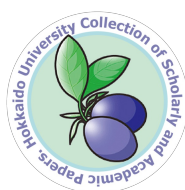




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Birth Cohort Consortium of Asia (BiCCA) - Current and Future Perspectives

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ABSTRACT

Background: The environmental health of children is one of the great global health concerns. What a developing child is exposed to *in utero* and in his/her early years has major consequences on later health. However, environmental risks or disease burdens vary from region to region. Birth cohort studies are ideal for investigating different environmental risks.

Methods: The principal investigators of three birth cohorts in Asia including the Taiwan Birth Panel Study (TBPS), the Mothers and Children's Environmental Health Study (MOCEH), and the Hokkaido Study on Environment and Children' Health (Hokkaido Study) co-established the Birth Cohort Consortium of Asia (BiCCA) in 2011. Through a series of five PI meetings, the enrolment criteria, aim of the consortium, and a first-phase inventory were confirmed.

Results: To date, 23 birth cohorts have been established in 10 Asian countries, consisting of approximately 70,000 study subjects in the BiCCA. This article provides the study framework, environmental exposure and health outcome assessments, as well as maternal and infant characteristics of the participating cohorts.

Conclusions: The BiCCA provide a unique and reliable source of birth cohort information in Asian countries. Further scientific cooperation is ongoing to identify specific regional environmental threats and improve the health of children in Asia.

INTRODUCTION

Asia contains half of the world's children, and the countries of Asia are the most rapidly industrializing nations in the world. Environmental threats to the health of children are diverse in Asia and include classic infectious disease hazards (i.e., pneumonia, dysentery, measles, Acquired Immune Deficiency Syndrome, and tuberculosis). Additionally, the prevalence of environmentally related diseases such as allergic disease, attention deficit hyperactivity disorder (ADHD), and autism is increasing dramatically.^{1,2} As industrial development proceeds and as nations in the region pass through the epidemiologic transition, rapid urbanization, unsustainable consumption, and an increase of industrial disposal such as e-waste, children are confronted by a rapidly multiplying array of new health threats posed by exposures to toxic chemicals.¹

To address these problems, local and national research efforts must focus on environmental risks. In 2002, the International Conference on Environmental Threats to the Health of Children was held in Bangkok to initiate the very first step towards awareness about the environmental health hazards affecting children in these regions. Several actions have been proposed to decrease environmental hazards, including removal of lead from gasoline, the India clean-water project, the mercury pollution

reduction project, international networking and anti-smoking campaigns.³ Nevertheless, new challenges continue to emerge. In 2008, hundreds of thousands of infants and young children suffered from renal dysfunction after exposure to Melamine that was deliberately added to milk and milk-containing products in China, Hong Kong and Taiwan.^{4,5} Later in 2011, plasticizers such as di(2-ethylhexyl) phthalate (DEHP) and di-iso-nonyl phthalate (DiNP) were found to be illegally added to clouding agents used in foods and beverages in Taiwan.⁶ These issues draw new attention to the importance of food safety. Another trans-boundary threat in the Asia-Pacific region is outdoor air pollution. Smog and sandstorm in China and Southeast Asia haze are not regional threats. Even more, we are facing the challenge of climate change and extreme weather globally. This issue has become the prominent target of policy reforms and public health efforts.

In response to these new threats, national governments in Asia have taken action since the 1970s to protect children against environmental threats to health, and in the past decade, they have developed new approaches to evaluating and managing toxic chemicals. In 2009, the Ministry of Environment in Korea held the Third International Conference for Children's Health and Environment in Busan, Korea in partnership with the World Health Organization.⁷ In July 2010, in Jeju, Korea, the Gov-

ernment of Korea hosted the Second Ministerial Regional Forum on Environment and Health in South-East and East Asian Countries, which was jointly organized by the United Nations Environment Program Regional Office for Asia and the Pacific and the World Health Organization Regional offices for the Western Pacific and South-East Asia.⁸ Some associated conferences have further pledged to advocate for the recognition, assessment and consideration of hazardous environmental influences on children's health and development.

Children's environmental health is an issue of both global and regional importance. Environmental hazards, lifestyle and genetic susceptibility vary across different regions and races. Thus, a single one cohort or study is unable to explore the whole picture of this issue. Population size is even the threshold of study investigating gene- environmental interactions or co-exposure effects. In addition, replication or validation is crucial for interpretation of results from omic technologies such as epigenomics and metabolomics. Harmonization of cohort studies has been successes by ENRIECO (Environmental Health Risks in European Birth Cohorts)⁹ and projects in Europe¹⁰, but not elsewhere. A useful network to exchange information will facilitate international cooperation for exploring regional and global hazards, understanding the health impact of environmental toxicants, and developing effective

prevention strategies not only in Asia but also across the world.

METHODS

Establishment of the Birth Cohort Consortium of Asia (BiCCA)

The Birth Cohort Consortium of Asia was co-established in 2011 by the principal investigators (PIs) of the following three birth cohorts in Asia: the Taiwan Birth Panel Study (TBPS) from Taiwan (PI: Chen), the Mothers and Children's Environmental Health Study (MOCEH) from Korea (PI: Ha), and the Hokkaido Study on Environment and Children's Health (Hokkaido Study) from Japan (PI: Kishi). The two main objectives of BiCCA are 1. to facilitate the exchange of knowledge and collaboration between cohorts and researchers, and 2. to explore the future need for children's environmental health research. The agenda of the BiCCA was first introduced at the PPTOXIII (Prenatal Programming and Toxicity III) held on May 14-15, 2012 in Paris, France. Later on, several symposia/seminar, workshop and PI meetings were held to increase the knowledge about the Asian birth cohorts and to build capacity related to conducting exposure measurements, and the latest techniques such as genetics and epigenetics analysis. These activities also determine the criteria to join BiCCA, complete the 1st phase inventory, prepare the introduction paper and plan for future direction of collaboration. The details are listed as eTable 1.

Definition and identification of Asian birth cohorts

Birth cohort studies were included in the project if they 1) were conducted in Asia; 2) collected information about both prenatal and postnatal exposures; 3) aimed to investigate environmental and health issues in children; and 4) enrolled more than 200 participants. The last criteria is a guideline but not an absolute exclusion criteria. Eligible cohorts were identified through a variety of sources, as follows: searchable websites, publications and personal contacts.

1st phase inventory

An inventory questionnaire was designed to collect detailed information from the various cohorts about their study design, biological sample collection, measurement of environmental exposure, and assessment of child health outcomes. The full questionnaire is listed as Online Supplemental Material. The questionnaire was divided into the following 3 sections:

- 1) Basic information: name of the birth cohort, information about the PI and contact person
- 2) Basic description: main aim, number of children/mother/father recruited, date and criteria of enrolment, and planned age of children at the end of the follow-up.
- 3) Questionnaire or registry date and biological samples: birth outcomes of the

children, the children's exposure, the children's growth and development, social factors, diet and nutrition, children's biological samples and outcome assessments; maternal characteristics, maternal exposure and biological samples; environmental exposure measurement including air pollution, phenol, heavy metals, pesticide, nutrients, persistent organic pollutants, plasticizers, flame retardants, tobacco smoke; genetic and epigenetic factors; outcome assessments including birth outcomes, malformation, allergic diseases, behaviours, neurodevelopment, sex differentiation and reproductive function.

RESULTS

The BiCCA includes 23 birth cohorts, totalling approximately 70,000 study subjects, that were conducted in 10 Asian countries (Figure 1), including three in China, four in Japan, five in Korea, one in Malaysia, one in Nepal, one in the Philippines, one in Singapore, one in Sri Lanka, three in Taiwan and three in Vietnam. Table 1 lists the full name of birth cohorts as well as the enrolment period and the numbers of participants.¹¹⁻²⁴ The CLHNS is the oldest cohort that began in 1983, while the Nanjing Medical University Birth Cohort (NJMUBC) and the Kalutara Children's Health Study (KCHS) are the newest two, beginning in 2014. The majority of the cohorts enrolled at least 200 participants, with the current largest cohort (Hokkaido Study) having 20,818 participants. Two exceptions were the Universiti Sains Malaysia Pregnancy Cohort Study (USM Pregnancy Cohort), which had enrolled 159 children and 188 mothers, and the Nepali Birth Cohort Study in Chitwan Valley (Nepali) from Nepal with 100 participants.

Figure 2 shows the different time points of enrolment and follow-up in the birth cohorts collaborating in the BiCCA. The predefined periods included pre-pregnancy, three trimesters of pregnancy, and newborn to the adolescent stage of participating children. Most of the cohorts recruited mothers during pregnancy (n=15) or before

pregnancy (n=2), and the remaining began at birth. Participating children were followed or were planned to be followed at least two points before the age of 2 years and then once every 2 to 5 years until puberty. The time points already performed and those planned are marked with different symbols. At our reference date (March 2015), children in the 10 cohorts were between 5 to 10 years of age, children in 6 cohorts were older than 10 years, and in seven cohorts, they were younger than 5 years of age (Figure 2).

Biological samples were collected in all cohorts with two exception [Panel Study on Korean Children (PSKC) and KCHS] from mothers and children, covering the prenatal and postnatal periods with various types of tissues including amniotic fluid, blood, breast milk, cord blood, deoxyribonucleic acid (DNA), hair, meconium, placenta, stool, nail, urine and umbilical cord collected (Table 2). The NJMUBC, SBC and The COhort for Childhood Origin of Asthma and allergic diseases (COCOA) collected blood and DNA from biological fathers. Urine and semen were collected additionally by the former two cohorts.

Heavy metals were the most commonly measured environmental exposure, but some cohorts (especially those conducted in Japan and Korea) only focused on mercury,

cadmium or lead. About half of the participating cohorts collected information about tobacco smoking by measuring biomarkers. COCOA, MOCEH and KCHS measured information about both indoor and outdoor air pollution. The Hokkaido Study from Japan collected indoor dust to measure mite allergens and phthalate, among others. The KCHS focused mainly on exposure to PM_{2.5} and Black carbon. Around half of the cohorts measured emerging environmental pollutants, such as persistent organic pollutants (dioxin and related compounds, polyfluoroalkyl substances or brominated flame retardants), bisphenol A and phthalate. The cohorts in Vietnam focused mainly on dioxin exposure (Table 3).

All of the studies had information about birth outcomes, including birth weight and gestational age, and most of them collected the body weight and height of children at a later follow-up visit. The GUSTO from Singapore performed comprehensive measurements of body composition of children including skinfolds and magnetic resonance imaging (MRI). Congenital malformations were recorded in about half of participating cohorts. Twelve studies assessed allergic diseases using The International Study of Asthma and Allergies in Childhood questionnaires (ISAAC). Neurodevelopment and behaviour problems were the most important outcomes for most of the studies, but the studies used a diverse set of measurement tools. Most studies

measured endocrine function and puberty status (or plan to do so in the future) (Table 4).

Maternal characteristics are shown in Table 5-1 and 5-2. The average maternal age and standard deviation among the cohorts ranged from 22.9 ± 3.7 (Nepali) to 33.5 ± 4.1 years (Children's Health and Environmental Chemicals in Korea, CHECK). The maternal pre-pregnancy BMI did not demonstrate large variations, ranging from 20.7 ± 2.6 (COCOA) to 23.7 ± 4.8 kg/m² (GUSTO). Comparisons of maternal educational levels among participants of the different cohorts are a little complex, as shown in Table 5-1 based on the education system of each country. The CLHNS had the highest percentages of multipara (76.9%), and the Laizhou Wan Birth Cohort (LWBC) in China had the highest percentage of primipara (67.3%) among cohorts (Table 5-2). The mothers in the Sapporo birth cohort (Japan) had the highest percentage of smokers (20.3%) and alcohol drinkers (30.9%) during pregnancy (Table 5-2).

The infants' gender ratio was diverse among the cohorts (Table 6); the percentage of males ranged between 45.1% (USM Pregnancy Cohort) and 57.4% (DaNang Dioxin Cohort Study, DaNang study). Although the average gestational ages were almost

the same, but the range of birth weights among the infants was wide; the infants' birth weight in the KCHS (2940 ± 567 g) was the lowest, and LWBC (3419 ± 500 g) had the highest infant birth weights among the cohorts. This variation may be due to differences in the recruitment and source of populations among the cohorts. The CLHNS study had the highest percentage of infants with preterm birth (15.6%), and low birth weight (14.1%).

DISCUSSION

The BiCCA enrolled cohorts established in Asia that were diverse in terms of industrialization and urbanization. The regional and/or global differences need to be discovered through an integrated platform; for example, we are able to explore the differences in cohort findings not only between developed versus developing Asian countries but also with European or North America cohorts. Information including standardized or state-of-art analytic methods, cohort design, assessments of health outcome can be smoothly exchanged. In addition, the experiences shared between studies or countries will help to promote environmental child health through health policy-making or strategy implementation. Furthermore, the knowledge derived from the BiCCA should note the future need for research of new emerging environmental threats or public health priorities that contribute towards organizing the next

generation of birth cohorts.

The theory “Developmental Origins of Health and Disease, DOHaD” illustrated that exogenous maternal malnutrition or environmental factors during pregnancy cause a lifelong, persisting adaptation of the foetus resulting in low birth weight, increased cardiovascular risk, and non-insulin dependent diabetes as adults.²⁵ However, the science underlying the impact of environmental factors on children’s health (from the stage of the foetus to the age of 18) is more complex. While most of the cohort studies in the BiCCA focused on environmental pollutants, CLHNS, GUSTO, USM Pregnancy Cohort and Nepali were designed to investigate the role of nutrients. Integration of participating cohorts in BiCCA with different study focus such as nutrition, social economic factors and environmental toxicants are promising to testify the DOHaD hypothesis and related mechanism.

From the aspect of the exposure assessment, many East Asian countries have some unique features compared with European countries and the USA. For example, the Perfluoroalkyl substances (PFASs) are persistent organic pollutants that are detected in humans worldwide. Their concentrations in plasma in Japan and Korea are quite a lot lower than in western countries, and the temporal trends of PFAS levels indicate

that PFOS (perfluorooctyl sulfonate) and PFOA (perfluorooctanoic acid) concentrations are decreasing every year due to the restriction of PFOS by the Stockholm convention on POPs in 2009. However, the levels of long-chain PFASs (i.e., PFNA, PFUnDA, and PFTrDA) seem to be increasing in Japan and Korea because they are manufactured primarily in Japan via oxidating a mixture of linear fluorotelomer olefins, and prenatal exposure to these compounds may have adverse health outcomes.^{26, 27} In Taiwan, the concentrations of PFOS and PFOA in rivers near semiconductor and electronics industries are higher than in other countries, and industrial wastewater treatment plants are a source of contamination.²⁸ Therefore, the related environmental hazards of PFASs could be an issue among countries with flourishing high-tech or electronics industries. In contrast, the use of polybrominated diphenyl ethers (PBDEs) in Japan diminished in the early 1990s following the recommendations of the Japanese Flame Retardants Conference for voluntary controls, and phosphate esters (PFRs) have been the most frequently used organic flame retardants. In 2003, the EU banned the use of PBDEs, and only a few epidemiological studies on the alternatives to PBDEs have been reported. Therefore, Asian cohort studies provide information about PFRs in indoor environments and their relationship to asthma and allergies in children.²⁹ The use of other alternative flame retardants, e.g., non-brominated flame retardants, is increasing and warrants further studies as well.

Different eating habit or culture may result in diverse chemical exposures or health impact. For example, the benefits of essential fatty acid and toxicity of chemical pollutants, such as mercury and dioxin related compounds, are always the scientific basis of fish consumption advisories. Maternal plasma fatty acid concentrations were significantly correlated with PFOS concentrations and may affected birth weight of female offsprings.³⁰ Associations between prenatal methylmercury exposure and cognitive deficits were reported in a Faroe Islands cohort, but few were found by the Seychelles Islands' study. Evidence of negative confounding by prenatal docosahexaenoic acid (DHA) which partially obscured the association of prenatal mercury with lower Intelligence quotient had reported.³¹ Meanwhile, the adverse health impacts of mercury were only observed among those children carrying the susceptible APOE (Apolipoprotein E) genotype in TBPS.³² Genetic variation between races or ethnicities could further impose a diverse susceptibility to environmental pollutants. In addition, canned food is common in Western countries whereas hot food in plastic containers is common in Asia. Whether these habits increase the exposure risk to certain endocrine disrupters such as bisphenol A or phthalate or not is another question to be solved. The complex interaction between diet or nutrients, co-exposure to environmental pollutants and genetic polymorphisms are crucial is-

sues in children's health.

Climate change and extreme weather are potential environmental threats. Season and weather especially cold ambient temperature have been identified as potential risk factors for lower birth weight and preterm birth.^{33, 34} Nevertheless, null association had been reported.³⁵ Meanwhile, evidence is growing that climate change has affect human health including mortality from extreme weather events, changes in quality of air and water and changes in the ecology of infectious disease. Humidity and temperature may change the composition of ambient air pollution and further cause diverse toxic effects. The survival and spread of infectious pathogens are highly correlated with weather. For example, the *Aedes species* mosquito carrying Zika virus is distributed in tropical and subtropical regions that Taiwan and the southern Chinese island province of Hainan could be at greater risk of locally transmitted cases. However, the effect of global warming is unclear. Climate change is a global issue and its related knowledge should be uncovered through international cooperation.

The BiCCA consortium intends to expand beyond Asia and provide collaborations among cohorts. One of the major challenges is the comparison of existing data

among the studies and harmonization of the exposure assessment and children's health outcome. Definition of basic demographic variables and questionnaires should be harmonized. The potential bias of environmental exposure measurements derived from various analytic methods or specimen could be verified by inter- and intra- laboratory tests. Homogeneity of country or language specific assessment tools needs to be identified. In addition, two different approach including pooled analysis and meta-analysis will be applied.³⁶ Reviewing existing data will provide a potential or direction for future collaborative analyses. Furthermore, evaluating new methods and technologies for future studies will be enhanced by aggregation of data from each cohort. After overcoming these challenges, combining and harmonizing cohort data in this consortium will help to improve statistical power, reduce publication bias, and assess the exposure-outcome relationship in emerging concerns of child health, even for relatively rare health outcomes. Further contribution will be made for researches of co-exposure effects, gene-environmental interaction and replication and validation in omic studies through transnational and interracial cooperation.

The BiCCA especially welcomes birth cohorts in Asia to collect epidemiological data across different Asian countries. The BiCCA provides detailed information

about the Asian birth cohorts and facilitates access to information regarding existing Asian cohort studies. Any group can contact us for further information or consider potential collaboration from all around the world. Enquiries and initial approaches regarding membership or detailed information are welcome. Please contact us at secretary@bicca.org; decisions will be made by the Executive Committee Professors Reiko Kish, Jun Jim Zhang, Eun-Hee Ha and Pau-Chung Chen. More information is available in our website (<http://www.bicca.org/>).

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FIGURE LEGENDS

Figure 1. Asian birth cohort studies collaborating in BiCCA.

Figure 2. Start of enrollment and time points of follow up participating studies in BiCCA. See Table 1 for full names and locations of cohorts.

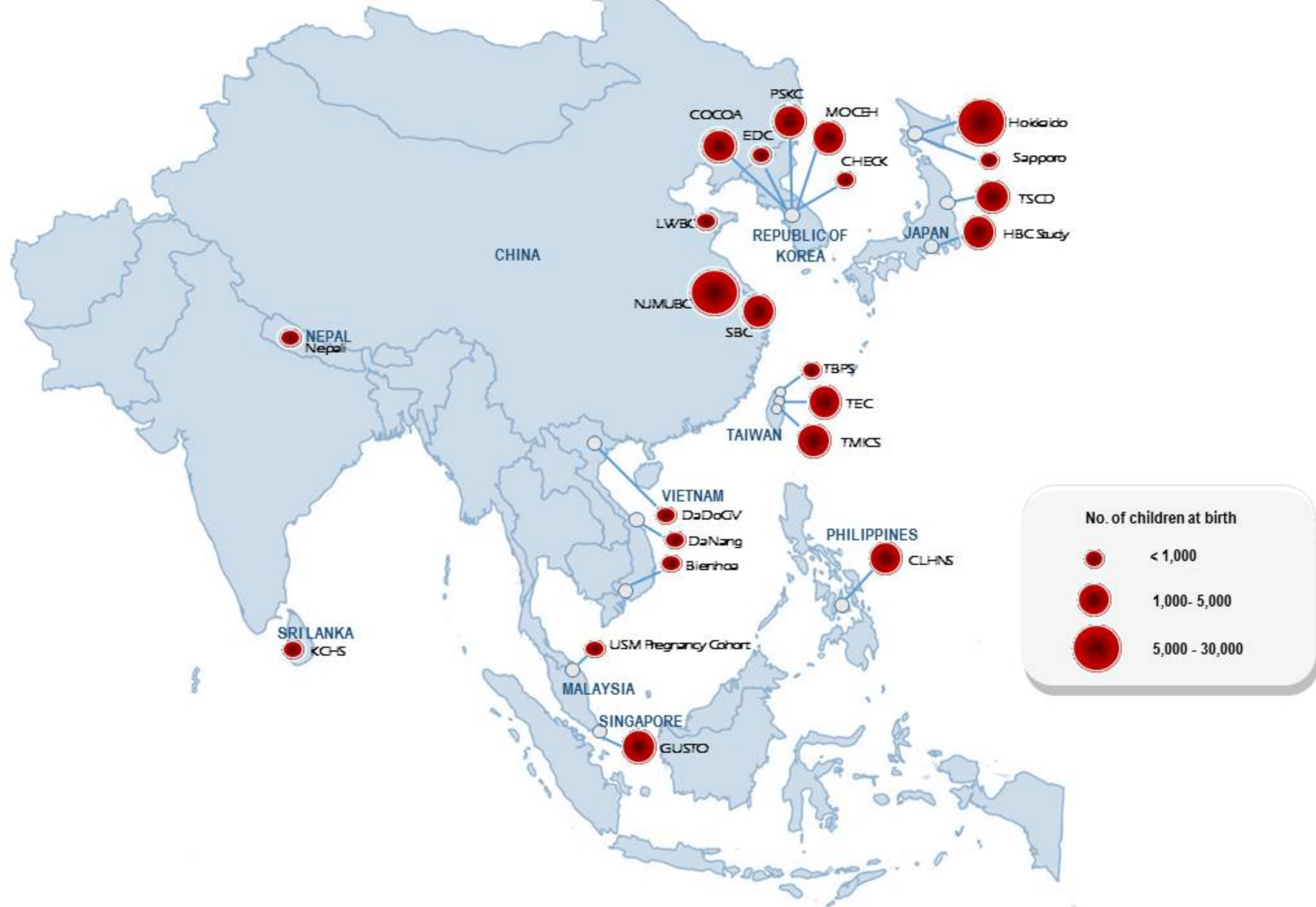


Fig. 1

Country	Cohort	Start	Pre-pregnancy	Prenatal period (trimester)			Postnatal period					
				First	Second	Third	Birth~1month	1~6 month	6~24 month	2~5 year	5~10 year	≥ 10 year
CHINA	LWBC	2010										
	NJMUBC	2014										
	SBC	2013										
JAPAN	HBC Study	2007										
	Hokkaido	2003										
	Sapporo	2002										
	TSCD	2001										
KOREA	CHECK	2011										
	COCOA	2007										
	EDC study	2008										
	MOCEH	2006										
	PSKC	2008										
MALAYSIA	USM Pregnancy Cohort	2010										
NEPAL	Nepali	2008										
PHILIPPINES	CLHNS	1983										
SINGAPORE	GUSTO	2009										
SRI LANKA	KCHS	2014										
TAIWAN	TBPS	2004										
	TEC	2004										
	TMICS	2000										
VIETNAM	BienHoa ²	2012										
	DaDoCiV	2008										
	DaNang ²	2008										

 Planned Study
 Ongoing Study

Fig. 2

Table 1. General description of participating studies in Birth Cohort Consortium of Asia

Country	Birth cohort	Full name and key reference	Regions covered	Source	Enrollment period	No. of children at birth	No. of mother enrolled
CHINA	LWBC	Laizhou Wan Birth Cohort	South coast area of Laizhou Wan of Bohai Sea, Shandong province, China	Hospital based	2010-2013	773	773
	NJMUBC	Nanjing Medical University Birth Cohort	Nanjing, Suzhou, Wuxi, Huai'an, Changzhou	Hospital & Community based	2014-2016	26,000*	30,000*
	SBC	Shanghai Birth Cohort	Shanghai	Hospital based	2013-2015	3,000	4,000
JAPAN	HBC Study	Hamamatsu Birth Cohort for Mothers and Children ¹¹	Hamamatsu	Hospital & Community based	2007-2011	1,258	1,138
	Hokkaido	Hokkaido cohort: Hokkaido Study on Environment and Children's Health ^{12,13}	Hokkaido	Hospital & Community based	2003-2013	20,818	20,929
	Sapporo	Sapporo cohort: Hokkaido Study on Environment and Children's Health ^{12,13}	Sapporo	Hospital based	2002-2005	504	514
	TSCD	The Tohoku Study of Child Development ¹⁴	Sendai	Hospital based	2001-2006	1,348	1,323

Country	Birth cohort	Full name and key reference	Regions covered	Source	Enrollment period	No. of children at birth	No. of mother enrolled
KOREA	CHECK	Children's Health and Environmental Chemicals in Korea	South Korea	University hospital based	2011-2013	352	352
	COCOA	COhort for Childhood Origin of Asthma and allergic diseases ¹⁵	Korea	Hospital & Community based	2007-2016	2,400	2,400
	EDC study	Environment and Development of Children Study	Seoul	Community based	2008-2014	698	698
	MOCEH	The Mothers and Children's Environmental Health study ¹⁶	Seoul, Ulsan and Cheonan	Hospital & Community based	2006-2010	1,751	1,751
	PSKC	Panel Study on Korean Children	Korea	Hospital based	2008	2,150	2,150
MALAYSIA	USM Pregnancy Cohort	Universiti Sains Malaysia Pregnancy Cohort Study ¹⁷	Kubang Kerian	Hospital based	2010-2011	159	188
NEPAL	Nepali	Nepali Birth Cohort Study in Chitwan Valley ¹⁸	Chitwan	Hospital & Community based	2008Sep-Oct	100	100
PHILIPPINES	CLHNS	Cebu Longitudinal Health and Nutrition Survey ¹⁹	Metro Cebu, Philippines	Community based	1983-1984	3,080	3,327
SINGAPORE	GUSTO	Growing Up in Singapore Towards healthy Outcomes ²⁰	Singapore	Hospital based	2009-2010	1,190	1,247

Country	Birth cohort	Full name and key reference	Regions covered	Source	Enrollment period	No. of children at birth	No. of mother enrolled
SRI LANKA	KCHS	Kalutara Children's Health Study	Kalutara, Sri Lanka	Community based	2014-2015	450	450
TAIWAN	TBPS	Taiwan Birth Panel Study ²¹	Taipei and New Taipei	Hospital based & Community based	2004-2005	486	486
	TEC	Taiwan Early-Life Cohort ²²	Hsinjuang, Jiayi, Yulin, Tainan, Kaohsiung, Taitung	Hospital based	2001-2005	1,589	1,589
	TMICS	Taiwan Maternal and Infant Cohort Study ²³	Taipei, Hsinchu, Taichung, Changjua, Kaohsiung, Hualien	Hospital based	2000-2014	1,616	2,577
VIETNAM	BienHoa study	BienHoa Dioxin Cohort study ²⁴	Bien Hoa	Hospital based	2012Sep-Nov	200	200
	DaDoCiV	Dioxin and Development of Children in Vietnam	Hanoi, Phu, Cat, Bien Hoa	Community based	2008-2013	200	200
	DaNang study	DaNang Dioxin Cohort study	DaNang	Hospital based	2008-2010	241	241

*Targeted recruitment numbers.

Table 2. Collected biological samples of participating studies in Birth Cohort Consortium of Asia

[illegible]

Cohort	Father	Mother				postpartum	Child					
		T1	T2	T3	at delivery ^a		Birth	1~6 mo	6~24 mo	2~5 year	5~10 year	≥ 10 year
USM												
Pregnancy Cohort			B	B	H	BM				H		
Nepali CLHNS					UC, H		CB, M		B, H			B
GUSTO	Ds		B, H, Db, Ds		B, P, Db	BM, H, Ds	UC, CB, Ds, M	Ds, S	Ds, S	Ds, H, S		
KCHS												
TBPS					B, Db, P, U		CB, Db		B, H, S, U	U	B, Db, Ds, U	
TEC					B, Db, P, U		CB, Db				B, Db, Ds, U	
TMICS		B, Db, U	U	B, Db, U	P	BM	CB, M		B, Db, U	B, Db, U	B, Db, H, U	B, Db, H, U
BienHoa						BM	CB, UC		U	U		
DaDoCiV					B	BM			Ds	Ds		
DaNang						BM				U		

Abbreviations: A, amniotic fluid; B, blood; BM, breast milk; CB, cord blood; Db, DNA from blood; Ds, DNA from buccal swab ; H, hair; M, meconium; P, placenta; T1, T2, T3, first, second and third trimesters; S, stool; Se, semen; N, nail; U, urine; UC, umbilical cord;

^a biosample collected during the hospital stay for delivery

^b Sapporo cohort did its first enrollment during T2-T3

Table 3. Measurements of selected environmental exposure/biomarker^a of participating studies in Birth Cohort Consortium of Asia

Cohort	Indoor air pollutions	Outdoor air pollutions	Tobacco smoking	Metals and Metalloids	Pesticides	Persistent organic pollutants	other chemical exposures
LWBC				18 metals ^e	Organophosphate, pyrethrin	PBDEs	BPA, trclosan, nonylphenol
NJMUBC ^b		PM _{2.5} , PM ₁₀	Cotinine, Nicotine, Myosmine	25 metals ^f	Organophosphate pesticides, Carbamate pesticides, Organochlorine insecticides, Pyrethroid pesticides, Herbicides, Fungicides	PCBs, PFASs, PBDEs	Pheonls, VOCs, Phthalates, Phytoestrogens, Polycyclic aromatic hydrocarbons
SBC	dust			18 metals ^e	Organophosphate, pyrethrin	PCBs, PFASs, PBDEs	BPA, trclosan, nonylphenol
HBC Study				Cu, Se, Zn			
Hokkaido	dust mite, phthalate		Cotinine ^c			Dioxin, PCBs, PFASs	BPA, phthalates
Sapporo			Cotinine	Hg	DDT, Drins, Chlordane, Heptaclor, HCH, Mirex, Toxaphene, HCB	Dioxin, PCBs, PFASs	BPA, phthalates
TSCD				MeHg, Pb, Cd	Organochlorine	Dioxin, PCBs	

Cohort	Indoor air pollutions	Outdoor air pollutions	Tobacco smoking	Metals and Metalloids	Pesticides	Persistent organic pollutants	other chemical exposures
CHECK				Pb, Cd	DDTs, chlordanes, HCB, HCHs, heptachlor, heptachlor epoxide, mirex	PBDEs, PCBs	BPA, phthalates, parabens
COCOA	PM, Dust, mite, Endotoxin	PM, NO ₂ , O ₃	Cotinine				Phthalates
EDC study		PM ₁₀ , NO ₂ , CO, O ₃ , SO ₂	Cotinine	Pb, Cd, Hg		PFASs	BPA, phthalates, Pyrethroids (3-PBA), PAHs, VOCs
MOCEH	PM _{2.5} , PM ₁₀ , NO ₂ , HCHO, VOCs, dust mite, endotoxin	PM _{2.5} , PM ₁₀ , NO ₂ , HCHO, VOCs	Cotinine ^b	Pb, Cd, Hg, Mn			BPA, phthalates, PAHs
PSKC	Humidity/ Mold		Nicotine				

Cohort	Indoor air pollutions	Outdoor air pollutions	Tobacco smoking	Metals and Metalloids	Pesticides	Persistent organic pollutants	other chemical exposures
USM Pregnancy Cohort			Nicotine ^c				
Nepali				Pb, As, Cd, Zn, Se, Cu			
CLHNS GUSTO		PM _{2.5}	Cotinine				
KCHS	PM _{2.5} , Black carbon	PM _{2.5} , Black carbon					
TBPS			Cotinine	18 metals ^e	chlorpyrifos, cypermethrin, Flucythrinate	PFASs	BPA, phenols, phthalates
TEC		PM _{2.5} , PM ₁₀ , NO ₂ , HCHO, VOCs		18 metals ^e		PFASs	
TMICS			Cotinine ^d	18 metals ^e	DDT, Chlordane, Heptaclor, HCH, HCB	PFASs, PCBs, Dioxin	BPA, phthalates, phenols
BienHoa						Dioxin	

Cohort	Indoor air pollutions	Outdoor air pollutions	Tobacco smoking	Metals and Metalloids	Pesticides	Persistent organic pollutants	other chemical exposures
DaDoCiV						Dioxin	
DaNang						Dioxin	

Abbreviations: BPA, bisphenol A; DDTs, dichlorodiphenyl trichloroethanes; HCB, hexachlorobenzene; HCHs, hexachlorocyclohexanes; PAHs, Polycyclic aromatic hydrocarbons; PBDEs, polybrominated diphenyl ester; PCB, polychlorinated biphenyl; PFASs, polyfluoroalkyl substances; VOCs, Volatile Organic Compounds;

^a prenatal exposure, unless specified

^b planned to measure in the future

^c measurement include prenatal and postal exposure

^d postnatal exposure

^e 18 metals: lead, arsenic, mercury, cadmium, beryllium, antimony, barium, cerium, platinum, thorium, manganese, zinc, copper, selenium, cobalt, molybdenum, gallium, uranium

^f 25 metals: Aluminum, Antimony, Arsenic, Barium, Beryllium, Cadmium, Calcium, Cesium, Chromium, Cobalt, Copper, Gallium, Iron, Lead, Manganese, Mercury, Molybdenum, Nickel, Platinum, Selenium, Thallium, Thorium, Tungsten, Uranium, Zinc

Table 4. Health outcomes/surrogate marker recorded by participating studies in Birth Cohort Consortium of Asia

Cohort	Fetal growth	Pregnancy outcome	Growth and obesity	Allergic disease and immune function	Neurodevelopment and behavior problems	Endocrine function and puberty	Others
LWBC	BW, BL	preterm birth, congenital malformation	weight, height		GESELL, CBCL, IQ (WPPSI/ WISC), ADHD-RS	thyroid function, sex hormone	
NJMUBC	fetal sonography, BW, BL	preterm birth, congenital malformation, miscarriage, stillbirth, FGR, LBW, SGA, macrosomia	weight, height, head, fat	ISAAC	CBCL, DDST, GESELL, PSQ, Japan S-M social adaptability scale, SPM, C-WISC	thyroid function, sex hormone	
SBC	fetal sonography, BW, BL	preterm birth, congenital malformation, stillbirth	weight, height, fat	ISAAC	ASQ, ASQ-SE, Bayley III, CBCL, M-CHAT, IQ (WPPSI/ WISC)	thyroid function, sex hormone	

Cohort	Fetal growth	Pregnancy outcome	Growth and obesity	Allergic disease and immune function	Neurodevelopment and behavior problems	Endocrine function and puberty	Others
HBC Study	fetal sonography, BW, BL	preterm birth, stillbirth, LBW, SGA	weight, height, head circumference	ISAAC	ADHD-RS, ADI-R, ADOS, BISQ, Early Child Behavioural Questionnaire, Edinburgh Handedness Inventory, MacArthur CDI, M-CHAT, MSEL, SDQ, WPPSI, VABS II		Eye gaze patterns for measuring sociability and attention using Gazefinder®
Hokkaido	BW, BL	preterm birth, congenital malformation, miscarriage, stillbirth, FGR, LBW, SGA	weight, height	ISAAC	SCQ, SDQ, DCDQ, M-CHAT, KIDS, CBCL, ADHD-Rating scale, Conners3P, WISC-IV	thyroid function, reproductive hormones	
Sapporo	BW, BL	preterm birth, congenital malformation, stillbirth, FGR, LBW, SGA	weight, height	IgE, ISAAC	Bayley II, CBCL, WISC-III, K-ABC, FT-II, DDST, WCST-KFS	thyroid function, reproductive hormones	

Cohort	Fetal growth	Pregnancy outcome	Growth and obesity	Allergic disease and immune function	Neurodevelopment and behavior problems	Endocrine function and puberty	Others
TSCD	BW, BL	preterm birth, congenital malformation	weight, height		ADHD-Rating scale, Bayley II, Boston Naming Test, CBCL, CPT, Fagan Test, K-ABC, KSPD, NABS, WISC-III, WISC_IV	thyroid function	
CHECK	BW, BL	preterm birth	weight, height		Bayley II, SMS tests	thyroid function	
COCOA	BW, BL	preterm birth	weight, height	IgE, IL-13, IFN γ , SPT, ISAAC	Mullen, ASQ, CBCL, IQ (WPPSI/ WISC), MSEL		
EDC study	fetal sonography, BW	preterm birth, congenital malformation	weight, height			thyroid function, sexual maturation, bone age	liver and kidney function
MOCEH	fetal sonography, BW, BL	preterm birth, congenital malformation FGR, LBW, SGA	weight, height, head	ISAAC	Bayley II, ASQ, WPPSI, CAT, CBCL, SRS, SDQ, ARS		

Cohort	Fetal growth	Pregnancy outcome	Growth and obesity	Allergic disease and immune function	Neurodevelopment and behavior problems	Endocrine function and puberty	Others
PSKC	BW, BL	preterm birth	weight, height, head, waist	ISAAC	ASQ(Korea), Bayley II, CBCL 1.5-5(Korea), DDST II(Korea), WPPSI(Korea), REVT		
USM Pregnancy Cohort	BW, BL		weight, height, head, fat (skinfold)		ASQ		
Nepali	BW, BL	preterm birth			Brazelton III, Bayley II		
CLHNS	BW, BL	preterm birth	weight, height, weight, height, head, mid-arm, abdominal circumference, body composition				
GUSTO	fetal sonography, BW, BL	preterm birth, congenital malformation FGR, LBW, SGA		ISAAC, SPT	ASQ, ASQ-SE, Bayley III, CBCL, CTS, ITSEA, PEDS, PEDS:DM, Q-CHAT		
KCHS	BW, BL	preterm birth, congenital malformation	weight, height				Respiratory Conditions (Symptom diaries, Pneumonia, etc.)

Cohort	Fetal growth	Pregnancy outcome	Growth and obesity	Allergic disease and immune function	Neurodevelopment and behavior problems	Endocrine function and puberty	Others
TBPS	fetal sonography, BW, BL	preterm birth, LBW, SGA	weight, height	IgE, ISAAC	CBCL, CDIIT, WPPSI	thyroid function, sexual maturation, bone age	
TEC	BW, BL	preterm birth	weight, height	IgE, ISAAC	CBCL	sexual maturation, bone age	
TMICS	BW, BL, fetal sonography	preterm birth, congenital malformation	weight, height	IgE, ISAAC	Bayley II, CBCL, WPPSI	thyroid function, sexual maturation, bone age	
BienHoa	BW, BL		weight, height, head and abdominal circumference		Bayley III	thyroid function, sex hormone, gender difference of behavior	

Cohort	Fetal growth	Pregnancy outcome	Growth and obesity	Allergic disease and immune function	Neurodevelopment and behavior problems	Endocrine function and puberty	Others
DaDoCiV	BW, BL	preterm birth				sex hormone	
DaNang	BW, BL		weight, height, head and abdominal circumference		Bayley III, Kauffman-ABC II, M-ABC2, Eating behavior, Autism Spectrum rating Scale (ASRS), ADHD	gender difference of behavior	

Abbreviations: ADHD rating scales, attention deficit hyperactivity disorder rating scales; ADI-R, Autism Diagnostic Interview Revised; ADOS, autism diagnostic observation scale; Bayley, Bayley Scales of Infant and Toddler Development; ASQ, Ages and Stages Questionnaire; ASQ-SE, ASQ- social Emotional; BIA, bioelectrical Impedance Analysis; BISQ, Brief Infant Sleep Questionnaire; BL, birth length; BW, birth weight; CBCL, Child Behavior Checklist; CPT, The Conners' Continuous Performance Test; Conners3P, The Conners Third edition Parent; CTS, Carey temperament Scales; DCDQ, developmental coordination disorder questionnaire; DDST, the Denver Developmental Screening Test; FGR, fetal growth restriction; FTII, The Fagan Test of Infant Intelligence; GA, gestational age; GESELL, the Gesell developmental schedules; IFN γ , Interferon gamma; IgE, immunoglobulin E; IL-13, Interleukin 13; ISAAC, The International Study of Asthma and Allergies in Childhood questionnaires; ITSEA, Infant Toddler Social Emotional Assessment; K-ABC, The Kaufman-Assessment Battery for Children; KIDS, Kinder Infant Development Scale; KSPD, Kyoto Scale of Psychological Development; LBW, low birth weight; MacArthur CDI, MacArthur Communicative Developmental Inventory; M-CHAT, modified checklist for autism in Toddlers; MSEL, Mullen Scales of Early learning; NABS, the Neonatal Behavioral Assessment Scale; PEDS, Parent's Evaluation of Developmental Status; PEDS:DM, PEDS: Developmental Milestones; PST, Parent Symptom Questionnaire; Q-CHAT, Quantitative Checklist for Autism in Toddlers; REVT, Receptive and Expressive Vocabulary Test; SCID, structured clinical interview for DSM-IV Axis-I disorders; SCQ, social communication questionnaire; SDQ, the strength and difficulties questionnaire; SGA, small for gestational age; SPT, skin prick test; SMS, Social Maturity Scale; VABS II, Vineland Adaptive

Behavior Scales, second edition; WCST-KFS, Wisconsin Card Sorting Test-Keio-F-S version; WISC-III The Wechsler Intelligence Scale for Children-Third edition; WISC-IV The Wechsler Intelligence Scale for Children-Forth edition; WPPSI, Wechsler Preschool and Primary Scale of Intelligence.

Table 5-1 Maternal characteristics

Birth cohort	Age (years), N (mean±SD)	Pre-pregnancy BMI (kg/m ²), N (mean±SD)	Educational level (years) N (%)						
			no education	elementary	junior high school	senior high school		university	graduate school
LWBC	756 (28.3±4.5)	741 (21.7±3.0)	5 (0.6)	46 (6.0)	303 (39.6)	216 (28.2)		189 (24.7)	7 (0.9)
NJMUBC	*	*	*	*	*	*	*	*	*
Shanghai	*	*	*	*	*	*	*	*	*
HBC Study	1138 (31.4 ± 5.1) ^a	1138 (21.0 ± 3.4)			<12y (junior high school) 68 (6.0)	12y (high school) 317 (27.9)	13-15y (vocational & college) 469 (41.2)	16y (university) 235 (20.7)	>16y (graduate school) 49 (4.3)
Hokkaido	18598 (29.8 ± 4.8)	19307 (21.2 ± 3.3)			≤9y (junior high school) 1084 (5.5)	10-15y (high school or junior college) 16553 (83.3)		university 2229 (11.2)	
Sapporo	510 (30.4 ± 4.9)	506 (21.2 ± 3.2)			≤12y 225 (44.3)	13-16y 274 (53.9)		≥17y 9 (1.8)	

Birth cohort	Age (years), N (mean±SD)	Pre-pregnancy BMI (kg/m ²), N (mean±SD)	Educational level (years)								
			N (%)								
TSCD	1348 (30.3 ± 4.8)	1348 (21.2 ± 3.1)									
CHECK	352 (33.5 ± 4.1)	352 (21.4 ± 3.3)	N.A.								
COCOA	2224 (32.6 ± 3.6)	2041 (20.7 ± 2.6)	no education 1 (0.1)	elementary 1 (0.1)	middle school 1 (0.1)	high school 110 (5.5)	vocational college 61 (3.0)	university 1415 (70.1)	graduate school 430 (21.3)		
EDC study	663 (31.4 ± 3.6)	662 (21.9 ± 3.0)					Junior high school 1 (0.15)	Senior high school 124 (18.7)	university 461 (69.5)	Graduate school 77 (11.6)	
MOCEH	1604 (30.30 ± 3.74)	1432 (22.9 ± 3.0)					<12y (high school) 397 (26.5)	>12y (university or graduated school) 1103 (73.5)			
PSKC	2077 (31.3 ± 3.7)	2067 (21.2±2.9)					below high school 14 (0.6)	high school 629 (30.5)	college 590 (28.6)	university 714 (34.6)	postgraduate degree 115 (5.6)
USM Pregnancy Cohort	153 (28.9 ± 4.5)	153 (22.6 ± 4.1)	no education 0	primary 1(0.7)	secondary 51(33.3)	diploma 64 (41.8)	university degree 26 (17.0)				postgraduate degree 11 (7.2)

Birth cohort	Age (years), N (mean±SD)	Pre-pregnancy BMI (kg/m ²), N (mean±SD)	Educational level (years) N (%)							
Nepali	100 (22.9 ± 3.7)	100 (23.2 ± 2.9)	Mean year (SD) 9.2 (3.8) and Range 0 to 17							
CLHNS	3327 (26.0 ± 6.0)	N.A.	no education 61 (1.8)	elementary 1984 (59.6)	high school 860 (25.8)	college 422 (12.7)				
GUSTO	1247 (30.6 ± 5.2)	1141 (23.7 ± 4.8)	no education 2 (0.2)	primary 55 (4.5)	secondary 451 (36.7)	GCE A Level/Diploma 311 (25.3)				
KCHS	375 (29.6 ± 5.2)	326 (22.6 ± 4.2)	Never gone to school 2 (0.5)	Primary education 3 (0.8)	Secondary education 96 (25.5)	G.C.E O/L 108 (28.6)	G.C.E O/L & Vocational education 2 (0.5)	G.C.E A/L 134 (35.5)	Degree 28 (7.4)	
TBPS	486 (30.9 ± 4.6)	486 (20.9 ± 3.0)	no education 3 (0.6)	elementary 10 (2.1)	junior high school 32 (6.6)	senior high school 113 (23.3)	specialized training school 112 (23.1)	university 149 (30.7)	graduate school 66 (13.6)	

Birth cohort	Age (years), N (mean±SD)	Pre-pregnancy BMI (kg/m ²), N (mean±SD)	Educational level (years) N (%)						
TEC	1521 (27.6 ± 8.9)	1265 (20.9 ± 3.3)	no education 15 (1)	elementary 50 (3.2)	junior high school 215 (13.8)	senior high school 823 (52.8)	specialized training school 303 (19.4)	university 132 (8.4)	graduate school 22 (1.4)
TMICS	1987 (31.1 ± 4.8)	1611 (21.9 ± 3.8)	no education 5 (0.2)	elementary 28 (1.4)	junior high school 203 (10.1)	senior high school 404 (20.1)	specialized training school/university 1141 (56.8)	graduate school 229 (11.4)	
BienHoa	210 (28.6 ± 4.6)	N.A.	no education 1 (0.5)	elementary 13(6.2)	junior high school 57 (27.1)	senior high school 70 (33.3)	specialized training school 39 (18.6)	university 30 (14.3)	
DaDoCiV	236 (24.8 ± 3.6)	N.A.		elementary 34 (14.8)	junior high school 99 (43.2)	high school 67 (29.3)		university 29 (12.7)	
DaNang	217 (27.8 ± 6.0)	N.A.	no education 9 (4.1)	elementary 44 (20.3)	junior high school 94 (43.3)	senior high school 48 (22.1)	specialized training school 19 (8.8)	university 3 (1.4)	

Abbreviations: N.A., not available.

^a number of participating parturient [1138]) is not equal to participating infants [1258] because of multiple births and multiple entry of some of the parturient

*: still recruiting subjects

Table 5-2 Maternal characteristics

Birth cohort	Parity		Smoking status during pregnancy, N (%)			Environmental tobacco smoke Exposure during pregnancy, N(%)	Alcohol drinking during pregnancy, N(%)
	primipara	multipara	non-smoker	Quitter	smoker	yes	yes
LWBC	489 (67.3)	238 (32.7)	766 (99.0)	4 (0.5)	4 (0.5)	339 (43.8)	0
NJMUBC	*	*	*	*	*	*	*
Shanghai	*	*	*	*	*	*	*
HBC Study	615 (54.0)	523 (46.0)	884 (77.6)	192 (16.8) ^a	62 (5.5) ^b	N.A.	145 (12.8) ^c
Hokkaido	8183 (43.8)	10498 (56.1)	9113 (54.5)	5284 (31.6)	2298 (13.7)	8662 (43.9) ^d	2438 (18.3)
Sapporo	240 (47.7)	263 (52.3)	228 (44.9)	177 (34.8)	103 (20.3)	372 (73.2) ^e	157 (30.9)
TSCD	725 (53.8)	623 (46.2)	1046(77.8)	222(16.5)	76(5.7)	N.A.	140 (10.4)
CHECK	136 (38.6)	216 (61.4)	252 (96.6)		9 (3.4)	131 (45.3)	37 (13.7)
COCOA	1099 (58.4)	782 (41.6)	164 (95.9)		7 (4.1)	1050 (60.6)	164 (9.4)
EDC study	374 (56.6)	287 (43.4)	531 (92.7)		42 (7.3)	163 (24.6)	173 (30.6)
MOCEH	681 (50.9)	657 (49.1)	1327 (88.2)	164 (10.9)	13 (0.9)	921 (65.1) ^d	75 (5.4)
PSKC	984 (47.5)	1088 (52.5)	1813 (97.3)	33 (1.8)	17 (0.9)	556 (60.3)	502 (26.9)
USM							
Pregnancy Cohort	43 (28.1)	110 (71.9)	153 (100.0)	0	0	65 (44.2)	0
Nepali	66 (66.0)	34 (34.0)			5 (5.0)		4 (4.0)
CLHNS	768 (23.1)	2559 (76.9)	2875 (86.4)		452 (13.6)		813 (24.4)
GUSTO	545 (45.9)	643 (54.1)	1149 (97.5)		29 (2.5)	432 (38.0)	21 (1.8)

Birth cohort	Parity		Smoking status during pregnancy, N (%)			Environmental tobacco smoke Exposure during pregnancy, N(%)	Alcohol drinking during pregnancy, N(%)
	primipara	multipara	non-smoker	Quitter	smoker	yes	yes
KCHS	105 (29.6)	227 (63.9)	377 (100)		0	5 (1.3)	0
TBPS	230 (47.3)	256 (52.7)	460 (94.7)		26 (5.30)	139 (28.6)	21 (4.3)
TEC	647 (47.2)	723 (52.8)	1452 (95.8)	16 (1.1)	48 (3.2)	618 (44.0)	32 (2.1)
TMICS	682 (43.5)	887 (56.5)	1974 (98.4)	12 (0.6)	20 (1.0)	N.A.	95 (4.7)
BienHoa	77 (36.7)	133 (63.3)	207 (98.6)	0	3 (1.4)	136 (64.8)	10 (4.8)
DaDoCiV	152 (64.7)	83 (35.3)	233 (99.2)	0	2 (0.8)	114 (48.5)	7 (3.0)
DaNang	73 (30.5)	163 (69.5)	241 (100)	0	0	198 (82.8)	17 (8.7)

^a quitted before 12wks of gestational age

^b any smoking at/after 12wks of gestational age (including those quitted after 12 wks)

^c any drinking at/after 12wks of gestational age

^d assessed based on exposure of pregnant women at home or workplace

^e pregnant women who lived with smoker(s) during pregnancy

*: still recruiting subjects

Table 6. Infant Characteristics

Birth cohort	Male, N (%)	Gestational age (weeks), N (mean±SD)	Birth weight (gm), N (mean±SD)	Preterm, N (%)	Low birth weight, N (%)
LWBC	391 (51.2)	756 (39.3 ± 2.0)	763 (3419 ± 501)	30 (4.0)	17 (2.2)
NJMUBC	*	*	*	*	*
SBC	*	*	*	*	*
HBC Study	648 (51.5)	1258 (38.9 ± 1.6)	1258 (2943 ± 435)	82 (6.5)	160 (12.7)
Hokkaido ^a	9204 (50.4)	18004 (38.7 ± 1.5)	18004 (3029 ± 420)	980 (5.4)	1592 (8.8)
Sapporo	242 (48.0)	504 (38.9 ± 1.5)	504 (3039 ± 521)	35 (6.9)	34 (6.7)
TSCD	696 (51.6)	1349 (39.6 ± 1.2)	1349 (3111 ± 355)	N.A.	N.A.
CHECK	177 (50.4)	352 (39.3 ± 1.2)	352 (3256 ± 388)	4 (1.1)	13 (3.7)
COCOA	1029 (52.0)	1915 (39.1 ± 1.3)	1690 (3184 ± 438)	80 (4.2)	94 (5.6)
EDC study	356 (53.7)	660 (38.7 ± 1.5)	608 (3240 ± 447)	8 (1.2)	26 (4.3)
MOCEH	774 (52.2)	1502 (39.0 ± 1.7)	1475 (3261 ± 444)	80 (5.3)	41 (2.8)
PSKC	1059 (51.0)	2066 (39.2 ± 1.2)	2073 (3258 ± 408)	63(3.0)	62(3.0)
USM					
Pregnancy Cohort	69 (45.1)	153 (38.8 ± 1.2)	153 (3110 ± 420)	0	11 (7.2)
Nepali	47 (47.0)	100 (38.9 ± 1.4)	100 (3029 ± 438)		
CLHNS	1632 (53.0)	3052 (38.9 ± 2.6)	3040 (2987 ± 442)	478 (15.6)	372 (14.1)
GUSTO	627 (52.7)	1190 (38.6 ± 1.7)	1190 (3065 ± 484)	103 (8.7)	117 (9.8)
KCHS	170 (48.0)	327 (38.3 ± 2.1)	354 (2940 ± 567)	38 (10.7)	43 (12.1)
TBPS	247 (50.8)	486 (38.5 ± 1.7)	486 (3158 ± 476)	42 (8.6)	28 (5.8)

Birth cohort	Male, N (%)	Gestational age (weeks), N (mean±SD)	Birth weight (gm), N (mean±SD)	Preterm, N (%)	Low birth weight, N (%)
TEC	809 (51.9)	1510 (38.9 ± 1.2)	1480 (3094 ± 429)	76 (5.0)	80 (5.4)
TMICS	712 (53.5)	1332 (38.4 ± 2.0)	1308 (3087 ± 465)	90 (6.8)	90 (6.9)
BienHoa	111 (52.9)	210 (38.9 ± 2.6)	210 (3297 ± 411)	6 (2.9)	2 (1.0)
DaDoCiV	125 (53.2)	N.A.	120 (3211 ± 433)	N.A.	6 (5.0)
DaNang	125 (57.4)	217 (39.5 ± 0.8)	217 (3228 ± 375)	0	4 (1.8)

Abbreviations: N.A., not available.

^a In Hokkaido cohort, gestational age, birth weight, preterm birth and low birth weight were calculated among subjects with live birth

*: still recruiting subjects