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BEING BORN STUNTED AND/OR WASTED NEED NOT BE INEVITABLE

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Impaired fetal growth is associated with a large proportion of stillbirths, as well as high neonatal and infant mortality rates, especially in low-middle income countries, and has long-term adverse effects on later growth, development and health. However, there is no consensus as to how babies should optimally grow *in utero*, or what defines 'healthy' size at birth. In fact, there are over 100 different fetal and newborn growth charts in use around the world, most of which are population-specific and of poor methodological quality.[1] This has significantly hampered our understanding of the etiology, epidemiology and long-term health consequences of impaired fetal and newborn growth, and limited research on potential interventions to address the problem. The lack of a unified approach to monitoring growth has almost certainly also resulted, at both population and individual levels, in a failure to identify babies that are stunted and/or wasted in utero and at birth, leading to missed opportunities to intervene both during and after pregnancy. Unfortunately, some of the differentials in fetal growth and birth size amongst populations have been mistakenly attributed to genetic diversity, and even considered 'normal' in some settings. This misconception was successfully challenged by the landmark study performed by the WHO Multicentre Growth Reference Study (MGRS), which produced the WHO Child Growth Standards describing optimally healthy growth from 0-5 years of age.[2]

Since their release in 2006, the WHO Child Growth Standards have been accepted and widely adopted for use in infants and children around the world.[2] They have provided a scientifically valid method by which the growth of all children can be compared, which has had a profound effect on the ability of countries to provide targeted interventions to prevent and treat stunting and wasting. Until recently, there were no equivalent standards for the fetus or newborn despite evidence that nutritional and environmental growth constraints often begin before birth.[3] An additional challenge is the commonly held belief amongst obstetricians that differences in birth weight around the world are largely due to ethnic/genetic factors. This has resulted in recommendations that the 'healthy' ranges for fetal growth and birth weight should be adjusted, or customised, for parental ethnicity.[4,5]

The INTERGROWTH-21st Project

The International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) was launched in 2008 to challenge the assumption that babies inherently grow differently around the world. We have conducted the largest, population based, multi-ethnic, multi-country, prospective study of fetal and newborn growth and development to date, involving over 300 researchers in 27 institutions. The conceptual and methodological approach used was the same as in the WHO MGRS **(FIGURE 1).** The project was conducted in eight diverse and geographically distinct urban areas where environmental, nutritional and social constraints on fetal growth were likely to be minimal, and women had access to evidence-based pregnancy and delivery care.[6]

The INTERGROWTH-21st Project comprised three complementary studies: the Fetal Growth Longitudinal Study (FGLS), the Newborn Cross-Sectional Study (NCSS) and the Preterm Postnatal Follow-up Study (PPFS). The study sites were in the cities of Pelotas, Brazil; Turin, Italy; Muscat, Oman; Oxford, UK; Seattle, USA; Shunyi County, a suburban district of the Beijing

municipality, China; the central area of the city of Nagpur (Central Nagpur), Maharashtra, India; and the Parklands suburb of Nairobi, Kenya. Nearly 60,000 consecutive deliveries were enrolled into NCSS, representing approximately 7,000 births at each site. Before commencing the project, all the sites agreed on a policy of providing ultrasound scans early in pregnancy. From the total population, 4,607 women with a certain last menstrual period and an ultrasound scan that confirmed the gestational age, who were at low risk of fetal growth problems - based on their social, reproductive and medical histories - were recruited to participate in FGLS. These women had ultrasound scans performed every 5±1 weeks from 14 weeks' gestation until delivery to measure skeletal fetal growth. The methodology used to measure the fetus was highly standardised, performed on identical ultrasound machines and subjected to strict external quality control protocols in order to minimise inter- and intra-observer error. Within 12 hours of delivery, birth weight, length, and head circumference were obtained for all 60,000 babies in NCSS (including the FGLS participants) using the same methodology employed in the WHO MGRS. Information was also collected on pregnancy, birth and newborn outcomes. The growth of all babies born preterm (<37 weeks' gestation) in the FGLS cohort was followed closely until 8 months of age in PPFS.

Main findings

The primary finding from the INTERGROWTH-21st Project was that fetal longitudinal skeletal growth and newborn size at birth are strikingly similar around the world when maternal health, social and nutritional conditions are optimal, and women have access to evidence-based pregnancy and delivery care.[7] These data are directly in keeping with the WHO MGRS findings on the similarity of growth in breast-fed, healthy children around the world.[8] Further evidence to support the concept of a common pattern of early human growth is provided by the observation that the birth lengths in the FGLS babies were almost identical to the distribution of birth lengths in the WHO MGRS population, despite the fact that the latter study was conducted nearly 10 years earlier. The total variability in fetal skeletal growth and length at birth due to between-site differences was 1.9% and 3.5% respectively, very similar to that observed in the WHO MGRS (3%).

These landmark findings led to the publication of the first international early pregnancy dating standards (using crown-rump length between 9 to 14 weeks' gestation)[9]; fetal growth standards (head circumference, femur length and abdominal circumference)[10], and newborn size at birth standards (weight, head circumference and length for gestational age and sex, **(FIGURE 2)**[11]. Standards for the postnatal growth of preterm infants, describing the growth of babies in PPFS without congenital abnormalities or major medical complications, are anticipated for release in 2015. All babies in the FGLS cohort are being followed to 2 years of age to develop the first international standards for neurodevelopmental assessment, based on a set of simple and replicable tests that can be scaled-up for clinical use in resource poor settings[12].

The public health significance of the INTERGROWTH-21st findings with regard to fetal growth and perinatal outcomes is substantial:

"The fact that when mothers are in good health, babies grow in the womb in very similar ways the world over is a tremendously positive message of hope for all women and their families," Professor Zulfiqar Bhutta, Chairman of the INTEGROWTH-21st Steering Committee shares. "But there is a challenge as well. There are implications in terms of the way we think about public health: This is about the health and life chances of future citizens everywhere on the planet. All those who are responsible for health care will have to think about providing the best possible maternal and child health."

Implications for clinical practice and research globally

These results offer paediatricians: a) new evidence-based tools to identify babies likely to have experienced growth and nutritional problems *in utero*; b) a common method for quantifying and comparing the prevalence of nutritional deficiencies in populations at birth, and c) the first evidence-based method for monitoring the postnatal growth of preterm infants. We estimate that each year an additional 13 million more newborns worldwide will be identified as being undernourished using the INTERGROWTH-21st Newborn Size Standards compared to current practice. "Being able to identify millions of additional undernourished babies at birth provides an opportunity for them to receive nutritional support and targeted treatment, without which close to 5% are likely to die in their first year or develop severe, long-term health problems," says co-Principal Investigator of the Project, Professor José Villar of the University of Oxford. "The huge improvement in health care we can achieve is unprecedented."

The project provides clear guidance on techniques for fetal biometry and newborn measurement, as well training and standardisation, all of which are available free online (www.intergrowth21.org). This unique resource has enormous potential to improve the quality of obstetric and newborn care around the world and correct recognition of babies with growth problems. The ability to recognise the earliest faltering of linear growth, or stunting, could enable more effective and timely interventions[7], avoiding the potential for metabolic problems and obesity associated with rapid catch-up growth.[13]

It is estimated that approximately 15 million babies are born preterm every year[14], with prematurity now accounting for the majority of neonatal and under-5 deaths.[15] In the FGLS cohort, the rate of preterm birth was 4.5%, less than half the current estimated global rate.[14] Thus, the message is clear, attention to maternal environment, wellbeing, nutrition and medical care in pregnancy could prevent many preterm births. Work is ongoing to develop a deeper understanding of the causes, pathways and potential opportunities to prevent preterm birth, with increasing recognition of the complexity of the problem and need for tailored solutions if rates are to be decreased.

The challenge now will be persuading paediatricians, obstetricians, professional societies and decision-makers in maternal and newborn health to endorse and adopt these international standards into clinical practice. It is hoped that use of the same approach to growth from conception through to childhood can promote integration of care across the disciplines of obstetrics, midwifery and paediatrics. It will also assist in screening for babies with evidence of stunting and/or wasting at birth.

Whilst implementing the standards into clinical practice is important, recognising and responding to the public heath importance of these findings is essential if we are to optimise the health of future generations everywhere in the world.

"Currently we are not all equal at birth, but we can be," says Professor José Villar. "We can create a similar start for all by making sure mothers are well educated and nourished, by treating infection and by providing adequate antenatal care. Don't tell us nothing can be done. Don't say that women in some parts of the world have small children because they are predestined to do so. It's simply not true."

To learn more about the INTERGROWTH-21st Project and download the publications and standards, please refer to www.intergrowth21.org. The INTERGROWTH-21st Project was generously supported by a grant from the Bill & Melinda Gates Foundation.

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FIGURE 1

Figure showing the close overlap between skeletal size in infants of the INTERGROWTH-21st FGLS cohort compared to the distribution observed in the WHO MGRS at 1 year of age.

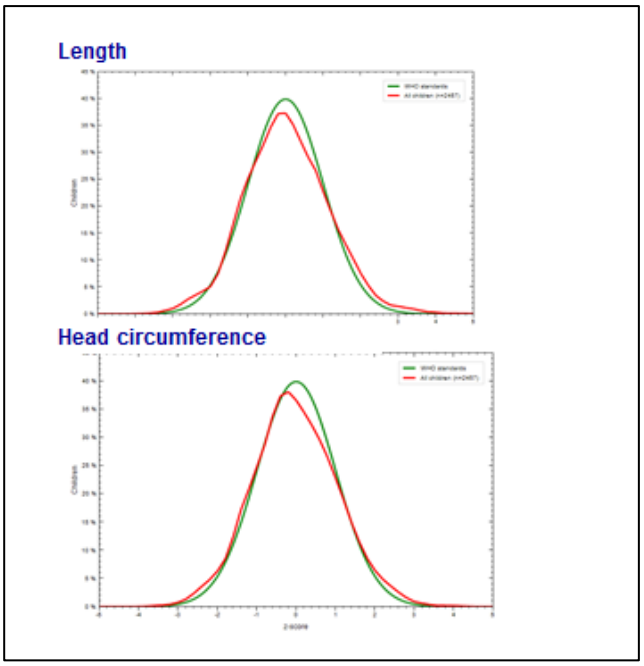
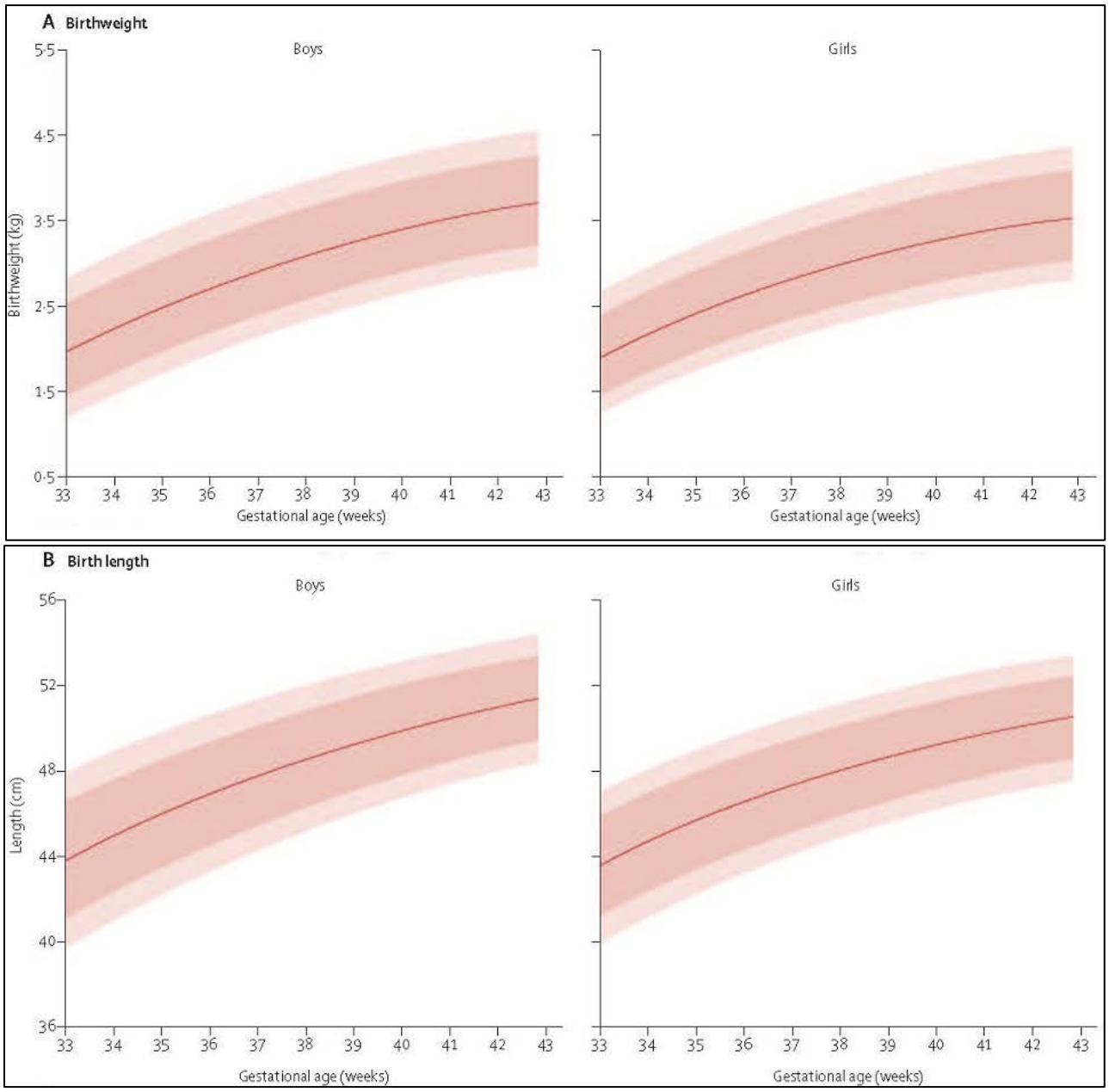


FIGURE 2

The 3rd, 10th, 50th, 90th, and 97th smoothed centile curves for (A) birthweight, (B) birth length, and (C) head circumference according to gestational age (Ref 11)



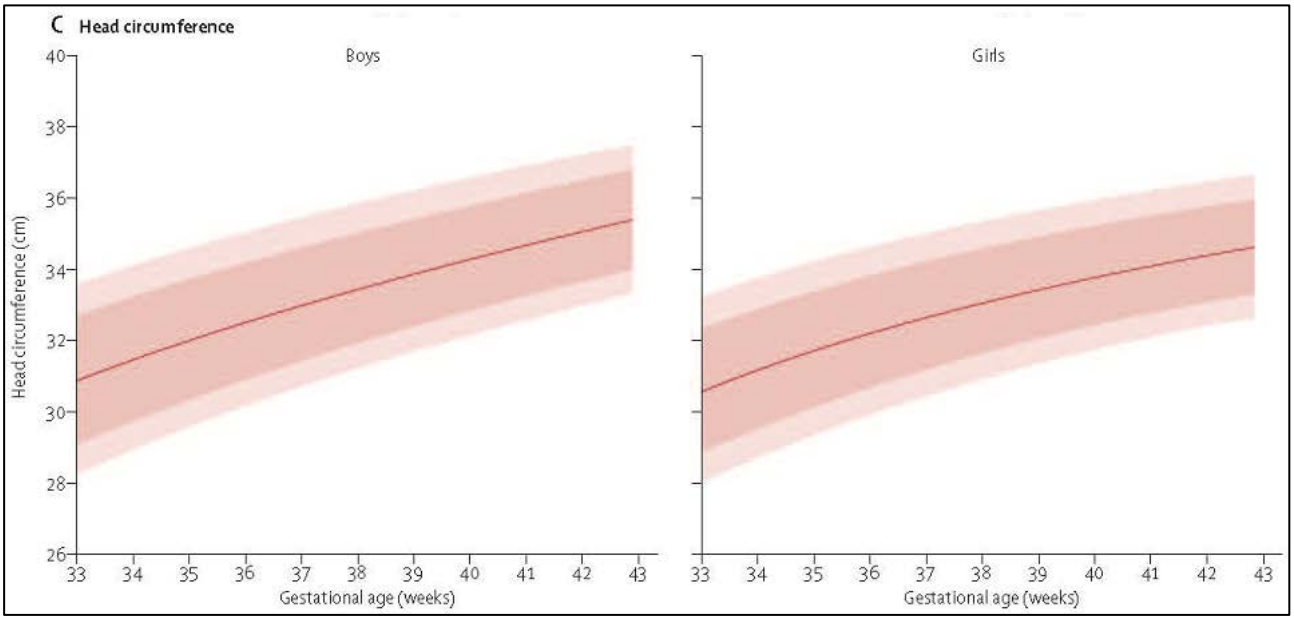


Figure 2 is also available in an appropriate size and higher resolution at International Pediatric Association's website under TAG-Nutrition-Resource Material. (www.ipa-world.org)