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The Shanghai Women's Asthma and Allergy Study: Objectives, Design, and Recruitment Results

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The Shanghai Women's Asthma and Allergy Study is the first population-based incidence study designed to assess the associations of dietary antioxidant intake and measures of oxidative stress and antioxidant enzyme activity with development of adult-onset asthma and allergic rhinitis. A total of 65,732 participants in the Shanghai Women's Health Study, an ongoing cohort study in seven districts of Shanghai, People's Republic of China, were recruited to the Shanghai Women's Asthma and Allergy Study from 2003 to 2007. Dietary intake was assessed in the parent study by using a validated and quantitative food frequency questionnaire at baseline recruitment and at the first biennial follow-up survey. Blood and urine samples were collected to measure baseline oxidative stress, antioxidant enzyme activity, and nutrient levels at the baseline survey. Incident asthma and allergic rhinitis were assessed by using a modification of the International Study of Asthma and Allergies in Childhood questionnaire during the biennial in-person survey of the Shanghai Women's Health Study. Diagnosis of asthma was confirmed by either methacholine challenge testing or test of reversibility to beta-agonists. Dietary antioxidant intake, plasma antioxidants, antioxidant enzymes, and urinary isoprostanes, a marker of oxidative stress, were measured prior to disease onset. This paper describes the study objectives, design, population demographics, and recruitment results.

antioxidants; asthma; diet; incidence; oxidative stress; rhinitis, allergic, perennial; rhinitis, allergic, seasonal

Abbreviations: FEV₁, forced expiratory volume in 1 second; SWAAS, Shanghai Women's Asthma and Allergy Study; SWHS, Shanghai Women's Health Study.

The etiology of incident adult-onset asthma is not well understood, and few longitudinal or case-control studies

characterize the development of adult-onset disease (1, 2). The striking variation in occurrence of asthma across the

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world, and the substantial increase in its prevalence in developed countries over recent decades, have called attention to environmental factors in asthma inception (2–5).

The rise in asthma prevalence in developed countries coincides with an increase in affluence and a marked change in the diet of these nations, characterized by decreased intake of fresh fruit and green vegetables and an increased intake of n-6 fatty acids (6–10). Diets containing increasing amounts of polyunsaturated fat susceptible to lipid peroxidation may also lead to greater requirements for dietary antioxidants (11–15).

Oxidants are thought to play a significant role in mediating the pathogenesis of both asthma and allergic rhinitis (13, 16). Epidemiologic studies have demonstrated a significant positive association between dietary antioxidant status and lung function and a protective effect of dietary antioxidant supplementation on asthma (11, 17–23). Most prior investigations of dietary antioxidants and asthma were cross-sectional studies; thus, it is not possible to determine whether the exposure preceded or resulted from the disease. Two large prospective cohort studies, the Dutch Zutphen Study and the US Nurses' Health Study, have shown that dietary antioxidant intake may have a protective effect on incident asthma (20, 24). Taken together, these studies highlight several important remaining questions that this study addresses. Can the Nurses' Health Study findings be generalized to other populations; do other dietary antioxidants, dietary patterns, serum concentrations of antioxidants, and systemic measures of oxidative stress predict asthma inception; and do these biomarkers interact with dietary antioxidant status in the development of asthma?

To fill these gaps in our knowledge, we designed the Shanghai Women's Asthma and Allergy Study (SWAAS). Its primary focus is to test the hypothesis that relative deficiencies in dietary antioxidants or antioxidant enzymes increase susceptibility to asthma.

MATERIALS AND METHODS

Study objectives and design

SWAAS is a prospective, population-based investigation of the relation among prior dietary antioxidant intake, measures of antioxidant status, biomarkers of oxidative stress, and adult-onset asthma. The initial study population for SWAAS was women who had been enrolled in the Shanghai Women's Health Study (SWHS) between 1997 and 2000. SWHS is an ongoing, population-based cohort study designed to investigate the effect of lifestyle factors, particularly diet, environmental exposures, and genetic susceptibility, on the etiology of cancer and other chronic diseases (25). The cohort of women is being followed by biennial in-person survey. The institutional review boards of Vanderbilt University School of Medicine, Zhongshan Hospital of Fudan University, and Shanghai Cancer Institute all approved the study. All participants gave informed consent. This study is supported by the US National Institute of Allergy and Infectious Diseases.

Using study instruments and protocols developed specifically for SWAAS, we carried out the first asthma and allergic disease screening examination between October 2003 and June 2007. Diagnosis of asthma was confirmed by methachol-

ine challenge or test of reversibility. Allergic rhinitis was assessed by using a previously validated questionnaire (26).

Additionally, we conducted a nested case-control study that includes all cases with incident asthma and two controls per case without asthma matched by subject's age at biospecimen collection (± 1 year); date of biospecimen collection (± 30 days); ever smoking (yes/no); and, because of the effect of obesity on asthma, body mass index (calculated as the ratio of weight to height squared (kg/m^2); ≤ 20 , >20 – 25 , >25 – 30 , >30) to determine whether plasma concentrations of antioxidants, antioxidant enzymes, and a urinary biomarker of oxidative stress predict the occurrence of asthma and allergic rhinitis.

Study population and subject recruitment

The parent study, SWHS, includes 74,942 women aged 40–69 years living in seven urban communities of Shanghai, the largest city on the southeast coast of China. Baseline interviews and comprehensive evaluations were conducted by trained interviewers at participants' homes. The participation rate was 93 percent. Recruitment of these women into SWAAS started in October 2003 during the in-person follow-up survey of the SWHS cohort and was completed in June 2007.

A flow diagram of participants through the enrollment, asthma screening, and analysis phases of this study is shown in figure 1. Eligibility screening was conducted in several stages on the basis of a predefined set of inclusion and exclusion criteria (table 1). Eligible women recruited to SWAAS underwent an in-home interview of approximately 2 hours.

Examination components of the baseline survey

The components of both the baseline in-person interviews and the asthma and allergic disease screening survey are listed in table 2. The baseline data for this study were collected between 1997 and 2000 as part of SWHS, prior to the initiation of SWAAS, and are described elsewhere (25). Briefly, information on demographic characteristics, medical history, menstrual and reproductive history, hormone use, physical activity, personal habits, residential and occupational history (work environment and products produced), environmental exposures (television, cooking fuel and oil, ventilation, water), and details on smoking, including age at which smoking started, number of cigarettes smoked per day, age at quitting smoking, current smoking, and second-hand smoke exposure, were collected via a self-administered questionnaire. Information on lifestyle factors, including a detailed dietary history, and dietary supplement use was obtained by using a validated food frequency questionnaire (27) via an in-person interview administered by trained health professionals. Height, weight, waist, and hip girth were measured following a standardized protocol (28). Physical activity was assessed by using a validated questionnaire, with regular physical activity defined as at least once a week for more than 3 months, continuously over the past 5 years (29). Biologic specimens, including urine and plasma, were obtained during the baseline survey.

The SWHS food frequency questionnaire lists 77 individual food items/groups that represent about 90 percent of

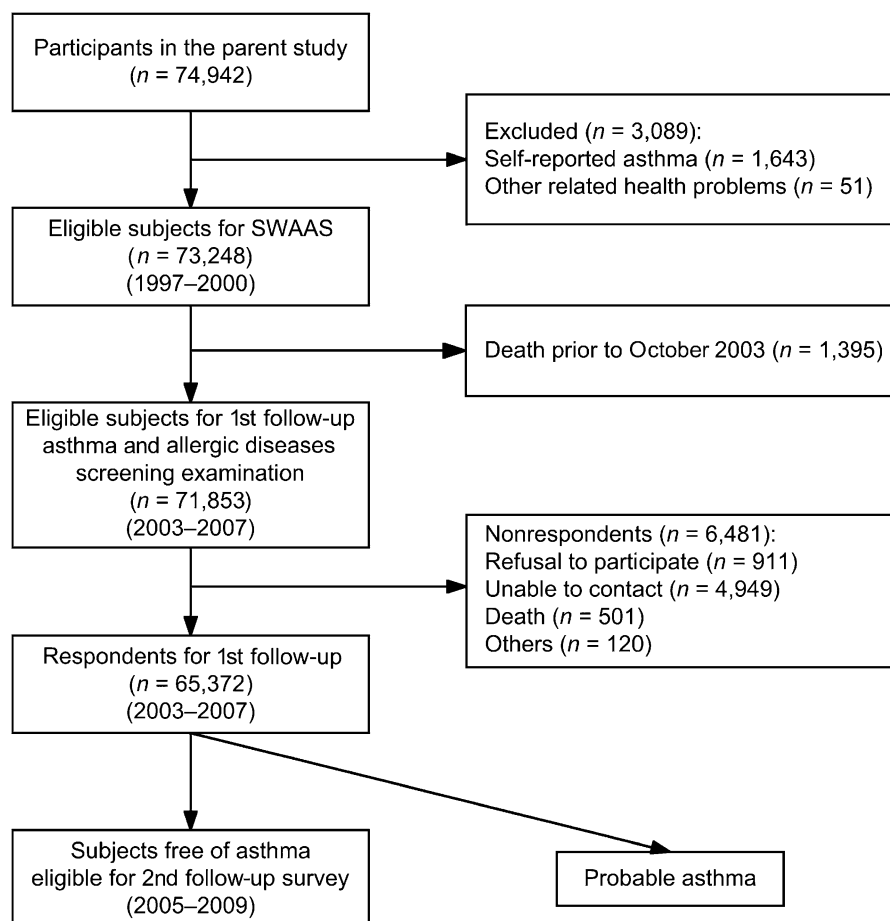


FIGURE 1. Flow diagram of participants through the enrollment, screening, and analysis phases of the Shanghai Women's Asthma and Allergy Study (SWAAS), 2003–present, Shanghai, China. Fifty-one subjects with the following comorbidities were excluded: emphysema and other reactive airway disease ($n = 32$), pulmonary fibrosis ($n = 1$), cystic fibrosis ($n = 2$), congestive heart failure ($n = 3$), hypogammaglobulinemia or immunodeficiency disorders ($n = 4$), and progressive or untreated lung cancer ($n = 9$).

food intake in the Shanghai population. The Chinese Food Composition Table (30) was used to estimate the intake level of major nutrients for the study participants. The validity of the food frequency questionnaire was evaluated by comparing intake levels of major nutrients and foods obtained from the food frequency questionnaire with those derived from multiple 24-hour dietary recalls. The correlation coefficients between food frequency questionnaire and 24-hour dietary recalls were 0.59–0.66 for macronutrients and 0.41–0.59 for micronutrients (27). Correlation coefficients for the antioxidant nutrients of interest were comparable to those reported by the Willett and Block food frequency questionnaires and ranged from 0.40 for carotene to 0.49 for vitamin E (31, 32).

First asthma and allergic diseases screening examination of the SWAAS cohort

A structured questionnaire, adapted from the International Study of Asthma and Allergies in Childhood questionnaire

as well as the European Community Respiratory Health Survey and the American Thoracic Society epidemiology standardization project, was used (33–39). The International Study of Asthma and Allergies in Childhood questionnaire has been validated in many cultures and languages, including among Chinese adolescents, and the Chinese questionnaire was used in this investigation (40). The questionnaire was translated and back-translated and then piloted among 500 women prior to initiation of SWAAS. Trained interviewers from the Shanghai Cancer Institute administered the initial screening questionnaire in person to all study subjects. Detailed information on physician-diagnosed disease; medication use; symptoms of asthma, allergic rhinitis, and atopic dermatitis; and a family history of these diseases was collected.

Asthma ascertainment and confirmation

Figure 2 provides the procedures for ascertaining and confirming incident asthma. Incident asthma was diagnosed

TABLE 1. SWAAS* inclusion and exclusion criteria at the time of study enrollment, China, 2003–2007

Inclusion criteria
Permanent residents of Shanghai
Females aged 40–69 years at enrollment in the Shanghai Women's Health Study
Willingness to participate in SWAAS
Informed consent
Exclusion criteria
Self-reported prevalent asthma
Other health-related problems
Emphysema and other reactive airway disease
Pulmonary fibrosis
Extrinsic allergic alveolitis
Cystic fibrosis
Alpha1-antitrypsin deficiency
Congestive heart failure
Hypogammaglobulinemia or immunodeficiency disorders
Progressive or untreated lung cancer
Not alive at the first screening survey
Absence during the study recruitment period

* SWAAS, Shanghai Women's Asthma and Allergy Study.

if the symptoms and treatment of the disease began after the baseline survey of the parent study (SWHS) and the subject had either a positive methacholine challenge test or a positive test of reversibility. Participants were considered to have “probable incident asthma” based on their responses to the in-home, in-person administered asthma and allergic diseases screening questionnaire if each of these two conditions was present: 1) a history of wheezing, whistling in the chest, or physician-diagnosed asthma; or asthma-specific medication use, any of which began after the SWHS baseline interview; and 2) absence of chronic bronchitis or chronic obstructive pulmonary disease (41–44) (table 3).

Women with “probable incident asthma” were recontacted and invited to undergo a methacholine challenge test or test of reversibility. All testing was performed at the Zhongshan Hospital of Fudan University in Shanghai pulmonary function test laboratory, the first such laboratory in China. Supplementary information from women with probable incident asthma was obtained by a second in-person follow-up questionnaire interview at the time of testing, including physician diagnosis, date of diagnosis and first asthma symptoms, seasonality, severity based on the Global Initiative for Asthma guidelines, precipitators, use of asthma-specific medications, and attacks requiring physician intervention (41–45).

Standard American Thoracic Society/European Respiratory Society protocol was used for methacholine challenge testing. In addition, all pulmonary function test results were read by both trained pulmonologists at the Pulmonary Function Laboratory at Zhongshan Hospital, as well as an independent pulmonary function test oversight committee

TABLE 2. SWAAS* examination components, China

Baseline examination (1997–2000)
Demographic characteristics
Age, residential history, education, marital status, family income, occupational status
Medical data
Personal and family medical history, reproductive history, menopausal status and hormone use, current medication use
Lifestyle habits
Physical activity, weight history, tobacco use, alcohol consumption, tea drinking, ginseng use, secondhand smoke exposure, work and home environmental exposures
Food frequency questionnaire
Dietary habits: usual dietary intake over the past 12 months and during adolescence (ages 13–15 years)
Physical measurements
Weight, height, girth, resting blood pressure
Biospecimen collection
Blood, urine, and exfoliated buccal cells
Screening examination for asthma and allergic diseases (2003–2007)
International Study of Asthma and Allergies in Childhood questionnaire
Signs, symptoms, and physician diagnosis of asthma, allergic rhinitis, and atopic dermatitis
Laboratory analyses of biospecimens
Plasma antioxidants and antioxidant enzyme activity
Urinary isoprostanes
Pulmonary function testing
Methacholine challenge test (performed if $FEV_1^* \geq 70\%$)
Test of reversibility to short-acting bronchodilators (performed if $FEV_1 < 70\%$)

* SWAAS, Shanghai Women's Asthma and Allergy Study, FEV_1 , forced expiratory volume in 1 second.

(J. R. S. and J. C.). Final determination of any discrepant cases was decided by the pulmonary function test oversight committee or by retesting the subject.

Spirometry was performed according to the Body Temperature and Pressure Saturated (BTPS) convention with a spirometer (JAEGER Co., Hoechberg, Germany; and the ASTOGRAPH TCK-6000M, Chest Corporation, Tokyo, Japan), which was calibrated and maintained to acceptable laboratory standards for respiratory function (46). Prior to spirometric testing, subjects were asked to withhold bronchodilator medications and those medications that interfere with methacholine. The following parameters were measured: forced expiratory volume in 1 second (FEV_1), forced vital capacity, forced expiratory flow at 25–75 percent, peak expiratory flow rate, and flow volume loops. These parameters were measured three times consecutively, and FEV_1 values had to be within 5 percent to be considered valid. For the analysis, the parameters from the test associated with the highest FEV_1 were used.

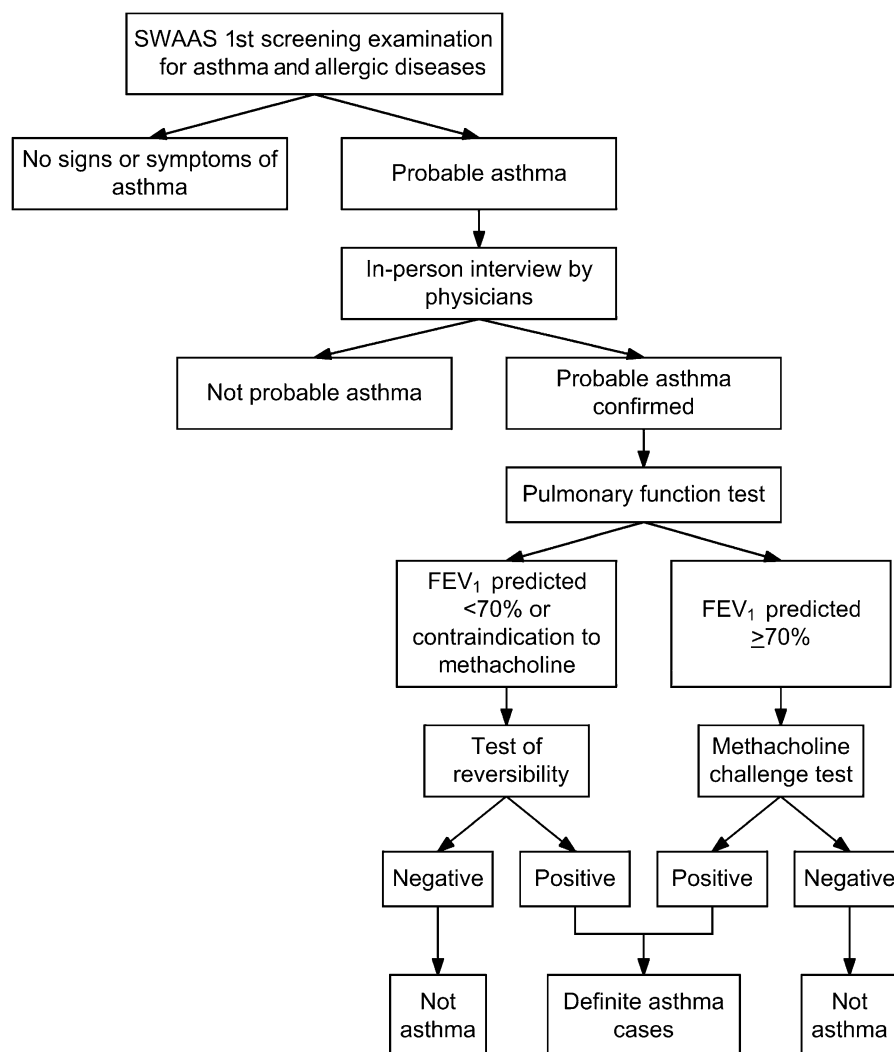


FIGURE 2. Procedures for ascertaining and confirming incident asthma in the Shanghai Women's Asthma and Allergy Study (SWAAS), 2003–present, Shanghai, China. FEV₁, forced expiratory volume in 1 second.

Methacholine challenge testing was performed if baseline FEV₁ was ≥ 70 percent of predicted. Twofold incremental concentrations of methacholine chloride (Tokyo Chemical Industry Co. Ltd., Tokyo, Japan) reconstituted with physiologic saline were prepared from 0.015–0.96 mg/ml. Methacholine was inhaled with a synchronized nebulizer/dosimeter (Methapharm Inc., Coral Springs, Florida). Five breaths at each dose up to 0.96 mg/ml (maximal dose) were used with a 0.6-second pulse duration. Spirometry was repeated 3 minutes after each dose of methacholine. A positive test was defined as a 20 percent decline from baseline FEV₁. Following testing, subjects received salbutamol (GlaxoSmithKline, Shanghai, China), and spirometry was repeated to assure recovery (47–49).

A test of reversibility to beta-agonist was performed on subjects whose baseline FEV₁ was < 70 percent of predicted by repeating spirometry 15 minutes following salbutamol

given by nebulizer. A positive test of reversibility was defined as an increase in FEV₁ of more than 12 percent and more than 0.2 liters (47, 49).

Ascertainment of allergic rhinitis

For this investigation, incident cases of allergic rhinitis were based on a set of positive responses to the International Study of Asthma and Allergies in Childhood screening questionnaire if either of two conditions was present, with symptom onset after the baseline SWHS survey: 1) a congested or a runny nose, or itchy-watery eyes during pollen season or when exposed to pollen, dust, or animal hair in the absence of a cold or the flu, with substantial variability in symptoms over time or seasonality; or 2) physician diagnosis of allergic rhinitis or prescription medication use for allergic rhinitis (26, 50).

TABLE 3. Definitions of incident asthma and allergic rhinitis, Shanghai Women's Asthma and Allergy Study, China

Probable asthma
Any of the following conditions beginning after 1997:
1. Wheezing or whistling in the chest
2. Use of medication for wheezing, whistling, or asthma
3. Ever physician diagnosis of asthma
4. An attack of asthma in the last 12 months
5. Woken by an attack of shortness of breath anytime in the last 12 months
6. Cough after a cold/flu (after recovering from cold/flu, continued frequent coughing for at least 3 weeks)
7. Cough not relieved by antibiotics when participant is exposed to irritants (cold air, irritating odor, etc.)
And in the absence of any of the following:
1. Chronic cough during the day, or night, in the winter for ≥ 3 months each year
2. Chronic phlegm production during the day, or night, ≥ 3 months each year
3. Physician diagnosis of chronic bronchitis
4. Chronic obstructive pulmonary disease or emphysema
Definite incident asthma
Meets the definition of probable asthma above <i>and</i> either of the following:
1. Positive methacholine challenge test in participants with $FEV_1^* \geq 70\%$
2. Positive test of reversibility to beta-agonist in participants with $FEV_1 < 70\%$ predicted
Incident allergic rhinitis
Either of the following conditions beginning after 1997:
1. Sneezing, or a runny or a blocked nose or itchy, watery, runny eyes in the absence of a cold or the flu, or congested or a runny nose, or itchy-watery eyes when exposed to pollen, dust, or animal hair in the absence of a cold, with substantial variability in symptoms over time or seasonality
2. Either a physician diagnosis of allergic rhinitis or use of prescription medication for allergic rhinitis

* FEV_1 , forced expiratory volume in 1 second.

Cohort follow-up

Biennially, subjects will be recontacted and undergo an in-person follow-up using a similar questionnaire to capture incident cases of asthma and allergic diseases among all SWAAS participants. The minimum duration of follow-up in the cohort is 6 years (total of 12 years, including the period of the SWHS). We anticipated that we would identify 300 participants with incident asthma from SWAAS over the 6-year study period.

Laboratory analyses for blood and urine samples

Blood and urine samples for the nested case-control study were retrieved from the biospecimen bank at Vanderbilt University School of Medicine, shipped on dry ice to the collaborating research laboratories at the University of Minnesota School of Public Health, and hand-delivered to the laboratory of author L. Jackson Roberts at Vanderbilt.

Plasma antioxidants and antioxidant enzyme activity were analyzed in samples from all incident asthma cases and matched controls. For analysis, matched sets were analyzed consecutively within the same batch. All major plasma carotenoids and tocopherols were measured simultaneously by an assay based on high-performance liquid chromatography (51). These antioxidants included lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin, zeaxanthin plus lutein, and alpha-tocopherol and gamma-tocopherol. Paraoxonase and platelet-activating factor acetylhydrolase were measured by spectrophotometer-based enzymatic assays. Plasma extracellular superoxide dismutase activity was assessed by measuring the dismutation of superoxide radicals generated by xanthine oxidase and hypoxanthine using the Superoxide Dismutase Assay Kit (Cayman Chemical, Ann Arbor, Michigan).

Oxidative stress was assessed by measuring F_2 isoprostanes in urine according to the methods of Roberts (Morris et al. (52)). The major urinary metabolite of the isoprostane, 15- F_{2t} -IsoP (8-iso-PGF $_{2\alpha}$), was measured in urine samples after purification and derivatization by a gas chromatographic mass/spectrometric assay. Endogenous 15- F_{2t} -IsoP-M was quantified by selected ion monitoring analysis of the ratios of intensities of m/z 543 to m/z 547. Concentrations were corrected for urinary creatinine.

Quality control procedures

The component-specific quality control procedures implemented in the field survey and laboratory testing were mentioned above. To standardize and monitor the quality of data collection and processing, all study personnel received centralized training and were certified for all study procedures including the home visit, interview, and examination components. All interviews were tape recorded, and a randomly selected sample of 10 percent of recordings was evaluated to monitor interview quality. All paper documentation was coded twice and was double entered to minimize errors due to data entry. Logical checks were performed by Shanghai Cancer Institute investigators and again by our statisticians. For laboratory analyses, six quality control samples were included in each biospecimen run. Blind quality control samples were labeled to resemble the subject samples and were randomly placed within each batch.

Statistical analyses

The outcome variables of interest are the incidence of asthma and of allergic rhinitis. The primary exposure variables of interest are dietary antioxidant status, plasma antioxidant concentrations, antioxidant enzyme activity, and urinary lipid peroxidation product levels at baseline prior to the onset of asthma or allergic rhinitis. Incidence will be calculated by dividing the number of incident cases by person-time of follow-up. Incidence rates will be determined by dividing the patient population into quartiles/quintiles of antioxidant intake. The association of risk of asthma and allergic rhinitis with dietary antioxidant intakes will be evaluated by using the Cox regression model. In the nested case-control study, biomarker concentrations will be

analyzed as both continuous and categorical variables on the outcomes of asthma and allergic rhinitis. Geometric means of plasma antioxidant and urinary isoprostane concentrations for cases and controls will be calculated and compared by using the paired *t* test. The conditional logistic regression models will be used to calculate odds ratios and 95 percent confidence intervals to estimate the association between these biomarkers and the risk of asthma and allergic rhinitis. The potential confounders considered in multivariable analyses will include demographic characteristics, age, cigarette smoking, secondhand smoke exposure, body mass index, alcohol consumption, supplemental multivitamin use, aspirin and nonsteroidal antiinflammatory drug use, physical activity, environmental exposures, and first- and second-degree family history of atopic disease.

RECRUITMENT RESULTS

SWAAS cohort participation rate

An overview of the SWAAS participants is presented in figure 1. Of 74,942 SWHS participants, 1,395 died prior to initiation of SWAAS, 1,643 were excluded because they had prevalent asthma at the baseline survey, and 51 with other comorbidities were also excluded. After these 3,089 women were excluded, 65,732 of 71,853 remaining eligible women were recruited for SWAAS, resulting in an overall participation rate of 91.5 percent. Among the 6,481 eligible non-participants, 911 refused, 501 died, 4,949 could not be contacted, and 120 did not participate for other reasons.

The final study sample included 65,732 women who were free of asthma at the SWHS baseline survey during 1997–2000 and completed the SWAAS screening examination for asthma and allergic diseases during 2003–2007. Blood and urine samples were collected for 50,364 (77.0 percent) and 58,197 (89.0 percent) of SWAAS subjects, respectively. SWAAS met its recruiting goals in June 2007, and the second follow-up survey is currently under way.

Three hundred seventy-seven women met the criteria for probable asthma and were invited to undergo the methacholine challenge test or test of reversibility. Seventy-five percent (*n* = 283) of them agreed to participate and underwent testing.

Sociodemographic characteristics and life habits of SWAAS women at baseline

Table 4 summarizes some of the sociodemographic characteristics of the SWAAS-eligible participants. Mean age and body mass index in this cohort were 51.9 years and 24.0, respectively. Nearly all study participants had worked outside the home; 89.2 percent were married. For most variables, few data are missing. Levels of cigarette smoking, alcohol consumption, hormone replacement therapy, and dietary supplement use were low among the study participants. There were no significant differences regarding most baseline demographic characteristics among those who did and did not participate in SWAAS. We found small differences in education, income, profession, and household size between women who did and did not participate.

TABLE 4. Demographic and lifestyle characteristics of the SWAAS* study cohort at baseline, China, 1997–2000

Characteristic	No. of subjects	%
Age group (years)		
40–50	32,202	49.3
51–60	16,029	24.6
61–69	17,141	26.2
Mean (SD)*	51.9 (9.0)	
Body mass index (kg/m ²)		
Normal (<25)	42,390	64.8
Overweight (25–<30)	19,663	30.1
Obese (≥30)	3,319	5.1
Mean (SD)	24.0 (3.4)	
Age at menarche (years)		
<12	544	0.8
≥12	64,831	99.2
Mean (SD)	14.9 (1.7)	
Pregnancy		
None	1,738	2.7
≥1	63,634	97.3
Menopausal status		
Premenopause	33,470	51.2
Postmenopause	31,892	48.8
Unknown	10	0.0
Education		
High school or above	27,000	41.3
Middle school	24,742	37.9
Elementary school or less	13,619	20.8
Unknown	11	0.0
Marital status		
Presently unmarried	7,052	10.8
Presently married	58,320	89.2
Occupation		
Professional	18,549	28.4
Clerical	13,529	20.7
Farmer/worker	33,082	50.6
Unknown	212	0.3
Family income		
Low	17,948	27.5
Middle	25,648	39.2
High	21,761	33.3
Unknown	15	0.0
Family history of allergy	10,574	16.2
Maternal allergy	2,714	4.2
Ever or current smoker†	1,724	2.6
Ever or current alcohol drinker	1,484	2.3
Ever or current tea drinker	19,495	29.8
Ever or current ginseng use	19,050	29.1
Dietary supplement use	4,736	7.2
Hormone replacement therapy	1,395	2.1
Regular physical activity‡	25,361	35.3

* SWAAS, Shanghai Women's Asthma and Allergy Study; SD, standard deviation.

† Current indicates smoking in the last 12 months.

‡ Defined as at least once a week for more than 3 months, continuously over the past 5 years.

TABLE 5. Nutrient intake of the SWAAS* cohort at baseline (1997–2000) compared with US women in the National Health and Nutrition Examination Survey and the US EAR*

Nutrient	SWAAS†	US women (53)†	US DRI* EAR‡ (55–57)
Energy (kcal)	1,685.6 (405.6)	1,776.3 (703.1)	1,869/2,055 (EER)§
Carbohydrate (g)	287.3 (68.1)	222.4 (96.9)	100
Protein (g)	67.3 (21.4)	67.00 (30.2)	0.8 g/kg body weight
Fat (g)	29.7 (13.5)	67.1 (36.4)	25–35% total energy
Fiber (g)	10.7 (4.2)	14.5 (9.2)	21 g total fiber (AI)¶
Total vitamin A (µg)	629.1 (321.1)	953.4 (1,122.0)	500
Vitamin C (mg)	93.9 (50.4)	94.00 (86.7)	60
Carotene (mg)	2,716.6 (1,484.1)	541.2 (898.00) (RE*)	—#
Total vitamin E (mg)	13.4 (6.4)	8.8 (8.1) (ATE*)	12 ATE only
Selenium (µg)	45.2 (21.5)	90.9 (48.71)	45

* SWAAS, Shanghai Women's Asthma and Allergy Study; EAR, Estimated Average Requirement; DRI, Dietary Reference Intakes; RE, retinol equivalents; ATE, alpha-tocopherol equivalents.

† Values in parentheses are standard deviations.

‡ EAR is defined as the daily intake value estimated to meet the requirement of half of the healthy individuals in an age and gender group.

§ The Estimated Energy Requirement (EER) is defined as the average dietary energy intake that should maintain energy balance in a healthy adult of a specific age, gender, and size and with an activity level consistent with good health. EER was calculated for a female aged 51 years, 5 feet 5 inches (1.65 m) tall, with a low activity level, and with a body mass index of 18.5 ($n = 1,869$) and 24.99 ($n = 2,055$).

¶ For fiber, an EAR cannot be set because the data are highly variable. Thus, an Adequate Intake (AI) is set for total fiber (sum of dietary and functional fiber) and is expected to meet or exceed the average amount needed to maintain health.

There are no EARs established for carotenoids; however, 3–6 mg/day of beta-carotene is the dietary intake level thought to be required to maintain blood levels in the range associated with chronic disease prevention.

Nutrient intake of SWAAS women at baseline

Table 5 shows the average daily intake levels of nutrients for all participants in this cohort. US nationally representative data for women of similar ages (40–69 years) from the National Health and Nutrition Examination Survey (1999–2000) are provided for comparison purposes (53). Compared with US women, the SWAAS cohort consumes similar levels of dietary vitamin C but higher levels of carotenoids and vitamin E. In contrast, US women consume higher levels of dietary selenium. Also included in table 5 (when available) are the recommended intakes by the US Food and Nutrition Board, Institute of Medicine for Estimated Average Requirements or Adequate Intake recommendations when the Estimated Average Requirements cannot be determined. The SWAAS cohort generally meets recommendations, particularly for the antioxidant nutrients of interest, without consuming the higher-fat diets typical of US women.

DISCUSSION

To our knowledge, SWAAS is the largest and most comprehensive prospective epidemiologic study to date to include direct measures of oxidative stress and antioxidant enzymes prior to disease onset, complementary measures

of nutrient intake, and food frequency data on the outcome of adult-onset asthma and allergic rhinitis. This study will provide important information about the role of oxidative stress and dietary intake (antioxidants, fatty acids, and other nutrients) in the development of adult-onset asthma and allergic rhinitis. It has the potential to identify new risk factors and biomarkers for asthma and allergic diseases. In addition, results of this study may help to identify risk profiles and biomarkers and may thus provide a basis for the design of new prevention strategies.

SWAAS is additionally unique because its objective is to observe the role of dietary intake in the development of asthma among women consuming high levels of antioxidants and having a very low rate of smoking. Women in SWAAS differ substantially from those in the United States regarding dietary exposure and other health-related factors. Their diet includes a high intake of tea, soy food, ginseng, and many other vegetables such as garlic, bok choy, and cruciferous and dark-green leafy vegetables but with marked heterogeneity in dietary intake. Over 92 percent of these women do not take vitamin supplements, which also facilitates the testing of dietary hypotheses. In comparison, 57 percent of US women participating in the 1999–2000 wave of the National Health and Nutrition Examination Survey reported using at least one dietary supplement in the previous month (54). A further strength of the present study is the strategy for

identifying incident asthma cases in this large cohort. The identification of new asthma cases considered both the positive response to a standard written questionnaire and the presence of bronchial hyperresponsiveness. Although such a diagnostic strategy might result in underdiagnosis of asthma, it is unlikely to result in false-positive diagnoses that might bias the hypothesis toward the null.

Several limitations of this study should be noted. First, the study sample was not randomly selected from the general population but instead was recruited from several districts of Shanghai to take advantage of the parent cohort of SWHS. However, the study communities participating were similar to the rest of the communities in Shanghai. The high response rate further assures the generalizability of our study results. Although, on the whole, dietary antioxidant intake is higher in this cohort compared with the United States, there is a wide distribution of intake, which will allow exploration of the mediating effects of dietary antioxidants and oxidative stress in the familial predisposition–asthma relation. In addition, although the correlation coefficients between Willett et al.'s (32) and our food frequency questionnaire are comparable, although low, we have complementary plasma nutrient levels that will be used in the analyses. Lastly, we encountered difficulty regarding participation (75.1 percent) of women with probable asthma who were invited to undergo pulmonary function testing. We have developed two strategies to address this problem. First, study personnel will visit subjects at home, explain the testing, demonstrate the use of a portable spirometer, and invite subjects again for testing. Second, we are currently assessing the predictive value of combinations of asthma questions, with methacholine challenge test confirmation of asthma, to create an algorithm for the outcome of “probable asthma” among those who refused formal testing.

Future reports from this cohort will help to untangle the complex relation among dietary antioxidants, oxidative stress, and development of asthma and other atopic diseases. Ultimately, this study has the potential to provide new approaches to both prevent the development of asthma and allergic diseases and control prevalent disease.

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