UNIVERSITY OF BIRMINGHAM
University of Birmingham Research at Birmingham

The Born in Guangzhou Cohort Study (BIGCS)

Xiu, Qiu; Lu, Jin-Hua; He, Jian-Rong; Lam, King-bong Hubert; Shen, Song-Ying ; Guo, Yong; Kuang, Ya-Shu; Yuan, Ming-Yang; Qiu, Lan ; Chen, Nian-Nian; Lu , Min-Shan; Li, Wei-Dong ; Xing , Yan-Fei; Bartington, Suzanne; Zhou, Feng-Juan; Cheng, Kar; Xia, Hui-Min

DOI:
10.1007/s10654-017-0239-x

License:
None: All rights reserved

Document Version
Peer reviewed version

Citation for published version (Harvard):
Xiu, Q, Lu, J-H, He, J-R, Lam, KH, Shen, S-Y, Guo, Y, Kuang, Y-S, Yuan, M-Y, Qiu, L, Chen, N-N, Lu , M-S, Li, W-D, Xing , Y-F, Bartington, S, Zhou, F-J, Cheng, K & Xia, H-M 2017, 'The Born in Guangzhou Cohort Study (BIGCS)', *European Journal of Epidemiology*, vol. 32, no. 4, pp. 337–346. https://doi.org/10.1007/s10654-017-0239-x

Link to publication on Research at Birmingham portal

Publisher Rights Statement:
The final publication is available at Springer via http://dx.doi.org/10.1007/s10654-017-0239-x

Eligibility for repository: Checked on 22/3/2017

General rights
Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

•Users may freely distribute the URL that is used to identify this publication.
•Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
•User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
•Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy
While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Download date: 24. Apr. 2024

Abstract

The Born in Guangzhou Cohort Study (BIGCS) is a large-scale prospective observational study investigating the role of social, biological and environmental influences on pregnancy and child health and development in an urban setting in southern China. Pregnant women who reside in Guangzhou and who attend Guangzhou Women and Children's Medical Center (GWCMC) for antenatal care in early pregnancy (less than 20 weeks' gestation) are eligible for inclusion. Study recruitment commenced in February 2012, with an overall participation rate of 76.3%. Study recruitment will continue until December 2018 to achieve the target sample size of 30 000 mother-child pairs. At 30 April 2016, a total of 75 422 questionnaires have been collected, while 14 696 live births have occurred with planned follow-up of cohort children until age 18 years. During the same period a total of 1 053 000 biological samples have been collected from participants, including maternal, paternal and infant blood, cord blood, placenta, umbilical cord, and maternal and infant stool samples. The dataset has been enhanced by record linkage to routine health and administrative records. We plan future record linkage to school enrolment and national examination records.

Keywords

Design; Cohort study; Child; Pregnancy; Record linkage

Introduction

Since initiating economic reform and opening-up trading policy in 1978, China has experienced an unprecedented period of economic and social development. Significant progress in healthcare delivery and utilization are reflected in improved human development indicators, best illustrated by the reduction in child mortality from 46.0 to 13.7 per 1000 live births (1996 - 2012) [1] and decline in maternal mortality from 141.7 to 20.1 per 100 000 (1996 - 2015) [2, 3]. Meanwhile, rapid economic ascendance has presented new health and social challenges, including an increasing burden of non-communicable diseases.

The Born in Guangzhou Cohort Study (BIGCS) is a large-scale prospective study of mothers and their children from the prenatal period to adult life in the urban setting of Guangzhou, China. Guangzhou is located on the Pearl River Delta in southern China (Figure 1), one of the first ports in China to initiate global trading, rapidly developing into a cosmopolitan city. The population has nearly tripled in the past 30 years, from 4.8 million in 1978 to 13.1 million in 2014, meanwhile during the same period the Per Capita Gross Domestic Product increased from < 1000 yuan to 128 000 yuan [4]. Undoubtedly, economic and social developments have had a profound impact on the health of the resident population. The contemporary generation of women of childbearing age in Guangzhou has experienced this phase of rapid economic development and social transition, including the now abolished one child family planning policy. Given these circumstances, a birth cohort of the contemporary generation of mothers and their children provides a unique opportunity to investigate the short- and long-term health consequences from a life course perspective. Compared to other contemporary birth cohorts in mainland China [5, 6], BIGCS has a larger sample size and more comprehensive collection of biological samples with the potential to assess internal exposure and address key research questions in maternal and child health. Most importantly, we anticipate the rapid economic development and social transition occurring in Guangzhou is likely to be replicated in other places China in the future. Thus BIGCS will provide information to

inform researchers, policy makers and other stakeholders in these areas.

In the context of this unique setting and period of historical importance, the objectives of BIGCS is to investigate the influence of social, genetic and environmental factors on a range of maternal, child and adolescent health outcomes to inform and improve the lives of future generations of children and their families, and to provide a basis for intervention strategies, of direct relevance to other cities in China and similar economic transition settings worldwide. Five major research themes will be explored: maternal health and pregnancy outcomes, fetal growth and development, immunological development in early life, neurodevelopmental pathways and parental risk factors for infant and child health outcomes.

Funding for BIGCS was provided by the Guangzhou Women and Children's Medical Center (GWCMC), the Guangzhou Science Technology and Innovation Commission, and Health and Family Planning Commission of Guangzhou Municipality.

Study cohort

The BIGCS recruits women during early pregnancy at two campuses of the GWCMC. This maternity center is one of the largest tertiary hospitals in China, with 18 000-20 000 annual deliveries of 220 000 total births in the Guangzhou municipality. In the antenatal outpatient clinic setting trained study personnel invite participation of pregnant women attending for early pregnancy examination. Eligible women are those of Chinese nationality, living in Guangzhou who are at less than 20 weeks of gestation and who intend to deliver at one of the two GWCMC campuses. Further criteria include ability to complete questionnaires in Mandarin or Cantonese language and an intention to remain in Guangzhou for at least three years after delivery. Partners of the eligible women are also invited to participate. Informed, written consent is obtained from all study participants and may be withdrawn at any stage of the study.

A three-month pilot study was conducted to evaluate the effectiveness of recruitment and follow-up methods, prior to the commencement of full-scale study recruitment in February 2012. The overall cohort sample size target is 30 000 mother-child pairs, which provides adequate power to detect moderately strong causal effects of common environmental, social and biological exposures. (Supplementary table 1)

By April 2016, we had approached 22 569 eligible pregnancies, of which 17 214 (from 17 050 women) provided consent (participation rate 76.3 %). Table 1 shows baseline characteristics among women who agreed and disagreed to participate in the study, with women of higher educational status being more likely to participate, although mean age was similar in both groups. Of those partners present at initial recruitment (n=7131, 41.4%) in early pregnancy, overall 4080 (57.2%) participated in the study.

Follow up

Maternal and paternal information, clinical measures and biological samples are collected at recruitment, 24-27 and 35-38 weeks of gestation. After delivery, maternal information including employment status, anthropometric measures and physical and mental health- related information would be followed up.

For cohort children, neonatal birth information including mode of delivery, birth characteristics (e.g. birth weight, birth length) and perinatal outcomes are obtained from routine medical records. Mothers are interviewed and children are examined in GWCMC's child health care clinics at age 6 weeks, 6, 12 and 36 months, or by telephone interview for those mothers who are unable to bring their child to the pediatric clinic. We plan to follow-up all cohort children until age 18 years.

Figure 2 shows study participant recruitment and follow-up until 30 April, 2016. At this stage of recruitment, a total of 1090 women (6.3%) had withdrawn consent for participation, with the following reasons (obtained by multiple choice item): (i) family disapproval (10.7%), (ii) reluctance to complete time-consuming questionnaire

(50.9%), (iii) unwilling to provide a blood sample (10.7%), (iv) selection of an alternative hospital for antenatal examination or delivery (14.4%), (v) moved out of Guangzhou (8.9%), and (vi) other reason (9.3%).

Table 2 presents the socio-demographic characteristics of those women who have withdrawn consent for study participation. Compared to those who continue in the study, women who opted out of the study were more likely to have lower levels of education, income and pre-pregnancy body mass index (BMI) and to be multiparous.

Data collection

For participating mothers, a summary of measures (questionnaire, clinical assessment, anthropometry and biological samples) collected at each follow-up phase are presented in Table 3. Semi-structured questionnaires are used to collect maternal data, including validated measures for socioeconomic status, occupational exposure, physical activity, dietary habits and mental health. Maternal dietary habits were evaluated using a validated food frequency questionnaire [7]. Mental health (depression and anxiety) during pregnancy was assessed by a 20-item self-rating depression scale (SDS) and a 20-item self-rating anxiety scale (SAS) [8, 9], and the postpartum depression was evaluated using the Chinese version of the Edinburgh Postnatal Depression Scale (EPDS) [10]. Clinical information during pregnancy including antenatal screening test results, ultrasound findings, obstetric complications and prescribed medication are obtained through medical records. At all contact points post-partum, we collect information on anthropometry, medical conditions and mental health.

For participating fathers, socio-demographic, family and personal medical history are recorded by the baseline questionnaire at recruitment, and blood samples (7 mL) are collected at the time of questionnaire completion (Table 3).

For participating children, data on newborn birth characteristics is obtained from delivery records. Cord

blood, umbilical cord, placenta were collected at birth. Heel prick dried blood spots (3 spots, each has a diameter of >8 mm) are collected within 48 hours after birth. Stool samples are collected at birth and at 6 weeks of age. In early childhood, we take advantage of the routine state health checks at 6 weeks, 6, 12 and 36 months of age, provided free of charge for children living in Guangzhou. Each check comprises a blood test, clinical assessment, physical measurements (weight, body length/ height, head/ chest/ abdomen/ upper arm circumference, skinfold thickness, bregmatic fontanel), clinical examination (dental eruption and breast/ testis volume) and neurobehavioral assessment using standardized tools (Chinese versions of Ages and Stages Questionnaire- III, ASQ-III and Gesell Development Scale, GDS), all of which are performed by trained members of the research team. The instruments of ASQ-III and GDS have been validated in Chinese population [11, 12]. The follow-up schedule of the preterm birth infants is chronologically the same as the full-term infants. Further clinical information including clinical test results, medication history and disease diagnosis are collected through record linkage to children's medical information. Data on immunization history and physical measurements of children before age 6 years are similarly extracted from community health records. In addition, during the pre-school period, blood samples (4 mL) will be collected at age 1 and 3 years (Table 4). We plan to obtain routine health and academic performance information after age 6 years by record linkage to the databases of the Guangzhou Bureau of Education.

Key findings and publications

The median maternal age at recruitment was 29.2 years. Of those participating in the study, 83.5% of mothers were primiparous, 65.3% had an educational level of undergraduate and above, 42.7% were in employment with modal category of maternal income 4501-9000 yuan per month, which is higher than the average level of per capita monthly income in China (4134 yuan in 2015) [13]. The mean total gestational weight gain was 14.98 kg

among 6085 primiparous women who delivered a term (≥ 37 weeks gestation) singleton baby. Within the same period (February 2012 to April 2016), there were 14 696 deliveries, resulting in 14 142 singleton and 332 multiple births. Among the 14 142 singleton births, 730 (5.2%) were preterm birth (PTB).

Using data on 9 044 singleton live births whose mothers were recruited between February 2012 and December 2014, we found maternal age (OR: 1.06, 95% CI: 1.03-1.09 for each year increase), history of preterm delivery (OR: 3.22, 95% CI: 1.55-6.67 for multiparous women with previous preterm delivery), vaginal bleeding during pregnancy (OR: 1.71, 95% CI: 1.39-2.10) and folic acid intake before pregnancy (OR: 0.77, 95% CI: 0.62-0.95) were associated with the risk of PTB (manuscript submitted).

Gestational diabetes mellitus (GDM) is one of the most prevalent major complications during pregnancy. Based on the findings from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study [14], the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommended a new set of criteria for diagnosing GDM in 2010 [15], resulting in higher diagnosed rates of GDM. For example, in China the prevalence has risen markedly from 5.0% in 2006 to 22.7% in 2011; while in BIGCS it is diagnosed in 14.2% of the mothers. We assessed the risk of LGA according to the different GDM diagnostic criteria among 6 993 participants who underwent a 2-h 75 g oral glucose tolerance test (OGTT) between 22 and 28 weeks gestational age. We found that a single measurement of fasting plasma glucose level can identify women at increased risk of delivering a LGA baby. The addition of 1-h and/or 2-h plasma glucose levels has only very limited additional value [16].

As a modifiable factor, maternal dietary habits may contribute to the development of GDM [17]. Using dietary information collected by the mid-pregnancy 64-item food-frequency questionnaire from 3063 mothers, we characterized four predominant dietary patterns during pregnancy (vegetable, protein-rich, prudent, and sweets and seafood patterns), and observed an increased risk of GDM associated with high intake of sweets and

seafood (OR: 1.23; 95% CI: 1.02, 1.49) and reduced risk among those had high intake of vegetables (OR: 0.79; 95% CI: 0.64, 0.97) [18].

We have also examined the association between maternal progesterone supplementation during early pregnancy (<14 weeks) and adverse birth outcomes in 6617 pregnant women. Our findings suggest that progesterone use in early pregnancy may offer limited benefit and could increase the risk of adverse birth outcomes. Due to the high prevalence of progesterone use in China, this could potentially have important public health significance [19].

We are also interested in the maternal mental health. We found evidence linking maternal exposure to passive smoking and depression during pregnancy. Among 6 247 pregnant women, high exposure to passive smoking (≥30 minutes/day) during early and late pregnancy both increased the risk of maternal depression during late pregnancy (RR: 1.49, 95% CI: 1.17-1.91 and RR: 1.45, 95%CI: 1.07-1.97, respectively) compared to those who were not exposed (< 1 minute/day). We also found an association between passive smoking during pregnancy and postpartum depression (RR: 1.60, 95%CI: 1.15, 2.22) [20]. This may be mediated by systemic inflammation, as demonstrated by an association between plasma c-reactive protein (a biomarker for inflammation) levels in late pregnancy and incidence of postpartum depression (OR: 1.13; 95% CI: 1.02, 1.26 per unit increase) in a subsample of 513 pregnant women from BIGCS [21].

Main strengths and weaknesses

This cohort has a number of strengths. (i) The large specific population in the BIGCS has undergone a unique and exceptionally rapid period of social, economic and epidemiological transition. (ii) We have collected detailed comprehensive information using a range of techniques, including clinical information (medical record linkage, measurements of medical examinations), self-report and multiple sequential biological samples. The

comprehensive biobank we have constructed is used to store a wide range of biological specimens at a central on-site facility, with standardised procedures for sample handling, processing and analysis to ensure high levels of validity and reproducibility. Also, the collection of stool samples enables us to investigate the effects of microbiota on maternal and child health. (iii) We are actively engaging with technical advances and rapid development of emerging new technologies, including metabolomics, metagenomics, immunomics, and proteomics. Such applications have the potential to provide insight into short- and long-term consequences of those fetal and early life macro and micro-environmental exposures which accompany social transition and economic development [22].

Several challenges of this ambitious cohort study should be considered. Social development in Guangzhou is at a much more advanced stage compared with many parts of China, particularly the more rural provinces in the west. It is not the intention of this study to recruit a nationally representative sample of pregnant women across China. In fact, our sample is not representative of the Guangzhou population because of mothers receiving antenatal care at the GWCMC are likely to be more affluent and older and have higher education than the contemporary pregnant women in Guangzhou, hence limiting generalizability of our findings. This selection bias had been recognized and acknowledged from an early design stage of our study. Nevertheless, even within our participants we were able to observe a relatively wide spread across all social-economic status (SES) indicators, hence enabling us to explore the differences in health consequences across different SES strata. Furthermore, the aim of the study is to examine and identify potential associations between exposure and key maternal and child health outcomes, and such estimates provide validity even when assessed within a non-representative sample of the overall study population. The collection of questionnaire information or biological samples during the preconception period remains a challenge as experienced within the majority of large-scale birth cohort studies. Although not possible for the entire cohort, we are planning a preconception recruitment of a subset of women

during the second recruitment phase.

Data available

The Born in Guangzhou Cohort Study welcomes collaboration and we are keen to establish BIGCS as a research platform. More information is provided on our website (http://www.bigcs.com.cn/).

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Wang Y, Li X, Zhou M, Luo S, Liang J, Liddell CA et al. Under-5 mortality in 2851 Chinese counties, 1996-2012: a subnational assessment of achieving MDG 4 goals in China. Lancet. 2015. doi:10.1016/S0140-6736(15)00554-1.
2. Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, Shackelford KA, Steiner C, Heuton KR et al. Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384 (9947):980-1004. doi: 10.1016/ S0140-6736 (14)60696-6.
3. National Health and Family Planning Commission of the People's Republic of China. Statistics of Health and Family Planning in 2015. http://wwwnhfpcgovcn/ewebeditor/uploadfile/2016/08201608051604103 98 pdf. In Chinese. Accessed 11 August, 2016.
4. Statistics Bureau of Guangzhou Municipality. Principal Aggregate Indicators on National Economic and Social Development and Growth Rates in Annual Statistics of 2015. http://data.gzstats.gov.cn/gzStat1/chaxun/njsj.jsp. Accessed 16 April, 2016.

5. Qiu J, He X, Cui H, Zhang C, Zhang H, Dang Y et al. Passive smoking and preterm birth in urban China. American journal of epidemiology. 2014;180(1):94-102. doi:10.1093/aje/kwu092.

6. Tao FB, Hao JH, Huang K, Su PY, Cheng DJ, Xing XY et al. Cohort Profile: the China-Anhui Birth Cohort Study. International journal of epidemiology. 2013;42(3):709-21. doi:10.1093/ije/dys085.

7. Yuan MY, He JR, Chen NN, Lu JH, Shen SY, Xiao WQ et al. Validity and Reproducibility of a Dietary Questionnaire for Consumption Frequencies of Foods during Pregnancy in the Born in Guangzhou Cohort Study (BIGCS). Nutrients. 2016;8(8). doi:10.3390/nu8080454.

8. Zung WW. A SELF-RATING DEPRESSION SCALE. Archives of general psychiatry. 1965;12:63-70.

9. Zung WW. A rating instrument for anxiety disorders. Psychosomatics. 1971;12(6):371-9. doi: 10.1016/ s0033- 3182(71)71479-0.

10. Lee DT, Yip SK, Chiu HF, Leung TY, Chan KP, Chau IO et al. Detecting postnatal depression in Chinese women. Validation of the Chinese version of the Edinburgh Postnatal Depression Scale. The British journal of psychiatry : the journal of mental science. 1998;172:433-7.

11. Wei M, Bian X, Squires J, Yao G, Wang X, Xie H et al. [Studies of the norm and psychometrical properties of the ages and stages questionnaires, third edition, with a Chinese national sample]. Zhonghua er ke za zhi = Chinese journal of pediatrics. 2015;53(12):913-8.

12. Group BMDC. Gesell Developmental Diagnosis Scale. Beijing Mental Development Cooperative Group. 1985.

13. Nation Bureau of Statistics of China. Annual data. http://data.stats.gov.cn/index.htm. Accessed 15 February, 2017.

14. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR et al. Hyperglycemia and adverse pregnancy outcomes. The New England journal of medicine. 2008;358(19):1991-2002.

doi:10.1056/NEJMoa0707943.

15. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes care. 2010;33 (3):676-82. doi: 10.2337/dc09-1848.

16. Shen S, Lu J, Zhang L, He J, Li W, Chen N et al. Single fasting plasma glucose measurement compared with 75 g oral glucose-tolerance test in prediction of adverse perinatal outcomes: a prospective cohort study from China. Lancet. 2016;388 Suppl 1:S8. doi:10.1016/S0140-6736(16)31935-3.

17. Zhang C, Ning Y. Effect of dietary and lifestyle factors on the risk of gestational diabetes: review of epidemiologic evidence. The American journal of clinical nutrition. 2011;94(6 Suppl):1975S-9S. doi:10.3945/ajcn.110.001032.

18. He JR, Yuan MY, Chen NN, Lu JH, Hu CY, Mai WB et al. Maternal dietary patterns and gestational diabetes mellitus: a large prospective cohort study in China. The British journal of nutrition. 2015;113(8):1292-300. doi:10.1017/S0007114515000707.

19. Shen SY, Lu JH, He JR, Liu Y, Chen NN, Yuan MY et al. Progesterone use in early pregnancy: a prospective birth cohort study in China. The Lancet. 2015; 386 S58. doi: http://dx.doi.org/ 10.1016/ S0140-6736 (15)00639-X.

20. He JR, Liu Y, Lu JH, Shen SY, Li WD, Guo Y et al. Passive smoking during pregnancy undermines maternal mental health: results from the Born in Guangzhou Cohort Study, China. Poster Abstract. The Lancet and Chinese Academy of Medical Sciences (CAMS) Health Summit; Beijing, China 2015.

21. Jin-hua L, Yong G, Song-ying S, Fang H, Nian-nian C, Ying-fang W et al. Association between inflammatory reaction at late pregnancy and the risk of postpartum depression: A prospective cohort stud. Chinese Journal of Woman and Child Health Research. 2014; 25 (3):391-3.

22. Swanson JM, Entringer S, Buss C, Wadhwa PD. Developmental origins of health and disease: environmental exposures. Seminars in reproductive medicine. 2009; 27(5):391-402. doi: 10.1055/ s-0029-1237427.

Figure legends

Figure 1 Geographical location of the BIGCS eligible study area in southern China and site of the two campuses of the Guangzhou Women and Children's Medical Centre

Figure 2 Flow chart of cohort participant recruitment and follow-up by 30 April, 2016

Figure 1

Click here to download Figure Figure 1.jpg

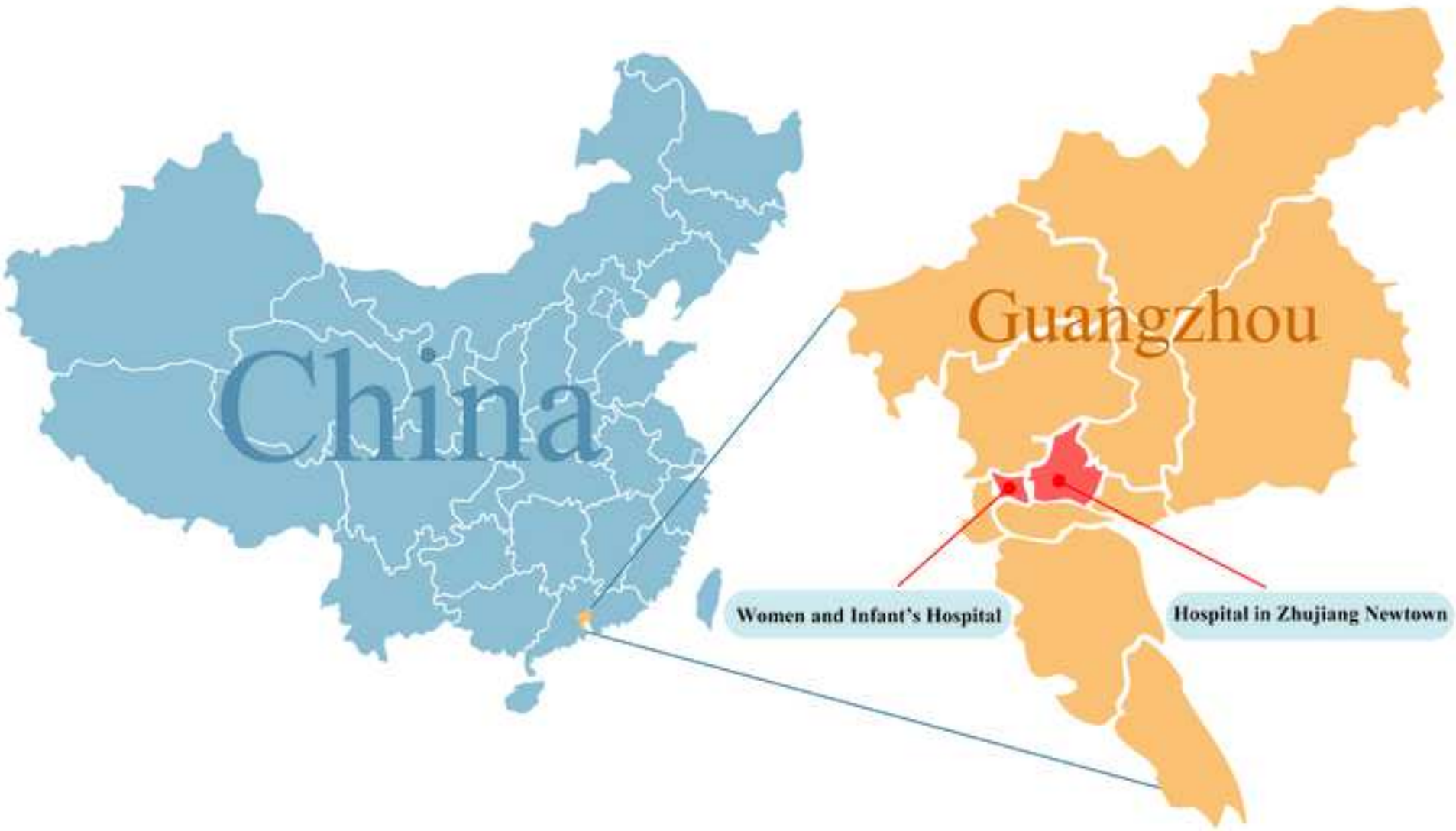
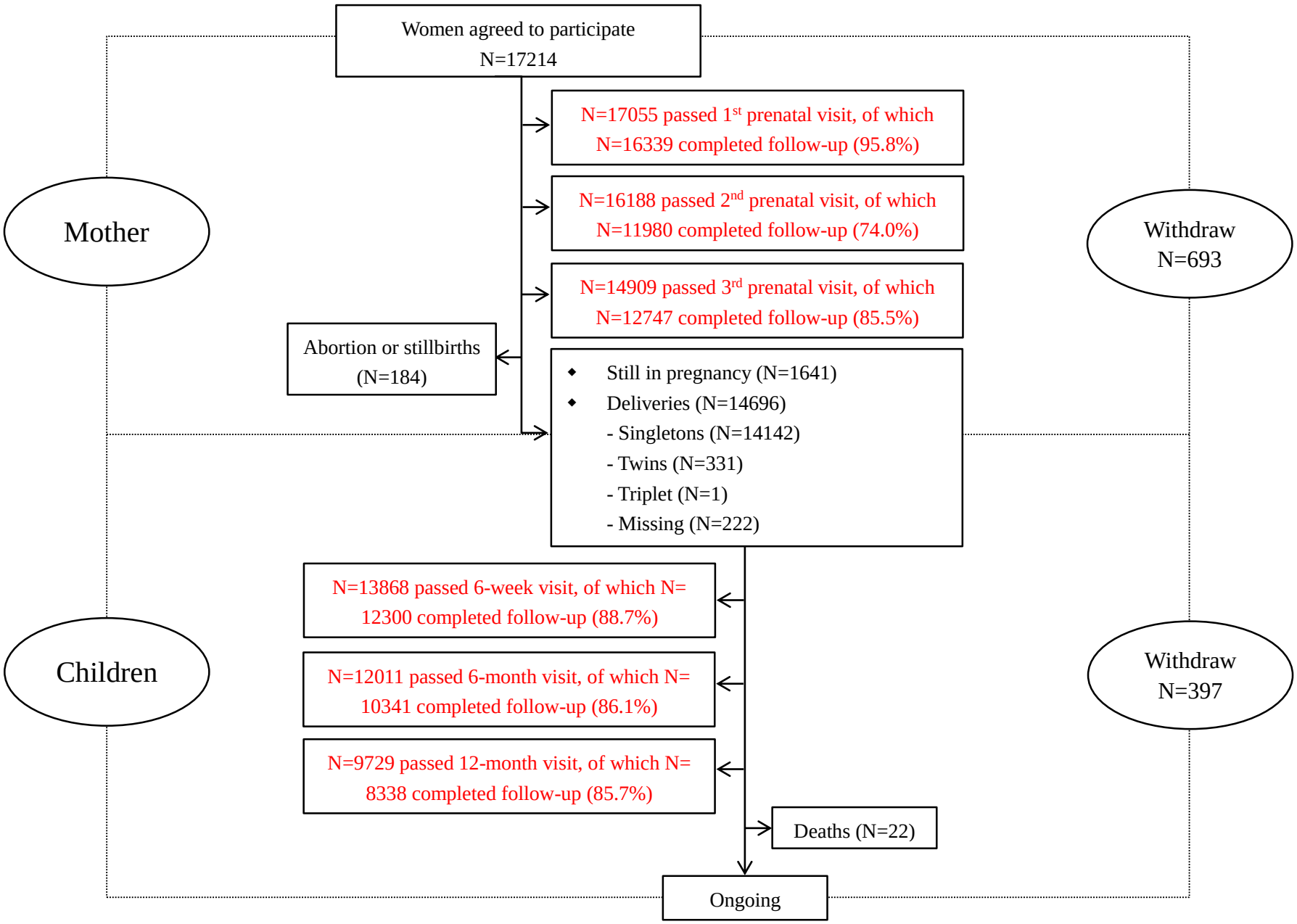


Figure 2

Click here to download Figure Figure 2-revised.docx



Click here to download table Tables-revised.docx

Table 1 Comparison of characteristics among women who agreed and disagreed to participate in BIGCS.

Characteristics	Agreed	Disagreed	*P* value *
N	17214	5355	
Age (years), mean (SD)	29.2 (3.5)	29.0 (3.6)	< 0.01
Education level, n (%)			
High school or below	1720 (10.0)	807 (15.1)	< 0.01
Vocational/technical college	4253 (24.7)	1452 (27.1)	
Undergraduate	9132 (53.1)	2487 (46.4)	
Postgraduate	2109 (12.3)	609 (11.4)	

* Significant differences across groups were tested by using t test or Wilcoxon rank test.

Table 2 Comparison of characteristics among women who remained in the cohort and those who have withdrawn.

Characteristics	Remained in the cohort	Consent withdrawn	*P* value *
N	16124	1090	
Age (years), mean (SD)	29.3 (3.5)	29.1 (3.8)	0.11
Education level, n (%)			
High school or below	1508 (9.4)	188 (17.3)	<0.01
Vocational/technical college	3955 (24.5)	285 (26.2)	
Undergraduate	8620 (53.5)	502 (46.1)	
Postgraduate	2041 (12.7)	115 (10.6)	
Monthly income (Yuan), n (%)			
<1500	1543 (10.1)	103 (13.8)	0.04
1500-4500	4367 (28.7)	211 (28.2)	
4501-9000	6503 (42.8)	304 (40.6)	
≥9001	2799 (18.4)	130 (17.4)	
Pre-pregnancy BMI (kg/m2), mean (SD)	20.4 (2.7)	20.1 (2.6)	<0.01
Parity, n (%)			
Primiparous	13189 (83.5)	720 (81.5)	0.01
Multiparous	2599 (16.5)	164 (18.6)	
Delivery mode, n (%)			
Vaginal labor	8679 (63.7)	215 (60.7)	0.26
Cesarean delivery	4953 (36.3)	139 (39.3)	
Preterm birth, n (%)			
No	13240 (94.0)	351 (92.1)	0.14
Yes	853 (6.1)	30 (7.9)	
Infant gender, n (%)			
Male	7516 (52.5)	194 (51.2)	0.61
Female	6795 (47.5)	185 (48.8)	
Birth weight(g), mean (SD)	3156 (458)	3159 (485)	0.88
Low birth weight, n (%)			
No	13228 (93.3)	344 (92.5)	0.52
Yes	947 (6.7)	28 (7.5)	

* Significant differences across groups were tested by using t test, Wilcoxon rank test or chi-square test.

Table 3 Data collection of mothers and their partners in BIGCS.

Maternal data	Antenatal (weeks)				Postnatal (months)				
	<20	24-27	35-38	Delivery	6 weeks	6	12	36	Continue
Mothers									
Demographics / Social									
Date of birth	√								
Ethnic group	√								
Education	√								
Marital status	√								
Family members	√								√
Housing, income	√								√
Occupation / employment									
Working status	√		√					√	√
Working category, hours and posture	√		√						√
Working environment	√		√						√
Dwelling environment									
Decoration	√								√
Pets	√		√						√
Mould	√		√						√
Lampblack, insecticide, incense	√		√						√
Lifestyle									
Smoking status, passive smoking	√		√		√				√
Alcohol	√	√							√
Beverage	√	√	√						
Drinking water	√	√	√						
Physical activity	√		√		√				√
Health									
Height	√								
Weight	√	√	√	√	√	√	√	√	√
Blood pressure		√	√		√	√	√	√	√
Blood glucose					√	√	√	√	√
Health status	√		√			√			√
Menstrual cycle	√								
Family medical history	√								
Medical history	√								
Medications	√		√		√	√	√	√	
Vaginal bleeding during pregnancy	√		√						
Micronutrient supplements	√		√		√				√
Mental health	√		√		√	√	√	√	√
Sleeping quality	√		√						
Diet (food frequency questionnaire)		√			√				
Biological samples									
Blood		√*	√						
Faeces		√	√						
Medical Records									
Clinical test results				√					
Ultrasound measurements				√					
Pregnancy complications (e.g. GDM, PIH)				√					

Medication			√
Delivery date, delivery mode			√
Fathers			
Demographics / Social			
Date of birth	√		
Ethnic group	√		
Education	√		
Housing, income	√		
Health			
Height	√		
Weight	√		
Medical history	√		
General health	√		
Family medical history	√		
Biological samples			
Blood		√	

* The first maternal blood sample was collected before 28 weeks of pregnancy.

Table 4 Data collection of children in BIGCS.

Children's data	Time points (months)					
	At birth	6 weeks	6	12	36	Continue
Gender	√	√*				
Date of birth	√	√*				
Birth weight / length, apgar score	√	√*				
Physical measurements		√	√	√	√	
Bregmatic fontanel		√	√	√		
Hip joint examination		√				
Dental eruption			√	√		
Breast/testis volume					√	
Diet						
Breastfeeding		√	√	√	√	
Milk or formula feeding		√	√	√	√	
Food frequency/preference			√	√		
Eating behavior/dietary restraint					√	
Chinese herbal medicine		√	√	√	√	
Water consumption		√	√	√		
Micronutrient supplements		√	√	√	√	
Family member, parenting practices		√	√	√	√	
Sleeping		√	√	√	√	
Dwelling environment						
Lampblack, insecticide, incense		√	√	√	√	√
Mould			√	√	√	√
Router use		√	√	√	√	√
Passive smoking status			√	√	√	√
Pets			√	√	√	√
Negative events						
Illnesses (fever, skin rash, wheeze& allergies)		√	√	√	√	√
Medications		√	√	√	√	
Immunization record		√	√	√		
Neurobehavioral development		√	√	√	√	
Language environment & learning languages					√	
ASQ-III			√	√	√	
Gesell				√		
Medical Records						
Clinical test results		√	√	√	√	
Medication		√	√	√	√	
Diagnosis		√	√	√	√	√
Biological samples						
Cord blood	√					
Umbilical cord, placenta	√					
Blood				√	√	√
Faeces	√	√				√

* This information is collected for the women who do not deliver at Guangzhou Women and Children's Medical Center.

Supplementary table 1

Click here to access/download
Supplementary material
Supplementary table 1.docx

COI form


Click here to access/download
Supplementary material
COI form.pdf