

Implementation of the INTERGROWTH-21st Project in the United States

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Accepted 20 November 2012.

The North American site in the INTERGROWTH-21st Project was North Seattle, Washington State, USA. The majority of the data were collected from within Seattle City, which has approximately 12 300 births per year. The sample for the Newborn Cross-Sectional Study (NCSS) was drawn from two hospitals (Swedish Medical Center and the University of Washington) covering almost 80% of deliveries within the target population. The Fetal Growth Longitudinal Study (FGLS) sample was recruited from several antenatal clinics serving the University of Washington Medical Center and Providence Everett Medical Center. Special activities to encourage participation and raise awareness of the studies included

furnishing the recruitment sites with fliers designed by the Project Coordinating Unit, and presenting the studies to clinical staff to encourage providers to refer appropriate patients. One of the major challenges at this site was the low recruitment rate in the early phase of the FGLS because of the high rates of smoking, maternal age >35 years and body mass index >30 years. This was remedied by the inclusion of other ancillary clinics, as well as increased advertising among the general public.

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

Please cite this paper as: Dighe M, Frederick I, Andersen H, Gravett M, Abbott S, Carter A, Algren H, Rocco D, Waller S, Sorensen T, Enquobahrie D, Blakey I, Knight H, Cheikh Ismail L, for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st). Implementation of the INTERGROWTH-21st Project in the United States. BJOG 2013;120 (Suppl. 2): 123–128.

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.

North Seattle was the North American site for the INTERGROWTH-21st Project. Seattle, Washington, is the centre of the Seattle–Tacoma–Bellevue metropolitan statistical area, the largest in the northwestern USA and the 15th largest in the USA. Seattle is the county seat of King County and is the major economic, cultural and educational centre in the region. As of April 2009, the city's population was approximately 617 000 within a metropolitan area of 4 158 000.² Seattle is consistently ranked as one of the two most literate cities among the USA's largest cities.³ Survey data from the US Census Bureau also indicates that Seattle has a higher percentage of college graduates than any other major US city, with approximately 53.8% of residents aged 25 and older holding a bachelor degree or higher, and 91.6% having a high school diploma.⁴

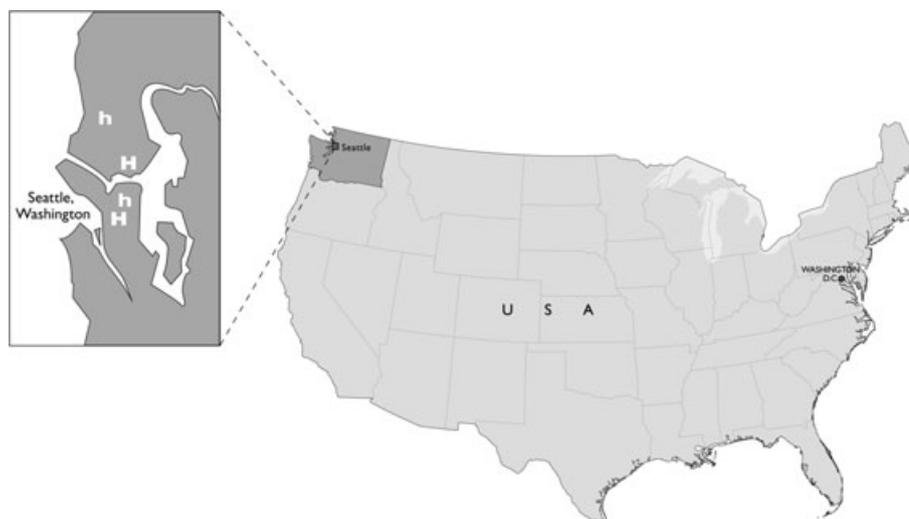


Figure 1. Location of Seattle City, WA, USA; H: hospital participating in the INTERGROWTH-21st Project; h: hospital not participating in the INTERGROWTH-21st Project.

In terms of per capita income, the Seattle metropolitan area was ranked 17th out of 363 metropolitan areas in 2006.⁵ Its gross domestic product (GDP) per capita, in 2005, was \$US 87,000.⁶ Recent statistics indicate that the mean female life expectancy in Seattle is 82.5 years.⁷ These data, therefore, support the inclusion of Seattle City, King County, in the INTERGROWTH-21st Project.

Seattle City also has relatively few risk factors for adverse outcomes. Infant mortality, in 2007, was 4.4 per 1000 live births. The low-birthweight rates for singleton and all pregnancies were 4.9 and 6.6 per 100 live births, respectively. The preterm birth rate was 9.8 per 100 live births.⁸ Therefore, Seattle City is the principal geographical area from which data were collected for the INTERGROWTH-21st Project, supplemented by one additional hospital in the North Seattle region (Figure 1).

Preparatory activities

Hospital selection

There are four hospitals in Seattle City with obstetric departments (Table 1). The two largest, the University of Washing-

Table 1. Delivery information for hospitals with an obstetric department in Seattle City, King County

Hospital name	No. of deliveries (2009)
University of Washington	2230
Northwest Hospital	1028
Group Health Cooperative	1712
Swedish Medical Center	7316
Total Seattle City	12 336

ton Medical Center (UWMC) and Swedish Medical Center (SMC), were selected to participate in the Newborn Cross-Sectional Study (NCSS). These hospitals cover almost 80% of the births in Seattle City, meeting the protocol requirement for the sample to be population-based (Figure 2).

UWMC has held Magnet status for excellence in nursing since 1994 and the hospital's birthing programme has received 'Baby Friendly' status from the WHO and UNICEF, the United Nation's Children's Fund. The centre is consistently ranked among the country's leading institutions in medical research. One of UWMC's missions is to participate in, and encourage, basic and clinical scientific investigation, including the evaluation of new technologies and patterns of practice. SMC is the largest, non-profit, healthcare provider in the Greater Seattle area, consisting of five hospital campuses and a network of more than 100 primary care and specialty clinics. SMC is consistently named the area's best hospital, with two of its campuses recently awarded an 'A' Hospital Safety Score by The Leap Frog Group, an independent national nonprofit group. SMC is known as a regional referral centre providing specialised treatment in various areas including high-risk obstetrics, women's and children's services, and clinical research. SMC had >7000 deliveries in 2011, making it the hospital with the highest number of deliveries in the region. SMC is also committed to ongoing medical research with as many as 600 clinical trials (federal and commercial) being conducted by SMC and SMC-affiliated investigators at any given time.⁹ This emphasis on research and high delivery statistics combined with Seattle's geographical location and other demographic features, are some of the driving factors in selecting these institutions as the North American sites for the INTERGROWTH-21st Project.

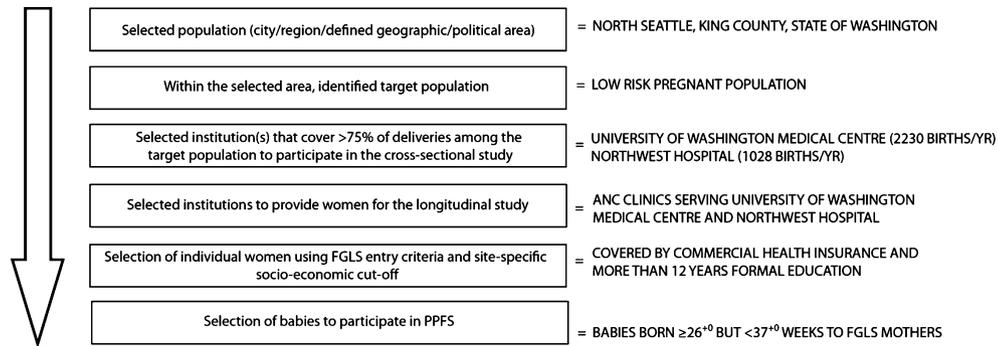


Figure 2. Summary of population-based sampling strategy in Seattle City, WA, USA.

UWMC was also selected as a recruitment site for the Fetal Growth Longitudinal Study (FGLS). The follow-up team and study ultrasound machine were located at UWMC because of its excellent reputation for clinical care and emphasis on research (both clinical and translational). Patients receiving care at UWMC are aware of research opportunities and are frequently approached to participate in studies. The research teams in the selected hospitals were highly qualified to conduct a large-scale, longitudinal study of this nature.

Recruitment and training of study personnel

The local Principal Investigator (PI) attended the ultrasound training session in Oxford in April 2009 and the anthropometry training session in Nairobi in July 2009. This training was then passed on to the ultrasonographers and other team members at the University of Washington. Four highly qualified ultrasonographers were trained by the local PI to perform measurements according to the ultrasound protocol and co-investigators were trained in the use of the anthropometric measurement techniques.^{10,11} A research coordinator was recruited to join the local team in October 2009; she served as the focal person for FGLS, under the supervision of the local PI. To prepare for NCSS at SMC, the local PI attended the UNICEF-sponsored anthropometric measurement training workshop in Amman, Jordan, in May 2012. This was followed by a 3 day infant measurement training session at SMC, conducted by the INTERGROWTH-21st Anthropometry Group in late May 2012. The local PI and manager also attended targeted in-house meetings and introduced the study to the physician and nursing groups upon whom the daily procedures involved in NCSS would impact. A total of two research coordinators and three research assistants were recruited and trained to collect data for NCSS under the supervision of the local PI. In addition, two existing research personnel were trained to provide additional coverage for study staff, as necessary, to ensure maximum

effort in infant measurement coverage in accordance with the study protocol.¹²

Organisational and advocacy activities

The INTERGROWTH-21st PI and Study Director visited the University of Washington site in August 2009 to meet the team and inspect the facility. All study equipment and materials were sent from the Project Coordinating Unit to the University of Washington in preparation for the study launch. Study questionnaires and assessment forms were then approved by the UWMC's Institutional Review Board (IRB) in November 2009 and were deemed appropriate for use with human subjects. All study measurement equipment and the data collection forms for NCSS at SMC were provided by the Project Coordinating Unit. The protocol, procedures, recruitment and data collection materials for NCSS were reviewed and approved by the SMC IRB in April 2012. The implementation of the INTERGROWTH-21st Project in the USA followed the overall protocol and the corresponding logistical strategies described in detail elsewhere.¹³

FGLS implementation

Enrolment logistics

Recruitment began in November 2009 (Figure 3). Screening initially took place at the Maternal Infant Care Center located in the hospital, as well as in several ancillary clinics that provide antenatal care under the University of Washington Medicine umbrella.

Once prescreened and found to be potentially eligible, women were approached during their antenatal appointments, as well as over the telephone. Fliers designed by the Project Coordinating Unit were provided to help recruitment. In addition, presentations were given to clinic staff to encourage providers to refer appropriate patients to the study.

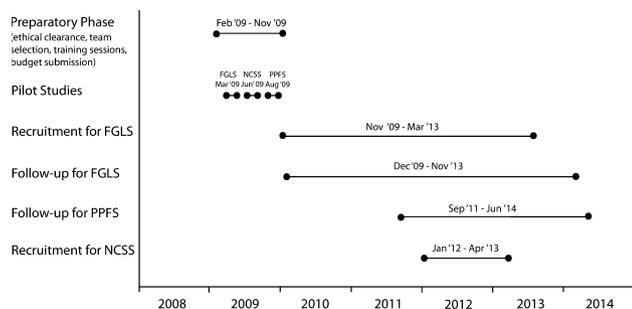


Figure 3. Project timeline in the USA.

In the first 10 months, >1000 women were prescreened via UWMC's online, medical record database. Of these women, only 74 were found to be eligible, 19 of whom declined to participate mostly citing time constraints as the reason for not wanting to participate. Major reasons for exclusion were gestational age >14 weeks, a history of health conditions requiring treatment, body mass index >30, and maternal age >35 years. The number of women >35 years old and with complicated health histories, posed a significant challenge to the recruitment efforts as many otherwise eligible women fell outside the criteria specified in the study protocol.¹²

In an attempt to overcome this very low enrolment rate, an additional recruitment centre at Providence Everett Medical Center (which is affiliated to the UWMC although located in north Seattle) was added to increase the pool of potentially eligible women. Training and standardisation were provided by the Project Coordinating Unit. Another strategy to improve the enrolment rate was to increase advertising efforts by placing articles on several University of Washington websites viewed by students and staff as well as members of the public. Lastly, advertisements were placed in local papers that had a wide circulation within the North Seattle community.

Follow-up logistics

Women enrolled in the study attended ultrasound scan appointments at intervals of 5 ± 1 weeks from 14⁺⁰ weeks of gestation onwards until delivery, but not beyond 42⁺⁰ weeks. The scans were performed using a Philips HD-9 ultrasound machine (Philips Ultrasound; Bothell, WA, USA). The same commercially available machine was used by ultrasonographers at all the study sites to ensure reliable measurements, to facilitate technical support and data transfer, and to ensure that a balance was struck between various criteria, e.g. cost, imaging quality, functionality etc.

Despite the below-target recruitment rate, participants expressed their enjoyment at taking part in the study, and were enthusiastic about the research and the level of care provided by the study team. The importance of attending

the follow-up visits was emphasised to all women recruited. Letters of confirmation were sent to participants informing them of upcoming appointments and they also received telephone calls the day before their appointments. Parking fees were reimbursed for each appointment and women received printed pictures of their ultrasound scan at the end of each appointment. After their baby was born, parents were each given a babygro and photo frame, printed with the study logo to thank them for their participation in the project.

Preterm follow-up logistics

All preterm newborns (born at >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 8 months after delivery to evaluate their postnatal growth according to the INTERGROWTH-21st protocol.¹² Preterm infants were managed according to recommended feeding patterns and clinical practice.¹⁴ Anthropometric measurements (weight, length and head circumference) were taken as soon as possible after birth, then every 2 weeks for the first 8 weeks, and monthly until 8 months. 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 made to reschedule the visit.

NCSS implementation

Enrolment logistics

Before the launch of NCSS at the University of Washington, the research team informed all hospital staff about the study, and held discussions with the neonatology and labour/delivery groups about the infant measurement protocol. As a result of these discussions, the groups agreed to adopt the INTERGROWTH-21st anthropometry protocol as the routine care procedure for the duration of the study.¹¹ This was a significant advantage because it meant that the measurements would not need to be duplicated by both clinical and study teams.

All personnel involved in the measurement of infants underwent rigorous training and standardisation to familiarise the teams with the new procedures and equipment, and to ensure that intra-observer and inter-observer differences in measurements were minimised. An international expert from the INTERGROWTH-21st Anthropometry Group oversaw the first of the quarterly standardisation sessions.¹⁵

The Study Coordinator supervised the collection and management of all data for NCSS. Teams of anthropometrists were organised into a rota to ensure daily coverage

for the duration of the study. Data were entered into an online data management system within 3 days of being collected and were kept confidential, with paper forms locked in drawers and all identifiers kept in a password-protected spreadsheet.¹⁶

Recruitment for NCSS at SMC started in June 2012 following a 3 day on-site anthropometry training and standardisation session. Furthermore, there were several introduction and strategy meetings with nursing staff to facilitate the introduction of the study's activities. All women that delivered at the First Hill campus of SMC were eligible. Women were approached within 24 hours of delivery in patient rooms. They were provided with a Study Information Sheet that introduced study procedures and allowed for a parent to opt out. Research staff answered any questions regarding study procedures before performing newborn measurements (weight, length, and head circumference). Maternal height was measured in the triage when possible or taken from the antenatal records.

During the first month of recruitment at SMC, the majority of babies were measured for NCSS. Reasons for non-measurement included not being able to approach women within 24 hours of delivery and parental refusal. We anticipate, however, that as the study progresses, the recruitment numbers and the rate of recruitment will increase. Training on medical record abstraction continues, and data entry is on-going.

Lessons learned and conclusions

The study teams in Seattle were enthusiastic about participating in this important international study. Women who completed the study reported high satisfaction rates and were pleased to have had the opportunity to participate. The major challenges faced by the team in Seattle were related to the low recruitment rate for FGLS. These challenges were overcome by the inclusion of other ancillary clinics, as well as by increased advertising and raising awareness of the study among the general public. For NCSS, overall institutional support and strategic planning, including introducing study procedures to relevant physician groups and nursing staff, have been central to the continuing success of the study.

Disclosure of interests

None.

Contribution to authorship

M Dighe and L Cheikh Ismail 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.

Funding

This Project was supported by the INTERGROWTH-21st Grant ID# 49038 from the Bill & Melinda Gates Foundation to the University of Oxford, for which we are very grateful.

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. ■

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