The Chinese Children and Families Cohort Study

The Nutrition, Physical Activity, and Ultraviolet Radiation Data Collection

Nancy Potischman, PhD
Liwen Fang, MD, PhD
Ling Hao, MD, PhD
Regan R. Bailey, PhD, MPH
David Berrigan, PhD, MPH
Robert John Berry, MD, MPHTM
Alison Brodie, PhD
Ann Chao, PhD
Jing Chen, MSc
Kevin Dodd, PhD
Yajing Feng, MSc
Guansheng Ma, PhD
Yuna He, PhD
Jing Fan, MSc
Michael Kimlin, PhD
Cari Kitahara, PhD
Martha Linet, MD, MPH
Zhu Li, MD, MPH
Ailing Liu, PhD
Yashan Liu, MD
Joshua Sampson, PhD
Joseph Su, PhD, MPH
Jiandong Sun, PhD
Natasha Tasevska, MD, PhD, MSc
Lichen Yang, MD, PhD
Ruilan Yang, MD
Qian Zhang, PhD
Ning Wang, MSc
Linhong Wang, MD, MS
Wang Yu, MD, PhD

Nancy Potischman, PhD, is the Director of Population Studies, in the Office of Disease Prevention in the Office of the Director of the National Institutes of Health and the principal investigator of the Chinese Children and Families Cohort Study (CFCS) Pilot Study 2.

Liwen Fang, MD, PhD, is Director of Cancer Division, National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China.

Ling Hao, MD, PhD, is a Project Officer, US Centers for Disease Control and Prevention China Office, Beijing, China.

Regan R. Bailey, PhD, MPH, formerly at the Office of Dietary Supplements, National Institutes of Health, Bethesda, Maryland.

David Berrigan, PhD, MPH, is a Program Director, Division of Cancer Control and Population Studies, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Robert John Berry, MD, MPHTM, is a medical epidemiologist, US Centers for Disease Control and Prevention, Atlanta, Georgia, and the US Principal Investigator of the Community Intervention Program in China (retired).

Alison Brodie, PhD, Queensland University of Technology, Brisbane, Australia.

Ann Chao, PhD, is a Senior Advisor for Cancer and Noncommunicable Diseases, Center for Global Health, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Jing Chen, MSc, Chinese Center for Disease Control and Prevention, Beijing, China.

Kevin Dodd, PhD, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Yajing Feng, MSc, Chinese Center for Disease Control and Prevention, Beijing, China.

Guansheng Ma, PhD, is Chair of Department of Nutrition and Food Safety, School of Public Health, Peking University, Beijing, China.

Yuna He, PhD, Chinese Center for Disease Control and Prevention, Beijing, China.

Jing Fan, MSc, Chinese Center for Disease Control and Prevention, Beijing, China.

Michael Kimlin, PhD, is professor of Cancer Prevention, University of the Sunshine Coast & Cancer Council Queensland, Brisbane, Australia.

Cari Kitahara, PhD, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Martha Linet, MD, MPH, served as Chief of the Radiation Epidemiology Branch from 2002 to 2014 in the Division of Cancer Epidemiology and Genetics of the National Cancer Institute and principal investigator of the larger CFCS Pilot Study 1.

Zhu Li, MD, MPH, is a consultant and Principal Investigator of the Community Intervention Program in China, Peking University Health Science Center, Beijing, China (retired).

Ailing Liu, PhD, Chinese Center for Disease Control and Prevention, Beijing, China.

Yashan Liu, MD, Department of Maternal and Child Health in Rural and Urban Centers in China.

Joshua Sampson, PhD, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Joseph Su, PhD, MPH, is a professor in the Department of Epidemiology and codirector of the Cancer Prevention and Population Sciences Program at the University of Arkansas, Little Rock.

Jiandong Sun, PhD, Queensland University of Technology, Brisbane, Australia.

Natasha Tasevska, MD, PhD, MSc, formerly at the National Cancer Institute, National Institutes of Health.

Lichen Yang, MD, PhD, is the nutrition team lead for CFCS and Director of Trace-Elements Division, National Center for Nutrition and Health, Chinese Center for Disease Control and Prevention, Beijing, China.

Ruilan Yang, MD, Department of Maternal and Child Health in Rural and Urban Centers in China.

Qian Zhang, PhD, Chinese Center for Disease Control and Prevention, Beijing, China.

Ning Wang, MSc, Chinese Center for Disease Control and Prevention, Beijing, China.

Linhong Wang, MD, MS, is the Director of the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China.

Wang Yu, MD, PhD, Director General (former), Chinese Center for Disease Control and Prevention, Beijing, China.

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This article reports the study design, methodological issues and early results of a pilot study testing methods for collecting nutrition, physical activity, and ultraviolet (UV) radiation exposure data in a groundbreaking study in China. Epidemiological studies suggest that exposures across the entire life course, including in utero, early childhood, and adolescence, may be important in the etiology of adult cancers and other chronic diseases. The Chinese Children and Families Cohort Study intends to follow-up subjects from the 1993 to 1995 Community Intervention Program of folic acid supplementation for the prevention of neural tube defects. This cohort is unique in that only folic acid exposure during pregnancy varies between groups as other supplements were not available, and there were nutrient deficiencies in the populations. Prior to launching a large-scale follow-up effort, a pilot study was conducted to assess the feasibility of recontacting original study participants to collect extensive diet, physical activity, and UV radiation exposure data in this population. The pilot study included 92 mothers and 184 adolescent children aged 14 to 17 years from 1 urban and 1 rural Community Intervention Program site. Subjects completed a Food Frequency Questionnaire, a 3-day food record, a physical activity questionnaire, a 3-day sun exposure diary together with 3 days of personal UV dosimetry, and 7 days of pedometry measurements and provided blood, saliva, and toenail samples. Grip strength and body composition measurements were taken, and ambient solar UV radiation was monitored in both study sites. While most of the assessments were successful, future studies would likely require different dietary intake instruments. The purpose of this report is to describe the study design and methodological issues emerging from this pilot work relevant for the follow-up of this large birth cohort.
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Emerging epidemiological evidence suggests that early-life exposures in conjunction with genetic makeup and variability may be important in the etiology of many common adult cancers.[1–10] However, methodological challenges exist for this type of research because there are relatively few health studies that include detailed exposure assessments across the entire lifecourse.[11] The majority of cancers have long latency periods and appear late in adulthood, making it difficult to study risk factors across time and to identify critical periods of susceptibility. Most of the current evidence on the role of early-life risk factors (particularly childhood and adolescent exposures) for cancer is based on adult recall of the past or record linkage studies of particular time points in the life span. Use of recalled lifetime lifestyle habits is challenging as the details are difficult to recollect and may result in a high degree of measurement error and bias, making it difficult to identify true associations.[12–14] Record linkage studies using national databases provide high-quality research data but are limited by being able to evaluate only 1 or 2 points in the life span[15–18] with no information on other time points or consideration of other potentially important covariates. Studies of the effects of diet and other exposures on diseases with long latencies such as cancers are methodologically challenging and require follow-up over many years. Evaluating the interrelationships among cancer risk factors, accumulating risk over time, critical time periods, or temporal changes in exposure have not been addressed in most population studies. Furthermore, the few cohorts with data over the life course are small and unable to address cancer etiology because of the limited number of cancers that occur. Large studies with prospectively collected information on neonatal, childhood, adolescent, and adulthood exposures are needed.

To overcome these limitations, we have developed a plan to carry out further follow-up of participants in the Community Intervention Program (CIP), which collected data from Chinese women during the periconception period through birth of offspring. The CIP is a large (n = 247 000) public health campaign conducted in China by Chinese and US collaborators from 1993 to 1995. Because approximately half of the women targeted in the campaign took folic acid supplements (400 μg/d) during the periconception period and half did not, it was possible to determine risk of neural tube defects in newborns in high-prevalence versus lower-prevalence regions. Compared with offspring of mothers who did not take folic acid supplements, the prevalence of neural tube defects in offspring of mothers who took supplements was reduced by 79% in the high-prevalence and by 41% in the low-prevalence regions.[19] At follow-up in 2000 to 2001, 93% of the original CIP subjects were located and evaluated, and no adverse health outcomes were reported in the folic acid–exposed women or offspring.

Prior to moving forward with a large-scale follow-up of CIP, it was necessary to test appropriate methods for locating, interviewing, and collecting data on mothers and their children. The Chinese Children and Families Cohort Study (CFCS) first conducted a pilot study to test methods for identifying the original cohort members, administering general questionnaires and obtaining physical measurements

Correspondence: Guansheng Ma, PhD, 38 Xue Yuan Road, Beijing, China 100191 (mags@bjmu.edu.cn); or Linhong Wang, MD, MS, No. 27, Nanwei Road, Beijing, China 1000050 (linhong@chinawch.org.cn).

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(Pilot Study 1).[20] Pilot Study 2, described in this article, tested the feasibility of a detailed multiday assessment of diet, physical activity, ultraviolet (UV) exposure, DNA methylation, and measures of nutritional status in a subset of Pilot Study 1 mother-child pairs. This article provides an overview of the Pilot Study 2 design and methods, an evaluation of methods used, and a summary of the data generated. Based on these results, we intend to implement a modified protocol in a large-scale follow-up study of the CFCS.

METHODS

Study Sample

One rural area in the north and 1 urban center in south central China from the original 21 counties where the CIP was carried out were selected for the pilot studies. Pilot Study 1[20] provided a letter to the 460 CIP mother-child pairs describing that they might be contacted for a nutrition and physical activity study (Figure 1). Using data from CIP, it was possible to select participants for Pilot Study 2 based on knowledge of in utero folic acid exposure. Sixty mother-child pairs were selected from lists of participants in Pilot Study 1 in each center so that half of the pairs had periconception folic acid exposure and half had no exposure. To increase the sample size of a substudy on DNA methylation patterns among adolescents, an additional sample of 65 children from the rural center and 34 children from the urban center was selected for a saliva collection. In the urban field site, the study staff approached 5 additional subjects who had refused involvement in the main part of Pilot Study 2 and requested their participation in the substudy. The intent of the substudy was to obtain saliva for the DNA methylation analyses using a protocol of collecting only saliva, Food Frequency Questionnaire (FFQ), and the Oral Health History Questionnaire, which may be important for the methylation analyses.

The institutional review boards and ethics committees of the participating institutions (US National Cancer Institute [NCI], US Centers for Disease Control and Prevention [CDC], and Chinese Center for Disease Control and Prevention [China CDC]) approved the project before data collection began and have continued to renew the project annually.

Training and Quality Control

Prior to study implementation, several workshops were held with the leadership from the Maternal and Child Health Hospitals (MCH) and county CDC from the study centers and collaborators from the China CDC, US CDC, and the US NCI to obtain input on protocol development and study logistics. Useful suggestions from the workshops were incorporated in revisions to the procedures. After the protocol was finalized and all of the forms and other data collection materials were developed and pretested, training and field manuals were developed for the interviewers and laboratory personnel. A 3-day training was conducted at each study center with the MCH staff interviewers, phlebotomists, and hospital laboratory staff. Team leads with various areas of expertise from the China CDC in Beijing, US CDC, NCI, and from Queensland University of Technology in Australia (the latter for the UV component of the study) led the trainings and practice sessions with the interviewers. A training manual that described all of the procedures in detail was developed to describe the overall framework and instruments for the study, including flowcharts and other materials to describe activities for each day of the study. A letter was developed to address frequently asked questions related to blood collection, which was provided to the participants prior to the blood collection. Approximately 1 month after the training, supervisory staff from Beijing returned to each center to oversee the data collection and monitor and retrain the staff as needed on various aspects of the data collection protocol. Two

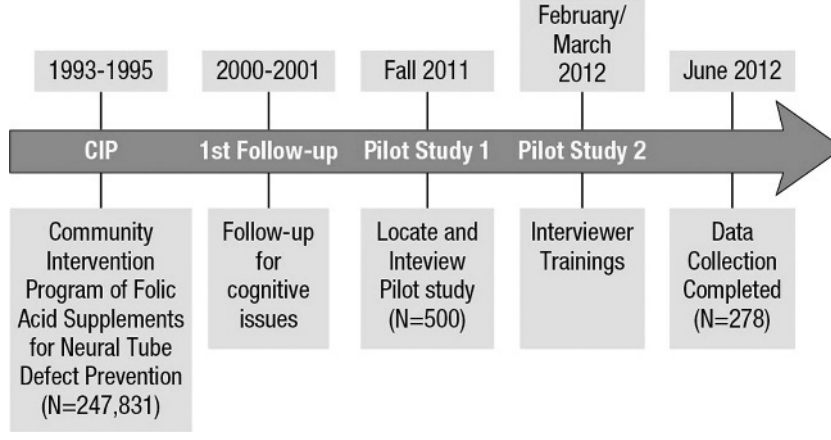

FIGURE 1. Timeline for CIP and follow-up studies.

other supervisory visits were implemented, separated by 2 to 3 weeks, to address questions and to provide further instructions related to logistics and administering the questionnaires.

Following data collection, a training workshop was held in Beijing for China CDC staff to address data cleaning and data management. Extensive review of the 3-day food records (3DFRs) and FFQ was required (described below) prior to data entry. Following manual review of all of the data, all of the questionnaires and forms were delivered to a data entry company with detailed directions for coding and for double entry to verify the data entry processes. Range and logic checks were carried out and were verified with the original paper forms, and corrections were made as needed.

Biological Specimens

Trained phlebotomists collected two 6-mL EDTA-coated purple top vacutainers for whole blood and one 6-mL red top vacutainer for serum from each participant. One vial was used for automated blood testing in the field MCH hospital laboratory, so the participant could be given relevant results relatively quickly by the local physician. The samples were processed in the hospital laboratory, and aliquots were stored in local freezers (−80°C) until the end of the study when they were transported to a central repository in Beijing without being thawed. Analyses were conducted by the China CDC National Institute for Nutrition and Health staff in Beijing for folate, homocysteine, and vitamin B_{12} on an automated analyzer.

Some aliquots for each participant were transported to the NCI repository in Maryland for further analyses. Specimens were sent to the US CDC laboratory in Atlanta and analyzed for multiple forms of folate, vitamin B_6, and vitamin D. This laboratory conducts analyses of the US National Health and Nutrition Examination Survey specimens. All of the saliva samples were transported to the repository in Maryland with the blood samples. Participants had cut their toenails and placed the clippings into bags. These were sent to the US for analyses of trace elements and metals.

Data Collection Logistics

The study was conducted in 2012 between April 7 and June 10 in the urban center and May 19 and June 17 in the rural center. Study managers at the central study office in Beijing sent a listing of the potential subjects and all of the study documents, instruments, supplies, and study ID labels. The local interviewers, including county, township, and village doctors, contacted the potential subjects on the weekend to describe the study and obtain informed consent from the mothers and assent from the adolescents. Most of the children were at boarding school, making it necessary to consent them while at home and then having another interviewer conduct the study components at the boarding school. A copy of the consent form was left with participants and included the telephone number for the central and local study managers. Incentives to complete the protocol included a small MP3 player (adolescent), a gift card to a grocery store (mother), the study pedometer, laboratory results from standard tests at the local hospital, and blood sample results from the research component. In addition, each participant received a certificate with their name imprinted to thank them for accepting participation and completion of the study.

After signed informed consent was obtained, participants began data collection (Figure 2). Participants completed the physical activity (PAQ) and oral health history questionnaires, provided saliva samples (OGR-500 Oragene DNA and RE-100 Oragene RNA vials), completed the first measure of grip strength, and were shown how to wear the UV dosimeter (YESDAS UVB pyranometers; Yankee Environmental Systems, Inc, Turner Falls, Massachusetts). Other components of the study were described for the rest of the week. Ultraviolet dosimeters were placed on roofs and other elevated locations daily to measure ambient UV radiation for the time period of the study.

On study day 1, participants started wearing the Omron HJ-151 pedometer (Omron Healthcare, Inc, Lake Forest, Illinois) clipped to clothing or a belt around their waistband and a UV dosimeter (polysulfone film) on a band around their arm or wrist all day. The UV dosimeter was attached to a reusable band with Velcro, and the instructions described wearing the band around the upper arm, but some participants wore the band around their wrists for convenience. The interviewer arrived in the evening to check the pedometer and address any issues related to it or the UV dosimeter. The participant completed a pedometer form with information about times when the pedometer was not worn. The interviewer then assisted with completion of the first day of the 3-day UV diary (3DUV diary), which elicited responses about indoor and outdoor activities and clothing covering the skin for each time period. At the end of the day, the UV dosimeters were placed in envelopes; this was done for each of the 3 days of dosimetry measurements. The FFQ was administered by an interviewer who also took a second measurement of grip strength. Because of a shortage of dynamometers to measure grip strength, there was flexibility to take the second grip strength measure at this visit or at the next interviewer visit on study day 6. The interviewer also reminded the participants not to cut their toenails until the last study day (study day 8). On study days 2 and 3, there was no contact with the interviewer.

On study day 4, the participants wore only the pedometer and received a call from the interviewer reminding them to begin the 3DFR the next day. There was no contact on study day 5, but the participants began the 3DFR and continued to wear the pedometers through study day 8. On study day 6, the interviewer visited and reviewed the

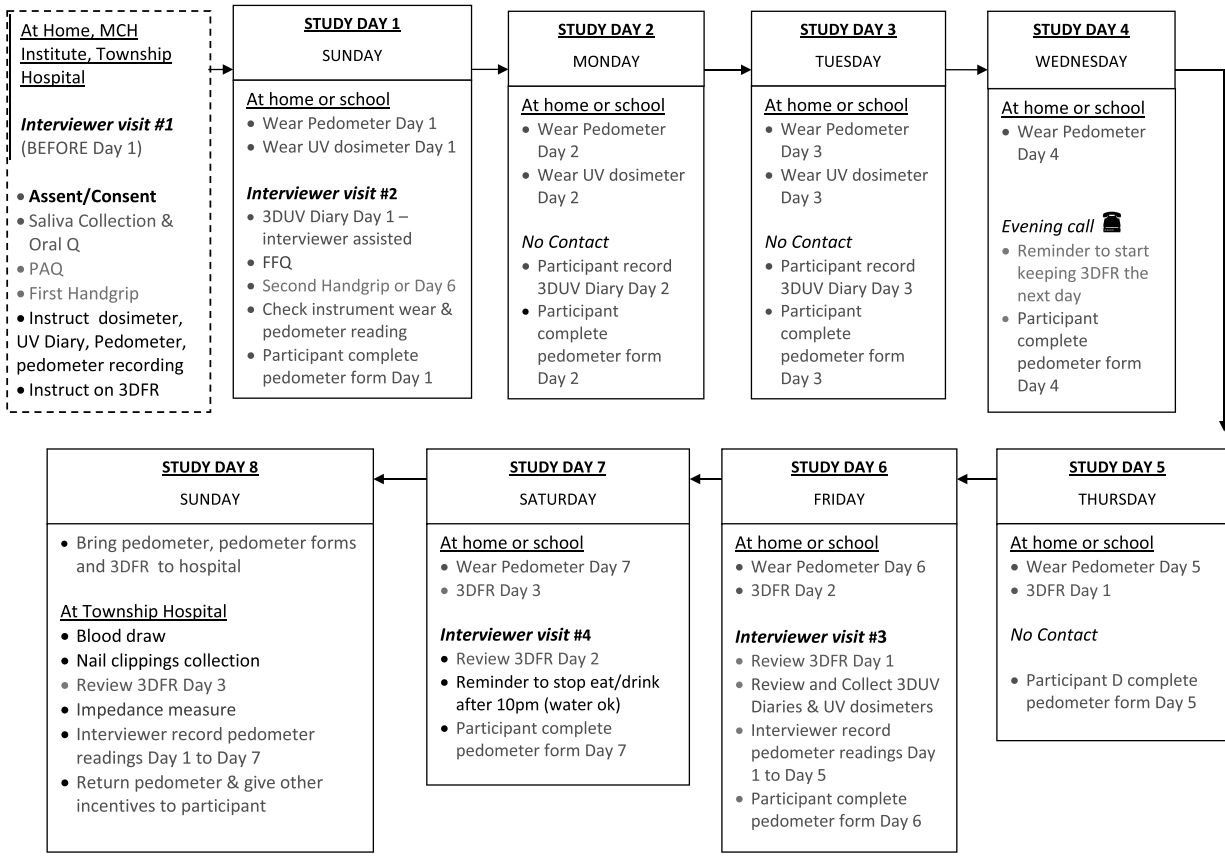

FIGURE 2. Study design for Pilot Study 2.

3DUV diaries and the first day of the 3DFR and acquired any missing details from the participants. A booklet with pictures of food portion sizes was provided to assist the interviewer in estimating the amounts consumed. The interviewer collected the 3 envelopes containing the UV dosimeters and 3DUV diaries. The interviewer also logged the number of steps on the pedometer recorded for study days 1 to 5. During the visit on study day 7, the interviewer reviewed the second day of the 3DFR and reminded the participants to fast after 10 PM that day in anticipation of the blood collection the following morning.

On study day 8, participants were transported to the local MCH hospital in the morning for the final day of the study. Upon arrival, the participants provided a fasting blood sample and then were given a snack. Female participants were queried about the dates of their last menstrual period and were instructed to note the date of their next menses. Interviewers called these participants approximately 1 month later to obtain the date of the next menses. After the blood collection, subjects were taken to another room, and toenail clippings were obtained. In addition, the third day of the 3DFR was reviewed, and staff recorded the pedometer readings for study days 1 to 7. A tetrapolar single-frequency (200 mA at 50 kHz) electrical bioimpedance analyzer (Imp DF50; ImpediMed Limited, Brisbane, Queensland, Australia) was used to measure impedance, resistance, and reactance. Participants laid down in a fully supine position on a nonconductive surface, with legs and arms abducted to each other and palms flat against the surface. Bioimpedance measurement was taken on the right side of the body. The bioimpedance prediction equation developed by Deurenberg et al[21] was used to calculate fat-free mass, and the percent body fat was then derived based on the 2-component model. The self-completed pedometer form was collected; any remaining incentives were given, and participants were asked for their input about the study logistics and instruments.

RESULTS

Participation Rates

The participation rates for Pilot Study 1 were high; 91% of rural and 90% of urban families who were traced completed the study (Table 1). For Pilot Study 2, each study site received a list of study IDs for 60 mother-child pairs who completed Pilot Study 1. Of these, 17 rural and 6 urban pairs refused participation, 1 urban pair quit (classified

TABLE 1 Overall Participation Rates

	Rural (Site 1)	Urban (Site 2)	Overall Pilot Study 2	Overall Pilot Study 1 and 2
Pilot Study 1	91%	90%		
Pilot Study 2				
Main Study 2 without blood	68%	87%	78%	70%
Main Study 2 with blood	66%	87%	76%	69%
Substudy saliva/ Food Frequency Questionnaire/ Oral Health History Questionnaire	83%	97%	88%	80%

as refusal), and 2 rural and 2 urban pairs were ineligible because they had moved out of the area or the mother was no longer available. The participation rate for Pilot Study 2 was 68% and 87% for the rural and urban sites, respectively. We attempted to avoid conflicts with school examinations, which helped with response rates in the children. The main reasons stated for refusal of the study centered on too much burden, too complicated, need for students to focus on school work, and too much of a time commitment for the mothers. For the substudy, 54 of the 65 adolescents (83%) in the rural site and 38 of the 39 subjects (97%) in the urban site completed the substudy.

A few additional subjects refused the blood-drawing component (Table 2). While the participation rate for collection of toenail clippings was high, some subjects did not have enough nail to cut and provided their sample a week or more later. Although it was suggested at the beginning of the week not to cut toenails, it is likely that this information was not delivered, instructions were not followed, or the time period was too short.

Participant Characteristics

Data from Pilot Study 1[20] provided information on demographic, measured anthropometry, and self-reported lifestyle factors. In the rural area, a higher percentage of Pilot Study 2 adolescents were female, whereas the opposite was true in the urban center (Table 3). As anticipated, the age of the children was 14 to 17 years, and mothers were 35 to 54 years of age at the time of the interviews. The heights were similar by gender and for the mothers across centers, but rural female adolescents and mothers weighed more, had higher body mass indices and fat mass, but higher fat-free mass compared with their urban counterparts. The percent body fat was lower in rural compared with urban adolescents but similar among the mothers. The majority of children at both centers were attending school; the majority of urban mothers reported working outside the home, whereas most of the rural mothers were working at home and often on home farms. None of the participants reported ever smoking cigarettes; most of the mothers and many male adolescents reported current alcohol consumption.

TABLE 2 Number of Subjects by Instrument, Devices,[a] and Specimens

	Rural Mothers	Rural Children	Rural Total	Urban Mothers	Urban Children	Urban Total	Total Mothers	Total Children
Main Study								
Approached	60	60	120	60	60	120	120	120
Completed questionnaires and devices	41	41	82 (68%)	52	52	104 (87%)	93 (78%)	93 (78%)
+Blood	39	40	79 (66%)	52	52	104 (87%)	91 (76%)	92 (77%)
+Saliva	41	40	79 (66%)	50	52	102 (85%)	91 (76%)	92 (77%)
+Toenail	41	40	81 (68%)	51	52	103 (86%)	92 (77%)	92 (77%)
Substudy								
Approached	N/A	65		N/A	39		N/A	104
Completed	N/A	54 (83%)		N/A	38 (97%)		N/A	92 (88%)
Total saliva							91	184 (82%)

[a]Devices include pedometer, hand grip tests, ultraviolet badges, and bioimpedance.

TABLE 3 Characteristics of Pilot Study 2 Population With Data From Pilot Study 1 (Mean [Range])

	Rural			Urban		
	Adolescents, n = 41			Adolescents, n = 52		
	Male	Female	Mothers, n = 41	Male	Female	Mothers, n = 52
No. of subjects	14 (35%)	27 (66%)	41	33 (63%)	19[a] (37%)	52
Age, y	15.1 (14–17)	15.4 (14–16)	41.5 (36–54)	15.1 (14–17)	15.1 (14–16)	38.7 (35–44)
Height, cm	170 (165–174)	161 (146–172)	157 (145–166)	171 (159–184)	162 (156–172)	157 (142–169)
Weight, kg	62 (48–83)	58 (44–78)	63 (42–86)	64 (49–92)	55 (44–84)	55 (41–76)
Body mass index, kg/m^2	21.5 (16.0–27.8)	22.3 (17.2–29.4)	25.5 (18.9–37.3)	21.9 (17.2–34.0)	21.0 (16.9–30.2)	22.4 (16.2–30.6)
Fat mass, kg	9.5[a]	15.3	19.4[b]	10.6[a]	14.3[c]	18.0[d]
Fat-free mass, kg	49.0[a]	42.6	41.5[b]	50.2[a]	39.4[c]	36.3[d]
% Body fat	16.6[a]	26.0	33.6[b]	18.6[a]	28.9[c]	33.6[d]
In school,[e] n	12	27	1	29	17	3
Working, n	1	—	9	2	1	43
Neither school or work, n	1	—	31	2	1	4[b]
Never smoked cigarettes, n	14	27	41	33	18	52
Current alcohol consumption, n	6 (43%)	1 (4%)	40 (98%)	18 (55%)	4 (21%)	48 (92%)

[a]Missing data for these variables on 1 child.
[b]Missing information on 2 mothers.
[c]Missing information on 2 girls.
[d]Missing information on 4 mothers.
[e]With or without work.

Study Instruments

The majority of the study instruments were completed properly by the interviewers. In each center, local supervisory staff reviewed the completed forms and questionnaires and sent them back to the interviewers for clarification or correction if needed. Site visits by supervisory staff from Beijing occurred early in the data collection, which provided clarifications, identified problems, and provided guidance to resolve problems. After data collection, the forms were reviewed by study managers in Beijing. One challenge encountered was that interviewers and local supervisors were not trained nutritionists and would have benefited from substantially more training and field visits to alleviate some of the issues encountered on the 3DFR or FFQ.

The 3DFR required careful review and some recoding of food items. Some interviewers did not obtain the level of detail required, quantified foods incorrectly, or assigned incorrect food codes. The interviewers did request more pictures in the booklets to help quantify amounts, which would have been beneficial, but the time period for this pilot study was too limited to generate new booklets. Although the FFQ had been used for previous national surveys in China, the personnel administering the questionnaire were different for this study and had no nutrition training. One problem with the FFQ was that some interviewers did not use the specified quantities and provided their own portions. It was determined that further training of field staff on the food records and FFQ would have been beneficial as well as more frequent supervision by qualified staff during data collection. In addition, there was some confusion over the "date of the next menses," and this would require better explanation during the training. If possible, early data entry and analysis of collected data would permit identification of misunderstandings and difficulties sooner and provide opportunities to address problems. Automated, standardized procedures would enhance collection of dietary data in this population.

The PAQ also presented a number of problems. Although it had previously been used in similar populations, the PAQ was complicated, and respondents sometimes failed to complete all 3 of the elements of the questionnaire (prevalence, frequency, and duration) for every activity. In addition, there was evidence of the cognitive challenges related to recall of the time spent in physical activity over the past year given time at school and at home. Substantial data cleaning is underway, as is incorporation of special statistical approaches to assist with analyses of these data, which will be reported separately.

Biospecimens and Monitors

Fasting and the blood draw protocol were accepted by the participants, and all of the field staff performed the necessary tasks appropriately. Most of the exported sample arrived in the United States unthawed, and others were flagged as having thawed. The folate values from the Chinese laboratory agreed well with those from the Chinese National Nutrition Survey. The analyte values for the CFCS samples from the US laboratory were in accordance with expectations; in particular, the folate values were similar to the US National Health and Nutrition Examination Survey values in the United States prior to food fortification. Several of the saliva tubes leaked during transport to the United States, suggesting that the field staff had not screwed on the tops properly, which should be addressed in future efforts. The saliva was determined to be of good quality with sufficient DNA for methylation analyses and for assessment of MTHFR polymorphisms.

The UV dosimeters and ambient UV detectors were sent to the Queensland University of Technology for readings analyses (Dr Kimlin's laboratory). Estimates from the ambient UV detectors were in line with expectations based on NASA data (http://aura.gsfc.nasa.gov/omi.html, accessed February 2015). Some subjects had problems with the UV dosimeters falling off the bands that were developed specifically for this study. Although replacement detectors were available, it was sometimes difficult to provide these to subjects in a timely manner. In such cases, the data for that day were lost. Future studies should use wristbands that secure the UV dosimeter tightly. The ascertainment of clothing covering skin and outdoor activity diaries were coded, and the data were entered and cleaned by investigators at the China CDC, in collaboration with an experienced team from the Queensland University of Technology.

The pedometers were clipped to specially made belts for the study as many of the students, especially girls, did not have belts or pockets for attaching the instrument. The pedometers were accepted well and utilized as requested in the study protocol. While the daily pedometer form requested information about time not wearing the instrument, the information provided did not appear to be useful. Pedometers were provided to interviewers as incentives and to improve their knowledge and experience in issues related to wearing and reading these devices so as to assist subjects. There were few dropped or missing pedometers during the data collection. The grip strength test was easily understood, and participants provided positive feedback about this task. Test-retest reliability for the dynamometry measurements was very high, and future studies would not require measurements of grip strength on 2 separate days.

Logistics

The collaborating investigators viewed the study to involve high participant burden, so they decided that using the township MCH physicians would lead to high levels of participation. Because of the geographical diversity of the study participants and local culture and spoken dialect, it

was necessary to have local interviewers conduct the data collection. Pilot Study 2 did involve a large number of interviewers who had to master a considerable amount of new data collection skills. If the local China CDC and MCH departments permitted, it would be more practical to have interviewers working in teams with each person having areas of expertise. Interviewers from nearby villages could collaborate together so that each person would have to master fewer procedures. The interviewers welcomed the concept of working in teams in the future.

The local interviewers provided direct feedback to the participants on the hospital laboratory results soon after the blood collection. Later, NCI and US CDC staff gave presentations to each center on the results from the nutrient analyses, including comparisons by study site, gender, and mother-child status. Interviewers were also briefed about the biological activities of the nutrients and how best to present this information to study participants. Fact sheets about the nutrients in the study were distributed to study staff. Letters were later sent to the sites with the nutrient results and lists of foods that contain these nutrients, and these were shared with the participants by the interviewers. Participants and health workers offered positive feedback about providing these blood results and being a part of this research project.

Site visits to the field proved useful early in the data collection. While there were no major problems with the consenting or phlebotomy, several issues arose related to the dietary questionnaire and PAQ, the UV monitors, and blood processing in the laboratory. For example, at 1 center, the freezer was set at −57°C and with study staff input was adjusted to −80°C, and an additional centrifuge had to be borrowed from another hospital to manage the high volume of bloods collected in a short period.

The 3DFR requested that participants record their food intake during or just after each eating occasion for 3 days, including information on the time, food description, specific components of the foods, and amounts or servings. The following day, the interviewers reviewed the participant's record face-to-face to complete the details needed for coding. The information added to the records included food suppliers, cooking methods, and verification of serving sizes. Then the interviewer coded the data applying food codes and portion sizes to each item. At the end of the study, trained nutritionists reviewed the records by hand and compared the interviewers' records with that of the participants'. Coding errors were corrected, but there were 6 mixed homemade foods that could not be coded. The review of each 3DFR entailed 20 minutes on average; examination of all 186 food records required 2 months of dedicated time by 1 reviewer and 5 consultants who were contacted on various issues and the resolutions documented.

Among 278 FFQs completed in the main study and substudy, a sample of approximately one-third (n = 95) were reviewed by hand before data entry. This sample was selected to represent each site, township, and interviewer involved in the study. Through the manual review, the study team summarized and discussed the problems and then created a list of principles for editing the data by hand in hardcopy or in data sets. The initial hardcopy review of the 95 FFQs by 2 staff members, in consultation with 2 nutritionists, required 10 days. Further data checks were conducted by the nutritionists to evaluate reported intake distributions and to identify subjects with unusually high energy or protein intakes.

All data were processed with double entry with reported error rates and error details in an acceptable range. Primary data checks aimed to identify missing values, outliers and logic checks, and possible data entry errors. Table 4 shows a list of exposure variables available from Pilot Study 2 study instruments. The dietary, physical activity, biomarker, and UV data were reviewed by appropriate experts on the study team. After the experts evaluated the data and made corrections, an updated version was sent to the data management team at the China CDC. Overall data cleaning was undertaken, but the first author and analysis team will be responsible for further data cleaning, generating derived variables, and publishing with greater detail on their exposures of interest. In general, all of the data seemed reasonable and will inform next drafts of the questionnaires and procedures for implementation of the full study.

Among the relatively few subjects who provided comments about the study, the main issue was that the study was burdensome and should be of shorter duration. Positive feedback was received about the pedometers and certificates of completion by both the participants and interviewers.

Discussion

Overall, Pilot Study 2 was deemed successful. Results indicate that use of the pedometers and personal and ambient UV badges; grip strength tests; and biospecimen collection, processing, transport, analyses, and reporting laboratory results back to participants were highly successful. Mothers, in general, were pleased to participate in the follow-up, while the pedometers and laboratory results were highly valued and appreciated. The PAQ, pedometer forms for location and nonwear time, impedance measures, and UV diaries were partially successful and would need some modification for future efforts. The FFQ and food records were more problematic and would require substantial modifications or use of other instruments for dietary intake assessment.

Having strong, dedicated team leads at each center was essential for recruiting appropriate staff, securing the space and laboratory equipment needed to conduct the trainings, and monitoring the staff and field work during data collection. In some cases, the leads had to borrow

TABLE 4 Exposure Variables for Pilot Study 2

Type of Exposure Data	Data Source	Variables for Exposures
Dietary data	FFQ and 3DFR	Food groups, nutrients, and energy intake
Self-reported physical activity	Physical Activity Questionnaire data on past year	Met-hours per day
Objective measures of physical activity	Pedometer data for 7 d, grip strength dynamometer	Steps per day, measured grip strength (kg)
Anthropometry	Measured and BIA	Height, weight, and % body fat
Nutrient status	Serum and plasma	Vitamins D, B_{12}, and B_6; folate, homocysteine
DNA measures related to folate exposures	Saliva using Oragene kits	DNA methylation and MTHFR polymorphisms
UV exposure	UV badge for 3 d, UV diary, and ambient UV measures	Skin exposure, sunscreen use, body UV radiation exposure
Trace element exposures	Toenail clippings	Se, Cd, Pb, Mg, Ca, Cr, Mn, Fe, Co, Cu, Zn, Cd, Ba, Ce, Nd
Demographics	Pilot Study 1 data	Age, marital status, onset of puberty, occupation, schooling, residence
Early-life data	CIP	Timing of folate exposure, gestational age, gender

Abbreviations: 3DFR, 3-day food record; BIA, bioimpedance; CIP, Community Intervention Program; FFQ, Food Frequency Questionnaire; UV, ultraviolet.

equipment, such as centrifuges and freezers, from other nearby hospitals for the study. The close relationship and trust between the township doctors and participants was an essential component of the high level of participation and cooperation in the study. In addition, the careful performance and amiable relationships set up from Pilot Study 1 helped with the success of Pilot Study 2.

During and following the training, the interviewers practiced on each other and were site visited by experienced staff from Beijing close in time to launching the field work. Nevertheless, the interviewers felt that it would take 2 to 3 weeks for the study logistics to run smoothly and successfully. In future work, interviewers may work together as teams so there would be fewer techniques to master, and they could support each other in the field activities.

Given that most of the children were at boarding schools, it was possible for a single interviewer to conduct a large number of interviews, but the available times for interviewing the students were limited by the boarding school schedules and obligations. In addition, it required more administrative efforts to partner with schools to enhance participation and to arrange for the data collection, being mindful of the examination and holiday schedules. In the future, it is unclear how we would approach the offspring who are now beginning to attend universities and to work outside the CIP areas as they find employment in many geographic regions. It may be necessary to conduct the work while the students are home for holidays or vacations. The study was viewed as successful in terms of field work, data collected, quality of the data, and collaboration among the study teams. Participants were cooperative and completed the tasks required. Newer methods may be available in the future including substitution of paper questionnaires and data collection forms with electronic versions of many of the instruments. This would make data collection faster, more standardized, and efficient. Clearly, future work in this unique cohort will require minimizing participant burden, additional training to interviewers for diet collection, improved devices used to hold UVR dosimeters, enhancing the quality of the initially collected data in the field, and timing some exposures to be measured after baseline. This is an important, unique cohort that should be followed up, particularly because the offspring are entering reproductive age themselves, which would permit transgenerational data analyses. Our pilot study suggests highly cooperative and interested participants who would be engaged in any follow-up efforts.

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CALENDAR

2018 Annual Conference—Canadian Nutrition Society
May 3 to 5, 2018
Halifax, Nova Scotia, Canada
E-mail: cara@cns-scn.ca
https://cns-scn.ca/2018-annual-conference/overview.

NUTRITION 2018, ASN's New Nutrition-Focused Annual Meeting
June 9 to 12, 2018
Boston, Massachusetts
http://nutrition.org/n18/

Transdisciplinary Research on Energetics and Cancer (TREC) Training Workshop
June 17 to 22, 2018
Westbrook, Connecticut
http://trectraining.yale.edu/

The National Association of College & University Food Services National Conference
July 11 to 14, 2018
Providence, Rhode Island
www.nacufs.org

IFT18
July 15 to 28, 2018
Chicago, Illinois
http://www.ift.org/meetings-and-events/calendar/events/2018/jul/ift18.aspx.

National Nutrient Databank Conference
July 23 to 26, 2018
Minneapolis, Minnesota
https://www.nutrientdataconf.org

Society for Nutrition Education and Behavior 51st Annual Conference
July 21 to 24, 2018
Minneapolis, Minnesota
https://www.sneb.org/2018

6th Annual International Conference on Nutrition in Medicine
August 10 and 11, 2018
Washington, DC
www.icnm18.org

American Association of Diabetes Educators Annual Meeting
August 17 to 20, 2018
Baltimore, Maryland
www.aademeeting.org

Academy of Nutrition and Dietetics Food and Nutrition Expo
October 20 to 23, 2018
Washington, DC
http://www.eatright.org/fnce

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