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Title: Maximising the potential of Chinese birth cohort studies: a systematic review of mother-baby

cohorts in Mainland China

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Word count text: 3494 words

Word count abstract 210 words

Figures: 4

Tables: 3

Supplementary file: 1

Conflict of interest: None declared

Abstract

Background: There is now a growing interest in early-life influences on adult diseases in China. A number of birth cohorts have been established. This systematic review provided a better understanding of the development of mother-baby cohorts in China.

Methods: We conducted a systematic review for research or profile papers in English/Chinese that reported data from mother-baby cohorts in mainland China, with ≥1y follow-up after birth. We identified 315 papers, corresponding to 31 cohorts from 19 provinces/mega-cities.

Results: All cohorts started in 1999-2017 (21 after 2010) and were set-up with broad objectives, or specific scientific focus. The baseline sample size varied, from <500 to >300,000 mothers. A majority of cohorts were initiated during pregnancy and followed children to <10y, only 6 to adolescence, none into adulthood. These cohorts mostly collected samples from mothers and babies, in addition to using interviews/questionnaires to collect information about pregnancy, birth and child health. Most cohorts recruited from a single province/city. The large Western region was under-studied.

Conclusions: Mother-baby cohorts have developed rapidly in China, but usually with short follow-up duration. Extending the follow-up of children and developing cross-cohort collaboration will increase the diversity, size and coverage of the sample, allow studying early influences on life-course health and identify targets for early intervention in Chinese population.

Key words: Mother-baby cohort, birth cohort, environmental exposure, maternal and child health, life course study, China, systematic review.

Funding: This work was supported by University College London Global Engagement Funds. The research was supported in part by the National Institute for Health Research (NIHR) Great Ormond Street Hospital Biomedical Research Centre.

Research in context

Evidence before this study

Until recently, few pregnancy and birth cohorts existed in China that were able to record changes in health over the life-course at population level. However, there is now a growing interest in research into maternal and early life influences on adult diseases, and a number of birth cohorts have been established. It is unclear how many birth cohorts have been set-up in recent years and their geographic distributions across China.

Added value of this study

To our knowledge, this is the first systematic review of existing mother-baby cohorts in China. We identified 31 mother-baby cohorts started between 1999 and 2017 from 19 Chinese provinces and mega-cities, and the marjority were set up after 2010. All cohorts followed children to at least one year, most followed to childhood, none into adult life. Most cohorts collected biomedical samples from mothers and babies, as well as information about pregnancy, birth, and child development and health. Some cohorts were set up with broad objectives, nearly two-thirds had a specific scientific focus on particular exposures and fetal or child outcomes.

Implications of all the available evidence

Mother-baby cohorts in China have developed rapidly in recent years, but most with short follow-up duration. Extending the follow-up of cohort children and building collaborations across cohorts will increase the diversity, size and coverage of the participant sample and enhance the potential of existing cohorts for the study of early life influences on health and disease risk across the life course.

Introduction

It is now well-established that biological, social and environmental factors across the lifespan are important influences on health and disease risk in later life¹. The life-course approach, originating from the fetal origin of adult diseases hypothesis, is supported by evidence of associations between adverse events during pregnancy, low birthweight and long-lasting health consequences, e.g. cardiovascular disease². One of the most important aspects of the life-course approach is to understand and intervene to improve maternal, in-utero and early childhood development, which is central for optimising lifelong health^{3,4}. Therefore, a key area of work for the World Health Organization is to improve the health and well-being of populations through the life-course by focusing on women of reproductive age, and children and adolescents who will become the adults of tomorrow⁵.

Population-based prospective cohorts are a key study design for investigating life-course influence on health⁶. 'Birth cohorts' commence with pregnancy or birth, continue throughout infancy and often follow children over long periods. Maternal or pregnancy-related risk factors can be collected prospectively or retrospectively, and follow-up may continue through childhood into adolescence or adulthood, thus contributing vital insights into early exposures and their impact on lifelong health.

Worldwide, there are many pregnancy and birth cohorts, with short and longer-term follow-up^{7,8}. In high-income countries, there are well-established cohorts, e.g. the UK Avon Longitudinal Study of Parents and Children^{9,10} and Born in Bradford Multi-ethnic Family Cohort Study¹¹, Norwegian Mother, Father and Child Cohort^{12,13}, and Danish National Birth Cohort¹⁴. In low or middle-income countries (LMICs), there are relatively fewer mother-baby cohorts¹⁵ and, although some have followed children into adulthood (e.g. 1982 Pelotas birth cohort¹⁶, 1990 birth to twenty study in South African¹⁷, South Delhi cohort¹⁸), most have small sample sizes, or are less mature with shorter follow-up durations¹⁵. Nevertheless, LMIC cohorts provide a diversity of exposures for disease risk and highlight the important contrasts between higher and lower income nations. For example, higher socio-economic

position appears associated with lower obesity risk in more affluent countries, but with higher risk in less affluent countries¹⁹.

China has the largest national population, with ~16 million babies born each year²⁰. Since the 1990s, China has made remarkable progress in science and health and exceeded the United Nations Millennium Development Goals on maternal, infant and under-5 mortality²¹. Changes in lifestyle and nutritional status, levels of pollution and birth policies in recent decades have had an impact on maternal and child health in China^{22,23}. Yet, substantial heterogeneity remains across regions. For example, the proportion of women receiving ≥ five antenatal check-ups is lower in central than western/eastern regions²⁴. The infant mortality rate is higher in inland than costal regions²⁵. The mortality rate for under-5 is higher in western than eastern regions²⁶.

Until recently, few mother-baby cohorts existed in China that were able to record population level changes in health over the life-course. However, there is now a growing interest in research into life-course influences on health and a number of birth cohorts have been established²⁷. Understanding the geographical coverage, representativeness and characteristics of existing birth cohorts in China is vital for maximising their values and informing future population health policy.

We conducted a systematic review of published papers that reported data from pregnancy and birth cohorts in China to identify the mother-baby cohorts and understand their development over time. We summarised their key characteristics, e.g. geographical locations, recruitment setting and periods covered, follow-up duration, sample sizes, and measures recorded on the mother and child. We identified the key scientific areas these cohorts addressed. We reported findings from our systematic review and discussed the potential of mother-baby cohorts for advancing studies on early determinants of health across the life-course in China.

Methods

Search strategy

We searched Medline, Embase, Web of Science, Scopus, and PsycINFO databases for papers published before the 8th February 2022. The search terms used were child (including infant, baby, fetus), mother (and maternal) and longitudinal or cohort study design. The main search strategy and set of search terms were developed in Medline (**Supplementary Table S1**) and then adapted for other databases. Duplicates were removed.

All titles and abstracts were screened against the inclusion and exclusion criteria for eligibility. Search results were screened. First, three reviewers (LL, RK, KL) separately reviewed two-thirds of titles and abstracts so that each abstract was independently reviewed by two reviewers. Any disagreements were resolved by consensus between all reviewers. Second, full-text papers were retrieved for all eligible abstracts and reviewed independently by two reviewers. Reference lists of selected papers and websites of cohort studies were reviewed. This process is illustrated in the PRISMA flow diagram (Figure 1).

Inclusion and exclusion criteria

We included peer reviewed original research or cohort profile papers in English or Chinese languages with an English abstract that were published before the 8th February 2022. We included cohorts conducted in China that collected maternal socio-demographic and pregnancy information (prospectively or retrospectively), fetal and birth outcomes, and development and health of children, with a minimum follow-up of one year after birth. We excluded studies that took place outside mainland China, were not observational or longitudinal (e.g. interventional clinical studies) and where planned or actual follow-up was less than one year after birth. Full inclusion and exclusion criteria are listed in **Supplementary Table S2**.

Data extraction

The final list of included papers was grouped by cohort. Two reviewers were randomly assigned to extract information about each cohort against a standardised data extraction proforma, that included the cohort lead, region of study (city, county, province), sample size, time of recruitment, demographic and clinical data collected, samples and measurements, number of waves, actual or expected follow-up duration, and published study outputs. Discrepancies were discussed and consensus was reached. Wherever published details were lacking, we contacted the cohort lead or article authors to request clarifications. Four responses (for five cohorts) were received and the data were added to **Tables 1-3** as indicated in the footnotes.

A complete PRISMA checklist is available in **Supplementary Table S5**. A protocol for this review has not been previously published. The review was not registered. Assessment of the risk of bias was not applicable in the context of the current review. The funders of this study had no role in study design, data collection, interpretation, or writing of the report.

Results

The searches yielded 12,500 abstracts. Additional 167 abstracts were identified from reference lists and cohort websites (**Figure 1**). After removal of duplicates, 6,165 abstracts/titles were screened for eligibility. A total of 5784 abstracts were excluded: 3900 were not longitudinal birth cohort, 1007 were trials or interventions, 714 were outside mainland China, 72 were reviews or reports, 91 were for other reason (e.g. no data on babies, or surveillance, special disease or animal studies). Of 381 full papers retrieved and assessed, 66 did not meet the inclusion criteria (56 without follow-up, 10 with no access to the paper). Data were extracted from 315 included papers, which corresponded to 31 mother-baby cohorts. The full paper list by cohort is given in **Supplementary Table S4**.

Mother-baby cohorts identified

We included 31 eligible mother-baby cohorts from mainland China. All cohorts were prospective and collected primary data, and had followed the child for a minimum of one year after birth. **Table 1**

provides an overview of these cohorts. **Tables 2** and **3** present the key measures collected on mothers and children from each cohort as reported in published papers or from personal communication where relevant. The earliest cohort to begin recruitment started in 1999 (*Jiaxing Birth Cohort*), but only 10 cohorts were established by 2010, 14 were set-up between 2011-14, and 7 have started since 2015 (**Figure 2**).

Sample sizes and regions covered

The sample size of each cohort varied considerably, from <500 (n=6) to >300,000 mothers, with 10 cohorts having >10,000 mothers at the baseline (**Table 1**).

Figure 3 shows the geographical distribution of the 31 identified cohorts that recruited participants from 19 provinces/mega-cities. The three largest cohorts recruited over half a million pregnant women from the Eastern (*Jiaxing Birth Cohort*), Northern (*Xi'an Longitudinal Mother–Child Cohort*) and Central regions (*Wuhan Maternal & Child Health Management Information System*). The large but less populated Western region was under-studied, with relatively small numbers from the Central-Western areas (Chongqing, Sichuan) recruited to four cohorts (*Chongqing Longitudinal Twin Study, Tongliang Birth Cohort, A Birth Cohort from Chengdu, China National Birth Cohort*). We did not identify any cohorts from the area north of Beijing and Liaoning.

The most frequently studied regions were Shanghai (in 8 cohorts), Hubei (6) and Jiangsu provinces (5). In most cohorts, participants were recruited from a single province or city, with notable exceptions being the *Nutrition in Pregnancy & Growth in South West China* (Guizhou, Sichuan, Yunnan), *Taicang & Wuqiang Mother-Baby Cohort* (Jiangsu, Hebei), *Prospective Cohort from Shenyang, Wuhan & Guangzhou*, and *China National Birth Cohort*. The *China National Birth Cohort* had the largest geographic coverage of any single cohort, comprising participants from 12 provinces/mega-cities (**Table 1**).

The participants of these cohorts were predominantly of Han ethnicity (>90% of Chinese population). Two cohorts recruited mothers from regions with high proportions of ethnic minorities (Supplementary Table S3). The *Birth Cohort from Daxin* had a small sample size, but had 85% of mothers of Zhuang ethnicity²⁸. The *Nutrition in Pregnancy & Growth in Southwest China Study* recruited pregnant women from three provinces with high minority ethnic populations. Most cohorts were located in urban settings, 13 included participants from rural areas (Table 1).

Cohort recruitment and follow-ups

In China, prenatal care is provided mostly by hospitals or community health centres. Pregnant women are referred to secondary or tertiary hospitals in late pregnancy for obstetric care. After birth, children receive regular check-ups at community health centres. Most cohorts (n=24) began enrolment during pregnancy. Two recruited before conception. The *Shanghai Birth Cohort* recruited women who were planning to become pregnant and the *China National Birth Cohort* recruited women undergoing assisted reproductive therapies (ART). Five cohorts recruited babies at birth and retrieved pregnancy data from prenatal records. Two recruited children after birth (*Changsha Kaifu Birth Cohort* at 4 weeks, *Jintan Child Cohort Study* at 3-5 years) and obtained pregnancy and birth information retrospectively (**Table 1, Supplementary Table S3**).

Figure 4 shows that follow-up duration varied between cohorts. The shortest was to 12 months after birth and the longest planned follow-up was to 18y. Eighteen cohorts followed children to early (1-5y), 10 to late childhood (6-10y) and 6 to adolescence (11-18y). Three had different follow-up durations for subsamples of children (**Figure 4**). In the *China-Anhui Birth Cohort*, only children from the Ma'anshan subsample had planned follow-up into adolescence. In the *Wuhan Twin Birth Cohort*, the subsample recruited most recently will be followed to 18y. In the *Wuhan Healthy Baby Cohort*, a subsample of 407 children were followed to 3y (the remainder to 2y). All cohorts had decreasing response rates over time. For example, in the *Wuhan Twin Birth Cohort*, 73.2% of children were followed to 12 months, but only one-in-ten remained at 6–7y²⁹.

Measurements and samples

Data were collected directly from participating mothers by questionnaires, interviews, clinical assessments, or as extracts from hospital records and health administration systems. A wide range of data items were collected from these cohorts. For mothers, nearly all cohorts had physical measurements during pregnancy. All cohorts recorded maternal demographic, socio-economic, obstetric, and health characteristics at baseline, and some recorded information on the father (n=17). Many of the cohorts had information on maternal physical and/or mental health (n=29), lifestyles (e.g. diet, smoking, alcohol consumption, physical activity) (n=29) and environmental exposures (n=24) (Table 2).

For children, all cohorts recorded birth outcomes (e.g. birth sizes, gestational age). Data were collected on breastfeeding (n=24), health (n=25), and physical (n=27), psychosocial (n=24), motor (n=11), and cognitive (n=25) development, and pubertal indicators (n=6) (**Table 3**).

Biological (e.g. blood, urine, stool) samples were collected from the mother (n=26) and the child (n=23) (**Tables 2 and 3**). Maternal or cord serum, or urine samples in some cohorts (or hair and nail in a few cases^{30,31}) were analysed to assess the environmental exposures (e.g. heavy metals³² or other pollutants³³⁻³⁵) to evaluate the mother-baby transmission.

Scope of study aims

Out of the 31 cohorts identified, 12 had broader aims/objectives relating to social, biological and environmental influences on pregnancy and child outcomes. Most cohorts were established with a specific focus, e.g. to investigate environmental pollutants, genetic influences in twins, or maternal factors (e.g. nutrition, sleeping patterns, stress). Some recruited from special populations, e.g. women receiving ART (*China National Birth Cohort*), women pregnant with twins (*Chongqing*

Longitudinal Twin Study, Wuhan Twin Birth Cohort), or pregnant women who lived near a coal-fired power plant (Chongqing Tongliang Birth Cohort).

Around one-third of 315 papers identified had a focus on prenatal environmental exposure, and reported associations of air pollution (e.g. fine particulate matter), heavy metals, or other chemicals (e.g. phthalates, polybrominated diphenyl ethers) with gestational diabetes and hypertension^{36,37}, adverse birth outcomes^{32,38-40}, and child health and physical/motor/cognitive/neuro-development^{33-35,39,41-44}

Discussion

To our knowledge, this is the first systematic review of existing mother-baby cohorts in China, and is important and timely. Until recently, there were few prospective birth cohorts in mainland China. The large *China Birth Cohort Study*⁴⁵ was set up in 2016 with planed follow-up to delivery, however, many smaller and earlier cohorts provide vital details about early exposures, and offer a unique opportunity to monitor their associations with child growth and development across regions. Some have published protocols or profile papers^{29-31,46-52}, whereas information on many cohorts needs to be extracted from individual papers. This review brings together existing birth cohorts and provides information (e.g. enrolment, inclusion criteria, data and biological sample collected) that is essential for identifying the strengths, gaps and potential for cross-cohort collaboration. Investigators of new cohorts will also benefit from knowledge gained from exiting cohort resources.

We identified 31 cohorts established between 1999-2017. The majority (26) started after 2007, reflecting a rapid recent increase in interest in birth cohorts. Most cohorts were initiated during pregnancy or delivery. Although all cohorts followed children to at least one year of age, only a few followed (or planned to follow) to adolescence, and none into adult life. Most cohorts collected biomedical samples from mothers and babies, in addition to using detailed interviews and questionnaires to collect information about pregnancy, birth, and child development and health.

Most cohorts were located in urban settings and recruited participants from a single province or city. The large Western region was under-represented. While several cohorts were set-up to fulfil broad objectives, many had a specific scientific focus, such as prenatal exposure to environmental pollutants and adverse maternal, birth and child outcomes. Together these cohorts comprise over 700,000 children born since 1999 in 19 provinces/mega-cities in China.

Challenges in existing mother-baby cohorts in China

All cohorts identified were established from 1999. Many cohorts did not follow-up children beyond early childhood due to difficulties in maintaining contact or funding, and therefore lack the data needed to study the long-term impacts of early exposures. For example, the *China National Birth Cohort*⁵³ which had a target sample of ~60,000 women who underwent ART or had spontaneous pregnancies from 12 provinces/cities will follow children to 3y, thus the long-term impacts of ART cannot be studied. As many of these cohorts are young, there are still opportunities to set-up longer term follow-ups that would markedly increase their value for monitoring health and wellbeing, and investigating the early origin of life-course diseases at an important time of China's fast social and economic development.

In addition to short follow-up periods, most cohorts had high attrition rates. Published analyses using these cohorts often have small samples sizes, thus have reduced statistical power and potential selection biases. The main difficulty to retention of the birth cohort beyond infancy includes the transfer of care from hospitals to community health centres. After a six-week postpartum check-up at the birth hospital, routine child healthcare (e.g. monitoring growth and development, providing vaccinations) is provided by local community health centres which may be widely dispersed depending on where children are registered. Tracing and maintaining contact with participants therefore is challenging²⁰.

The scientific outputs from each cohort varied considerably. Frequently, publications were based on subsamples of a cohort, thus the value of these cohorts as representative samples may not have been fully exploited.

Most cohorts had limited geographical coverage. Few included samples from Western or Northeast China, and rural or minority populations. Cohorts with longer follow-up into adulthood and participants from populations or regions underserved by research are crucial for investigating the long-term influences of early exposures on health in the population. However, such cohorts require considerable investment in time and resources, and may not be practical in China.

Our search strategy was restricted to published sources, and this could introduce publication bias.

For example, some cohorts may not have published papers during this timeframe, in particular those that have commenced recently. We excluded cohorts with no actual or planned follow-up beyond one year after birth, e.g. the *China Birth Cohort Study*⁴⁵ covered a large number of geographical areas and was set-up to investigate the risk factors for birth defects, but only undertook follow-up of pregnant women to delivery. However, some birth defects may not be obvious at birth and are diagnosed in infancy or childhood⁵⁴.

Although our search strategy was comprehensive and rigorous, involving both English and Chinese publications, we recognise that we may not have identified all mother-child cohorts that existed during this period in China. Nevertheless, given our extensive literature search, it is unlikely that we have missed a substantial number of eligible cohorts, therefore this review provides a representative picture of current and recent Chinese birth cohort studies.

Values and potential of mother-baby cohorts in China

Over thirty mother-baby cohorts have been set-up in China within less than 20 years. The data from these cohorts reflect prenatal and early-life exposures, and maternal, fetal and child health during

recent decades when China has experienced remarkable advances in economic development and improvement of healthcare. Maternal and child health (MCH) care system is well-established in China with near-universal coverage. There are MCH hospitals or centres across provinces, counties or cities to provide systematic healthcare for pregnant women and children⁵⁵. Thus, the health system in China is well-suited to facilitating the establishment of the cohort studies and recruiting participants in early pregnancy. Moreover, the collection of data and samples during the prenatal period is important for measuring exposures to risk factors for a wide range of investigations. This success in recruitment is demonstrated by the large sample sizes achieved by many cohorts.

Many of the cohorts identified focused on environmental pollutants and their associations with adverse maternal, birth and child outcomes, reflecting concerns about the impact of pollution on health due to the rapid urbanisation experienced in China^{20,56}. Findings from these cohorts have important implications for many urban environments worldwide.

The wealth of the detailed longitudinal data collected from these cohorts is a valuable resource and provides a unique opportunity to investigate the links between prenatal and postnatal exposures and maternal and child health in China, and to identify knowledge gaps in the current body of evidence. There is clear potential for extending the follow-up of the existing cohorts into adulthood, and for developing collaboration between cohorts to create larger and more diverse samples that will support a wider range of research topics and comparisons between different regions, population groups and time periods.

Conclusions

The establishment of large population-based birth cohorts to investigate maternal and child health has developed rapidly in China over the last two decades. Research into the possible links between early exposures (including in-utero or perinatal) and health later in life has included important investigation of risk factors and exposures resulting from China's economic development, including

demographic and nutritional transitions. However, these cohorts often lack the longer-term follow-up of children into adulthood that has brought critical insights into the links between the early life environment and adult health in other countries. There is an urgent need to extend the follow-up of mother-baby cohort studies in China to enhance the potential for studying life-course influences on adult health and identifying targets for early intervention.

The mother-child cohorts identified in this review have individually made important contributions to understanding the impact of early life exposures on maternal, fetal and child outcomes in specific geographical areas. However, their full potential can only be realised with collaborations between cohorts from different Chinese regions to increase diversity of the participant sample.

Combining and harmonising data from different cohorts would increase the sample size and allow the study of important but infrequent outcomes. Moreover, as the types of exposure may differ across regions, these differences could be examined by cross-cohort comparisons.

To encourage the collaboration across cohorts, it is essential to increase their visibility and improve data sharing, for example, by publishing information on study characteristics in 'cohort profiles' and opening access to their resources for academic collaboration. Cross-cohort collaborations would enable researchers to address major scientific challenges using existing cohorts and capitalize on the investments already made in data and sample collection.

Contributors

LL and RK conceived the study. LL, RK and KL designed the search strategy and reviewed papers. KL conducted the literature search and data extraction, and prepared the figures. LL wrote the first draft of the paper. All authors made substantial contributions to interpretation of the data, revised the manuscript and approved the final version.

Declaration of interests

We declare no competing interests.

Acknowledgments

This work is supported by the University College London Global Engagement Funds. The funder played no part in the review. The research was supported in part by the National Institute for Health Research (NIHR) Great Ormond Street Hospital Biomedical Research Centre. The authors would like to thank Professors Chao Tong and Xiu Qiu who responded to our enquiries. We would also like to thank Dr Mingyue Gao and Ms Zhonghui Huang for their help to produce the figure for geographic distribution of cohorts.

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Figure 1. Prisma flow chart for study selection (31 mother-baby cohorts were identified)

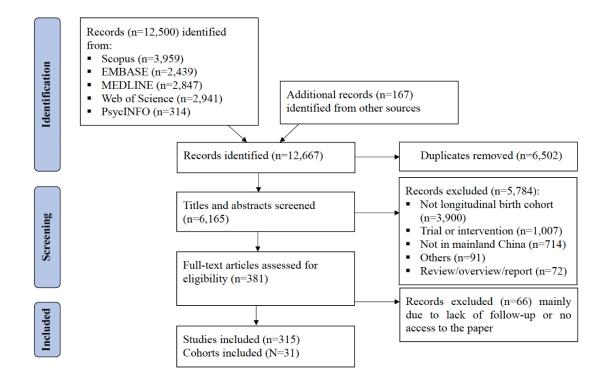
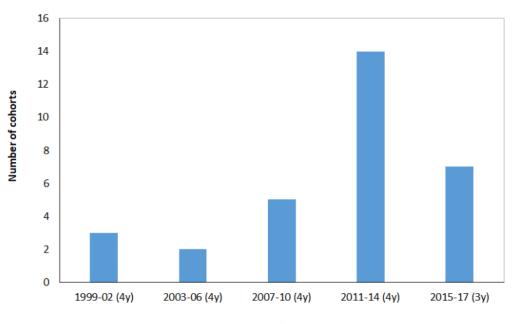


Figure 2. Distribution of year at the start of recruitment of 31 identified mother-baby cohorts in China



Year at start of recruitment

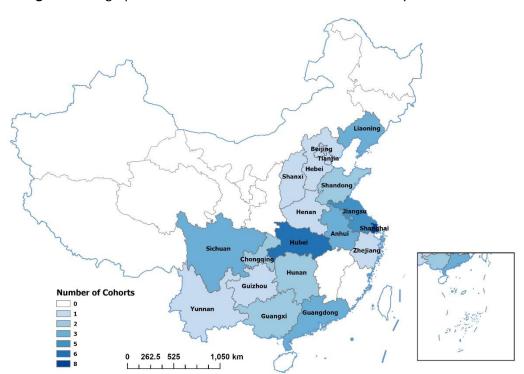


Figure 3. Geographical distribution of 31 identified mother-baby cohorts in China

Figure 4 Follow-up durations of the 31 mother-baby cohorts identified in China

Cohort: recruitment year(s)	Prenatal	Infancy (<1y)	Early childhoo	d (1-5y)	Late childh	ood (6-10y)	Adolescence	(11-18y)
5.Born in Guangzhou Cohort Study 2012 -								18y#
9.Wuhan Twin Birth Cohort: sample 3: 2016-20*								18y#
1.China-Anhui Birth Cohort -Ma'anshan sub-sample 2008–10*							14-15y#	
2.Ma'anshan Birth Cohort 2013-14							14-15y#	
14.Jintan Child Cohort Study 2004-05	ŧ	ŧ					13-15y	
27.Xi'an Longitudinal Mother–Child Cohort 2013-23							12y#	
10.Tongji MCH Cohort 2013-16						10y#		
15.Sheyang Mini Birth Cohort Study 2009-10	†					10y		
20.Shanghai birth cohort 2013-16 ; 2013-15						8y#		
9. Wuhan Twin Birth Cohort: samples 1: 2006-12 & sample 2: 2013-20*					7y#			
30.Jiaxing Birth Cohort 1999-2013					6-7y			
13.Jiangsu Birth Defect Intervention Cohort 2002-04					4-7y			
11. Wuhan MCH Management Information System 2011-13								
22.Shanghai Minhang birth cohort 2012								
25.Shanghai Sleep Cohort 2012-13								
29.Tianjin Birth Cohort 2017-21								
3.Chongqing Longitudinal Twin Study 2016-18				5y				
4.Tongliang Birth Cohort 2002, 2005	†							
12.Changsha Kaifu Birth Cohort 2015	†							
23.Shanghai obesity and Allergy Cohort 2012-15	†							
24.Shanghai Prenatal Cohort 2011-13								
6.Birth Cohort from Daxin 2013-14			Зу					
7. Nutrition in Pregnancy & Growth in Southwest China 2014-18								
8. Wuhan Healthy Baby Cohort 2012-14: sub-sample of 407 babies*								
16.Taicang & Wuqiang Mother–Child Cohort 2013-17; 2016-21								
26.Shanghai Stress Birth Cohort 2010	†							
31.China National Birth Cohort 2016-ongoing								
8. Wuhan Healthy Baby Cohort 2012-14			2y	•				
18. Prospective cohort from Shenyang, Wuhan, Guangzhou 2009-10; 2014-16	†		-					
19.Laizhou Bay Birth Cohort 2010-12	+							
21.Shanghai Maternal-Child Pairs Cohort 2016 -								
1.China-Anhui Birth Cohort (excluding Ma'anshan subsample) 2008-10*		12m						
17.Born in Shenyang Cohort Study 2017								
28. A birth cohort from Chengdu 2015								
MCH – Maternal and Child Health			•					

MCH – Maternal and Child Health

^{*}sub-sample(s) of a cohort

[†] recruited at delivery, pregnancy data retrieved from prenatal records

[‡] recruited at 3-5y, pregnancy and birth data obtained from medical records and questionnaire

[#] planned follow-up duration

Table 1. Characteristics of 31 identified mother-baby cohorts (by province/mega-city) with broad exposures or outcomes

	Cohort name	Province/mega-city (counties/cities)	Recruited site(s)	Recruitment period	Mothers/babies recruited	Recruitment time	Child follow-ups	Leas Institute(s)
1	China-Anhui Birth Cohort (C-ABC) ⁴⁷	Anhui (6 cities: Hefei, Jieshou, Lu'an, Ma'anshan, Ningguo, Wuhu)†	Maternity hospitals	2008–10	16,766 pregnant women/13,454 singleton livebirths	1 st /2 nd trimester	Birth, 6w, 3, 6, 9, 12m, for Ma'anshan 18, 24, 36m, 4.5-6y, planned to 14y (girls) &15y (boys)*	School of Public Health, Anhui Medical University
2	Ma'anshan Birth Cohort (MABC) ³³	Anhui (Ma'anshan)†	MCH Centre	2013-14	3474 pregnant women/3273 singleton livebirths	8-14w gestation*	Birth, 6w, 3, 6, 9, 12m, every 6m to 6y, planned to 14 (girls) & 15y (boys)*	School of Public Health, Anhui Medical University
3	Chongqing Longitudinal Twin Study (LoTiS) ³⁰	Chongqing†	1 st Affiliated Hospital of Chongqing Medical University, Chongqing MCH Centre	2016-18	439 pregnant women with twins	11-16w gestation	Birth, 6w, 3, 6, every 6m to 36m, 48, 60m,*	1 st Affiliated Hospital of Chongqing Medical University
4	Tongliang Birth Cohort (TBC) ³⁹	Chongqing (Tongliang)‡	Bachuan Hospital, Tongliang County Hospital, Traditional Chinese Medicine Hospital, MCH Hospital	2002/2005 (before/after power plant closure)	150 mothers/150 singletons) in 2002; 158/158 in 2005	Delivery	Birth, 18, 24, 30, 36m, 5y ⁵⁷	Children's Hospital, Chongqing Medical University; Dept of Environmental Health Sciences, Columbia University
5	Born in Guangzhou Cohort Study (BIGCS) ⁵¹	Guangdong (Guangzhou)†	Guangzhou MCH Centre (2 campuses)	2012–ongoing	55,000 mothers/51,000 babies by 2023*	<20w gestation	Birth, 6w, 6m, 12m, 3y, 6y, 9-10y, planned to 18y*	Women's & Children's Medical Centre, Guangzhou Medical University
6	A Birth Cohort from Daxin ⁵⁸	Guangxi Zhuang Autonomous Region (Daxin County)‡	MCH Centre in County hospital	2013-14	398 mothers/398 babies	4w before delivery to 1w postpartum	Birth, 12m, 36m	Xinhua Hospital, Shanghai Jiao Tong University School of Medicine; University of South Carolina
7	Nutrition in Pregnancy & Growth in Southwest China ⁵⁹	Guizhou, Sichuan, Yunnan#	12 urbans/15 rural hospitals or community health centres	2014-18	12,989 women /12,846 babies	9-11w gestation	Birth, 3, 6, 12, 18, 24, 30, 36m	Centre for Translational Medicine, Key Laboratory of Birth Defects & related diseases of women & children, West China 2 nd university hospital, Sichuan university
8	Wuhan Healthy Baby Cohort ^{32,60}	Hubei (Wuhan, Ezhou, Macheng counties)#	Maternal & Child Care Centres/Hospitals	2012-14	11,311 pregnant women with singletons	<16w gestation	Birth, 6m, 12m, 24m, sub-sample (N=407) to 3y ⁶¹	School of Public Health, Tongji Medical College, Huazhong University of Science & Technology
9	Wuhan Twin Birth Cohort (WTBC) ²⁹	Hubei (Wuhan)†.	Samples 1&2: Wuhan Pre- /Post-natal Twin Birth Registry;	Sample 1: 2006- 12; Sample 2:	Sample 1: 6,920 twin pairs;	1 st trimester	Samples 1&2: 1, 3, 6, 8, 12, 18, 24, 30, 36m, 4, 5, 6, 7y.	Wuhan Maternal & Child Healthcare Hospital, Tongji Medical

	1		Comple 2, antonotally at	2012 20.	Sample 2: 6 040: Sample		Comple 2: 1 2 6 9 12	College Hugghens
			Sample 3: antenatally at Wuhan MCH Centre	2013-20; <u>Sample3</u> : 2016-20	<u>Sample 2</u> : 6,949; <u>Sample</u> <u>3</u> : 1000 (target), and		Sample 3: 1, 3, 6, 8, 12, 18, 24, 30, 36m, 4, 5, 6,	College, Huazhong University of Science &
10	Tongji MCH Cohort ⁶²	Hubei (Wuhan)†	Hubei MCH Hospital, Central Hospital of Wuhan, Jiang'an MCH Hospital	2013-16	their mothers 8649 pregnant women	<16w gestation	7y, planned to 18y Birth, 1, 3, 6, 12, 24, 72m, planned to 10y	Technology School of Public Health, Tongji Medical College, Huazhong University of Science & Technology
11	Wuhan MCH Management Information System ^{38,42}	Hubei (Wuhan)†	Wuhan MCH Hospital	2011–13	105,927 mother-baby pairs ³⁸	1 st trimester	Birth, 1, 3, 6, 12, 18, 24, 30, 36m, 4, 5, 6y ⁴²	Wuhan Maternal & Child Healthcare Hospital, Tongji Medical College, Huazhong University of Science & Technology
12	Changsha Kaifu Birth Cohort ⁶³	Hunan (Changsha)†	Community Health Centres on 3 streets in Kaifu District	2015	976 mother-child pairs	Delivery to 4w after birth ⁶⁴ , retro data retrieved from 12w gestation from Community Health Management Information System	Birth, 1, 3, 6, 8, 12m, follow to 5y ⁶⁵	Xiangya School of Public Health, Central South University
13	Jiangsu Birth Defect Prevention Cohort ⁶⁶	Jiangsu#	110 communities Jiangsu	2002-04	26,803 pregnant women/25,809 babies	15-20w gestation	2-4y, 4-7y.	Jiangsu Institute of Planned Parenthood Research
14	Jintan Child Cohort ⁶⁷	Jiangsu (Changzhou)‡	4 pre-schools (Jianshe, Huacheng, Xuebu, Huashan) administrated by Jintan MCH Centre	2004-05	1656 preschool children	3-5y (prenatal and birth data from questionnaire and medical records)*	3-6y, 7-13y, 13-15y	Schools of Nursing & Medicine, University of Pennsylvania
15	Sheyang Mini Birth Cohort Study ^{40,68}	Jiangsu (Sheyang County)‡	Sheyang Maternity Hospital	June 2009- Jan 2010	1149 pregnant women (1,100 mother-child pairs).	Delivery	Birth, 3, 7, 10y	School of Public Health, Fudan University
16	Taicang and Wuqiang Mother— Child Cohort Study (TAWS) ⁴⁹	Jiangsu (Taicang), Hebei (Wuqiang)‡	Early pregnant cohort: Prenatal & childcare clinics in 22 community health centres in Taicang; 8 health centres and MCH hospital in Wuqiang. Delivery cohort: Wuqiang County Hospital	Taicang: 2013-17; Wuqiang: 2016- 21	Early pregnancy cohort: 4035 mothers from 2 sites; Delivery cohort: 3005 mothers in Wuqiang	Early pregnancy cohort: <16w gestation; Delivery cohort: at delivery	Taicang: 4w, 3, 6, 8, 12, 18, 24, 30, 36m; Wuqiang: 1, 2, 3, 6, 8, 12, 18, 24, 30, 36m, then annually to 12y	National Institute for Nutrition & Health, Chinese Centre for Disease Control & Prevention
17	Born in Shenyang Cohort Study (BISCS) ⁶⁹	Liaoning (Shenyang)†	54 hospitals and community health centres	Apr-Sep 2017	1338 pregnant women/1260 live singletons (801 pairs included)	21-24w gestation	1, 3, 6, 12m	Institute of Health Sciences, China Medical University
18	A Prospective Cohort from Shenyang, Wuhan and Guangzhou ⁷⁰	Liaoning (Shenyang), Hubei (Wuhan), Guangdong (Guangzhou for	Community health centre. Info was obtained from municipal MCH Info System	Cohort A: 2009- 10 Cohort B: 2014- 16	Cohort A: 2066 mother/neonate pairs; Cohort B: 1970 pairs	Delivery	1, 3, 5, 6, 7, 9, 12, 18, 24m	Dept of MCH, School of Public Health, Tongji Medical College, Huazhong University of Science & Technology

		cohort A, Zhuhai for cohort B)†						
19	Laizhou Bay Birth Cohort ³⁴	Shandong (Laizhou Wan)‡	County hospital	2010-12	232 mother-child pairs	Birth-mothers recruited when preparing for labor	Birth, 1y, 2y.	Dept of Environmental Health, School of Public Health, Shanghai Jiao Tong University School of Medicine
20	Shanghai Birth Cohort ³¹	Shanghai#	6 hospitals in urban, suburban, semi-rural areas	Pregnancy cohort: 2013-16 Preconception cohort: 2013-15	4127 mothers, 3692 singleton babies; pregnancy cohort: 3426; pre-conception cohort: 701	Pregnancy cohort: 1st trimester (≤16w). Preconception cohort: pre-pregnancy	Birth, 6w, 6, 12, 24m, 4y, planned follow-up at 6, 8y	Xinhua Hospital, Shanghai Jiao Tong University School of Medicine
21	Shanghai Maternal- Child Pairs Cohort (MCPC) ⁷¹	Shanghai†	Shanghai Pudong Hospital; Songjiang MCH Hospital	2016- (last reported recruitment Dec 2018)	4178 children born before Oct 2018	1 st prenatal visit	Birth, 2, 6, 12, 24m	School of Public Health, Fudan University
22	Shanghai Minhang Birth Cohort ^{43,72}	Shanghai†	Minhang MCH Hospital	2012	1292 mothers; 1225 singletons babies	12-16w gestation	6m, 1, 2, 4, 6y	Shanghai Institute of Planned Parenthood Research, Fudan University
23	Shanghai Obesity and Allergy Cohort ^{41,73}	Shanghai†	Xinghua Hospital, International Peace MCH Hospital	2012-15	1143 mother-child pairs (singletons)	Delivery	Birth, 1y, 2y, 3y, 4y, 5y.	Xinhua Hospital, Shanghai Jiao Tong University School of Medicine
24	Shanghai Prenatal Cohort ^{35,74}	Shanghai†	Xinghua Hospital, International Peace MCH Hospital	2011-13	1269 mother-child pairs	29-41w gestation	Birth, 1y, 2y, 3y, 4y, 5y	Xinhua Hospital, Shanghai Jiao Tong University School of Medicine
25	Shanghai Sleep Birth Cohort ⁵⁰	Shanghai†	Renji Hospital, Shanghai Children's Medical Centre	2012-13	277 pregnant women	≥28w gestation	6w, 3m, 6m, 9m, 12m, 18m, 24m, 3y, 4y, 6y	Shanghai Children's Medical Centre, Shanghai Jiao Tong University School of Medicine
26	Shanghai Stress Birth Cohort (SSBC) ^{75,76}	Shanghai†	Xinghua Hospital, International Peace MCH Hospital	2010	398 mother-infant pairs (singletons)	28-36w gestation	24-36m (follow to 3y)	Xinhua Hospital, Shanghai Jiao Tong University School of Medicine
27	Xi'an Longitudinal Mother–Child Cohort (XAMC) ⁷⁷	Shanxi (Xi'an)†	Northwest MCH Hospital (2 campuses)	2013-23 A sub-cohort recruited from 01.01.2017	114, 946 mothers/124,454 neonates enrolled in 2013-19 4642 mother–child pairs enrolled from Jan 2007 to June 2019	<20w gestation	Mother interview and child examination at 6w, 6, 12, 24m, mother telephone interview every 2y to 12y. Random sample of >10% mother—child pairs for clinical visits at 3–5y and 8–12y	Nutrition & Food Safety, School of Public Health, Xi'an Jiaotong University; Northwest Women's & Children's Hospital (Xi'an)
28	A Birth Cohort from Chengdu ⁵²	Sichuan (Chengdu)†	4 MCH hospitals	May-Aug 2015	1901 pregnant women	15-20w gestation	1, 3, 6, 12m	West China Hospital, Sichuan University

29	Tianjin Birth Cohort (TJBC) ⁷⁸	Tianjin#	6 urban & 3 sub-urban district level MCH centres	2017–21 (planned for 4y)	Target: 10,000 families. Achieved: 3924 pregnant women Aug 2017-Jan	≤14w gestation	Birth, 6w, 6m, annually to 6y	Tianjin Women's & Children's Health Centre
					2019			
30	Jiaxing Birth Cohort ⁷⁹	Zhejiang (Jiaxing)‡	Medical clinics in 7 county- level divisions	1999-2013	363,416 pregnant women/338,413 livebirths (mother-child pairs)	1 st trimester	1-2m, every 3m in infancy (3-12m), every 6m in toddler stage (1- 3y), annually to 6-7y	Women's & Children's Hospital, Jiaxing University; Institute of Nutrition & Health, Qingdao University
31	China National Birth Cohort (CNBC) ⁵³	12 provinces/mega cities (Anhui, Beijing, Guangdong, Guangxi, Henan, Hubei, Hunan, Jiangsu, Liaoning, Shandong, Shanghai, Sichuan)#	Hospitals, maternity care units	2016–ongoing	ART Cohort 27,044 families and Natural Pregnancy Cohort 29,589 pregnant women by June 2020 (target 30,000 in each cohort)	Natural Pregnancy Cohort: 1st trimester (8-14w). ART Cohort: pre- treatment/conception.	6w, 6m, 1y, 3y	School of Public Health, State Key Laboratory of Reproductive Medicine, Nanjing Medical University

MCH=Maternal and Child Health; years=y, months=m, weeks=w, days=d

^{*} Information was based on personal communications

[†]urban; ‡rural; #both urban & rural regions

Table 2. Measurements recorded for mothers in each cohort

	2. Measurements recorded for		cal measur			alth		Lifestyle fa	actors		В	iomarker	'S			
		Height	Weight	ВР	Physical Health	Mental health	Smoking	Physical activity	Diet	Alcohol	Blood	Urine	Stool	Demography	Environmental exposures	Father
1	China-Anhui Birth Cohort	✓	√	√	✓	✓	✓	,	✓	√	✓	✓		✓	✓	✓
2	Ma'anshan Birth Cohort	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓	✓	✓
3	Chongqing Longitudinal Twin Study*	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓
4	Tongliang Birth Cohort	✓	✓		✓		✓		✓	✓	✓			✓	✓	
5	Born in Guangzhou Cohort Study	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
6	A Birth Cohort from Daxin	✓	✓		✓		✓		✓	✓	✓			✓	✓	✓
7	Nutrition in Pregnancy and Growth in Southwest China	√	√	✓	✓		✓	✓	√	√	✓	√		✓		
8	Wuhan Healthy Baby Cohort	✓	✓	✓	✓		✓	✓		✓	✓	✓		✓	✓	
9	Wuhan Twin Birth Cohort	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓	✓	✓
10	Tongji Maternal and Child Health Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓
11	Wuhan Maternal and Child Health Management Information System	√	√	✓	√		√			√				✓	✓	
12	Changsha Kaifu Birth Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓		✓
13	Jiangsu Birth Defect Intervention Cohort				✓		✓			✓				✓	✓	
14	Jintan Child Cohort*				✓	✓	✓							✓	✓	
15	Sheyang Mini Birth Cohort Study		✓		✓						✓	✓		✓	✓	
16	Taicang and Wuqiang Mother-Child	✓	✓		✓	✓		✓	✓		✓	✓		✓		✓
	Cohort Study															
17	Born in Shenyang Cohort Study		✓				✓							✓		✓
18	A Prospective Cohort Study from Shenyang, Wuhan and Guangzhou	✓	√	✓	√		√							✓		✓
19	Laizhou Bay Birth Cohort	✓	✓		✓		✓		✓	✓	✓	✓		✓	✓	
20	Shanghai Birth Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓
21	Shanghai Maternal-Child Pairs Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	
22	Shanghai-Minhang Birth Cohort	✓	✓	✓	✓		✓		✓	✓	✓	✓		✓	✓	✓
23	Shanghai Obesity and Allergy Cohort	✓	✓	✓			✓				✓	✓		✓	✓	
24	Shanghai Prenatal Cohort	✓	✓		✓		✓		✓		✓			✓	✓	
25	Shanghai Sleep Birth Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓		✓
26	Shanghai Stress Birth Cohort				✓	✓					✓			✓	✓	
27	Xi'an Longitudinal Mother-Child Cohort	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	
28	A Birth Cohort from Chengdu	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓		
29	Tianjin Birth Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
30	Jiaxing Birth Cohort	✓	✓	✓	✓		✓			✓	✓	✓		✓	✓	✓
31	China National Birth Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓

BP=blood pressure; MCH=Maternal and Child Health
* Information was based on personal communications

Table 3. Measurements recorded for children in each cohort

	able 3. Measurements recorded			rth			Bioma	rkers		Development/health						
		Pregnancy outcomes	Birth size	Gestation	Birth defect	Cord blood	Blood sample	Urine	Stool	Infant feeding	Body size	Psychosocial /behavior	Motor	Cognition	Health	Puberty
1	China-Anhui Birth Cohort	✓	✓	✓	√	✓	✓				✓	√		✓		√
2	Ma'anshan Birth Cohort	✓	✓	✓		✓	✓			✓	✓	✓		✓	✓	✓
3	Chongqing Longitudinal Twin Study*	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓	
4	Tongliang Birth Cohort	✓	✓	✓	✓	✓					✓	✓	✓	✓	✓	
5	Born in Guangzhou Cohort Study	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
6	A Birth Cohort from Daxin	✓	✓	✓					✓	✓	✓	✓	✓	✓	✓	
7	Nutrition in Pregnancy and Growth in Southwest China	√	✓	√	√		√			√	√	✓		√	√	
8	Wuhan Healthy Baby Cohort	✓	✓	✓	✓	✓	✓				✓	✓		✓	✓	
9	Wuhan Twin Birth Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓
10	Tongji Maternal and Child Health Cohort	✓	✓	✓	✓					✓	✓	✓		✓	✓	
11	Wuhan Maternal and Child Health Management Information System	✓	✓	✓	√					✓	✓					
12	Changsha Kaifu Birth Cohort	✓	✓	✓	✓					✓	✓				✓	
13	Jiangsu Birth Defects Intervention Cohort	✓	✓	✓	✓						✓	✓	✓	✓	✓	
14	Jintan Child Cohort*	✓	✓	✓	✓		✓			✓	✓	✓	✓	✓	✓	✓
15	Sheyang Mini Birth Cohort Study		✓	✓		✓		✓			✓	✓		✓	✓	✓
16	Taicang and Wuqiang Mother-Child Cohort Study	√	✓	√		√	√	√	✓	✓	✓	✓	√	√	√	
17	Born in Shenyang Cohort Study	✓	✓							✓	✓	✓			✓	
18	A Prospective Cohort Study from Shenyang, Wuhan and Guangzhou		√	√	√					✓	✓					
19	Laizhou Bay Birth Cohort	✓	✓	✓	✓	✓								✓		
20	Shanghai Birth Cohort	✓	✓	✓	✓	✓	✓	✓		✓	✓			✓	✓	
21	Shanghai Shanghai Maternal-Child Pairs Cohort	√	✓	√					✓	✓		✓	√	√	√	
22	Shanghai Minhang Birth Cohort	✓	✓	✓		✓		✓			✓	✓		✓		
23	Shanghai Obesity and Allergy Cohort	✓	✓	✓	✓	✓	✓			✓	✓				✓	
24	Shanghai Prenatal Cohort	✓	✓	✓		✓	✓			✓					✓	
25	Shanghai Sleep Birth Cohort	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓	
26	Shanghai Stress Birth Cohort	✓	✓	✓	✓					✓		✓		✓		
27	Xi'an Longitudinal Mother-Child Cohort Study	√	√	√	√	√	√	✓	√	✓	✓	√	√	✓	√	
28	A birth Cohort from Chengdu	✓	✓	✓	✓					✓	✓	✓		✓	✓	
29	Tianjin Birth Cohort	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	
30	Jiaxing Birth Cohort	✓	✓	✓	✓		✓			✓	✓	✓		✓	✓	
31	China National Birth Cohort	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓	_

MCH = Maternal and Child Health

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