Annex 2

Japan Environment and Children's Study

International Advisory Board

Fact Sheet

December 2015

Japan Environment and Children's Study

1. Executive summary

Japan Environment and Children's Study (JECS) started in 2011 as a national birth cohort study that examines environmental impacts on children's health and development. The goal of JECS is to identify environmental factors that affect children's health in order to facilitate better environmental risk management. Specifically, the JECS focuses on the effect of exposure to chemical substances during foetal period and/or in early childhood. JECS gives priority to five major health domains: Reproduction and pregnancy complications; congenital anomalies; neuropsychiatric/developmental disorders; allergy and immune system disorders; and metabolic and endocrine system dysfunctions. In JECS, the environment is defined broadly such as global/ambient environment including chemical substances and physical conditions, built environment, behaviours/habits, socio-economic factors, family/community support and genetic factors. JECS recruits and collects outcome and exposure data/biological specimens from expecting mothers and then periodically follows their children until they reach 13 years of age as a main part of the study (Main Study). Additionally, a Sub-Cohort Study, involving 5,000 children randomly selected from the Main Study, is also designed to investigate the environmental factors and outcome variables more thoroughly, including home visits, ambient air measurements, psycho-developmental tests and paediatricians' examination.

The JECS is operated in cooperation among several research institutions. The Programme Office, or National Centre for JECS, which is situated in the National Institute for Environmental Studies (NIES), takes a directive role for the JECS, such as preparing standard operating procedures (SOPs) and storing collected data and biospecimens. The Medical Support Centre, which is organised within the National Centre for Child Health and Development, supports the Programme Office providing medical expertise. The Programme Office and Medical Support Centre cooperate together with 15 Regional Centres that are located in universities and other research institutions throughout Japan. The Regional Centres select study areas involving a single or multiple administrative district(s), taking account of their number of births, regional representativeness and level of potential exposure to chemical substances. The Regional Centres are responsible for recruiting and maintaining study participants and gathering data in their selected study areas at each study phase.

The participants of the Main Study are 100,000 pregnant women, their children and the children's fathers (when accessible). The participants of the Sub-Cohort Study are 5,000 children who are randomly extracted from those of the Main Study. The exposure assessment is conducted through chemical analyses of biospecimens collected from the participants (pregnant women, their children and the children's fathers), questionnaires, environmental monitoring and modelling/computer simulations. The biospecimens include blood, urine, umbilical cord blood, breast milk and hair. The health outcomes are measured primarily through questionnaires and medical record transcriptions, while medical examination and clinical blood testing are also performed. For the Sub-Cohort Study, more extensive methods of measurement for both environmental factors and health outcomes are employed, such as ambient air monitoring, a neurodevelopmental test, paediatricians' examinations and blood tests.

By March 2014, participants (pregnant women) solicitation for the Main Study was completed. The registered mothers reached 103,106, resulting in 100,169 births. The number of fathers counted 51,943 (those numbers are being confirmed). For each participant, questionnaires are administered twice during pregnancy, at birth, a month after birth, 6 months old and every subsequent 6 months. The response rate for each questionnaire administered after their children became 6 months old has been maintained over 80%. To date, two articles have been published in peer-reviewed journals, and two additional articles have been accepted for publication.

Attachment:

1. Japan Environment and Children's Study (JECS) Study Protocol
2. Japan Environment and Children's Study (JECS) Sub-Cohort Study Protocol

2. Study overview

2.1 History

Throughout the world, there has been a growing concern regarding the effects of environmental pollution and chemical contaminants in the environment on children's health and development. In 1997, the Miami Declaration on Children's Environmental Health was adopted at the G8 Environment Ministers' Meeting. In late 1990's, Denmark, Norway and the United States commenced large-scale birth cohort studies of the 100,000 size to investigate the effects of the environment. In 2009, the importance of children's environmental health was highlighted again at the G8 Environment Ministers' Meeting held in Syracuse, Italy, where ministers agreed to cooperate in scientific research to push this movement forward.

Along with such development, a great deal of research has been conducted to evaluate the impact of the environment on human health. However, as most of such studies were conducted with laboratory animals, their findings may not necessarily address possible effects occurring under the current exposure levels in humans. This led Japan to recognize the importance to conduct its own birth cohort research, which enables us to directly observe the effects of environmental factors on humans. (Report of the Conference on Epidemiological Study of Children's Environmental Health, March 2008).

In August 2006, the MOE held a conference focusing on children's vulnerability to environmental hazards. In April 2008, MOE organised the Expert Group on the Epidemiological Research for Children's Environmental Health (later converted to JECS Working Group) and started planning a nation-wide epidemiological study. After small-scale pilot studies were conducted at several locations in Japan to examine the appropriateness and feasibility of the study plan, in March 2010, the Working Group published a conceptual plan for a large-scale birth cohort study which defined JECS.

2.2 Study objectives

JECS is a nation-wide birth-cohort study that follows children before birth to age 13. The goal of the JECS is to identify environmental factors that affect children's health and development during the foetal period and/or in early childhood, in order to help the government formulates measures to safeguard the environment for future generations. To search environmental factors with potential impacts as broadly as possible, JECS created an extensive list of chemical compounds and evaluate their effects on children. The target compounds include metals/elements, chlorinated persistent organic pollutants (POPs), brominated POPs, pesticides, organofluorine compounds, aroma compounds, phthalate metabolites, phenols, and many other compounds (Table 1). The chemical compounds subject to analyses are selected from Table 1, taking into account the needs and importance for the examination of core hypotheses.

Table 1: JECS selected target compounds

Group	Target compounds
Metals/elements	Lead, cadmium, elemental mercury, methyl mercury, manganese, selenium, arsenic, organic arsenic compounds, iodine
Chlorinated POPs (persistent organic pollutants)	Polychlorinated biphenyls (PCBs), hydroxylated PCBs (OH-PCBs), dioxins and furans (PCDDs, PCDFs, co-PCBs), hexachlorobenzenes (HCBs), pentachlorobenzenes (PeCBs)
Brominated POPs	Polybromodiphenylethers (PBDEs), polybromobiphenyls (PBBs), hexabromocyclododecans (HBCDs)
Pesticides	Chlordanes, DDT and its metabolites (DDE, etc.), drins (dieldrin, etc.), heptachlor, hexachlorocyclohexanes (HCHs), mirex, chlordecone, toxaphene, organophophorus pesticide metabolites (DMP, DEP, DMTP, DETP, etc.), fenitrothion metabolite (methylnitrophenol), acephate metabolite (methamidophos), pyrethroid metabolites (PBA, DCCA, etc.), dithiocarbamate fungicide metabolites (ethylene thiourea, etc.), neonicotinoid metabolites, pentachlorophenol (PCP), atrazine, dymron, glyphosate, flutolanil, iprodione, flusulfamide
Organofluorine compounds	Perfluorinated alkyl acids (PFAAs), polyfluorinated telomer compounds
Aroma compounds	Nitromusks, cyclic musks
Phthalate metabolites	Mono (2-ethylhexyl) phthalates
Phenols	Bisphenol A, Nonyphenols, Parabens
Others	Triclosan, benzophenone, *N*,*N*-diethyl-meta-toluamide (DEET), polyaromatic hydrocarbons (PAHs) and their metabolites (1-hydroxypyrene, 3-hydroxyphenanthrene, etc.), cotinine, thiocyanate, dichlorobenzene, phytoestrogen, caffeine, pyridine, acrylamide, tributyl phosphate, tributoxyethyl phosphate, 8-hydroxydeoxyguanosine (8-OHdG)

The JECS priority health outcomes are reproduction and pregnancy complications, congenital anomalies, neuropsychiatric/developmental disorders, allergy and immune system disorders and metabolic/endocrine system dysfunctions (Table 2).

Table 2: Health Outcomes

Category	Items
Pregnancy/reproduction	Sex ratio, abnormal pregnancy, miscarriage, stillbirth, preterm delivery, birth weight, physical development after birth (e.g., motor function, kidney function, and lung function), etc.
Congenital anomalies	Hypospadias, cryptorchidism, cleft lip and palate, intestinal atresia, ventricular septal defect, chromosome aberration
Neuropsychiatric developmental disorders	Developmental delay or deviation (mental retardation and other cognitive difficulties), autism spectrum disorder, learning disorder (LD), attention deficit hyperactivity disorder (ADHD), mental disorders (e.g., gender identity disorder), and other symptoms and behavioural characteristics
Allergy and immune system disorders	Food allergy, atopic dermatitis, asthma, allergic rhinitis, Kawasaki disease, etc.
Metabolic and endocrine system disorders	Abnormal glucose tolerance, obesity, effects on reproductive organs, genital dysplasia, sex differentiation of the brain, etc.
Childhood tumours	Leukaemia, brain tumours, etc.

2.3 Study method

2.3.1 Study design

JECS is a longitudinal birth cohort study involving 100,000 mother–child pairs, and if accessible fathers. The Main Study includes all the participants. The information about pregnancy and children's health outcomes is collected by questionnaires and medical record transcriptions during pregnancy and after birth until children become 13 years of age. Besides the Main Study involving all the participants, 5,000 children are randomly selected from the Main Study and subject to more extensive measurements of both environmental factors and health outcomes, including ambient air monitoring, a neurodevelopmental test, paediatricians' examinations and blood tests.

2.3.2 Participants

In the Main Study, the participants are 100,000 pregnant women, their children and the children's fathers if accessible. The inclusion criteria are: 1) their expected delivery date is between 1 August 2011 and 31 March 2014 and 2) they live in one of the study areas selected by Regional Centres at the time of recruitment.

The participants are recruited by the Regional Centres through the following two methods. The first is to recruit through cooperating health care providers (CHCPs). Regional Centres request cooperation from all of the health care providers that pregnant women living in the study areas possibly visit for prenatal care and/or delivery. The pregnant women living in the study areas who visit the CHCPs are asked to participate in the study. The second recruitment method is to use local government offices such as public health departments. When pregnant women living in the study areas apply for the Mother and Child Health Handbook[1], or a pregnancy journal, at the local government offices, Regional Centres contact them and ask for their participation. When they show interest in the study, trained field staff, or Research Coordinators, from the Regional Centres acquire the information from the pregnant women about which health care providers they would visit for prenatal care and delivery. If the health care providers are designated as CHCPs, the pregnant women are then asked to participate in the study.

The participants of the Sub-Cohort Study are 5,000 children who are randomly selected from those of the Main Study. The Programme Office creates soliciting lists by extracting children randomly from those who are born during a certain period so that the age of the participants at the time of data collection falls within a limited

[1] An official booklet given complimentary to all expecting mothers in Japan when they get pregnant in order to receive municipal services for pregnancy, delivery and childcare.

range (e.g., 24–27 months). The total number of the children on each recruiting list is estimated based on the results of recruitment of participants for the Main Study. The number of the children extracted for the list who reside in the study area of each Regional Centre is designed to be proportional to the number of the participants of the Main Study in the area. The parents/legal guardians of the selected children are reached through phone-call and asked their consent of children's participation in the Sub-Cohort Study.

2.3.3 Instruments

Environmental factors

In JECS, the environment is defined broadly such as global/ambient environment including chemical substances and physical conditions, built environment, behaviours/habits, socio-economic factors, family/community and genetic factors. The exposure analyses are conducted through chemical analyses of biospecimens collected from the participants (pregnant women, their children and the children's fathers), questionnaires, environmental monitoring and modelling/computer simulations. The biospecimens include blood, urine, umbilical cord blood, breast milk and hair. The Programme Office develops analytical methods, procedures and models which are provided to contract laboratories that meet the required specifications including ISO/IEC 17025:2005 accreditation and the analysis specific quality assurance/quality control requirements. Resulting data are sent back to the Programme Office in the specified format (i.e. electronic data deliverable) and then stored in the central data management system (DMS) after the automated data review process.

Health outcomes

JECS' priority outcomes are reproduction and pregnancy complications; congenital anomalies; neuropsychiatric/developmental disorders; allergy and immune system disorders; and metabolic and endocrine system disorders. These outcomes are measured not only by diagnoses but also by symptoms and signs. Questionnaires and medical record transcriptions are the two major instruments for the outcome measurements. Paediatricians' and psychologists' examinations as well as clinical blood testing are also conducted at certain ages (planned at 6 and 12 years old). For highly prioritized outcomes, the detailed information (i.e., phenotypes, clinical test results) are collected from the corresponding medical records. Some of the measurements, such as neurodevelopmental examinations and clinical blood tests at ages 2 and 4 years, are conducted only in the Sub-Cohort Study.

Covariates and potential confounders

JECS collects the information about outcome and exposure covariates and potential confounders. Such include demographic variables (e.g. address, education, employment, house-hold income), lifestyle/behaviour factors (e.g. stress level, diet, smoking and alcohol habits, exercise, sleep condition), physical environment (e.g., heat, ionising radiation, housing condition, and neighbourhood), social/psychological factors (e.g., personality, social/community support), medical history (including pregnancy history) and medical history of family members.

2.3.4 Milestones

The recruitment of participants starts in January 2011 and continues for three years. The participating children are followed until they reach the age of 13 years. The JECS is planned to continue until 2032, allowing five years for data analysis after all the data collection are completed.

During their pregnancy, the data of the enrolled mothers are collected twice, once in early pregnancy and once in the mid-to-late pregnancy through administering questionnaires, gathering biospecimens and referring their medical record during pregnancy. After the mothers give birth, questionnaires are sent to them every 6 months. The information in the Mother and Child Health Handbook is transcribed to gather additional data regarding the children's growth and development. Table 3 shows the milestones of the Main Study and Sub-Cohort Study. Study protocols for 6 years and later are under development.

Table 3: JECS milestones

Milestones	Instruments (Main Study)	Instruments (Sub Study)
At recruitment (first trimester)	Medical record, Questionnaire Biospecimen (Mother: blood (30 ml) and urine (50 ml), Father: blood (30 ml))	
Second or third trimester	Questionnaire Biospecimen (Mother: blood (30 ml) and urine (50 ml))	
At delivery	Medical record Biospecimen (Child: umbilical cord blood (20–35 ml))	
Within a few days after birth (during hospitalization)	Biospecimen (Mother: blood (20 ml), hair (2 mg), Child: dried blood spot)	
1 month old	Medical record, Questionnaire Biospecimen (Mother: breast milk (20 ml); Child: hair (2 mg))	
6 months old	Questionnaire	
1 year old	Questionnaire	
1.5 years old	Questionnaire	Environmental measurements
2 years old	Questionnaire	Developmental test Medical examination (blood test, skin examination, etc.)
2.5 years old	Questionnaire	
3 years old	Questionnaire Mother and Child Health Handbook transcription	Environmental measurements
3.5 years old	Questionnaire	
4 years old	Questionnaire	Developmental test Medical examination (blood test, skin examination, etc.)
4.5–5.5 years old	Questionnaire (once every 6 months)	
6 years old	Questionnaire Paediatric examination Body measurement (height, weight, etc.) Biospecimen (Child: urine (50 ml) and possibly blood (under consideration)) Mother and Child Health Handbook transcription	Developmental/Neuropsychological test and/or interviews (at 6, 8, 10 and 12 years old) Medical examination (blood test, height measurement, etc.; at 6, 8, 10 and 12 years old) Environmental measurements (once or twice, under consideration)
6.5–11.5 years old	Questionnaire (once every 6 months) School records	
12 years old	Questionnaire Paediatric examination Physical measurement (body height, body weight, etc.) Biospecimen (Child: urine (50 ml) and possibly blood (under consideration)) School records	

2.4 Organisation

The JECS is conducted in cooperation among several different organizations: Programme Office, Medical Support Centre and 15 Regional Centres.

The Programme Office, or National Centre for JECS, which is situated in the National Institute for Environmental Studies (NIES), is taking a leading role for the JECS, including accumulating data collected by Regional Centres; maintaining the database, or data management system (DMS); maintaining the repository of biological and environmental specimens; and performing exposure measurements including chemical analyses on the specimen. The Programme Office prepares standard operating procedures (SOPs); carries out administrative tasks; provides administrative and technical support for Regional Centres and is responsible for risk management and public communication.

The Medical Support Centre is established in the National Centre for Child Health and Development. The Medical Support Centre develops outcome measurement instruments. The Medical Support Centre is also responsible for preparing SOPs, training personnel who are responsible for collecting data regarding to health outcome variables at each Regional Centres and providing Regional Centres with medical advices when necessary.

The Regional Centres are placed in universities and other research institutions in different locations of Japan. The Regional Centres are responsible for recruiting study participants and contacting them, such as explaining the study protocol, obtaining the written consent, registering the participants, collecting biospecimens, transcribing medical records, entering questionnaires into the DMS and field operation for the Sub-Cohort Study home visits.

The Steering Committee is the highest decision making body of the JECS. Subcommittees are formed under the Steering Committee to discuss specific aspects of the study such as publication, communication/outreach, exposure analysis, pilot study conducts, epidemiological/statistical methodologies and ethics. In addition to these committees. Working groups are placed under the Programme Office and Medical Support Centre to draft study protocols and procedures, including developing questionnaires, planning the Sub-Cohort Study and selecting chemistry methods.

The organisational chart of the JECS is presented in Figure 1.

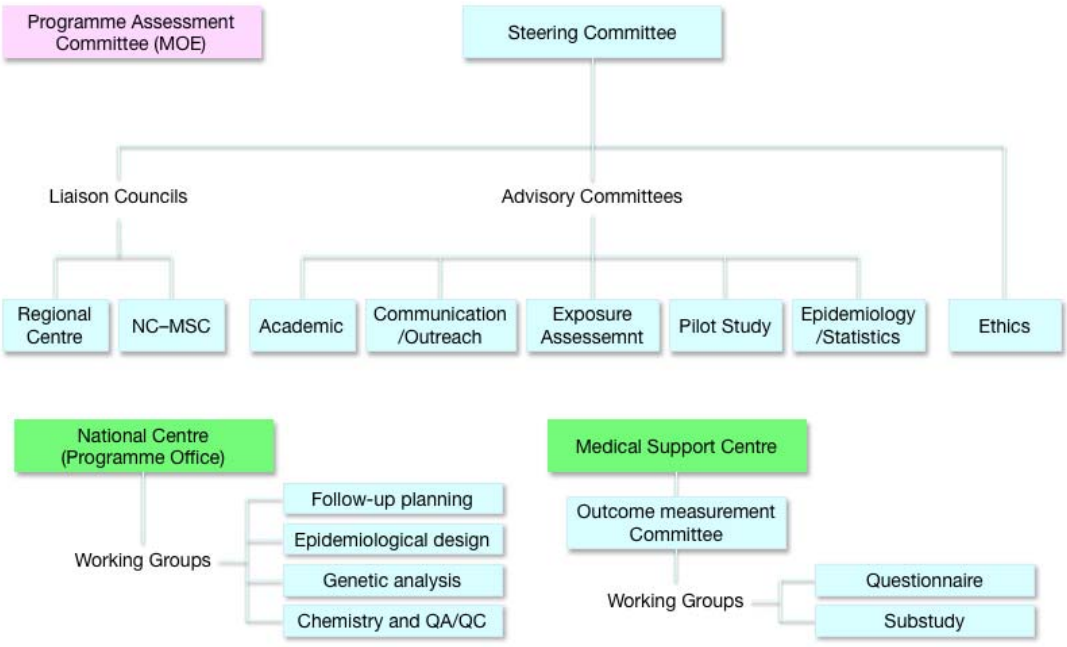

Figure 1: JECS Organisation

2.5 Funding

JECS is funded directly by the MOE under parliament approval. The annual budget is shown in Table 4.

Table 4: Annual funding for JECS

Fiscal year (April–March)	Billion yen[2]	US dollar (rate = 1 USD/110 yen)
2010	3.1	28 m
2011	4.6	42 m
2012	6.1	55 m
2013	6.1	55 m
2014	5.7	52 m
2015	5.7	52 m

2.6 International collaboration

The MOE organised a workshop in February 2011 in Tokyo and initiated a discussion about possible study harmonisation among some large-scale 21st century birth cohort studies. Investigators associated with major studies decided it was worthwhile to harmonise study protocols and procedures prior to, or in conjunction with, each study's progress in order to make future data pooling easier. A working group was formed to define a list of core elements for inclusion in the new birth cohort studies, such as health outcome measurements, biomarkers, exposure measurements, questionnaire harmonisation, data management and study process. France, Germany, Shanghai (China) and the United States that were planning or conducting new large-scale studies of environmental influences on children's health and development showed interest in participating in the group. In late 2011, experts from these five countries constituted the Environment and Child Health International Birth Cohort Group (ECHIBCG). The group meets periodically along with monthly telephone conferences to exchange information about each study protocol and process and to discuss possible measures of harmonisation. Recently the group also shared a common biological sample and performed a round-robin trial for lead and mercury analysis in order to identify potential quality assurance/quality control problems. JECS plays a key role in this group.

The sample size of JECS, 100,000, is not considered sufficient to evaluate the association between environmental exposures and childhood cancers. JECS collects the information about cancers in order to contribute to international pooled data analyses. JECS is a participant of the International Childhood Cancer Cohort Consortium (I4C).

3. Current status

3.1 Participation

Recruitment of participants (pregnant women) for the Main Study was completed in March 2014. The consent rate of mothers was approximately 80%. As of 31 August 2015, 103,086 mothers and 51,943 fathers are registered with 100,169 live births being recorded (Table 5, Figure 2). For each participant, questionnaires are administered during pregnancy, at birth, a month after birth, 6 months old and every subsequent 6 months. The eldest children have become 4 years old as of 1 October 2015.

Selection of the participants for the Sub-Cohort Study and their recruitment through phone call started in October 2014. By the end of March 2015, all the Regional Centres completed the selection of participants from the first wave (those born between April and June 2013) and the second wave (those born between July and

[2] Budget includes funding for the Programme Office, Medical Support Centre and Regional Centres.

September 2013). The Regional Centres started to contact participants selected from the third wave. Approximately 50% of the participants contacted have agreed for their children's participation.

Table 5: Number of participants as of August 2015

Regional Centre	Recruitment			Follow-up
	Mothers	Children	Fathers	Children
Hokkaido	8,362	7,930	2,956	7,618
Miyagi	9,217	9,002	4,160	8,854
Fukushima	13,134	12,830	8,695	12,638
Chiba	6,192	5,961	3,978	5,807
Kanagawa	6,652	6,411	2,444	6,259
Koshin	7,335	7,157	5,016	6,995
Toyama	5,584	5,383	3,280	5,291
Aichi	5,721	5,554	2,575	5,467
Kyoto	3,984	3,884	3,151	3,834
Osaka	8,043	7,847	3,003	7,754
Hyogo	5,174	5,040	1,892	5,009
Tottori	3,059	3,029	1,149	3,003
Kochi	7,094	6,917	2,385	6,822
Fukuoka	7,691	7,509	3,809	7,409
South Kyushu/Okinawa	5,845	5,708	3,487	5,628
	103,087	100,162	51,980	98,388

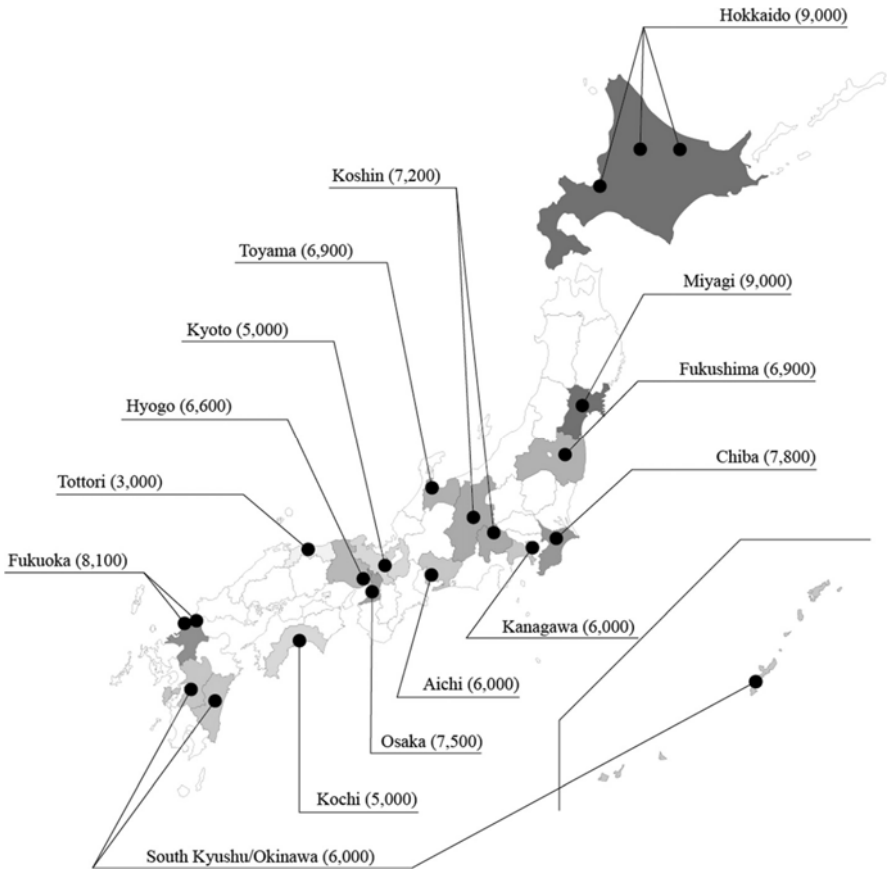

Figure 2: Programme Office, Medical Support Centre and Regional Centres and targeted sample sizes

3.2 Follow-up programme

As a part of the Main Study, the participants (mothers) are asked to fill out questionnaires every 6 months after their children become 6 months old.

The response rate[3] for each questionnaire are presented in Table 6. As seen in the table, the total response rate has been maintained as over 80%, with some variance between different regional areas, though it decreases slightly as the study proceeded. We are going to make as much effort as possible to maintain high response rate.

The data collection for the Sub-Cohort Study began in November 2014. Participants at the age of 18 months have been receiving home visits for volatile organic compounds (VOCs) measurements, particulate matter collection and dwelling observation. Since April 2015, the participants has been administered a psychological developmental test (adjusted version of Kyoto Scale of Psychological Development), neuromotor test, paediatricians' examination and blood testing when they became 2 years old.

Table 6: Response rate for each questionnaire administration as of 28 August 2015

Regional Centres	6 months old	1 year old	1.5 years old	2 years old	2.5 years old	3 years old
Hokkaido	93.7%	91.2%	90.4%	89.0%	86.2%	83.9%
Miyagi	90.2%	86.1%	83.6%	82.8%	81.7%	80.2%
Fukushima	96.7%	94.4%	91.9%	89.0%	88.6%	88.0%
Chiba	93.4%	91.4%	88.7%	87.0%	85.6%	83.5%
Kanagawa	95.3%	92.6%	89.9%	88.4%	88.6%	89.1%
Koshin	94.3%	90.2%	88.1%	86.0%	84.0%	83.2%
Toyama	96.6%	93.9%	92.5%	91.7%	91.2%	90.1%
Aichi	92.1%	89.0%	86.6%	84.4%	82.3%	80.5%
Kyoto	95.0%	93.0%	91.0%	90.0%	89.0%	87.7%
Osaka	92.9%	90.3%	88.3%	86.4%	84.8%	82.3%
Hyogo	95.1%	91.9%	89.8%	88.0%	86.5%	83.3%
Tottori	95.1%	93.0%	91.2%	88.7%	88.4%	86.8%
Kochi	91.4%	88.6%	85.5%	84.1%	83.3%	79.6%
Fukuoka	93.9%	90.1%	87.9%	86.2%	84.2%	80.9%
South Kyushu /Okinawa	93.5%	90.9%	88.3%	87.2%	82.7%	82.6%
Total	93.9%	90.9%	88.6%	86.8%	85.3%	83.5%

3.3 Collection and analyses of biospecimens

The collection of biospecimens during pregnancy and at birth was completed in the end of January 2015. The numbers of collected samples are listed in Table 7. The collected samples are stored in three different bio-repository facilities. In 2014, 20,000 mothers' blood samples during late pregnancy and 12,000 urine samples were analysed for heavy metals (lead, cadmium, mercury, manganese and selenium) and nicotine metabolites, respectively.

[3] Response rate is calculated by the number of questionnaires sent back from the participants within 6 months after sending them divided by the total number of questionnaires sent to the participants

Table 7: Biological samples collected during pregnancy and at birth

Sample type	Participant		Number
Blood	Mother	Early pregnancy	91,935
		Mid–late pregnancy	97,979
		At birth	98,818
	Father		49,796
	Umbilical cord blood		87,802
	Child		94,841
Breast milk	Mother		89,364
Hair	Mother		78,719
	Child		94,990

3.4 Data cleaning

In October 2013, the data collected at recruitment, during pregnancy and at birth from those who gave birth or were born before December 2011 was fixed and distributed to the Regional Centres for analyses. The second data set, including the data collected at a month after birth, for those who gave birth or were born by September 2013 was fixed and distributed in the Summer of 2015. The rest of the birth data is being cleaned and all birth data will be confirmed by March 2016.

3.5 Publication

Considering the potential impact of the study results, JECS has publication and presentation rules. It requires data users to be registered by the Programme Office and authors are to submit the manuscript and presentation abstract to the Programme Office and obtain approval from the MOE for publication.

3.5.1 Selected publication

1. Kawamoto T, Nitta H, Murata K, Toda E, Tsukamoto N, Hasegawa M, Yamagata Z, Kayama F, Kishi R, Ohya Y, Saito H, Sago H, Okuyama M, Ogata T, Yokoya S, Koresawa Y, Shibata Y, Nakayama S, Michikawa T, Takeuchi A, Satoh H and Working Group of the Epidemiological Research for Children's Environmental Health. (2014) Rationale and study design of the Japan environment and children's study (JECS). *BMC Public Health 14*:25
2. Michikawa, T., Nitta, H., Nakayama, S. F., Ono, M., Yonemoto, J., Tamura, K. et al (2015). The Japan Environment and Children's Study (JECS): A Preliminary Report on Selected Characteristics of Approximately 10 000 Pregnant Women Recruited During the First Year of the Study. *Journal of Epidemiology 25*, 452-458
3. Suzuki K, Shinohara R, Sato M, Otawa S, Yamagata Z. (in press). Association between maternal smoking during pregnancy and birth weight: an appropriately adjusted model from the Japan Environment and Children's Study. *Journal of Epidemiology* (in press)
4. Watanabe Z, Iwama N, Nishigori H, Nishigori T, Mizuno S, Sakurai K, Ishikuro M, Obara T, Tatsuta N, Nishijima I, Fujiwara I, Nakai K, Arima T, Takeda T, Sugawara J, Kuriyama S, Metoki H, Yaegashi N, Japan Environment & Children's Study Group. (in press). Psychological distress during pregnancy in Miyagi after the Great East Japan Earthquake: The Japan Environment and Children's Study. *Journal of Affective Disorders* (in press)