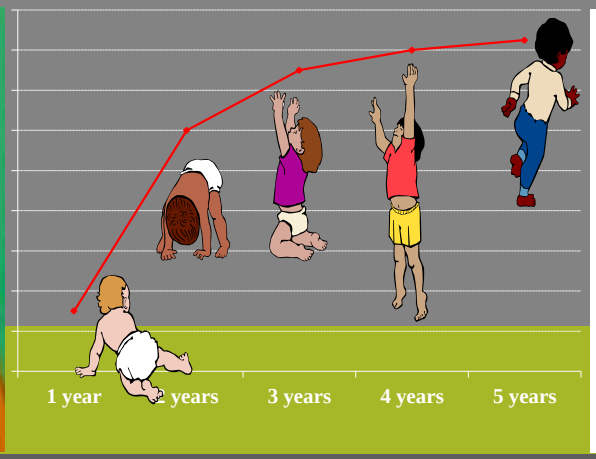
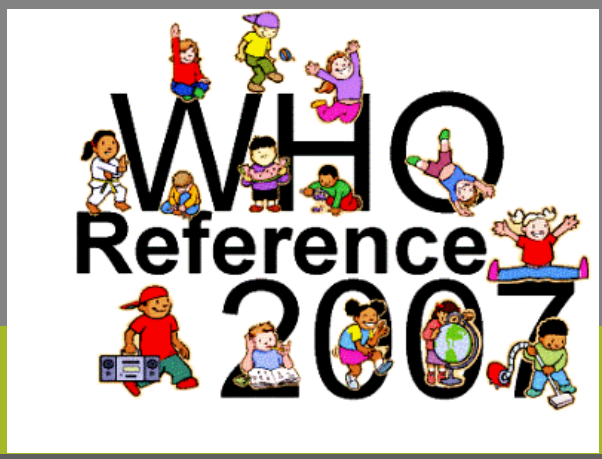
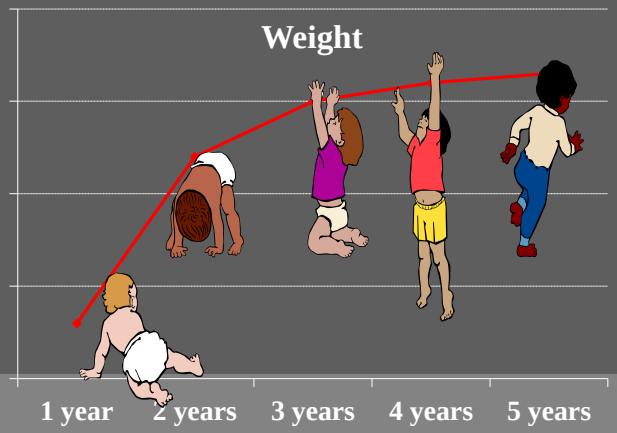
MONITORING HUMAN GROWTH FROM THE WOMB TO ADULTHOOD





Dr Leila Cheikh Ismail
INTERGROWTH-21st Project Leader
Nuffield Department of Obstetrics and Gynaecology
Women's Centre, John Radcliffe Hospital
University of Oxford
Oxford, UK



WHO CHILD GROWTH STANDARDS

Background and Global Overview

WHY?

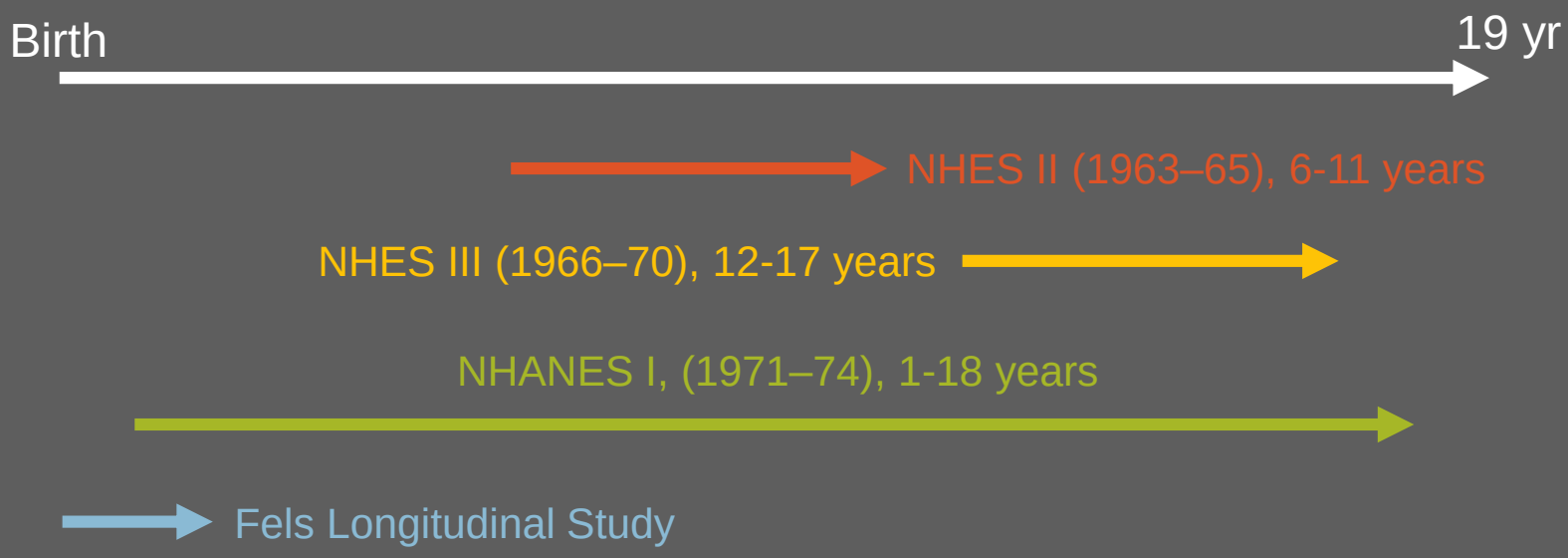
RATIONALE

Prior to 2006, WHO recommended the use of the growth references developed by the United States National Center for Health Statistics (NCHS) of the CDC, based on national survey data collected in the 1960s and 1970s.

→ WHO growth references, the NCHS/WHO growth references, or the NCHS/WHO growth chart

→ Included growth charts for infants from birth to 36 months and for older children from 2 to 18 years of age

NCHS/WHO GROWTH CHART
SAMPLE ORIGINS



This reference was based on data from **several unrelated samples** of children from a **single country** and suffered from a number of **technical and biological drawbacks** that made it inadequate to monitor early childhood growth.

CONCEPTUAL LIMITATIONS

WHO 1995 RECOMMENDATIONS

- Data from multiple countries and geographic regions (including less-developed countries)
- Data should reflect the status of healthy populations with unconstrained growth (even when not representative of the whole population)
- Data for children from birth to adolescence should be included
- Sample size and data-collection procedures should be appropriate and well documented

Wang et al. (2006) Food and Nutrition Bulletin 27(4)

NCHS/WHO GROWTH CHART
LIMITATIONS

- Data from multiple countries and geographic regions (including less-developed countries)

→NCHS/WHO growth chart were derived from samples form **one country:** the United States

NCHS/WHO GROWTH CHART
LIMITATIONS

- Data should reflect the status of healthy populations with unconstrained growth (even when not representative of the whole population)

→ Sample selection used a **descriptive** approach, which when applied to a population like that of the United States, which has an increasing prevalence of obesity, was likely to result in a **non-healthy sample**.

NCHS/WHO GROWTH CHART
LIMITATIONS

- Data should reflect the status of healthy populations with unconstrained growth (even when not representative of the whole population)

→ Data collected may not reflect the **desirable eating and growth patterns** for these age groups or the more **recent patterns** worldwide.

For example, the Fels dataset reflects the growth of **formula-fed** rather than breastfed infants.

NCHS/WHO GROWTH CHART
LIMITATIONS

- Sample size and data-collection procedures should be appropriate

→ For most sex and age groups in the NCHS/WHO references, the sample size was **approximately 120**.

WHO RECOMMENDATION (1995)

Human growth worldwide should be evaluated using

international standards describing how individuals should grow

Report of WHO Expert Committee 1995
Physical Status: The Use and Interpretation of Anthropometry,
Technical Report Series No. 854

REFERENCES vs. STANDARDS

Reference charts describe how fetuses and newborns ***have*** grown at a particular time and/or place

International standards describe how fetuses and newborns ***should*** grow when nutritional, environmental and health constraints on growth are minimal

REFERENCES vs. STANDARDS

Reference charts describe how fetuses and newborns ***have*** grown at a particular time and/or place

International standards describe how fetuses and newborns ***should*** grow when nutritional, environmental and health constraints on growth are minimal

HOW?

A GROWTH CURVE FOR THE 21ST CENTURY

The WHO Multicentre Growth Reference Study

World Health Organization

MILESTONES IN THE DEVELOPMENT OF THE WHO CHILD GROWTH STANDARDS

1991-1993 WHO Working Group on Infant Growth

- Comprehensive review shows growth patterns of healthy breastfed infants differ from the current NCHS/WHO international reference

- A new growth reference is needed to improve infant health management

WHO MGRS GROUP (2006) Acta Pædiatrica Suppl 450:76

MILESTONES IN THE DEVELOPMENT OF THE WHO CHILD GROWTH STANDARDS

1993 WHO Expert Committee

- Recommends development of a new international growth reference
- Based on an international sample of "healthy" infants

1994 WHA resolution (WHA 47.5)

- Endorses need for new reference
- Requests it to be based on breastfed infants

WHO GROWTH REFERENCE STUDY

Optimal Nutrition

- Breastfed infants
- Appropriate complementary feeding

Optimal Environment

- No microbiological contamination
- No smoking

Optimal Health Care

- Immunization
- Paediatric routines

WHO CHILD GROWTH STANDARDS
STUDY SAMPLE

Six countries where there are:

- <5% stunting, wasting, underweight
- At least 20% mothers breastfeeding
- No health/environmental constraints on growth

And where mothers are:

- Non-smoking
- Willing to follow feeding recommendations
- Single, term birth
- No significant morbidity

WHO Multicentre Growth Reference Study (MGRS)

WHO 03.125

MGRS STUDY DESIGN

Longitudinal (0-24mo)

→ 1743 total enrolled
(1542, 88.5% completed FUP)

Cross-sectional (18-71mo)

→ 6669 (3450 boys/3219 girls)

The following links provide access to the first and second set of the WHO child growth standards (0-60 months):

:: Length/height-for-age

:: Weight-for-age

:: Weight-for-length

:: Weight-for-height

:: BMI-for-age

:: Head circumference-for-age

:: Arm circumference-for-age

:: Subscapular skinfold-for-age

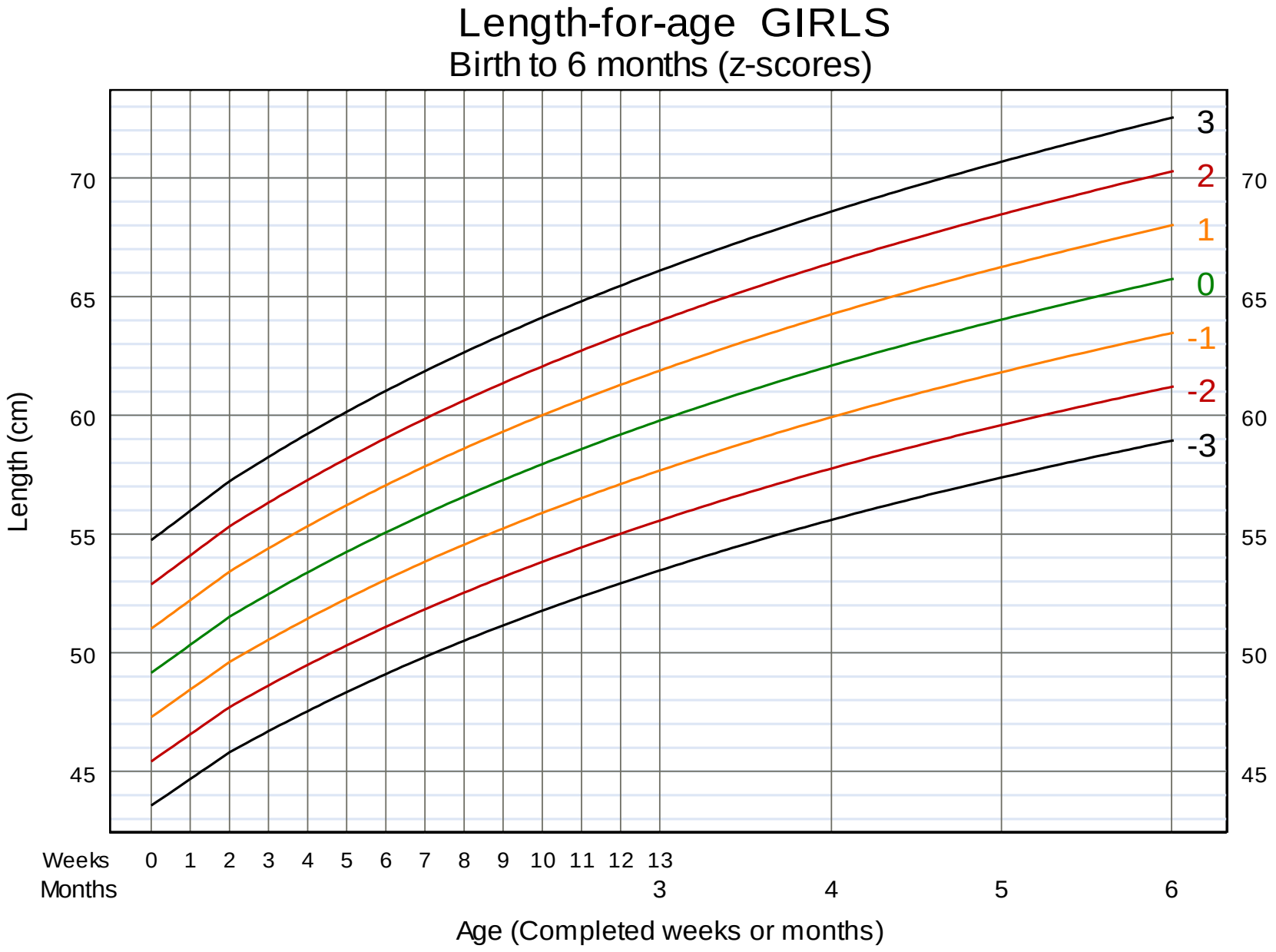
:: Triceps skinfold-for-age

:: Motor development milestones

LENGTH/HEIGHT-FOR-AGE

Z-scores by gender

- Length-for-age: Birth to 6 months
- Length-for-age: Birth to 2 years
- Length-for-age: 6 months to 2 years
- Height-for-age: 2 to 5 years
- Length/height-for-age: Birth to 5 years


Length-for-age GIRLS
Birth to 6 months (z-scores)
Length (cm)
70
65
60
55
50
45
3
2
1
0
-1
-2
-3
Weeks 0 1 2 3 4 5 6 7 8 9 10 11 12 13
Months 3 4 5 6
Age (Completed weeks or months)

INTERPRET PLOTTED POINTS FOR GROWTH INDICATORS

- The curved lines printed on the growth charts will help you interpret the plotted points that represent a child's growth status. The line labeled 0 on each chart represents the median, which is, generally speaking, the average
- The other curved lines are z-score lines which indicate distance from the average
- Z-score lines on the growth charts are numbered positively (1, 2, 3) or negatively (–1, –2, –3). In general, a plotted point that is far from the median in either direction (for example, close to the 3 or –3 z-score line) may represent a growth problem, although other factors must be considered, such as the growth pattern, the health condition of the child and the height of the parents

DEFINITION OF GROWTH PROBLEMS

Z-scores	Growth indicators			
	Length/height-for-age	Weight-for-age	Weight-for-length/height	BMI-for-age
Above 3	*See note 1*	*See note 2*	Obese	Obese
Above 2		*See note 2*	Overweight	Overweight
Above 1		*See note 2*	Possible risk of overweight *(see note 3)*	Possible risk of overweight *(see note 3)*
0 (median)				
Below 1				
Below 2	Stunted *(see note 4)*	Underweight	Wasted	Wasted
Below 3	Severely stunted *(see note 4)*	Severely underweight *(see note 5)*	Severely wasted	Severely wasted

GROWTH REFERENCE DATA FOR 5-19 YEARS

Background and Global Overview

De Onis (2007) Bulletin of the World Health Organization 85(9)

RATIONALE

- In 2006, the WHO released the new Child Growth Standards from birth to 5 years of age

- Need to harmonize growth assessment tools conceptually and pragmatically

HISTORY

- In early 2006, a group of expert was tasked to evaluate the feasibility of developing a single international growth reference for school-aged children and adolescents.

- Several options were considered…

HOW?

OPTION 1

A growth standard could be constructed for this age group by conducting a similar study to the one that led to the development of the WHO Child Growth Standards for 0 to 5 years.

→ It was agreed that such a study would not be feasible for older children, as it would not be possible to control the dynamics of their environment.

OPTION 2

A growth reference could be constructed for this age group using existing historical data and discussed the criteria for selecting the data sets.

→ This approach was abandoned due to the great heterogeneity in methods and data quality, sample size, age categories, socioeconomic status of participating children and various other factors critical to growth curve construction.

OPTION 3

To reconstruct the 1977 NCHS/WHO growth reference from 5 to 19 years, using the original sample (a non-obese sample with expected heights), supplemented with data from the WHO Child Growth Standards (to facilitate a smooth transition at 5 years), and applying the state-of-the-art statistical methods

→ WHO Growth reference 5-19 years

The links below provide access to the reference charts and tables by indicator:

:: BMI-for-age (5-19 years)

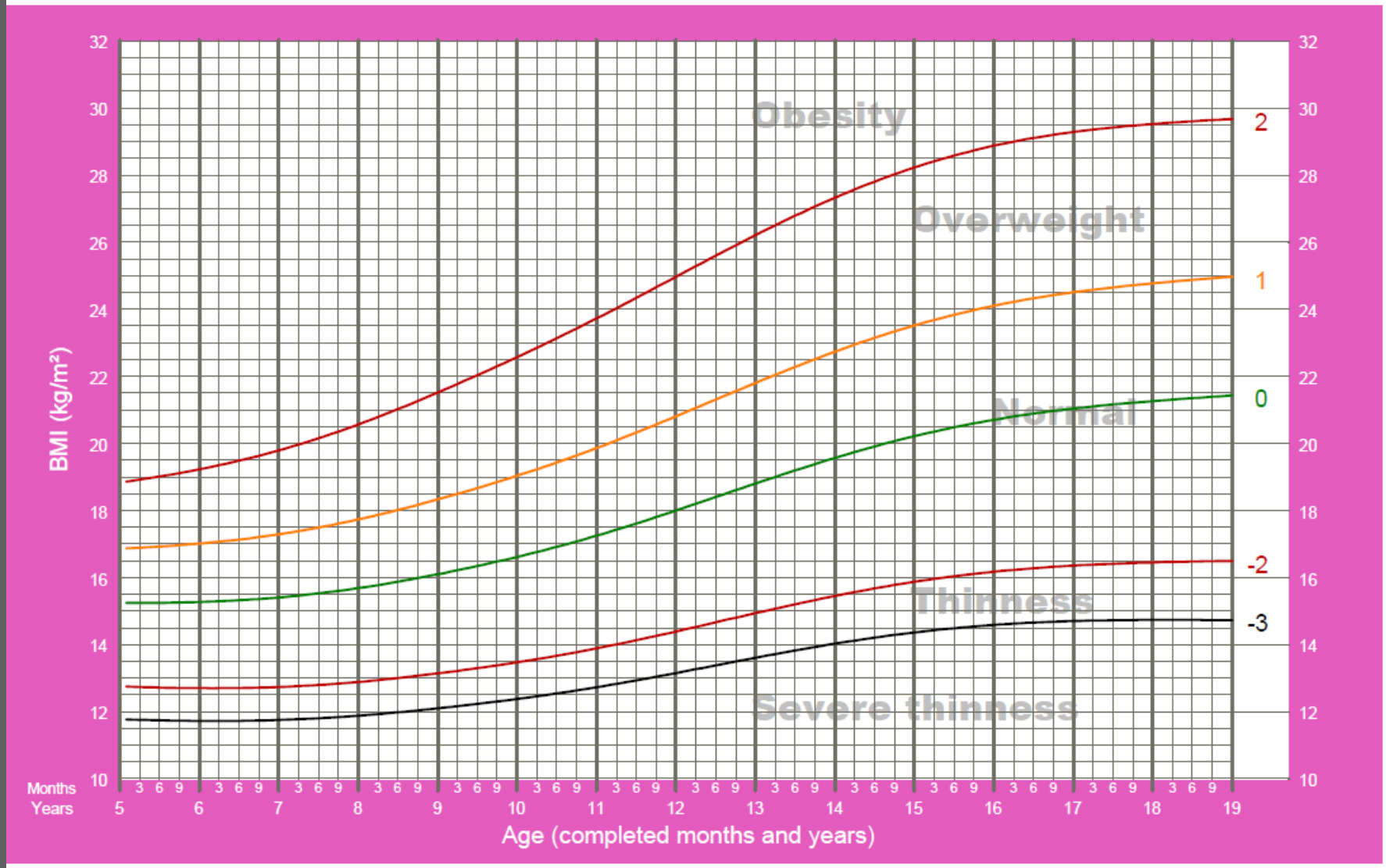
:: Height-for-age (5-19 years)

:: Weight-for-age (5-10 years)

BMI-for-age GIRLS

5 to 19 years (z-scores)

World Health Organization



2007 WHO Reference

WHO BMI-FOR-AGE (5-19 YEARS)

Cut-offs:

Overweight: above +1 Z-score

Obesity: above +2 Z-score

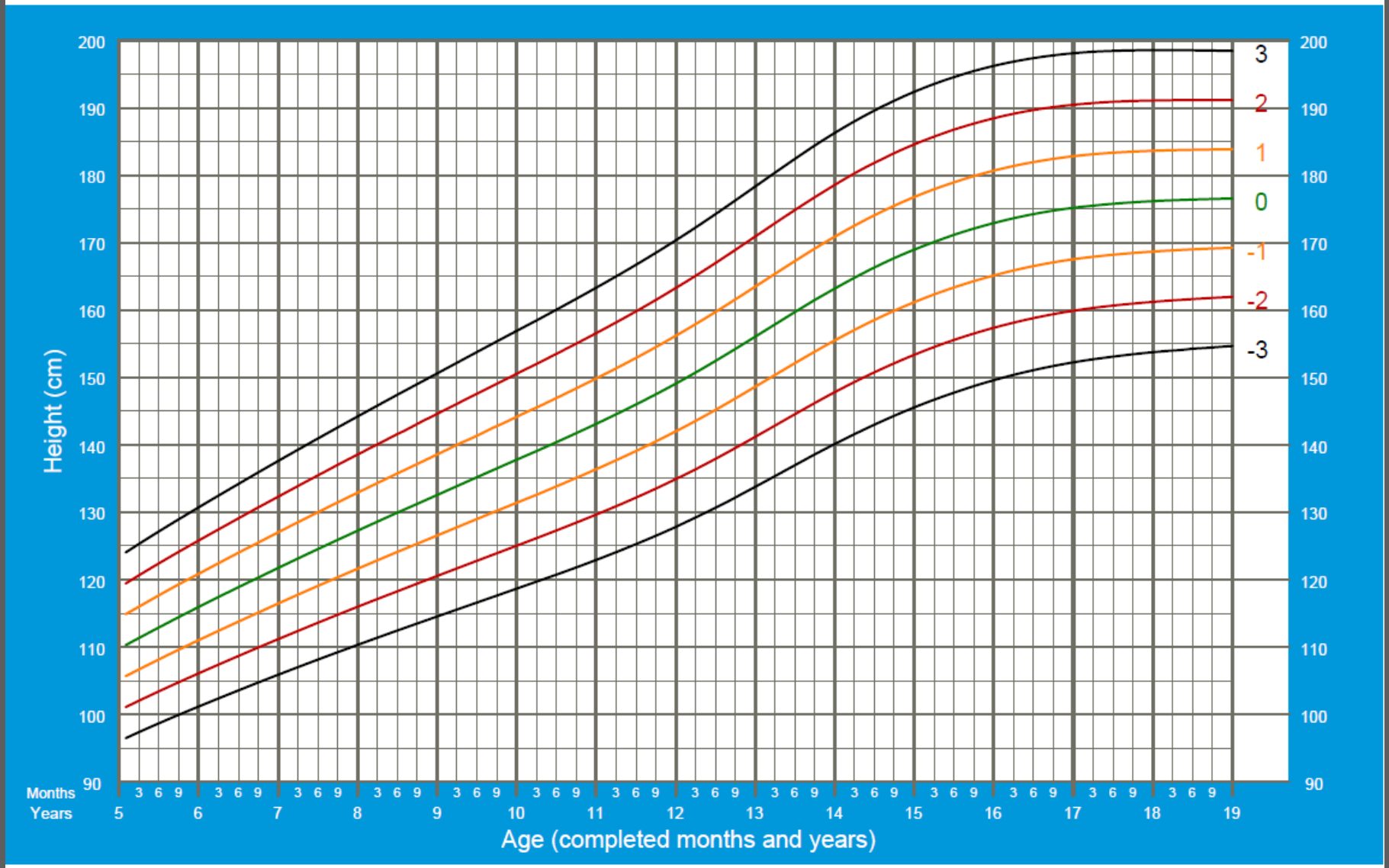
Thinness: below -2 Z-score

Severe thinness: below -3 Z-score

Height-for-age BOYS

5 to 19 years (z-scores)

World Health Organization



2007 WHO Reference

WHO HEIGHT-FOR-AGE (5-19 YEARS)

Cut-offs:

Above +3 Z-score: Tallness is rarely a problem, unless it is so excessive that it may indicate an endocrine disorder.

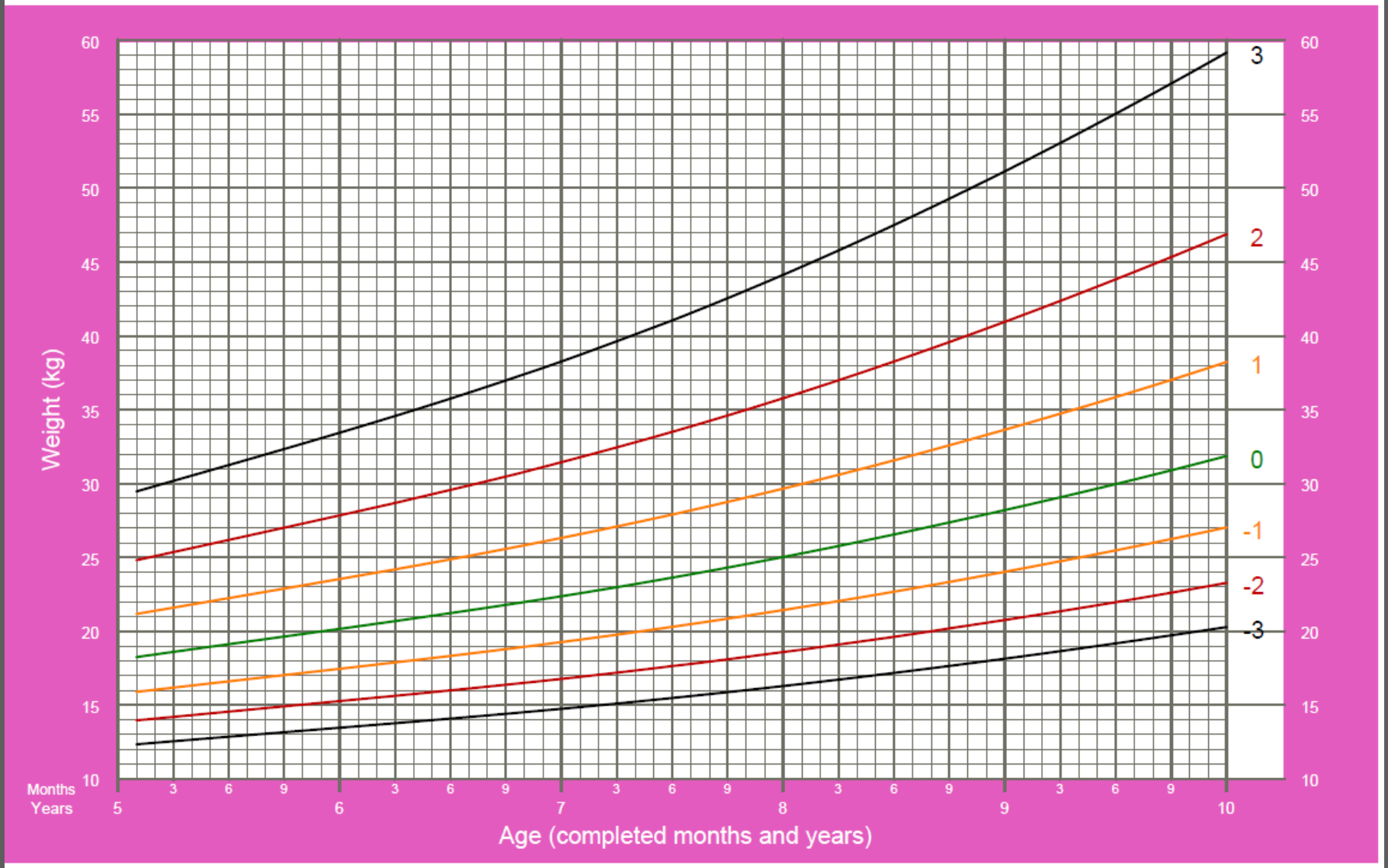
Stunted: below -2 Z-score

Severely stunted: below -3 Z-score

Weight-for-age GIRLS

5 to 10 years (z-scores)

World Health Organization



2007 WHO Reference

WHO WEIGHT-FOR-AGE (5-10 YEARS)

Cut-offs:

Z-score > +1: A child whose weight-for-age falls in this range may have a growth problem, but this is better assessed from weight-for-length/height or BMI-for-age

Underweight: below -2 Z-score

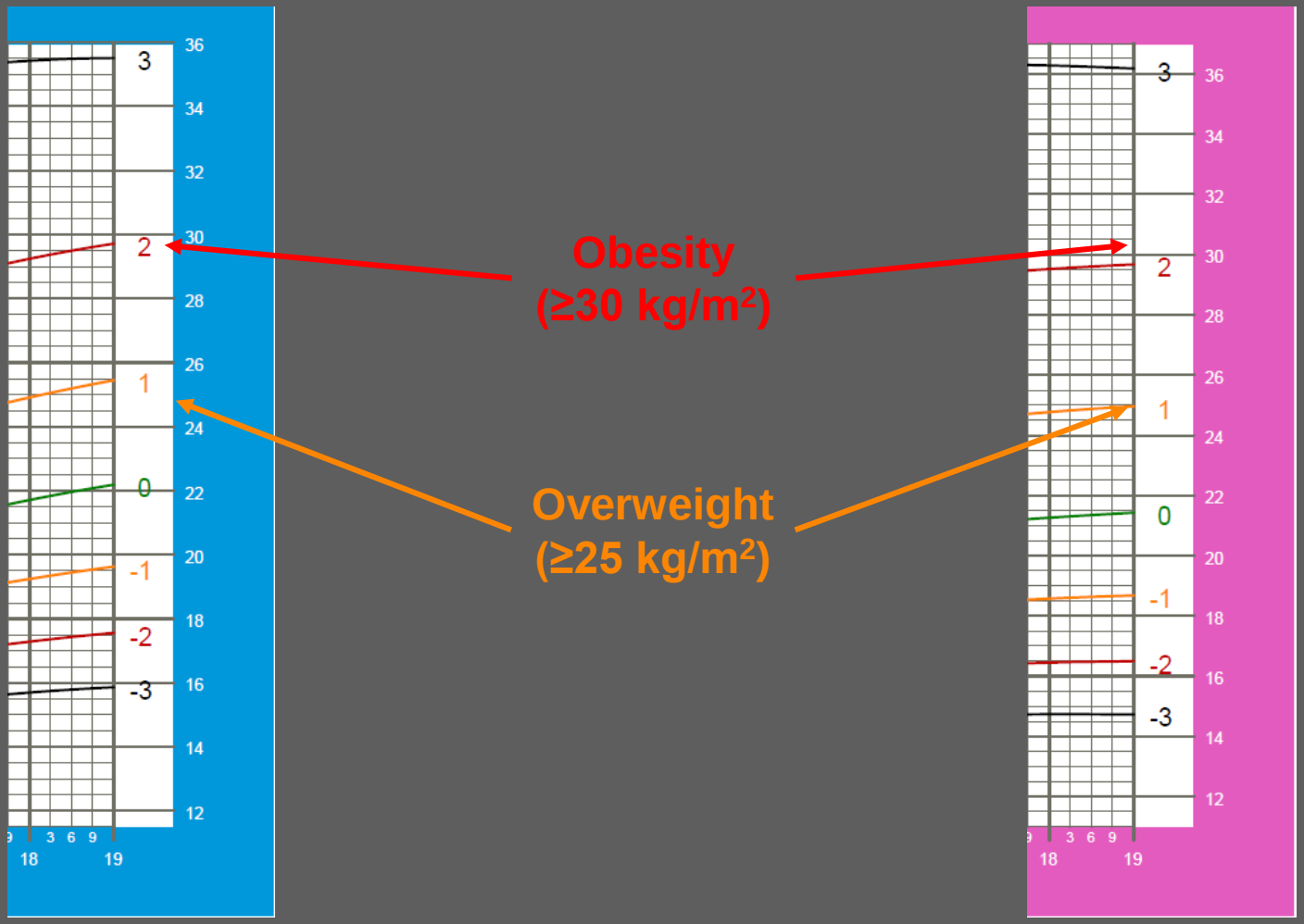
Severely underweight: below -3 Z-score

TRANSITION TO ADULT CUT-OFFS

In the 2007 BMI-for-age at 19 years of age:

- +1 SD (25.4 kg/m² for boys and 25.0 kg/m² for girls) are equivalent to the overweight cut-off used for adults (> 25.0 kg/m²)
- +2 SD (29.7 kg/m² for both sexes) compares closely with the cut-off for obesity (> 30.0 kg/m²)

TRANSITION TO ADULT CUT-OFFS



INTERGROWTH-21ST STANDARDS AND REFERENCES

Background and Global Overview

WHY?

RATIONALE

WHO child growth standards (0-60 months):

- Length/height-for-age
- Weight-for-age
- Weight-for-length/height
- BMI-for-age
- Head circumference-for-age
- Arm circumference-for-age
- Subscapular skinfold-for-age
- Triceps skinfold-for-age
- Motor development milestones

What is missing?

No information on:

- Growth during pregnancy
- Size at birth by GA
- Postnatal growth of preterm infants

HOW?

CHALLENGES

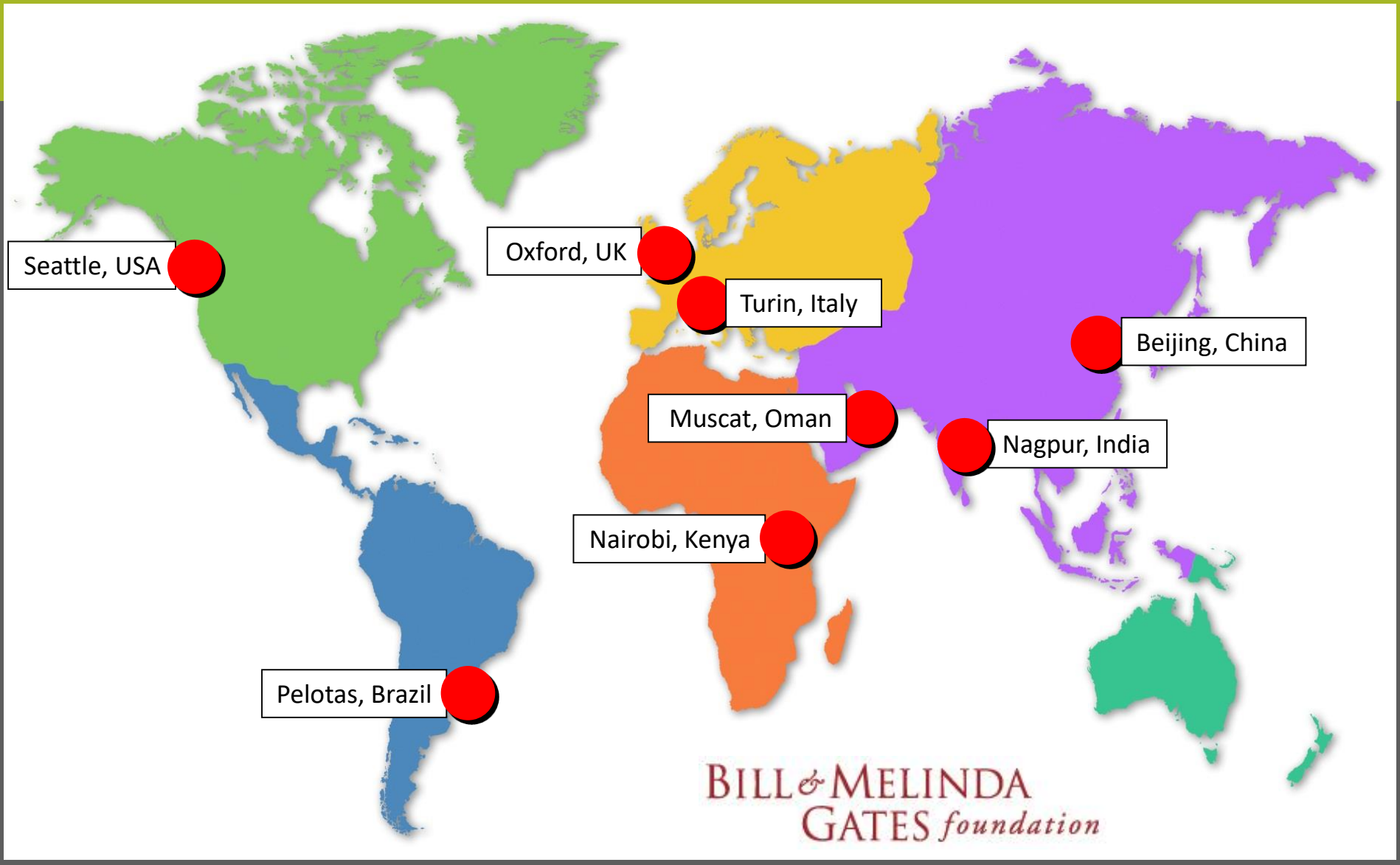
Practical considerations:

Where?	→ Site selection
Who?	→ Population selection

Methodological considerations:

Multicentre study	→ Same equipment, protocols, level of care and recommendations
Complement WHO charts	→ Same anthropometric equipment and protocol
Pooling the results	→ Ensuring good data quality throughout the study and across sites

INTERGROWTH-21ST SITES



POPULATION SELECTION
LOW-RISK PREGNANCY CRITERIA

a) aged ≥18 and ≤35 years;
b) BMI ≥18.5 and <30 kg/m^2;
c) height ≥ 153 cm;
d) singleton pregnancy;
e) a known LMP with regular cycles (defined as a 26-30 day cycle in the previous 3 months), without hormonal contraceptive use, pregnancy or breastfeeding in the 3 months before pregnancy;
f) natural conception
g) no relevant past medical history (refer to screening form), with no need for long-term medication (including fertility

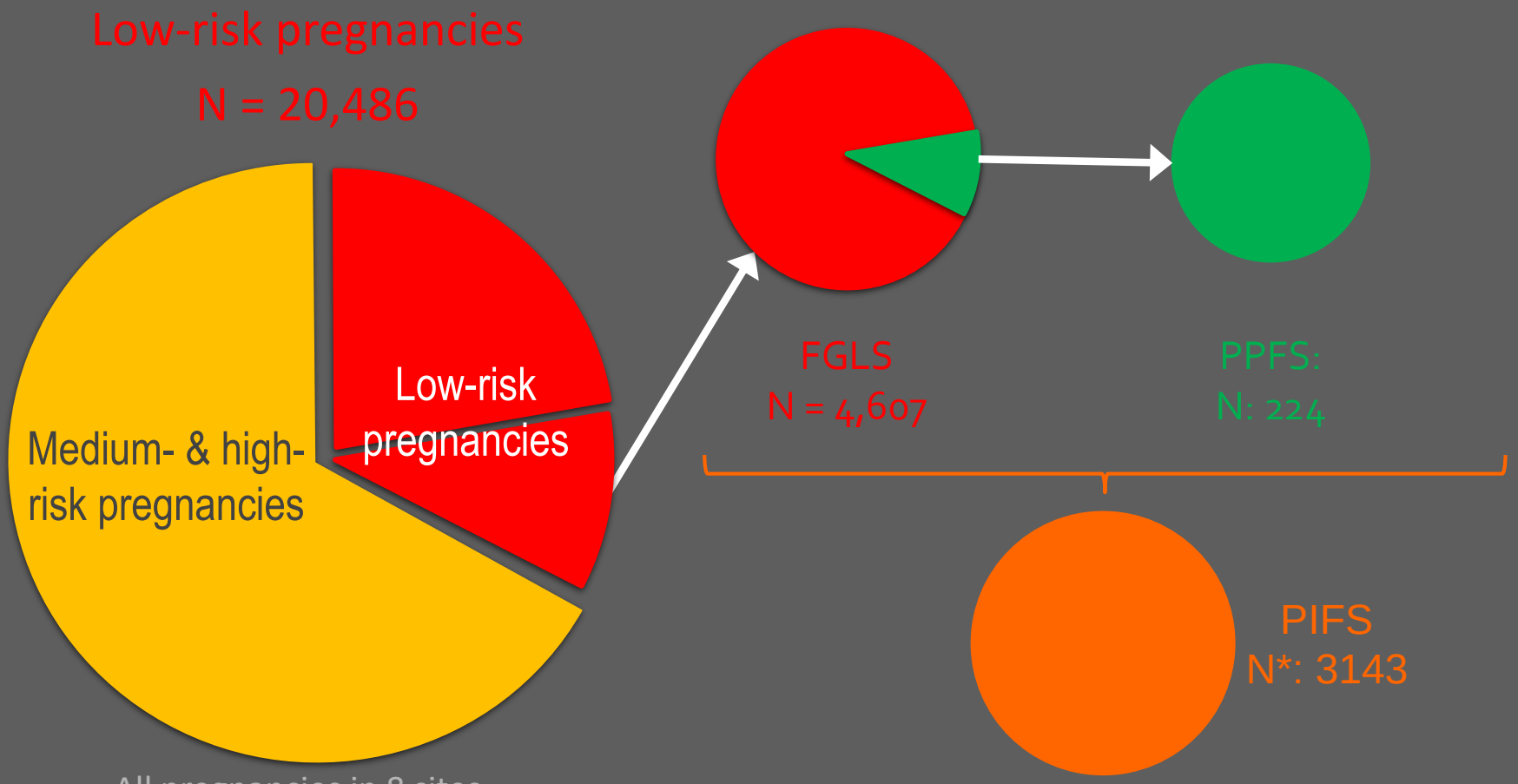
Criteria defining a low-risk study population as healthy and well-nourished (both before and during pregnancy) to ensure that fetal growth is optimal

o) no clinically significant atypical red cell alloantibodies;
p) negative urinalysis;
q) systolic blood pressure <140 mmHg and diastolic blood pressure < 90 mmHg;
r) haemoglobin ≥11 g/dl;
s) negative syphilis test and no clinical evidence of any other sexually transmitted diseases, including clinical Trichomoniasis;
t) not in an occupation with risk of exposure to chemicals or toxic substances, or very physically demanding activity to be evaluated by local standards. Also women should not be conducting vigorous or contact sports, as well as scuba diving or similar activities

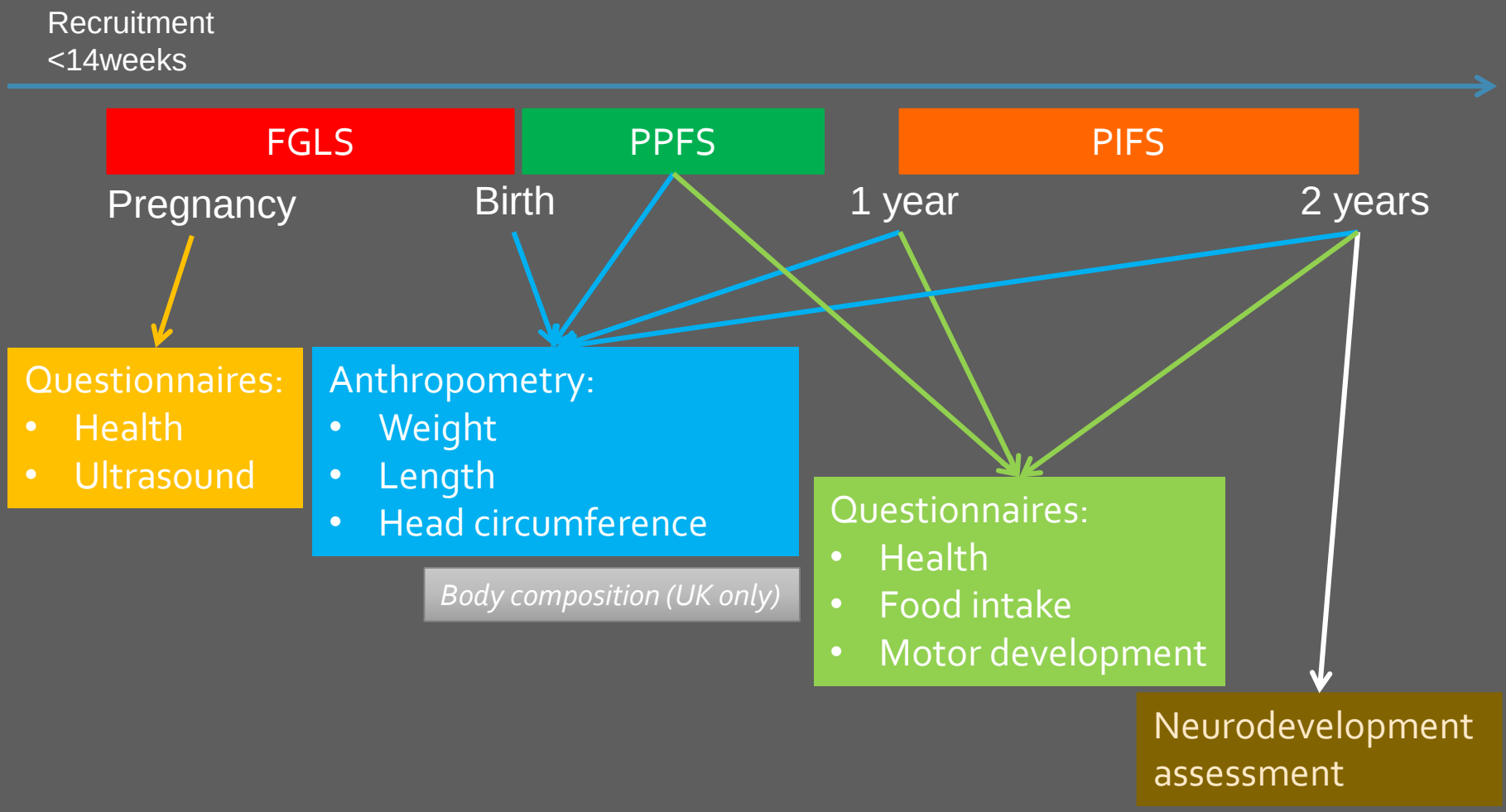
INTERGROWTH-21ST PROJECT

1. **Fetal Growth Longitudinal Study (FGLS) from <14+0 weeks gestational age to birth:** to monitor and measure fetal growth clinically and by ultrasound in a healthy population
2. **Preterm Postnatal Follow-up Study (PPFS) of preterm infants (>26+0 but <37+0** weeks) in the FGLS to describe their postnatal growth pattern
3. **Newborn Cross-sectional Study (NCSS)** of all newborns at the study centres over 12 months, obtaining anthropometric measures and neonatal morbidity and mortality rates

INTERGROWTH-21ST POPULATIONS



OVERVIEW


Recruitment
<14weeks
FGLS
PPFS
PIFS
Pregnancy
Birth
1 year
2 years
Questionnaires:
• Health
• Ultrasound
Anthropometry:
• Weight
• Length
• Head circumference
Body composition (UK only)
Questionnaires:
• Health
• Food intake
• Motor development
Neurodevelopment assessment

PRODUCTS

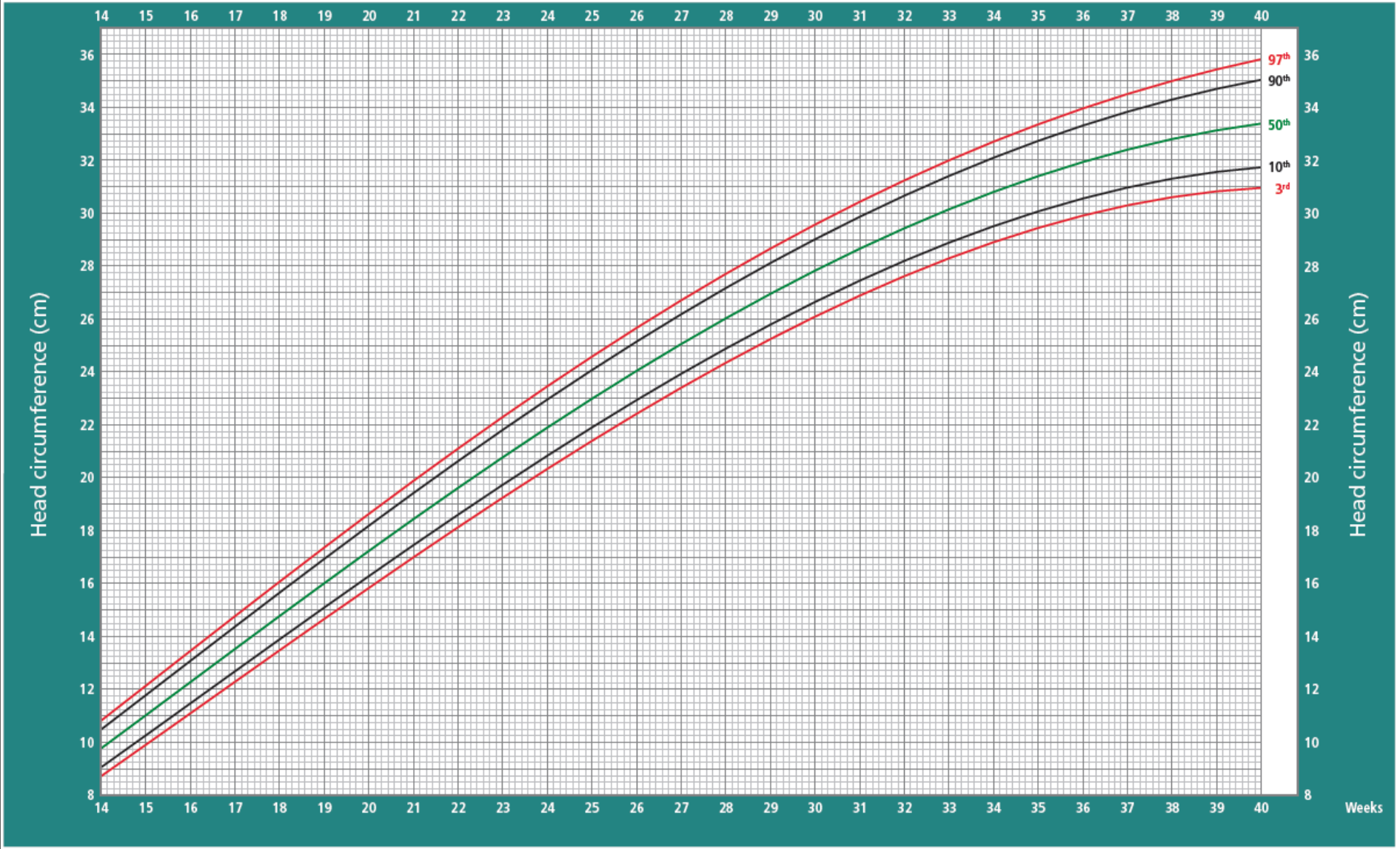
INTERGROWTH-21st Project:

Fetal growth	Growth standards: HC, AC and FL
Newborn size at birth	Growth references (27+0 to 32+6 weeks) and standards (33+0 to 42+6 weeks): Weight, length, and HC
Postnatal Preterm growth	Growth standards: Weight, length, and HC

UNIVERSITY OF OXFORD

International Fetal Growth Standards
Head circumference

INTERGROWTH-21st



Ref: Papageorghiou AT et al. Lancet 2014; 384: 869-79.

PRODUCTS

INTERGROWTH-21st Project:

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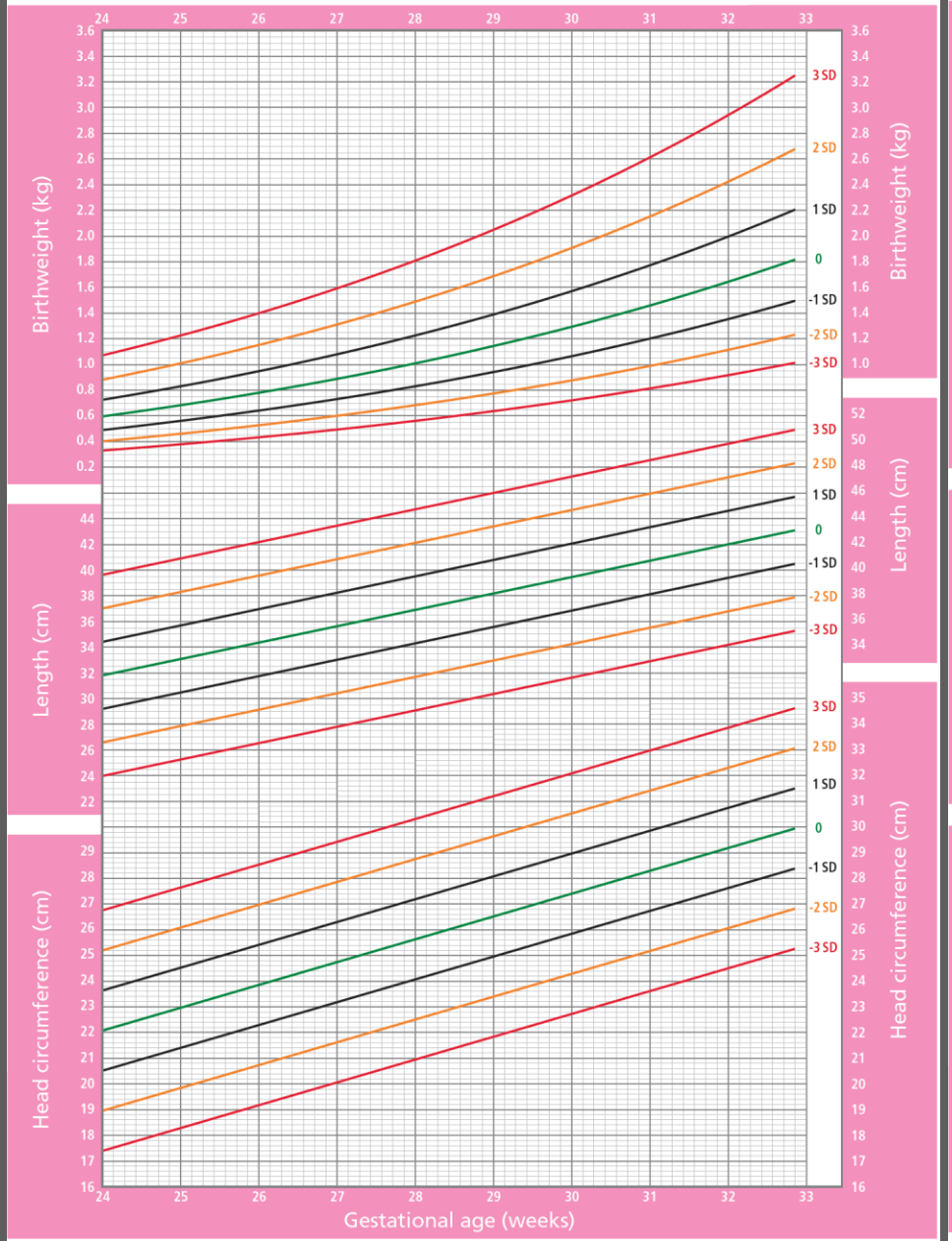
Postnatal Preterm growth	Growth standards: Weight, length, and HC

International Very Preterm Size at Birth Reference charts (Girls)

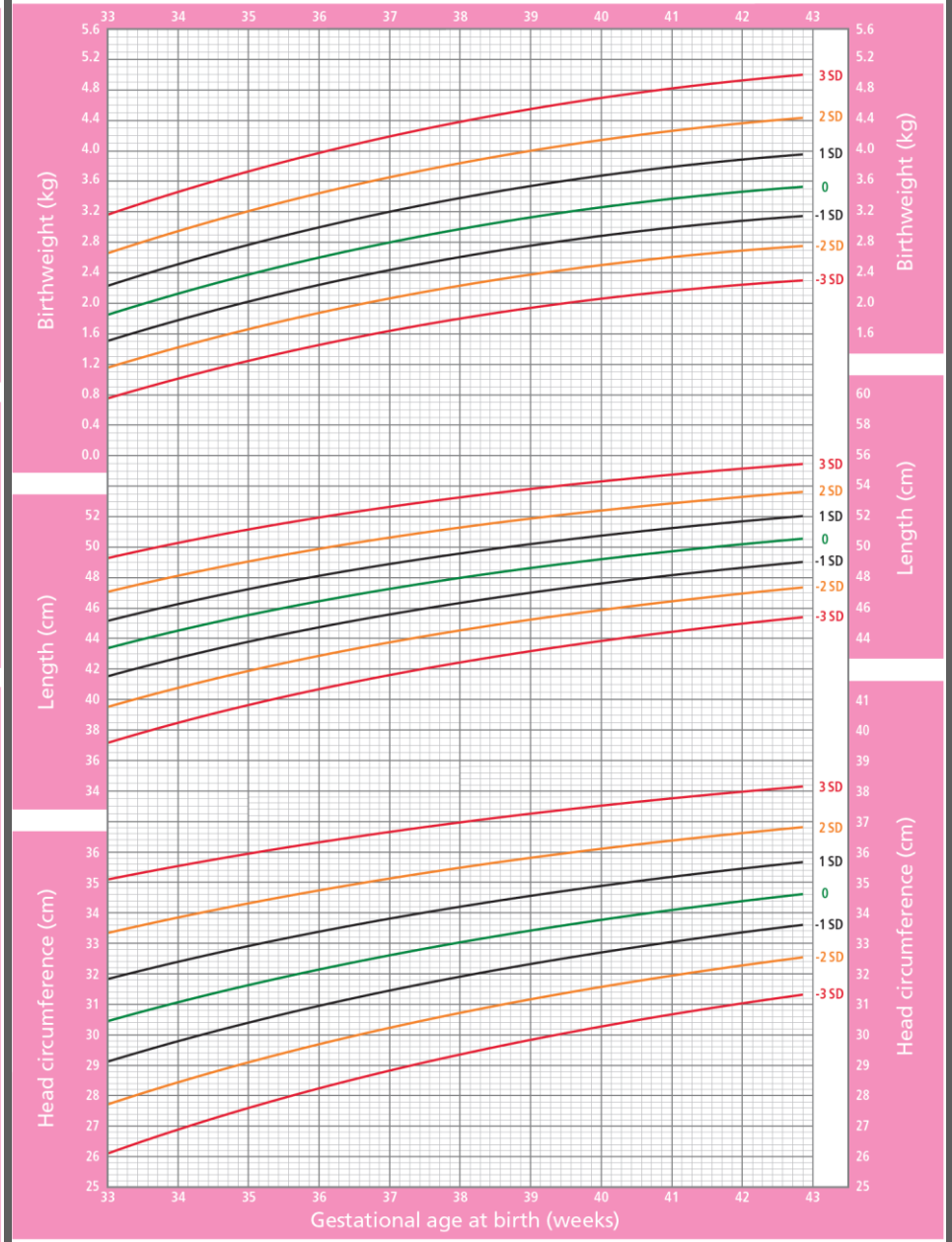
INTERGROWTH-21st



Ref: Villar J et al. Lancet 2016; 387: 844-845

International Standards for Size at Birth (Girls)

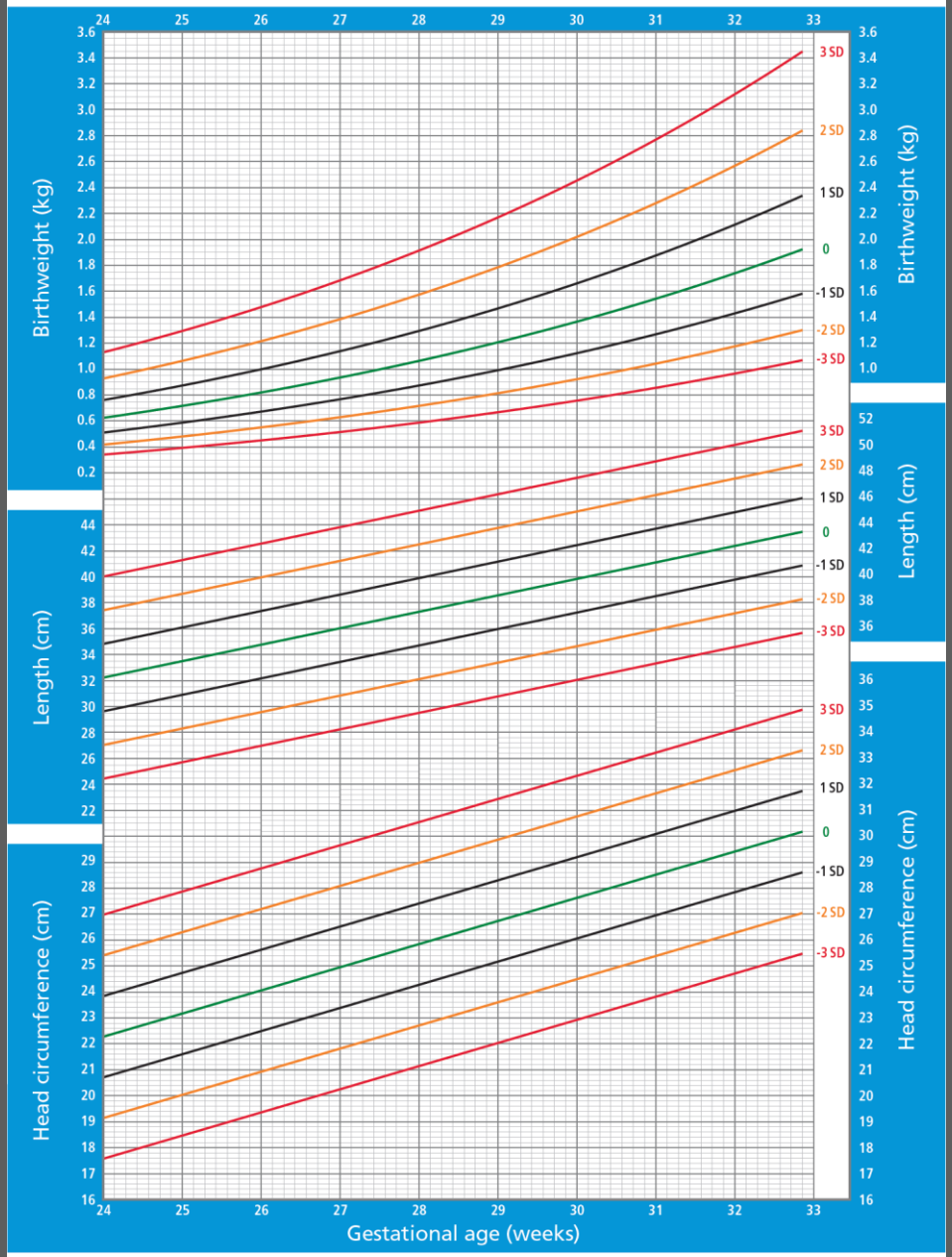
INTERGROWTH-21st



Ref: Villar J et al. Lancet 2014; 384: 857-868

International Very Preterm Size at Birth Reference charts (Boys)

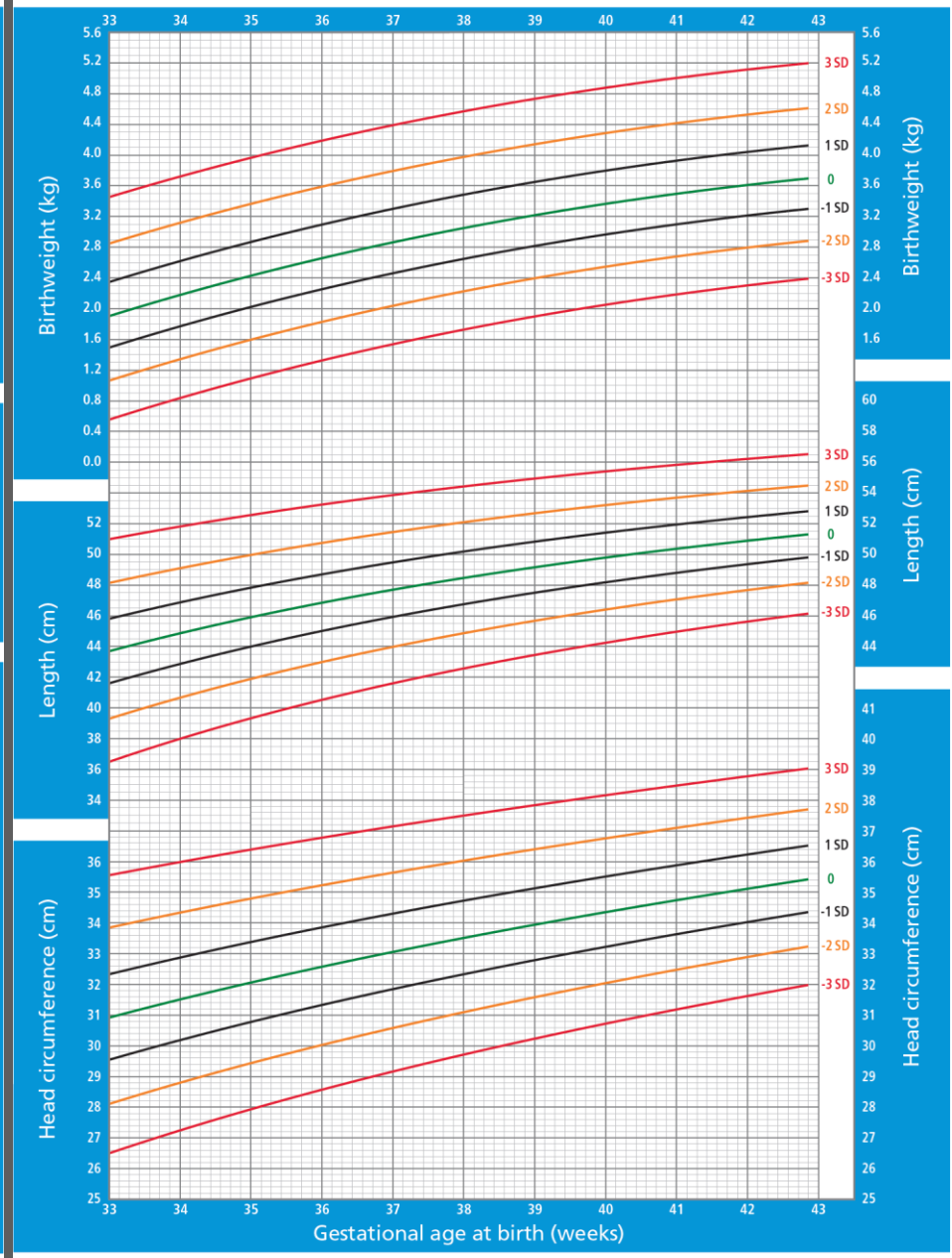
INTERGROWTH-21st



Ref: Villar J et al. Lancet 2016; 387: 844-845

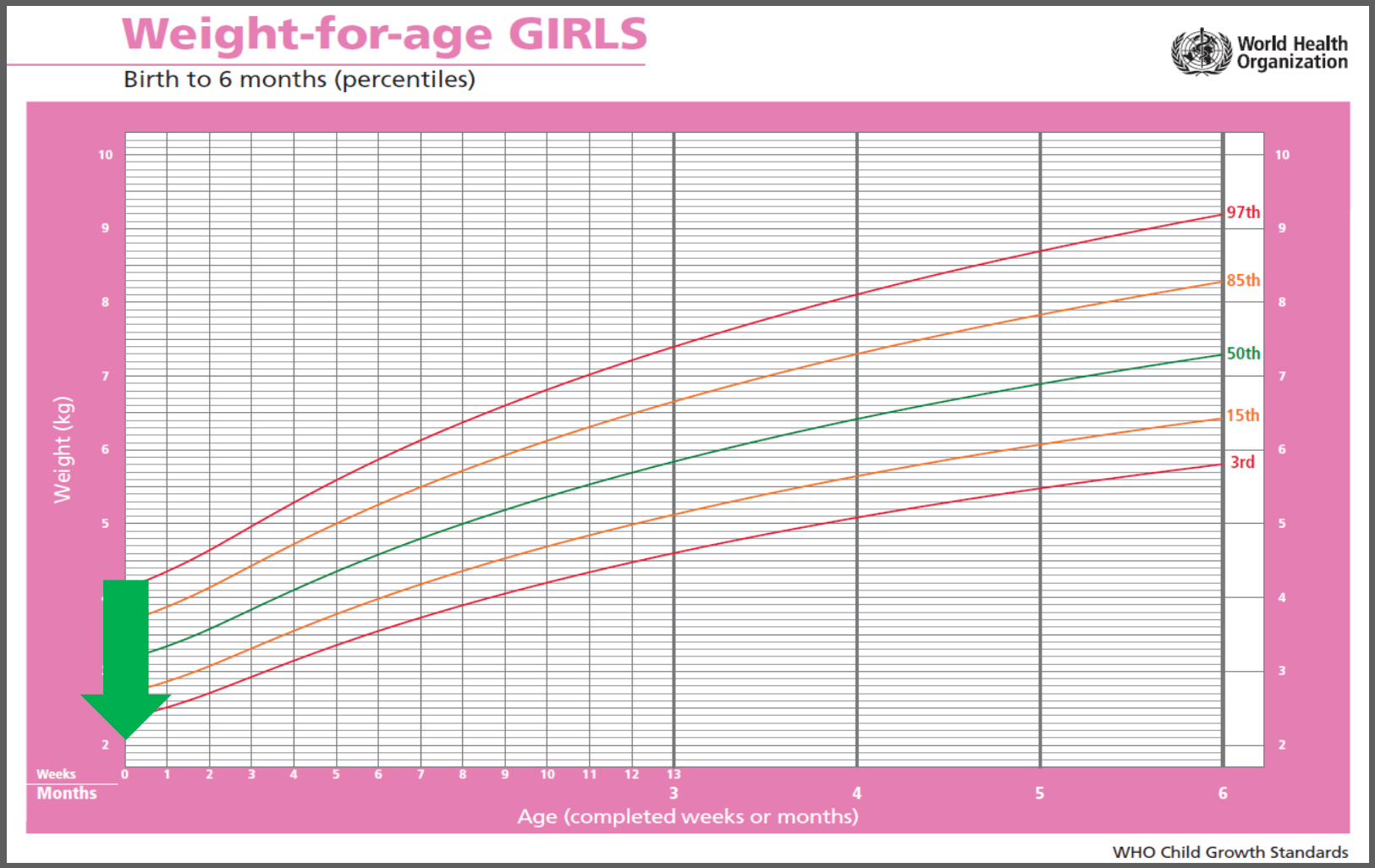
International Standards for Size at Birth (Boys)

INTERGROWTH-21st



Ref: Villar J et al. Lancet 2014; 384: 857-868

COMPARISON OF WHO AND INTERGROWTH CHARTS



USING THE WHO'S CHARTS

Baby Melissa's (X) birthweight: 2.82kg

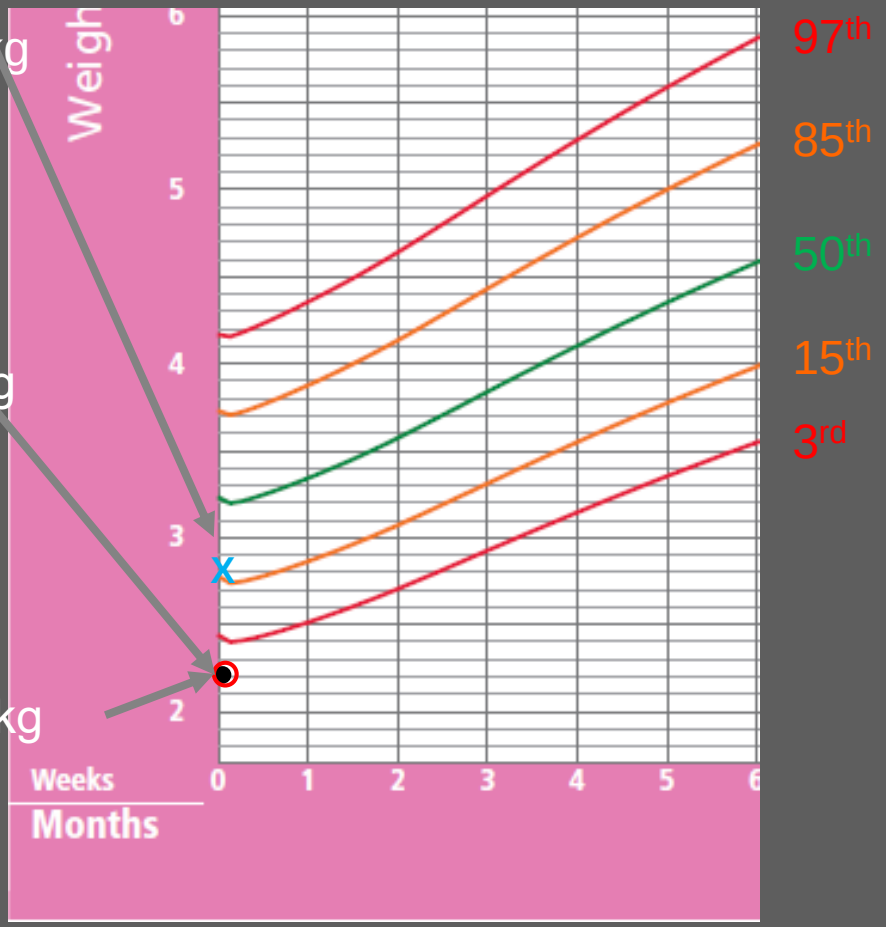
→ Gestational age: 36+5 weeks

Baby Sophie's (●) birthweight: 2.17kg

→ Gestational age: 40+1 weeks

Baby Michelle's (○) birthweight: 2.19kg

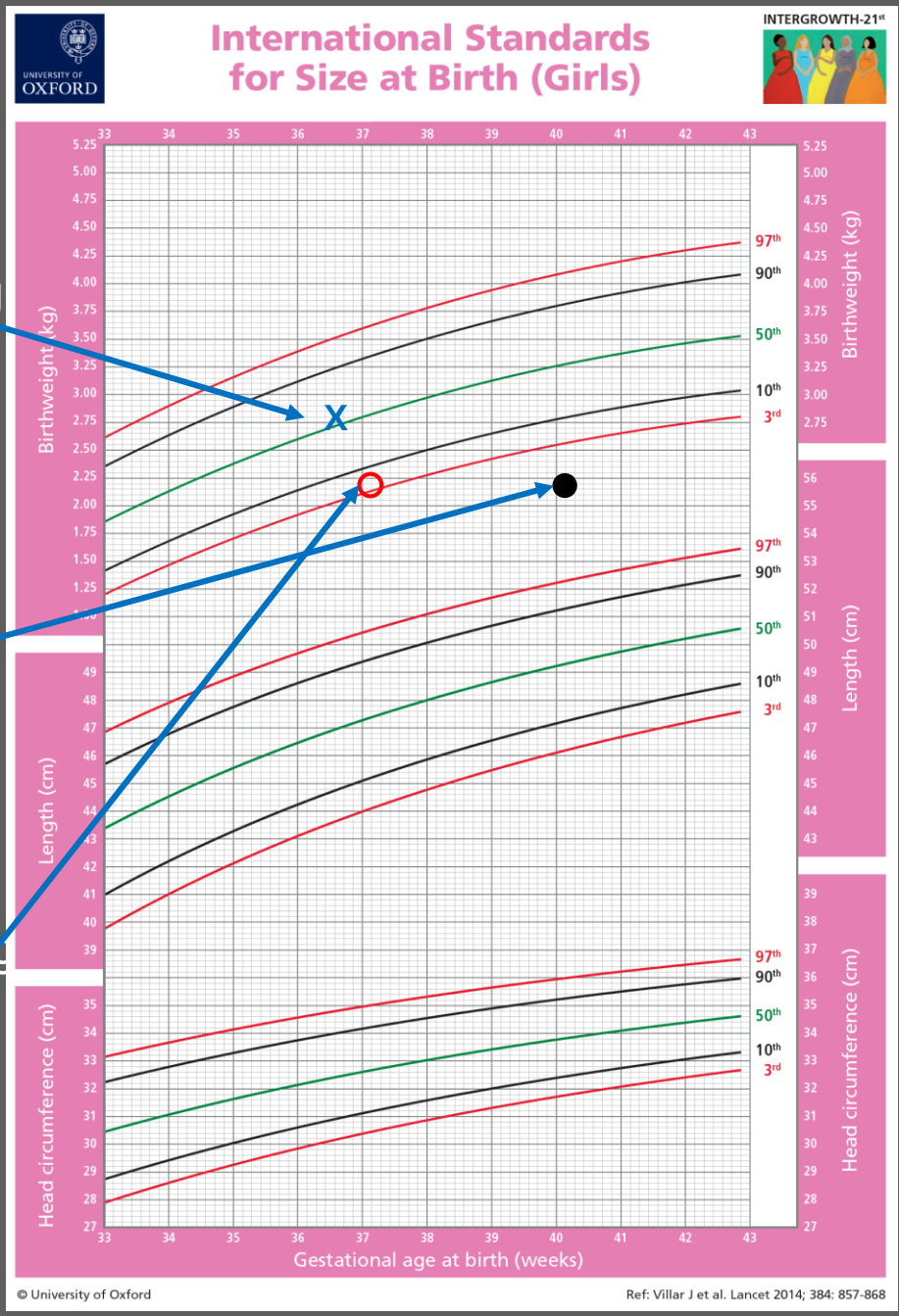
→ Gestational age: 37+1 weeks



Baby Melissa's (X) birthweight: 2.82kg
And GA: 36+5 weeks

Baby Sophie's (●) birthweight: 2.17kg
and GA: 40+1 weeks

Baby Michelle's (○) birthweight: 2.19kg
And GA: 37+1 weeks



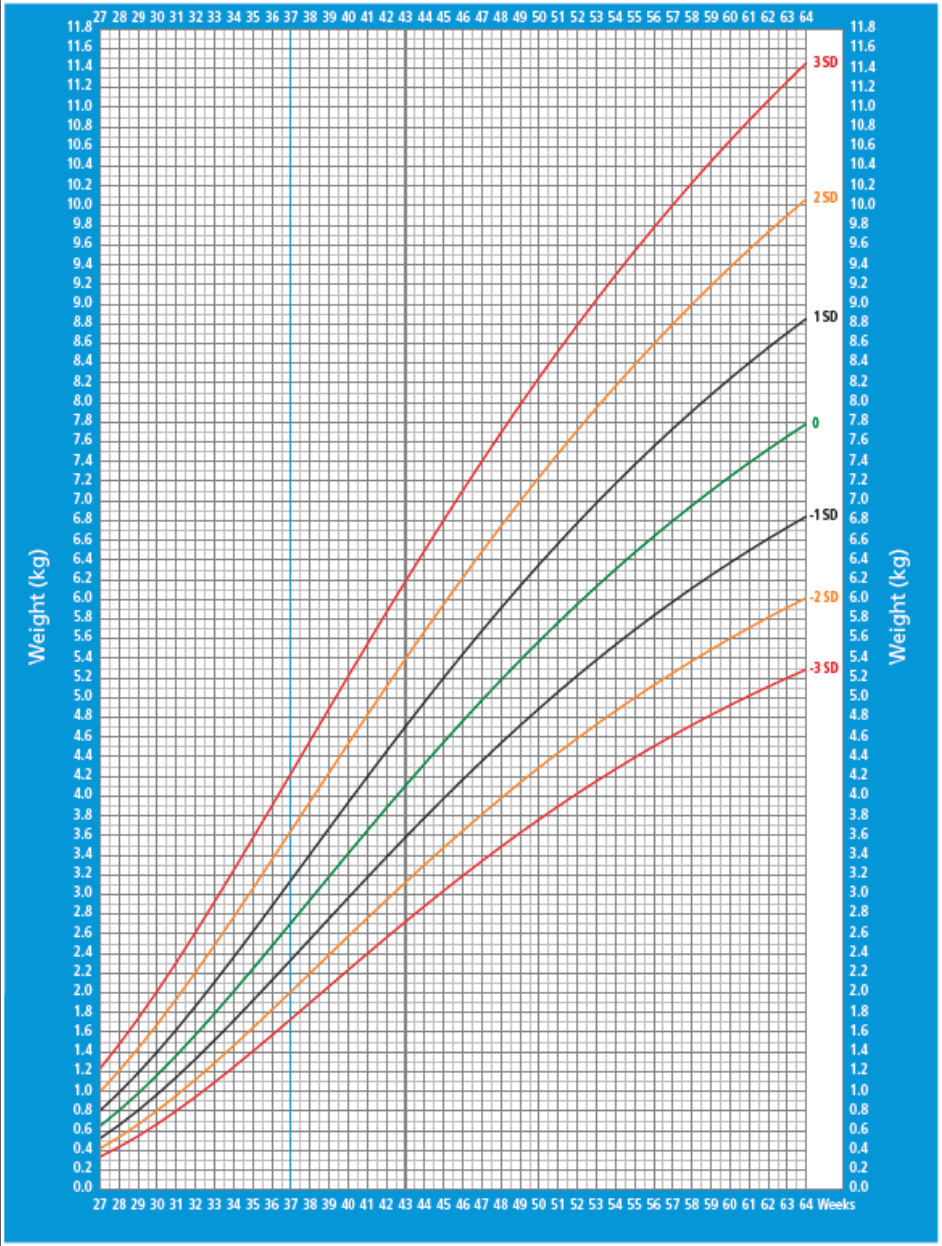
PRODUCTS

INTERGROWTH-21st Project:

Fetal growth	Growth standards: HC, BPD, OFD, AC, and FL
Newborn size at birth	Growth references (27+0 to 32+6 weeks) and standards (33+0 to 42+6 weeks): Weight, length, and HC
Postnatal Preterm growth	Growth standards: Weight, length, and HC

International Postnatal Growth Standards for Preterm Infants (Boys)

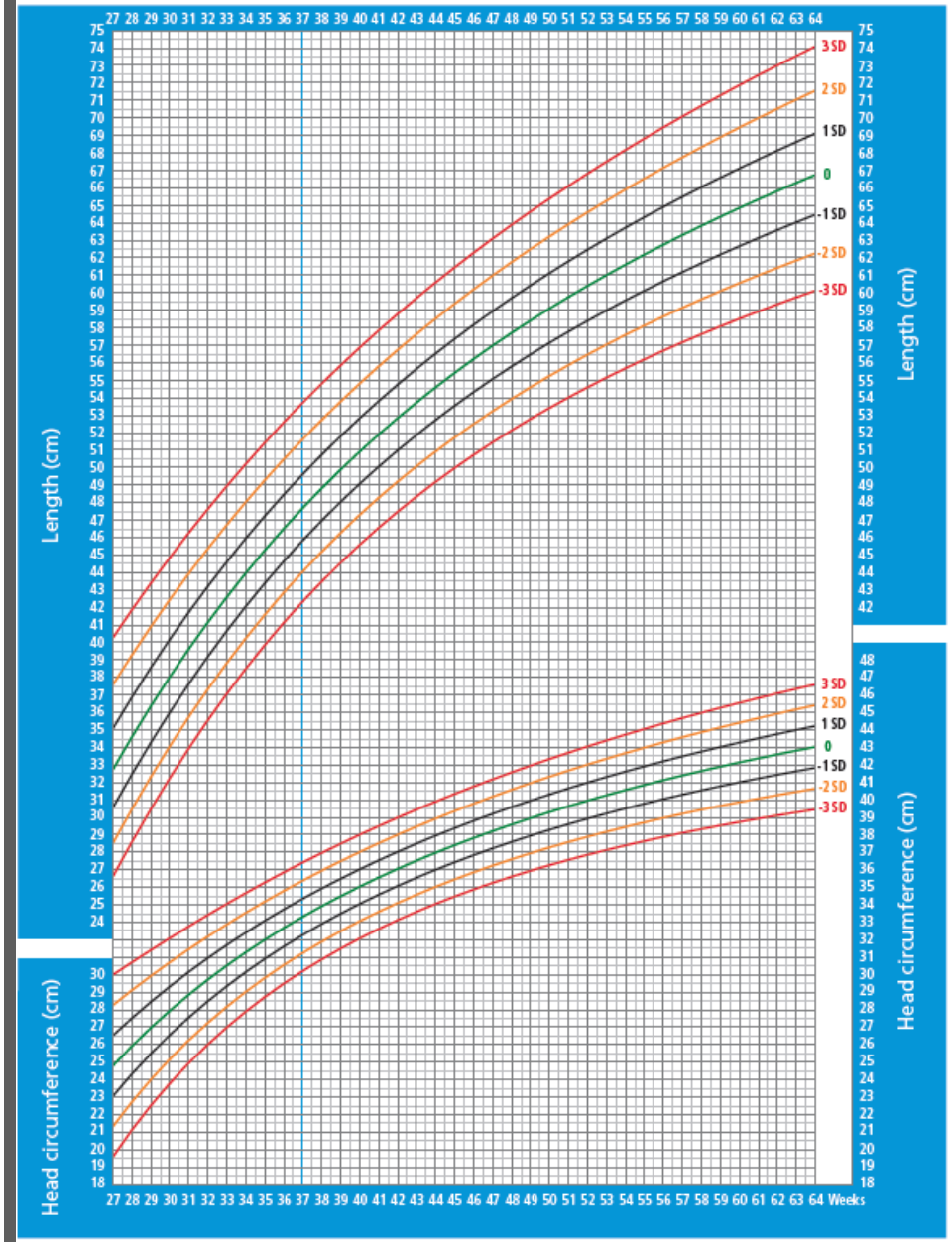
INTERGROWTH-21st



Ref: Villar et al *Lancet Glob Heath* 2015;3:e681-91.

International Postnatal Growth Standards for Preterm Infants (Boys)

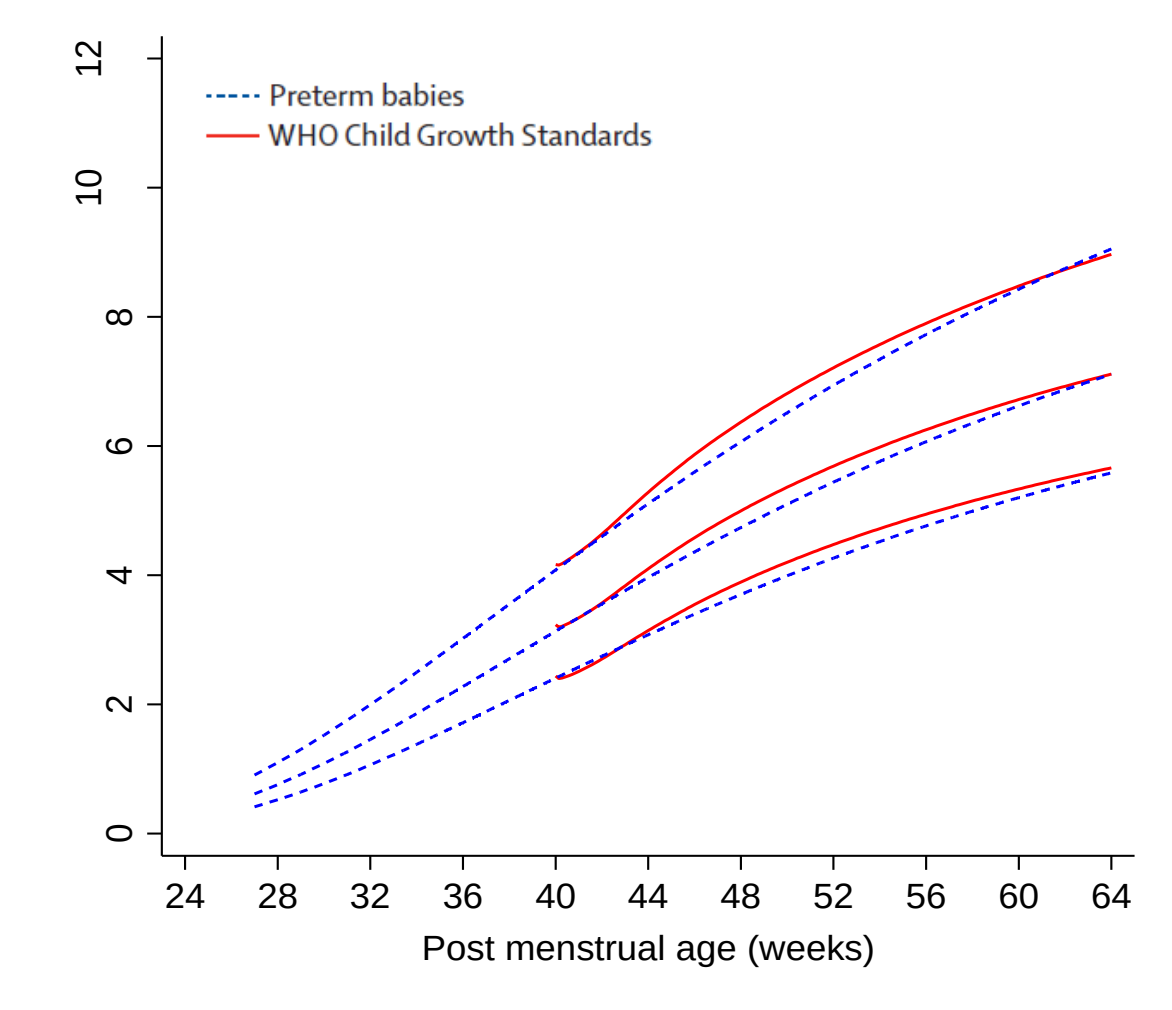
INTERGROWTH-21st



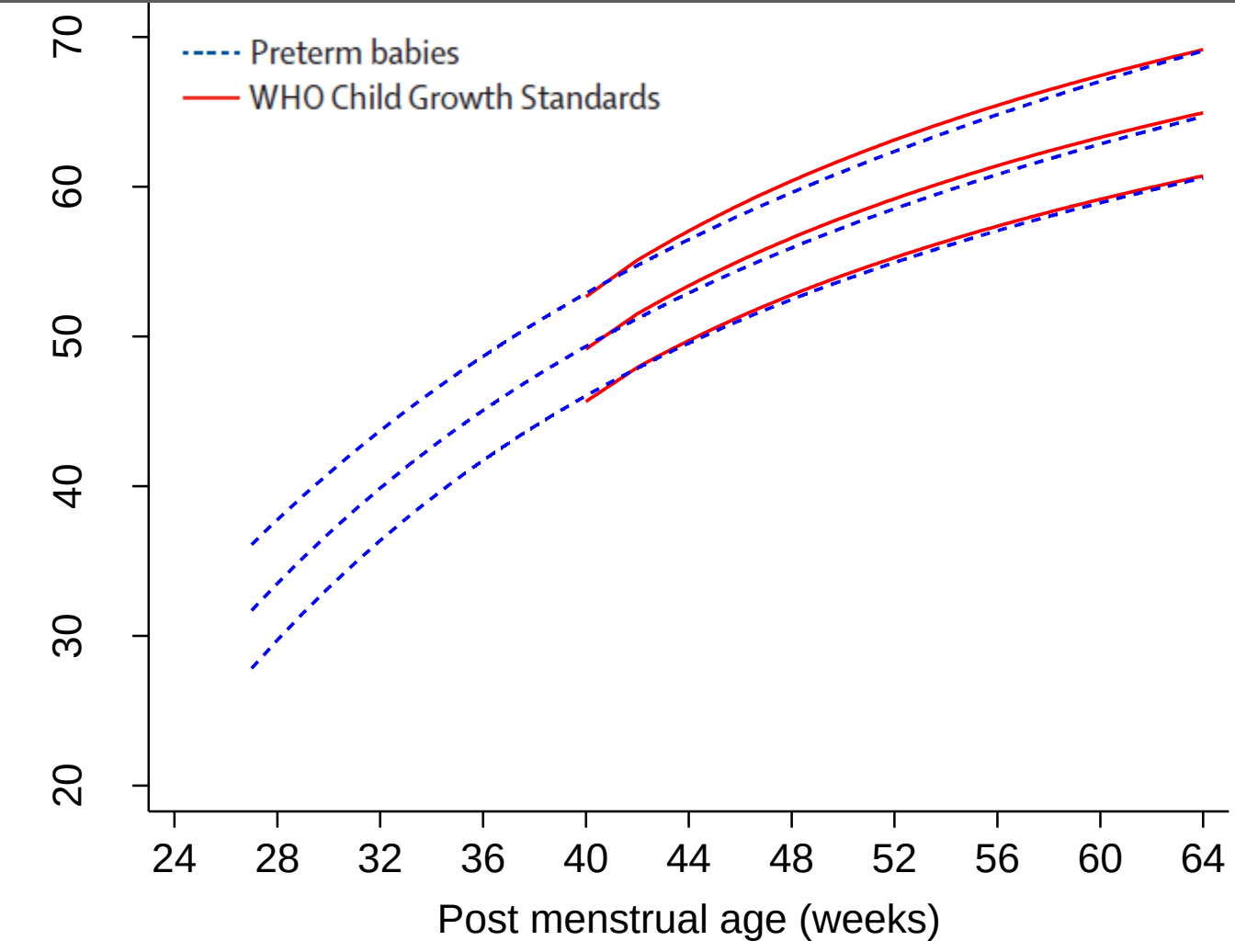
Ref: Villar et al *Lancet Glob Heath* 2015;3:e681-91.

PRETERM POSTNATAL STANDARDS VS. WHO CHILD GROWTH STANDARDS

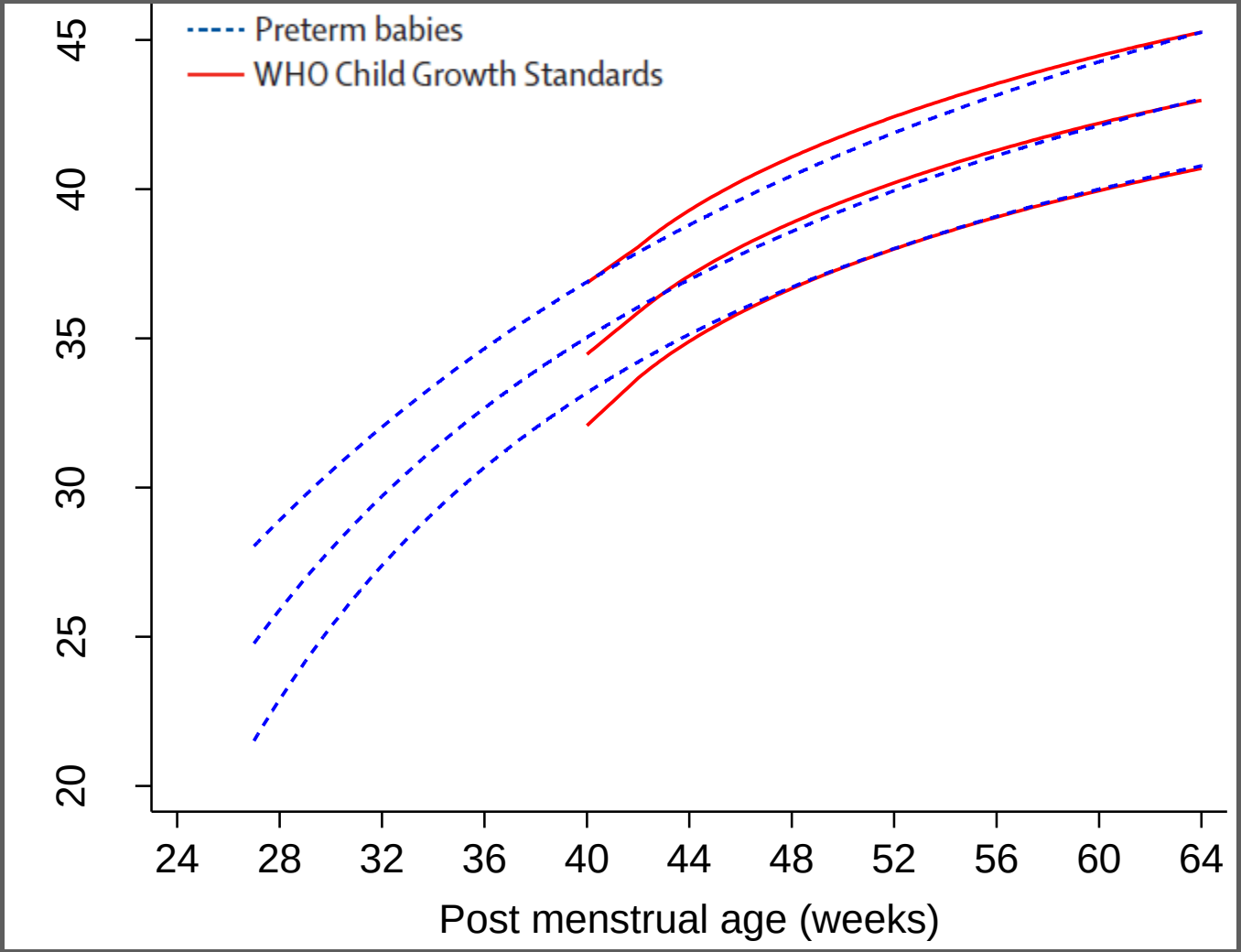
FITTED 3RD, 50TH, AND 97TH CENTILE CURVES FOR POSTNATAL **WEIGHT** OVER TIME IN PRETERM BABIES COMPARED WITH THE WHO CHILD GROWTH STANDARDS: **GIRLS**



FITTED 3RD, 50TH, AND 97TH CENTILE CURVES FOR POSTNATAL **LENGTH** OVER TIME IN PRETERM BABIES COMPARED WITH THE WHO CHILD GROWTH STANDARDS: **GIRLS**



FITTED 3RD, 50TH, AND 97TH CENTILE CURVES FOR POSTNATAL **HEAD CIRCUMFERENCE** OVER TIME IN PRETERM BABIES COMPARED WITH THE WHO CHILD GROWTH STANDARDS: **BOYS**



PRODUCTS

INTERGROWTH-21st Project:

Gestational weight gain

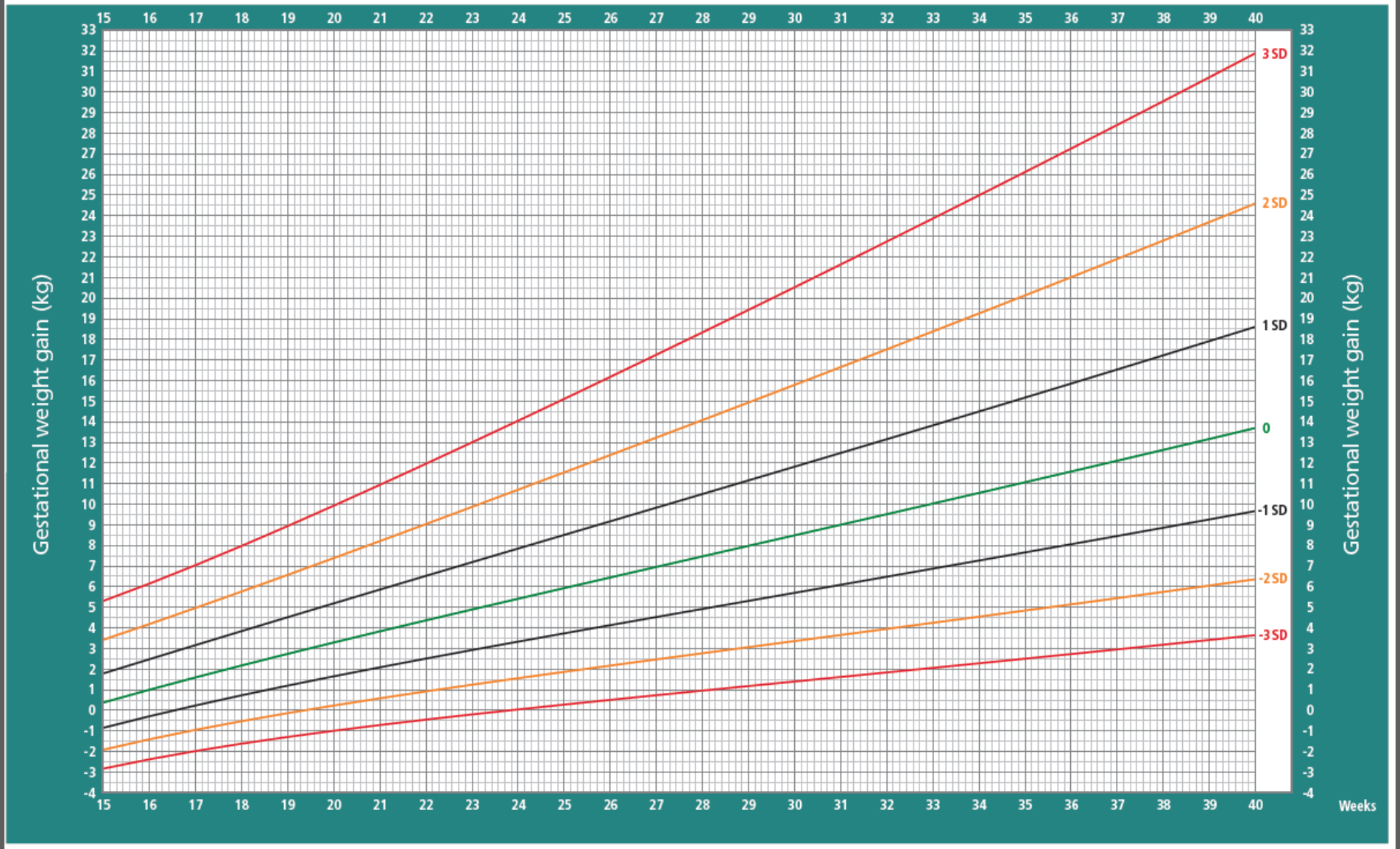
Growth standards:
women with a normal 1st trimester BMI

Women, overweight in the 1st trimester *(in preparation)*

UNIVERSITY OF OXFORD

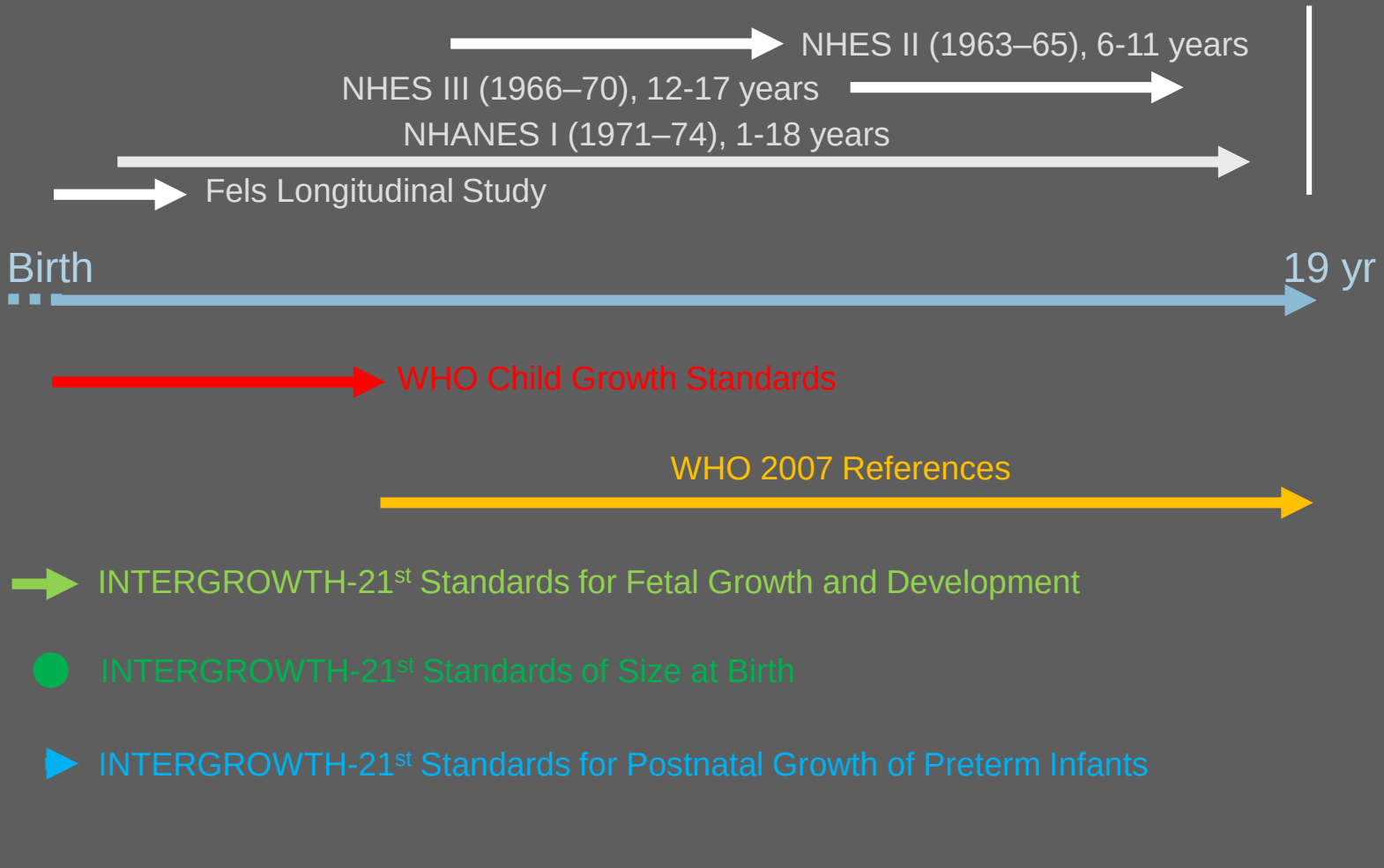
The International Gestational Weight Gain Standards

INTERGROWTH-21st



Ref: Cheikh Ismail et al. BMJ 2016; 352: i555

CONCLUSION


NHES II (1963–65), 6-11 years
NHES III (1966–70), 12-17 years
NHANES I (1971–74), 1-18 years
Fels Longitudinal Study
Birth
19 yr
WHO Child Growth Standards
WHO 2007 References
INTERGROWTH-21st Standards for Fetal Growth and Development
INTERGROWTH-21st Standards of Size at Birth
INTERGROWTH-21st Standards for Postnatal Growth of Preterm Infants

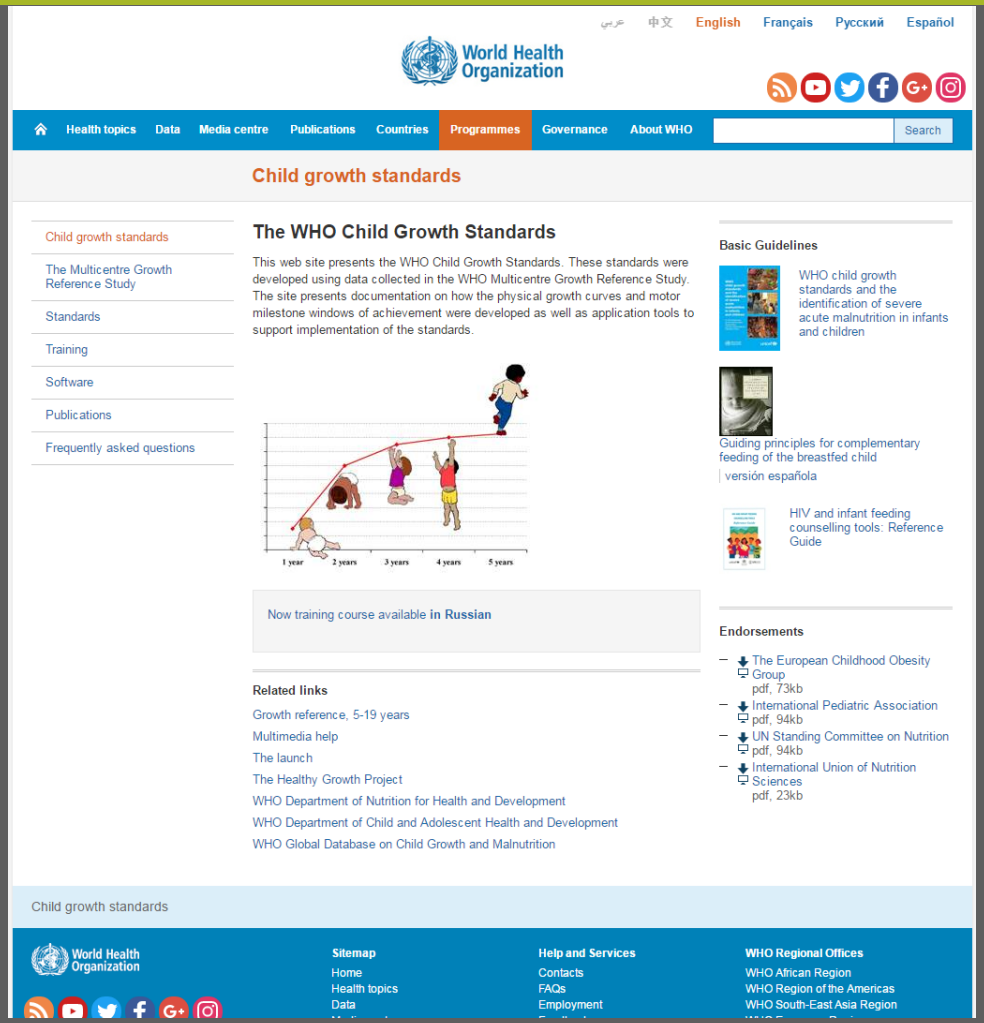
CONCLUSION

Growth monitoring promotes continuity of care from the womb to the classroom worldwide

The WHO Child Growth Standards, the WHO Growth Reference 5-19 years, and the INTERGROWTH-21st Growth Standards monitor growth from conception up to 19 years of age

WHO STANDARDS WEBSITE:

HTTP://WWW.WHO.INT/CHILDGROWTH/EN/



WHO REFERENCE WEBSITE:

HTTP://WWW.WHO.INT/GROWTHREF/EN/

INTERGROWTH-21ST WEBSITE:

HTTPS://INTERGROWTH21.TGHN.ORG/

THANK YOU!