# Introduction

# ZA Bhutta, for the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>)

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From an annual birth cohort of approximately 125 million globally, it is estimated that 20 million newborns (16%) are low birthweight, i.e. weigh <2500 g at birth.<sup>1</sup> The term 'low birthweight' encompasses prematurity, intrauterine growth restriction (IUGR), or both, which are conditions associated with a significantly increased risk of mortality and morbidity. The vast majority, more than 95%, of these births are in developing countries.<sup>1</sup> More than two-thirds (68%) of all low-birthweight infants are born with evidence of IUGR, the majority in south-central Asia, where more than one-quarter (27%) of all newborns are low birthweight.<sup>2</sup> Such IUGR infants mostly include those born at term (about 9.6% of all newborns weigh between 2000 and 2499 g at birth), but may also include preterm infants (crudely estimated at about 1.3% of infants born globally weighing between 1500 and 1999 g at birth), or those born with both prematurity and IUGR (Figure 1).<sup>2</sup>

It is recognised that IUGR infants have much higher rates of morbidity and neonatal complications, including a higher risk of mortality.<sup>2</sup> Newborns weighing 2000–2499 g (those representing the majority with term IUGR) are 2.8 (95% confidence interval [CI], 1.8–4.4) times more likely to die during the neonatal period than those weighing more than 2499 g at birth. Despite limited data from community settings, it is also known that the corresponding relative risks of dying from birth asphyxia and infectious diseases are 2.3 (95% CI, 1.3–4.1) and 2.0 (95% CI, 1.2–3.4), respectively, for those weighing 2000–2499 g at birth.<sup>2</sup> More importantly, the well-documented long-term effects of low birthweight, coupled with postnatal factors, also highlight important links with the growing epidemic of noncommunicable diseases.<sup>3</sup>

A major limitation in our understanding of the significance of low birthweight and various connotations of the condition is the lack of standardised patterns of intrauterine growth. The common understanding of the antecedents of the condition are that these are multifactorial and may be related to a combination of factors, such as undernutrition, micronutrient deficiencies, environmental stresses, lifestyle issues and genetics. A key factor limiting our understanding of some of these factors and the epidemiology of the condition is the singular absence of a global standard for intrauterine growth for comparison of deviations and determinants thereof. In the absence of such comparative

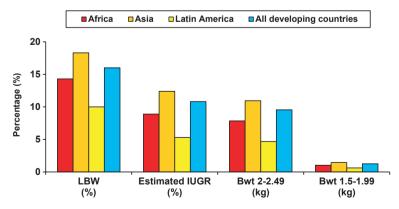


Figure 1. Prevalence of low birthweight (LBW) and intrauterine growth restriction (IUGR) globally. Bwt, birthweight.

benchmark(s), there have even been calls for local growth standards and, indeed, a redefinition of the cut-offs for low birthweight.<sup>4</sup> Others have made the call for the definition of international intrauterine or perinatal growth references based on either cross-sectional data from mixed ethnic populations in developed countries,<sup>5</sup> or representative local populations from the developed world.<sup>6</sup> Others have suggested modifications of existing growth trajectories,<sup>7</sup> or have attempted to define standards using existing data from cross-sectional surveys across various countries.<sup>8</sup>

Given the importance of optimal growth, fetal programming and long-term outcomes,<sup>9,10</sup> the definition of optimal intrauterine growth in representative populations with no identifiable risk factors is a priority. A comparable approach was used by the World Health Organization in defining postnatal growth and in developing a single set of internationally representative infant growth reference standards.<sup>11</sup>

The International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>) Project is the largest prospective study aimed at the definition of such standards.<sup>12</sup> It is also easily the largest collaborative venture in this field to date using standardised methods and protocols across five continents. The objectives include not only the definition of growth patterns in utero, but also an effort to define postnatal growth among preterm infants prospectively, an area that has not been the subject of attention in developing countries.

This supplement to *BJOG* describes the genesis and protocol development process for the INTERGROWTH-21<sup>st</sup> Project and its various components. Given the recognised variability in intrauterine measurement methods using ultrasonography,<sup>13</sup> extreme care was exercised in the development of uniform methods and quality assurance protocols. These sets of papers present the study background, protocols and implementation strategy for the INTERGROWTH-21<sup>st</sup> Project.

#### **Disclosure of interests** None.

#### Contribution to authorship

ZA Bhutta wrote the manuscript.

#### Details of ethics approval

The INTERGROWTH-21<sup>st</sup> Project was approved by the Oxfordshire Research Ethics Committee 'C' (reference: 08/ H0606/139), and the research ethics committees of the individual participating institutions and corresponding health authorities where the Project was implemented.

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