

# Implementation of the INTERGROWTH-21<sup>st</sup> Project in India

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The South Asian site in the INTERGROWTH-21<sup>st</sup> Project was the city of Nagpur, in Maharashtra State, India, with approximately 4500 births per year among the target population with middle to high socio-economic status. These deliveries are mainly concentrated in 20 small private hospitals, most of which are in the city centre. The sample for the Newborn Cross-Sectional Study (NCSS) was drawn from ten of these hospitals, covering 76% of the target low-risk pregnant population. The Fetal Growth Longitudinal Study (FGLS) sample was recruited from the largest of these institutions, Ketkar Hospital, as well as several ancillary antenatal

care clinics. Special activities to encourage participation and raise awareness of the study at this site included translating patient information leaflets into local languages and securing local media interest. Among the unique challenges of the Indian site was the coordination of the large number of hospitals involved in NCSS, a task that required careful planning and organisation by the field teams.

**Keywords** Fetal growth, INTERGROWTH-21<sup>st</sup>, nutrition, standards.

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## Introduction

The International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>) is a large-scale, population-based, multicentre project involving health institutions from eight geographically diverse countries, which aims to assess fetal, newborn and preterm growth under optimal conditions, in a manner similar to that adopted by the World Health Organization (WHO) Multicentre Growth Reference Study (MGRS).<sup>1</sup> The INTERGROWTH-21<sup>st</sup> Project has three major components, which were designed to create: (1) longitudinally derived, prescriptive, international, fetal growth standards using both clinical and ultrasound measures; (2) preterm, postnatal growth standards for those infants born  $\geq 26^{+0}$  but  $<37^{+0}$  weeks of gestation in the longitudinal cohort, and (3) birthweight-for-gestational-age standards derived from

all newborns delivering at the study (FGLS) sites over an approximately 12 month period.<sup>2</sup>

The South Asian site for the INTERGROWTH-21<sup>st</sup> Project was the Indian city of Nagpur, in the state of Maharashtra (Figure 1). Nagpur is the largest city in central India, with an urban population of 2 129 500 inhabitants. The city is the main centre of commerce, education and politics in the Vidarbha region and is an important trading location.

Nagpur was selected to participate in the INTERGROWTH-21<sup>st</sup> Project for several reasons. First, it is a middle-income city with a monthly gross domestic product (GDP) per capita of INR11 666 (US\$208) and mean life expectancy of 70 years,<sup>3</sup> making it suitable for a prescriptive study of this nature. Second, early antenatal booking is common among the low-risk pregnant population and the vast majority of births in the city take place in a health institution. Third, the research team, which includes some of India's leading experts in

antenatal and neonatal care, have considerable experience in implementing large-scale, longitudinal studies and could therefore be relied upon to execute the protocol effectively.<sup>4</sup>

## Preparatory activities

### Hospital selection

Preparation began with a census to identify health institutions in Nagpur serving the middle to high socio-economic pregnant population. The census identified 20 institutions, most of which were located in the central part of the city; of these, the ten hospitals with the highest number of annual deliveries were selected to represent the NCSS population (Figure 1). These ten hospitals cover approximately 76% (3400/4500) of births occurring among the target population in Nagpur (Table 1 and Figure 2). The INTERGROWTH-21<sup>st</sup> Principal Investigator and Project Leader visited each of these hospitals during the preparatory phase to brief the hospital directors about the study and ascertain their willingness to participate.

Ketkar Hospital (KH) was chosen as the focal point for the Fetal Growth Longitudinal Study (FGLS) because of its



**Figure 1.** Location of Nagpur. H: hospital participating in the INTERGROWTH-21<sup>st</sup> Project

**Table 1.** Delivery information for selected hospitals.

Hospital	Number of deliveries (2009)
Avanti Hospital	432
Avantika Hospital	234
Gurukrupa Maternity Home	105
Ketkar Hospital	700
Mulik Hospital & Research Center	400
Om Women Hospital	368
Renuka Nursing Home	369
Saboo Nursing Home	274
Somani Nursing Home	352
Nandlok Hospital	130
Total	3364

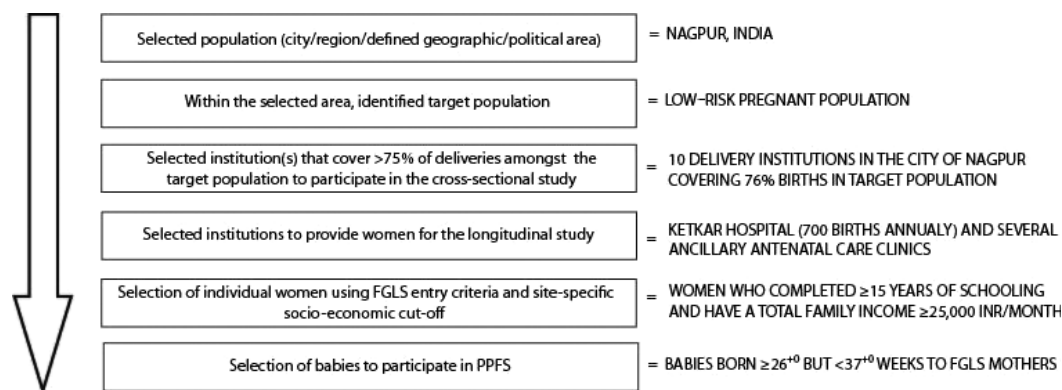
central location and status as the largest of the selected institutions. Although the majority of women enrolled in FGLS were recruited from KH's antenatal service, some were also recruited from five other hospitals in the locality that participated in NCSS; all served comparable populations of high socio-economic status and shared similar standards of antenatal care.

The population served by KH met the protocol requirement for being at low risk of fetal growth impairment, as indicated by the hospital's low birthweight rate (<2500 g) and mean birthweight of 7.6% and 3109 g, respectively. In 2009, the hospital's perinatal mortality rate was 9.5/1000 and >80% of women had secondary-level or university-level education. In addition, the mean number of antenatal care appointments was >12 and the Federation of Obstetrics and Gynaecological Societies of India (FOGSI) has recognised KH as a training centre in ultrasonography for senior medical staff. Moreover, the management team at KH were willing to provide space for the study equipment and the skilled staff based there were keen to assist with the implementation of the project.

As KH is not a specialist neonatal hospital, all preterm infants born to mothers in the FGLS cohort were referred to Rajan New Born Care Unit, located 1 km from KH, where they were followed up according to the protocol.

### Recruitment and training of study personnel

The members of the FGLS team underwent training for various tasks before the study started. The data manager and lead ultrasonographer were trained in Oxford at the centralised training sessions in April 2009, as described elsewhere in this supplement.<sup>5,6</sup> The data management training focused on data collection principles and use of the on-line data entry and management system. The ultrasound training focused on teaching standardised measurement techniques designed to minimise intra-



**Figure 2.** Summary of population-based sampling strategy in Nagpur, India.

observer and inter-observer variation. Each team leader then conducted similar training sessions with their respective local teams in Nagpur.

Ten anthropometrists were selected and trained by the lead anthropometrist, who completed the centralised anthropometry team standardisation session in Nairobi, Kenya, as described elsewhere in this supplement.<sup>7</sup> The first local standardisation session in Nagpur was conducted in April 2010 and was overseen by a senior member of the INTERGROWTH-21<sup>st</sup> Anthropometry Group. A second standardisation session was conducted before starting NCSS as per protocol, and subsequent standardisation sessions took place on a quarterly basis.

### Organisational and advocacy activities

A team of researchers comprising obstetricians, ultrasonographers and a neonatologist was formed in January 2009 to plan and implement the INTERGROWTH-21<sup>st</sup> Project in Nagpur. Institutional ethical clearance was obtained and the project was registered at the International Health Division, Indian Council of Medical Research, New Delhi. Clearance from the Indian Ministry of Health and Family Welfare was received on schedule in April 2009. However, obtaining Foreign Contribution Regulation Act (FCRA) clearance to accept the funds for the project proved a major challenge, partly because Government elections occurred during the process. This delayed the start of the studies. As per Government regulations, the ultrasound machine was registered with the Nagpur Municipal Corporation, Health Department Government of Maharashtra under the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act 1994 and the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Rules 1996. The team were required to state that the machine would not be used for sex determination. All the problems were eventually resolved with the help of the local authorities and the study site began recruiting in November 2009.

Patient information leaflets and consent forms were translated into the regional (Marathi) and national (Hindi) languages by the local study team. Members of the Nagpur Obstetrics and Gynaecology Society and the Nagpur branch of the Indian Medical Association were apprised of the project. Information was also published in leading English and local language newspapers to encourage women to participate (see Supporting Information, Appendix S1).

## FGLS implementation

### Pilot phase

During the pilot phase, 50 women were screened over 4 weeks at KH, of whom 25 were found to be eligible, i.e. a potential recruitment rate of 50%. The most common reasons for exclusion were low maternal height, a history of medical problems or pregnancy complications and assisted conception. No major issues were identified and no adaptations to the forms were required.

### Enrolment logistics

Recruitment for FGLS began in November 2009 (Figure 3). Based on the team's previous experience of conducting complex studies of this nature, a local Study Monitoring Committee was formed to monitor various aspects of the study implementation such as recruitment and retention. Well-defined tasks and specific responsibilities were delegated to members who were required to report back on their progress at the regular team meetings.

The screening criteria identified pregnant women at low risk for factors known to affect fetal growth and development, including socio-economic constraints. The country-specific cut-off point indicator for low socio-economic status used in India was  $< 15$  years of female education or an annual family income  $< \text{INR}25\,000$ .<sup>8-10</sup> Women were first screened for eligibility for the study at the hospital reception where they report for their appointments. Prescreening criteria were used

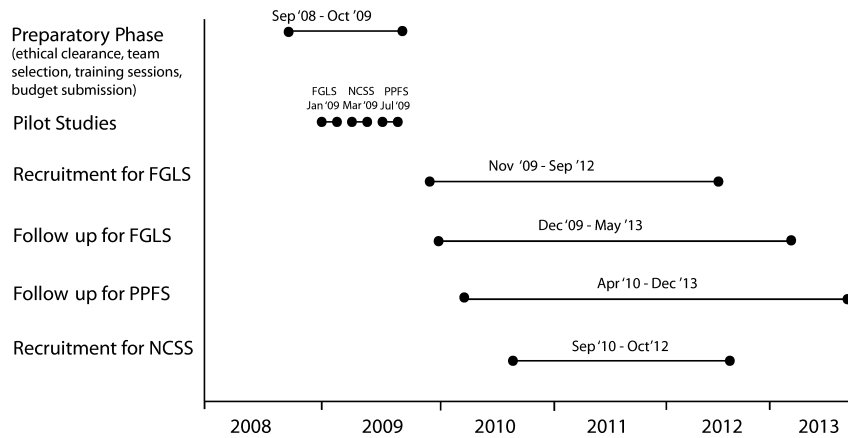


Figure 3. Project timeline in India.

to identify women within the 9<sup>+0</sup> to 13<sup>+6</sup> weeks of gestation limit who appeared to meet the study criteria. Potentially eligible women who were <9<sup>+0</sup> weeks of gestation were approached again at their next appointment.

Once a potentially eligible woman was identified, the receptionist alerted the medical social worker who explained the study to the woman, gave her the information sheet and confirmed her eligibility. Women willing to participate in the study were fast-tracked to minimise the waiting period for the dating scan, which was usually performed on the same day.

If the woman was still eligible after the dating scan (i.e. the difference in her gestational age estimation based on her last menstrual period and crown-rump length was  $\leq 7$  days), the research officer explained the study objectives and participation requirements again to the woman and her relatives (usually husband and mother-in-law), in the local language if necessary. Written consent was then obtained and the follow-up visits were scheduled.

#### Follow-up logistics

Every  $5 \pm 1$  weeks until delivery, fetal growth scans were performed at KH by the study's trained ultrasonographer, with the Philips HD9 ultrasound machine (Philips Ultrasound, Bothell, WA, USA), according to the INTERGROWTH-21<sup>st</sup> protocol.<sup>5,11</sup> The same commercially available machine was used by ultrasonographers at all the INTERGROWTH-21<sup>st</sup> participating centres to ensure reliable measurements; facilitate technical support and data transfer, and ensure that a balance was struck between various criteria, e.g. cost, imaging quality, functionality etc.

Each woman was assigned a logbook for the duration of the study, containing the dates of all follow-up visits and the expected date of delivery. To minimise loss to follow-up, at least three contact addresses were recorded, including the mother's family. Each woman was given an appointment card with her visit dates; women were also phoned the day before each scan visit. To maximise compliance, the flexibility in the

follow-up schedule outlined in the study protocol was used if a woman wished to change her visit date, e.g. if she was visiting family outside Nagpur. If a woman missed an appointment, a telephone call was made immediately to reschedule the scan. If more than one appointment was missed, a home visit was arranged to assess the situation.

#### Implementation of the Preterm Postnatal Follow-up Study

All preterm newborns ( $\geq 26^{+0}$  but  $<37^{+0}$  weeks of gestation) born to mothers in the FGLS cohort were included in the Preterm Postnatal Follow-up Study (PPFS) and followed for 24 months after delivery to evaluate their postnatal growth. Preterm infants were managed according to recommended feeding patterns and clinical practice.<sup>12</sup> Anthropometric measurements (weight, length and head circumference)

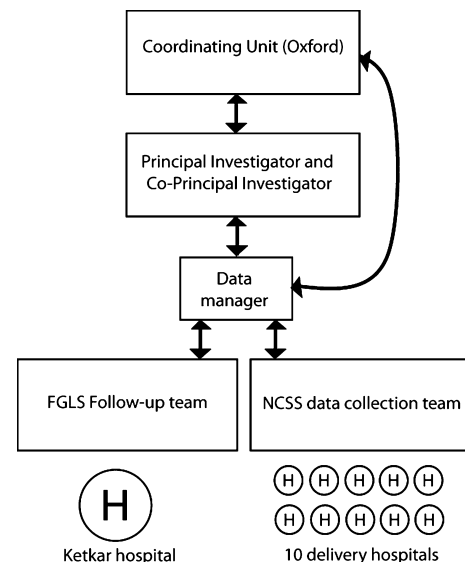


Figure 4. Team coordination.

were taken as soon as possible after birth, then every 2 weeks for the first 8 weeks, and monthly until 8 months. The same anthropometric measurements were taken at 1 year, 15, 18, 21 months and 2 years of age. All follow-up measurements, interviews and clinical evaluations were conducted at a special follow-up clinic at the Rajan New Born Care Unit. After discharge, follow-up appointments were arranged with the parents and each mother was given an appointment card with the visit dates; mothers also received a telephone call the day before each visit to remind them of the appointment. If an appointment was missed, a telephone call was immediately made to reschedule the visit. If more than one appointment was missed, a home visit was arranged to collect data and anthropometric measurements.

## NCSS implementation

### Data collection logistics

Data collection began in September 2010, once the anthropometric equipment was installed at the ten collaborating hospitals.

The study team for NCSS comprised a research coordinator, anthropometrists and nursing staff. The team organised a rota to ensure coverage at every hospital 7 days per week. The research coordinator visited each hospital every day to complete the data collection forms using the hospital medical records. Anthropometric data were collected for all newborns at the ten hospitals preferably within 12 hours, and no later than 24 hours, of birth.

The data manager performed visual checks on all NCSS forms before entering the data into the online database. Any queries concerning missing values or outliers were resolved with the data collection teams.

### Lessons learned and conclusions

The implementation of the INTERGROWTH-21<sup>st</sup> Project in India was a challenging task that required careful planning and implementation because of its population-based nature. The requirement of the protocol to collect the newborn anthropometric measurements within 12 hours of birth was particularly challenging because of the large number of hospitals participating in NCSS. Hence, to obtain data from at least 80% of the deliveries among the target population in Nagpur required excellent coordination and communication between the various study units, and extraordinary levels of commitment on the part of the Research Coordinator and anthropometric team. Another significant challenge was the delay in receiving the study funds because of the need to obtain FCRA clearance; however, once clearance was obtained the team in Nagpur did not face any significant challenges in meeting the target recruitment rate for FGLS of 25 women per month. Regular communication with the INTERGROWTH-21<sup>st</sup> Project Coordinating Unit and

frequent site visits also played important roles in the early identification and quick resolution of any problems that arose during the course of the project.

### Disclosure of interests

None.

### Contribution to authorship

MP, HEK and LCI wrote the manuscript and all the authors read and approved the final version.

### 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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A full list of Members of the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>) and its Committees appears in the preliminary pages of this supplement.

## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Appendix S1.** Example of newspaper article published to encourage women to participate. ■

## References

- 1 de Onis M, Garza C, Victora CG, Bhan MK, Norum K. The WHO Multicentre Growth Reference Study (MGRS): rationale, planning, and implementation. *Food Nutr Bull* 2004;25:S1–90.
- 2 Villar J, Altman DG, Purwar M, Noble JA, Knight HE, Ruyan P, et al. for the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>). The objectives, design and implementation of the INTERGROWTH-21<sup>st</sup> Project. *BJOG* 2013; DOI: 10.1111/1471-0528.12047.
- 3 *Environmental Status Report for Nagpur Corporation City 2010–2011*. Nagpur, India: Global Scientific Inc., 2011.
- 4 Villar J, Abdel-Aleem H, Merialdi M, Mathai M, Ali MM, Zavaleta N, et al. World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. *Am J Obstet Gynecol* 2006;194:639–49.
- 5 Sarris I, Ioannou C, Ohuma EO, Altman DG, Hoch L, Cosgrove C, et al. for the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>). Standardisation and quality

- control of ultrasound measurements taken in the INTERGROWTH-21<sup>st</sup> Project. *BJOG* 2013; DOI: 10.1111/1471-0528.12315.
- 6** Ohuma EO, Hoch L, Cosgrove C, Knight HE, Cheikh Ismail L, Juodvirsiene L, et al. for the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>). Managing data for the international, multicentre INTERGROWTH-21<sup>st</sup> Project. *BJOG* 2013; DOI: 10.1111/1471-0528.12080.
- 7** Cheikh Ismail L, Knight HE, Ohuma EO, Hoch L, Chumlea WC for the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>). Anthropometric standardisation and quality control protocols for the construction of new international fetal and newborn growth standards: the INTERGROWTH-21<sup>st</sup> Project. *BJOG* 2013; DOI: 10.1111/1471-0528.12127.
- 8** Kumar N, Shekhar C, Kumar P, Kundu AS. Kuppuswamy's socioeconomic scale: updating income ranges for the year 2012. *Indian J Public Health* 2012;56:103–4.
- 9** Kumar N, Shekhar C, Kumar P, Kundu AS. Kuppuswamy's socioeconomic status scale—updating for 2007. *Indian J Pediatr* 2007;74:1131–2.
- 10** Available from: [www.cyberjournalist.org.in/manisana/aicpinew.html](http://www.cyberjournalist.org.in/manisana/aicpinew.html). Accessed 1 December 2010.
- 11** Ioannou C, Sarris I, Hoch L, Salomon L, Papageorghiou AT, for the International Fetal and Newborn Growth Consortium for the 21<sup>st</sup> Century (INTERGROWTH-21<sup>st</sup>). Standardisation of crown–rump length measurement. *BJOG* 2013; DOI: 10.1111/1471-0528.12056.
- 12** INTERGROWTH-21<sup>st</sup> Neonatal Manual. Available from: [www.intergrowth21.org.uk](http://www.intergrowth21.org.uk). Accessed 15 November 2010.