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Analysis of non-respondent pregnant women who were registered in the Japan Environment and Children's Study: a longitudinal cohort study

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Abstract

Objectives: Non-response to questionnaires in a longitudinal study reduces the effective sample size and introduces bias. We identified the characteristics of non-respondent pregnant women, and compared them with respondents in the Japan Environment and Children's Study (JECS) during the gestational period. **Design:** This was a questionnaire-based, longitudinal cohort study. **Setting:** Questionnaires were provided by research coordinators to mothers at prenatal examinations (at obstetrics clinics) or by mail. Mothers were measured twice: during the first trimester and during the second/third trimester. **Participants:** Data were collected from the participating mothers of the 10,288 children surveyed in the 2011 baseline JECS. We excluded responses from mothers who had a miscarriage or still birth; therefore, we analysed data from 9,649 participants. **Primary and secondary outcome measures:** Data concerning demographics, medical history, health characteristics, health-related behaviour, and environmental exposure were collected via self-administered questionnaires. The response status of participants' partners and contact with their obstetrician were also examined. Multivariate logistic regression analysis was used to examine factors related to non-response. **Results:** Response was associated with living with one's mother-in-law (odds ratio [OR]: 0.47, 95% confidence interval [CI]: 0.24–0.85), positive participation of

participants' partner (OR: 0.25, 95% CI: 0.17–0.35), and multiple visits to the obstetrician (OR: 0.02, 95% CI: 0.02–0.03). Participants who had a medical history of allergic rhinitis, had body pain, or drank alcohol had higher odds of responding (ORs: 0.68, 0.96, and 0.36, 95% CIs: 0.48–0.95, 0.95–0.98, and 0.16–0.72, respectively); those exposed to secondary smoke had lower odds of responding (OR: 1.59, 95% CI: 1.12–2.23).

Conclusions: The non-response rate decreased when participants reported health-related behaviour or characteristics. Obtaining the understanding of people around each participant might help increase response rates.

Strengths and limitations of this study

- The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that includes 10,129 mothers with confirmed obstetric outcomes in the first year of recruitment.
- During the gestational period, we provided self-administered questionnaires to mothers twice.
- The study is strengthened by its assessment of the effects of non-response on prevalence estimates as well as the exposure–outcome relationship.
- The sample size of this study was sufficient to examine the risk factors of

non-response.

▪ We were unable to examine the effects of some socioeconomic factors on non-response.

Background

Population-based studies are used to provide epidemiological data on the occurrence of disease and to identify risk factors that may be relevant to these outcomes. The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that started recruiting expectant mothers in January 2011. [1]

In the first year of recruitment, approximately 10,000 registered pregnant women had confirmed obstetric outcomes. Data on participants' health-related behaviour, marital status, socioeconomic status, and education level were collected via self-administered questionnaires provided twice during the gestational period.[2]

In recent years, the response rates have decreased in several epidemiological studies, which may lead to selection biases.[3,4] Although a study may achieve a high response rate, the prevalence estimates may still be biased if the non-responses are not random. The characteristics of non-respondents therefore need to be confirmed. Systematic differences in the characteristics of respondents and non-respondents detract from the outcomes of interest. Therefore, the presence and extent of such bias should be investigated.[5] In a cross-sectional health survey, Pietila and colleagues compared the backgrounds of responding and non-responding young men and found that their socioeconomic status and education level were related to their response status.[6]

Furthermore, the response status in the Atherosclerosis Risk in Communities Study differed according to sex and ethnicity.[7]

Long-term follow-up studies are hampered by a decrease in response rate due to the lapse of time between birth and follow-up. A systematic review of randomized controlled trials using postal questionnaires showed that the response rate was related to the length and/or design of questionnaire, use of personalized letters, and follow-up contact, and matched the interests of participants and originating sources.[8] In longitudinal cohort studies, various factors have been shown to be related to response status, including age, sex, marital status, education, health status, health-related behaviour, lifestyle, ethnicity, study objectives, contact modes, number and order of contact modes, and use of incentives.[9-12]

Some authors have suggested that non-response increases the proportion of infants with adverse outcomes in the remaining study population; however, how these factors influence study outcomes is unclear.[13] Therefore, we performed this study to describe the characteristics of non-responders. We studied pregnant women who were registered in a prospective, cohort study and who did not return the second questionnaire during the gestational period.

Methods

Design of the JECS

In the JECS, self-administered questionnaires were provided to mothers twice: during the first trimester (MT1) and during the second/third trimester (MT2). Questionnaires were provided by research coordinators at prenatal examinations (in the obstetrics clinic) or by mail and returned either by hand at subsequent prenatal visits (in the obstetrics clinic) or by mail. The partners of registered mothers were also asked to participate. We collected data from registered partners during the women's pregnancy through self-administered questionnaires returned by hand or by mail. Women's medical records were transcribed three times, by obstetricians, midwives/nurses, or research coordinators at the obstetrics clinic: during the first trimester, during the second/third trimester, and after delivery.

Design of the non-responder study

This study was based on a data set (i.e. jecs-ag-ai-20131008), which was released in October 2013 (The dataset supporting the conclusions of this article will be available after the steering committee of the JECS permits its accessibility). The participant flow is illustrated in Figure 1.

Comment [31]: INSERT FIGURE 1 ABOUT HERE

Using the MT1 questionnaire, demographic data (age, marital status, and cohabiting

family members), medical and obstetric history, health-related behaviour (smoker/exposure to secondary smoke, and alcohol consumption), and occupational data were collected. The SF-8™ questionnaire (Japanese version) (Medical Outcomes Trust, Health Assessment Lab, Quality Metric, Fukuhara S) was used to assess participants' health-related quality of life (QOL). The K6 questionnaire (Japanese version) was used to assess participants' psychological distress.[14] Age was divided into four categories: <25 years, 25–29 years, 30–34 years, and ≥35 years. We collected data of cohabiting family members via multiple-choice questionnaires.

The response data from participants' partners and a transcription sheet regarding health status data during the gestational period were linked with each participant.

Definitions

Health status data during pregnancy was defined as positive based on multiple visits to obstetricians and using transcription sheet data. Partners' participation status was defined as positive when partners returned the questionnaire.

We collected information on occupation and types of employment of participants with the MT1 questionnaire. We focused on the following settings: homemakers or unemployed, worked from home, and employed. For allocation of these settings, we used the Japan Standard Occupational Classification and the classification of positions in

employment by the Ministry of Internal Affairs and Communication.

Regarding exposure to secondary smoke before pregnancy, 'daily' was defined as when participants answered with 'exposed at least once a week'.

Patient and Public Involvement

JECS started recruiting expectant mothers in January 2011 with the aim of assessing environmental factors that affect children's health, with the goal of providing a foundation for policymaking to safeguard the environment for the next generation. JECS study aimed to recruit approximately 100,000 pregnant women and their partners over 3 years, to collect biological samples, and to collect data on their children until they turned 13 years old.[1]

Written informed consent for participation in JECS was obtained from individual mothers. In addition to the JECS main study, adjunct studies were conducted by the member of JECS group, or any combination of them. The adjunct studies may have included procedures that were not adopted by the main study, e.g., collection and examination of placenta. This study was one of the adjunct studies of JECS, based on an existing dataset, and hence, patients were not directly involved in the sampling process.

Ethical considerations

The JECS protocol was reviewed and approved by the Ministry of the Environment's

Institutional Review Board on Epidemiological Studies and by the Ethics Committees of all participating institutions. Written informed consent was obtained from all participating women and their partners.

Statistical analyses

The following variables were considered in the analyses for mothers: demographic data (age, marital status, and cohabiting family members), medical and obstetric history, physical and mental health, health-related behaviour, occupation, environmental exposure, contact status with their obstetrician, and partners' response status. Student's t-test or Welch's t-test for independent groups was used for continuous variables and Pearson's chi-square test or Fisher's exact test was used for categorical variables. The variables that had significant associations with non-response to the MT2 questionnaire in the bivariate logistic regression models were included in the multivariate models. Prevalence odds ratios and 95% confidence intervals for non-response were estimated using multivariate logistic regression analyses. The contribution of a variable to the regression model was assessed using the likelihood ratio test.

A significance level of .05 (two-tailed) was used for all statistical tests. JMP® Pro version 11 (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

Results

The overall response rate to the questionnaire in the second/third trimester was 97.7% (9432/9649). Table 1 shows participants' characteristics at the first trimester, their partners' participating status, and visits to the obstetrician among responders and non-responders. The proportions of marital status, family members, medical history, exposure to secondary smoke, and job status significantly differed between responders and non-responders. The responders were more likely to be married, living with in-laws, have a history of allergic rhinitis or allergic conjunctivitis, have better physical functioning, have a high response rate from their partner, and make more visits to the obstetrician. Additionally, responders were less likely to have a history of migraines or polycystic ovary syndrome than were non-responders. Non-responders were more likely to have been exposed to secondary smoke than were responders. Participants who were employed were more likely to respond than were their counterparts. The SF-8 Physical Functioning and Body Pain scales were significantly higher for responders than for non-responders.

Two variables showed significant associations—living with one's mother-in-law and having allergic rhinitis—with non-response according to the bivariate logistic

Comment [32]: INSERT TABLE 1 ABOUT HERE

regression model. Table 2 shows the odds ratios for non-response according to the various demographic and clinical characteristics, partners' participation status, and visiting obstetricians in the multivariate logistic regression analyses. Model 1 included the variables that had significant associations with non-response of MT2.

Comment [33]: INSERT TABLE 2 ABOUT HERE

The odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS[1]; had a positive QOL; were living with their mother-in-law; had partners who active participated; and had maintained contact with obstetricians. However, the odds of non-response were higher in participants who had been exposed to secondary smoke. Marital status, job site, and the SF-8 physical functioning scale did not match the model, and thus were excluded.

Model 2 excluded variables that did not show significance in Model 1. The odds of non-response were higher in participants who had been exposed to secondary smoke; however, the odds were lower in participants who lived with their mother-in-law, had a history of allergic rhinitis, had a positive QOL regarding body pain, had partners who participated, and visited the obstetrician.

Discussion

Using data collected during pregnancy, we evaluated non-response bias in

approximately 10,000 pregnant women who participated in the JECS. Many factors were independently associated with response to the follow-up questionnaire. The characteristics associated with a greater probability of response included being married, living with one's mother-in-law, and where the participants worked. Having a medical history of allergic rhinitis or allergic conjunctivitis resulted in a higher probability of response. The number of partners with positive participation in the JECS and multiple visits to the obstetrician were significantly lower in non-responders than in responders.

The odds ratios for non-response were correlated with demographic and clinical characteristics, partners' participation status, and visiting the obstetrician in the multivariate logistic regression analysis. Specifically, the odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS; who had a positive QOL; who were living with their mother-in-law; whose partners participated; and who maintained contact with obstetricians. The odds of non-response were higher in participants who had been exposed to secondary smoke. Baron and colleagues reported that passive smoking showed disparity across educational levels.[15] We could not consider the effects of education; however, the relationship between non-response and exposure to secondary smoke might be affected by participants' education.

One of the objectives of the JECS was to assess environmental factors that affect children's health (e.g. allergic diseases). The prevalence of allergic rhinitis in the Japanese population was 44.2% in 2006–2007[16] and that of allergic conjunctivitis disease was 14.8% in 1993.[17] Both were higher than those reported in the current study (35.9% and 10.9%, respectively). Macera and colleagues reported that responders were individuals who had family members with certain chronic conditions in their health-related survey.[18] Leadbetter and colleagues examined the perceived risk of cancer by comparing early and late responders. They reported that the salience of the survey topic was associated with a prompt response.[19] In this survey, participants with interest in children's allergic diseases were more likely to respond; however, daily exposure to secondary smoke made non-responses more likely. In health-related surveys, participants with risky health behaviours are more likely to be non-respondents than are those who exhibit healthier behaviour.[20]

Etter and colleagues reported that respondents had better general health than did non-respondents.[21] Martikainen and colleagues evaluated non-response bias in analyses of social class inequalities in health.[22] They found that female non-respondents had an approximately 20–30% higher sickness absence rate per 100 person-years than did respondents. Our results from the Body Pain scale showed that

respondents were healthier than were non-respondents, which is consistent with these previous results. The response rate was higher among participants who lived with their mother-in-law, those who had partners who positively participated, and those who maintained contact with an obstetrician. Alessi and colleagues suggested that general practitioners' understanding of the study could influence the attitude of their patients.[23] Our results indicate that the same is true for people close to the participants. Hatta and colleagues reported that parents-in-law were perceived as the least cohesive persons among close family members in Japan.[24] Another study of postpartum depression in China reported that the underlying cultural setting of the daughter-in-law/mother-in-law relationship contributed to depression among daughters-in-law.[25] In our survey, the presence of a mother-in-law may have acted as a stressor to motivate the participants to return the questionnaires. Further, we collected participants' job status and categorized it into three modes: homemakers or unemployed, worked from home, and employed. The response rate depended on participants' job, with a higher response rate being found among participants working from home than among those whose job location was outside of their home. In the Survey on Time Use and Leisure Activities in 2011,[26] women who worked from home (family workers) spent more time on housework and less time on self-education/training

and hobbies/amusement than did those who were employed outside of their home. Associations with response to the questionnaire were also observed for job location and time spent answering the questionnaire; however, these relationships were weak.

The limitations of this study are as follows: 1) a lack of information on education level and participants' socioeconomic status, 2) a lack of information on the survey mode, and 3) a lack of information on partners' registration status. However, we know that socioeconomic status and education level are related to response status.[6,27-29] Although we collected socioeconomic and educational data on the MT2 questionnaire, we failed to consider these effects because they were beyond the scope of our objectives. In addition, several researchers have reported that response status differs according to survey mode.[30-33] In this study, we collected questionnaires by hand or by mail. Because we were unable to collect data on the mode used, we did not evaluate the effect of these distinct modes. We were also unable to collect information regarding the extent of partners' participation—any response was considered positive. Finally, we could not confirm participants' medical or obstetric history using clinical data. Relying solely on data collected by self-administered questionnaires introduces the risk of response bias.

Conclusions

In conclusion, this study showed that obtaining understanding of the research objectives from people who are close to the participants was associated with a higher odds of response. To reduce the non-response rate in future follow-up surveys, additional efforts should be made to maintain contact and encourage participation among individuals who display relevant characteristics of potential non-responders.

Declarations

Data sharing statement

The dataset supporting the conclusions of this article will be available after the steering committee of the JECS allows it to become available.

The dataset supporting the conclusions of this article is unsuitable for public deposition due to ethical restrictions and legal framework of Japan. The Act on the Protection of Personal Information (Act No. 57 of 30 May 2003; amendment on 9 September 2015) prohibits publicly depositing data containing personal information. The Ethical Guidelines for Medical and Health Research Involving Human Subjects, which are enforced by the Japan Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare, also restrict the open sharing of epidemiologic data. All inquiries about access to these data should be sent to Dr. Shoji F. Nakayama, JECS Programme Office, National Institute for Environmental

Studies; email: jecs-en@nies.go.jp.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MK designed and conducted the study, performed the statistical analyses, and wrote the manuscript. KM helped draft the manuscript. AT conducted the data collection and helped draft the manuscript. MI and TT conducted data collection and helped critically revise the manuscript. KH and HI participated in the study design and helped critically revise the manuscript. HO assisted with the statistical analyses. YA and SS helped critically revise the manuscript. All authors have read and approved the final manuscript.

Figure legend

Figure 1. Participant (expecting mothers) flow

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Table 1. Baseline characteristics of sample

	Responder (n=9,432)	Non-responder (n= 217)	
	%	%	p value
Age			0.205
< 25	9.1	10.4	
25 – 29	27.3	24.2	
30 – 34	35.8	42.3	
>= 35	27.8	23.1	
Marital status			0.024
Married	95.8	93.9	
Unmarried	3.2	3.3	
Divorced/widowed	1.0	2.8	
Family member participants living with			
none	0.7	0.9	0.661*
Partner	93.0	91.7	0.471
Children	55.3	54.8	0.892
Father	7.6	5.5	0.298*
Mother	9.9	8.8	0.646*
Brother / sister	4.2	5.9	0.218
Father-in-law	9.4	5.5	0.045*
Mother-in-law	11.6	5.5	0.005*
Brother / sister-in-law	3.1	0.9	0.071*
1st pregnancy	30.5	31.0	0.940*
Medical history			
Have allergic rhinitis	35.9	26.7	0.005*
Have allergic conjunctivitis	10.9	6.4	0.035*
Smoking habits during early pregnancy			0.072
Never smoked	56.8	50.0	
Ex-smokers who quit before pregnancy	24.2	25.2	
Ex-smokers who quit after pregnancy	13.5	15.9	
Smoker	5.5	8.9	
Exposed to secondary smoke before pregnancy [a]			< 0.001
Rarely	80.2	71.0	
Daily	19.8	29.0	

Alcohol consumption during early pregnancy			0.006*
Never drinker	35.0	40.4	
Ex-drinkers	55.0	55.4	
Drinkers	10.0	4.2	
Job site of participants			0.011
Housewife / unemployed	42.2	52.2	
Work from home	3.4	3.9	
Employed	54.4	43.9	
Relationship with others			
Visits obstetrician [b]	97.8	54.3	< 0.001*
Positive participation of partners [c]	60.4	23.9	< 0.001*
	Mean, SE	Mean, SE	p value
No. of household member	3.3, 0.01	3.1, 0.09	0.094+
Health Related Quality of Life (SF-8)			
General Health	46.9, 0.1	46.7, 0.5	0.772
Physical Functioning	46.6, 0.1	45.5, 0.5	0.027
Role Physical	43.7, 0.1	43.5, 0.6	0.756
Body Pain	50.0, 0.1	48.7, 0.6	0.025
Vitality	47.5, 0.1	47.2, 0.5	0.452
Social Functioning	44.2, 0.1	43.4, 0.6	0.203
Mental Health	47.0, 0.1	46.2, 0.5	0.062
Role Emotional	47.2, 0.1	46.5, 0.5	0.198
Physical Component Summary	45.5, 0.1	44.8, 0.5	0.203
Mental Component Summary	46.3, 0.1	45.6, 0.5	0.164
Self-Administered mental health (K6)	9.6, 0.0	10.1, 0.3	0.097+

*: Fisher's exact test, +: Welch's t test

a: 'Daily' defined as subjects exposed at least once a week.

b: Participants who collected the transcription sheet defined as multiple visits with obstetrician.

c: Positive participation of partner was those who answered the questionnaire .

Table 2. (a) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response : model 1

Variable	OR (95% CI)	p value
Marital status		
Married	Reference	
Unmarried	0.64 (0.23, 1.48)	0.324
Divorced/widowed	1.22 (0.28, 3.52)	0.750
Living with mother-in-law (yes / no)	0.50 (0.25, 0.90)	0.020
Job site of participants		
Housewife or unemployed	Reference	
Work from home	1.58 (0.67, 3.26)	0.173
Employed	0.86 (0.62, 1.19)	0.107
Medical history of allergic rhinitis (yes / no)	0.62 (0.43, 0.88)	0.007
Health Related Quality of Life (Physical Functioning)	0.98 (0.96, 1.00)	0.135
Health Related Quality of Life (Body Pain)	0.97 (0.95, 0.98)	0.002
Exposed to secondary smoke during early pregnancy (daily / rarely)	1.48 (1.03, 2.11)	0.034
Alcohol consumption		
Drinker during early pregnancy / never drunk	0.34 (0.14, 0.71)	0.002
Drinker during early pregnancy / ex-drinkers	0.45 (0.19, 0.92)	0.027
Relationship with others		
Visits to obstetrician (yes / no)	0.02 (0.02, 0.04)	<0.001
Positive participation of partners (yes / no)	0.26 (0.18, 0.36)	<0.001

AICc: 1427.9, LOF: p=1.000

Table 2. (b) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response : model 2

Variable	OR (95% CI)	p value
Living with mother-in-law (yes / no)	0.47 (0.24, 0.85)	0.011
Having history of allergic rhinitis (yes / no)	0.68 (0.48, 0.95)	0.024
Health Related Quality of Life (Body Pain)	0.96 (0.95, 0.98)	<0.001
Exposed to secondary smoke (daily / rarely)	1.59 (1.12, 2.23)	0.009
Alcohol consumption (drinker / never drinker)	0.36 (0.16, 0.72)	0.002
Alcohol consumption (drinker / ex-drinker)	0.47 (0.21, 0.92)	0.026
Visits obstetrician (yes / no)	0.02 (0.02, 0.03)	<0.001
Positive participation of participants' partners (yes / no)	0.25 (0.17, 0.35)	<0.001

AICc: 1507.8, LOF: p=1.000

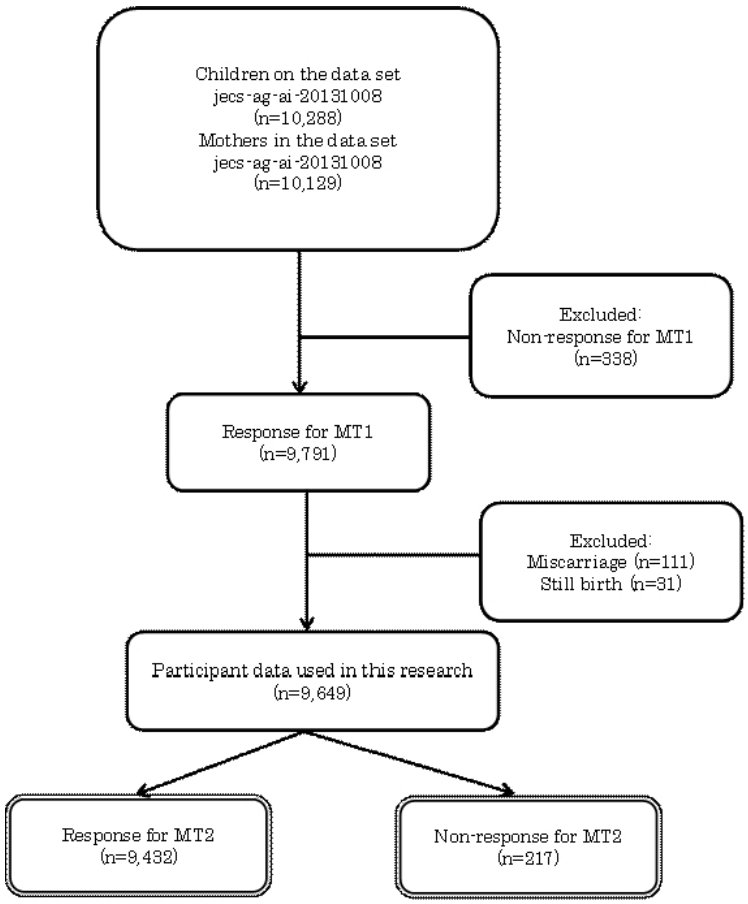

Figure 1. Inclusion of subjects (expecting mothers)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	The page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	p. 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	p. 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	p.6-8
Objectives	3	State specific objectives, including any prespecified hypotheses	p.8 l.1-4
Methods			
Study design	4	Present key elements of study design early in the paper	p.9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p.9-10
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	p.9 Fig.1
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p.9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*p.9-10*
Bias	9	Describe any efforts to address potential sources of bias	p.16-17
Study size	10	Explain how the study size was arrived at	Fig.1 p.11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p.9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P10-11
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and	

	controls was addressed
	Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy
	(*e*) Describe any sensitivity analyses

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	p.11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	p.11 Tab.1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*p.11-12 Tab.2*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p.12-13 Tab.2
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	p.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p.14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	p.17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.8, 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Analysis of non-respondent pregnant women who were registered in the Japan Environment and Children's Study: a longitudinal cohort study

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Analysis of non-respondent pregnant women who were registered in the Japan Environment and Children's Study: a longitudinal cohort study

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Abstract

Objectives: Non-response to questionnaires in a longitudinal study reduces the effective sample size and introduces bias. We identified the characteristics of non-respondent pregnant women, and compared them with respondents in the Japan Environment and Children's Study (JECS) during the gestational period. **Design:** This was a questionnaire-based, longitudinal cohort study. **Setting:** Questionnaires were provided by research coordinators to mothers at prenatal examinations (at obstetrics clinics) or by mail. Mothers were measured twice: during the first trimester and during the second/third trimester. **Participants:** Data were collected from the 10,129 participating mothers of the 10,288 children surveyed in the 2011 baseline JECS. We excluded responses from mothers who had a miscarriage or still birth; therefore, we analysed data from 9,649 participants. **Primary and secondary outcome measures:** Data concerning demographics, medical history, health characteristics, health-related behaviour, and environmental exposure were collected via self-administered questionnaires. The response status of participants' partners and contact with their obstetrician were also examined. Multivariate logistic regression analysis was used to examine factors related to non-response. **Results:** Response was associated with living with one's mother-in-law (odds ratio [OR]: 0.47, 95% confidence interval [CI]: 0.24–0.85), positive participation of

participants' partner (OR: 0.25, 95% CI: 0.17–0.35), and multiple visits to the obstetrician (OR: 0.02, 95% CI: 0.02–0.03). Participants who had a medical history of allergic rhinitis, had body pain, or drank alcohol had higher odds of responding (ORs: 0.68, 0.96, and 0.36, 95% CIs: 0.48–0.95, 0.95–0.98, and 0.16–0.72, respectively); those exposed to secondary smoke had lower odds of responding (OR: 1.59, 95% CI: 1.12–2.23).

Conclusions: The non-response rate decreased when participants reported health-related behaviour or characteristics. Obtaining the understanding of people around each participant might help increase response rates.

Strengths and limitations of this study

- The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that includes 10,129 mothers with confirmed obstetric outcomes in the first year of recruitment.
- During the gestational period, we provided self-administered questionnaires to mothers twice.
- The study is strengthened by its assessment of the effects of non-response on prevalence estimates as well as the exposure–outcome relationship.
- The sample size of this study was sufficient to examine the risk factors of non-response.

- We were unable to examine the effects of some socioeconomic factors on non-response.

Background

Population-based studies are used to provide epidemiological data on the occurrence of disease and to identify risk factors that may be relevant to these outcomes. The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that started recruiting expectant mothers in January 2011. [1]

In the first year of recruitment, approximately 10,000 registered pregnant women had confirmed obstetric outcomes. Data on participants' health-related behaviour, marital status, socioeconomic status, and education level were collected via self-administered questionnaires provided twice during the gestational period.[2]

In recent years, the response rates have decreased in several epidemiological studies over time, which may lead to selection biases.[3,4] Although a study may achieve a high response rate, the prevalence estimates may still be biased if the non-responses are not random. The characteristics of non-respondents therefore need to be confirmed. Systematic differences in the characteristics of respondents and non-respondents detract from the outcomes of interest. Therefore, the presence and extent of such bias should be investigated.[5] In a cross-sectional health survey, Pietila and colleagues compared the backgrounds of responding and non-responding young men and found that their socioeconomic status and education level were related to their response

status.[6] Furthermore, the response status in the Atherosclerosis Risk in Communities Study differed according to sex and ethnicity.[7]

Long-term follow-up studies are hampered by a decrease in response rate due to the lapse of time between birth and follow-up. A systematic review of randomized controlled trials using postal questionnaires showed that the response rate was related to the length and/or design of questionnaire, use of personalized letters, and follow-up contact, and matched the interests of participants and originating sources.[8] In longitudinal cohort studies, various factors have been shown to be related to response status, including age, sex, marital status, education, health status, health-related behaviour, lifestyle, ethnicity, study objectives, contact modes, number and order of contact modes, and use of incentives.[9-12]

Some authors have suggested that non-response increases the proportion of infants with adverse outcomes in the remaining study population [13]; however, how these factors influence study outcomes is unclear. Therefore, we performed this study to describe the characteristics of non-responders. We studied pregnant women who were registered in a prospective, cohort study and who did not return the second questionnaire during the gestational period.

Methods

Design of the JECS

In the JECS, self-administered questionnaires were provided to mothers twice: during the first trimester (MT1) and during the second/third trimester (MT2). Questionnaires were provided by research coordinators at prenatal examinations (in the obstetrics clinic) or by mail and returned either by hand at subsequent prenatal visits (in the obstetrics clinic) or by mail. The partners of registered mothers were also asked to participate. We collected data from registered partners during the women's pregnancy through self-administered questionnaires returned by hand or by mail. Women's medical records were transcribed three times, by obstetricians, midwives/nurses, or research coordinators at the obstetrics clinic: during the first trimester, during the second/third trimester, and after delivery.

Design of the non-responder study

In this study, we defined 'non-respondents' as JECS participants who did not return the questionnaire of 2nd/3rd trimesters. This study was based on a data set (i.e. jecs-ag-ai-20131008), which was released in October 2013 (The dataset supporting the conclusions of this article will be available after the steering committee of the JECS permits its accessibility). The participant flow is illustrated in Figure 1.

Using the MT1 questionnaire, demographic data (age, marital status, and cohabiting family members), medical and obstetric history, health-related behaviour (smoker/exposure to secondary smoke, and alcohol consumption), and occupational data were collected. The SF-8™ questionnaire (Japanese version) [14] was used to assess participants' health-related quality of life (QOL). The K6 questionnaire (Japanese version) was used to assess participants' psychological distress. [15] Age was divided into four categories: <25 years, 25–29 years, 30–34 years, and ≥35 years. We collected data of cohabiting family members via multiple-choice questionnaires.

The response data from participants' partners and a transcription sheet regarding health status data during the gestational period were linked with each participant.

Definitions

Health status data during pregnancy was defined as positive based on multiple visits to obstetricians and using transcription sheet data. Partners' participation status was defined as positive when partners returned the questionnaire.

We collected information on occupation and types of employment of participants with the MT1 questionnaire. We focused on the following settings: homemakers or unemployed, worked from home, and employed. For allocation of these settings, we used the Japan Standard Occupational Classification and the classification of positions in

employment by the Ministry of Internal Affairs and Communication.

Regarding exposure to secondary smoke before pregnancy, 'daily' was defined as when participants answered with 'exposed at least once a week'.

Patient and Public Involvement

JECS started recruiting expectant mothers in January 2011 with the aim of assessing environmental factors that affect children's health, with the goal of providing a foundation for policymaking to safeguard the environment for the next generation. JECS study aimed to recruit approximately 100,000 pregnant women and their partners over 3 years, to collect biological samples, and to collect data on their children until they turned 13 years old.[1]

Written informed consent for participation in JECS was obtained from individual mothers. In addition to the JECS main study, adjunct studies were conducted by the member of JECS group, or any combination of them. The adjunct studies may have included procedures that were not adopted by the main study, e.g., collection and examination of placenta. This study was one of the adjunct studies of JECS, based on an existing dataset, and hence, patients were not directly involved in the sampling process.

Ethical considerations

The JECS protocol was reviewed and approved by the Ministry of the Environment's

Institutional Review Board on Epidemiological Studies and by the Ethics Committees of all participating institutions. Written informed consent was obtained from all participating women and their partners.

Statistical analyses

The following variables were considered in the analyses for mothers: demographic data (age, marital status, and cohabiting family members), medical and obstetric history, physical and mental health, health-related behaviours, occupation, environmental exposure, contact status with their obstetrician, and partners' response status. A Student's t-test or Welch's t-test for independent groups was used for continuous variables, and a Pearson's chi-square test or Fisher's exact test was used for categorical variables. The variables that had significant associations with non-response to the MT2 questionnaire in the bivariate logistic regression models were included in the multivariate models. Prevalence odds ratios and 95% confidence intervals for non-response were estimated using multivariate logistic regression analyses. The contribution of a variable to the regression model was assessed using the likelihood ratio test.

A significance level of .05 (two-tailed) was used for all statistical tests. JMP® Pro version 11 (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

Results

The overall response rate to the questionnaire in the second/third trimester was 97.7% (9432/9649). Table 1 shows participants' characteristics at the first trimester, their partners' participating status, and visits to the obstetrician among responders and non-responders. The proportions of marital status, family members, medical history, exposure to secondary smoke, and job status significantly differed between responders and non-responders. The responders were more likely to be married, living with in-laws, have a history of allergic rhinitis or allergic conjunctivitis, have better physical functioning, have a high response rate from their partner, and make more visits to the obstetrician. Additionally, responders were less likely to have a history of migraines or polycystic ovary syndrome than were non-responders. Non-responders were more likely to have been exposed to secondary smoke than were responders. Participants who were employed were more likely to respond than were their counterparts. The SF-8 Physical Functioning and Body Pain scales were significantly higher for responders than for non-responders.

Two variables showed significant associations—living with one's mother-in-law and having allergic rhinitis—with non-response according to the bivariate logistic regression

model. Table 2 shows the odds ratios for non-response according to the various demographic and clinical characteristics, partners' participation status, and visiting obstetricians in the multivariate logistic regression analyses. Model 1 included the variables that had significant associations with non-response of MT2.

The odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS[1]; had a positive QOL; were living with their mother-in-law; had partners who actively participated; and had maintained contact with obstetricians. However, the odds of non-response were higher in participants who had been exposed to secondary smoke. Marital status, job site, and the SF-8 physical functioning scale did not match the model, and thus were excluded.

Model 2 excluded variables that did not show significance in Model 1. The odds of non-response were higher in participants who had been exposed to secondary smoke; however, the odds were lower in participants who lived with their mother-in-law, had a history of allergic rhinitis, had a positive QOL regarding body pain, had partners who participated, and visited the obstetrician.

Discussion

Using data collected during pregnancy, we evaluated non-response bias in

approximately 10,000 pregnant women who participated in the JECS. Many factors were independently associated with response to the follow-up questionnaire. The characteristics associated with a greater probability of response included being married, living with one's mother-in-law, and where the participants worked. Having a medical history of allergic rhinitis or allergic conjunctivitis resulted in a higher probability of response. The number of partners with positive participation in the JECS and multiple visits to the obstetrician were significantly lower in non-responders than in responders.

The odds ratios for non-response were correlated with demographic and clinical characteristics, partners' participation status, and visiting the obstetrician in the multivariate logistic regression analysis. Specifically, the odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS; who had a positive QOL; who were living with their mother-in-law; whose partners participated; and who maintained contact with obstetricians. The odds of non-response were higher in participants who had been exposed to secondary smoke. Baron and colleagues reported that passive smoking showed disparity across educational levels.[16] We could not consider the effects of education; however, the relationship between non-response and exposure to secondary smoke might be affected by participants' education.

One of the objectives of the JECS was to assess environmental factors that affect children's health (e.g. allergic diseases). The prevalence of allergic rhinitis in the Japanese population was 44.2% in 2006–2007 [17] and that of allergic conjunctivitis disease was 14.8% in 1993. [18] Both were higher than those reported in the current study (35.9% and 10.9%, respectively). Macera and colleagues reported that responders were individuals who had family members with certain chronic conditions in their health-related survey. [19] Leadbetter and colleagues examined the perceived risk of cancer by comparing early and late responders. They reported that the salience of the survey topic was associated with a prompt response. [20] In this survey, participants with interest in children's allergic diseases were more likely to respond; however, daily exposure to secondary smoke made non-responses more likely. In health-related surveys, participants with risky health behaviours are more likely to be non-respondents than are those who exhibit healthier behaviour. [21]

Etter and colleagues reported that respondents had better general health than did non-respondents.[22] Martikainen and colleagues evaluated non-response bias in analyses of social class inequalities in health.[23] They found that female non-respondents had an approximately 20–30% higher sickness absence rate per 100 person-years than did respondents. Our results from the Body Pain scale showed that

respondents were healthier than were non-respondents, which is consistent with these previous results. The response rate was higher among participants who lived with their mother-in-law, those who had partners who positively participated, and those who maintained contact with an obstetrician. Alessi and colleagues suggested that general practitioners' understanding of the study could influence the attitude of their patients. [24] Our results indicate that the same is true for people close to the participants. Hatta and colleagues reported that parents-in-law were perceived as the least cohesive persons among close family members in Japan. [25] Another study of postpartum depression in China reported that the underlying cultural setting of the daughter-in-law/mother-in-law relationship contributed to depression among daughters-in-law. [26] In our survey, the presence of a mother-in-law may have acted as a stressor to motivate the participants to return the questionnaires. Further, we collected participants' job status and categorized it into three modes: homemakers or unemployed, worked from home, and employed. The response rate depended on participants' job, with a higher response rate being found among participants working from home than among those whose job location was outside of their home. In the Survey on Time Use and Leisure Activities in 2011,[27] women who worked from home (family workers) spent more time on housework and less time on self-education/training and hobbies/amusement than did those who were

employed outside of their home. Associations with response to the questionnaire were also observed for job location and time spent answering the questionnaire; however, these relationships were weak.

The limitations of this study are as follows: 1) a lack of information on education level and participants' socioeconomic status, 2) a lack of information on the survey mode, and 3) a lack of information on partners' registration status. However, we know that socioeconomic status and education level are related to response status. [6,28-30] Although we collected socioeconomic and educational data on the MT2 questionnaire, we failed to consider these effects because they were beyond the scope of our objectives. In particular, it seems that the investigators' interpretation of 'secondary smoke' was inconsistent with their results regarding alcohol consumption or health-related variables. These variables were related to socioeconomic and education status. In addition, several researchers have reported that response status differs according to survey mode.[31-34] In this study, we collected questionnaires by hand or by mail. Because we were unable to collect data on the mode used, we did not evaluate the effect of these distinct modes. We were also unable to collect information regarding the extent of partners' participation—any response was considered positive. Finally, we could not confirm participants' medical or obstetric history using clinical data. Relying solely on data

collected by self-administered questionnaires introduces the risk of response bias.

Conclusions

In conclusion, this study showed that obtaining understanding of the research objectives from people who are close to the participants was associated with a higher odds of response. To reduce the non-response rate in future follow-up surveys, additional efforts should be made to maintain contact and encourage participation among individuals who display relevant characteristics of potential non-responders. Because the data collected from pregnant women participating in JECS were used in this study, it means the participants may have been influenced by the Japanese culture and/or their socioeconomic situation. It is necessary to consider the results obtained from other participants from different cultures or nationalities.

Declarations

Data sharing statement

The dataset supporting the conclusions of this article will be available after the steering committee of the JECS allows it to become available.

The dataset supporting the conclusions of this article is unsuitable for public deposition due to ethical restrictions and legal framework of Japan. The Act on the

Protection of Personal Information (Act No. 57 of 30 May 2003; amendment on 9 September 2015) prohibits publicly depositing data containing personal information. The Ethical Guidelines for Medical and Health Research Involving Human Subjects, which are enforced by the Japan Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare, also restrict the open sharing of epidemiologic data. All inquiries about access to these data should be sent to Dr Shoji F. Nakayama, JECS Programme Office, National Institute for Environmental Studies; email: jecs-en@nies.go.jp.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MK designed and conducted the study, performed the statistical analyses, and wrote the manuscript. KM helped draft the manuscript. AT conducted the data collection and

helped draft the manuscript. MI and TT conducted data collection and helped critically revise the manuscript. KH and HI participated in the study design and helped critically revise the manuscript. HO assisted with the statistical analyses. YA and SS helped critically revise the manuscript. All authors have read and approved the final manuscript.

Figure legend

Figure 1. Participant (expecting mothers) flow

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Table 1. Baseline characteristics of sample

	Responder (n=9,432)	Non-responder (n= 217)	
	%	%	p value
Age			0.205
< 25	9.1	10.4	
25 – 29	27.3	24.2	
30 – 34	35.8	42.3	
>= 35	27.8	23.1	
Marital status			0.024
Married	95.8	93.9	
Unmarried	3.2	3.3	
Divorced/widowed	1.0	2.8	
Family member participants living with			
None	0.7	0.9	0.661*
Partner	93.0	91.7	0.471
Children	55.3	54.8	0.892
Father	7.6	5.5	0.298*
Mother	9.9	8.8	0.646*
Brother / sister	4.2	5.9	0.218
Father-in-law	9.4	5.5	0.045*
Mother-in-law	11.6	5.5	0.005*
Brother / sister-in-law	3.1	0.9	0.071*
1st pregnancy	30.5	31.0	0.940*
Medical history			
Have allergic rhinitis	35.9	26.7	0.005*
Have allergic conjunctivitis	10.9	6.4	0.035*
Smoking habits during early pregnancy			0.072
Never smoked	56.8	50.0	
Ex-smokers who quit before pregnancy	24.2	25.2	
Ex-smokers who quit after pregnancy	13.5	15.9	
Smoker	5.5	8.9	
Exposed to secondary smoke before pregnancy [a]			< 0.001
Rarely	80.2	71.0	
Daily	19.8	29.0	
Alcohol consumption during early pregnancy			0.006*

Never drinker	35.0	40.4	
Ex-drinkers	55.0	55.4	
Drinkers	10.0	4.2	
Job site of participants			0.011
Housewife / unemployed	42.2	52.2	
Work from home	3.4	3.9	
Employed	54.4	43.9	
Relationship with others			
Visits obstetrician [b]	97.8	54.3	< 0.001*
Positive participation of partners [c]	60.4	23.9	< 0.001*
	Mean, SE	Mean, SE	p value
No. of household member	3.3, 0.01	3.1, 0.09	0.094+
Health Related Quality of Life (SF-8)			
General Health	46.9, 0.1	46.7, 0.5	0.772
Physical Functioning	46.6, 0.1	45.5, 0.5	0.027
Role Physical	43.7, 0.1	43.5, 0.6	0.756
Body Pain	50.0, 0.1	48.7, 0.6	0.025
Vitality	47.5, 0.1	47.2, 0.5	0.452
Social Functioning	44.2, 0.1	43.4, 0.6	0.203
Mental Health	47.0, 0.1	46.2, 0.5	0.062
Role Emotional	47.2, 0.1	46.5, 0.5	0.198
Physical Component Summary	45.5, 0.1	44.8, 0.5	0.203
Mental Component Summary	46.3, 0.1	45.6, 0.5	0.164
Self-Administered mental health (K6)	9.6, 0.0	10.1, 0.3	0.097+

*: Fisher's exact test, +: Welch's t test

a: 'Daily' defined as subjects exposed at least once a week.

b: Participants who collected the transcription sheet defined as multiple visits with obstetrician.

c: Positive participation of partner was those who answered the questionnaire.

Table 2. (a) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response: model 1

Variable	OR (95% CI)	p value
Marital status		
Married	Reference	
Unmarried	0.64 (0.23, 1.48)	0.324
Divorced/widowed	1.22 (0.28, 3.52)	0.750
Living with mother-in-law (yes / no)	0.50 (0.25, 0.90)	0.020
Job site of participants		
Housewife or unemployed	Reference	
Work from home	1.58 (0.67, 3.26)	0.173
Employed	0.86 (0.62, 1.19)	0.107
Medical history of allergic rhinitis (yes / no)	0.62 (0.43, 0.88)	0.007
Health Related Quality of Life (Physical Functioning)	0.98 (0.96, 1.00)	0.135
Health Related Quality of Life (Body Pain)	0.97 (0.95, 0.98)	0.002
Exposed to secondary smoke during early pregnancy (daily / rarely)	1.48 (1.03, 2.11)	0.034
Alcohol consumption		
Drinker during early pregnancy / never drunk	0.34 (0.14, 0.71)	0.002
Drinker during early pregnancy / ex-drinkers	0.45 (0.19, 0.92)	0.027
Relationship with others		
Visits to obstetrician (yes / no)	0.02 (0.02, 0.04)	<0.001
Positive participation of partners (yes / no)	0.26 (0.18, 0.36)	<0.001

For this model, data of 9,298 people were used.

AICc: 1427.9, LOF: p=1.000

Table 2. (b) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response: model 2

Variable	OR (95% CI)	p value
Living with mother-in-law (yes / no)	0.47 (0.24, 0.85)	0.011
Having history of allergic rhinitis (yes / no)	0.68 (0.48, 0.95)	0.024
Health Related Quality of Life (Body Pain)	0.96 (0.95, 0.98)	<0.001
Exposed to secondary smoke (daily / rarely)	1.59 (1.12, 2.23)	0.009
Alcohol consumption (drinker / never drinker)	0.36 (0.16, 0.72)	0.002
Alcohol consumption (drinker / ex-drinker)	0.47 (0.21, 0.92)	0.026
Visits obstetrician (yes / no)	0.02 (0.02, 0.03)	<0.001
Positive participation of participants' partners (yes / no)	0.25 (0.17, 0.35)	<0.001

For this analysis, data of 9,634 people were used.

AICc: 1507.8, LOF: p=1.000

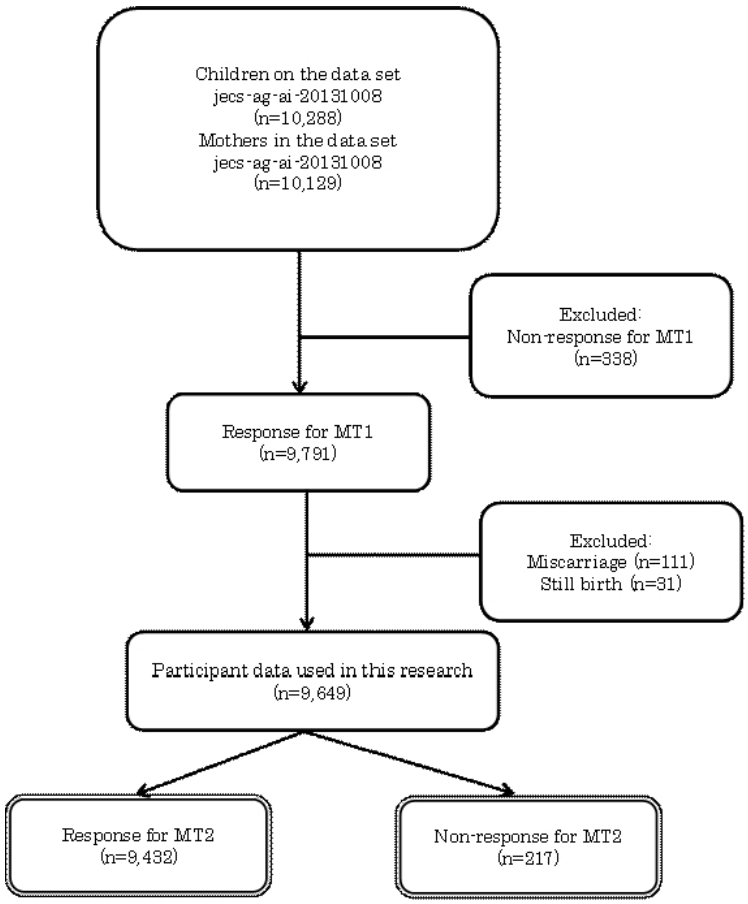

Figure 1. Inclusion of subjects (expecting mothers)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	The page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	p. 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	p. 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	p.6-8
Objectives	3	State specific objectives, including any prespecified hypotheses	p.8 l.1-4
Methods			
Study design	4	Present key elements of study design early in the paper	p.9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p.9-10
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	p.9 Fig.1
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p.9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*p.9-10*
Bias	9	Describe any efforts to address potential sources of bias	p.16-17
Study size	10	Explain how the study size was arrived at	Fig.1 p.11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p.9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P10-11
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and	

	controls was addressed
	Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy
	(*e*) Describe any sensitivity analyses

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	p.11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	p.11 Tab.1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*p.11-12 Tab.2*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p.12-13 Tab.2
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	p.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p.14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	p.17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.8, 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Analysis of non-respondent pregnant women who were registered in the Japan Environment and Children's Study: a longitudinal cohort study

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Analysis of non-respondent pregnant women who were registered in the Japan Environment and Children's Study: a longitudinal cohort study

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Abstract

Objectives: Non-response to questionnaires in a longitudinal study reduces the effective sample size and introduces bias. We identified the characteristics of non-respondent pregnant women, and compared them with respondents in the Japan Environment and Children's Study (JECS) during the gestational period. **Design:** This was a questionnaire-based, longitudinal cohort study. **Setting:** Questionnaires were provided by research coordinators to mothers at prenatal examinations (at obstetrics clinics) or by mail. Mothers were measured twice: during the first trimester and during the second/third trimester. **Participants:** Data were collected from the 10,129 participating mothers of the 10,288 children surveyed in the 2011 baseline JECS. We excluded responses from mothers who had a miscarriage or still birth; therefore, we analysed data from 9,649 participants. **Primary and secondary outcome measures:** Data concerning demographics, medical history, health characteristics, health-related behaviour, and environmental exposure were collected via self-administered questionnaires. The response status of participants' partners and contact with their obstetrician were also examined. Multivariate logistic regression analysis was used to examine factors related to non-response. **Results:** Response was associated with living with one's mother-in-law (odds ratio [OR]: 0.47, 95% confidence interval [CI]: 0.24–0.85), positive participation of

participants' partner (OR: 0.25, 95% CI: 0.17–0.35), and multiple visits to the obstetrician (OR: 0.02, 95% CI: 0.02–0.03). Participants who had a medical history of allergic rhinitis, had body pain, or drank alcohol had higher odds of responding (ORs: 0.68, 0.96, and 0.36, 95% CIs: 0.48–0.95, 0.95–0.98, and 0.16–0.72, respectively); those exposed to secondary smoke had lower odds of responding (OR: 1.59, 95% CI: 1.12–2.23).

Conclusions: The non-response rate decreased when participants reported health-related behaviour or characteristics. Obtaining the understanding of people around each participant might help increase response rates.

Strengths and limitations of this study

- The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that includes 10,129 mothers with confirmed obstetric outcomes in the first year of recruitment.
- During the gestational period, we provided self-administered questionnaires to mothers twice.
- The study is strengthened by its assessment of the effects of non-response on prevalence estimates as well as the exposure–outcome relationship.
- The sample size of this study was sufficient to examine the risk factors of non-response.

- We were unable to examine the effects of some socioeconomic factors on non-response.

Background

Population-based studies are used to provide epidemiological data on the occurrence of disease and to identify risk factors that may be relevant to these outcomes. The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that started recruiting expectant mothers in January 2011. [1]

In the first year of recruitment, approximately 10,000 registered pregnant women had confirmed obstetric outcomes. Data on participants' health-related behaviour, marital status, socioeconomic status, and education level were collected via self-administered questionnaires provided twice during the gestational period.[2]

In recent years, the response rates have decreased in several epidemiological studies over time. Although a particular study may achieve a high response rate, the prevalence estimates may still be biased if the non-responses are not random. The non-response bias may be related to selection bias; thus, the characteristics of non-respondents need to be confirmed.[3,4] Systematic differences in the characteristics of respondents and non-respondents detract from the outcomes of interest. Therefore, the presence and extent of such bias should be investigated.[5] In a cross-sectional health survey, Pietila and colleagues compared the backgrounds of responding and non-responding young men and found that their socioeconomic status and education level were related to their

response status.[6] Furthermore, the response status in the Atherosclerosis Risk in Communities Study differed according to sex and ethnicity.[7]

Long-term follow-up studies are hampered by a decrease in response rate due to the lapse of time between birth and follow-up. A systematic review of randomized controlled trials using postal questionnaires showed that the response rate was related to the length and/or design of questionnaire, use of personalized letters, and follow-up contact, and matched the interests of participants and originating sources.[8] In longitudinal cohort studies, various factors have been shown to be related to response status, including age, sex, marital status, education, health status, health-related behaviour, lifestyle, ethnicity, study objectives, contact modes, number and order of contact modes, and use of incentives.[9-12]

Some authors have suggested that non-response increases the proportion of infants with adverse outcomes in the remaining study population [13]; however, how these factors influence study outcomes is unclear. Therefore, we performed this study to describe the characteristics of non-responders. We studied pregnant women who were registered in a prospective, cohort study and who did not return the second questionnaire during the gestational period.

Methods

Design of the JECS

In the JECS, self-administered questionnaires were provided to mothers twice: during the first trimester (MT1) and during the second/third trimester (MT2). Questionnaires were provided by research coordinators at prenatal examinations (in the obstetrics clinic) or by mail and returned either by hand at subsequent prenatal visits (in the obstetrics clinic) or by mail. The partners of registered mothers were also asked to participate. We collected data from registered partners during the women's pregnancy through self-administered questionnaires returned by hand or by mail. Women's medical records were transcribed three times, by obstetricians, midwives/nurses, or research coordinators at the obstetrics clinic: during the first trimester, during the second/third trimester, and after delivery.

Design of the non-responder study

In this study, we defined 'non-respondents' as JECS participants who did not return the questionnaire of 2nd/3rd trimesters. This study was based on a data set (i.e. jecs-ag-ai-20131008), which was released in October 2013 (The dataset supporting the conclusions of this article will be available after the steering committee of the JECS permits its accessibility). The participant flow is illustrated in Figure 1.

Using the MT1 questionnaire, demographic data (age, marital status, and cohabiting family members), medical and obstetric history, health-related behaviour (smoker/exposure to secondary smoke, and alcohol consumption), and occupational data were collected. The SF-8™ questionnaire (Japanese version) [14] was used to assess participants' health-related quality of life (QOL). The K6 questionnaire (Japanese version) was used to assess participants' psychological distress. [15] Age was divided into four categories: <25 years, 25–29 years, 30–34 years, and ≥35 years. We collected data of cohabiting family members via multiple-choice questionnaires.

The response data from participants' partners and a transcription sheet regarding health status data during the gestational period were linked with each participant.

Definitions

Participants' obstetric visiting status was a binary variable and was defined as present for a participant when the transcription sheet was returned if they had reported "multiple obstetric visits to collaborating hospitals during pregnancy." Partners' participation status was defined as positive when partners returned the questionnaire.

We collected information on occupation and types of employment of participants with the MT1 questionnaire. We focused on the following settings: homemakers or unemployed, worked from home, and employed. For allocation of these settings, we used

the Japan Standard Occupational Classification and the classification of positions in employment by the Ministry of Internal Affairs and Communication.

Regarding exposure to secondary smoke before pregnancy, 'daily' was defined as when participants answered with 'exposed at least once a week'.

Patient and Public Involvement

JECS started recruiting expectant mothers in January 2011 with the aim of assessing environmental factors that affect children's health, with the goal of providing a foundation for policymaking to safeguard the environment for the next generation. JECS study aimed to recruit approximately 100,000 pregnant women and their partners over 3 years, to collect biological samples, and to collect data on their children until they turned 13 years old.[1]

Written informed consent for participation in JECS was obtained from individual mothers. In addition to the JECS main study, adjunct studies were conducted by the member of JECS group, or any combination of them. The adjunct studies may have included procedures that were not adopted by the main study, e.g., collection and examination of placenta. This study was one of the adjunct studies of JECS, based on an existing dataset, and hence, patients were not directly involved in the sampling process.

Ethical considerations

The JECS protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and by the Ethics Committees of all participating institutions. Written informed consent was obtained from all participating women and their partners.

Statistical analyses

The following variables were considered in the analyses for mothers: demographic data (age, marital status, and cohabiting family members), medical and obstetric history, physical and mental health, health-related behaviours, occupation, environmental exposure, contact status with their obstetrician, and partners' response status. Of these variables, a Student's t-test or Welch's t-test for independent groups was used for physical and mental health variables (SF-8, K6), or number of cohabiting family members (continuous variables), and a Pearson's chi-square test or Fisher's exact test was used for other variables (categorical variables). The variables that had significant associations with non-response to the MT2 questionnaire in the bivariate logistic regression models were included in the multivariate models. Prevalence odds ratios and 95% confidence intervals for non-response were estimated using multivariate logistic regression analyses. The contribution of a variable to the regression model was assessed using the likelihood ratio test.

A significance level of 0.05 (two-tailed) was used for all statistical tests. JMP® Pro version 11 (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

Results

The overall response rate to the questionnaire in the second/third trimester was 97.7% (9432/9649). Table 1 shows participants' characteristics at the first trimester, their partners' participating status, and visits to the obstetrician among responders and non-responders. The proportions of marital status, family members, medical history, exposure to secondary smoke, and job status significantly differed between responders and non-responders. The responders were more likely to be married, living with in-laws, have a history of allergic rhinitis or allergic conjunctivitis, have better physical functioning, have a high response rate from their partner, and make more visits to the obstetrician. Additionally, responders were less likely to have a history of migraines or polycystic ovary syndrome than were non-responders. Non-responders were more likely to have been exposed to secondary smoke than were responders. Participants who were employed were more likely to respond than were their counterparts. The SF-8 Physical Functioning and Body Pain scales were significantly higher for responders than for non-responders.

Two variables showed significant associations—living with one's mother-in-law and having allergic rhinitis—with non-response according to the bivariate logistic regression model. Table 2 shows the odds ratios for non-response according to the various demographic and clinical characteristics, partners' participation status, and visiting obstetricians in the multivariate logistic regression analyses. Model 1 included the variables that had significant associations with non-response of MT2.

The odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS[1]; had a positive QOL; were living with their mother-in-law; had partners who actively participated; and had maintained contact with obstetricians. However, the odds of non-response were higher in participants who had been exposed to secondary smoke. Marital status, job site, and the SF-8 physical functioning scale did not match the model, and thus were excluded.

Model 2 excluded variables that did not show significance in Model 1. The odds of non-response were higher in participants who had been exposed to secondary smoke; however, the odds were lower in participants who lived with their mother-in-law, had a history of allergic rhinitis, had a positive QOL regarding body pain, had partners who participated, and visited the obstetrician.

Discussion

Using data collected during pregnancy, we evaluated non-response bias in approximately 10,000 pregnant women who participated in the JECS. Many factors were independently associated with response to the follow-up questionnaire. The characteristics associated with a greater probability of response included being married, living with one's mother-in-law, and where the participants worked. Having a medical history of allergic rhinitis or allergic conjunctivitis resulted in a higher probability of response. The number of partners with positive participation in the JECS and multiple visits to the obstetrician were significantly lower in non-responders than in responders.

The odds ratios for non-response were correlated with demographic and clinical characteristics, partners' participation status, and visiting the obstetrician in the multivariate logistic regression analysis. Specifically, the odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS; who had a positive QOL; who were living with their mother-in-law; whose partners participated; and who maintained contact with obstetricians. The odds of non-response were higher in participants who had been exposed to secondary smoke. Baron and colleagues reported that passive smoking showed disparity across educational levels.[16] We could not consider the effects of education; however, the

relationship between non-response and exposure to secondary smoke might be affected by participants' education.

One of the objectives of the JECS was to assess environmental factors that affect children's health (e.g. allergic diseases). The prevalence of allergic rhinitis in the Japanese population was 44.2% in 2006–2007 [17] and that of allergic conjunctivitis disease was 14.8% in 1993. [18] Both were higher than those reported in the current study (35.9% and 10.9%, respectively). Macera and colleagues reported that responders were individuals who had family members with certain chronic conditions in their health-related survey. [19] Leadbetter and colleagues examined the perceived risk of cancer by comparing early and late responders. They reported that the salience of the survey topic was associated with a prompt response. [20] In this survey, participants with interest in children's allergic diseases were more likely to respond; however, daily exposure to secondary smoke made non-responses more likely. In health-related surveys, participants with risky health behaviours are more likely to be non-respondents than are those who exhibit healthier behaviour. [21]

Etter and colleagues reported that respondents had better general health than did non-respondents.[22] Martikainen and colleagues evaluated non-response bias in analyses of social class inequalities in health.[23] They found that female non-

respondents had an approximately 20–30% higher sickness absence rate per 100 person-years than did respondents. Our results from the Body Pain scale showed that respondents were healthier than were non-respondents, which is consistent with these previous results. The response rate was higher among participants who lived with their mother-in-law, those who had partners who positively participated, and those who maintained contact with an obstetrician. Alessi and colleagues suggested that general practitioners' understanding of the study could influence the attitude of their patients. [24] Our results indicate that the same is true for people close to the participants. Hatta and colleagues reported that parents-in-law were perceived as the least cohesive persons among close family members in Japan. [25] Another study of postpartum depression in China reported that the underlying cultural setting of the daughter-in-law/mother-in-law relationship contributed to depression among daughters-in-law. [26] In our survey, the presence of a mother-in-law may have acted as a stressor to motivate the participants to return the questionnaires.

Further, we collected participants' job status and categorized it into three modes: homemakers or unemployed, worked from home, and employed. The response rate depended on participants' job, with a higher response rate being found among participants working from home than among those whose job location was outside of

their home. In the Survey on Time Use and Leisure Activities in 2011,[27] women who worked from home (family workers) spent more time on housework and less time on self-education/training and hobbies/amusement than did those who were employed outside of their home. Associations with response to the questionnaire were also observed for job location and time spent answering the questionnaire; however, these relationships were weak.

The limitations of this study are as follows: 1) a lack of information on education level and participants' socioeconomic status, 2) a lack of information on the survey mode, and 3) a lack of information on partners' registration status. However, we know that socioeconomic status and education level are related to response status. [6,28-30]. In the JECS study, however, the socioeconomic and education status data were collected with the MT2 questionnaire, which was used to examine the non-response factor. Thus, We could not examine these factors. In particular, it seems that the investigators' interpretation of 'secondary smoke' was inconsistent with their results regarding alcohol consumption or health-related variables. These variables were related to socioeconomic and education status. In addition, several researchers have reported that response status differs according to survey mode.[31-34] In this study, we collected questionnaires by hand or by mail. Because we were unable to collect data on the mode used, we did not

evaluate the effect of these distinct modes. We were also unable to collect information regarding the extent of partners' participation—any response was considered positive. Finally, we could not confirm participants' medical or obstetric history using clinical data. Relying solely on data collected by self-administered questionnaires introduces the risk of response bias.

Conclusions

In conclusion, this study showed that obtaining understanding of the research objectives from people who are close to the participants was associated with a higher odds of response. To reduce the non-response rate in future follow-up surveys, additional efforts should be made to maintain contact and encourage participation among individuals who display relevant characteristics of potential non-responders. Because the data collected from pregnant women participating in JECS were used in this study, it means the participants may have been influenced by the Japanese culture and/or their socioeconomic situation. It is necessary to consider the results obtained from other participants from different cultures or nationalities.

Declarations

Data sharing statement

The dataset supporting the conclusions of this article will be available after the steering committee of the JECS allows it to become available.

The dataset supporting the conclusions of this article is unsuitable for public deposition due to ethical restrictions and legal framework of Japan. The Act on the Protection of Personal Information (Act No. 57 of 30 May 2003; amendment on 9 September 2015) prohibits publicly depositing data containing personal information. The Ethical Guidelines for Medical and Health Research Involving Human Subjects, which are enforced by the Japan Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare, also restrict the open sharing of epidemiologic data. All inquiries about access to these data should be sent to Dr Shoji F. Nakayama, JECS Programme Office, National Institute for Environmental Studies; email: jecs-en@nies.go.jp.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MK designed and conducted the study, performed the statistical analyses, and wrote the manuscript. KM helped draft the manuscript. AT conducted the data collection and helped draft the manuscript. MI and TT conducted data collection and helped critically revise the manuscript. KH and HI participated in the study design and helped critically revise the manuscript. HO assisted with the statistical analyses. YA and SS helped critically revise the manuscript. All authors have read and approved the final manuscript.

Figure legend

Figure 1. Participant (expecting mothers) flow

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Table 1. Baseline characteristics of sample

	Responder (n=9,432)	Non-responder (n= 217)	
	%	%	p value
Age			0.205
< 25	9.1	10.4	
25 – 29	27.3	24.2	
30 – 34	35.8	42.3	
>= 35	27.8	23.1	
Marital status			0.024
Married	95.8	93.9	
Unmarried	3.2	3.3	
Divorced/widowed	1.0	2.8	
Family member participants living with			
None	0.7	0.9	0.661*
Partner	93.0	91.7	0.471
Children	55.3	54.8	0.892
Father	7.6	5.5	0.298*
Mother	9.9	8.8	0.646*
Brother / sister	4.2	5.9	0.218
Father-in-law	9.4	5.5	0.045*
Mother-in-law	11.6	5.5	0.005*
Brother / sister-in-law	3.1	0.9	0.071*
1st pregnancy	30.5	31.0	0.940*
Medical history			
Have allergic rhinitis	35.9	26.7	0.005*
Have allergic conjunctivitis	10.9	6.4	0.035*
Smoking habits during early pregnancy			0.072
Never smoked	56.8	50.0	
Ex-smokers who quit before pregnancy	24.2	25.2	
Ex-smokers who quit after pregnancy	13.5	15.9	
Smoker	5.5	8.9	
Exposed to secondary smoke before pregnancy [a]			< 0.001
Rarely	80.2	71.0	
Daily	19.8	29.0	
Alcohol consumption during early pregnancy			0.006*

Never drinker	35.0	40.4	
Ex-drinkers	55.0	55.4	
Drinkers	10.0	4.2	
Job site of participants			0.011
Housewife / unemployed	42.2	52.2	
Work from home	3.4	3.9	
Employed	54.4	43.9	
Relationship with others			
Visits obstetrician [b]	97.8	54.3	< 0.001*
Positive participation of partners [c]	60.4	23.9	< 0.001*
	Mean, SE	Mean, SE	p value
No. of household member	3.3, 0.01	3.1, 0.09	0.094+
Health Related Quality of Life (SF-8)			
General Health	46.9, 0.1	46.7, 0.5	0.772
Physical Functioning	46.6, 0.1	45.5, 0.5	0.027
Role Physical	43.7, 0.1	43.5, 0.6	0.756
Body Pain	50.0, 0.1	48.7, 0.6	0.025
Vitality	47.5, 0.1	47.2, 0.5	0.452
Social Functioning	44.2, 0.1	43.4, 0.6	0.203
Mental Health	47.0, 0.1	46.2, 0.5	0.062
Role Emotional	47.2, 0.1	46.5, 0.5	0.198
Physical Component Summary	45.5, 0.1	44.8, 0.5	0.203
Mental Component Summary	46.3, 0.1	45.6, 0.5	0.164
Self-Administered mental health (K6)	9.6, 0.0	10.1, 0.3	0.097+

*: Fisher's exact test, +: Welch's t test

a: 'Daily' defined as subjects exposed at least once a week.

b: Participants who collected the transcription sheet defined as multiple visits with obstetrician.

c: Positive participation of partner was those who answered the questionnaire.

Table 2. (a) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response: model 1

Variable	OR (95% CI)	p value
Marital status		
Married	Reference	
Unmarried	0.64 (0.23, 1.48)	0.324
Divorced/widowed	1.22 (0.28, 3.52)	0.750
Living with mother-in-law (yes / no)	0.50 (0.25, 0.90)	0.020
Job site of participants		
Housewife or unemployed	Reference	
Work from home	1.58 (0.67, 3.26)	0.173
Employed	0.86 (0.62, 1.19)	0.107
Medical history of allergic rhinitis (yes / no)	0.62 (0.43, 0.88)	0.007
Health Related Quality of Life (Physical Functioning)	0.98 (0.96, 1.00)	0.135
Health Related Quality of Life (Body Pain)	0.97 (0.95, 0.98)	0.002
Exposed to secondary smoke during early pregnancy (daily / rarely)	1.48 (1.03, 2.11)	0.034
Alcohol consumption		
Drinker during early pregnancy / never drunk	0.34 (0.14, 0.71)	0.002
Drinker during early pregnancy / ex-drinkers	0.45 (0.19, 0.92)	0.027
Relationship with others		
Visits to obstetrician (yes / no)	0.02 (0.02, 0.04)	<0.001
Positive participation of partners (yes / no)	0.26 (0.18, 0.36)	<0.001

For this model, data of 9,298 people were used.

AICc: 1427.9, LOF: p=1.000

Table 2. (b) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response: model 2

Variable	OR (95% CI)	p value
Living with mother-in-law (yes / no)	0.47 (0.24, 0.85)	0.011
Having history of allergic rhinitis (yes / no)	0.68 (0.48, 0.95)	0.024
Health Related Quality of Life (Body Pain)	0.96 (0.95, 0.98)	<0.001
Exposed to secondary smoke (daily / rarely)	1.59 (1.12, 2.23)	0.009
Alcohol consumption (drinker / never drinker)	0.36 (0.16, 0.72)	0.002
Alcohol consumption (drinker / ex-drinker)	0.47 (0.21, 0.92)	0.026
Visits obstetrician (yes / no)	0.02 (0.02, 0.03)	<0.001
Positive participation of participants' partners (yes / no)	0.25 (0.17, 0.35)	<0.001

For this analysis, data of 9,634 people were used.

AICc: 1507.8, LOF: p=1.000

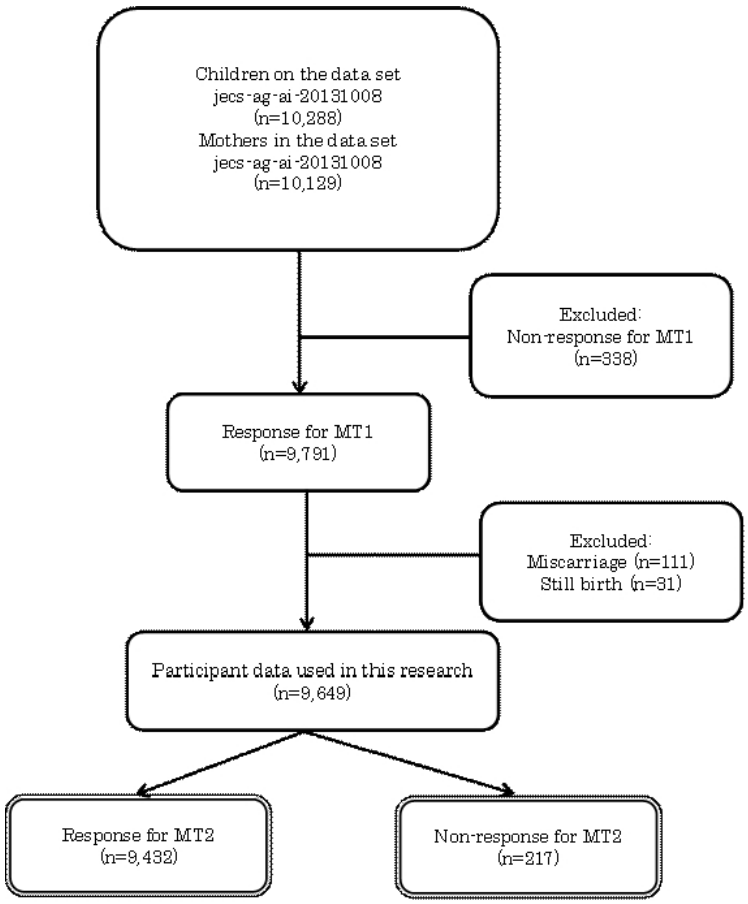

Figure 1. Inclusion of subjects (expecting mothers)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	The page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	p. 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	p. 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	p.6-8
Objectives	3	State specific objectives, including any prespecified hypotheses	p.8 l.1-4
Methods			
Study design	4	Present key elements of study design early in the paper	p.9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p.9-10
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	p.9 Fig.1
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p.9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*p.9-10*
Bias	9	Describe any efforts to address potential sources of bias	p.16-17
Study size	10	Explain how the study size was arrived at	Fig.1 p.11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p.9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P10-11
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and	

	controls was addressed
	Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy
	(*e*) Describe any sensitivity analyses

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	p.11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	p.11 Tab.1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*p.11-12 Tab.2*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p.12-13 Tab.2
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	p.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p.14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	p.17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.8, 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Analysis of non-respondent pregnant women who were registered in the Japan Environment and Children's Study: a longitudinal cohort study

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Analysis of non-respondent pregnant women who were registered in the Japan Environment and Children's Study: a longitudinal cohort study

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Abstract

Objectives: Non-response to questionnaires in a longitudinal study reduces the effective sample size and introduces bias. We identified the characteristics of non-respondent pregnant women, and compared them with respondents in the Japan Environment and Children's Study (JECS) during the gestational period. **Design:** This was a questionnaire-based, longitudinal cohort study. **Setting:** Questionnaires were provided by research coordinators to mothers at prenatal examinations (at obstetrics clinics) or by mail. Mothers were measured twice: during the first trimester and during the second/third trimester. **Participants:** Data were collected from the 10,129 participating mothers of the 10,288 children surveyed in the 2011 baseline JECS. We excluded responses from mothers who had a miscarriage or still birth; therefore, we analysed data from 9,649 participants. **Primary and secondary outcome measures:** Data concerning demographics, medical history, health characteristics, health-related behaviour, and environmental exposure were collected via self-administered questionnaires. The response status of participants' partners and contact with their obstetrician were also examined. Multivariate logistic regression analysis was used to examine factors related to non-response. **Results:** Response was associated with living with one's mother-in-law (odds ratio [OR]: 0.47, 95% confidence interval [CI]: 0.24–0.85),

positive participation of participants' partner (OR: 0.25, 95% CI: 0.17–0.35), and multiple visits to the obstetrician (OR: 0.02, 95% CI: 0.02–0.03). Participants who had a medical history of allergic rhinitis, had body pain, or drank alcohol had higher odds of responding (ORs: 0.68, 0.96, and 0.36, 95% CIs: 0.48–0.95, 0.95–0.98, and 0.16–0.72, respectively); those exposed to secondary smoke had lower odds of responding (OR: 1.59, 95% CI: 1.12–2.23). **Conclusions:** The non-response rate decreased when participants reported health-related behaviour or characteristics. Obtaining the understanding of people around each participant might help increase response rates.

Strengths and limitations of this study

- The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that includes 10,129 mothers with confirmed obstetric outcomes in the first year of recruitment.
- During the gestational period, we provided self-administered questionnaires to mothers twice.
- The study is strengthened by its assessment of the effects of non-response on prevalence estimates as well as the exposure–outcome relationship.
- The sample size of this study was sufficient to examine the risk factors of

non-response.

- We were unable to examine the effects of some socioeconomic factors on non-response.

Background

Population-based studies are used to provide epidemiological data on the occurrence of disease and to identify risk factors that may be relevant to these outcomes. The Japan Environment and Children's Study (JECS) is a nationwide birth cohort study that started recruiting expectant mothers in January 2011. [1]

In the first year of recruitment, approximately 10,000 registered pregnant women had confirmed obstetric outcomes. Data on participants' health-related behaviour, marital status, socioeconomic status, and education level were collected via self-administered questionnaires provided twice during the gestational period.[2]

In recent years, the response rates have decreased in several epidemiological studies over time. Although a particular study may achieve a high response rate, the prevalence estimates may still be biased if the non-responses are not random. The non-response bias may be related to selection bias; thus, the characteristics of non-respondents need to be confirmed.[3,4] Systematic differences in the characteristics of respondents and non-respondents detract from the outcomes of interest. Therefore, the presence and extent of such bias should be investigated.[5] In a cross-sectional health survey, Pietila and colleagues compared the backgrounds of responding and non-responding young men and found that their socioeconomic status

and education level were related to their response status.[6] Furthermore, the response status in the Atherosclerosis Risk in Communities Study differed according to sex and ethnicity.[7]

Long-term follow-up studies are hampered by a decrease in response rate due to the lapse of time between birth and follow-up. A systematic review of randomized controlled trials using postal questionnaires showed that the response rate was related to the length and/or design of questionnaire, use of personalized letters, and follow-up contact, and matched the interests of participants and originating sources.[8] In longitudinal cohort studies, various factors have been shown to be related to response status, including age, sex, marital status, education, health status, health-related behaviour, lifestyle, ethnicity, study objectives, contact modes, number and order of contact modes, and use of incentives.[9-12]

Some authors have suggested that non-response increases the proportion of infants with adverse outcomes in the remaining study population [13]; however, how these factors influence study outcomes is unclear. Therefore, we performed this study to describe the characteristics of non-responders. We studied pregnant women who were registered in a prospective, cohort study and who did not return the second questionnaire during the gestational period.

Methods

Design of the JECS

In the JECS, self-administered questionnaires were provided to mothers twice: during the first trimester (MT1) and during the second/third trimester (MT2). Questionnaires were provided by research coordinators at prenatal examinations (in the obstetrics clinic) or by mail and returned either by hand at subsequent prenatal visits (in the obstetrics clinic) or by mail. The partners of registered mothers were also asked to participate. We collected data from registered partners during the women's pregnancy through self-administered questionnaires returned by hand or by mail. Women's medical records were transcribed three times, by obstetricians, midwives/nurses, or research coordinators at the obstetrics clinic: during the first trimester, during the second/third trimester, and after delivery.

Design of the non-responder study

In this study, we defined 'non-respondents' as JECS participants who did not return the questionnaire of 2nd/3rd trimesters. This study was based on a data set (i.e. jecs-ag-ai-20131008), which was released in October 2013 (The dataset supporting the conclusions of this article will be available after the steering committee of the JECS

permits its accessibility). The participant flow is illustrated in Figure 1.

Using the MT1 questionnaire, demographic data (age, marital status, and cohabiting family members), medical and obstetric history, health-related behaviour (smoker/exposure to secondary smoke, and alcohol consumption), and occupational data were collected. The SF-8™ questionnaire (Japanese version) [14] was used to assess participants' health-related quality of life (QOL). The K6 questionnaire (Japanese version) was used to assess participants' psychological distress. [15] Age was divided into four categories: <25 years, 25–29 years, 30–34 years, and ≥35 years. We collected data of cohabiting family members via multiple-choice questionnaires.

The response data from participants' partners and a transcription sheet regarding health status data during the gestational period were linked with each participant.

Definitions

Participants' obstetric visiting status was a binary variable and was defined as present for a participant when the transcription sheet was returned if they had reported "multiple obstetric visits to collaborating hospitals during pregnancy." Partners' participation status was defined as positive when partners returned the questionnaire.

We collected information on occupation and types of employment of participants with the MT1 questionnaire. We focused on the following settings: homemakers or

unemployed, worked from home, and employed. For allocation of these settings, we used the Japan Standard Occupational Classification and the classification of positions in employment by the Ministry of Internal Affairs and Communication.

Regarding exposure to secondary smoke before pregnancy, 'daily' was defined as when participants answered with 'exposed at least once a week'.

Patient and Public Involvement

JECS started recruiting expectant mothers in January 2011 with the aim of assessing environmental factors that affect children's health, with the goal of providing a foundation for policymaking to safeguard the environment for the next generation. JECS study aimed to recruit approximately 100,000 pregnant women and their partners over 3 years, to collect biological samples, and to collect data on their children until they turned 13 years old.[1]

Written informed consent for participation in JECS was obtained from individual mothers. In addition to the JECS main study, adjunct studies were conducted by the member of JECS group, or any combination of them. The adjunct studies may have included procedures that were not adopted by the main study, e.g., collection and examination of placenta. This study was one of the adjunct studies of JECS, based on an existing dataset, and hence, patients were not directly involved in the sampling process.

Ethical considerations

The JECS protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and by the Ethics Committees of all participating institutions. Written informed consent was obtained from all participating women and their partners.

Statistical analyses

The following variables were considered in the analyses for mothers: demographic data (age, marital status, and cohabiting family members), medical and obstetric history, physical and mental health, health-related behaviours, occupation, environmental exposure, contact status with their obstetrician, and partners' response status. Of these variables, a Student's t-test or Welch's t-test for independent groups was used for physical and mental health variables (SF-8, K6), or number of cohabiting family members (continuous variables), and a Pearson's chi-square test or Fisher's exact test was used for other variables (categorical variables). The variables that had significant associations with non-response to the MT2 questionnaire in the bivariate logistic regression models were included in the multivariate models. Prevalence odds ratios and 95% confidence intervals for non-response were estimated using multivariate logistic regression analyses. The contribution of a variable to the regression model was

assessed using the likelihood ratio test.

A significance level of 0.05 (two-tailed) was used for all statistical tests. JMP® Pro version 11 (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

Results

The overall response rate to the questionnaire in the second/third trimester was 97.7% (9432/9649). Table 1 shows participants' characteristics at the first trimester, their partners' participating status, and visits to the obstetrician among responders and non-responders. The proportions of marital status, family members, medical history, exposure to secondary smoke, and job status significantly differed between responders and non-responders. The responders were more likely to be married, living with in-laws, have a history of allergic rhinitis or allergic conjunctivitis, have better physical functioning, have a high response rate from their partner, and make more visits to the obstetrician. Additionally, responders were less likely to have a history of migraines or polycystic ovary syndrome than were non-responders. Non-responders were more likely to have been exposed to secondary smoke than were responders. Participants who were employed were more likely to respond than were their counterparts. The SF-8 Physical Functioning and Body Pain scales were significantly higher for responders than for

non-responders.

Two variables showed significant associations—living with one's mother-in-law and having allergic rhinitis—with non-response according to the bivariate logistic regression model. Table 2 shows the odds ratios for non-response according to the various demographic and clinical characteristics, partners' participation status, and visiting obstetricians in the multivariate logistic regression analyses. Model 1 included the variables that had significant associations with non-response of MT2.

The odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS[1]; had a positive QOL; were living with their mother-in-law; had partners who actively participated; and had maintained contact with obstetricians. However, the odds of non-response were higher in participants who had been exposed to secondary smoke. Marital status, job site, and the SF-8 physical functioning scale did not match the model, and thus were excluded.

Model 2 excluded variables that did not show significance in Model 1. The odds of non-response were higher in participants who had been exposed to secondary smoke; however, the odds were lower in participants who lived with their mother-in-law, had a history of allergic rhinitis, had a positive QOL regarding body pain, had partners who participated, and visited the obstetrician.

Discussion

Using data collected during pregnancy, we evaluated non-response bias in approximately 10,000 pregnant women who participated in the JECS. Many factors were independently associated with response to the follow-up questionnaire. The characteristics associated with a greater probability of response included being married, living with one's mother-in-law, and where the participants worked. Having a medical history of allergic rhinitis or allergic conjunctivitis resulted in a higher probability of response. The number of partners with positive participation in the JECS and multiple visits to the obstetrician were significantly lower in non-responders than in responders.

The odds ratios for non-response were correlated with demographic and clinical characteristics, partners' participation status, and visiting the obstetrician in the multivariate logistic regression analysis. Specifically, the odds of non-response were lower in participants who had a medical history of allergies, which is one of the priority outcomes of the JECS; who had a positive QOL; who were living with their mother-in-law; whose partners participated; and who maintained contact with obstetricians. The odds of non-response were higher in participants who had been exposed to secondary smoke. Baron and colleagues reported that passive smoking

showed disparity across educational levels.[16] We could not consider the effects of education; however, the relationship between non-response and exposure to secondary smoke might be affected by participants' education.

One of the objectives of the JECS was to assess environmental factors that affect children's health (e.g. allergic diseases). The prevalence of allergic rhinitis in the Japanese population was 44.2% in 2006–2007 [17] and that of allergic conjunctivitis disease was 14.8% in 1993. [18] Both were higher than those reported in the current study (35.9% and 10.9%, respectively). Macera and colleagues reported that responders were individuals who had family members with certain chronic conditions in their health-related survey. [19] Leadbetter and colleagues examined the perceived risk of cancer by comparing early and late responders. They reported that the salience of the survey topic was associated with a prompt response. [20] In this survey, participants with interest in children's allergic diseases were more likely to respond; however, daily exposure to secondary smoke made non-responses more likely. In health-related surveys, participants with risky health behaviours are more likely to be non-respondents than are those who exhibit healthier behaviour. [21]

Etter and colleagues reported that respondents had better general health than did non-respondents.[22] Martikainen and colleagues evaluated non-response bias in

analyses of social class inequalities in health.[23] They found that female non-respondents had an approximately 20–30% higher sickness absence rate per 100 person-years than did respondents. Our results from the Body Pain scale showed that respondents were healthier than were non-respondents, which is consistent with these previous results. The response rate was higher among participants who lived with their mother-in-law, those who had partners who positively participated, and those who maintained contact with an obstetrician. Alessi and colleagues suggested that general practitioners' understanding of the study could influence the attitude of their patients. [24] Our results indicate that the same is true for people close to the participants. Hatta and colleagues reported that parents-in-law were perceived as the least cohesive persons among close family members in Japan. [25] Another study of postpartum depression in China reported that the underlying cultural setting of the daughter-in-law/mother-in-law relationship contributed to depression among daughters-in-law. [26] In our survey, the presence of a mother-in-law may have acted as a stressor to motivate the participants to return the questionnaires.

Further, we collected participants' job status and categorized it into three modes: homemakers or unemployed, worked from home, and employed. The response rate depended on participants' job, with a higher response rate being found among

participants working from home than among those whose job location was outside of their home. In the Survey on Time Use and Leisure Activities in 2011,[27] women who worked from home (family workers) spent more time on housework and less time on self-education/training and hobbies/amusement than did those who were employed outside of their home. Associations with response to the questionnaire were also observed for job location and time spent answering the questionnaire; however, these relationships were weak.

Michikawa and colleagues reported that there was no difference in the distribution of maternal age at delivery between the JECS participants and the general population, further revealing that characteristics of selected infants in the JECS population (singleton birth, gestational age at birth, gender, birth weight) were similar to those of national survey data from the general population in Japan. [2] The association between non-response and the relative factors found in this study was observed in Japanese pregnant women.

The limitations of this study are as follows: 1) a lack of information on education level and participants' socioeconomic status, 2) a lack of information on the survey mode, and 3) a lack of information on partners' registration status. However, we know that socioeconomic status and education level are related to response status. [6,28-30]. In the

JECS study, however, the socioeconomic and education status data were collected with the MT2 questionnaire, which was used to examine the non-response factor. Thus, We could not examine these factors. In particular, it seems that the investigators' interpretation of 'secondary smoke' was inconsistent with their results regarding alcohol consumption or health-related variables. These variables were related to socioeconomic and education status. In addition, several researchers have reported that response status differs according to survey mode.[31-34] In this study, we collected questionnaires by hand or by mail. Because we were unable to collect data on the mode used, we did not evaluate the effect of these distinct modes. We were also unable to collect information regarding the extent of partners' participation—any response was considered positive. Finally, we could not confirm participants' medical or obstetric history using clinical data. Relying solely on data collected by self-administered questionnaires introduces the risk of response bias.

Conclusions

In conclusion, this study showed that obtaining understanding of the research objectives from people who are close to the participants was associated with a higher odds of response. To reduce the non-response rate in future follow-up surveys,

additional efforts should be made to maintain contact and encourage participation among individuals who display relevant characteristics of potential non-responders. Because the data collected from pregnant women participating in JECS were used in this study, it means the participants may have been influenced by the Japanese culture and/or their socioeconomic situation. It is necessary to consider the results obtained from other participants from different cultures or nationalities.

Declarations

Data sharing statement

The dataset supporting the conclusions of this article will be available after the steering committee of the JECS allows it to become available.

The dataset supporting the conclusions of this article is unsuitable for public deposition due to ethical restrictions and legal framework of Japan. The Act on the Protection of Personal Information (Act No. 57 of 30 May 2003; amendment on 9 September 2015) prohibits publicly depositing data containing personal information. The Ethical Guidelines for Medical and Health Research Involving Human Subjects, which are enforced by the Japan Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare, also restrict the open sharing of epidemiologic data. All inquiries about access to these data should be sent to

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Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MK designed and conducted the study, performed the statistical analyses, and wrote the manuscript. KM helped draft the manuscript. AT conducted the data collection and helped draft the manuscript. MI and TT conducted data collection and helped critically revise the manuscript. KH and HI participated in the study design and helped critically revise the manuscript. HO assisted with the statistical analyses. YA and SS helped critically revise the manuscript. All authors have read and approved the final manuscript.

Figure legend

Figure 1. Participant (expecting mothers) flow

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Table 1. Baseline characteristics of sample

	Responder (n=9,432)	Non-responder (n= 217)	
	%	%	p value
Age			0.205
< 25	9.1	10.4	
25 – 29	27.3	24.2	
30 – 34	35.8	42.3	
>= 35	27.8	23.1	
Marital status			0.024
Married	95.8	93.9	
Unmarried	3.2	3.3	
Divorced/widowed	1.0	2.8	
Family member participants living with			
None	0.7	0.9	0.661*
Partner	93.0	91.7	0.471
Children	55.3	54.8	0.892
Father	7.6	5.5	0.298*
Mother	9.9	8.8	0.646*
Brother / sister	4.2	5.9	0.218
Father-in-law	9.4	5.5	0.045*
Mother-in-law	11.6	5.5	0.005*
Brother / sister-in-law	3.1	0.9	0.071*
1st pregnancy	30.5	31.0	0.940*
Medical history			
Have allergic rhinitis	35.9	26.7	0.005*
Have allergic conjunctivitis	10.9	6.4	0.035*
Smoking habits during early pregnancy			0.072
Never smoked	56.8	50.0	
Ex-smokers who quit before pregnancy	24.2	25.2	
Ex-smokers who quit after pregnancy	13.5	15.9	
Smoker	5.5	8.9	
Exposed to secondary smoke before pregnancy [a]			< 0.001
Rarely	80.2	71.0	
Daily	19.8	29.0	
Alcohol consumption during early pregnancy			0.006*

Never drinker	35.0	40.4	
Ex-drinkers	55.0	55.4	
Drinkers	10.0	4.2	
Job site of participants			0.011
Housewife / unemployed	42.2	52.2	
Work from home	3.4	3.9	
Employed	54.4	43.9	
Relationship with others			
Visits obstetrician [b]	97.8	54.3	< 0.001*
Positive participation of partners [c]	60.4	23.9	< 0.001*
	Mean, SE	Mean, SE	p value
No. of household member	3.3, 0.01	3.1, 0.09	0.094+
Health Related Quality of Life (SF-8)			
General Health	46.9, 0.1	46.7, 0.5	0.772
Physical Functioning	46.6, 0.1	45.5, 0.5	0.027
Role Physical	43.7, 0.1	43.5, 0.6	0.756
Body Pain	50.0, 0.1	48.7, 0.6	0.025
Vitality	47.5, 0.1	47.2, 0.5	0.452
Social Functioning	44.2, 0.1	43.4, 0.6	0.203
Mental Health	47.0, 0.1	46.2, 0.5	0.062
Role Emotional	47.2, 0.1	46.5, 0.5	0.198
Physical Component Summary	45.5, 0.1	44.8, 0.5	0.203
Mental Component Summary	46.3, 0.1	45.6, 0.5	0.164
Self-Administered mental health (K6)	9.6, 0.0	10.1, 0.3	0.097+

*: Fisher's exact test, +: Welch's t test

a: 'Daily' defined as subjects exposed at least once a week.

b: Participants who collected the transcription sheet defined as multiple visits with obstetrician.

c: Positive participation of partner was those who answered the questionnaire.

Table 2. (a) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response: model 1

Variable	OR (95% CI)	p value
Marital status		
Married	Reference	
Unmarried	0.64 (0.23, 1.48)	0.324
Divorced/widowed	1.22 (0.28, 3.52)	0.750
Living with mother-in-law (yes / no)	0.50 (0.25, 0.90)	0.020
Job site of participants		
Housewife or unemployed	Reference	
Work from home	1.58 (0.67, 3.26)	0.173
Employed	0.86 (0.62, 1.19)	0.107
Medical history of allergic rhinitis (yes / no)	0.62 (0.43, 0.88)	0.007
Health Related Quality of Life (Physical Functioning)	0.98 (0.96, 1.00)	0.135
Health Related Quality of Life (Body Pain)	0.97 (0.95, 0.98)	0.002
Exposed to secondary smoke during early pregnancy (daily / rarely)	1.48 (1.03, 2.11)	0.034
Alcohol consumption		
Drinker during early pregnancy / never drunk	0.34 (0.14, 0.71)	0.002
Drinker during early pregnancy / ex-drinkers	0.45 (0.19, 0.92)	0.027
Relationship with others		
Visits to obstetrician (yes / no)	0.02 (0.02, 0.04)	<0.001
Positive participation of partners (yes / no)	0.26 (0.18, 0.36)	<0.001

For this model, data of 9,298 people were used.

AICc: 1427.9, LOF: p=1.000

Table 2. (b) Multivariate Logistic Regression Predicting the likelihood of Survey Non-response: model 2

Variable	OR (95% CI)	p value
Living with mother-in-law (yes / no)	0.47 (0.24, 0.85)	0.011
Having history of allergic rhinitis (yes / no)	0.68 (0.48, 0.95)	0.024
Health Related Quality of Life (Body Pain)	0.96 (0.95, 0.98)	<0.001
Exposed to secondary smoke (daily / rarely)	1.59 (1.12, 2.23)	0.009
Alcohol consumption (drinker / never drinker)	0.36 (0.16, 0.72)	0.002
Alcohol consumption (drinker / ex-drinker)	0.47 (0.21, 0.92)	0.026
Visits obstetrician (yes / no)	0.02 (0.02, 0.03)	<0.001
Positive participation of participants' partners (yes / no)	0.25 (0.17, 0.35)	<0.001

For this analysis, data of 9,634 people were used.

AICc: 1507.8, LOF: p=1.000

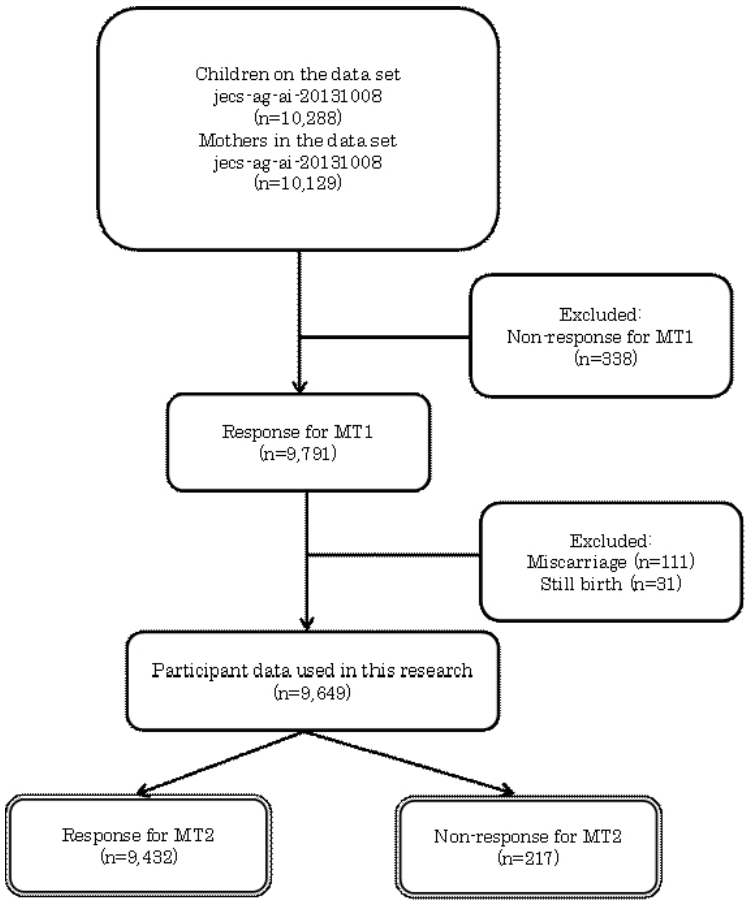

Figure 1. Inclusion of subjects (expecting mothers)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	The page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	p. 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	p. 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	p.6-8
Objectives	3	State specific objectives, including any prespecified hypotheses	p.8 l.1-4
Methods			
Study design	4	Present key elements of study design early in the paper	p.9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p.9-10
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	p.9 Fig.1
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p.9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*p.9-10*
Bias	9	Describe any efforts to address potential sources of bias	p.16-17
Study size	10	Explain how the study size was arrived at	Fig.1 p.11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p.9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P10-11
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and	

	controls was addressed
	Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy
	(*e*) Describe any sensitivity analyses

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	p.11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	p.11 Tab.1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*p.11-12 Tab.2*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p.12-13 Tab.2
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	p.13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p.14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	p.17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.8, 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.