

Implementation of the INTERGROWTH-21st Project in Italy

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Turin, Italy, was one of the two European sites for the INTERGROWTH-21st Project. The sample for the Newborn Cross-Sectional Study (NCSS) was drawn from two obstetric hospitals that together account for 79% of the city's approximately 12 000 births per year. Women were recruited for the Fetal Growth Longitudinal Study (FGLS) from ten antenatal clinics serving the city's largest obstetric hospital, Azienda Ospedaliera OIRM—S. Anna. Special activities to encourage participation and raise awareness of the project in this population included obtaining an endorsement from the coordinator of the city's antenatal care service, and

disseminating information about the project to women through posters and leaflets in antenatal clinics. One of the major challenges at this site was the low recruitment rate in the early phase of FGLS because of the high prevalence of smoking and of women >35 years old in the population. The addition of six extra recruiting clinics served to increase the pool of potentially eligible women who could be screened and led to a marked improvement in the recruitment rate.

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.

The city of Turin, located in the Piemonte region of Northern Italy (Figure 1), was one of the two European

sites selected for the INTERGROWTH-21st Project. Turin has a population of 910 504 and a crude birth rate of 9.3/1000.² Eighty-seven per cent of the population are native Italian; other Europeans and North Africans represent the dominant immigrant groups. In 2008, the average female life expectancy for the Piemonte region was 84 years, and, like many north Italian cities, the population is ageing.² The city has a gross domestic product of US \$58 billion and is a major industrial centre, well-known for its car manufacturing and aerospace industries. Thirteen per cent of city-dwellers hold a university degree, which is close to the Italian national average.³ In short, the population of Turin is relatively affluent, healthy and well-educated.

The team selected to coordinate the study in Turin is based at the Department of Obstetrics & Neonatology of the University of Turin, located in Azienda Ospedaliera OIRM—S. Anna, a large hospital complex. The team has considerable experience in conducting research related to fetal and newborn growth.^{4–7}



Figure 1. Location of Turin, Italy. H: hospital participating in the INTERGROWTH-21st Project; h: hospital not participating in the INTERGROWTH-21st Project.

Preparatory activities

Hospital selection

A census of hospitals with obstetric units in the city was undertaken (Table 1). Based on these data, two hospitals were selected to carry out the Newborn Cross-Sectional Study (NCSS): Ospedale Mauriziano Umberto I and Azienda Ospedaliera OIRM—S. Anna, which has six obstetric units. Together these hospitals have almost 10 000 births per year, covering 79% of the city's deliveries, making the sample truly population-based (Figure 2).

The Azienda Ospedaliera OIRM—S. Anna was selected as the site for recruitment into the Fetal Growth Longitudi-

nal Study (FGLS) as it has a low-birthweight rate of <10%, a mean birthweight of 3108 g and a perinatal mortality rate of 4.8 per 1000, thereby meeting the study protocol requirement to serve pregnant women at low risk of fetal growth impairment.

Organisational and advocacy activities

The implementation of the INTERGROWTH-21st Project in Italy followed the overall protocol and the corresponding logistical strategies described in detail elsewhere.⁸ Initial preparatory activities included obtaining approval from the local Ethics Committee and the endorsement of the Director of the Azienda. Once these approvals were granted, the coordinator of the antenatal care units in Turin was contacted and briefed about FGLS. The INTERGROWTH-21st Principal Investigator and Project Leader visited the site in the early stages of the study to meet the team and present the research aims and objectives. Other FGLS preparatory activities included the dissemination of information leaflets about the study to increase both awareness in antenatal clinics and self-referral of pregnant women from the local area. Before the launch of NCSS, a presentation was made to the consultants and senior nurses on the neonatal ward. The routine hospital policy at S. Anna already involved measuring weight, length and head circumference so written consent from the mothers was not required. Meetings were held to familiarise the anthropometrists with the study protocol and the instructions for completing the data collection forms.

Preparation of study materials

All study forms and materials were translated into Italian and then back-translated to ensure that errors were not introduced during the translation process. A flip chart showing different glass sizes in relation to units of alcohol and a list of high-risk activities were given to each team of interviewers for use during the FGLS screening interview. Meetings were held to familiarise all study staff with the data collection tools and operation manuals before starting recruitment.

Recruitment and training of study personnel

The local principal investigator and co-principal investigator hired a study team comprising a study coordinator, two ultrasonographers, a data manager and seven anthropometrists. Central training sessions in Oxford and Kenya were attended by the lead ultrasonographer and lead anthropometrist, respectively, as described elsewhere in this supplement.^{9,10} The leaders then arranged local training sessions for their teams before starting recruitment. The Italian data manager attended a training workshop in Oxford in April 2009.

Table 1. Delivery information for hospitals with an obstetric department in Turin.

Hospital name	No. of deliveries (2008)
Azienda Ospedaliera OIRM—S. Anna	8760
Ospedale Maria Vittoria	1541
Ospedale Mauriziano Umberto I	1131
Presidio Ospedaliero Martini	1055
Total	12 487

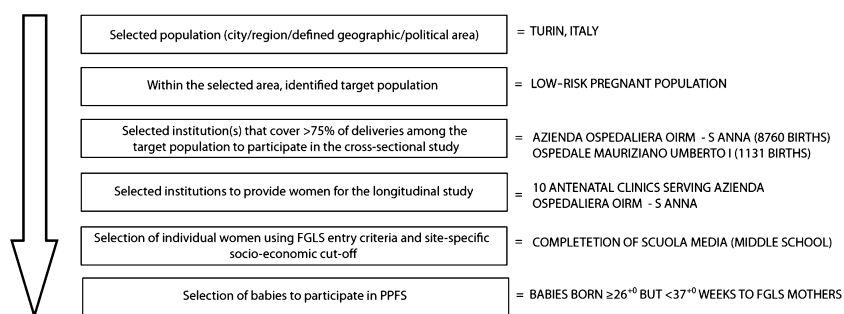


Figure 2. Summary of population-based sampling strategy in Turin, Italy.

FGLS implementation

Screening logistics

Recruitment for FGLS began in October 2009 (Figure 3). Antenatal care in Turin takes place in 17 clinics in the city, all but one of which are located outside the Azienda. In the initial phase of FGLS, four of these clinics were approached and asked to refer eligible women for the study. At first, the recruitment rate in Italy was very low. Part of the reason was the high prevalence of smoking (33.3% among the women prescreened for the study). As in the UK and US centres, maternal age >35 years was also a major reason for exclusion. After 3 months of low recruitment, a review was carried out with members of the Project Coordinating Unit. As a result of these discussions, the decision was taken to enrol several additional clinics to provide recruitment support, bringing the total number of centres to ten. In addition, several obstetricians working in private practice were approached and asked to refer eligible women.

A crucial issue in the recruitment process was to establish and maintain good communication between the study team based in the Azienda and the recruitment centres. To ensure regular contact, a member of the study team was given the specific task of arranging follow-up visits every 2 weeks to collect the screening forms from the antenatal clinics and to discuss any issues related to the recruitment process (Figure 4).

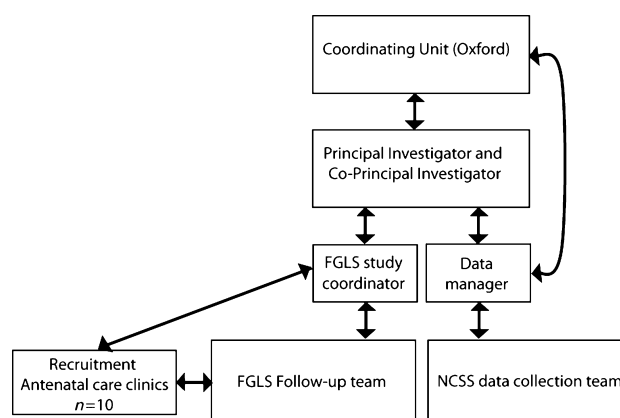


Figure 4. Team coordination in Turin, Italy.

Follow-up logistics

Eligible women were referred by the antenatal clinics to the study team, based at S. Anna, where their eligibility was confirmed and informed consent was obtained. The women attended ultrasound scan appointments at intervals of 5 ± 1 weeks from 14^{+0} weeks of gestation until delivery, but not beyond 42^{+0} weeks. The scans were performed using a Philips HD-9 ultrasound machine (Philips Ultrasound; Botolph Claydon, UK). 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.

To ensure a high retention rate, several strategies were implemented. The study team endeavoured to provide a highly personalised service, giving antenatal advice to women concerned about any aspect of their pregnancy. A 24 hour contact number was also provided to allow women to change the time of their visits if necessary, within the limits defined in the study protocol.¹¹ At each scan appointment, women were thanked for their participation and given printed ultrasound images of their baby. Once women began the follow-up scans and developed a rela-

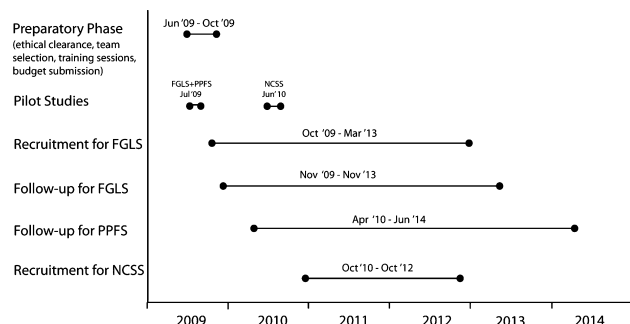


Figure 3. Project timeline in Turin, Italy.

relationship with the research team it was highly unusual for them to withdraw.

Implementation of the Preterm Postnatal Follow-up Study

The first preterm baby from the FGLS cohort in Italy was born in April 2010. From then on, the lead anthropometrists organised outpatient clinics for infant follow-up. Appointments were scheduled according to the study protocol. A contact number was provided to allow mothers to change the time of the visit if necessary, within the limits defined by the study protocol.¹¹ To ensure the lowest possible rate of loss to follow-up, several strategies were implemented. The presence of a paediatrician at each visit proved to be an effective strategy, because mothers appreciated the possibility of getting advice about any aspect of their babies' health, nutrition and growth.

NCSS implementation

The NCSS began in October 2010 (Figure 3). Seven doctors were selected from those that worked in the unit to form the anthropometric data collection team who measured all infants born in both the S. Anna and Mauriziano Hospitals during the NCSS study period according to the anthropometry protocol.¹² An initial training and standardisation session was conducted by a leading expert from the INTERGROWTH-21st Anthropometry Group.

The lead anthropometrist organised the rota to ensure that all maternity wards were visited every day by a pair of anthropometrists, who measured infants born in the previous 24 hours. The anthropometrists also completed the data collection forms using maternal data obtained from the medical records. Neonatal outcomes were monitored daily and recorded on the data collection forms upon hospital discharge. All forms were checked for completeness and accuracy before being sent to the data manager, who entered the data into the central electronic database. Any queries were resolved with the data collection and clinical care teams.

Challenges and lessons learned

The implementation of the INTERGROWTH-21st Project at the Italian site was a demanding task, which carried with it several major challenges. The critical issue for the Italian team in the early phase was the low recruitment rate. To select a healthy target population upon which a standard could be built proved difficult, mainly as a consequence of the high rate of smoking, high body mass index and maternal age > 35 years in the Italian population.¹³ In addition, although staff in the antenatal clinics were enthusiastic about being involved in FGLS, the recruitment rate initially remained low. However, employing someone whose specific role was to maintain good communication with the

recruitment clinics proved remarkably useful in overcoming this problem.

Another critical issue in both FGLS and NCSS was the high volume of data, which occasionally led to a lag between data collection and entry. By facilitating more direct contact between the data manager and ultrasonographers, and by ensuring the timely transfer of completed forms, the study coordinator was able to reduce this lag time dramatically.

A key factor in the successful implementation of the project in Italy was the development of strong personal relationships between the study staff and the women enrolled. Participants were given regular updates about the progress of FGLS in the belief that such feedback would increase their motivation to complete their follow-up scans. Most mothers viewed their participation as contributing to a larger international goal of improving infant and child health and were grateful that the site in Turin played a pivotal role in developing the new growth standards.

Disclosure of interests

None.

Contribution to authorship

FG 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 by 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 21st Century (INTERGROWTH-21st) and its Committees appears in the preliminary pages of this supplement. ■

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–S90.
- 2 ISTAT. Indicatori demografici: febbraio 2008. [www.istat.it/en]. Accessed 18 January 2011.
- 3 Organisation for Economic Cooperation and Development website [www.oecd.org]. Accessed 22 July 2010.

- 4 Bertino E, Spada E, Occhi L, Coscia A, Giuliani F, Gagliardi L, et al. Neonatal anthropometric charts: the Italian Neonatal Study compared with other European studies. *J Pediatr Gastroenterol Nutr* 2010;51:353–61.
- 5 Bertino E, Coscia A, Boni L, Rossi C, Martano C, Giuliani F, et al. Weight growth velocity of very low birth weight infants: role of gender, gestational age and major morbidities. *Early Hum Dev* 2009;85:339–47.
- 6 Bertino E, Coscia A, Mombrò M, Boni L, Rossetti G, Fabris C, et al. Postnatal weight increase and growth velocity of very low birthweight infants. *Arch Dis Child Fetal Neonatal Ed* 2006;91:F349–56.
- 7 Bertino E, Di Battista E, Bossi A, Pagliano M, Fabris C, Aicardi G, et al. Fetal growth velocity: kinetic, clinical, and biological aspects. *Arch Dis Child Fetal Neonatal Ed* 1996;74:F10–15. Erratum in: *Arch Dis Child Fetal Neonatal Ed* 1996;75:F144.
- 8 Villar J, Altman DG, Purwar M, Noble JA, Knight HE, Ruyan P, et al. for the International Fetal and Newborn Growth Consortium (INTERGROWTH-21st). The objectives, design and implementation of the INTERGROWTH-21st Project. *BJOG* 2013: DOI: 10.1111/1471-0528.12047.
- 9 Sarris I, Ioannou C, Ohuma EO, Altman DG, Hoch L, Cosgrove C, et al. for the International Fetal and Newborn Growth Consortium (INTERGROWTH-21st). Standardization and quality control of ultrasound measurements. *BJOG* 2013: DOI: 10.1111/1471-0528.12315.
- 10 Cheikh Ismail L, Knight H, Ohuma EO, Hoch L, Chumlea C. Anthropometric standardisation and quality control protocols for the construction of new international fetal and newborn growth standards: the INTERGROWTH-21st Project. *BJOG* 2013: DOI: 10.1111/1471-0528.12127.
- 11 The International Fetal and Newborn Growth Standards for the 21st Century (INTERGROWTH-21st) Study Protocol. International Fetal and Newborn Growth Consortium. [www.intergrowth21.org.uk]. Accessed 11 October 2010.
- 12 INTERGROWTH-21st Anthropometry Protocol. [www.intergrowth21.org.uk]. Accessed 7 January 2011.
- 13 Ministry of Occupation, Health and Social Politics - Health Department [www.salute.gov.it/imgs/C_17_primopianoNuovo_255_documenti_it emDocumenti_0_fileDocumento.pdf]. Accessed 31 August 2010.