

Implementation of the INTERGROWTH-21st Project in China

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The East Asian site in the INTERGROWTH-21st Project was Shunyi County, Beijing, China, which is an affluent suburb of north Beijing delivering approximately 7000 women annually. The Newborn Cross-Sectional Study (NCSS) sample was drawn from two hospitals, covering >85% of births in the county. The Fetal Growth Longitudinal Study sample (FGLS) was recruited from the antenatal clinic of Shunyi Maternal & Child Health Hospital, the larger of the two institutions. Special activities to promote the study in this population included: (1) the distribution of health education materials about the importance of antenatal care and (2) the organisation of seminars by the study team to brief key

stakeholders at the two hospitals about the goals of the research. One of the major challenges at this site in the early stages of the study was a reluctance to have an early ultrasound dating scan (<14⁺⁰ weeks of gestation). This challenge was overcome after a thorough evaluation of the literature regarding the benefits of an early ultrasound scan for dating purposes, as a result of which there was a formal change in hospital policy.

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

The East Asian site for the INTERGROWTH-21st Project was Shunyi County, Beijing, China (Figure 1). Beijing municipality comprises 18 administrative subdivisions: eight urban, eight suburban and two rural/semi-rural. Shunyi is a suburban district approximately 30 km north of the central business district of Beijing. The county lies at a low altitude (250 m) and covers an area of over 1000 km². The population of Shunyi is largely urban, with 636 479 inhabitants recorded at the last census in 2000.³ According to vital registration data, there are approximately 7000 births in the county annually.

In 2007, the average annual income in Shunyi was 19 843 RMB (US\$2950) per person, ranking it fourth richest among the 18 subdivisions of Beijing. The agricultural science and construction industries are major employers in Shunyi and the county is also home to China's largest international exhibition centre. Sixty-nine percent of the population of Shunyi have at least 9 years of education and 90 000 children are currently enrolled in schools within the

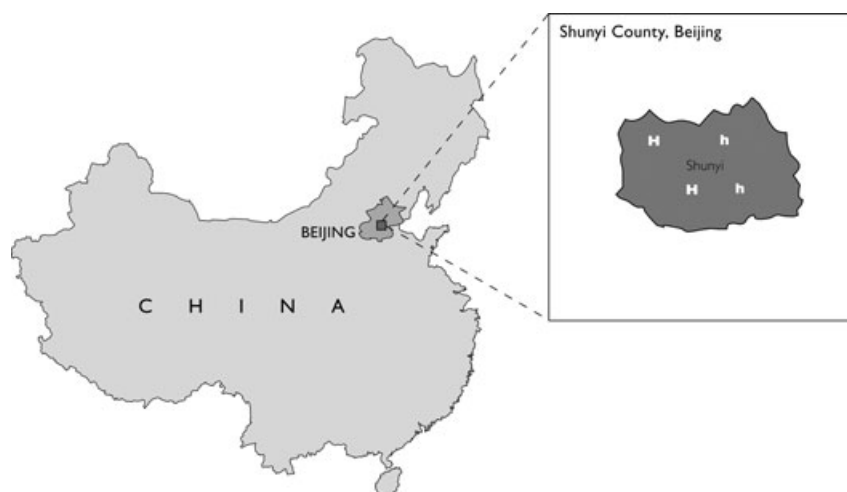


Figure 1. Location of Shunyi County. H: hospital participating in the INTERGROWTH-21st Project; h: hospital not participating in the INTERGROWTH-21st Project.

county.⁴ In short, the population of Shunyi is relatively affluent and well-educated.

The coordinating unit of the study in China was located at Beijing Obstetrics and Gynaecology (OBS/GYN) Hospital Maternal & Child Health (MCH) Institute, a tertiary research hospital affiliated to Capital Medical University. This team was responsible for the overall implementation of the study in China and was in constant contact with the selected hospitals in Shunyi throughout the duration of the project.

Preparatory activities

Hospital selection

We identified four hospitals with obstetric departments in Shunyi County, covering close to 100% of all deliveries in the

county (Table 1). Together, Shunyi MCH Hospital (SMCHH) and Shunyi General Hospital (SGH) account for almost 85% of the total number of deliveries in Shunyi County. These two hospitals were therefore selected to participate in the Newborn Cross-Sectional Study (NCSS) (Figure 2). The Traditional Chinese Medicine Hospital and the Second General Hospital were not selected because of their relatively small number of births and neonatal care arrangements.

SMCHH was selected as the leading research institution for the Fetal Growth Longitudinal Study (FGLS) for several reasons. First, the hospital accounts for 46.8% of the births in Shunyi; second, the facility met the protocol requirement to serve a population of middle to high socio-economic status (24% of the women who deliver in the hospital are university graduates), and third, the obstetric team based there has considerable research experience, having collaborated with both Peking University and WHO on other research projects. The hospital also met all the protocol requirements to serve a population at low risk of fetal growth impairment for FGLS, as indicated by routinely collected hospital data (Table 2).

Recruitment and training of study personnel

Two lead data managers and two lead ultrasonographers were selected and standardised at the centralised training sessions in Oxford in April 2009. A third ultrasonographer attended a 1-week training and standardisation course in Oxford in May 2010. Each team leader conducted similar training sessions with their respective local teams in China. Three research nurses were hired specifically for FGLS to complete the screening forms, arrange the ultrasound dating scans, take informed consent, schedule follow-up appointments and perform online data entry (Figure 3).

Table 1. Perinatal information for hospitals in Shunyi county with obstetric services (2008)

Hospital name	Deliveries (2008)	Perinatal deaths (2008) n (%)	Preterm births (2008) n (%)	Low birthweight deliveries (2008) n (%)
Shunyi MCH Hospital	3328	18 (0.5)	117 (3.5)	78 (2.3)
Shunyi General Hospital	2467	9 (0.4)	80 (3.2)	11 (0.4)
Traditional Chinese Medicine Hospital	1064	3 (0.3)	6 (0.6)	18 (0.2)
The Second General Hospital	13	0 (–)	0 (–)	0 (–)
Total	6872	30 (0.4)	203 (2.9)	107 (1.6)

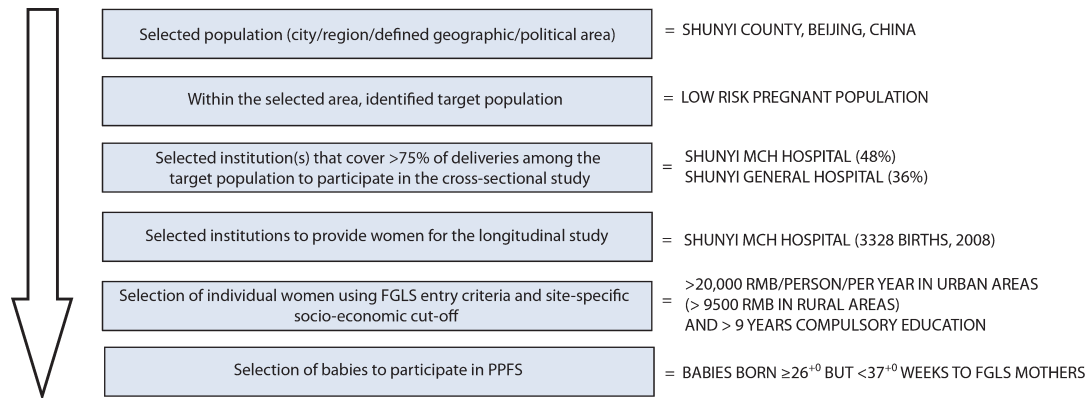


Figure 2. Summary of population-based sampling strategy in Beijing, China.

Table 2. Shunyi MCH Hospital data, indicator of population at low risk of fetal growth impairment

	Value	Protocol requirement met
Low-birthweight rate (%)	2.3	Yes
Perinatal mortality rate (per 1000 live births)	5.4	Yes
Mean birthweight (g)	3322	Yes
Maternal secondary education (%)	71	Yes
Altitude (m above sea level)	250	Yes

For NCSS, two lead anthropometrists were selected from the pool of 11 paediatric nurses and obstetricians, based on their previous experience. They attended the central anthropometric training and standardisation session in Nairobi, Kenya, in June 2009, as described elsewhere in this supplement.⁵ Upon their return to China, the lead anthropometrists took responsibility for organising a similar session for the local teams in Shunyi, in accordance with the anthropometry protocol.⁶ The first two quarterly standardisation sessions were overseen by senior staff from the INTERGROWTH-21st Anthropometry Group.

Organisational and advocacy activities

The Ethics Committee of Beijing OBS/GYN Hospital/MCH Institute approved the study in December 2008. All study materials (protocol, forms, manuals and leaflets) were translated into Mandarin by the coordinating team in Beijing. Translated forms were back-translated to check for consistency and then pre-tested in both hospitals during June 2009. Field teams were trained to complete the forms during the INTERGROWTH-21st Project Leader's visit in October 2009.

Health education leaflets about antenatal care were designed and printed. The leaflets contained information in

Mandarin about the project, antenatal follow-up instructions, advice on what to do in case of hospital admission and contact information for healthcare providers and study personnel.

A number of public relations and advocacy activities took place in the initial stages of the study. During her first site visit to China, the INTERGROWTH-21st Project Leader met officials from the Shunyi Health Bureau and all the senior staff in the Obstetric and Neonatology departments. Press coverage of this event was also secured (see Appendix S1). During the second site visit in October 2009, the Project Leader presented NCSS to obstetric nurses from both SMCHH and SGH to highlight the importance and international significance of the study. This meeting was also attended by the directors of both hospitals, who encouraged their staff to support the study.

FGLS implementation

Recruitment of women for FGLS began in June 2009 (Figure 4). Screening for enrolment took place in the SMCHH ultrasound department, where the FGLS team, HD9 ultrasound machine (Philips Ultrasound, Bothell, WA, USA) and other study equipment were located.

Pilot phase

During the pilot phase, 77 women were screened in 1 week at SMCHH, of whom 23 were found to be eligible, i.e. a potential recruitment rate of 30%. The major reasons for ineligibility were first presentation $> 14^{+0}$ weeks of gestation and reluctance to give informed consent. This highlighted two issues: (1) the need to promote early pregnancy booking and ultrasound dating in this population and (2) that many women were unwilling to participate in research because of local concerns about the use of ultrasound technology in early pregnancy. Before launching the study, the ultrasound dating policy at SMCHH was to perform the

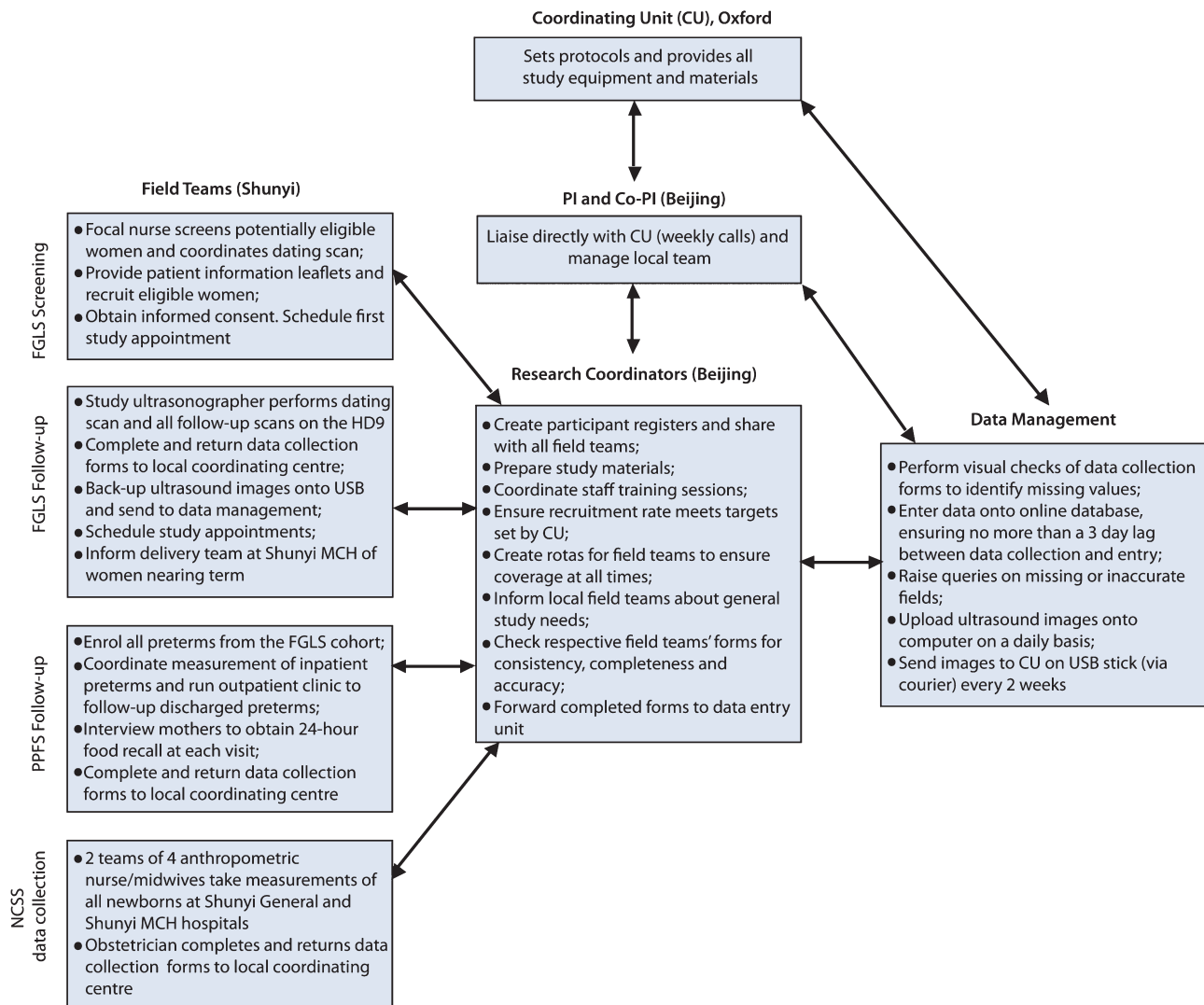


Figure 3. Team coordination in China.

first scan at approximately 20 weeks. However, the literature on ultrasound dating strongly suggests that fetal measurements obtained $>14^{+0}$ weeks are less accurate than those obtained between 9^{+0} and 14^{+0} weeks.⁷ Agreement was therefore reached with the Director of SMCHH that the ultrasound dating policy would change: scans would be performed between 9^{+0} and 14^{+0} weeks of gestation to improve the accuracy of gestational age estimation in accordance with the study protocol. In addition, the coordinating team in China held a seminar for all staff on the advantages of early ultrasound dating. Once the obstetricians and midwives understood the importance of early ultrasound dating, they found it easier to convince women to take part in the research. This represented an important practical contribution of the study to the improvement of antenatal care in the county.

Enrolment logistics

Once the recruitment phase began, all potentially eligible women attending the antenatal clinic at SMCHH were screened according to the INTERGROWTH-21st criteria, which involved identifying women at low risk for all factors known to affect fetal growth and development.² We also used country-specific criteria and cut-off points to identify women at low risk of fetal growth restriction as the result of socio-economic constraints; those failing to meet these criteria were considered not to be eligible for FGLS. The indicator for low socio-economic status used in China was an income of $<20\,000$ RMB/person/per year in urban areas (<9500 RMB/person/per year in rural areas) <9 years of compulsory education.⁴

Gestational age was confirmed by measuring the crown-rump length with the Philips HD9 ultrasound machine

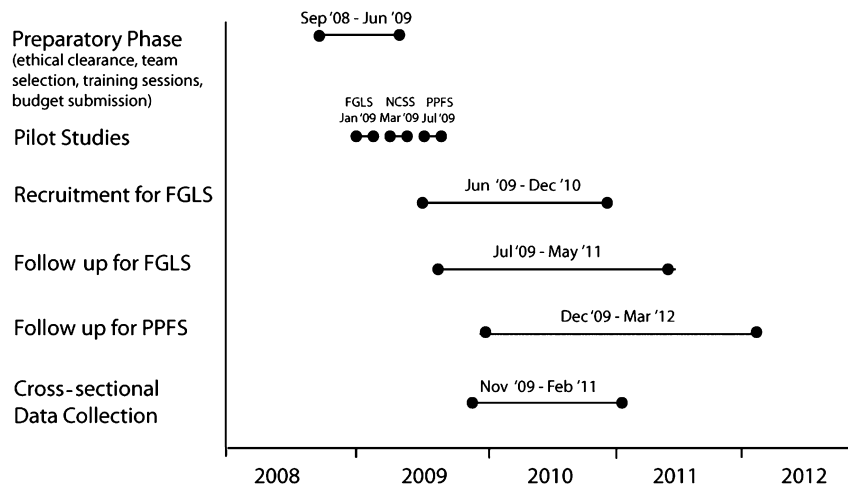


Figure 4. Project timeline in China.

according to the INTERGROWTH-21st protocol.⁸ The same commercially available machine was used by ultrasonographers at all the INTERGROWTH-21st participating centres 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. In the early stages of the study, the recruitment team saw large numbers of women who would have been eligible to participate but were $>14^{+0}$ weeks. As the new ultrasound dating policy was implemented in the hospital, the number of women attending for a dating scan at $<14^{+0}$ weeks of gestation steadily rose.

At the first 6-month review, the INTERGROWTH-21st Project Coordinating Unit identified a problem with the clustering of ultrasound data points at exactly 5-weekly intervals. This pattern arose because the majority of women in China were recruited at exactly 12^{+0} weeks of gestation, and the Chinese team rigorously followed the 5-week interval between scans recommended by the protocol. The recruitment team were, therefore, asked to adapt their early recruitment strategy so that data points were more evenly distributed across the gestational age range. After the review, the recruitment team started visiting the pre-pregnancy clinic to publicise the study and identify all potential candidates who could be recruited between 9^{+0} and 11^{+0} weeks.

Follow-up logistics

A very high retention rate in FGLS was achieved by emphasising to the research team the importance of providing a friendly and personalised service. For example, the Director of the OBS/GYN Department personally saw each woman participating in FGLS at least once in the antenatal clinic. Women in FGLS were also given priority appoint-

ments for antenatal check-ups, which helped to improve compliance. If a woman was late for an appointment, she was contacted immediately by telephone and messages were left if necessary. As a consequence of these strategies, the level of compliance was extremely high and very few women failed to complete the follow-up. To thank mothers for their participation, at the end of the study each was given a bag with the INTERGROWTH-21st logo, which contained baby products.

Preterm follow-up logistics

All preterm babies born at SMCHH are routinely given special observation and attention. Two paediatricians took responsibility for the follow-up of all preterm infants born to mothers in the FGLS cohort. Both were trained to follow the Preterm Postnatal Follow-up Study (PPFS) protocol, including the anthropometric components. During follow-up visits, they measured the infant and provided additional services, including a careful medical check-up and breastfeeding consultation. During the first PPFS visit, a small gift was given to the parents. This attentive and friendly service further strengthened the relationship between the study team and the parents, who reported a high satisfaction rate. There were no significant problems with loss to follow-up or non-attendance.

Challenges arose when FGLS mothers were occasionally referred as having high-risk pregnancies to other tertiary hospitals, where they subsequently delivered. In one of these pregnancies, the birth was not reported to the study team for 48 hours. Cases like this served to remind the team of the importance of good communication with participants. Special efforts were made to remind women to inform the team immediately if they delivered in other hospitals.

Data entry and quality control

The local coordinating team from Beijing OBS/GYN MCH Institute visited SMCHH twice weekly throughout the study. During the visits, data forms were randomly checked against the medical records and the data were entered online. The lag time between data collection and entry was usually no more than 3 days, which enabled queries and missing values to be swiftly resolved.

NCSS implementation

The NCSS began in November 2009 (Figure 4). Data were collected for all babies born at SMCHH and SGH over the following 14 months.

Data collection logistics

Newborns were measured by two teams of four nurses/midwives in each hospital. A rota was organised, with each group divided into pairs, to ensure that all newborns born at the hospitals were measured within 12 hours of delivery, 7 days per week. A paediatrician was also hired to assist with the measurements and supervise the teams at SMCHH, which had a greater number of deliveries (15–20 per day). An obstetrician was responsible for completing the data collection forms from the mothers' medical notes. One problem encountered was that not all women had complete medical records, despite all preparatory activities. In particular, early ultrasound dating and antenatal care information from the first trimester was often missing. The head nurse of the delivery room and the Director of the OBS/GYN Department oversaw all data collection.

Quality control/data entry

The data entry for NCSS in China was carried out by a postgraduate student who checked the forms before entering the data online and queried any missing or suspicious values with the data collection team. No systematic errors were reported after the first quality control exercise on a random 10% sample of the first 1000 deliveries; overall, only 0.11% of variables were entered incorrectly, well within acceptable limits.

Lessons learned and conclusions

The key factors in the successful implementation of the INTERGROWTH-21st Project in China were the strong level of cooperation offered by the health authorities in the region and the close working relationships among the Project Coordinating Unit, the country coordination team and the field teams. The Project Coordinating Unit maintained regular contact with the country coordination team and provided timely assistance when problems arose. Regular site visits were made to motivate the field teams. The country coordination team built a strong relationship with the field teams during the twice-weekly visits to Shunyi and

regularly monitored all aspects of data collection and quality control. Incentives were offered to the field teams to reward their dedication and enthusiasm. The support of the hospital directors and the strong leadership of the project coordinators in both hospitals were other essential factors in the success. We consider that the conditions of the health system in this region of China are ideal for implementing complex clinical and healthcare research projects of this nature.

Disclosure of interests

None.

Contribution to authorship

YP, RYP, HEK and LCI wrote the manuscript and all 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. ■

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