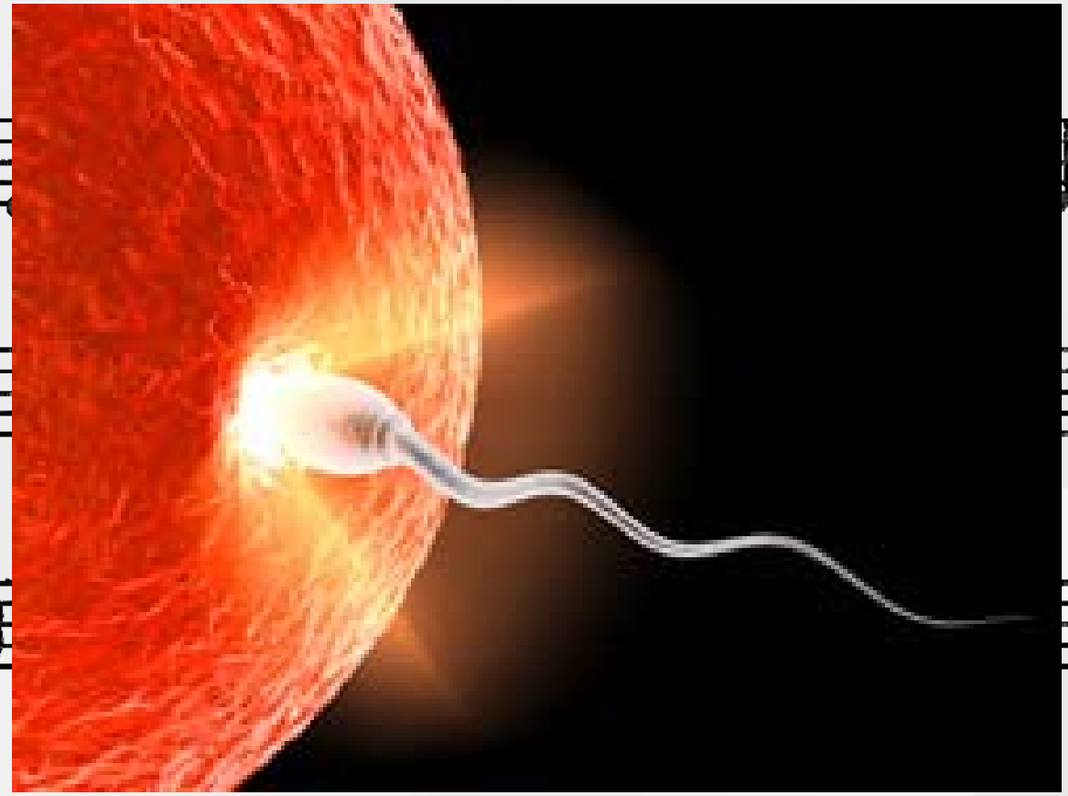
The assessment of biological age and maturity

Noël Cameron

School of Sport, Exercise & Health Sciences,
Loughborough University, UK

Email: N.Cameron@lboro.ac.uk

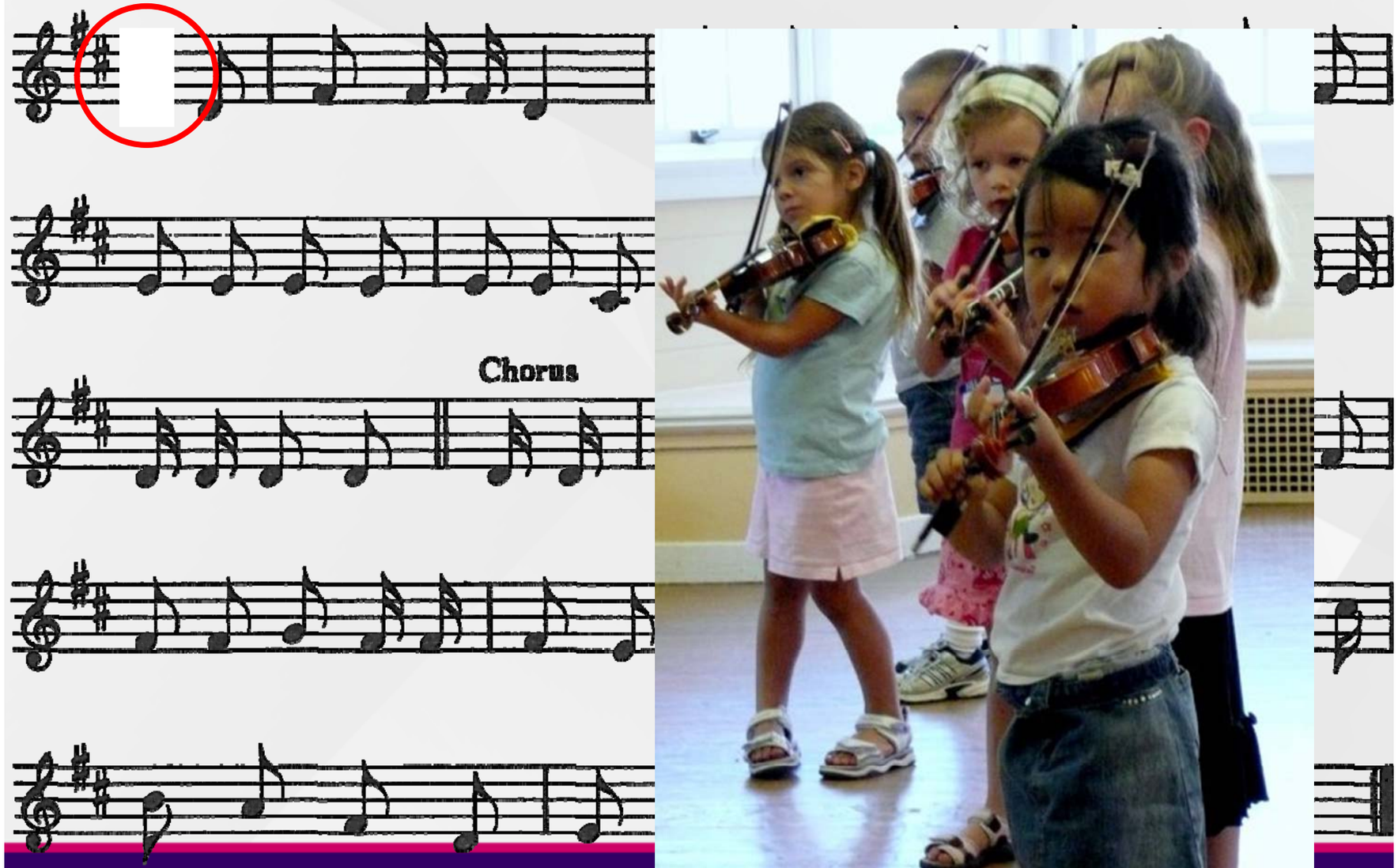
James M Tanner 1920 - 2010



Loughborough University

#InspiringWinners since 1909

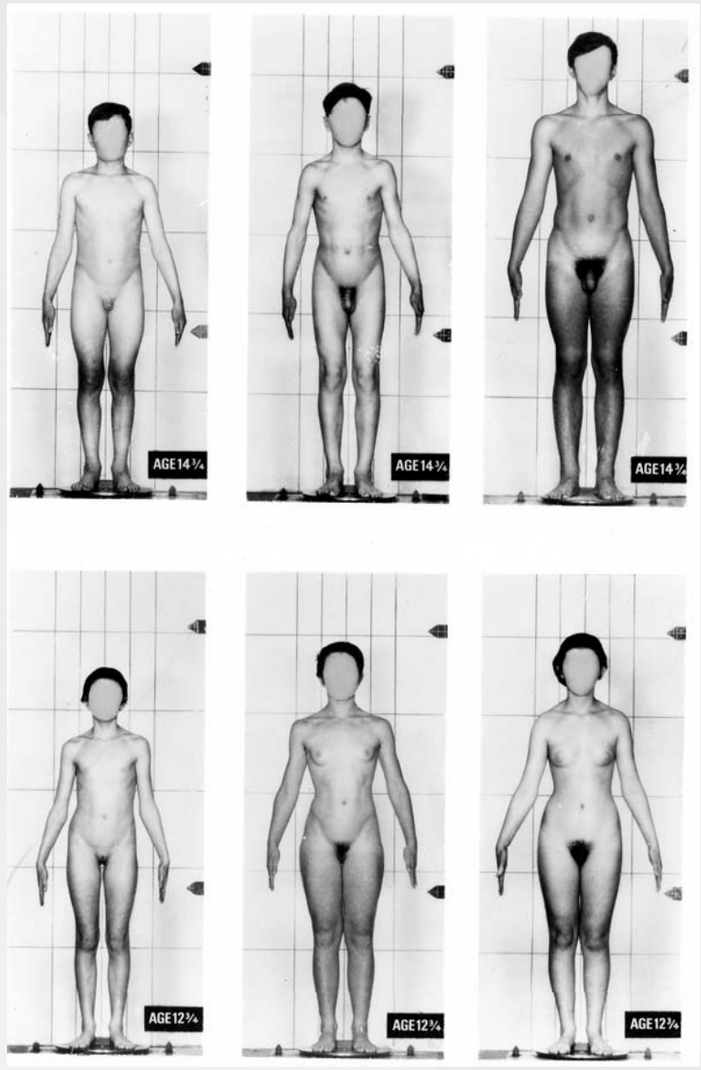
Chorus


Chorus

Childhood

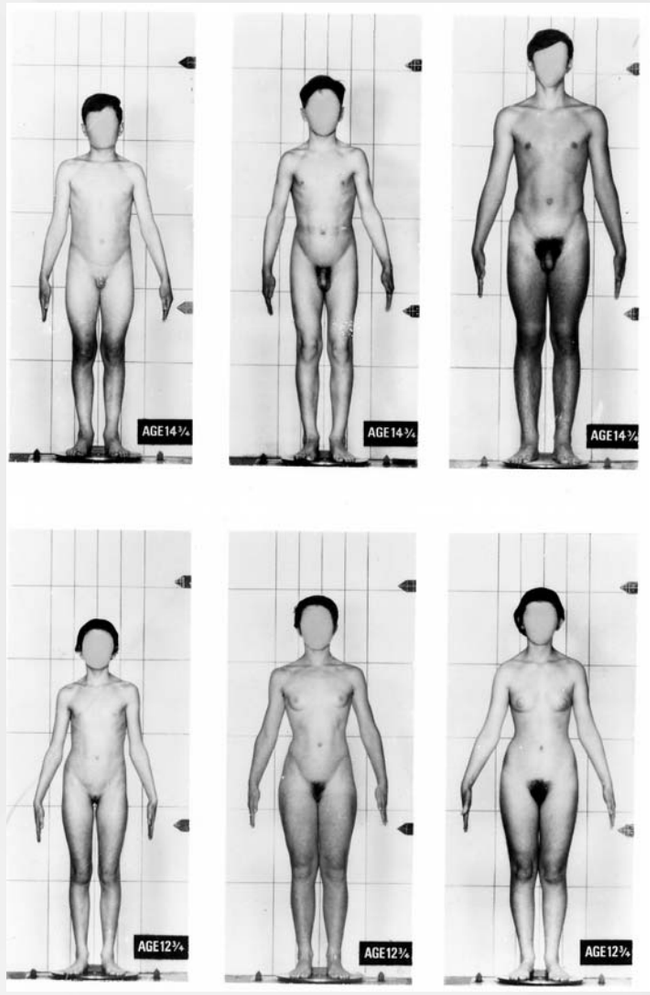
Adolescence

Adolescence



lento *moderato* *allegro*

Variation in the tempo of growth



3 boys aged
14.75 years

3 girls aged
12.75 years

Growth analysis requires somatic and developmental variables

At a clinical level the individual status of the child (the amount of deviation from normal) depends on her/his size (height, weight, etc.) corrected for her/his stage of maturity in relation to age

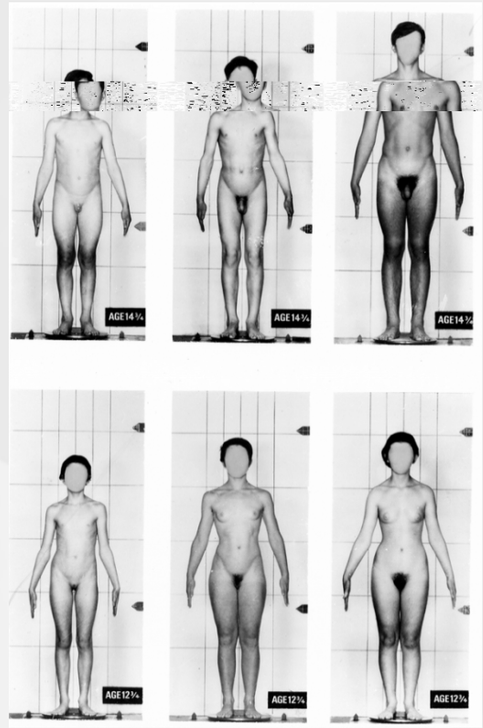
At a sample or population level the average size (e.g. height-for age) and the average age of attainment of developmental milestones (e.g. age at menarche) reflects not only the health and wellbeing of the society but also its socio-economic wellbeing

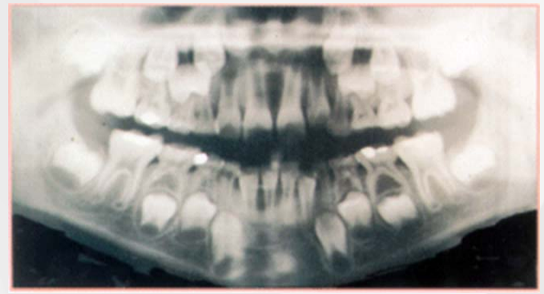
How do we measure maturity?

Maturity Processes v Events

Processes:

- Skeletal maturation
- Dental maturation
- Sexual maturation



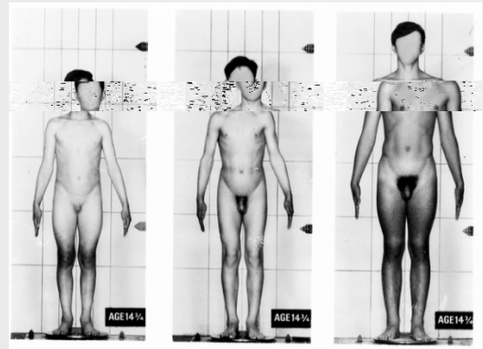


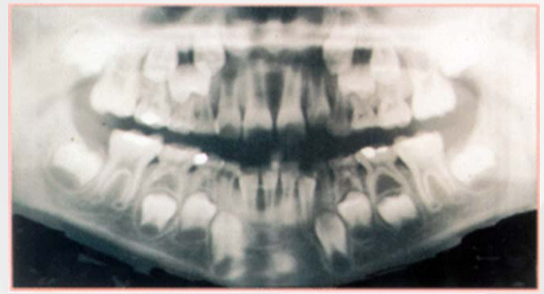
Maturity Processes

Atlas v Bone-specific scoring methods

Tanner scaling

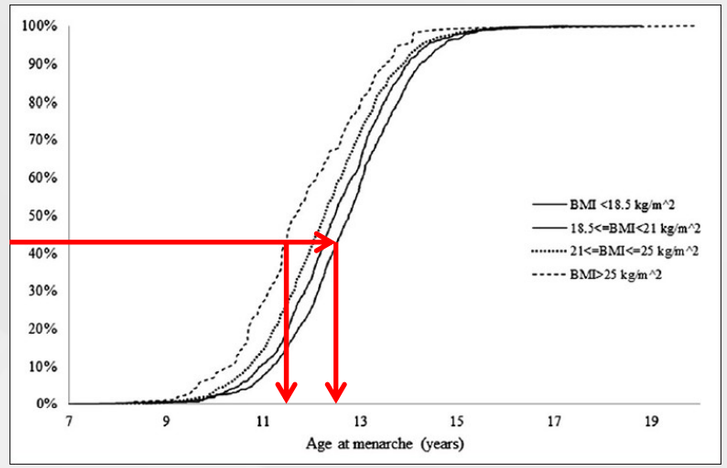
Age of Emergence
Tooth-specific scroing

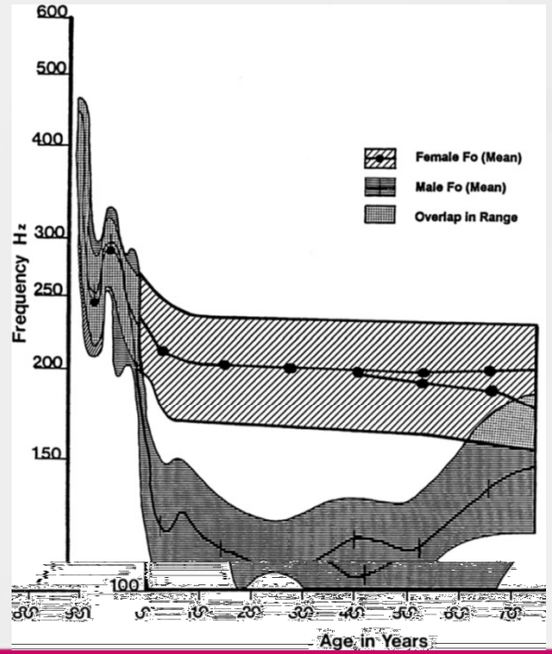


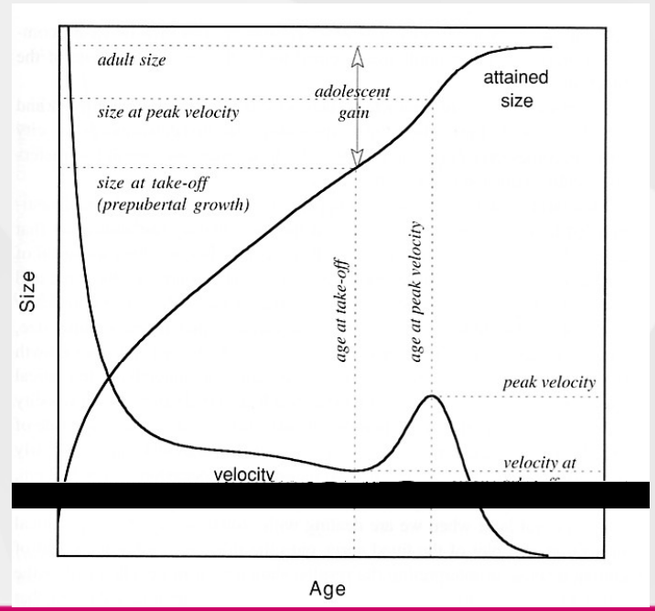


Maturity Processes v Events:

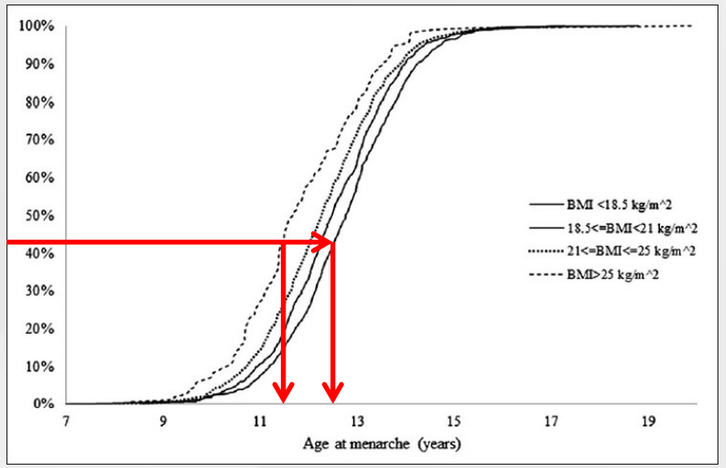
- Menarche
- Spermarche
- Voice change
- Peak Height Velocity
- 95% adult height

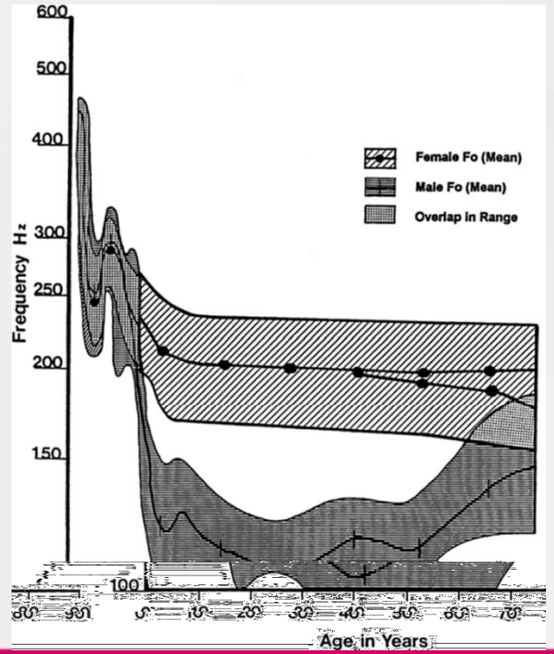


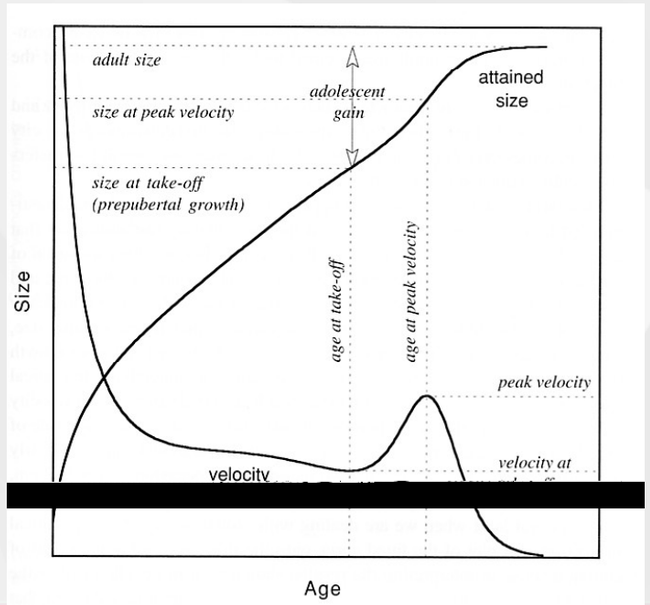




Maturity Events:
Status quo, prospective, recall
Fundamental Frequency Modelling





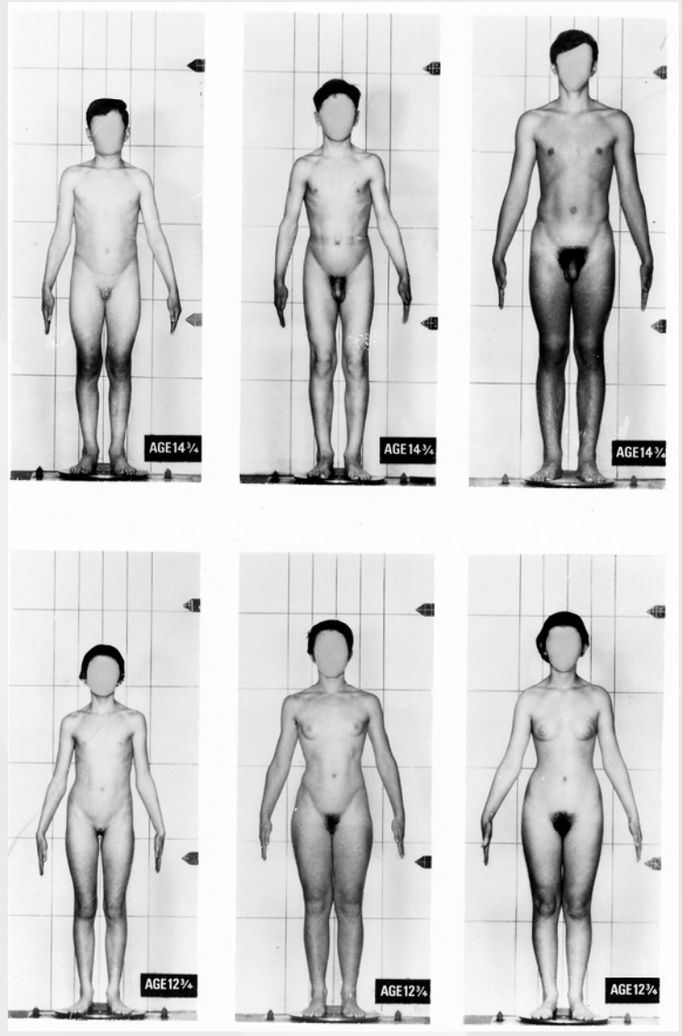


Maturity indicator criteria:

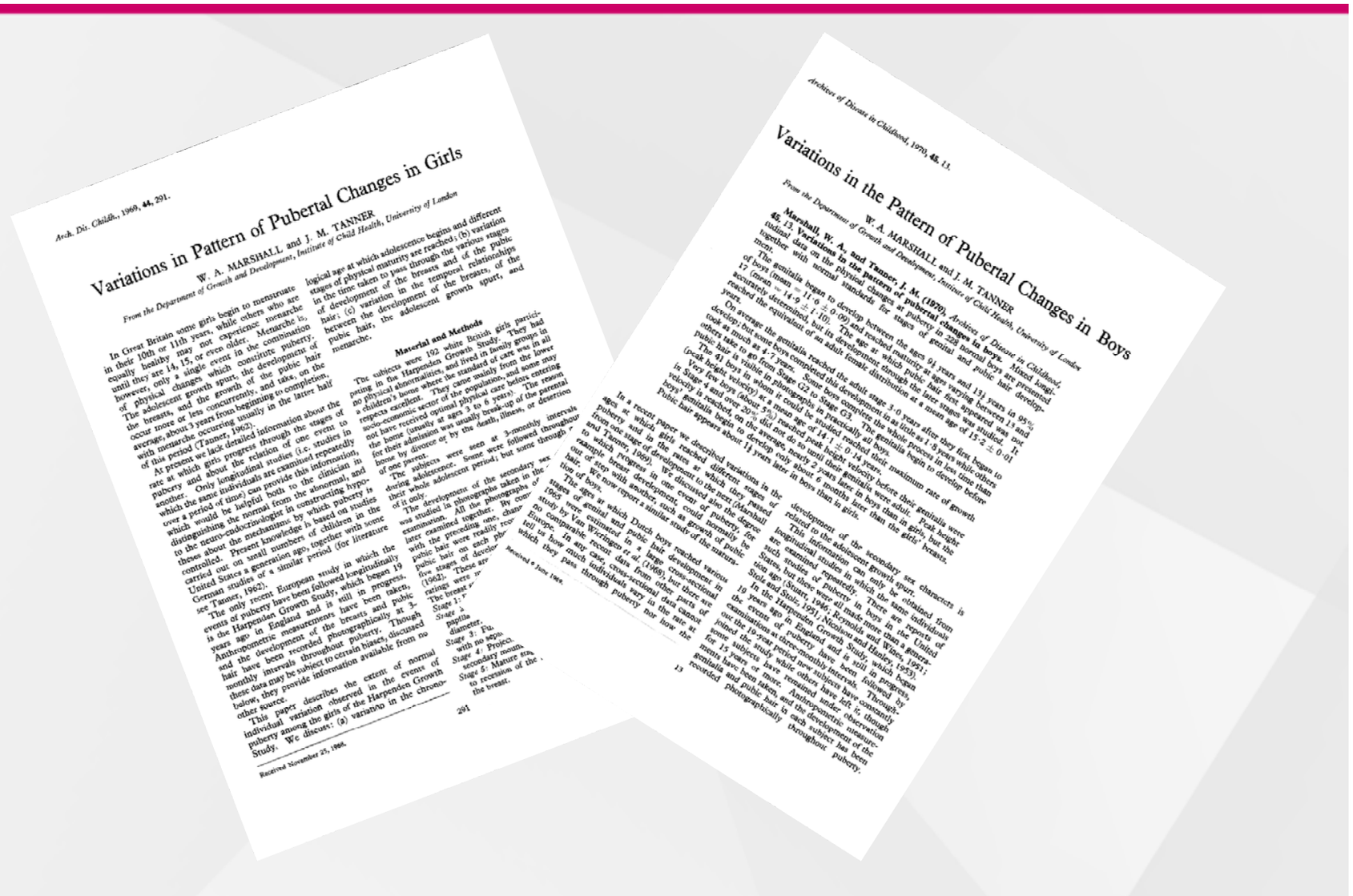
1. Universal
2. Sequential
3. Discrimination
4. Reliability
5. Validity
6. Completeness

Six considerations:

1. Maturity v Time
2. Discrete Maturity Indicators
3. Independence of maturational processes
4. Uneven maturation
5. Sexual dimorphism
6. Maturity v size



In vivo assessment of secondary sexual development in normal children was not an established or recommended procedure…



Arch. Dis. Childh., 1969, 44, 291.

Variations in Pattern of Pubertal Changes in Girls

W. A. MARSHALL and J. M. TANNER

From the Department of Growth and Development, Institute of Child Health, University of London

In Great Britain some girls begin to menstruate in their 10th or 11th years, while others who are equally healthy may not experience menarche until they are 14, 15, or even older. Menarche is, however, only a single event in the combination of physical changes which constitute puberty. The adolescent growth spurt, the development of the breasts, and the growth of the pubic hair occur more or less concurrently, and take, on the average, about 3 years from beginning to completion, with menarche occurring usually in the latter half of this period (Tanner, 1962).

At present we lack detailed information about the rate at which girls progress through the stages of puberty and about the relation of one event to another. Only longitudinal studies (i.e. studies in which the same individuals are examined repeatedly over a period of time) can provide this information, which would be helpful both to the clinician in distinguishing the normal from the abnormal, and to the neuro-endocrinologist in constructing hypotheses about the mechanisms by which puberty is controlled. Present knowledge is based on studies carried out on small numbers of children in the United States a generation ago, together with some German studies of a similar period (for literature see Tanner, 1962).

The only recent European study in which the events of puberty have been followed longitudinally is the Harpenden Growth Study, which began 19 years ago in England and is still in progress. Anthropometric measurements have been taken, and the development of the breasts and pubic hair have been recorded photographically at 3-monthly intervals throughout puberty. Though these data may be subject to certain biases, discussed below, they provide information available from no other source.

This paper describes the extent of normal individual variation observed in the events of puberty among the girls of the Harpenden Growth Study. We discuss: (a) variation in the chronological age at which adolescence begins and different stages of physical maturity are reached; (b) variation in the time taken to pass through the various stages of development of the breasts and of the pubic hair; (c) variation in the temporal relationships between the development of the breasts, of the pubic hair, the adolescent growth spurt, and menarche.

Material and Methods

The subjects were 192 white British girls participating in the Harpenden Growth Study. They had no physical abnormalities, and lived in family groups in a children's home where the standard of care was in all respects excellent. They came mainly from the lower socio-economic sector of the population, and some may not have received optimal physical care before entering the home (usually at ages 3 to 6 years). The reason for their admission was usually break-up of the parental home by divorce or by the death, illness, or desertion of one parent.

The subjects were seen at 3-monthly intervals during adolescence. Some were followed throughout their whole adolescent period; but some through [illegible] of it only.

The development of the secondary sex [illegible] was studied in photographs taken in the [illegible] examination. All the photographs of [illegible] later examined together. By com[illegible] with the preceding one, chan[illegible] pubic hair were readily rec[illegible] pubic hair on each phe[illegible] five stages of develop[illegible] (1962). These are [illegible] ratings were [illegible] The breast [illegible] Stage 1: [illegible] Stage 2: [illegible] papilla [illegible] diameter. Stage 3: Fu[illegible] with no sepa[illegible] Stage 4: Project[illegible] secondary mound[illegible] Stage 5: Mature sta[illegible] to recession of the [illegible] the breast.

Received November 25, 1968.

Received 9 June 1969.

Archives of Disease in Childhood, 1970, 45, 13.

Variations in the Pattern of Pubertal Changes in Boys

W. A. MARSHALL and J. M. TANNER

From the Department of Growth and Development, Institute of Child Health, University of London

Marshall, W. A., and Tanner, J. M. (1970), *Archives of Disease in Childhood,* **45, 13. Variations in the pattern of pubertal changes in boys.** Mixed longitudinal data on the physical changes at puberty in 228 normal boys are presented together with normal standards for stages of genital and pubic hair development.

The genitalia began to develop between the ages 9½ years and 13½ years in 95% of boys (mean = 11·6 ± 0·09) and reached maturity at ages varying between 13 and 17 (mean = 14·9 ± 1·10). The age at which pubic hair first appeared was not accurately determined, but its development through the later stages was studied. It reached the equivalent of an adult female distribution at a mean age of 15·2 ± 0·01 years.

On average the genitalia reached the adult stage 3·0 years after they first began to develop; but some boys completed this development in as little as 1·8 years while others took as much as 4·7 years. Some boys complete the whole process in less time than others take to go from Stage G2 to Stage G3. The genitalia begin to develop before pubic hair is visible in photographs, and in practically all boys.

The 91 boys in whom it could be studied reached their maximum rate of growth (peak height velocity) at a mean age of 14·1 ± 0·14 years.

Very few boys (about 5%) reached peak height velocity before their genitalia were in Stage 4 and over 20% did not do so until their genitalia were adult. Peak height velocity is reached, on the average, nearly 2 years later in boys than in girls, but the boys' genitalia begin to develop only about 6 months later than the girls' breasts. Pubic hair appears about 1½ years later in boys than in girls.

In a recent paper we described variations in the ages at which girls reached different stages of puberty and in the rates at which they passed from one stage of development to the next (Marshall and Tanner, 1969). We discussed also the degree to which progress in one event of puberty, for example breast development, could normally be out of step with another, such as growth of pubic hair. We now report a similar study of the maturation of boys.

The ages at which Dutch boys reached various stages of genital and pubic hair development in 1965 were estimated in a large cross-sectional study by Van Wieringen *et al.* (1968), but there are no comparable recent data from other parts of Europe. In any case, cross-sectional data cannot tell us how much individuals vary in the rate at which they pass through puberty nor how the development of the secondary sex characters is related to the adolescent growth spurt, obtained from longitudinal studies in which the same individuals are examined repeatedly. There are no United States studies of puberty in boys in the United States, but these were all made more than a generation ago (Stuart, 1946; Reynolds and Wines, 1951; Stolz and Stolz, 1951; Nicolson and Hanley, 1953).

In the Harpenden Growth Study, which began 19 years ago in England and is still in progress, the events of puberty have been followed by examinations at three-monthly intervals. Throughout the 19-year period new subjects have constantly joined the study while others have left it; though some subjects have remained under observation for 15 years or more. Anthropometric measurements have been taken, and the development of the genitalia and pubic hair in each subject has been recorded photographically throughout puberty.

Loughborough University

#InspiringWinners since 1909

Marshall & Tanner 1969:

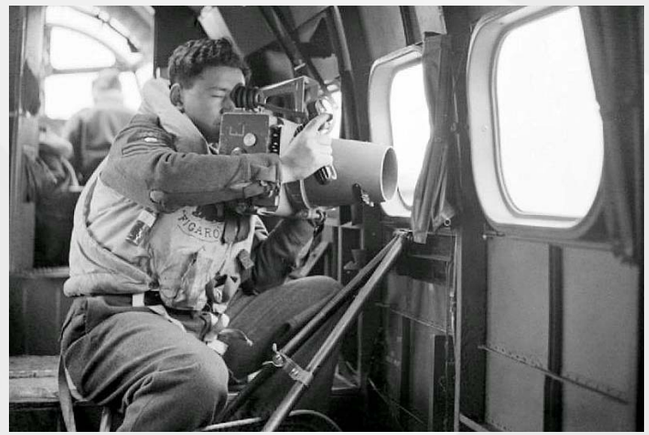
"The development of secondary sexual characters was studied in photographs taken in the nude at each examination. All the photographs of each girl were later examined together. By comparing each picture with the preceding one, changes in the breasts and pubic hair were readily recognized." (pp 291)

Age on reaching stages:

"The figures *[mean and SD]* for PH2 must be treated with reserve as the first appearance of pubic hair cannot readily be seen on photographs. The mean…is...almost certainly too high and the standard deviation...too large." (pp 294)

Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in girls/boys. Arch. Dis. Childh. 44/45, 291-303/13-23. 1969/1970.

F24 Aerial Mapping Camera
c 1939-45



In vivo assessment of secondary sexual development in normal children was not an established or recommended procedure…

Concerns over:

- right to privacy
- taboo on touching or palpation
- qualifications and background of observer
- presence of same sex chaperone

In non-clinical research settings Tanner staging is a barrier to participant compliance because of cultural and religious beliefs and practices

Assessments of skeletal maturity require unacceptable radiation exposure

Hand-wrist Radiation exposure values: 0.003 mSv

1/10th exposure for air travellers

1/6th background in UK
(except Aberdeen 1/3rd)

Alternative methods for maturity characteristics?

- Questionnaires
- Self-assessment (Puberty Development Scale - PDS)
- Blood bio-markers

The questions for girls are:

- Have you started puberty i.e. do you have any pubic hair or have your breasts enlarged since you were a child?
- Do you have regular menstrual cycles i.e. periods?
- If so, have you been having periods for more than two years?
- How old were you when you started to have periods?

The questions for boys are:

- Have you started puberty i.e. do you have any pubic hair or have your genitalia enlarged since you were a child?
- Has your voice broken i.e. do you speak in a deeper voice then when you were a child?
- If so, have you been speaking in a deeper voice for more than two years?
- How old were you when your voice broke?
- Do you shave?
- How often do you shave e.g. per week/month?
- When did you start shaving?

Artículo original

Arch Argent Pediatr 2009; 107(5):423-429 / 423

Método no invasivo para la evaluación del desarrollo sexual en la adolescencia

A non invasive method for assessing development at adolescence

Dr. Horacio Lejarraga et al

Loughborough University

#InspiringWinners since 1909

The highest concordance were found in the questions: "Have you started puberty?", with Tanner's stages III, IV or V (Kappa value= 0.60); "Have you already had your first menstrual period?" with stages IV-V (K= 0.69); and "Do you shave?" with stages IV-V (K= 0.66). In most cases, these questions showed high (≥ 0.80) sensitivity and specificity for detecting the mentioned puberty periods.

Lejarraga et al 2009

ORIGINAL ARTICLES

www.jpeds.com • THE

Clin Endocrinol (Oxf). 2012 October ; 77(4): 555–563. doi:10.1111/j.1365-2265.2012.04393.x.

Inhibin B and luteinizing hormone levels in girls aged 6-11 years from NHANES III, 1988-1994

Emily K. Sims, M.D.[1], O. Yaw Addo, Ph.D.[2], Audra L. Gollenberg, Ph.D.[3], John H. Himes, Ph.D.[2], Mary L. Hediger, Ph.D.[4], and Peter A. Lee, M.D, Ph.D.[1,5]

[1]Department of Pediatric Endocrinology and Diabetology, Indiana University School of Medicine, Riley Hospital for Children, Indianapolis, IN.

[2]Division of Epidemiology and Community Health, University of Minnesota School of Public Health, Minneapolis, MN.

[3] Department of Public Health, College of Arts & Sciences, Shenandoah University, Winchester, VA.

[4]Epidemiology Branch, Division of Epidemiology, Statistics and Prevention Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Department of Health and Human Services, Bethesda, MD.

[5]Department of Pediatrics, Penn State College of Medicine, The Milton S. Hershey Medical Center, Hershey, PA.

Abstract

Objective—Evaluate inhibin B and luteinizing hormone (LH) levels in a large, r… cross-sectional sample of U.S. girls and characterize the relationships of these … with age, clinical signs of puberty, and other correlates.

Articles | Population Study

nature publishing group

Child Dev. 2009 ; 80(2): 327–337. doi:10.1111/j.1467-8624.2009.01263.x.

Assessment of Pubertal Development: Correspondence between hormonal and physical development

Elizabeth A. Shirtcliff, PhD, Ronald E. Dahl, MD, and Seth D. Pollak, PhD

Abstract

Puberty marks the advent of adolescence and plays an important role in many changes and adjustments that adolescents must face. Pubertal maturation is advanced by sex hormones, yet it is not clear how best to measure puberty and how well existing measures capture hormone levels. We compared multiple indices of puberty to determine their interrelationships, including the Pubertal Development Scale (PDS), a picture-based interview about puberty (PBIP) and a physical exam. We also examined how physical pubertal measures were associated with basal hormones responsible for advancing pubertal development. Participants included 160 early adolescents (82 boys, 78 girls), 9-14 years of age. Basal hormones were derived using hierarchical linear modeling from 32 repeated saliva samples of testosterone and dehydroepiandrosterone (DHEA) in both sexes and 5 repeated measures of estradiol in girls. The two self-report measures were moderately concordant with the exam and with each other, with approximately half of the adolescents self-reporting the same stage as the physical exam. The different indices of puberty were highly correlated with each other, suggesting that self-report may be adequate when precise agreement is not necessary. Nevertheless, adolescents who were substantially more or less physically developed than their same-aged peers were most likely to self-report a stage that was different from the physical exam. The physical exam stages correlated well with boys' and girls' testosterone and DHEA, and less so with girls' estradiol. With a few exceptions, the PDS and PBIP were generally related to basal hormones in parallel with the exam. Multiple measures of pubertal development are viable options, each with respective strengths.

CONCLUSIONS: Pubertal assessment by the chil… pubertal staging and should be augmented by a physical examinat… epidemiologic studies self-assessment can be sufficiently accurate for a simple distinc… between prepuberty and puberty.

Loughborough University

#InspiringWinners since 1909

Table IV. Spearman correlations among self-assessment, physician assessment, hormone status, and true sexual maturation status

Self-assessments	Physician-assessment	SP*	SH†	PH‡	ST§ (95% CI)	PT¶ (95% CI)
Girls						
Breast	Breast	0.71	0.73	0.66	0.83 (0.73-0.97)	0.80 (0.70-0.89)
Pubic hair	Pubic hair	0.91	0.62	0.57	1.00 (0.95-1.00)	0.91 (0.84-0.97)
Boys						
Genitalia	Genitalia	0.38	0.40	0.61	0.50 (0.31-0.65)	0.75 (0.56-0.93)
Genitalia	Testicular volume (largest)	0.40	0.40	0.65	0.50 (0.31-0.66)	0.80 (0.62-0.98)
Genitalia	Testicular volume (average)	0.39	0.40	0.66	0.49 (0.30-0.65)	0.80 (0.62-0.97)
Pubic hair	Pubic hair	0.73	0.61	0.54	0.91 (0.79-1.00)	0.80 (0.57- 0.97)

NB: Self-assessment by questions and drawings of Tanner scale

Chavarro et al 2017 Validity of self-assessed sexual maturation against physician assessments and hormone levels. J.Pediatr. 2017;186:182-8

Table IV. Spearman correlations among self-assessment, physician assessment, hormone status, and true sexual maturation status

Self-assessments	Physician-assessment	SP*	SH†	PH‡	ST§ (95% CI)	PT¶ (95% CI)
Girls						
Breast	Breast	0.71	0.73	0.66	0.83 (0.73-0.97)	0.80 (0.70-0.89)
Pubic hair	Pubic hair	0.91	0.62	0.57	1.00 (0.95-1.00)	0.91 (0.84-0.97)
Boys						
Genitalia	Genitalia	0.38	0.40	0.61	0.50 (0.31-0.65)	0.75 (0.56-0.93)
Genitalia	Testicular volume (largest)	0.40	0.40	0.65	0.50 (0.31-0.66)	0.80 (0.62-0.98)
Genitalia	Testicular volume (average)	0.39	0.40	0.66	0.49 (0.31-0.65)	0.80 (0.62-0.97)
Pubic hair	Pubic hair	0.73	0.61	0.54	0.91 (0.79-1.00)	0.80 (0.57- 0.97)

Chavarro et al 2017 Validity of self-assessed sexual maturation against physician assessments and hormone levels. J.Pediatr. 2017;186:182-8

Puberty Development Scale (PDS) v
Picture Based Interview about Puberty (PBIP) v
Physical exam (physician)

N=160 boys= 82; girls = 78

Setting : Wisconsin, USA

Gonadal signals: ♀ AGS, B,
Men; ♂ AGS, Voice, facial hair
Adrenal signals: ♀/♂ PH, “skin changes”

Shirtcliffe et al Child Dev. 2009

Comp	K	%Acc.	%Acc. ♂	%Acc. ♀	%Over	%♂/♀	%Under	%♂/♀
Phys v PDS Gon	0.36	52	54	47	18	15/27	30	31/27
Phys v PDS Adr	0.36	50	60	44	29	26/34	21	14/23
Phys v PBIP B/G	0.36	49	41	57	26	35/17	25	24/17
Phys v PBIP PH	0.43	56	54	58	24	26/21	20	19/21
PDS v PBIP B/G	0.29	44	37	52				
PDS v PBIP PH	0.37	52	47	57				

Comp	K	%Acc.	%Acc. ♂	%Acc. ♀	%Over	%♂/♀	%Under	%♂/♀
Phys v PDS Gon	0.36	52	54	47	18	15/27	30	31/27
Phys v PDS Adr	0.36	50	60	44	29	26/34	21	14/23
Phys v PBIP B/G	0.36	49	41	57	26	35/17	25	24/17
Phys v PBIP PH	0.43	56	54	58	24	26/21	20	19/21
PDS v PBIP B/G	0.29	44	37	52				
PDS v PBIP PH	0.37	52	47	57				

Comp	K	%Acc.	%Acc. ♂	%Acc. ♀	%Over	%♂/♀	%Under	%♂/♀
Phys v PDS Gon	0.36	52	54	47	18	15/27	30	31/27
Phys v PDS Adr	0.36	50	60	44	29	26/34	21	14/23
Phys v PBIP B/G	0.36	49	41	57	26	35/17	25	24/17
Phys v PBIP PH	0.43	56	54	58	24	26/21	20	19/21
PDS v PBIP B/G	0.29	44	37	52				
PDS v PBIP PH	0.37	52	47	57				

Self-assessment Summary:

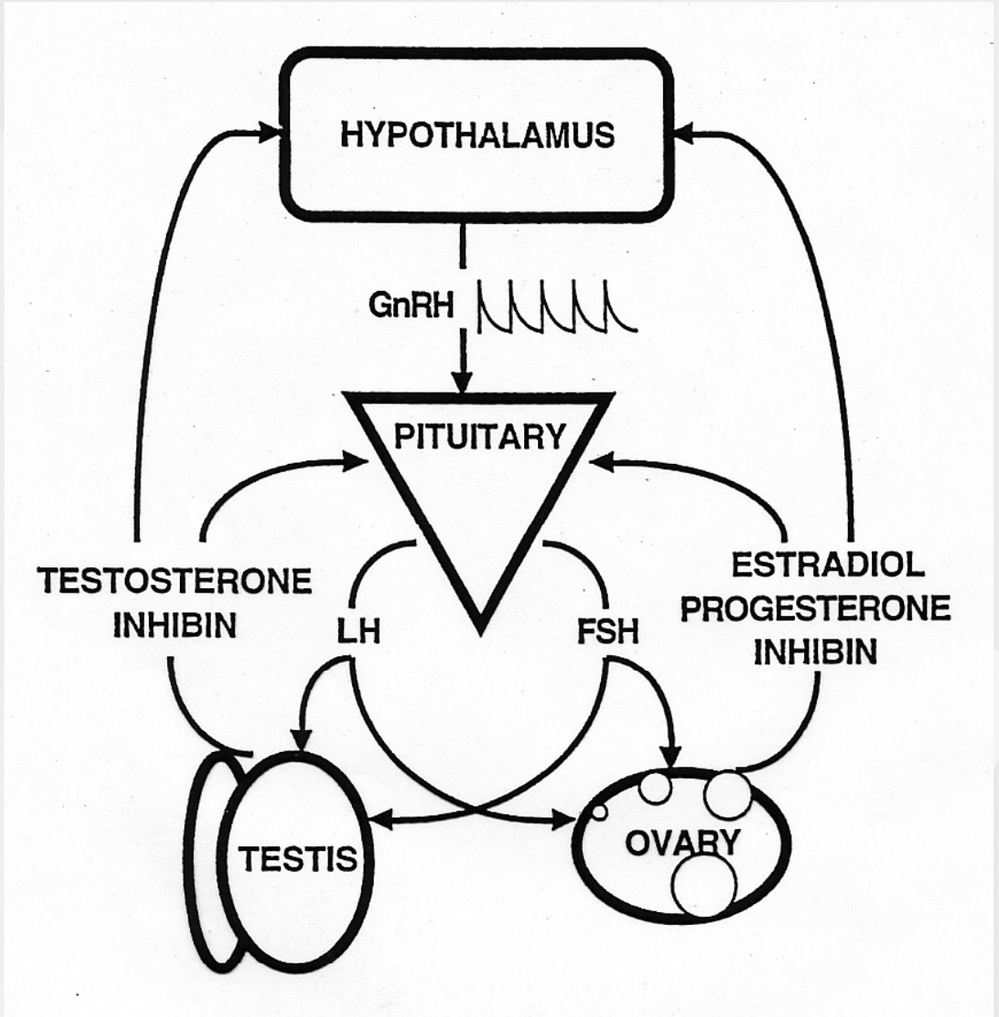
- Questions demonstrate a good concordance between self assessment and physician's assessment
- Self assessments from pictures have moderate concordance with physician's assessments
- Concordance from PDS and PBIP is modest except for PBIP and Physicians assessment which is good
- Boys are worse than girls in general except for PH
- Early and late developers are worse than average developers

But…the timing of the initiation and duration of puberty is fundamentally important in:

- Critical period for social and emotional development
- The long term effects of early adversity
- The development of patterns of habitual dietary intake and physical activity
- Critical changes in body composition and the development of obesity
- The development of risk for CVD, CHD, etc.

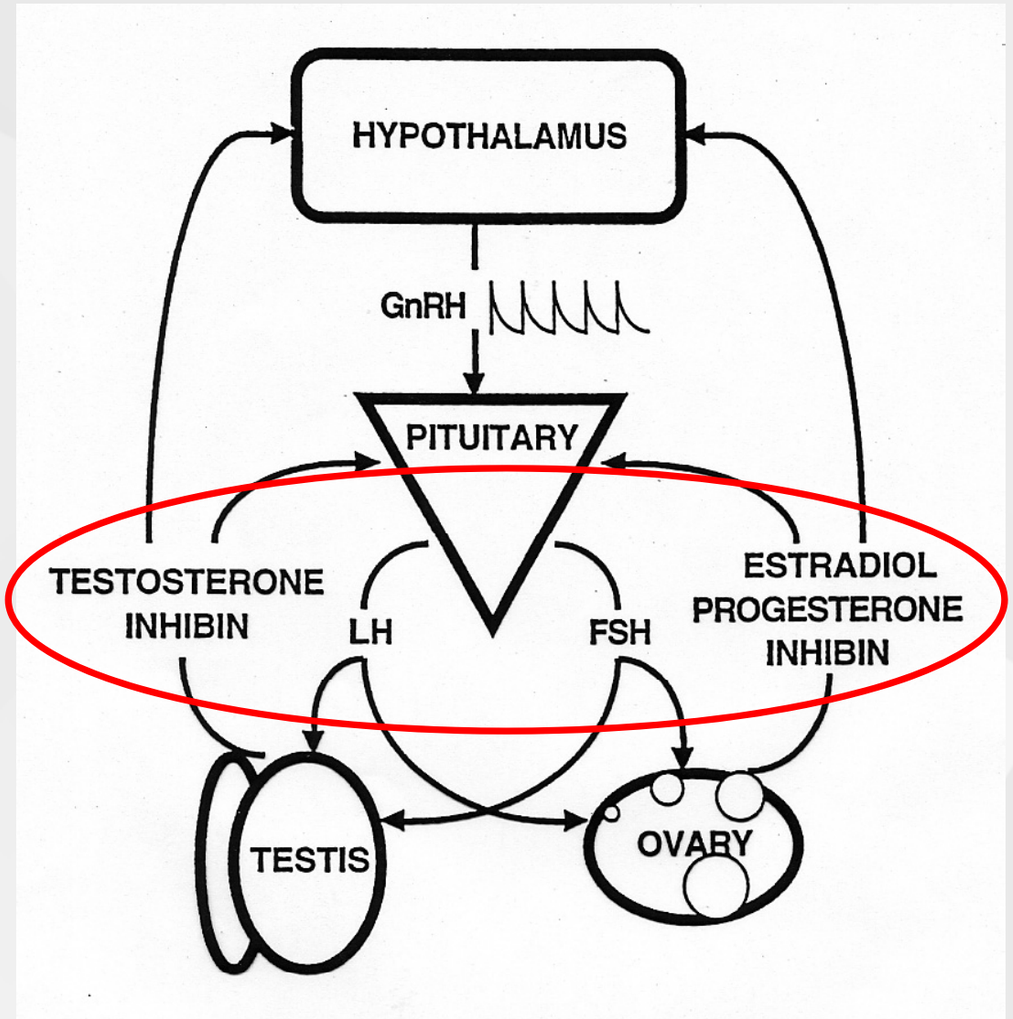
If traditional methods are no longer acceptable and self-assessment is good but not great, what can be assessed as an acceptable maturity indicator of pubertal initiation and duration?

HPG axis


HYPOTHALAMUS
GnRH
PITUITARY
TESTOSTERONE
INHIBIN
LH
FSH
ESTRADIOL
PROGESTERONE
INHIBIN
TESTIS
OVARY

HPG axis

Threshold values of gonadotrophins and sex steroids from body fluids?

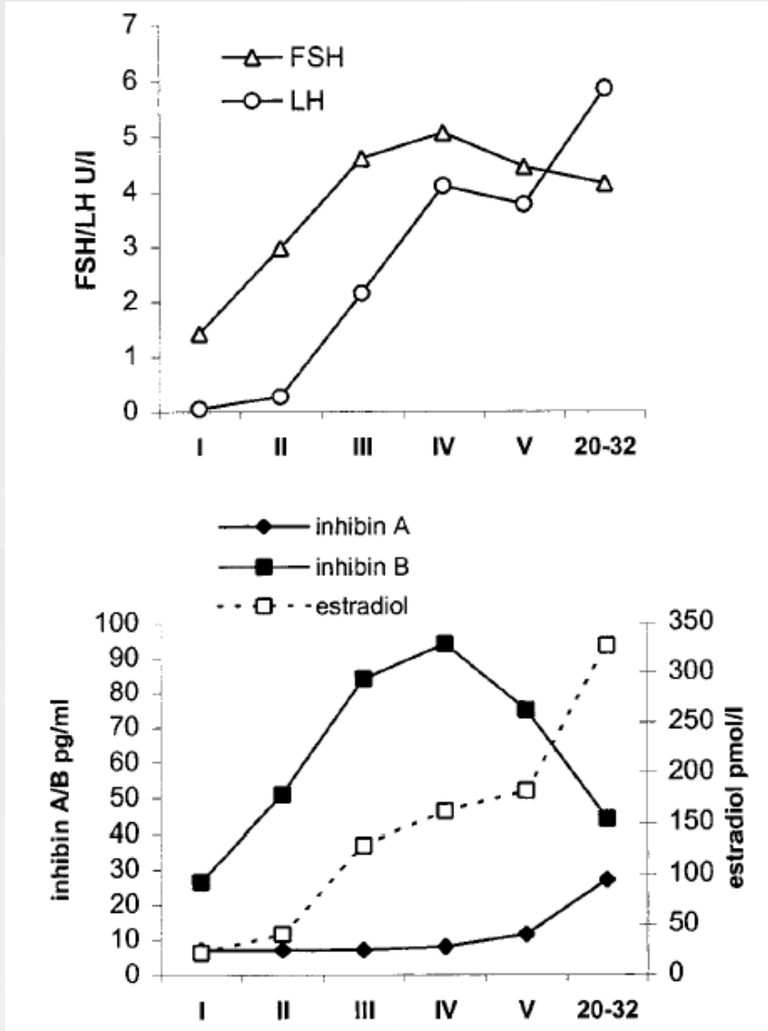


Girls:

FSH, LH, Inhibin (A&B) Estradiol v Tanner stage

XS, N=403 6-20 yrs

Sehested et al J Clin Endoc Metab 85(4): 1634-1640. 2000

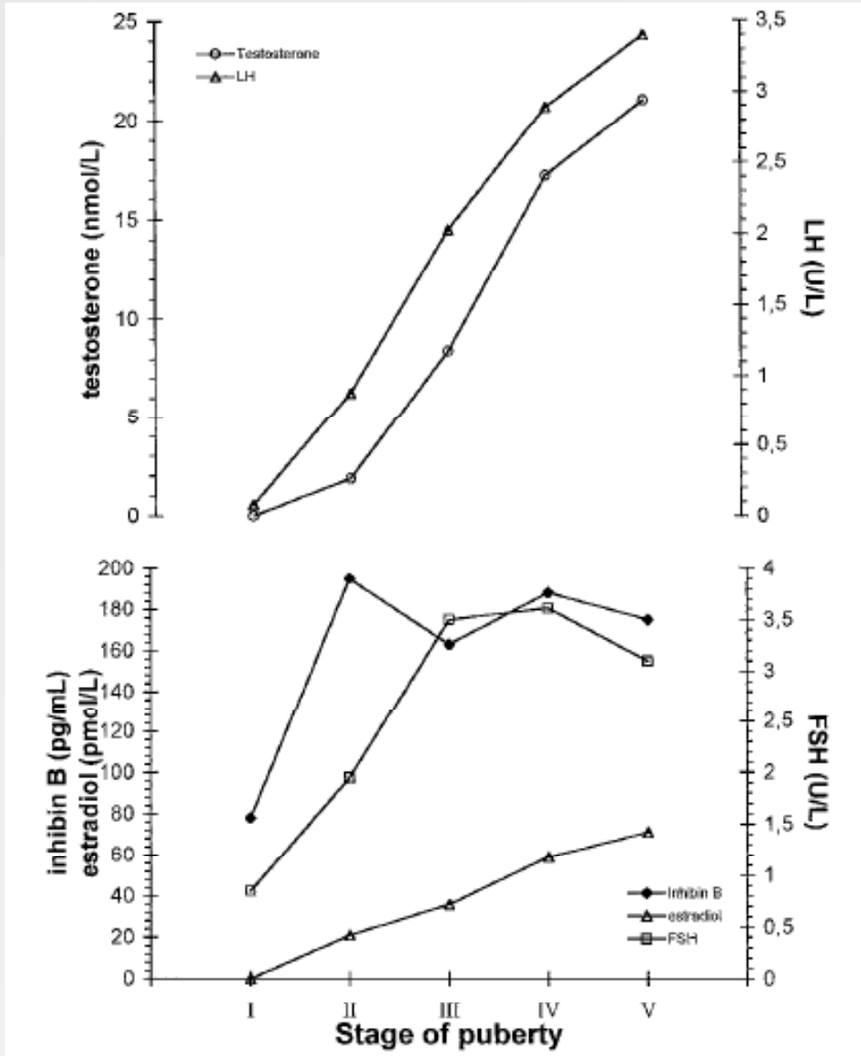


Boys:

Inhibin B, FSH, LH, testosterone, and estradiol v Tanner stage

XS N=400 6-20 yrs

AM Anderson et al J Clin Endoc Metab 82(12): 3976-3981. 1997



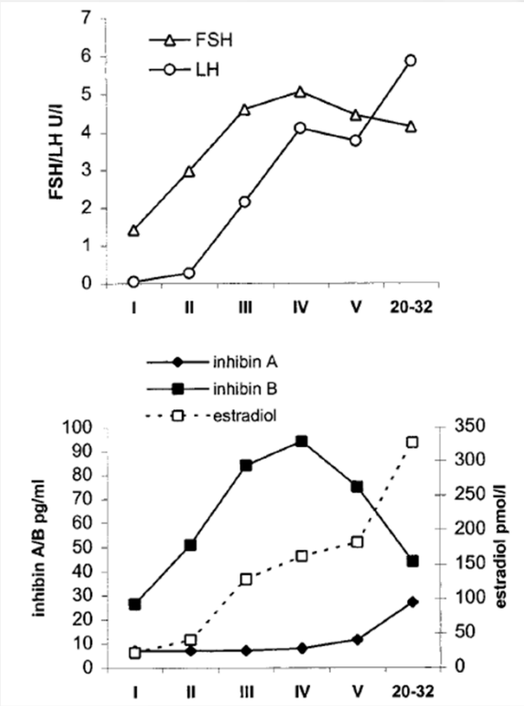
Importance of scaling by pubertal status rather than age is demonstrated by:

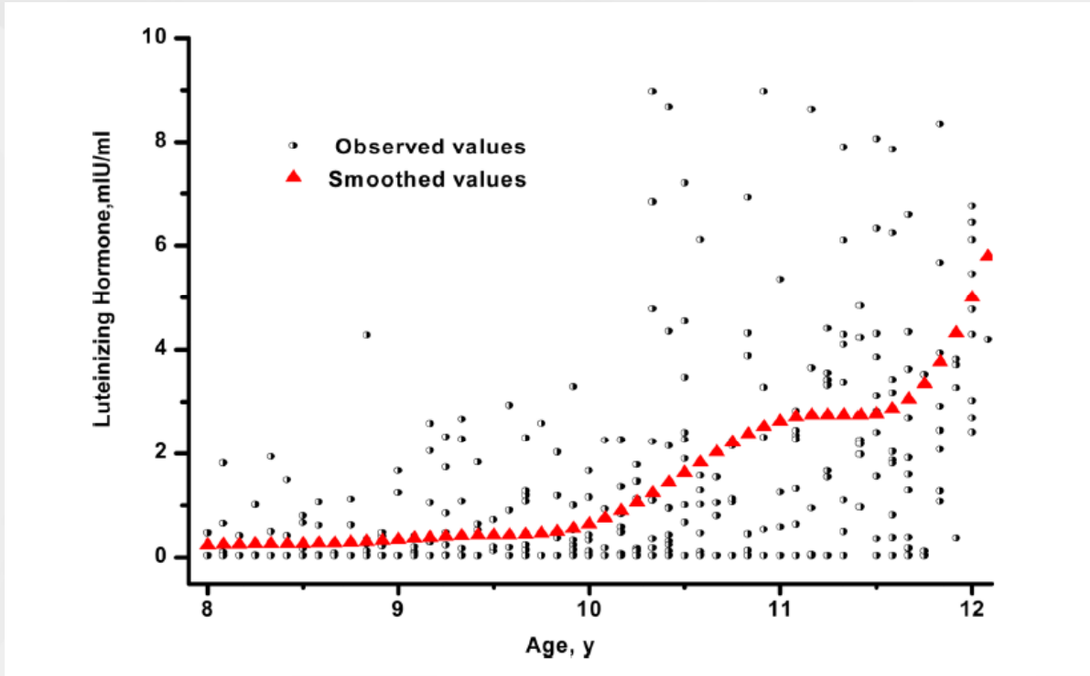
Sims et al 2012 Clin Endocrinol

NHANES III 1988-1994

Girls: LH, Inhibin B

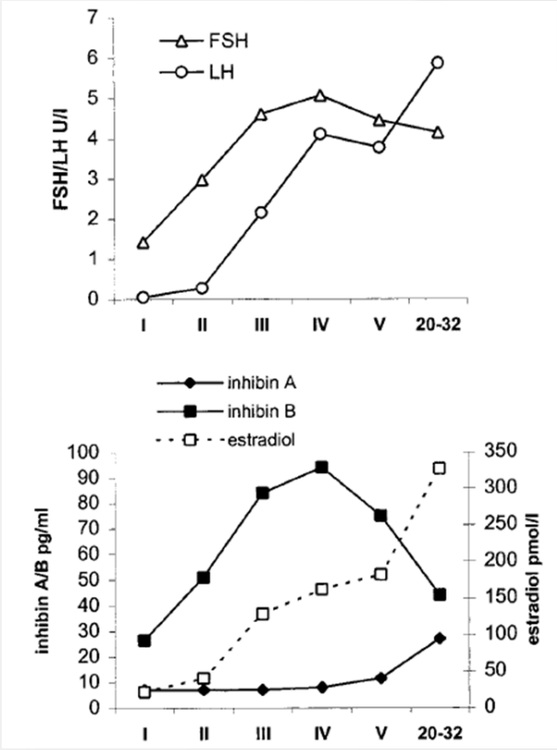
N=705

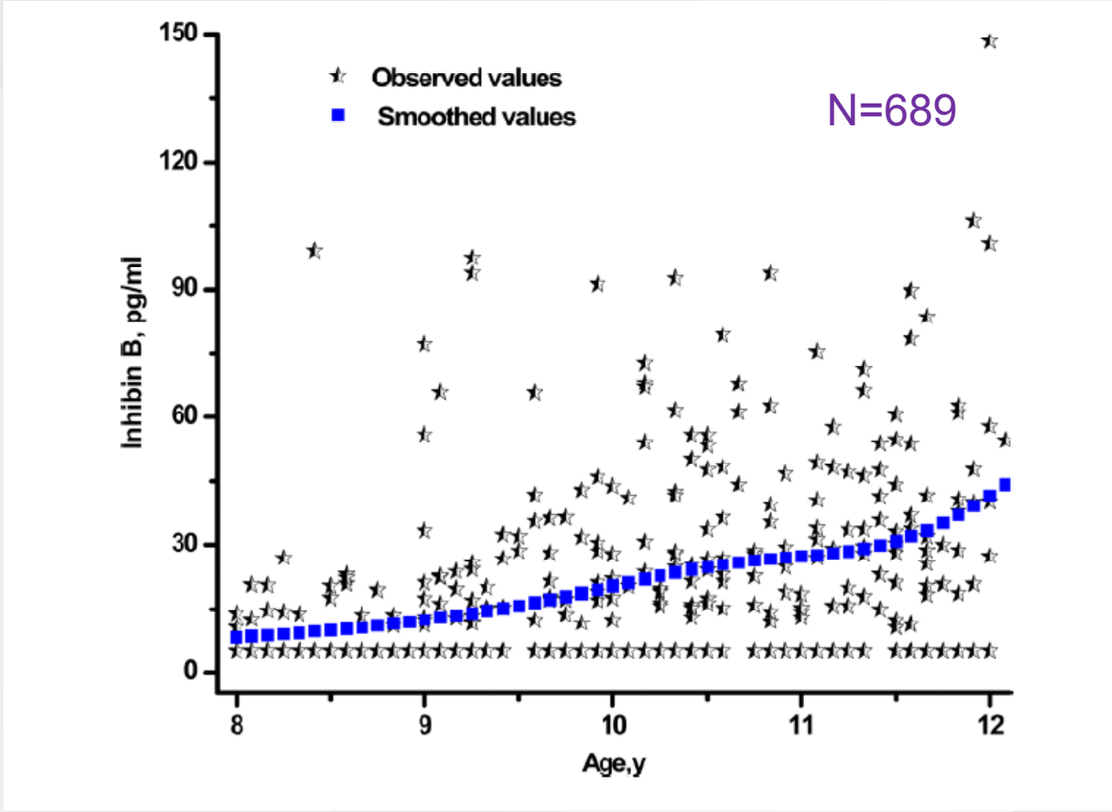




Sehested et al J Clin Endoc Metab 85(4): 1634-1640. 2000

Sims et al NHANES III 88-94 Clin Endoc 2012 77:55-63





Sehested et al J Clin Endoc Metab 85(4): 1634-1640. 2000

Sims et al NHANES III 88-94 Clin Endoc 2012 77:55-63

UK Border

What indicators of maturity were being used to estimate chronological age (CA)?

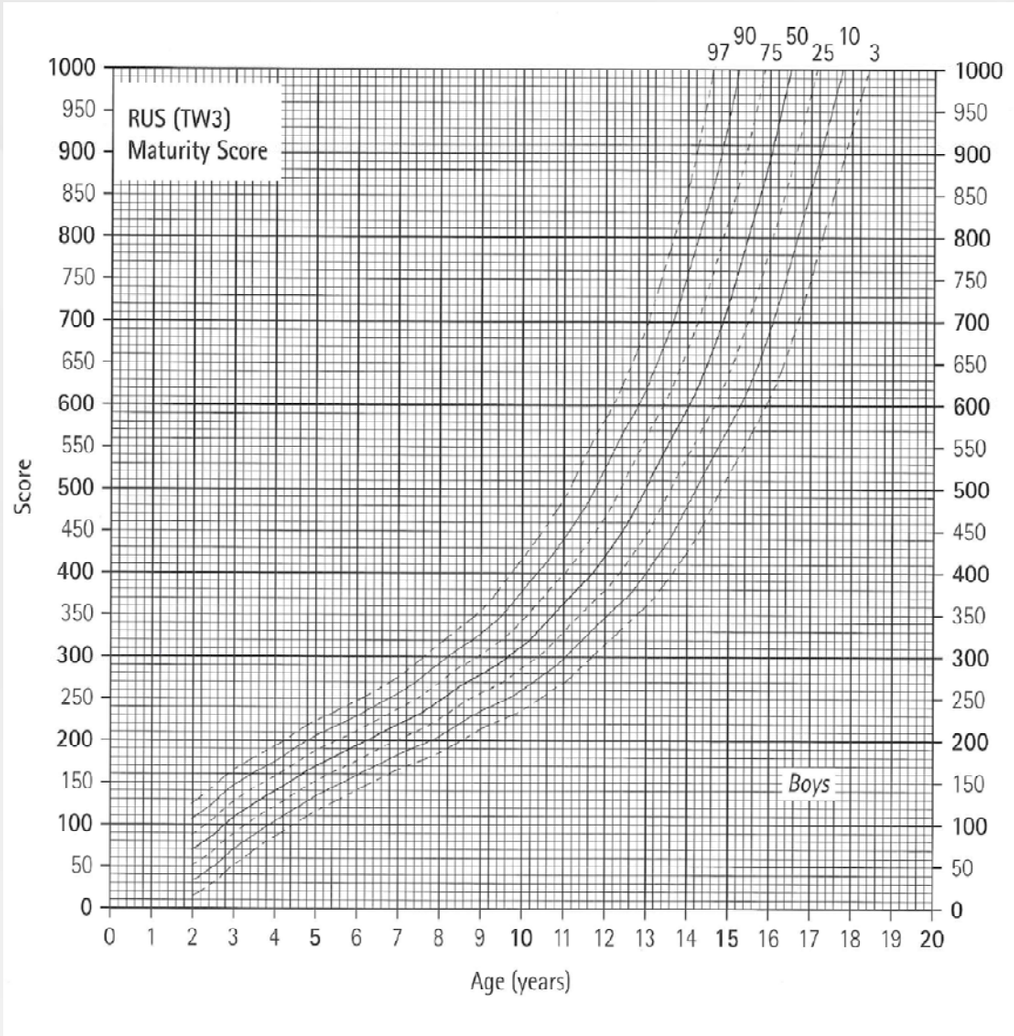
- Times of appearance and fusion of ossification centres
- Number of erupted teeth
- Present/absent 2y sexual development
- Normal/abnormal gait
- Normal/abnormal skin elasticity

What indicators of maturity were being used to estimate chronological age?

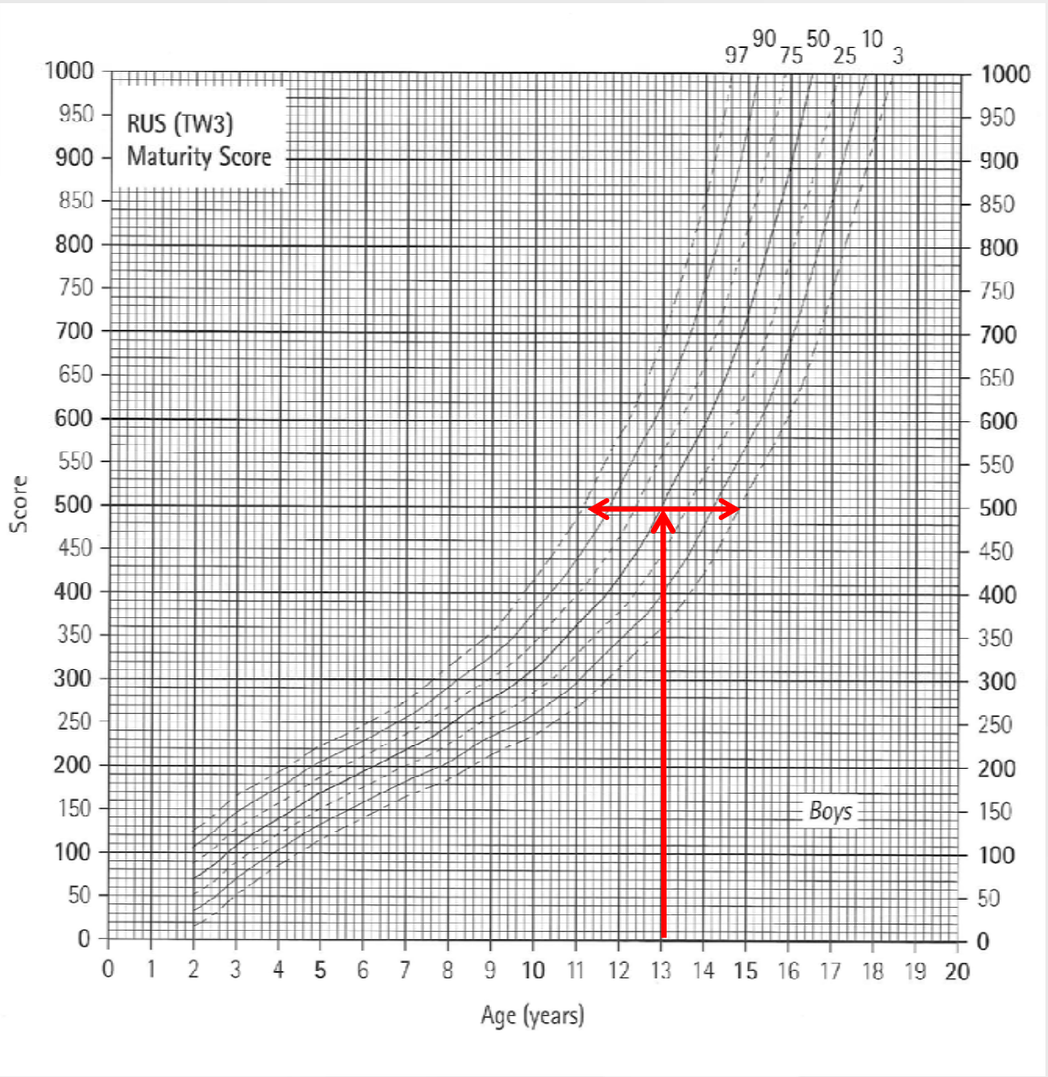
- Times of appearance and fusion of ossification centres
- Number of erupted teeth
- Present/absent 2y sexual development
- Normal/abnormal gait
- Normal/abnormal skin elasticity

Validity? Relationship to Chronological age?

TW3 RUS bone maturity score



TW3 RUS bone maturity score



Maturity indicators:

T. Wingate Todd (1937) Atlas of Skeletal Maturation

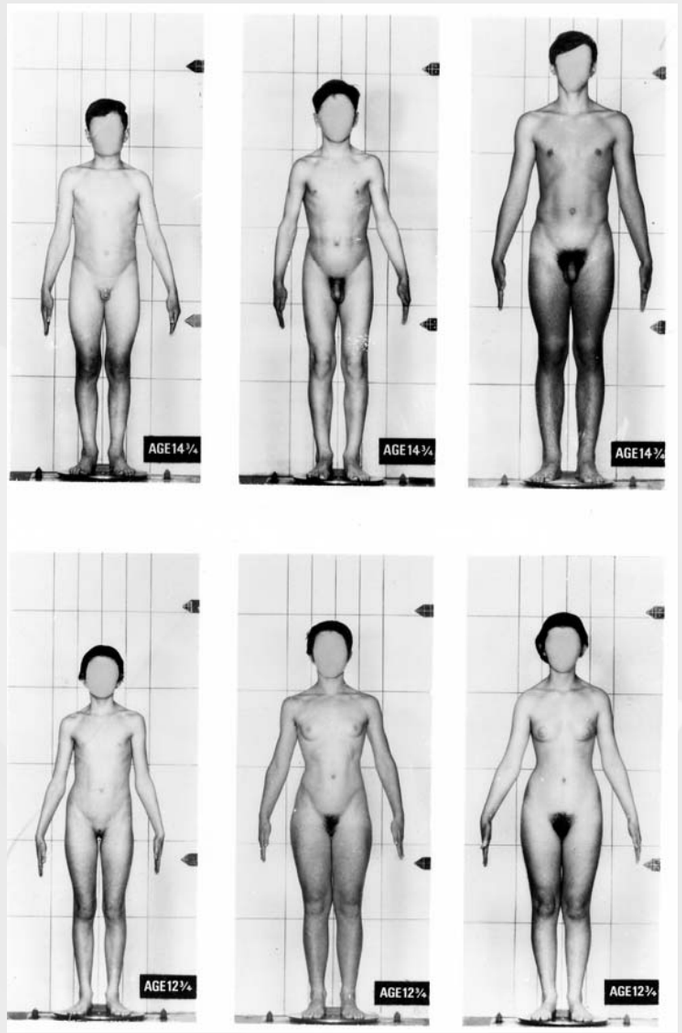
“…those features…which, because they tend to occur regularly and in a definitive and irreversible order, mark…progress towards maturity.”

The future of non-clinical pubertal assessment…

Culturally sensitive questionnaire
HPG hormones - body fluid analysis

1. Maturity v Time

- One maturational year is not equal to one chronological year

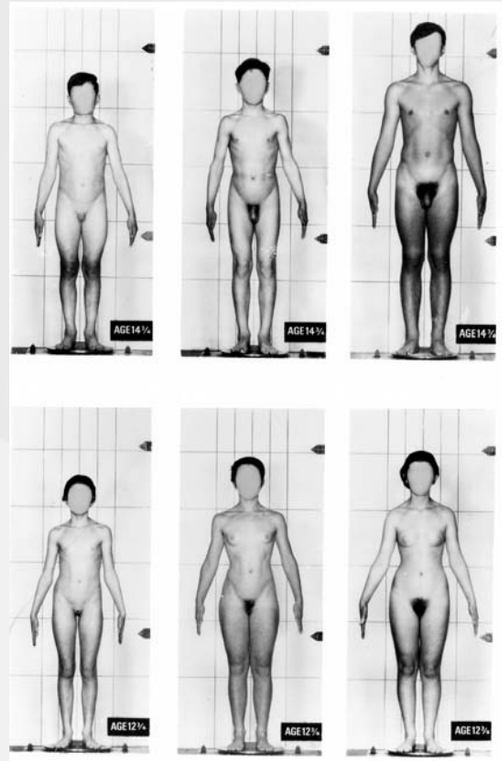


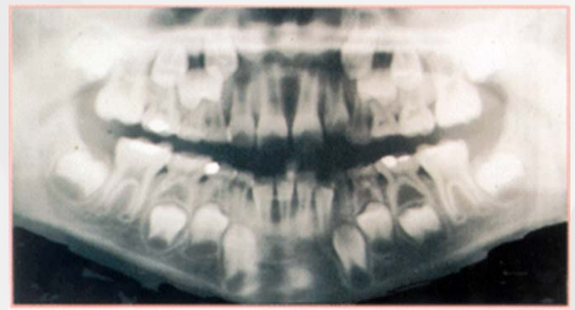
1. Maturity v Time
2. Discrete indicators

- Maturity indicators are discrete indicators of continuous processes

1. Maturity v Time
2. Discrete indicators
3. Independence of processes

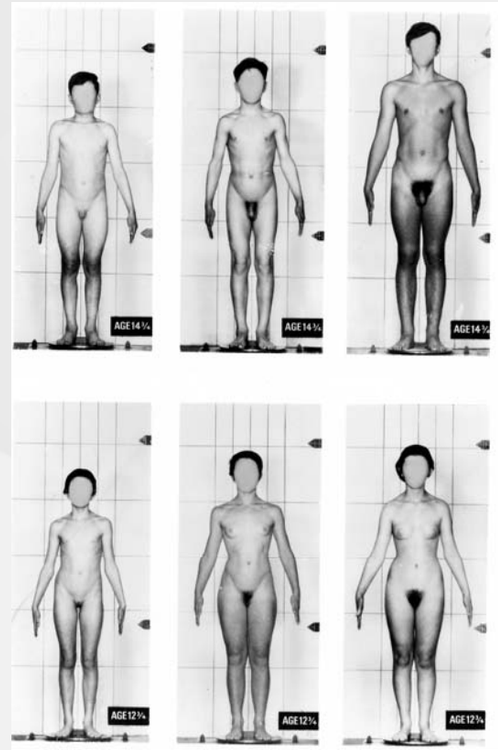
- different aspects of maturation are under different biological control

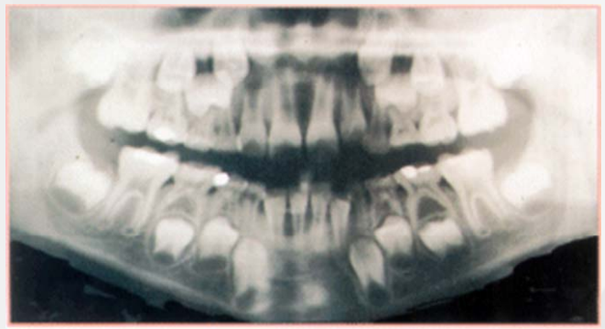




1. Maturity v Time
2. Discrete indicators
3. Independence of processes
4. Uneven maturation

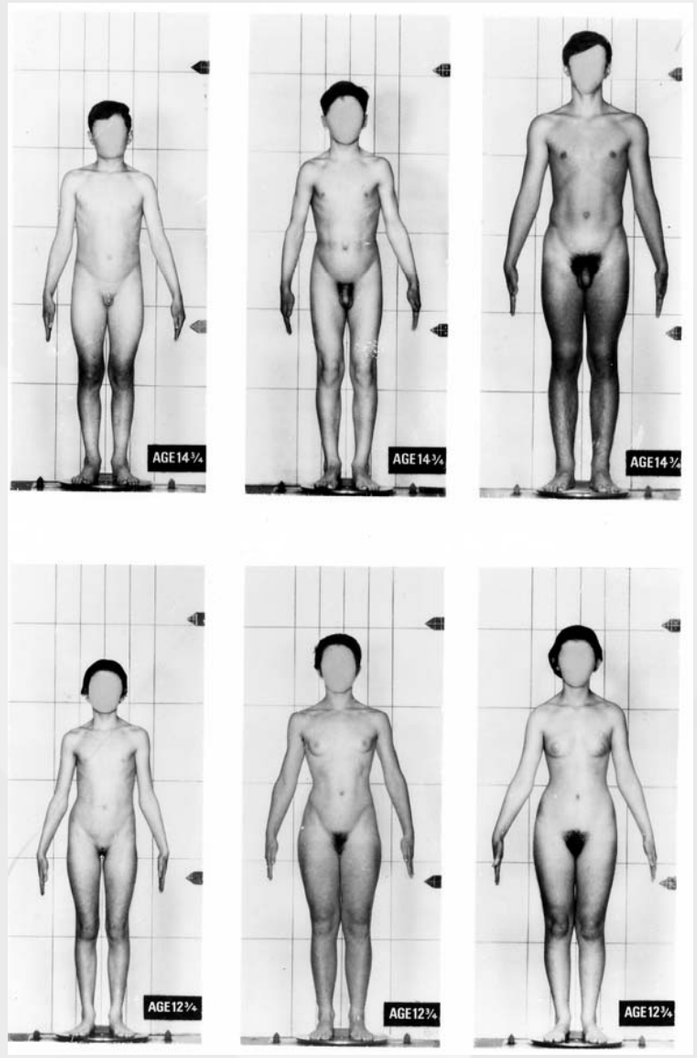
• no two process mature at the same rate





1. Maturity v Time
2. Discrete indicators
3. Independence of processes
4. Uneven maturation
5. Sexual dimorphism

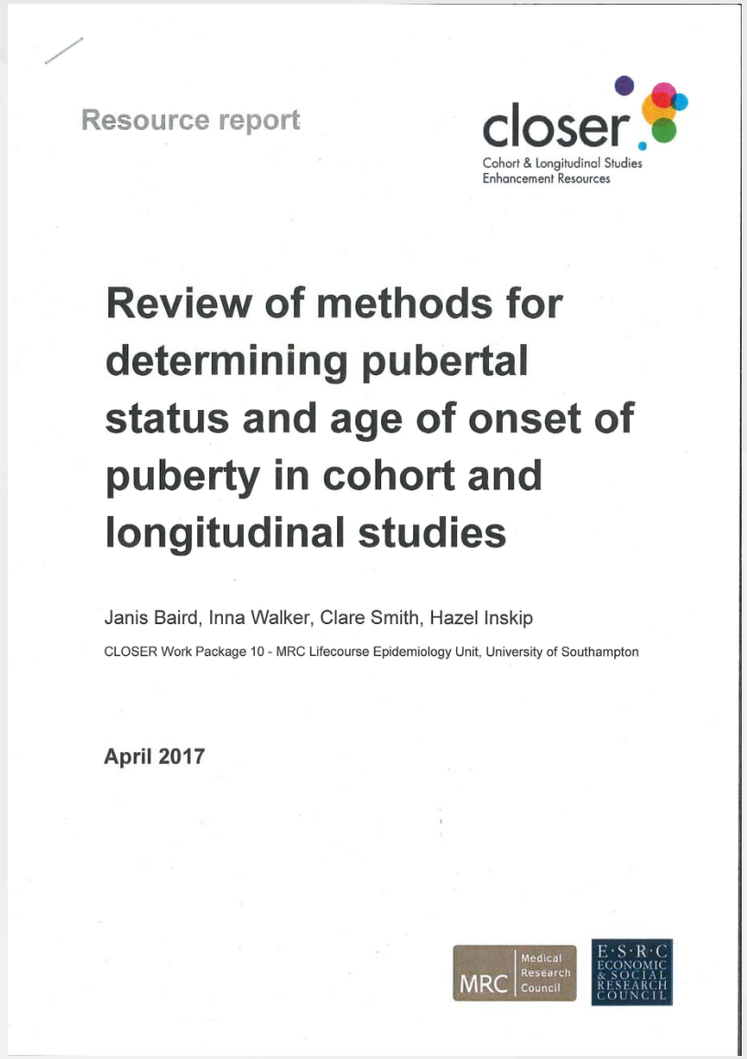
- Maturation rates differ between the sexes



1. Maturity v Time
2. Discrete indicators
3. Independence of processes
4. Uneven maturation
5. Sexual dimorphism
6. Maturity v Size

- a general but not specific relationship exists between size and maturity

What indicators of maturity were being used to estimate chronological age?



Loughborough University
#InspiringWinners since 1909

Resource report

closer
Cohort & Longitudinal Studies Enhancement Resources

Review of methods for determining pubertal status and age of onset of puberty in cohort and longitudinal studies

Janis Baird, Inna Walker, Clare Smith, Hazel Inskip

CLOSER Work Package 10 - MRC Lifecourse Epidemiology Unit, University of Southampton

April 2017

MRC Medical Research Council

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

Conclusions:

- Clinical (physicians) assessment were best
- Growth analysis (SITAR) when longitudinal data height and foot length(?)
- Biomarkers
- Voice change

Adolescent's opinions: (N=10 6♂/4♀):

- Questionnaires - paper not digital
- Growth – height, foot length…
- Voice change
- Same sex professional