for hand-wrist radiographs to be taken for orthodontic patients.

Conclusions

- The findings of this study demonstrate the relationship between cervical vertebral maturation (CVM) and statural height growth velocity with statistically significant

differences being found in the mean annualized height growth velocity between all the CVM stages except between Stages 2 and 4.

- The peak in statural height growth velocity occurred at CVM Stage 3 in both males and females.
- At CVM Stage 3, females were significantly older than the males.
- The CVM method can be used to augment other diagnostic tools available to the orthodontist, as it is already available on the lateral cephalogram and may obviate the need for hand-wrist radiographs for orthodontic patients to assess skeletal maturation and hence growth potential.

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Figure Captions

Figure I. Changes in height growth velocity from infancy to adulthood. Modified from McNamara et al.⁶

Figure II: Flow of patients through study

Figure III: Box plot of mean annualised growth velocity MAGV at different CVM stages

Figure IV: Line graph showing MAGVs at different CVM stages for this study and its comparison to the Franchi et al. (2000) study.²⁰

Table Captions

Table I: Mean Annualised Growth Velocity by CVM Stage (cm^y⁻¹)

Table II: Mean annualised growth velocity at each CVM group for Females and Males

Table III: Mean age of males and females at CVM stage 3

Table IV: Tukey Post-hoc Pairwise Comparisons of Differences in growth velocity between CVM Stages

Figure 1

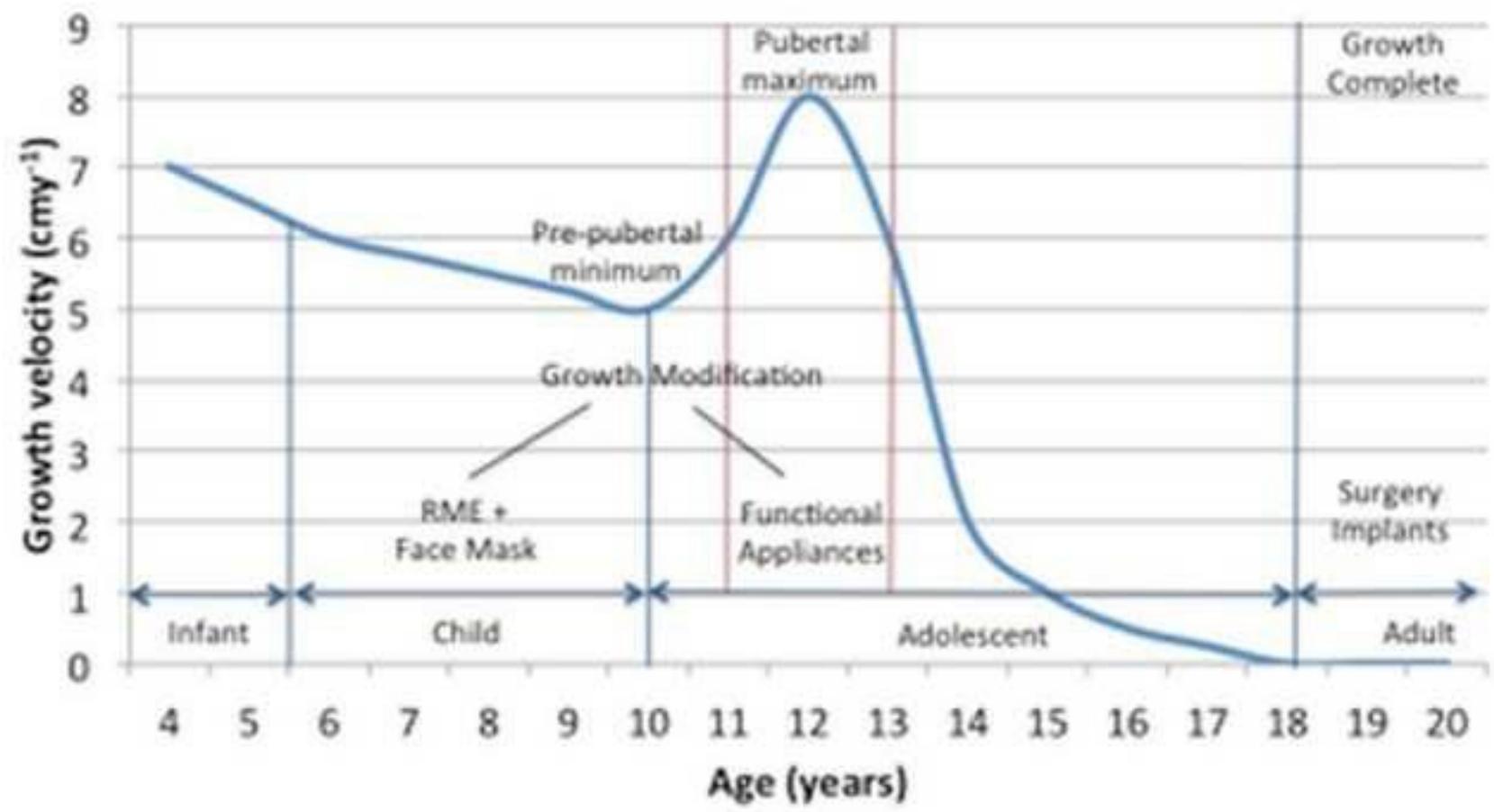


Figure II

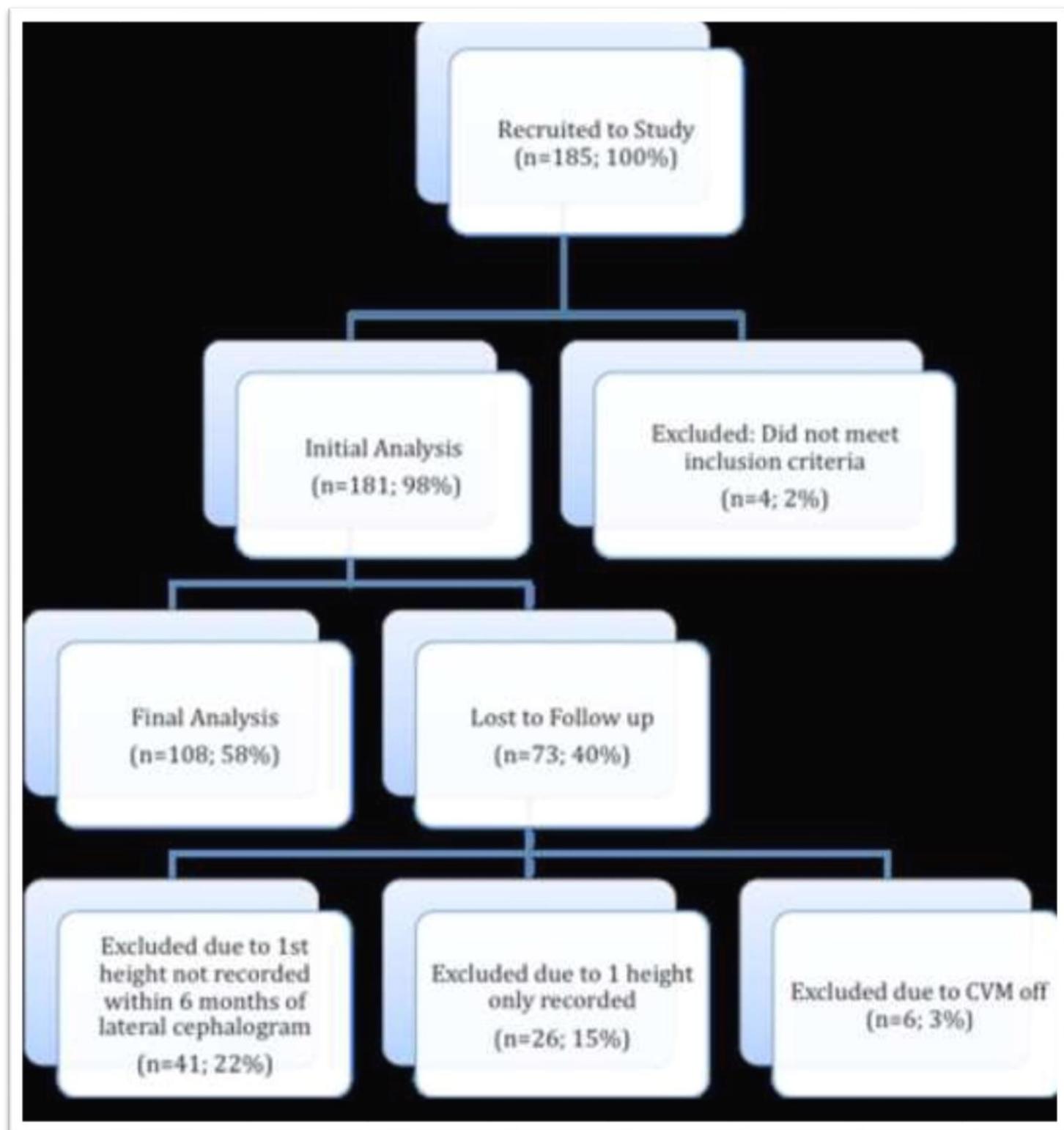


Figure III

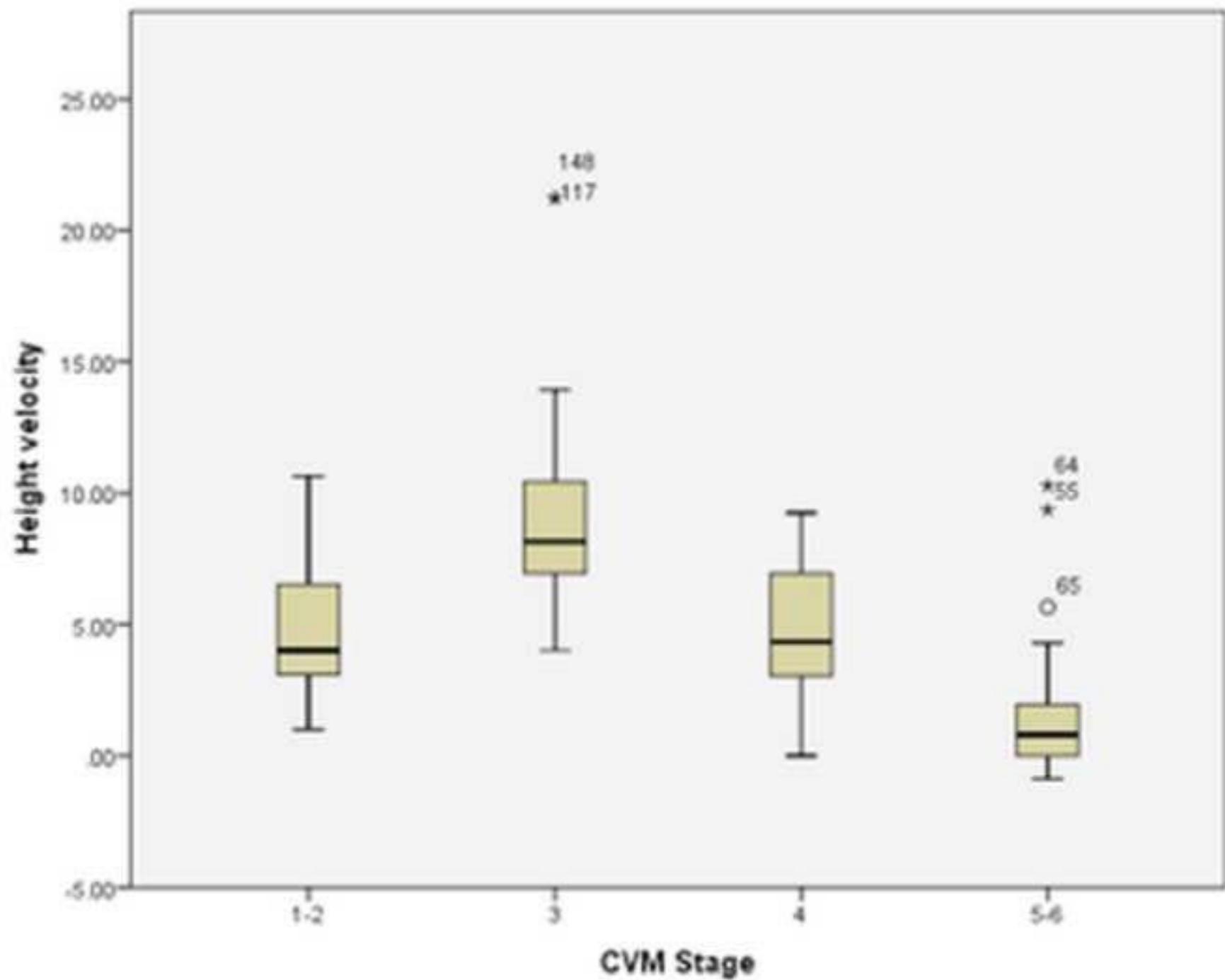


Figure IV

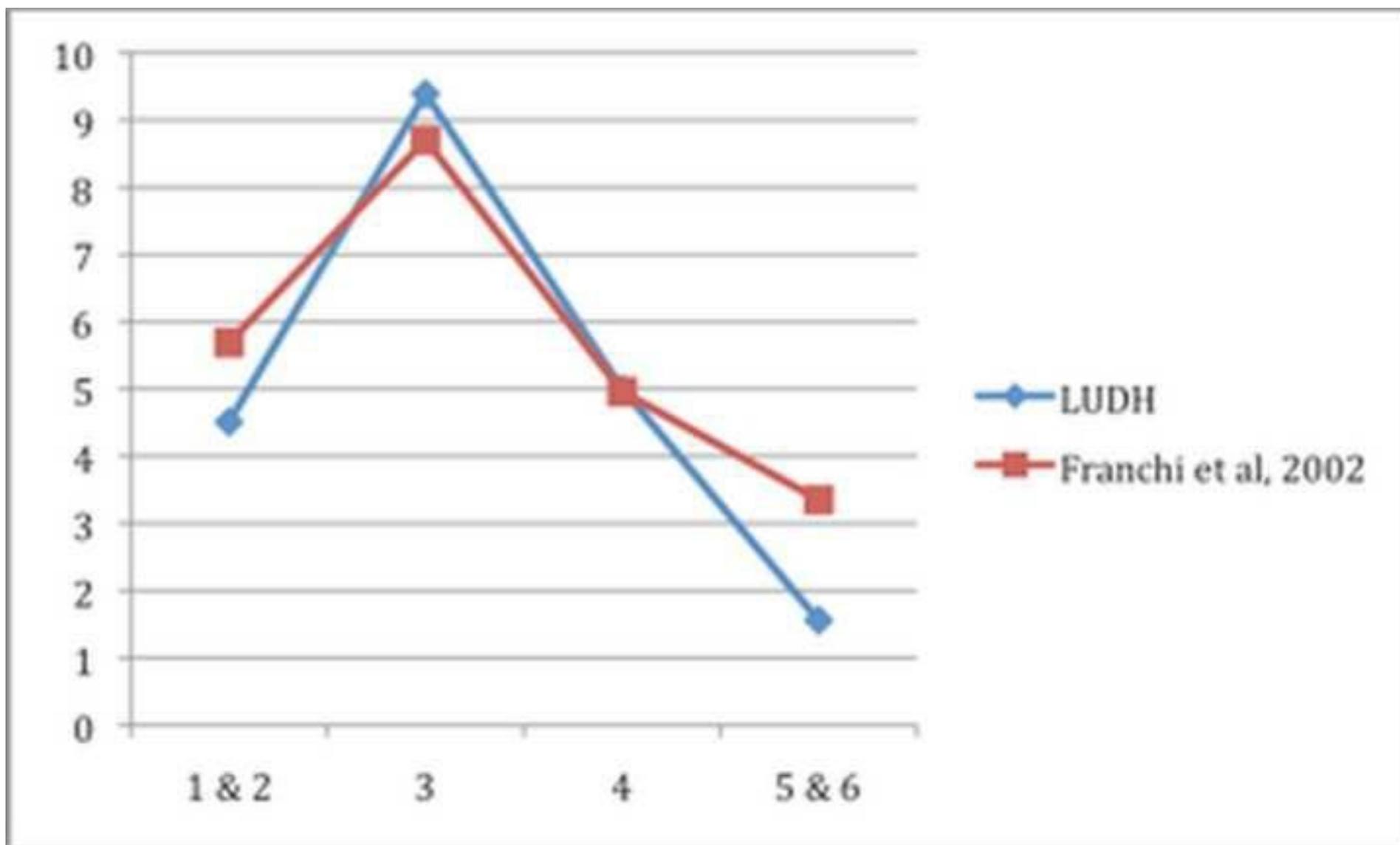


Table I

CVM Stage	Number of patients	Mean annualized growth rate (cm ^y ⁻¹)	Standard deviation (cm ^y ⁻¹)
1 & 2	14	4.51	2.71
3	22	9.39	4.44
4	33	5.00	2.33
5 & 6	39	1.56	2.34
Total	108	4.59	4.06

Table I: Mean Annualised Growth Rate by CVM Stage (cm^y⁻¹)

Table II

CVM Stage	Number of Patients		Mean annualized growth velocity (MAGV) Standard Deviation (SD) (cm ^y ⁻¹)				95% Confidence Interval			
							Lower Bound		Upper Bound	
							Girls	Boys	Girls	Boys
			Girls		Boys					
			MAGR	SD	MAGR	SD	Girls	Boys	Girls	Boys
1 & 2	9	5	3.87	2.16	5.65	3.47	2.21	1.34	5.53	9.96
3	8	14	7.54	3.25	10.44	4.79	4.83	7.68	10.26	13.2
4	17	16	4.43	2.20	5.60	2.38	3.31	4.33	5.57	6.87
5 & 6	26	13	1.77	2.70	1.13	1.39	0.68	0.29	2.86	1.97

Table II: Mean annualised growth velocity at each CVM group for Females and Males

Table III

Gender	Number of Patients	Mean Age (years)	Standard Deviation	Minimum	Maximum	95%CI	
						Lower Bound	Upper Bound
Female	8	12.4	1.14	10.55	13.61	11.46	13.36
Male	14	13.6	0.90	11.80	14.51	13.06	14.09
Total	22	13.2	1.12	10.55	14.51	12.65	13.65

Table III: Average age of males and females at CVM stage 3

Table IV

CVM Stage (a)	CVM Stage (b)	Mean Difference (a-b)	Significance	95% Confidence Interval	
				Lower Bound	Upper Bound
2	3	-4.88	0.000*	-7.50	-2.27
	4	-0.50	0.951	-2.94	1.94
	5	2.94	0.009*	0.56	5.33
3	4	4.38	0.000*	2.28	6.49
	5	7.83	0.000*	5.79	9.86
4	5	3.44	0.000*	1.63	5.25

* The mean difference is significant at the 0.05 level

Table IV: Tukey Post-hoc Pairwise Comparisons of Differences in growth velocity between CVM Stages