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Implementation of the INTERGROWTH-21st Project in Brazil

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The Latin American site in the INTERGROWTH-21st Project was Pelotas, Brazil, with approximately 4000 births per year. The sample for the Newborn Cross-Sectional Study (NCSS) was drawn from four hospitals, covering 99% of births in the city. The Fetal Growth Longitudinal Study (FGLS) sample was recruited from one of the largest private ultrasound clinics in the city and 30 smaller, private, antenatal clinics serving middle to high socioeconomic status women. Among this site's major challenges was the recruitment of women for FGLS from numerous different clinics. Several public relations activities were conducted to improve collaborative efforts between the research team and obstetricians, paediatricians and community leaders in Pelotas.

Keywords Fetal growth, INTERGROWTH-21st, nutrition, standards.

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Introduction

The International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) 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).[1] The INTERGROWTH-21st 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 at $\geq 26^{+0}$ 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 sites over an approximately 12 month period.[2]

Brazil was the Latin American site for the INTERGROWTH-21st Project. Data were collected in the middle-income city of Pelotas, in the southernmost region of the country (Figure 1). Pelotas is the third most populous city in the state of Rio Grande de Sul, with 350 000 inhabitants (92% living in urban areas) and 4000 births per year. More than 99% of these births take place in the city's four maternity hospitals.

In economic terms, the richer states in Brazil are found in the southern and southeastern regions of the country, where Pelotas is located. In 2007, Pelotas had a per capita gross domestic product (GDP) of R$8248 (US$4933).[3] Forty-seven percent of women in Pelotas receive >9 years of formal education, with 21% receiving more than 12 years.[3] Data from the Pelotas 2004 birth cohort study indicate that the rates of low birthweight (<2500 g) and intrauterine growth restriction are 10% and 12%, respectively, and that the mean birthweight of newborns in Pelotas is 3150 g (Table 1).[4] These statistics serve to indicate

Figure 1. Location of Pelotas. H: hospital participating in the INTERGROWTH-21st Project.

Table 1. INTERGROWTH-21st protocol requirements

Indicator of population at low risk of fetal growth impairment	Value	Protocol requirement met
Low birthweight rate (%)	10	Yes
Perinatal mortality rate (per 1000 live births) (2004)	18.5	Yes
Mean birthweight (g)	3150	Yes
>4 years maternal education (%)	92	Yes
Altitude (m above sea level)	<500	Yes

that Pelotas meets the project's requirements for a population at low risk of fetal growth impairment.

The city has an Epidemiology Research Centre based at the Federal University of Pelotas. The centre has been conducting epidemiological research on maternal and child health nutrition for more than 30 years and is also a WHO Collaborating Centre in the area of nutrition.[5,6] The same research team also participated in MGRS.[7] It was partly due to this research experience in conducting large-scale longitudinal studies that Pelotas was chosen as a site for the INTERGROWTH-21st Project.

Preparatory activities

Hospital selection

There are four hospitals with maternity services in Pelotas, delivery information for which is presented in Table 2. A small proportion of the deliveries at these hospitals occur to non-Pelotas residents who are referred from nearby cities and the surrounding areas. All four hospitals were selected to participate in the Newborn Cross-Sectional Study (NCSS) to ensure that the sample was truly population-based (Figure 2). These hospitals also received pregnant women from the Fetal Growth Longitudinal Study (FGLS) cohort at delivery.

Table 2. Delivery information for hospitals included in FGLS and NCSS

Maternity hospital	Number of deliveries (2009)	Deliveries in Pelotas (%)
Hospital Miguel Piltcher	245	5
Hospital São Francisco de Paula	2235	46
Hospital Escola UFPEL	887	18
Santa Casa de Misericordia	1480	30
Total	4847	99*

*The remaining 1% of births in Pelotas take place at home.

Organisational and advocacy activities

Large research projects such as INTERGROWTH-21st require close collaboration between the city's hospitals, doctors and families. Several public relations activities were, therefore, conducted to increase levels of cooperation between the research team and obstetricians, paediatricians and community leaders. The Principal Investigator of the INTERGROWTH-21st Project organised a session at the annual Pelotas Medical Association meeting to present the project to a large number of obstetricians and paediatricians working in the city. The INTERGROWTH-21st Project Leader also visited the site to introduce the studies to the teams at the local hospitals and emphasise the Project's international importance.

The research coordinators visited the four largest hospitals in the city and the private obstetric clinics in the locality to introduce the aims and objectives of the project and encourage them to refer eligible women. Contact was also made with local newspapers, as well as TV and radio stations, to raise awareness of the project among the local population (see Appendix S1).

The study was approved by the Ethical Committee of the Medical School, Federal University of Pelotas in February 2009.

Recruitment and training of study personnel

A Study Coordinator was hired to work in conjunction with the local Principal Investigator to oversee the implementation of FGLS in Brazil. A data manager and lead ultrasonographer were trained in Oxford at the centralised training sessions in April 2009. Each team leader then conducted similar training sessions with their respective local teams in Brazil.

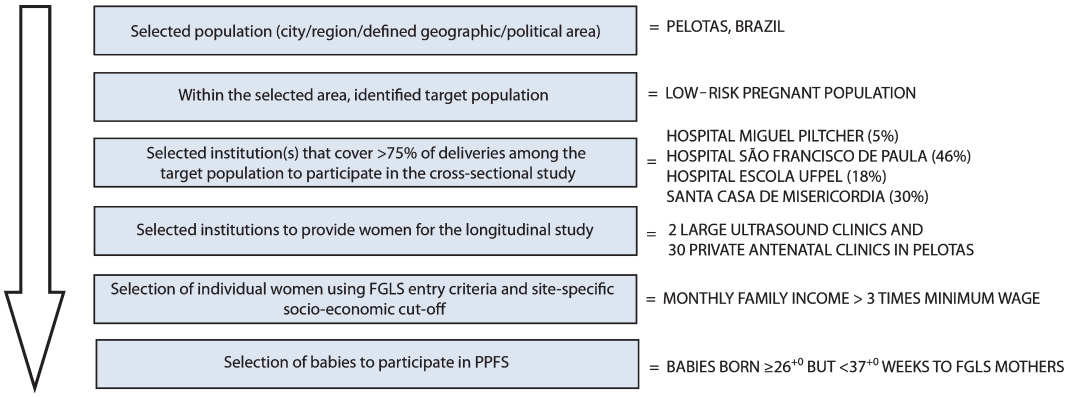

Figure 2. Summary of population-based sampling strategy in Pelotas, Brazil.

Eleven female interviewers were initially recruited to form the NCSS data collection team. A lead anthropometrist was selected and attended the anthropometry team standardisation programme session in Kenya, described elsewhere in this supplement.[8] The lead anthropometrist trained the other members of the team to use the data collection forms and anthropometric equipment, under the supervision of an expert member of the INTERGROWTH-21st Anthropometry Group. Following this, a full standardisation session took place in accordance with the anthropometry protocol.[9] Based on the results of this session and a simple anthropometric knowledge test, the ten interviewers with the best performance were recruited to work full-time on the project.

Preparation of study materials

All the study documents and data collection instruments were translated from English into Portuguese and piloted by the local study team. Back translation was performed for all forms to ensure that errors were not introduced during the translation process. A flip chart showing alcohol units, iron and vitamin products and high-risk activities was given to each team of interviewers for use during the FGLS screening interview. To prepare for NCSS and the Preterm Postnatal Follow-up Study (PPFS), a list including the main brands of infant formula was also prepared for coding information on nonhuman milk intake, as well as a list of prenatal vitamins, so the field interviewers could have the composition of the main brands.

FGLS implementation

Antenatal care in Pelotas is delivered in both public health institutions and approximately 40 private obstetric clinics; approximately 20% of births in Pelotas are covered by health insurance or private care schemes. The FGLS recruitment team concentrated efforts in this population because of the strict needs of the inclusion criteria to select a pregnant population at low risk of fetal growth impairment.[10]

Obstetricians running the private obstetric clinics and the three private ultrasound clinics were contacted by members of the research team and asked to refer eligible women to the Epidemiology Research Centre, where the study's ultrasound machine was located. One of the largest ultrasound clinics and 30 of the smaller obstetric clinics agreed to do so. Ultrasonographers in this clinic took part in the standardisation exercise for crown–rump length measurement, described elsewhere in this supplement.[11]

Pilot phase

During the pilot phase, 20 women were randomly selected to complete the FGLS screening interview at one of the local participating ultrasound clinics, of whom 16 were found to be eligible, i.e. a potential recruitment rate of 80%. The reasons for ineligibility were age >35 years, smoking, past medical history and an uncertain date of the last menstrual period. The pilot phase served to familiarise the study team with the data collection tools and resolve any queries before launching FGLS.

Recruitment started in October 2010 (Figure 3). This was much later than planned because of delays in importing the HD9 ultrasound machine (Philips Ultrasound, Bothell, WA, USA) caused by the manufacturer having to apply for national authorisation as it was new to the market. It was essential to wait for authorisation rather than use an alternative machine because the HD9 was used at all the INTERGROWTH-21st participating centres.

Enrolment logistics

All potentially eligible women were screened according to the INTERGROWTH-21st criteria, which involved identifying pregnant women at low risk for all factors known to affect fetal growth and development.[11] We also used country-specific criteria and cut-off points to identify women at low risk of fetal growth restriction because of socio-eco-

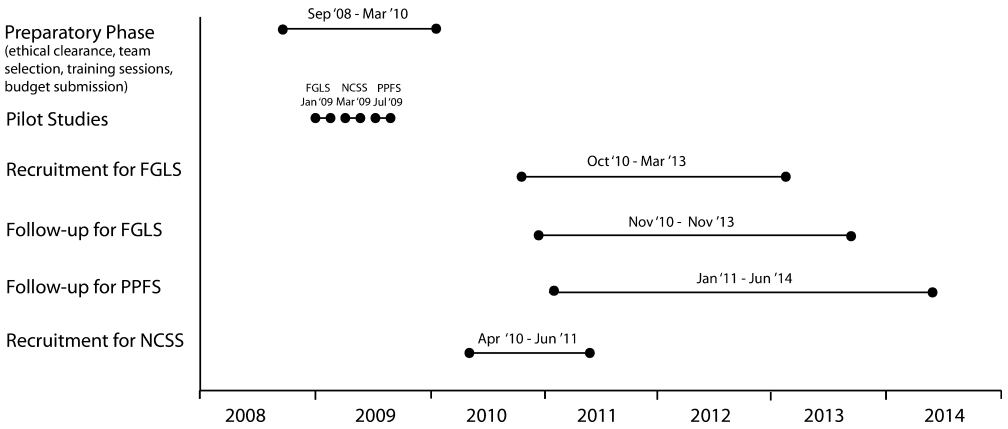

Figure 3. Project timeline in Brazil.

nomic constraints; those not meeting these criteria were considered to be not eligible for FGLS. Data from the 2004 Pelotas Birth Cohort Study, which covered all births in the city that year, were analysed to identify a socio-economic cut-off above which fetuses would have a <10% prevalence of impaired growth.[4] Based on this analysis, a monthly family income of at least three times the minimum wage (R$1800) was chosen as a cut-off to define middle to high socio-economic status.

Two full-time interviewers were recruited to enrol women into FGLS: one was based at the larger of the private ultrasound clinics referring women to the study and the other was 'on-call' to travel to any of the other ultrasound or obstetric clinics whenever an eligible woman was identified. All eligible women willing to participate in the study signed a written consent form and completed the study entry questionnaire, administered by a trained interviewer.

Follow-up logistics

Several strategies were implemented to ensure a high rate of compliance with the strict study follow-up schedule. Telephone calls were made to women 1 week before their next ultrasound scan appointment to confirm the time and remind them to attend. At the end of each appointment each woman was given a free DVD with images of her baby to take home; this was greatly appreciated as women are typically expected to pay for this service in private clinics. Each woman who completed the study was given a small gift to thank her for her participation.

Preterm follow-up logistics

For the PPFS, all the preterm infants born to the mothers in FGLS were screened and included if they fulfilled the study criteria. When such a preterm birth occurred, the fieldworker alerted one of the two study paediatricians, who then interviewed the mother, measured the newborn and completed the data entry forms. The follow-up visits were performed by one of the paediatricians together with an anthropometrist who repeated the measures. The study secretary telephoned the mothers before each appointment to confirm the scheduled visit. Usually the visits occurred at the ultrasound clinic but, in the event that a mother had difficulty attending the clinic the team conducted home visits to avoid missing an appointment.

NCSS implementation

Data collection

The four hospitals selected to participate in NCSS, which began in April 2010, were visited beforehand by the local Study Coordinator and the INTERGROWTH-21st Project Leader to explain the study objectives and request authorisation for data collection. In addition, the local Principal Investigator sent formal requests to the hospital directors and, as a goodwill gesture, the offer was made to donate the study equipment to each hospital if NCSS was successfully completed.

Five fieldwork teams collected data for NCSS: one was based in each of the four hospitals and a fifth covered weekends, sickness and holiday periods. Follow-up team meetings were scheduled twice-weekly throughout the study.

All women who gave birth in Pelotas during the study period were invited to participate in NCSS. After gaining written consent from mothers, the anthropometrists took infant measurements in pairs according to the protocol, and collected pregnancy and delivery information. The teams liaised with the head paediatrician to ascertain the best time to measure babies in the Neonatal Intensive Care Unit. Information was also collected from antenatal care cards, hospital files and relevant clinicians. The mother's contact details were recorded in case any additional clinical information, not available at the hospital, was required.

Quality control procedures

Anthropometric standardisation sessions were carried out every 3 months for the duration of the study. A database

was created with these measurements and sent to the INTERGROWTH-21st Anthropometry Group for quarterly review.

In general, the interviewers returned the completed questionnaires to the Assistant Study Coordinator within 4 days of the interview. The fieldwork supervisors then checked the forms before the data were entered into the online database. Whenever possible, problems encountered at this stage were discussed at the next weekly team meeting so that the entire group could agree on how they should be handled. After any necessary revisions, the questionnaires were given to the data manager for data entry.

Conclusions and lessons learned

The team encountered difficulties and delays in importing the HD9 ultrasound machine as it had not been approved for use in Brazil. It took nearly a year to obtain the licence to import the equipment, which inevitably altered the study timelines causing FGLS not to start until 5 months after NCSS.

One of the challenges associated with conducting NCSS in Pelotas was that many women either did not have an early ultrasound scan for dating purposes or they did not have a copy of the ultrasound report. In some cases, the crown–rump length measurement was not even obtainable. As a result, these values were missing for some women despite our best efforts to contact the ultrasound clinics and obstetricians for the information.

Another challenge was to ensure that the teams of anthropometrists could cover all four hospitals without missing any deliveries as discharges in Pelotas can occur very early, within 12 hours of a normal vaginal delivery. It was, therefore, necessary to perform more than one round of data collection per day in each hospital to ensure that the measurements were recorded before mothers were discharged. A positive aspect of this component of NCSS, however, was that strong relationships were established with the clinicians and that, in turn, improved the willingness of mothers to participate in the study.

Ultimately, the key to the overall success of the project in Pelotas was regular and effective communication between the various field teams and the research coordinators. The weekly team meetings served to ensure that all problems were resolved in a timely manner. Regular communication with the INTERGROWTH-21st Project Coordinating Unit in Oxford and frequent site visits also played an important role in maintaining the enthusiasm and motivation of the data collection team over the long duration of the study.

Disclosure of interests

None.

Contribution to authorship

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

Details of ethics approval

The INTERGROWTH-21st 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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Acknowledgements

A full list of Members of the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) 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. Media coverage of the INTERGROWTH-21st Project in Brazil. ■

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