The INTERGROWTH-21st
Postnatal Growth Standards for Preterm Infants

Dr Leila Cheikh Ismail
Project Leader
University of Oxford

on behalf of:
The International Fetal and Newborn Growth Consortium for the 21st Century
1. Prescriptive growth standards for infants born at term

NOT APPROPRIATE

✓ When growth parameters of preterm infants are plotted, these measures often fall far below the lowest centiles or z-scores, as the postnatal growth of preterm is different from that of term infants.
2. Fetal weight estimation curves based on ultrasound measurements

- Fetal weight is by definition, an *estimation of actual* weight and large measurement errors exist.

- The ‘intrauterine’ growth charts do not consider the physiological weight loss that occurs in the neonatal period particularly among preterm infants.
3. Birth weight for gestational age charts

Data used to construct them are cross-sectional and do not represent the actual growth of preterm infants that occurs during extrauterine life as they are based on anthropometric measures taken at birth in infants born at different gestational ages.
Systematic review
Postnatal growth charts for infants born preterm

• Assessment of methodological quality of longitudinal studies design the produce postnatal growth charts for preterm infants.

• **61** published **longitudinal** charts

• Methodologic quality was fair to low, with very few that were of high quality

• Considerable limitations in gestational age estimation, anthropometric measures, feeding and morbidities
INTERGROWTH-21\textsuperscript{st} 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 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.

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PPFS

**SELECTION LEVELS**

1. Site selection
2. Maternal population selection
3. Preterm population selection

**CRITERIA**

- Low-birthweight rate <10%
- Mean birth weight >3100g
- Perinatal mortality <20 per 1000 live births
- >75% mothers have attained an educational level/SES indicator greater than the locally defined cut-off points
- Lack of known, major, non-microbial environmental contaminants
- Altitude <1600m

Selection of the 8 INTERGROWTH-21st participating centres
PPFS

SELECTION LEVELS

1. Site selection
2. Maternal population selection
3. Preterm population selection

CRITERIA

• Low-risk study population
• Healthy and well-nourished
• Extensive list of maternal criteria including age, height, BMI, medical history, gynecological and obstetrical history, known LMP...
• Early evaluation of gestational age confirmed by CRL <14 weeks

Selection of INTERGROWTH-21st FGLS cohort
PPFS

SELECTION LEVELS

1. Site selection
2. Maternal population selection
3. Preterm population selection

CRITERIA

• Exclusion of fetuses with impaired fetal growth
• No major neonatal complications, neonatal surgery, congenital malformations or death in the follow-up period
• Standardisation of feeding practices and newborn care

Selection of the INTERGROWTH-21st PPFS cohort
PPFS
To develop new Growth Standards for Preterm Infants

Low-risk pregnancies
N = 20,486

Medium- & high-risk pregnancies

FGLS
N = 4,607

PPFS:
N: 224

International Preterm Postnatal Growth Standards

All pregnancies in 8 sites, N = 60,268
Number of women consented and enrolled into FGLS  n = 4607

Preterm singleton births  n = 224

Excluded from PPFS due to:
1. Sepsis  n = 6
2. Died  n = 6
3. Abnormal fetal growth  n = 2
4. HIV/AIDS  n = 1
5. <24wks at birth  n = 1
6. Congenital malformation  n = 7
Total excluded  n = 23

Final preterm analysis population  n = 201

Overall incidence of preterm delivery: 4.8%
Prematurity worldwide

- World: 9.6%  
- Europe: 6.2%  
- Asia: 9.1%  
- Africa: 11.9%  
- LA and Caribbean: 8.1%  
- Oceania: 6.4%  
- NA: 10.6%

Standardisation of neonatal clinical practice & nutrition

INTERGROWTH-21st
International Fetal and Newborn Growth Standards for the 21st Century

The International Fetal and Newborn Growth Consortium

BASIC NEONATAL CARE MANUAL

April 2010

UNIVERSITY OF OXFORD

Standardisation of neonatal clinical practice

ZA Bhutta, a F Giuliani, b A Haroon, a HE Knight, c E Albernaz, d,e M Batra, f B Bhat, g E Bertino, b K McCormick, h R Ochieng, i V Rajan, j P Ruyan, k L Cheikh Ismail, c V Paul, l for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st)
Breastfeeding promotion

Standardized nutritional strategies

Goal: promotion of exclusive breast feeding of the preterm infant at the time of hospital discharge.

Preferred feed:

1. Mother’s own milk from breast or expressed
2. Donor human milk
3. Preterm formula
PPFS Timeline

Birth

48-72h

Fortnightly

Monthly

Anthropometry:
• Weight
• Length
• Head circumference

Questionnaires:
• Health
• Food intake
• Motor development (from 4mo)
Preterm Postnatal Follow-up Study Results
Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21st Project

José Villar, Francesca Giuliani, Zulfiqar A Bhutta, Enrico Bertino, Eric O Ohuma, Leila Cheikh Ismail, Fernando C Barros, Douglas G Altman, Cesar Victora, Julia A Noble, Michael G Gravett, Manorama Purwar, Ruyan Pang, Ann Lambert, Aris T Papageorghiou, Roseline Ochieng, Yasmin A Jaffer, and Stephen H Kennedy, for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st)
Gestational age distribution

- <32 wks (10.2%)
- 32-33 wks (11.7%)
- 34-36 wks (78.1%)
Maternal characteristics

<table>
<thead>
<tr>
<th></th>
<th>Preterm (N = 201)</th>
<th>Term (N = 4116)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal age (years)</strong></td>
<td>28.5 (4.1)</td>
<td>28.3 (3.8)</td>
</tr>
<tr>
<td>Maternal height (cm)</td>
<td>162.0 (5.8)</td>
<td>162.2 (5.8)</td>
</tr>
<tr>
<td>Maternal weight (kg)</td>
<td>61.9 (9.2)</td>
<td>61.2 (9.1)</td>
</tr>
<tr>
<td><strong>Maternal BMI (kg/m^2)</strong></td>
<td>23.5 (3.1)</td>
<td>23.2 (3.0)</td>
</tr>
<tr>
<td>Paternal height (cm)</td>
<td>173.4 (7.3)</td>
<td>174.4 (7.3)</td>
</tr>
<tr>
<td>Gestational age at 1st antenatal visit (weeks)</td>
<td>11.7 (1.4)</td>
<td>11.8 (1.4)</td>
</tr>
<tr>
<td>Years of formal education</td>
<td>14.6 (2.9)</td>
<td>15.0 (2.8)</td>
</tr>
<tr>
<td>Haemoglobin level &lt;15 weeks’ gestation</td>
<td>12.4 (1.1)</td>
<td>12.5 (1.1)</td>
</tr>
<tr>
<td>Married/cohabiting (%)</td>
<td>192 (95.5)</td>
<td>4008 (97.4)</td>
</tr>
<tr>
<td>Nulliparous (%)</td>
<td>146 (72.6)</td>
<td>2806 (68.2)</td>
</tr>
</tbody>
</table>
## Labour and neonatal characteristics

<table>
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<tr>
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<th>Preterm (N = 201)</th>
<th>Term (N = 4116)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age at birth (weeks)</strong></td>
<td>35.5 (1.7)</td>
<td>39.6 (1.2)</td>
</tr>
<tr>
<td>Caesarean section (%)</td>
<td>80 (39.8)</td>
<td>1459 (35.4)</td>
</tr>
<tr>
<td>NICU admission &gt;1 day (%)</td>
<td>82 (40.8)</td>
<td>151 (3.7)</td>
</tr>
<tr>
<td>Low-birth weight (&lt;2.5kg) (%)</td>
<td>108 (53.7)</td>
<td>123 (3.0)</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>99 (49.3)</td>
<td>2048 (49.8)</td>
</tr>
<tr>
<td>Exclusive breastfeeding at discharge (%)</td>
<td>145 (72.1)</td>
<td>3642 (88.5)</td>
</tr>
<tr>
<td><strong>Birth weight (kg)</strong></td>
<td><strong>2.452 (519)</strong></td>
<td><strong>3.268 (443)</strong></td>
</tr>
<tr>
<td>Birth length (cm)</td>
<td>45.6 (2.7)</td>
<td>49.4 (1.9)</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>31.7 (1.8)</td>
<td>33.9 (1.3)</td>
</tr>
</tbody>
</table>
## Infant conditions (0 - 2 months)

<table>
<thead>
<tr>
<th>Conditions</th>
<th>N = 201 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient tachypnoea of the newborn</td>
<td></td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>21 (10.4)</td>
</tr>
<tr>
<td>Meconium aspiration with respiratory distress</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>No oral feeds for &gt;24hrs but &lt;7days</td>
<td>24 (11.9)</td>
</tr>
<tr>
<td>Stoppage of enteral feeding for &gt;3 consecutive days</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Apnoea of prematurity</td>
<td>14 (7.0)</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia*</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Hyperbilirubinaemia</td>
<td>46 (22.9)</td>
</tr>
<tr>
<td><strong>Hypoglycaemia</strong></td>
<td><strong>16 (8.0)</strong></td>
</tr>
<tr>
<td>Hypotension requiring ionotrophic treatment or steroids</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Pneumonia / Bronchiolitis</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>Other infection</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Anaemia requiring transfusion</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Patent ductus arteriosus requiring pharmacological treatment</td>
<td>4 (2.0)</td>
</tr>
<tr>
<td>Intraventricular haemorrhage, Grade I-II</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Retinopathy of prematurity</td>
<td>1 (0.5)</td>
</tr>
</tbody>
</table>

With normal growth and development during follow-up *
Diagnosis and treatments include those at neonatal ICU or special care unit
**Infant conditions (0 - 6 months)**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>3-4 months (N = 161)*</th>
<th>5-6 months (N = 160)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia/Acute respiratory infection / Bronchiolitis</td>
<td>23 (14.3)</td>
<td>25 (15.6)</td>
</tr>
<tr>
<td>Otitis</td>
<td>2 (1.2)</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td>Febrile episode</td>
<td>27 (16.8)</td>
<td>27 (16.9)</td>
</tr>
<tr>
<td><strong>Diarrhoea</strong></td>
<td><strong>5 (3.1)</strong></td>
<td><strong>11 (6.9)</strong></td>
</tr>
<tr>
<td>Gastro-esophago-pharyngeal reflux</td>
<td>6 (3.7)</td>
<td>5 (3.1)</td>
</tr>
<tr>
<td>Skin problems</td>
<td>14 (8.7)</td>
<td>16 (10.0)</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Injury / trauma</td>
<td>0 (0.0)</td>
<td>1 (0.6)</td>
</tr>
</tbody>
</table>

* Number of infants followed up at this time interval
Breastfeeding promotion
Standardized nutritional strategies

**Goal:** promotion of exclusive breast feeding of the preterm infant at the time of hospital discharge.

**Preferred feed:**
1. Mother’s own milk from breast or expressed
2. Donor human milk
3. Preterm formula
Preterm feeding recommendations are achievable in large-scale research studies

Leila Cheikh Ismail1,12*, Francesca Giuliani2, Bashir A. Bhat3, Deborah Bishop1, Aris T. Papageorghiou1, Roseline Ochieng4, Fabien Puglia1, Douglas G. Altman5, Michael Maia-Schlüssel1, Julia A. Noble6, Enrico Bertino2, Michael G. Gravett7, Manorama Purwar8, Lui Yajing9, Denise Mota10, Eric Ohuma1,5, Ann Lambert1, Stephen H. Kennedy1, Zulfiqar A. Bhutta11, José Villar1 and for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st)
Achievement of WHO milestones for gross motor development

<table>
<thead>
<tr>
<th>Months (SD)</th>
<th>INTERGROWTH-21st PPFS cohort</th>
<th>WHO MGRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting without support</td>
<td>6.9 (1.3)</td>
<td>6.0 (1.1)</td>
</tr>
<tr>
<td>Standing without assistance</td>
<td>9.8 (1.3)</td>
<td>7.6 (1.4)</td>
</tr>
<tr>
<td>Walking alone</td>
<td>13.1 (1.5)</td>
<td>12.1 (1.8)</td>
</tr>
</tbody>
</table>
PRETERM POSTNATAL STANDARDS VS. NEWBORN SIZE AT BIRTH STANDARDS
Fitted 3\textsuperscript{rd}, 50\textsuperscript{th}, and 97\textsuperscript{th} centile curves for postnatal weight over time in preterm babies compared with INTERGROWTH-21\textsuperscript{st} Newborn Size Standards: Girls
Fitted 3\textsuperscript{rd}, 50\textsuperscript{th}, and 97\textsuperscript{th} centile curves for postnatal length over time in preterm babies compared with INTERGROWTH-21\textsuperscript{st} Newborn Size Standards: Boys
Fitted 3\textsuperscript{rd}, 50\textsuperscript{th}, and 97\textsuperscript{th} centile curves for postnatal head circumference over time in preterm babies compared with INTERGROWTH-21\textsuperscript{st} Newborn Size Standards: Girls
PRETERM POSTNATAL STANDARDS VS. WHO CHILD GROWTH STANDARDS
Fitted 3\textsuperscript{rd}, 50\textsuperscript{th}, and 97\textsuperscript{th} 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
THE INTERGROWTH-21ST PRETERM POSTNATAL GROWTH STANDARDS
International Postnatal Growth Standards for Preterm Infants
Weight (Girls)
Project websites:

The Global health network:

https://intergrowth21.tghn.org/
The International Fetal and Newborn Growth Consortium for the 21st Century

Home
The International Fetal and Newborn Growth Consortium for the 21st Century, or INTERGROWTH-21st, is a global, multidisciplinary network of more than 300 researchers from 18 countries worldwide and coordinated from the University of Oxford. We are dedicated to reducing the millions of preventable newborn deaths that occur as a result of preterm birth.

News
INTERGROWTH 21st - Head circumference training video
Head circumference training video now available to support and enhance use of the latest INTERGROWTH 21st head circumference measurement tools
READ MORE

Zika Virus
In response to the recent news about the Zika virus, we draw your attention to the International INTERGROWTH-21st Standards for Head Circumference of newborns and very preterm infants.

Access the INTERGROWTH-21st tool browser version

(Access the translated tool: Português / Español)
Download INTERGROWTH-21st Standards & Tools Below

3-score calculator for fetal growth standards

This website provides clinicians and researchers access to the INTERGROWTH-21st Global Perinatal Package. This package is comprised of new, globally-validated standards and practical training resources. To download the standards please use the download links to the right of this page.

These standards are paired with an expanding Training Toolkit and a rich body of literature on our methods.
News

INTERGROWTH 21st - Head circumference training video

Head circumference training video now available to support and enhance use of the latest INTERGROWTH-21st head circumference measurement tools.

Z-score calculator for fetal growth standards now available

This tool is currently available in Excel format and will be updated by a web and PC/MAC application developed early in 2016.

INTERGROWTH-21st Newborn Size Application Tool – Mac and web versions now available.

The INTERGROWTH-21st Newborn Size Application Tool for calculating centiles and z-scores for birth weight, length and head circumference is now available for download for Windows and Mac users, along with a web browser version.

Read more news stories from INTERGROWTH-21st here.

These standards are paired with an expanding Training Toolkit and a rich body of literature on our methods.

Policymakers may be interested in learning our progress with dissemination so far, and the implications of our new standards for health policy.

A selection of INTERGROWTH-21st-related news articles from around the world and information regarding press inquiries is available on our Media page.

INTERGROWTH-21st course on maternal, fetal and newborn growth monitoring

This three module course communicates the methodology of maternal, fetal and newborn growth monitoring and the application of the INTERGROWTH-21st international growth standards to make...
Gender
Serial measurements
GA (in weeks and days)
Anthropometric measurements
Male 357 postmenstrual age (days)

<table>
<thead>
<tr>
<th>Length (cm)</th>
<th>Weight (kg)</th>
<th>Head circumference (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>57.5 cm</td>
<td>5.2 kg</td>
<td>38 cm</td>
</tr>
</tbody>
</table>

- z-score: -1.1456, centile: 12.60
- z-score: -0.8074, centile: 20.97
- z-score: -1.5924, centile: 5.56

Length [cm]

Postmenstrual Age [weeks]
Conclusions

• Fetal, newborn and infant growth are similar across populations when constraints on growth are minimal, justifying the construction of International Growth Standards

• The INTERGROWTH-21st & WHO Child Growth Standards monitor growth up to 5 years of age using the same instruments

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


• Cheikh Ismail L, Giuliani F, Bhat BA, et al. Preterm feeding recommendations are achievable in large-scale research studies BMC Nutrition 2016 2:9

In 2016, we still believe in global solutions to global health problems