ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

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ΕΙΔΙΚΕΥΣΗ ΣΤΗΝ ΟΡΘΟΔΟΝΤΙΚΗ

«ΑΞΙΟΛΟΓΗΣΗ ΤΗΣ ΕΠΑΝΑΛΗΨΙΜΟΤΗΤΑΣ ΤΗΣ ΜΕΘΟΔΟΥ ΩΡΙΜΑΝΣΗΣ ΑΥΧΕΝΙΚΩΝ ΣΠΟΝΔΥΛΩΝ (CVM). ΜΠΟΡΕΙ Η CVM ΝΑ ΕΚΤΙΜΗΣΕΙ ΤΗ ΧΡΟΝΟΛΟΓΙΚΗ ΗΛΙΚΙΑ;»

«A REPRODUCIBILITY STUDY OF CERVICAL VERTEBRAL MATURATION (CVM) METHOD. CAN CHRONOLOGICAL AGE BE ASSESSED BASED ON CVM METHOD?»

ΣΧΟΡΕΤΣΑΝΙΤΗ Γ. ΛΥΔΙΑ

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Επιβλέπων Καθηγητής για την εκπόνηση της Μεταπτυχιακής Διπλωματικής Εργασίας: Μαργαρίτα Μάκου, Ομότιμη Καθηγήτρια Εργαστηρίου Ορθοδοντικής

Τριμελής Επιτροπή για την αξιολόγηση της Μεταπτυχιακής Διπλωματικής Εργασίας:

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Πρόλογος

Η παρούσα διπλωματική εργασία προέκυψε ως αποτέλεσμα συζητήσεων κατά τη φοίτησή μου στο μεταπτυχιακό της Ορθοδοντικής. Ένα θέμα που συχνά επανερχόταν ήταν κατά πόσο διαγνωστικά εργαλεία που χρησιμοποιούμε στην καθημερινή κλινική ορθοδοντική πράξη θα μπορούσαν να βρουν εφαρμογή και σε διαφορετικά πεδία. Η ανάγκη για εκτίμηση της ηλικίας σε περιπτώσεις Ιατροδικαστικού ενδιαφέροντος που αφορούν ζώντα άτομα αλλά και πτωματικό υλικό τέθηκε από την κα Αναστασία Μητσέα, Λέκτορα της Κλινικής Διαγνωστικής και Ακτινολογίας Στόματος του ΕΚΠΑ. Η εξειδίκευσή της στην Ιατροδικαστική, η καθοδήγηση και η συμμετοχή της στη διεξαγωγή της έρευνας έδρασαν καταλυτικά. Για όλους τους παραπάνω λόγους και για την εξαιρετική συνεργασία που είχαμε θα ήθελα να την ευχαριστήσω από τα βάθη της ψυχής μου.

Ακόμη θα ήθελα να ευχαριστήσω τον κ. Ιωσήφ Σηφακάκη, Λέκτορα του Εργαστηρίου της Ορθοδοντικής του ΕΚΠΑ, για τη διάθεσή του να μοιραστεί απλόχερα τις γνώσεις του μαζί μου. Συνέβαλε σημαντικά στην αρχική σύλληψη του θέματος, αλλά και στην επιτυχή ολοκλήρωση της εργασίας, με τις συμβουλές και τις εύστοχες διορθώσεις του μέχρι και την τελευταία στιγμή.

Η εργασία δεν θα μπορούσε να έχει γραφεί χωρίς την αρωγή και την καθημερινή ενθάρρυνση της κας Μαργαρίτας Μάκου, Ομότιμης Καθηγήτριας του Εργαστηρίου Ορθοδοντικής του ΕΚΠΑ. Η επιστημονική της επίβλεψη, με τρόπο καθοριστικό, προσδιόρισε την επιτυχή έκβαση της εργασίας αυτής.

Οι συμβουλές του κ. Δημήτρη Χαλαζωνίτη, Αναπληρωτή Καθηγητή και Διευθυντή του Εργαστηρίου Ορθοδοντικής του ΕΚΠΑ, ήταν πάντα απολύτως εύστοχες και με βοήθησαν στην οργάνωση της δομής της έρευνας, καθώς και στην ανάλυση των αποτελεσμάτων. Για

τους λόγους αυτούς, αλλά και για την επιστημονική του καθοδήγηση όλα αυτά τα χρόνια, θα ήθελα να εκφράσω την ειλικρινή ευγνωμοσύνη μου.

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Αισθάνομαι, τέλος, την ανάγκη να ευχαριστήσω τους γονείς μου, τους φίλους και τους συμφοιτητές μου για την υπομονή και τη συμπαράστασή τους καθ' όλη τη διάρκεια φοίτησής μου στο μεταπτυχιακό της Ορθοδοντικής.

Contents

Περίληψη

Σκοπός: Οι σκοποί της παρούσας εργασίας ήταν: α) η αξιολόγηση της επαναληψιμότητας της μεθόδου CVM όπως έχει περιγραφεί από τους Baccetti και συν. 2005, β) η αξιολόγηση της συσχέτισης μεταξύ της χρονολογικής ηλικίας και της σκελετικής ωρίμανσης, όπως αυτή προσδιορίζεται από τα στάδια ωρίμανσης των αυχενικών σπονδύλων, γ) ο προσδιορισμός της ακρίβειας με την οποία η μέθοδος αυτή μπορεί να εκτιμήσει τη χρονολογική ηλικία.

Υλικά και μέθοδος: Το δείγμα της έρευνας αποτελούταν από 474 πλάγιες κεφαλομετρικές ακτινογραφίες Ελλήνων ασθενών, ηλικίας από 6.4 έως 22.4 χρονών. Οι ακτινογραφίες επιλέχθηκαν με βάση συγκεκριμένα κριτήρια. Έξι παρατηρητές με διαφορετική εμπειρία εκπαιδεύτηκαν στη μέθοδο CVM. Η αξιολόγηση του δείγματος πραγματοποιήθηκε κάτω από τις ίδιες συνθήκες και επαναλήφθηκε αφού μεσολάβησε διάστημα τεσσάρων εβδομάδων. Η ενδο- και δια- βαθμολογική αξιοπιστία εκτιμήθηκε με τους στατιστικούς δείκτες συνάφειας Cohen's weighted kappa και intraclass correlation coefficient. Η συσχέτιση της χρονολογικής ηλικίας με τα στάδια της μεθόδου CVM πραγματοποιήθηκε με έλεγχο ανάλυσης διακύμανσης (ANOVA). Η ακρίβεια με την οποία η μέθοδος CVM μπορεί να εκτιμήσει τη χρονολογική ηλικία ελέγχθηκε με το γενικό μοντέλο γραμμικής παλινδρόμησης.

Αποτελέσματα: Η ενδο-βαθμολογική αξιοπιστία ήταν υψηλή και κυμάνθηκε από 0.857 έως 0.931. Τα ποσοστά της απόλυτης ενδο-βαθμολογικής συμφωνίας υπολογίσθηκαν από 77% έως 87.3%. Η δια-βαθμολογική αξιοπιστία ήταν 0.90, ενώ το ποσοστό της απόλυτης δια-βαθμολογικής συμφωνίας βρέθηκε λιγότερο από 50%. Επιπλέον, η επαναληψιμότητα του 3^{ου} σταδίου αυχενικής ωρίμανσης (CS3) ήταν η μικρότερη κατά σειρά μεταξύ των σταδίων. Οι μέσοι όροι της χρονολογικής ηλικίας κάθε σταδίου διέφεραν μεταξύ τους στατιστικά σημαντικά (εκτός από τη διαφορά μεταξύ των σταδίων CS2 και CS3), ενώ η ηλικία αυξανόταν όσο τα στάδια προχωρούσαν. Σε κάθε στάδιο τα κορίτσια ήταν μικρότερα από

τα αγόρια μέχρι και ένα χρόνο. Το γενικό μοντέλο γραμμικής παλινδρόμησης έδειξε ότι παρόλο που το φύλο και η ηλικία συσχετίζονται στατιστικά σημαντικά με τα στάδια ωρίμανσης, αυτές οι δύο μεταβλητές μπορούν να εξηγήσουν σχεδόν το 60% (adjusted R^2=0.61) της ηλικιακής διακύμανσης του δείγματος.

Συμπεράσματα: Η CVM μέθοδος βρέθηκε στατιστικά αξιόπιστη και επαναλήψιμη. Ωστόσο, δεν μπορεί να αποτελέσει επαρκές διαγνωστικό εργαλείο για τον καθορισμό της εφηβικής αύξησης, εφόσον η επαναληψιμότητα του CS3 ήταν η μικρότερη κατά σειρά μεταξύ των σταδίων. Ακόμα, η ηλικία αυξανόταν όσο τα στάδια προχωρούσαν. Τέλος, είναι εφικτό η μέθοδος να εφαρμοσθεί και σε πεδία (πχ Ιατροδικαστική), όπου οι απαιτήσεις προσδιορισμού του σταδίου ωρίμανσης είναι λιγότερο αυστηρές, προσφέροντας πληροφορίες σχετικές με την ηλικία.

Abstract

Aim: The aims of this study were to 1) assess the reproducibility of Cervical Vertebral Maturation (CVM) method as described by Baccetti et al., 2) evaluate the relationship between chronological age and skeletal maturation according to this method and 3) investigate the potential for age estimation of Bacceti's CVM method.

Materials and Method: The sample of this cross-sectional study consisted of 474 Greek patients' lateral cephalograms, age ranging from 6.4 to 22.4 years, following specific inclusion criteria. Six raters of various educational backgrounds were trained to CVM method. All images were assessed twice under the same conditions. Between the two assessments there was a four week interval. Intra- and inter-rater agreement were assessed by Cohen's weighted kappa and intraclass correlation coefficient, respectively. A factorial (2X6) analysis of variance was fitted to investigate the correlation between chronological age and cervical maturation stages. The potential for age prediction was tested by general linear model regression analysis.

Results: Intra-rater reliability was high and ranged from 0.857 to 0.931. Intra-rater absolute agreement ranged from 77% to 87.3%. Inter-rater reliability was nearly perfect (0.90), whereas inter-rater absolute agreement was <50%.The lowest reproducibility was found for the 3rd Cervical Maturation Stage (CS3). The differences in mean ages among the 6 CS stages were statistically significant (with the exception of CS2 and CS3), and increased as the CS increased. Females reached each stage earlier than males. Linear model regression analysis showed that although gender and CS are correlated with age statistically significantly, these two variables could explain roughly 60% (adjusted R^2=0.61) of the age variance of the sample.

Conclusions: CVM method presented with high intra- and inter-rater agreement. However, CVM cannot by itself predict accurately the pubertal growth spurt, as CS3 was the least reproducible of all stages. A direct and expected correlation was found between chronological age and cervical stages. CVM method could be more effectively applied in other fields (e.g. Forensics), providing information about age.

Introduction

Identification of an unknown deceased person is of major importance not only in sole cases but also in natural and unnatural mass disasters (Disaster Victim Identification, DVI). Even when identification is impossible, it is crucial to reconstruct the profile of the unidentified person by gathering information about their gender and age. Moreover, age estimation might be necessary in cases of living individuals without legal documents that verify their chronological age. Age estimation might be based on dental and skeletal maturity (Beauthier et al., 2009; Black et al., 2010; Berketa et al., 2012; Timmins et al., 2012).

The evaluation of skeletal maturation is also important in orthodontic treatment. In this field, it is essential to predict future growth and recognize growth acceleration and deceleration periods, as well as growth peak and completion, mainly in cases of skeletal discrepancies. This information is useful in clinical decisions regarding the treatment initiation time and timing for orthognathic surgery (Baccetti et al., 2005; Gabriel et al., 2009; Wong et al., 2009; Santiago et al., 2012; Melion et al., 2013; Perinetti et al., 2014).

Several biological indices have been introduced since the early 1900s in order to assess skeletal maturity. These indices include among others: chronological age, dental age, the appearance of secondary gender characteristics, stature changes, ossification of hand and wrist and maturation of the cervical vertebrae (CVM) (Greulich & Pyle, 1959; Lewis & Garm, 1960; Hunter, 1966; Fishman, 1979; Hagg & Taranger, 1982). Lamparski pioneered in 1972 by studying the cervical vertebrae morphology from lateral cephalograms to assess skeletal maturity (Lamparski, 1972).

Since then, a plethora of CVM studies have been performed varying from qualitative to quantitative assessment of height, width and depth of the lower concavity of the vertebrae, to geometric morphometric analysis or linear regression formulae (Chatzigianni &

Halazonetis, 2009; Santiago et al., 2012). The studies conducted by Hassel and Farman in 1995 and by Baccetti et al. in 2005 stand out as the most influential (Hassel & Farman, 1995; Baccetti et al., 2005). Both describe maturation stages based on the initiation of the concavity at the lower border of the cervical vertebrae as well as their shape.

CVM method presents with high reliability compared to both the ossification of hand and wrist method and the increments of the mandible (Lamparski, 1972; O'Reilly & Yannielo, 1988; Hassel & Farman, 1995; Santiago et al., 2012). Specifically, a recent systematic review concluded that «both CVM methods (Hassel & Farman, 1995, Baccetti et al., 2002) are reliable to replace the hand-wrist radiograph in predicting the pubertal growth spurt» (Cericato et al., 2015). Furthermore, an advantage of the CVM method is that the patients are not exposed to additional radiation, since lateral cephalograms are taken as a part of the initial orthodontic records.

Unfortunately, the verdict is still out on the method's accuracy and reproducibility. Some researchers have reported high percentages of accuracy and reproducibility (Kucukkeles et al., 1999; Pasciuty et al., 2013; Perinetti et al., 2014) whereas others observed a wide discrepancy in the definition of the maturation stages among observers (Gabriel et al., 2009; Nestman et al., 2011; Zhao et al., 2012).

According to recent systematic reviews, most studies present with methodological deficiencies related to study design (sample size and sample randomization, blinding), statistical analysis, interpretation of the results (Santiago et al., 2012; Cericato et al., 2015). Both studies underline the need for further research concerning the reproducibility of CVM method.

It has been indicated that ethnicity, environment, diet and socioeconomic status might be associated with variations in skeletal maturity (Mappes et al., 1992; Mansourvar et al.,

2014). The skeletal age according to the CVM method as described by Baccetti et al. 2005 has not been assessed hitherto in Greek subjects.

The aims of this study were to 1) assess the reproducibility of CVM method, as described by Baccetti et al. 2005, 2) evaluate the relationship between chronological age and skeletal maturation according to this method and 3) investigate the potential for age estimation of the CVM method.

Aim

The aims of this study were to 1) assess the reproducibility of CVM method, as described by Baccetti et al. 2005, 2) evaluate the relationship between chronological age and skeletal maturation according to this method and 3) investigate the potential for age estimation of the CVM method.

Material and methods

Digital lateral cephalograms from 474 Caucasian patients (217 males and 257 females), with Greek origin were included in this study. The images were selected from the archives of the Department of Orthodontics, Dental School, University of Athens and were taken as part of the Orthodontic treatment planning and not for the purpose of this study. Gender and age were recorded for each subject.

Lateral cephalograms were included, as long as they fulfilled the following inclusion criteria: taken from 2005 to 2015, good image quality with the 2nd, 3rd and 4th cervical vertebrae (C2-C4) visible, belonging to children, adolescent and young adults with Greek origin, with free medical history, no previous trauma, inherited or acquired craniofacial deformities, and no previous orthodontic treatment. Cephalograms belonging to subjects with metabolic or developmental diseases and nutritional problems, syndromes, cleft lip and/or palate, and receiving any medication were excluded.

All images were performed with the same x-ray equipment Planmenca Promax with max KV 84, 26mm Al filter, 1700 VA (Plamnenca, Helsinki, Finland) using identical source-subject and subject-film distances. Since vertical and horizontal measurements were not performed, distortion of the image was not considered.

Skeletal maturation was evaluated according to Baccetti's method. This 6-stage method is based on the assessment of anatomical changes of the 2nd, 3rd and 4th cervical vertebrae (C2, C3 and C4). In particular, two parameters are assessed: a) the existence or nonexistence of the concavity of the lower border of the C2, C3 and C4 and b) the shapes of C2, C3 and C4; four shapes might be observed: trapezoid, rectangular horizontal, square and rectangular vertical (Figure1) (Baccetti et al., 2005; Baidas 2012).

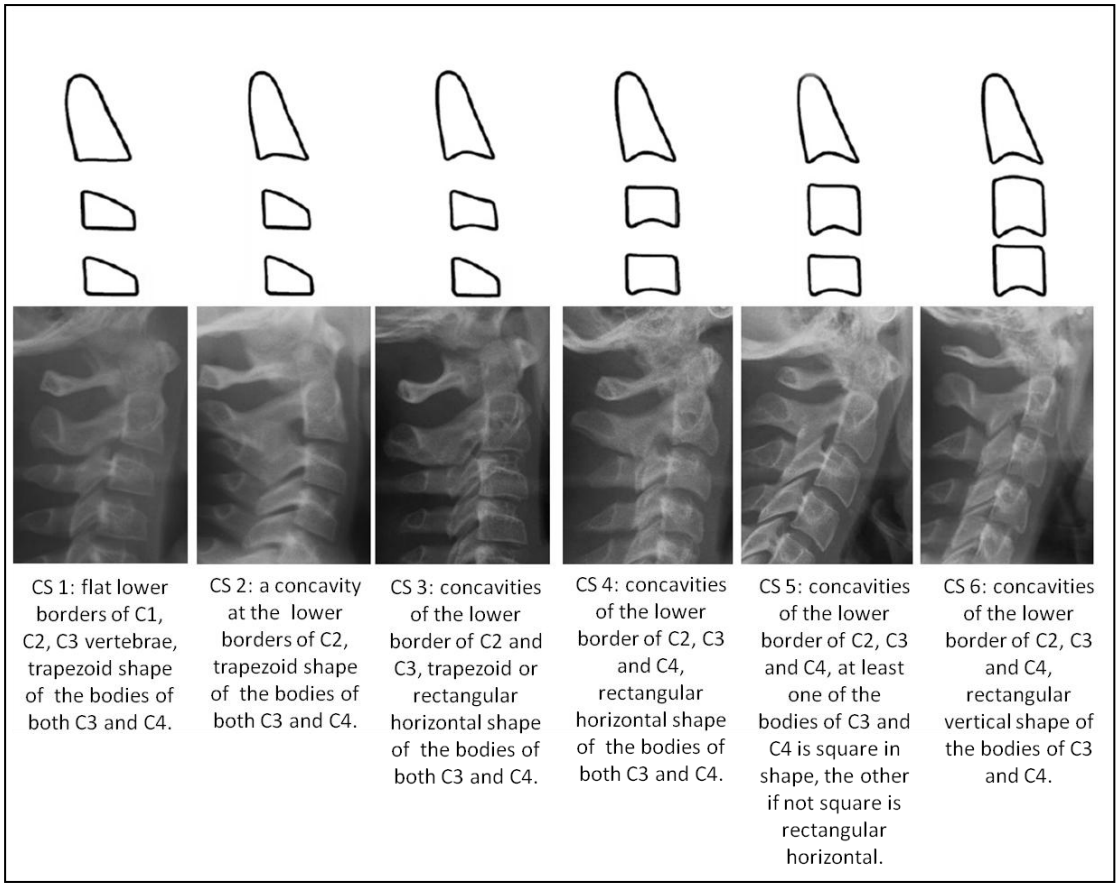

Figure 1. Cervical vertebral maturation stages according to Baccetti et al. 2005, with example images from the present study's sample (Baccetti et al., 2005; Baidas 2012)

A person other than the raters cropped all cephalograms in order to restrict visualization to the cervical vertebrae and hide the dentition. The random function of Microsoft Excel® was applied to randomize these cropped images and a database was formed, where gender and age were not evident. This database was then distributed to the raters.

Two orthodontists (OR1 and OR2), one dentomaxillofacial radiologist (DR), one medical radiologist (MR), one dentist (D) and one 3rd year orthodontic postgraduate student (OPS) acted independently and blindly as raters in the study. A detailed calibration session took place prior to rating, in which raters assessed 40 images (not included in the sample). In this session raters were given a comprehensive description of this CVM method (Baccetti et al., 2005) with example images of all stages. Moreover, it was clarified that in case of uncertainty, the earlier maturation stage between two consecutive stages had to be

allocated. A discussion followed the calibration session, where the results were commented upon by the six raters. All ratings were performed under the same conditions in a diagnostic monitor, no later than 5 days after the calibration session. There was no time limit on the rating session's duration, but no more than 30 images were observed consecutively (without break) to minimize errors due to raters' fatigue. Each rater reevaluated all images after an interval of one month. The images' order was randomly changed for this second rating.

Statistical analysis

Statistical analysis was performed using the STATISTICA 10 software package and MedCalc 14 (Ostend, Belgium) for MS Windows, followed by descriptive analysis (mean and standard deviation). Statistical significance was read at 5% probability level.

Method's reliability was evaluated based on intra- and inter-rater agreement. Intra-rater agreement was assessed by Cohen's weighted kappa. Kappa values indicates the following levels of agreement: slight agreement (0.01-0.20), fair agreement (0.21-0.40), moderate agreement (0.41-0.60), substantial agreement (0.61-0.80) and perfect agreement (0.80-1) (Viera and Garrett, 2005). Moreover, inter-rater agreement was measured using the intraclass correlation coefficient.

A factorial (2X6) analysis of variance was fitted to investigate the correlation between the chronological age and the CVM stages, using gender and mean CS (the evaluations by the six raters combined into an average CS for each image, rounded to the nearest integer) as grouping factors and chronological age as the dependent variable.

Furthermore, the CVM method's potential for age estimation was tested by general linear model regression analysis using age as the dependent variable and gender and mean CS as the predictor variables (Winer, 1971; Tabachnik & Fidel, 2007).

Results

The lateral cephalograms belonged to 474 patients (mean age 13.38 years, range 6.40 - 22.40 years), 217 males (mean age 12.93 years, range 6.90 - 22.30 years) and 257 females (mean age 13.77, range 6.40 - 22.40 years). Further descriptive statistics of the sample can be seen in Table 1 (Table 1).

Table 1. Sample descriptive statistics

Gender	n (%)	Mean Age	SD	Std. Err	95% CI	Minimum Age	Maximum Age
Male	217 (45.78)	12.93	3.79	0.26	12.42 - 13.43	6.90	22.30
Female	257 (54.21)	13.77	4.15	0.26	13.26 - 14.28	6.40	22.40
Total	474 (100.0)	13.38	4.01	0.18	13.02 - 13.75	6.40	22.40

Intra-rater agreement, assessed by Cohen's weighted kappa was found high, ranging from 0.857 to 0.931, whereas intra-rater absolute agreement ranged from 77% (367/474) to 87.3% (414/474) (Table 2).

Table 2. Intra-rater agreement and absolute agreement

Rater	Cohen's weighted kappa	95% CI	Std. Err	Absolute agreement n (%)
OR1	0.902	0.880- 0.924	0.011	398 (83.9)
OR2	0.931	0.913 - 0.948	0.009	414 (87.3)
OPS	0.916	0.896 - 0.937	0.010	408 (86.0)
DR	0.908	0.888 - 0.928	0.010	397 (83.7)
D	0.857	0.829 - 0.884	0.014	367 (77.0)
MR	0.888	0.864 - 0.911	0.012	384 (81.0)

Furthermore, intra-rater absolute agreement by stage was calculated by dividing the number of repeated observations of each stage by the sum of this stage's observations (both assessments); CS3 was found to be the least reproducible of the six (Table 3).

Table 3. Intra-rater absolute agreement by stage

	OR1	OR2	OPS	DR	D	MR
CS1	120/135=89%	216/222=98%	150/169= 89%	194/211=92%	138/170=81%	170/193=88%
CS2	104/125=83%	102/117=87%	116/140=83%	96/123= 78%	88/123=71%	92/122 =75%
CS3	84/112=75%	56/78=71%	88/105=84%	52/71= 73%	64/99 =65%	56/86=65%
CS4	208/235=88%	136/171=79%	154/178=87%	144/176= 82%	148/197=75%	142/168=84%
CS5	162/200=81%	242/274=89%	204/234=87%	123/284= 86%	160/202=79%	158/198=80%
CS6	118/141=84%	76/86=88%	104/122=85%	31/83= 75%	136/157=87%	150/181=83%

Inter-rater agreement, measured by the intraclass correlation coefficient showed a strong statistical agreement between raters (Table 4). Inter-rater agreement ranging from absolute agreement to 5 stages apart disagreement is also presented in Table 4 (Table 4).

Table 4. Inter-rater agreement

	First assessment	Second assessment
Intraclass correlation coefficient	0.919	0.934
95% CI	0.908 - 0.931	0.925 - 0.943
Absolute agreement n (%)	203/474 (42,82)	234/474 (49,36)
One stage apart n (%)	222/474 (46,83)	200/474 (42,19)
Two stages apart n (%)	31/474 (6,54)	30/474 (6,32)
Three stages apart n (%)	18/474 (3,79)	10/474 (2,10)
Four stages apart	0	0
Five stages apart	0	0

Taking into account the high intra- and inter-rater reproducibility, it was considered safe to combine all evaluations from the six raters into an average Cervical Maturation Stage (CS). A mean age for each CS stage was calculated for the total sample as well as for each gender separately. Clearly chronological age increased as CVM stages progressed (Table 5, Figure 2). CS5 was the most frequently observed stage in the total sample (n=123), followed by CS4

(n=82). In particular, in females CS5 was also the most frequently observed stage (n=82), followed by CS4 (n=49). On the contrary, in males CS2 was the most frequently observed stage (n=48), followed by CS1 (n=45). CS3 was the less frequently observed stage in the total sample (n=53). Females were less frequently observed in CS3 (n=23), whereas males were less frequently observed in CS6 (n=20). Further descriptive statistics for the sample are presented in table 5 (Table 5). It was shown that females reach CS3 and CS4 earlier than males. Males' mean age in CS3 and CS4 was 11.14 years and 14.19 years, respectively, while females' mean age in CS3 and CS4 was 10.74 years and 13.22 years, respectively.

Table 5. Sample distribution of chronological age among CVM stages

Stage		N	Mean age	Std.Dev.	Std.Err	-95%	+95%	Min Age	Max Age
Total	**CS1**	78	9.21	1.36	0.15	8.91	9.52	6.40	13.20
	CS2	76	10.34	1.61	0.18	9.97	10.71	6.40	13.80
	CS3	53	10.97	1.41	0.19	10.58	11.36	6.90	16.00
	CS4	82	13.61	2.90	0.32	12.98	14.25	7.90	20.90
	CS5	123	16.63	3.06	0.28	16.09	17.18	10.80	22.40
	CS6	62	17.68	2.89	0.37	16.95	18.42	12.30	22.40
Males	**CS1**	45	9.53	1.41	0.21	9.11	9.96	7.60	13.20
	CS2	48	10.63	1.61	0.23	10.17	11.10	7.50	13.80
	CS3	30	11.14	1.62	0.29	10.54	11.75	6.90	16.00
	CS4	33	14.19	2.52	0.44	13.30	15.09	9.20	20.70
	CS5	41	17.06	2.83	0.44	16.17	17.95	11.90	22.10
	CS6	20	18.19	2.49	0.56	17.03	19.35	13.30	22.30
Females	**CS1**	33	8.78	1.17	0.20	8.36	9.19	6.40	11.20
	CS2	28	9.83	1.51	0.29	9.24	10.42	6.40	12.70
	CS3	23	10.74	1.08	0.23	10.28	11.21	8.80	13.20
	CS4	49	13.22	3.09	0.44	12.34	14.11	7.90	20.90
	CS5	82	16.42	3.16	0.35	15.72	17.11	10.80	22.40
	CS6	42	17.44	3.06	0.47	16.49	18.40	12.30	22.40

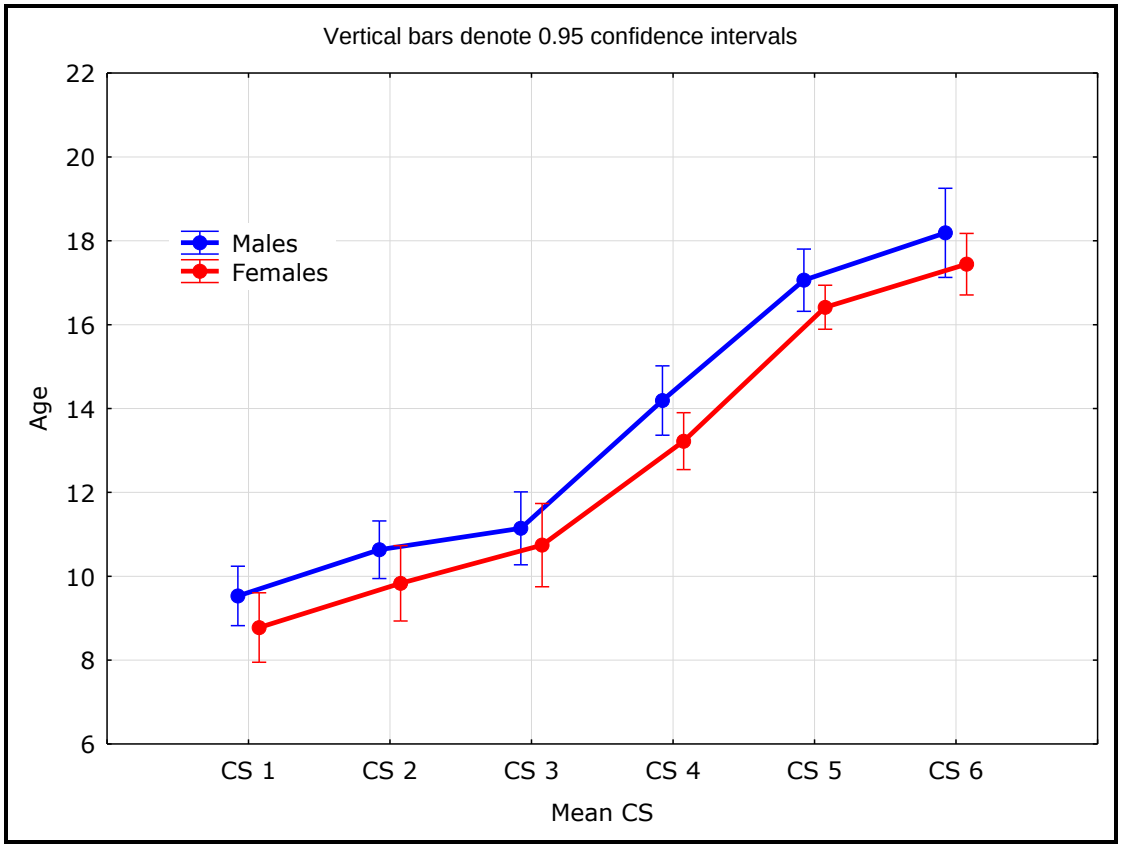

Figure 2. Sample distribution of chronological age among CVM stages in both genders

The Age Confidence intervals among CS1, CS2 and CS3 appeared to overlap in the total sample, as well as in each gender group. The same finding appeared between CS5 and CS6. However, a clear distinction among CS3, CS4 and CS5 was observed in the total sample as well as in each gender group (Figure 2). Accordingly, males aged ≤ 11.75 years and females aged ≤ 11.21 years belong to CS1 or CS2 or CS3. Males aged ≥16.17 years, and females aged ≥15.72 years belong to CS5 or CS6.

Analysis of variance results are presented in table 6 (Table 6).

Table 6. Analysis of variance

	F	**P**
Gender	9.15	0.002629
CS	159.43	<0,001
Gender *CS	0.10	0.992637

LSD test showed that the differences in mean ages among the 6 CS stages were statistically significant and increased as the CS increased. The only exception was CS2 and CS3 that did not show any statistically significant difference, albeit the difference was in the expected direction as it is presented in Table 7 (Table 7).

Table 7. LSD test; differences in mean ages among the 6 CS stages

CVM stage	{CS 1} - 9.2128	{CS 2} - 10.338	{CS 3} - 10.970	{CS 4} - 13.612	{CS 5} - 16.631	{CS 6} - 17.684
CS 1		0.004118	0.000054	0.000000	0.000000	0.000000
CS 2	0.004118		• 0.145620	0.000000	0.000000	0.000000
CS 3	0.000054	• 0.145620		0.000000	0.000000	0.000000
CS 4	0.000000	0.000000	0.000000		0.000000	0.000000
CS 5	0.000000	0.000000	0.000000	0.000000		0.005457
CS 6	0.000000	0.000000	0.000000	0.000000	0.005457	

• denotes absence of statistical significance

Linear model regression analysis was based on highly significant relationships as shown in Table 8 (Table 8).

Table 8. Linear model regression analysis

	B	Std.Err. - of b	t	p-value
Intercept	6.928794	0.278102	24.91457	<0.001
Gender	-0.638936	0.236061	-2.70666	0.007043
CS	1.891935	0.069632	27.17068	0.000000

R= 0.78408099, **R^2= 0.61478299,** Adjusted R^2= 0.61314725

The adjusted coefficient of determination (adjusted R^2=0.61) reveals that the regression line fit the data relatively well; gender and CS, could explain 60% of the age variance in the sample.

The following regression equation for age prediction was calculated:

Predicted age=6.928794-Sex*0.638936+CS*1.891935

Predicted ages according to the regression equation are presented in Table 9 (Table 9).

Table 9. Values of predicted age in years

CVM stage	Males	Females
CS 1	8.82	8.18
CS 2	10.71	10.07
CS 3	12.60	11.96
CS 4	14.49	13.85
CS 5	16.38	15.74
CS 6	18.28	17.64

The accuracy of the age prediction was rather high with only 27 out of the 474 subjects (6%) appearing as outliers using the ±2SD approach. The majority of the 27 outliers (22/27, i.e. 81%) were ≥20 years old. The residuals were mostly positive indicating a tendency to underestimate chronological age in the subjects (Figure 3).

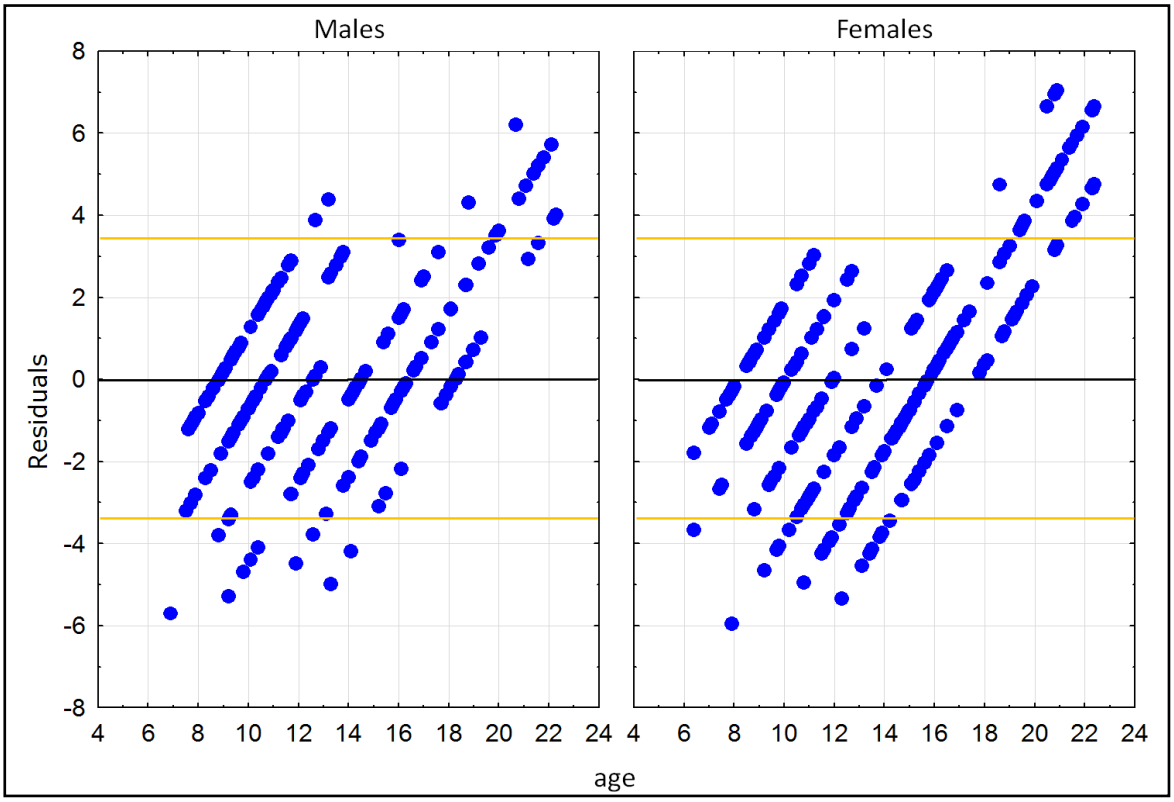

Figure 3. Scatterplot of Residuals against chronological age; categorized by gender

Discussion

Although there are several CVM methods, the one described by Baccetti et al. 2005 was selected for being a simple visual method and easily comprehensible, focusing on just three cervical vertebrae (C2, C3, C4) (Baccetti et al., 2005; Pichai et al., 2014). Moreover, this method was selected for comparison purposes since it has been used in previous studies (Lai et al., 2008; Gabriel et al., 2009; Mellion et al., 2013; Perinetti et al., 2014).

The evaluation of the CVM method's reliability in predicting the pubertal spurt was not a direct objective for the present study. Being a cross-sectional study, no reliable results relative to growth could be obtained (Chen et al., 2008; Soegiharto et al., 2008; Santiago et al., 2012). Longitudinal studies are generally more suitable to evaluate reliability. However, such a study would not be feasible due to the lack of longitudinal radiographic databases of Greek subjects that are not under orthodontic treatment. Besides, taking consecutive radiographs of a subject without clear medical reasons would be ethically unacceptable.

Recently, CVM method has gained popularity for radiation protection reasons replacing the hand and wrist method, in evaluating skeletal growth (Lai et al., 2008; Soegiharto et al., 2008). Since a cephalogram (in which the area of cervical vertebrae is visible by default) is part of the standard documentation used in orthodontic diagnosis, further radiation exposure is avoided. However, the thyroid gland is an extremely radiosensitive organ. Since patient's exposure doses should be kept as low as reasonably achievable (ALARA), the use of a thyroid collar or a collimated beam that could exclude the thyroid might be more beneficial than the information gained from the imaging of the cervical vertebrae. Thus, in cases where skeletal maturity assessment is required, in addition to an ALARA complied cephalogram, a hand-wrist radiograph might be preferable (Hassel & Farman, 1995; Baccetti et al., 2005; Kamal et al., 2006; Chen et al., 2008; Wong et al., 2009; Patcas et al., 2013; Pichai et al., 2014; EC guidelines, 2015).

Recent studies call in question the method's reproducibility (Gabriel et al., 2009; Nestman et al., 2011; Zhao et al., 2012). Gabriel et al. found moderate scores of CVM reproducibility and argued that the CVM method "is too variable to be used as a strict clinical guideline". In a recent systematic review the need for "further studies to assess the reproducibility of the method" was stated (Cerricato et al., 2015).

The present study aimed to address the reproducibility issue by redeeming previous methodological flaws in the literature. A sample consisting of 474 x-rays will likely give a precise image on the method's applicability, while strict inclusion and exclusion criteria guarantee the sample's homogeneity. In order to avoid overstating results, the rater team in our study consisted of three of the authors plus an additional three raters. Moreover, a person not belonging to the rater team cropped the cephalograms and randomized them in a database. Furthermore, the six raters had different educational backgrounds and clinical experience.

Raters were in absolute agreement or in only 1 stage-apart disagreement 85% of the times. Regarding the second rating assessment each rater agreed with their previous assessment at least 3/4 of the times. The consistency of these results can point to the reproducibility of the CVM method. Statistical analysis confirms this perspective: inter- and intra-rater agreement (measured by intraclass correlation coefficient and weighted kappa respectively) were both found high. Based on the above findings and since a cervical staging can be repeated with similar results, the reliability of the CVM method appears to be high. This is in agreement with previous studies (Lai et al., 2008; Soegiharto et al., 2008; Zhao et al., 2012).

However, the level of absolute agreement among raters were lower than 50% and the reproducibility of CS3, the stage that represents the beginning of pubertal growth (Baccetti et al., 2005) was the lowest among all stages. Consequently the present data support Gabriel's conclusion that CVM is an unsafe method for recognizing the pubertal spurt.

Unfortunately, the CVM method is not without limitations. Evidently, identification of a concavity at the lower border of the vertebrae, as well as the assessment of its shape as rectangular horizontal, square or rectangular vertical enclose subjectivity (Zhao et al., 2012). Transition between stages is slow and gradual and there can be morphological vertebrae variations that do not correspond to any of the six stages described above (Figure 4). Development of a software application that would provide objective criteria for the use of CVM method and an automatic staging might overcome the aforementioned difficulties.

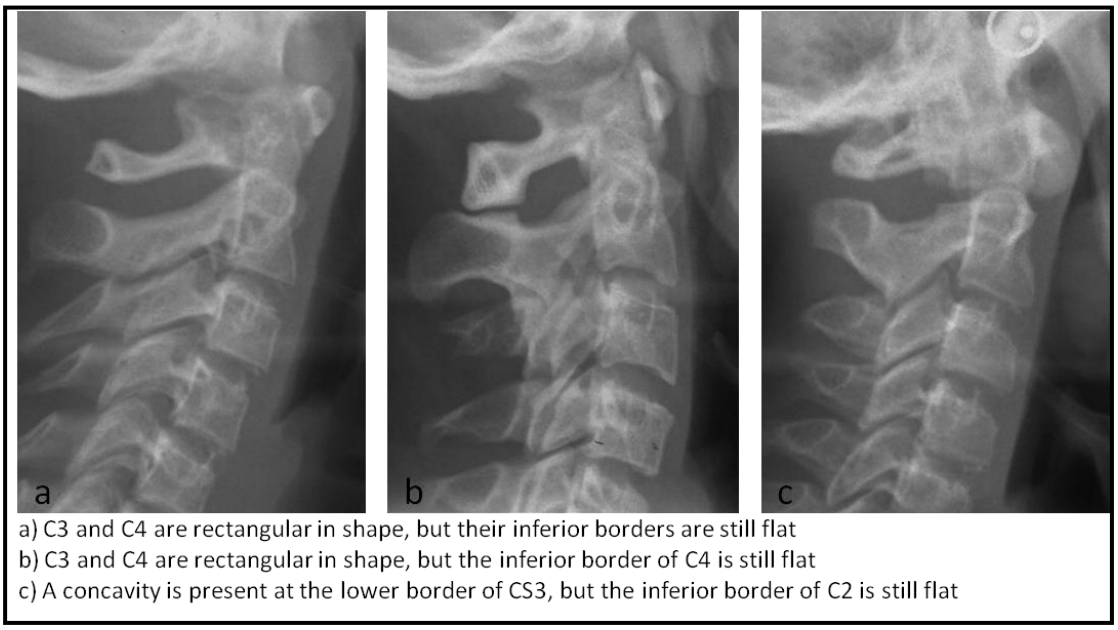

Figure 4. Morphological vertebrae variations that do not correspond to any of the six stages described by Baccetti et al. 2005

Moreover, during evaluation of the radiographs in this study and in case of doubt, the raters were instructed to choose the earlier maturation stage between the two consecutive stages. It is possible that this guideline had an influence on intra- and inter-rater agreement.

A range of ±1 CS when assessing agreement, while making statistical sense, might be quite wide in the context of Orthodontics. However, in potential application of CVM method in different fields (i.e. Forensics) the same range could be tolerated.

A direct, and expected, correlation was found between chronological age and cervical stage (Lamparski, 1972; Baccetti et al., 2005); as cervical stages progress corresponding ages increase, for males and females alike. The differences in mean chronological age between CS1-CS2, CS2-CS3 and CS5-CS6 are all about 1 year. However, the difference in mean ages between CS3-CS4 and CS4-CS5 is almost triple. Thus, the graph reflects a stable and consistent growth rhythm disrupted and decelerated between CS3 and CS5 (Figure 2). To avoid any errors affecting results interpretation, the pubertal acceleration in skeletal growth should be taken into account. This acceleration occurs at different times for different individuals (Buckler, 1984). The undeniable existence of early and late developers that reach their pubertal growth spurt years apart is reflected in the increased age range of CS3 and CS4 and accounts for this inconsistency. Growth rhythm is restored between CS5 and CS6; being a clear indication that CS5 is beyond the peak of the growth spurt.

Furthermore, ages (with a ±95% confidence interval) for CS1, CS2, CS3 and CS5, CS6 overlap, thus forming two distinct groups. Subjects up to 12 years of age will most likely be in the CS1-CS3 group, while children over 16 years old will be in the CS5-CS6 group. We can conclude that in Greek population adult individuals (≥18 years old) will have a skeletal maturation of CS6 or at least CS5 and no less.

This study, conducted in Greek population, shows that overall females reach each stage earlier than males. This comes in accordance with the general developmental pattern stating that girls mature earlier than boys (Hunter, 1966; Molinari et al., 2013).

Age estimation can be of major importance in Forensic science (Rai et al., 2008; Timmins et al., 2011). CVM method could provide a framework to gather information about chronological age and also has the extra advantage of being applicable in various fields, apart from Orthodontics. Regression analysis of our data was used to determine the CVM method's age predicting potential.

Taking into consideration that this study was carried out in children and young adults, it seems reasonable that the age prediction will be valid mainly for CS1-CS4. Cephalograms indicating CS5 and CS6 might belong to adult subjects aged well beyond the predicted values of this study's equation. Despite this limitation, given an arbitrary range of ±3.5 years, chronological age can be estimated safely for subjects of both genders and CS1-CS4 (Figure 3). CS4 values of predicted age are 14.49 years and 13.85 years for boys and girls, respectively. Consequently, subjects with skeletal maturity up to - and including - CS4 will most likely be underage, even in the +3.5 years margin. This finding might be a practical guide in Forensic identification or even in determining legal responsibility.

Based on the present analysis, the CVM method, while helpful in providing a broad estimation about chronological age, should be used in conjunction with other indices if a more accurate prediction is needed.

Conclusions

-With appropriate training, the CVM method described by Baccetti et al. 2005 can be used by professionals without orthodontic background. Thus, CVM could find application in different scientific fields (e.g. Forensics).

-The CVM method presents high reliability in the present study.

-Reproducibility of the CVM method for absolute agreement and 1 stage apart disagreement in the present study is over 77%.

-The CVM method is unsafe for recognizing pubertal spurt, as CS3 is the least reproducible stage.

-A direct, and expected, correlation was found between chronological age and cervical stage; as cervical stages progress corresponding ages increase.

-Regarding age prediction, gender and CS could roughly explain 60% of the age variance in our sample.

-Greek subjects with skeletal maturity up to - and including - CS4 will most likely be underage.

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Appendix A: Statistical Analysis

Intra-rater agreement (Weighted kappa)

Rater:DR

DR	Observation 1						
Observation 2	CS 1	CS 2	CS 3	CS 4	CS 5	CS 6	
CS 1	97	13	1	1	0	0	112 (23.6%)
CS 2	2	48	4	3	0	0	57 (12.0%)
CS 3	0	4	26	6	0	0	36 (7.6%)
CS 4	0	1	4	72	3	0	80 (16.9%)
CS 5	0	0	0	14	123	14	151 (31.9%)
CS 6	0	0	0	0	7	31	38 (8.0%)
	99 (20.9%)	66 (13.9%)	35 (7.4%)	96 (20.3%)	133 (28.1%)	45 (9.5%)	474

Weighted Kappa[a]	0.908
Standard error	0.010
95% CI	0.888 to 0.928

[a] Linear weights

Concordance correlation coefficient (DR)

Sample size	474
Concordance correlation coefficient	0.9645
95% Confidence interval	0.9576 to 0.9702
Pearson ρ (precision)	0.9649
Bias correction factor C_b (accuracy)	0.9996

Rater:D

D Observation 2	Observation 1						
	CS 1	CS 2	CS 3	CS 4	CS 5	CS 6	
CS 1	69	15	6	7	0	0	97 (20.5%)
CS 2	4	44	8	4	0	0	60 (12.7%)
CS 3	0	3	32	6	1	0	42 (8.9%)
CS 4	0	1	11	74	1	0	87 (18.4%)
CS 5	0	0	0	19	80	7	106 (22.4%)
CS 6	0	0	0	0	14	68	82 (17.3%)
	73 (15.4%)	63 (13.3%)	57 (12.0%)	110 (23.2%)	96 (20.3%)	75 (15.8%)	474

Weighted Kappa[a]	0.857
Standard error	0.014
95% CI	0.829 to 0.884

[a] Linear weights

Concordance correlation coefficient (D)

Sample size	474
Concordance correlation coefficient	0.9297
95% Confidence interval	0.9167 to 0.9407
Pearson ρ (precision)	0.9327
Bias correction factor C_b (accuracy)	0.9968

Rater:MR

MR / Observation 2	Observation 1						
	CS 1	CS 2	CS 3	CS 4	CS 5	CS 6	
CS 1	85	12	6	3	0	0	106 (22.4%)
CS 2	1	46	10	3	0	0	60 (12.7%)
CS 3	1	4	28	4	0	1	38 (8.0%)
CS 4	0	0	4	71	4	1	80 (16.9%)
CS 5	0	0	0	7	79	19	105 (22.2%)
CS 6	0	0	0	0	10	75	85 (17.9%)
	87 (18.4%)	62 (13.1%)	48 (10.1%)	88 (18.6%)	93 (19.6%)	96 (20.3%)	474

Weighted Kappa[a]	0.888
Standard error	0.012
95% CI	0.864 to 0.911

[a] Linear weights

Concordance correlation coefficient (MR)

Sample size	474
Concordance correlation coefficient	0.9501
95% Confidence interval	0.9406 to 0.9581
Pearson ρ (precision)	0.9523
Bias correction factor C_b (accuracy)	0.9977

Rater:OPS

OPS	Observation 1						
Observation 2	CS 1	CS 2	CS 3	CS 4	CS 5	CS 6	
CS 1	75	6	2	0	0	0	83 (17.5%)
CS 2	8	58	2	1	0	0	69 (14.6%)
CS 3	1	5	44	4	0	0	54 (11.4%)
CS 4	2	2	3	77	4	0	88 (18.6%)
CS 5	0	0	0	8	102	8	118 (24.9%)
CS 6	0	0	0	0	10	52	62 (13.1%)
	86 (18.1%)	71 (15.0%)	51 (10.8%)	90 (19.0%)	116 (24.5%)	60 (12.7%)	474

Weighted Kappa[a]	0.916
Standard error	0.010
95% CI	0.896 to 0.937

[a] Linear weights

Concordance correlation coefficient (OPS)

Sample size	474
Concordance correlation coefficient	0.9633
95% Confidence interval	0.9562 to 0.9693
Pearson ρ (precision)	0.9635
Bias correction factor C_b (accuracy)	0.9998

Rater:OR2

OR2	Observation 1						
Observation 2	CS 1	CS 2	CS 3	CS 4	CS 5	CS 6	
CS 1	108	3	2	0	0	0	113 (23.8%)
CS 2	1	51	6	1	0	0	59 (12.4%)
CS 3	0	3	28	5	0	0	36 (7.6%)
CS 4	0	1	6	68	5	0	80 (16.9%)
CS 5	0	0	0	17	121	1	139 (29.3%)
CS 6	0	0	0	0	9	38	47 (9.9%)
	109 (23.0%)	58 (12.2%)	42 (8.9%)	91 (19.2%)	135 (28.5%)	39 (8.2%)	474

Weighted Kappa[a]	0.931
Standard error	0.009
95% CI	0.913 to 0.948

[a] Linear weights

Concordance correlation coefficient (OR2)

Sample size	474
Concordance correlation coefficient	0.9749
95% Confidence interval	0.9700 to 0.9789
Pearson ρ (precision)	0.9754
Bias correction factor C_b (accuracy)	0.9995

Rater:OR1

OR1 Observation 2	Observation 1						
	CS 1	CS 2	CS 3	CS 4	CS 5	CS 6	
CS 1	60	7	3	0	0	0	70 (14.8%)
CS 2	1	52	5	0	0	0	58 (12.2%)
CS 3	3	7	42	6	0	0	58 (12.2%)
CS 4	1	1	4	104	8	0	118 (24.9%)
CS 5	0	0	0	7	81	13	101 (21.3%)
CS 6	0	0	0	0	10	59	69 (14.6%)
	65 (13.7%)	67 (14.1%)	54 (11.4%)	117 (24.7%)	99 (20.9%)	72 (15.2%)	474

Weighted Kappa[a]	0.902
Standard error	0.011
95% CI	0.880 to 0.924

[a] Linear weights

Concordance correlation coefficient (OR1)

Sample size	474
Concordance correlation coefficient	0.9581
95% Confidence interval	0.9500 to 0.9649
Pearson ρ (precision)	0.9581
Bias correction factor C_b (accuracy)	1.0000

Inter-rater agreement (Intraclass correlation coefficient)

Intraclass correlation coefficient (First assessment)

Number of subjects (n)	474
Number of raters (k)	6
Model	The same raters for all subjects. Two-way model.
Type	Absolute agreement
Measurements	AM_1 CR_1 GS_1 LS_1 MM_1 SS_1

Intraclass Correlation Coefficient

	Intraclass correlation [a]	95% Confidence Interval
Single measures [b]	0.9198	0.9075 to 0.9308
Average measures [c]	0.9857	0.9833 to 0.9878

[a] The degree of absolute agreement among measurements.

[b] Estimates the reliability of single ratings.

[c] Estimates the reliability of averages of *k* ratings.

Intraclass correlation coefficient (Second assessment)

Number of subjects (n)	474
Number of raters (k)	6
Model	The same raters for all subjects. Two-way model.
Type	Absolute agreement
Measurements	AM_2 CR_2 GS_2 LS_2 MM_2 SS_2

Intraclass Correlation Coefficient

	Intraclass correlation [a]	95% Confidence Interval
Single measures [b]	0.9348	0.9251 to 0.9435
Average measures [c]	0.9885	0.9867 to 0.9901

[a] The degree of absolute agreement among measurements.

[b] Estimates the reliability of single ratings.

[c] Estimates the reliability of averages of *k* ratings.

Intraclass correlation coefficient (All assessments)

Number of subjects (n)	474
Number of raters (k)	12
Model	The same raters for all subjects. Two-way model.
Type	Absolute agreement

Intraclass Correlation Coefficient

	Intraclass correlation [a]	95% Confidence Interval
Single measures [b]	0.9294	0.9199 to 0.9382
Average measures [c]	0.9937	0.9928 to 0.9945

[a] The degree of absolute agreement among measurements.

[b] Estimates the reliability of single ratings.

[c] Estimates the reliability of averages of *k* ratings.

Intra observer agreement as assessed by Cohen's weighted Kappa was high and ranged from 0.857 to 0.931. Precision was also high (0.9581) and accuracy too (1.000),

Finally, inter observer agreement as measured by the Intraclass Correlation Coefficient was nearly perfect (0.9937) In the light of these findings we concluded it was safe to combine all the evaluations from the six observers into an average CS rounded to the nearest integer. Thus we used the Mean CS for the final analysis with age as the dependent variable and Mean CS and Sex as the predictor variables.

Sample

Age		N	Mean	Std.Dev.	Std.Err	-95%	+95%	Min	Max
Total		474	13.38	4.01	0.18	13.02	13.75	6.40	22.40
Males		217	12.93	3.79	0.26	12.42	13.43	6.90	22.30
Females		257	13.77	4.15	0.26	13.26	14.28	6.40	22.40
CS1		78	9.21	1.36	0.15	8.91	9.52	6.40	13.20
CS2		76	10.34	1.61	0.18	9.97	10.71	6.40	13.80
CS3		53	10.97	1.41	0.19	10.58	11.36	6.90	16.00
CS4		82	13.61	2.90	0.32	12.98	14.25	7.90	20.90
CS5		123	16.63	3.06	0.28	16.09	17.18	10.80	22.40
CS6		62	17.68	2.89	0.37	16.95	18.42	12.30	22.40
Males	CS1	45	9.53	1.41	0.21	9.11	9.96	7.60	13.20
	CS2	48	10.63	1.61	0.23	10.17	11.10	7.50	13.80
	CS3	30	11.14	1.62	0.29	10.54	11.75	6.90	16.00
	CS4	33	14.19	2.52	0.44	13.30	15.09	9.20	20.70
	CS5	41	17.06	2.83	0.44	16.17	17.95	11.90	22.10
	CS6	20	18.19	2.49	0.56	17.03	19.35	13.30	22.30
Females	CS1	33	8.78	1.17	0.20	8.36	9.19	6.40	11.20
	CS2	28	9.83	1.51	0.29	9.24	10.42	6.40	12.70
	CS3	23	10.74	1.08	0.23	10.28	11.21	8.80	13.20
	CS4	49	13.22	3.09	0.44	12.34	14.11	7.90	20.90
	CS5	82	16.42	3.16	0.35	15.72	17.11	10.80	22.40
	CS6	42	17.44	3.06	0.47	16.49	18.40	12.30	22.40

Analysis of Variance

	SS	Degr. of - Freedom	MS	F	p
Intercept	71204.24	1	71204.24	12143.58	0.000000
Sex	53.64	1	53.64	9.15	0.002629
Mean CS	4674.23	5	934.85	159.43	0.000000
Sex*Mean CS	2.84	5	0.57	0.10	0.992637
Error	2708.95	462	5.86		

LSD test; variable Age

MEAN CS	{CS 1} - 9.2128	{CS 2} - 10.338	{CS 3} - 10.970	{CS 4} - 13.612	{CS 5} - 16.631	{CS 6} - 17.684
CS 1		0.004118	0.000054	0.000000	0.000000	0.000000
CS 2	0.004118		0.145620	0.000000	0.000000	0.000000
CS 3	0.000054	0.145620		0.000000	0.000000	0.000000
CS 4	0.000000	0.000000	0.000000		0.000000	0.000000
CS 5	0.000000	0.000000	0.000000	0.000000		0.005457
CS 6	0.000000	0.000000	0.000000	0.000000	0.005457	

As a first step we proceeded with factorial (2X6) Analysis of Variance using Sex and the Mean CS as grouping factors and Age as the dependent variable. The results are summarized in the tables above.

The Analysis of Variance table clearly showed a Sex and Mean CS effect (p=0.002 and 0.000 respectively) whereas there was no statistically significant interaction.

Overall boys were slightly younger than girls but only for about one year. Although this finding was statistically significant we did not consider it to be of any real significance. However we did use sex as an independent variable in the regression analysis that followed.

The differences in means (=age mean for each CS stage) between the 6 CS categories were statistically significant (LSD test) and increased as the CS increased. The only exception was categories 2 and 3 that did not show statistically significant difference albeit the difference was in the expected direction.

Following this analysis we continued with a General Linear Model Regression Analysis using Age as the dependent variable and Sex and Mean CS categories as the predictor variables. As it can be seen in the tables below the R value was rather high (0.78) and the Adjusted R^2 was 0.61 meaning that the two variables, Sex and Mean CS could explain roughly 60% of the age variance in our sample. Special mention should be made to the totally neutral Durbin-Watson statistic which was 1.90 indicating no relationship whatsoever between the residuals in the regression analysis. The results of the regression analysis are summarized in the table below.

[1]

Regression Summary for Dependent Variable: Age R= 0.78408099 R²= 0.61478299 Adjusted R²= 0.61314725 F(2,471)=375.84 p						
	b*	**Std.Err. - of b***	**b**	**Std.Err. - of b**	**t(471)**	**p-value**
Intercept			6.928794	0.278102	24.91457	0.000000
Sex	-0.079556	0.029393	-0.638936	0.236061	-2.70666	0.007043
Mean CS	0.798621	0.029393	1.891935	0.069632	27.17068	0.000000

Regression equation: Age=6.928794-Sex*0.638936+CS*1.891935

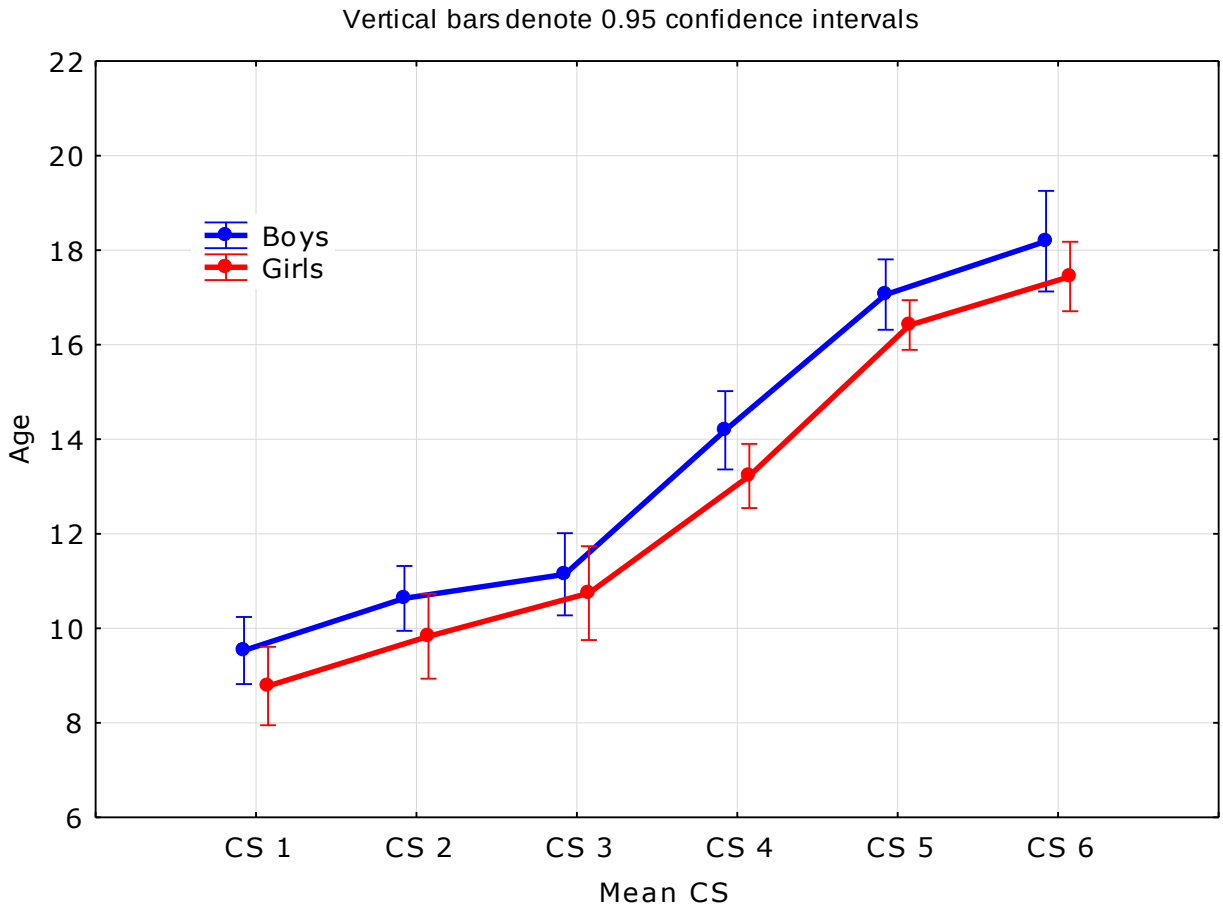
Durbin-Watson d and serial correlation of residuals		
	Durbin-Watson d[1]	**Serial - Corr.**
Estimate	1.904958	0.047373

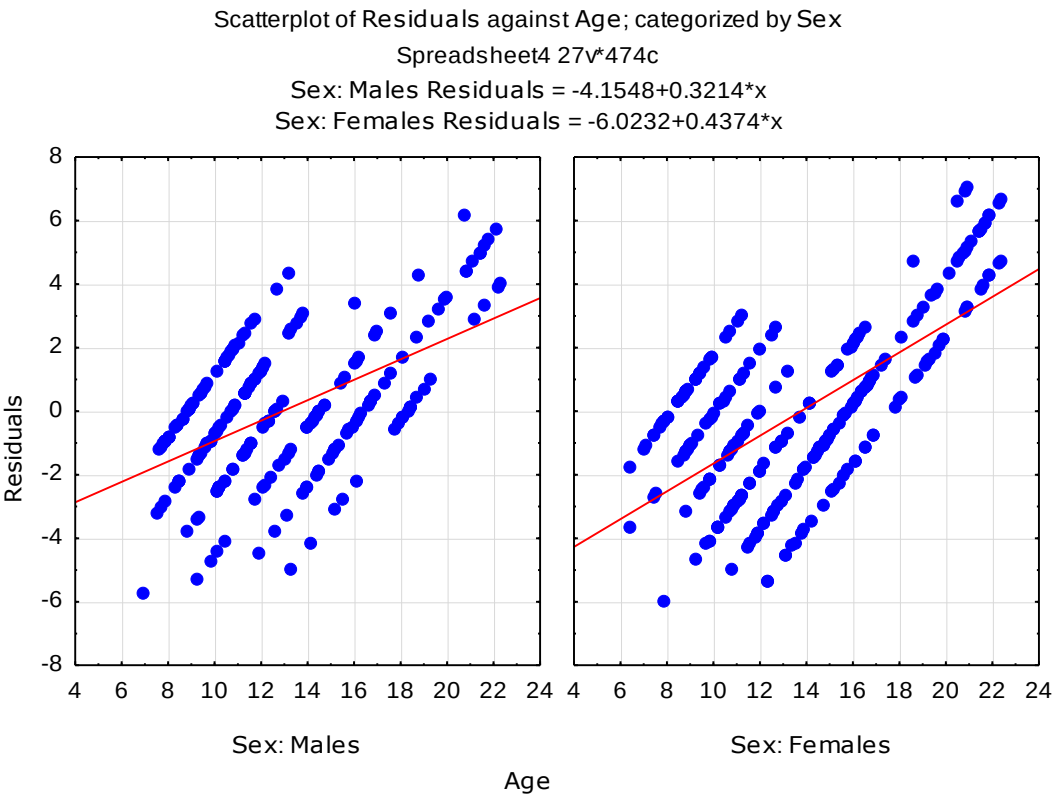
[1] Independence of Residuals - Durbin-Watson Statistic: The assumption is that the residuals are not correlated serially from one observation to the next. This means the size of the residual for one case has no impact on the size of the residual for the next case. The Durbin-Watson Statistic is used to test for the presence of serial correlation among the residuals. The value of the Durbin-Watson statistic ranges from 0 to 4. As a general rule of thumb, the residuals are uncorrelated is the Durbin-Watson statistic is approximately 2. A value close to 0 indicates strong positive correlation, while a value of 4 indicates strong negative correlation. For our problem, the value of Durbin-Watson is 1.94950, approximately equal to 2, indicating no serial correlation.

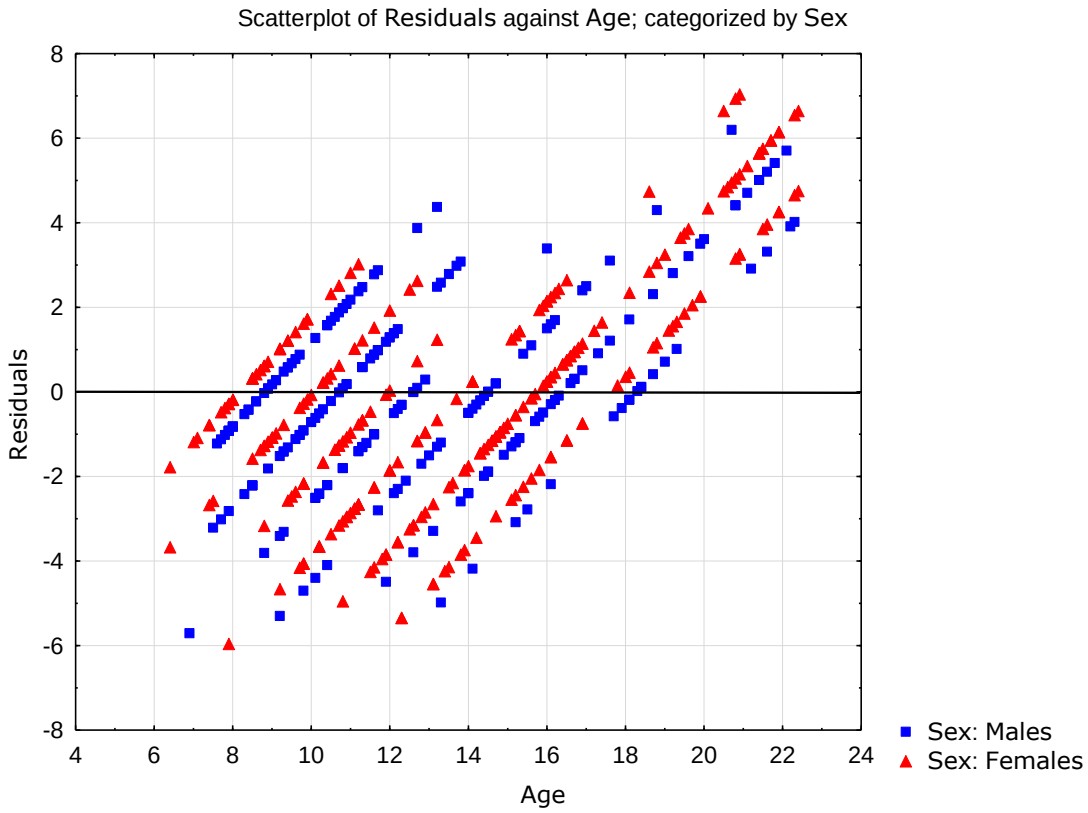
The accuracy of the age prediction was rather high with only 27 out of the 474 subjects (6%) appearing as outliers using the ±2SD approach. Of the 22 outliers the majority (22/27, i.e. 81%) were 20 years old or over. The residuals were mostly positive indicating a tendency to underestimate age in the subjects.

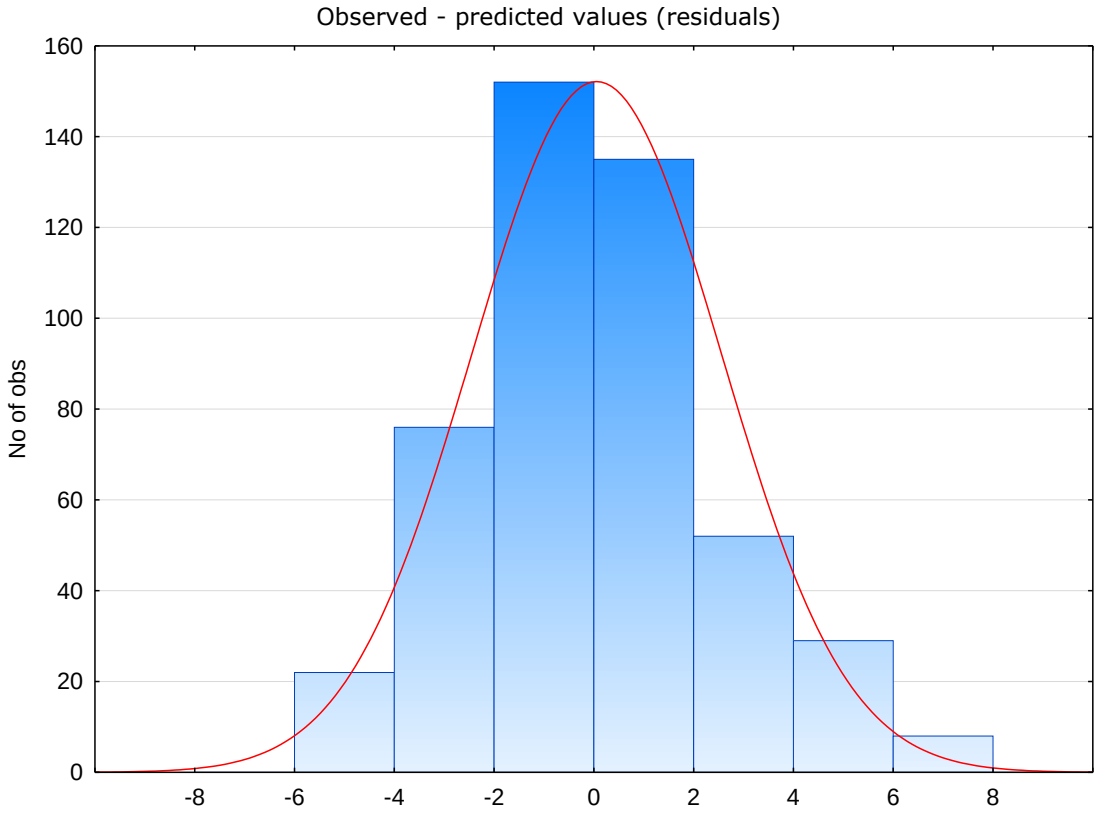
Standard Residual: Age Outliers

	Observed - Value	Predicted - Value	Residual	Standard - Pred. v.	Standard - Residual	Std.Err. - Pred.Val
6 . . . |* . . .	21.40	15.75	5.65	0.75	2.27	0.17
46 . . . |* . . .	21.40	16.39	5.01	0.96	2.01	0.21
88 . . . |* . . .	21.50	15.75	5.75	0.75	2.31	0.17
91 . . . | * . . .	20.50	13.86	6.64	0.15	2.67	0.16
92 . . . | * . . .	21.90	15.75	6.15	0.75	2.47	0.17
94 . . . |* . . .	21.40	15.75	5.65	0.75	2.27	0.17
117 . . . | * . . .	20.70	14.50	6.20	0.35	2.49	0.18
120 . . . |* . . .	20.80	15.75	5.05	0.75	2.03	0.17
141 . . . | *. . .	20.80	13.86	6.94	0.15	2.79	0.16
146 . . . |* . . .	21.40	15.75	5.65	0.75	2.27	0.17
159 . . . | * . . .	22.30	15.75	6.55	0.75	2.63	0.17
167 . . . | * . . .	21.70	15.75	5.95	0.75	2.39	0.17
175 . . . | *. . .	20.90	13.86	7.04	0.15	2.83	0.16
181 . . . |* . . .	21.40	16.39	5.01	0.96	2.01	0.21
211 . . . * . . .	12.30	17.64	-5.34	1.36	-2.14	0.21
218 . . . *| . . .	7.90	13.86	-5.96	0.15	-2.39	0.16
245 . . . *| . . .	6.90	12.60	-5.70	-0.25	-2.29	0.17
305 . . . * . . .	12.30	17.64	-5.34	1.36	-2.14	0.21
343 . . . |* . . .	21.80	16.39	5.41	0.96	2.17	0.21
375 . . . | * . . .	22.40	15.75	6.65	0.75	2.67	0.17
398 . . . | * . . .	21.70	15.75	5.95	0.75	2.39	0.17
411 . . . * . . .	9.20	14.50	-5.30	0.35	-2.13	0.18
414 . . . |* . . .	22.10	16.39	5.71	0.96	2.29	0.21
416 . . . |* . . .	20.90	15.75	5.15	0.75	2.07	0.17
421 . . . |* . . .	21.60	16.39	5.21	0.96	2.09	0.21
427 . . . |* . . .	21.10	15.75	5.35	0.75	2.15	0.17
465 . . . | * . . .	21.90	15.75	6.15	0.75	2.47	0.17
Minimum . . . * | . . .	6.90	12.60	-5.96	-0.25	-2.39	0.16
Maximum . . . | *. . .	22.40	17.64	7.04	1.36	2.83	0.21
Mean . . . |* . . .	19.27	15.52	3.75	0.68	1.50	0.18
Median . . . |* . . .	21.40	15.75	5.65	0.75	2.27	0.17

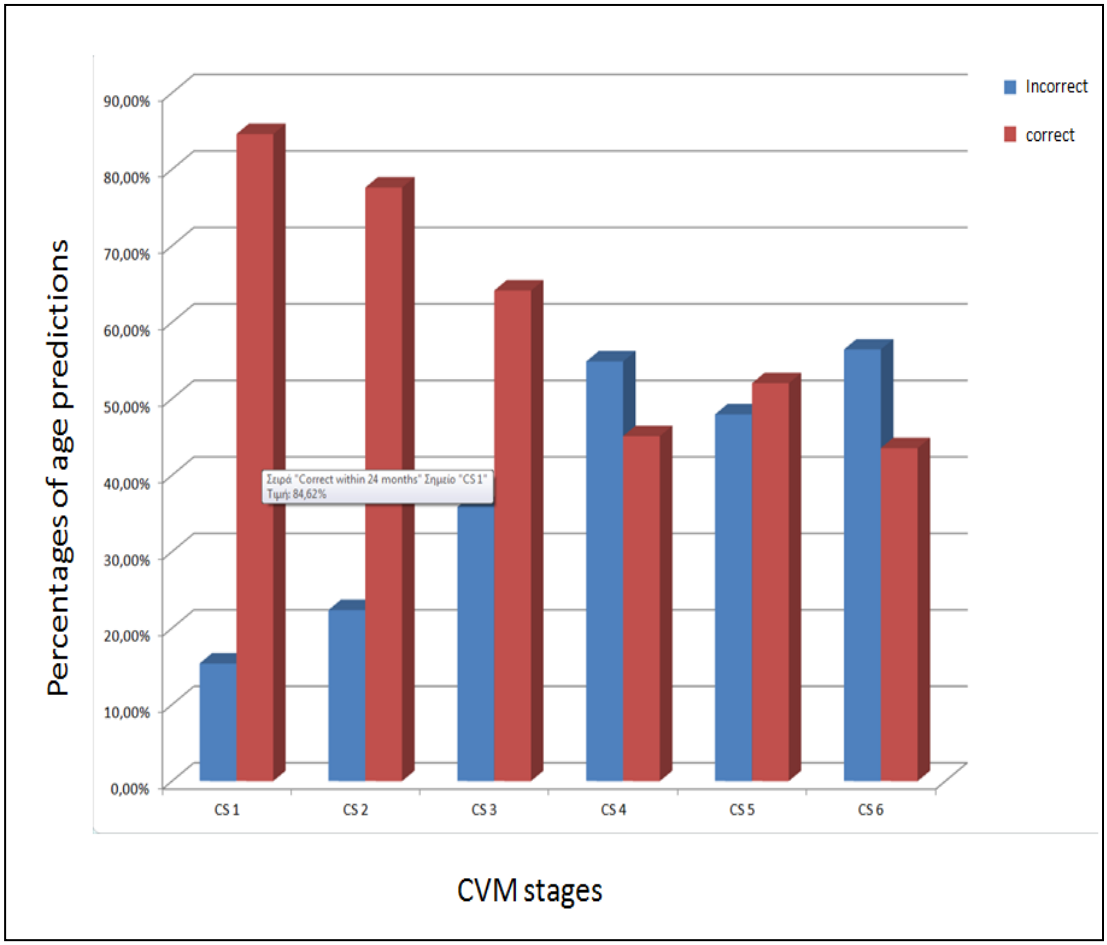

Vertical bars denote 0.95 confidence intervals
Boys
Girls
Age
22
20
18
16
14
12
10
8
6
CS 1
CS 2
CS 3
CS 4
CS 5
CS 6
Mean CS


Scatterplot of Residuals against Age; categorized by Sex
Spreadsheet4 27v*474c
Sex: Males Residuals = -4.1548+0.3214*x
Sex: Females Residuals = -6.0232+0.4374*x
Residuals
8
6
4
2
0
-2
-4
-6
-8
4 6 8 10 12 14 16 18 20 22 24
4 6 8 10 12 14 16 18 20 22 24
Sex: Males
Sex: Females
Age


Scatterplot of Residuals against Age; categorized by Sex
Residuals
Age
Sex: Males
Sex: Females


Observed - predicted values (residuals)
No of obs

Percentages of correct versus incorrect age prediction within 24months for each CVM stage.



Appendix B: Raw Data

*Values (1-6) refer to CS

X-ray No	Gender	Age	OPS 1ST assessment	OPS 2nd assessment	DR 1ST assessment	DR 2nd assessment	D 1ST assessment	D 2nd assessment	MR 1ST assessment	MR 2nd assessment	OR1 1ST assessment	OR1 2nd assessment	OR2 1ST assessment	OR2 2nd assessment
1	M	17,3	5	5	5	5	5	5	5	5	4	4	5	5
2	F	14,8	5	5	5	5	6	6	5	6	5	5	5	5
3	M	14,4	4	4	4	4	4	4	4	4	4	4	4	4
4	M	15,8	5	5	5	5	5	5	5	5	4	4	4	5
5	F	21,6	6	6	6	6	6	6	5	6	6	6	5	6
6	F	21,4	5	5	5	5	5	6	5	6	6	5	5	6
7	M	8,4	1	1	1	1	1	1	1	1	1	1	1	1
8	F	16,4	5	5	5	5	5	5	6	6	5	5	5	5
9	M	12,8	4	4	4	4	3	4	4	4	3	4	3	4
10	M	11,9	5	5	5	5	5	5	5	5	5	5	5	5
11	F	20,1	5	5	5	5	5	5	5	6	5	5	5	5
12	M	10,2	3	3	3	3	3	3	3	3	3	3	3	3
13	F	16	5	6	5	5	5	6	5	6	5	6	5	5
14	M	9,7	2	2	2	1	2	2	2	2	2	2	2	1
15	F	11,5	5	5	5	5	5	5	5	5	5	5	5	5
16	F	10,3	1	1	1	1	1	2	2	2	2	2	2	1
17	M	19,3	6	6	5	5	6	6	6	6	5	6	5	6

18	M	13,3	4	3	4	3	3	4	4	4	4	4	4	3
19	M	22,2	6	6	6	6	6	6	6	6	6	6	6	6
20	M	9,4	1	1	1	1	1	1	1	1	1	1	2	1
21	M	14,7	4	4	4	4	3	3	3	4	3	3	3	4
22	M	15,9	5	5	5	5	5	5	5	5	5	4	5	4
23	M	7,7	1	1	1	1	1	1	1	1	1	1	1	1
24	M	12,1	2	3	2	2	2	2	2	2	2	3	3	2
25	F	18,8	6	6	6	6	6	6	6	6	6	6	6	6
26	M	10	2	1	1	2	3	2	3	3	3	3	3	2
27	M	9,8	2	1	2	1	1	1	2	1	2	2	1	2
28	F	18,6	4	4	4	4	4	4	4	5	4	4	4	4
29	M	14	4	4	5	4	4	5	5	5	4	4	4	5
30	F	10,9	4	4	4	3	3	4	4	4	4	4	4	4
31	F	20,5	5	6	5	5	6	6	6	6	5	5	5	5
32	F	19,9	5	5	5	5	6	6	6	6	5	5	6	6
33	F	10,5	4	4	4	4	3	4	4	4	4	4	4	3
34	M	15,4	5	4	4	5	4	4	4	4	4	4	4	4
35	F	11,2	4	4	4	4	4	4	4	4	4	4	4	4
36	F	21,9	6	6	6	6	6	6	6	6	6	6	6	6
37	F	13,9	5	6	5	5	6	6	6	6	6	6	5	5

38	F	9,8	2	3	3	3	3	3	4	4	2	3	3	2
39	M	11,6	2	4	2	3	4	2	2	2	2	3	4	2
40	F	15,2	5	5	5	5	5	5	5	5	5	5	5	5
41	F	9,8	2	1	1	1	1	1	3	1	1	1	3	1
42	M	10,9	2	2	2	2	2	2	2	2	2	2	2	2
43	F	14,4	4	4	5	5	4	4	5	5	4	4	5	5
44	M	10,1	3	3	3	3	3	3	2	3	3	3	3	2
45	M	12,2	2	3	3	2	2	2	2	2	2	3	3	2
46	M	21,4	5	5	5	5	5	5	5	6	5	5	6	6
47	F	12	4	4	4	4	4	4	4	4	4	4	4	4
48	F	8,6	1	1	1	1	1	1	1	1	1	1	1	1
49	M	19,6	5	5	5	5	5	5	4	4	4	4	5	5
50	F	16,6	5	5	5	5	5	5	5	5	5	5	5	5
51	F	10,5	1	1	1	1	1	1	1	1	1	1	1	1
52	F	12,9	4	4	4	4	4	4	4	4	4	4	4	4
53	M	13,3	5	6	6	5	5	6	6	6	5	6	6	6
54	M	14	5	5	5	5	5	5	5	5	5	5	5	5
55	M	20,8	5	5	5	5	5	5	6	5	5	6	6	6
56	M	16,9	5	5	5	6	5	5	6	6	5	5	5	5
57	F	9,9	1	1	1	1	1	1	1	1	1	1	1	1

58	M	13,8	5	5	5	5	5	5	5	5	4	5	4	5
59	F	14,2	6	6	5	5	6	6	6	5	5	6	5	5
60	M	14,7	4	4	3	4	4	4	4	4	4	4	3	4
61	M	10,4	4	3	4	4	3	4	4	4	3	4	3	4
62	M	18,8	5	4	4	5	4	4	4	4	5	4	4	4
63	F	8,9	1	2	1	1	1	2	2	1	2	2	1	1
64	M	17,6	5	5	5	5	5	5	5	5	5	5	5	5
65	F	15,8	6	5	5	5	6	6	6	6	5	6	6	6
66	F	15,6	5	5	5	5	5	5	5	5	5	5	5	5
67	M	10,1	4	4	4	4	4	4	4	4	4	4	4	4
68	F	10,7	4	4	5	5	4	4	4	5	4	4	4	5
69	M	10,4	3	3	3	3	3	3	3	3	3	3	3	3
70	F	13,2	3	3	3	4	3	4	3	3	4	3	4	4
71	F	11	3	3	2	2	3	3	2	3	3	3	3	3
72	M	16,1	4	4	4	4	4	4	4	4	4	4	4	4
73	F	12,5	2	2	2	1	2	2	2	2	1	1	2	2
74	M	19	6	6	6	6	6	6	6	6	6	6	6	6
75	M	10,9	1	1	1	1	1	1	1	1	1	1	1	1
76	F	10,8	4	4	4	4	4	4	4	4	4	4	4	4
77	F	16,1	5	5	5	5	5	5	6	5	6	5	5	5

78	F	11,6	1	4	1	1	4	1	1	1	3	1	3	4
79	F	15,4	6	6	6	6	6	6	6	6	6	6	6	6
80	M	11,7	1	2	2	1	2	1	1	1	1	1	1	1
81	M	18,4	6	6	6	6	6	6	6	6	6	6	6	6
82	F	9,9	1	1	1	1	1	1	1	1	1	1	1	1
83	M	9,4	1	2	2	1	1	1	1	1	2	1	2	2
84	M	10,7	2	2	1	1	1	1	1	1	1	1	2	2
85	M	14	4	4	4	4	4	4	4	4	4	4	4	4
86	F	9,8	4	4	4	4	4	4	4	4	4	4	4	4
87	M	16,1	5	5	6	5	5	5	6	6	5	5	5	5
88	F	21,5	5	5	5	5	4	5	4	5	4	4	4	5
89	M	9,5	1	1	1	1	1	1	1	1	1	1	1	1
90	M	14,4	4	4	4	4	4	4	4	4	4	4	4	4
91	F	20,5	4	4	5	5	4	4	4	4	4	4	4	5
92	F	21,9	5	5	5	5	6	5	5	5	6	5	6	6
93	M	13,2	1	2	1	1	1	2	2	2	1	3	3	1
94	F	21,4	5	5	6	5	5	5	6	5	5	5	5	5
95	F	11,2	4	4	4	4	4	4	4	4	4	4	4	4
96	F	16,1	6	6	6	6	6	6	5	6	6	6	5	6
97	F	16,7	5	5	5	5	5	5	5	5	5	5	5	5

98	M	11,7	4	4	4	3	4	4	4	4	4	4	4	3
99	F	9,2	4	4	4	4	4	4	4	4	4	4	4	4
100	F	16,2	4	4	4	5	4	5	4	4	4	4	4	4
101	F	17,8	6	6	5	5	6	6	6	5	6	5	6	6
102	F	15,6	6	6	6	6	6	6	6	6	6	6	6	6
103	F	20,8	6	6	5	5	6	6	6	6	6	6	5	5
104	M	13,5	2	2	2	2	2	2	2	2	2	2	2	2
105	F	10,6	3	3	2	2	3	3	3	3	3	4	3	3
106	F	12,9	5	5	5	5	5	5	6	5	5	5	5	5
107	F	9,8	4	4	3	4	4	4	4	4	4	4	4	3
108	F	10,9	4	3	3	3	3	4	3	4	4	4	3	4
109	F	14,9	5	5	5	5	5	5	6	5	5	6	5	5
110	M	18,4	6	6	5	5	6	6	6	6	6	6	6	6
111	M	14,4	4	4	5	5	5	5	5	5	4	4	4	5
112	M	15,7	5	5	5	5	4	5	5	5	4	5	4	5
113	M	19,9	5	5	6	5	6	5	5	5	5	5	5	6
114	M	17,6	5	5	4	4	4	4	4	4	4	4	4	5
115	F	10,2	4	4	4	4	3	4	3	4	4	4	4	4
116	M	13.1	5	5	4	5	5	5	5	5	4	5	5	5
117	M	20,7	4	5	4	5	4	4	4	4	4	4	4	5

118	F	13,1	6	6	5	5	6	6	6	6	6	6	5	6
119	M	10,6	1	1	1	1	1	1	1	1	1	1	1	1
120	F	20,8	5	5	5	5	5	6	6	5	5	5	5	5
121	M	15,3	5	5	6	5	6	6	6	6	5	5	5	5
122	M	14,5	5	4	4	5	4	4	5	5	4	5	4	5
123	F	12.9	4	4	4	4	4	4	4	4	4	4	4	4
124	M	11,5	1	2	2	1	1	1	1	1	2	2	2	2
125	F	16,5	6	6	5	5	6	6	6	6	5	6	6	6
126	F	21,5	6	6	6	6	6	6	6	6	6	6	6	6
127	M	11,4	3	3	2	2	3	3	2	2	3	3	2	2
128	F	19,3	6	6	6	6	6	6	6	6	6	6	6	6
129	F	18,1	5	6	6	5	6	6	6	6	6	6	5	5
130	M	18,3	6	6	5	5	6	6	6	6	6	6	5	5
131	F	11,1	4	4	4	4	4	4	4	4	4	4	4	4
132	F	10,4	2	2	2	2	2	3	2	2	2	2	2	2
133	F	18,8	6	5	5	5	5	5	6	5	6	5	5	5
134	F	19,6	5	5	5	5	5	5	5	5	5	5	5	5
135	M	18,1	5	5	5	5	4	5	6	4	4	5	5	5
136	M	11,3	2	2	2	2	2	2	4	3	1	4	1	1
137	F	18,7	6	6	6	6	6	6	6	6	6	6	5	5

138	M	18,4	6	6	6	6	6	6	6	6	6	6	6	6
139	F	9,6	1	1	1	1	1	1	1	1	1	1	1	1
140	F	16,9	6	6	6	6	6	6	6	6	6	6	6	6
141	F	20,8	4	4	4	4	4	4	4	4	4	4	4	4
142	F	14,3	5	5	5	5	5	5	5	5	5	5	5	5
143	F	14,8	5	5	6	5	6	6	6	6	5	5	5	5
144	F	16	5	5	5	5	5	5	5	5	6	5	5	5
145	M	11,9	3	1	1	1	1	1	3	1	3	3	1	1
146	F	21,4	5	5	5	5	5	5	6	6	5	5	5	5
147	F	14,1	4	5	5	4	4	4	5	5	4	4	4	4
148	M	22,3	6	6	6	6	6	6	6	6	6	6	6	6
149	F	13,9	5	5	5	5	6	6	6	6	5	5	5	5
150	F	15,1	6	6	6	6	6	6	6	6	6	6	6	6
151	F	11,9	4	4	5	5	5	4	4	5	5	5	5	4
152	M	11	1	1	1	1	1	1	1	1	1	1	1	1
153	F	12.7	5	5	4	2	4	5	4	5	3	3	2	4
154	F	15,2	6	5	5	5	6	6	6	6	6	6	5	5
155	M	10,8	3	3	3	3	3	3	3	3	3	3	3	3
156	F	10,8	5	5	5	5	5	5	5	5	5	5	5	5
157	M	18,1	6	6	6	6	6	6	6	6	6	6	6	6

158	M	12,3	3	4	3	3	3	4	3	4	3	3	4	4
159	F	22,3	5	5	5	5	5	5	5	5	5	5	5	5
160	F	10,7	2	4	3	4	4	4	4	4	3	4	2	2
161	M	9,4	2	2	2	2	2	2	2	2	2	2	2	2
162	F	18	6	6	6	6	6	6	6	6	6	6	6	6
163	M	10,4	1	1	1	1	1	1	1	1	1	1	1	1
164	M	10	2	2	2	2	2	2	2	2	2	2	2	2
165	F	19,1	6	6	6	6	6	6	6	6	6	6	6	6
166	F	10	2	2	3	3	2	2	2	2	3	3	2	2
167	F	21,7	5	5	6	5	5	5	6	5	5	6	5	5
168	F	11.2	2	1	1	1	1	1	2	1	1	2	1	1
169	F	10,9	4	3	3	3	4	4	4	4	3	3	3	3
170	M	12,1	2	2	2	1	2	2	2	2	1	1	1	1
171	F	13,5	5	5	5	5	4	5	4	5	4	4	4	4
172	F	10,3	3	3	3	3	3	3	3	3	3	3	3	3
173	F	22,4	6	6	6	6	6	6	6	6	6	6	6	6
174	M	14,5	4	4	4	4	4	4	4	4	4	4	4	4
175	F	20,9	4	4	4	4	4	4	4	4	4	4	4	4
176	M	10,9	1	1	1	1	1	1	1	1	4	4	1	1
177	M	10,1	1	1	2	1	1	1	1	1	1	1	1	1

178	F	16,7	5	4	4	5	5	5	5	5	4	4	4	5
179	M	16,6	4	5	4	5	4	5	5	5	5	4	4	5
180	M	10,2	2	2	2	2	2	2	2	2	2	2	1	1
181	M	21,4	5	5	5	5	5	5	5	5	5	5	5	5
182	F	11,6	5	5	5	5	5	5	5	6	6	5	5	5
183	F	16,6	5	5	5	5	5	5	5	5	5	5	5	5
184	M	9,6	1	1	1	1	1	1	1	1	1	1	1	1
185	M	16,2	4	4	4	4	4	4	4	4	4	4	4	4
186	M	12,6	4	2	2	2	4	2	2	2	4	4	2	2
187	F	8	1	1	1	1	1	1	1	1	3	1	1	1
188	M	12,9	1	4	4	1	4	1	4	1	4	4	1	1
189	M	11,2	1	1	1	1	1	1	1	1	1	1	1	1
190	F	9,8	3	3	2	2	3	2	2	3	4	4	2	2
191	F	14	5	5	5	5	5	5	5	5	5	5	5	5
192	M	8	1	1	1	1	1	1	1	1	1	1	1	1
193	F	17,2	5	5	5	5	5	5	5	5	5	4	5	4
194	M	15,5	6	6	6	6	6	6	6	6	6	6	6	6
195	M	11,7	3	3	1	1	3	3	3	1	4	4	1	1
196	F	18,6	5	5	5	5	5	5	5	5	5	5	5	5
197	M	19,2	5	5	5	5	5	5	5	5	5	5	5	5

198	M	11,6	3	3	3	1	4	4	4	1	4	4	1	1
199	F	12,2	5	5	5	5	5	5	5	5	5	5	5	5
200	F	20,6	5	5	5	5	5	5	5	5	5	5	5	5
201	M	12,2	4	4	4	4	4	4	4	4	4	4	4	4
202	F	12,2	5	5	5	5	5	5	6	5	5	5	5	5
203	F	13,1	5	5	4	5	5	5	5	5	5	4	5	5
204	F	15,2	4	4	4	4	4	4	4	4	4	4	4	4
205	F	9,5	2	2	2	3	4	4	4	4	2	2	1	1
206	M	11,3	2	3	2	4	3	2	4	2	2	2	2	2
207	M	8	1	1	1	1	1	1	1	1	1	1	1	1
208	F	8,9	3	2	2	2	3	3	3	2	2	3	2	2
209	M	12,4	4	4	4	4	4	4	4	4	4	4	4	4
210	M	10,8	1	1	2	2	1	1	1	1	2	2	1	1
211	F	12,3	5	6	6	5	6	6	6	6	6	6	6	6
212	M	13	4	4	4	3	4	4	4	3	4	3	4	3
213	M	13,2	4	4	4	4	4	4	4	4	4	4	4	4
214	M	10,8	2	2	2	2	2	4	4	4	4	4	3	2
215	F	13,2	4	4	4	4	4	4	4	4	4	4	4	4
216	F	8,7	1	1	1	1	2	1	1	1	1	1	1	1
217	M	8,8	1	2	4	2	4	4	4	2	4	4	2	2

218	F	7,9	3	4	4	4	3	4	4	3	4	3	3	3
219	F	11,2	3	3	3	3	3	3	3	3	3	3	3	3
220	M	11,2	3	3	3	3	4	3	3	2	4	4	3	3
221	F	10,3	2	2	2	2	2	2	2	1	2	2	1	1
222	F	10,7	1	1	1	1	1	1	1	1	1	1	1	1
223	M	12,7	2	2	4	4	3	4	4	2	5	5	2	2
224	M	12	3	3	2	2	3	3	2	2	2	2	2	2
225	F	14,8	5	5	5	5	5	5	5	6	6	5	5	5
226	F	10,3	3	3	3	3	3	3	3	3	3	3	3	3
227	M	10,8	1	1	1	1	1	1	1	1	1	1	1	1
228	M	10,4	1	1	1	1	2	1	1	1	2	2	1	1
229	M	11,3	3	3	2	2	4	2	3	2	3	3	2	2
230	M	13,3	1	2	1	1	4	1	1	1	2	2	1	1
231	M	8,3	2	2	2	2	2	1	1	2	1	1	1	1
232	M	12,2	3	3	3	3	3	3	3	3	3	3	3	3
233	M	11,3	2	2	2	1	2	2	2	1	2	1	1	1
234	F	9,8	2	2	2	2	2	2	2	2	2	2	2	2
235	F	11,6	4	4	4	4	4	4	4	4	4	4	4	4
236	F	12,6	5	5	5	5	5	5	5	5	5	5	5	5
237	M	12	2	2	2	2	2	2	2	2	2	2	2	2

238	F	12,6	5	5	5	5	5	5	5	5	5	5	5	5
239	F	11,5	3	3	4	4	3	3	3	3	4	4	3	3
240	M	10,8	2	2	2	2	2	3	3	2	2	2	2	2
241	M	14,5	5	5	5	5	5	5	5	5	6	6	5	5
242	F	9,6	3	3	3	3	3	3	2	2	3	3	2	2
243	M	10,7	2	2	2	2	1	1	2	2	1	3	1	1
244	M	8,5	3	3	1	1	3	3	3	3	3	3	1	1
245	M	6,9	3	3	3	3	3	3	3	3	3	3	3	3
246	M	11,3	2	2	1	1	3	1	1	1	3	3	1	1
247	M	10,1	3	3	3	3	3	3	3	3	3	3	3	3
248	F	12	4	4	4	4	4	4	4	4	4	4	4	4
249	F	11,3	1	1	2	1	4	1	3	1	4	4	1	1
250	F	11	2	2	1	1	2	1	1	1	2	2	1	1
251	F	12,2	4	4	4	4	4	4	4	4	4	4	4	4
252	M	8,8	1	1	1	1	1	1	1	1	1	1	1	1
253	M	11,6	2	2	2	1	2	1	1	1	2	4	2	2
254	M	12,1	4	4	4	4	4	4	4	4	4	4	4	4
255	M	11,6	3	3	3	3	3	3	3	3	3	3	3	3
256	F	12,8	5	5	5	5	4	5	5	5	5	5	4	5
257	F	12,7	4	4	4	4	4	5	5	5	5	5	4	4

258	F	13,1	5	5	6	6	5	6	6	6	5	6	5	5
259	M	11,6	2	2	2	2	2	2	2	2	2	2	2	2
260	F	10,7	2	2	4	4	2	2	2	2	4	4	2	2
261	M	10,5	2	2	2	1	2	2	2	2	2	2	1	1
262	F	19,5	6	5	5	5	5	6	6	6	5	5	5	5
263	F	13,4	5	5	6	6	5	5	6	6	6	6	5	5
264	F	11,2	3	4	4	4	4	3	3	3	3	3	4	4
265	F	12	3	3	4	3	4	3	3	3	4	4	3	3
266	F	16,1	6	6	5	5	6	6	6	6	6	6	5	5
267	F	6,4	1	1	1	1	1	1	1	1	1	1	1	1
268	M	12,6	4	4	5	5	4	5	4	5	4	5	5	4
269	F	10,8	3	3	3	3	3	3	3	2	4	4	3	3
270	F	11,6	4	4	4	4	4	4	4	4	4	4	4	4
271	M	10,4	3	3	2	3	3	2	3	2	4	3	2	2
272	M	13,7	2	2	3	2	2	2	2	2	2	2	2	2
273	F	10,7	2	2	3	2	2	2	3	2	3	2	2	2
274	M	10,2	3	3	4	3	4	3	3	3	3	3	3	3
275	F	11,1	3	1	1	1	3	1	1	1	3	3	1	1
276	F	8,5	1	1	1	1	1	1	1	1	1	1	1	1
277	F	11,3	3	3	3	3	3	3	3	3	3	3	3	3

278	M	13,2	2	2	1	1	2	1	1	1	2	2	1	1
279	M	10,4	2	2	1	1	2	1	1	1	1	1	1	1
280	F	13,6	5	5	5	5	5	5	5	5	5	5	5	5
281	M	9,6	3	3	1	1	3	1	3	1	1	3	1	1
282	M	11,2	3	3	2	2	3	2	3	2	3	3	2	2
283	F	11,9	3	3	2	2	4	2	3	2	4	3	2	3
284	M	16,1	5	5	6	5	6	5	6	6	6	6	5	5
285	F	11,8	3	3	6	5	5	3	6	3	6	5	5	5
286	F	11,1	2	2	2	2	2	2	2	2	2	2	2	2
287	F	11,9	5	5	5	5	5	5	5	5	5	5	5	5
288	M	10,2	2	2	4	2	4	4	4	3	4	4	3	3
289	F	16,7	5	5	5	5	6	5	5	5	6	6	6	6
290	F	10,2	4	4	4	4	4	4	4	4	4	4	4	4
291	F	13,8	6	6	6	6	6	6	6	6	6	6	6	5
292	F	13,9	4	4	5	5	5	5	5	5	5	4	4	5
293	M	10,1	3	3	1	1	4	1	1	1	3	3	1	1
294	F	10,5	2	2	2	2	2	2	2	1	2	2	1	1
295	M	11,7	2	2	1	1	3	1	1	1	3	3	1	1
296	F	12,5	5	5	5	5	5	5	5	5	5	5	5	5
297	F	13,7	4	4	4	4	4	4	4	4	4	4	4	4

298	F	8,7	2	2	2	2	2	2	2	2	2	2	2	2
299	M	11,3	2	1	1	1	2	1	1	1	2	1	1	1
300	F	12,7	2	2	1	1	3	1	1	1	3	3	1	1
301	M	11,6	2	2	1	1	2	1	1	1	2	2	1	1
302	M	13,8	3	2	2	2	3	3	2	2	3	2	2	2
303	F	12	3	3	1	1	3	1	3	1	1	1	1	1
304	M	12,7	1	1	1	1	1	1	1	1	1	1	1	1
305	F	12,3	6	6	6	6	6	6	6	6	6	6	6	6
306	F	10,2	4	4	4	4	4	4	4	4	4	4	4	4
307	M	12,1	3	3	3	3	3	3	3	3	3	3	3	3
308	M	11,3	2	2	2	2	2	2	2	1	2	2	2	2
309	F	12,7	3	3	3	3	3	3	3	3	4	4	4	4
310	F	11,1	4	4	4	4	4	4	4	4	4	4	4	4
311	M	7,7	2	2	2	2	2	2	3	3	2	3	2	2
312	F	11	4	4	4	4	4	4	4	4	4	4	4	4
313	M	9,3	1	1	1	1	1	1	1	1	1	1	1	1
314	M	7,5	2	2	3	2	2	2	2	2	2	2	2	2
315	M	12,6	3	3	2	3	3	3	3	3	3	3	3	3
316	M	10,3	2	2	2	2	2	2	2	2	2	2	2	2
317	F	13,5	6	6	5	6	6	6	6	6	6	6	6	6

318	M	9,3	2	2	2	2	2	2	2	2	2	1	1	1
319	F	20,9	6	5	6	5	6	6	6	6	6	6	6	6
320	M	11,3	1	1	2	1	4	1	4	1	4	4	1	1
321	F	11,3	3	3	3	3	3	2	2	2	3	2	2	2
322	M	12,3	3	3	4	4	3	3	3	3	4	4	3	3
323	F	8,8	3	3	3	3	3	3	3	3	3	3	3	3
324	F	15,9	4	4	4	4	4	4	4	4	4	4	4	4
325	M	17	4	4	4	4	4	4	4	4	4	4	4	4
326	M	20,8	5	6	5	5	5	6	5	5	6	5	5	5
327	F	15,4	5	5	5	5	5	5	5	5	5	5	5	5
328	F	16,9	6	6	6	6	6	6	6	6	6	6	5	6
329	M	9,7	2	2	1	1	2	2	2	1	2	2	1	1
330	F	15,7	5	5	5	5	5	5	6	5	5	5	5	5
331	F	19,5	6	6	6	6	6	6	6	6	6	6	6	6
332	F	7,8	1	1	1	1	1	1	1	1	3	1	1	1
333	F	19,2	6	6	6	5	6	6	6	6	6	6	6	6
334	M	15,2	6	6	5	6	6	6	6	6	6	6	5	5
335	F	21,9	5	6	5	5	6	6	6	6	6	6	5	5
336	M	9,1	1	1	1	1	1	1	1	1	1	1	1	1
337	F	14,7	5	5	5	5	5	5	5	5	6	6	5	5

338	F	8,8	2	2	2	2	2	2	2	2	2	2	2	2
339	M	15,6	4	4	4	4	4	4	5	5	4	5	4	5
340	F	14,7	4	5	5	5	5	5	5	5	5	5	5	5
341	F	9	1	1	1	1	3	2	3	2	3	3	1	1
342	M	18,7	6	5	5	5	6	6	6	6	6	5	5	5
343	M	21,8	5	5	5	5	5	5	6	6	5	5	5	5
344	F	8,8	2	2	2	2	2	2	2	2	2	2	2	2
345	M	7,9	1	1	1	1	1	1	1	1	1	1	1	1
346	M	14	5	5	5	5	5	5	6	6	6	6	5	5
347	F	22,3	6	6	5	5	6	6	6	6	6	6	5	5
348	F	15,2	5	5	5	5	5	5	5	5	5	5	5	5
349	M	18,1	6	6	6	6	6	6	6	6	6	6	6	6
350	M	9,8	1	1	1	1	4	1	1	1	4	4	1	1
351	M	16,7	5	5	5	5	5	6	6	5	5	5	5	5
352	F	16,5	4	5	4	5	4	5	5	4	5	5	4	4
353	M	8,9	1	1	1	1	1	1	1	1	1	1	1	1
354	F	18,1	5	5	5	5	5	5	5	5	5	5	5	5
355	F	9,4	1	1	1	1	1	1	1	1	1	1	1	1
356	F	17,4	5	5	6	5	6	5	5	6	5	5	5	5
357	M	8,9	1	1	1	1	2	1	1	1	1	1	1	1

358	F	15,1	4	4	4	4	4	4	4	4	4	4	4	4
359	M	9,2	1	3	1	1	4	3	2	3	4	3	2	3
360	F	8,8	1	1	1	1	1	1	1	1	1	1	1	1
361	M	9	1	1	1	1	1	1	1	1	1	1	1	1
362	F	7,4	1	1	1	1	1	1	1	1	1	1	1	1
363	F	8,8	1	1	1	1	2	1	1	1	1	1	1	1
364	M	9,2	1	1	1	1	1	2	2	2	3	2	1	1
365	M	14,1	6	6	5	5	6	6	6	6	6	6	5	5
366	F	9,2	1	1	1	1	1	1	2	1	2	2	1	1
367	M	7,6	1	1	1	1	1	1	1	1	1	1	1	1
368	F	9,8	3	3	3	3	3	3	3	3	3	3	3	3
369	F	20,7	5	5	5	5	5	5	6	5	6	6	5	5
370	F	7,9	1	1	1	1	1	1	1	1	1	1	1	1
371	F	8,5	1	1	1	1	1	1	1	1	2	2	1	1
372	F	9	2	2	2	2	2	2	2	2	2	2	2	2
373	F	19,9	6	6	5	5	6	6	6	6	6	6	5	6
374	F	19,4	4	4	5	5	5	5	5	5	5	5	4	5
375	F	22,4	5	5	4	5	5	5	5	5	4	4	5	5
376	M	7,9	1	1	1	1	1	1	1	1	1	1	1	1
377	F	19,7	6	6	6	6	6	6	6	6	6	6	6	6

378	F	9,7	4	4	4	4	4	4	4	4	4	4	4	4
379	M	16,3	6	5	5	5	6	5	6	6	5	5	5	5
380	F	14,7	6	6	5	5	6	6	6	6	6	6	5	6
381	F	15	5	5	5	6	6	6	6	5	5	5	5	5
382	F	16,5	5	5	5	5	6	5	6	5	5	5	5	5
383	F	16,2	5	5	4	5	5	5	5	5	5	4	5	5
384	M	15,2	5	5	5	5	5	5	5	5	5	5	5	5
385	M	8,9	1	1	1	1	4	4	1	1	4	4	1	1
386	M	8,4	1	1	1	1	1	1	1	1	2	2	1	1
387	F	16,5	6	6	5	5	6	6	6	6	6	6	5	5
388	M	14,5	4	4	4	4	4	4	4	4	4	4	4	4
389	F	16,4	5	6	5	5	5	6	6	6	5	5	5	5
390	M	16	4	4	4	4	4	4	4	4	4	4	5	5
391	M	14,1	4	5	4	4	4	5	4	4	5	4	4	4
392	M	21,6	6	6	6	6	6	6	6	6	6	6	6	6
393	F	7,4	2	2	2	2	2	2	2	2	2	2	2	2
394	M	16,7	5	5	4	5	4	5	5	5	4	4	4	4
395	F	8	1	1	1	1	1	1	1	1	1	1	1	1
396	F	8,8	1	1	1	1	1	1	1	1	1	1	1	1
397	F	14,6	5	6	5	6	5	6	6	5	6	5	5	5

398	F	21,7	5	5	5	5	5	5	5	5	5	5	5	5
399	F	16,1	5	5	5	5	5	5	5	5	5	5	5	5
400	F	7,4	1	1	1	1	1	1	1	1	1	1	1	1
401	F	9,9	2	2	2	2	2	2	2	2	2	2	2	2
402	M	18,7	5	5	5	5	5	5	5	5	5	5	5	5
403	M	14,9	4	4	5	4	5	5	5	5	4	4	5	5
404	F	7,5	2	2	2	2	2	2	2	2	3	3	2	2
405	M	9,8	4	4	4	4	4	4	4	4	4	4	4	4
406	M	21,2	6	6	5	5	6	6	6	6	6	6	5	5
407	F	16,3	4	4	4	4	4	4	4	4	4	4	4	4
408	F	15,3	4	4	4	4	4	4	5	4	4	4	5	5
409	M	10,5	2	1	1	1	2	2	1	1	2	2	1	1
410	F	16,1	4	5	4	4	4	5	5	5	4	4	4	4
411	M	9,2	4	4	4	4	4	4	4	4	4	4	4	4
412	F	15,6	5	5	5	5	5	5	5	5	5	5	5	5
413	F	9,2	1	1	1	1	1	1	2	1	2	1	1	1
414	M	22,1	5	5	5	5	5	5	5	5	5	5	5	5
415	F	8,5	1	1	1	1	1	1	1	1	2	2	1	1
416	F	20,9	6	6	5	5	6	6	5	5	5	5	5	5
417	F	9,7	1	1	2	2	2	2	3	3	2	3	2	3

418	F	8,5	2	2	1	1	2	1	1	1	2	2	2	2
419	F	15,3	4	4	4	4	4	4	5	4	4	4	4	4
420	F	20,9	6	6	5	6	6	6	6	6	6	6	5	5
421	M	21,6	5	5	5	5	5	5	5	5	5	5	5	5
422	F	16	4	4	4	4	4	4	4	4	4	4	4	4
423	F	6,4	2	2	2	2	2	2	2	2	2	2	2	2
424	M	17,9	6	6	5	6	6	6	6	6	6	6	5	5
425	F	14,5	5	5	5	5	5	5	5	5	6	5	5	5
426	M	16,7	6	6	5	5	5	6	6	6	5	5	5	5
427	F	21,1	5	5	5	5	5	5	5	5	5	5	5	5
428	M	16,2	5	5	5	5	6	6	5	5	5	5	5	5
429	M	8	1	1	1	1	1	1	1	1	2	1	1	1
430	F	16,5	4	4	4	4	4	4	4	4	4	4	4	4
431	F	7,7	1	1	1	1	1	1	1	1	1	1	1	1
432	F	14,3	6	6	5	5	6	6	6	5	5	5	5	5
433	F	16,8	4	4	4	4	4	5	5	5	5	5	5	5
434	F	16	4	4	4	4	4	4	5	5	4	4	4	4
435	M	17,7	6	6	6	6	6	6	6	6	6	6	6	6
436	F	7,1	1	1	1	1	1	1	1	1	2	1	1	1
437	M	16	2	3	2	2	2	2	2	2	2	2	5	4

438	F	14,1	4	4	4	4	4	4	4	4	4	4	4	4
439	M	8,6	1	1	1	1	1	1	1	1	1	1	1	1
440	F	9,4	1	1	1	1	1	1	1	1	1	1	1	1
441	F	7	1	1	1	1	1	1	1	1	2	2	1	1
442	M	21,1	5	5	5	5	5	5	5	5	5	5	5	5
443	F	7,9	1	1	1	1	1	1	1	1	1	1	1	1
444	M	16,9	4	4	4	4	4	4	4	4	4	4	4	4
445	M	20	5	5	5	5	5	6	6	6	5	5	5	5
446	F	16,9	5	5	5	5	5	6	6	6	6	6	5	5
447	M	15,2	5	5	5	5	5	5	5	5	5	5	5	5
448	M	7,9	1	1	1	1	1	1	1	1	1	1	1	1
449	M	7,9	1	1	1	1	1	1	1	1	1	1	1	1
450	M	9,7	2	2	1	1	2	1	1	1	2	2	1	1
451	M	9,3	3	3	4	4	4	3	4	4	3	3	3	3
452	M	9,3	2	2	2	2	3	2	2	2	3	3	2	2
453	M	14,2	4	4	4	4	4	5	5	4	4	4	4	4
454	F	19	5	5	5	5	5	5	5	5	5	5	5	5
455	F	9,3	2	2	2	2	2	2	2	2	3	3	2	2
456	M	9,1	1	1	1	1	1	1	1	1	1	1	1	1
457	F	14,7	5	5	5	5	5	6	6	6	5	5	5	5

458	M	8,6	1	1	1	1	1	1	1	1	1	1	1	1
459	M	8,3	1	1	1	1	1	1	1	1	1	1	1	1
460	F	9,2	1	1	1	1	2	1	2	1	2	2	1	1
461	F	14,6	5	5	4	5	5	5	5	5	5	5	5	5
462	F	9,4	3	3	3	3	3	3	3	3	4	4	3	3
463	F	9,1	2	2	2	2	2	2	2	1	2	2	2	2
464	F	15,9	6	5	5	5	6	6	6	5	5	5	5	5
465	F	21,9	5	5	5	5	4	5	5	5	4	4	5	5
466	F	15,8	4	4	4	4	4	4	4	4	4	4	4	4
467	M	15,1	4	5	5	5	4	5	5	5	5	5	5	5
468	M	8,9	1	1	1	1	1	1	1	1	1	1	1	1
469	M	8,5	2	2	2	2	2	2	2	2	3	2	2	2
470	F	14,1	4	4	4	4	4	4	4	4	4	4	4	4
471	M	7,8	1	1	1	1	1	1	1	1	1	1	1	1
472	M	8,5	1	1	1	1	2	3	1	3	3	3	1	1
473	M	7,9	1	2	1	2	2	2	2	2	2	2	1	1
474	M	14,3	4	4	4	4	4	4	4	4	4	4	4	4