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The Chinese National Twin Registry: An Update

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The Chinese National Twin Registry (CNTR), established in 2001, is the first and largest population-based twin registry in China. Based on the CNTR, a new twin cohort was recruited from 2011 to study the relationship between environmental risk factors and chronic diseases. So far, 33,874 twin pairs from nine provinces have been recruited, in which hundreds of disease-discordant twin pairs and even thousands of exposure-discordant twin pairs were found in this cohort. The updates of the CNTR will be introduced in detail in this article.

■ **Keywords:** registries, twins, China, chronic disease, environment

The Chinese National Twin Registry (CNTR), established in 2001, is the first national twin registry in China, and it has now become the largest twin registry in China. Recently, the CNTR obtained a large amount of funding for a project entitled 'Cohort study on environmental epidemiology in China', which was supported by Specific Research Project of Health Pro Bono Sectors, Ministry of Health, China (Project ID 201002007). This project aimed to establish a twin cohort. The CNTR is led by the School of Public Health, Peking University, and collaborates with nine other research centers: the Qingdao Center for Disease Control and Prevention (CDC), Zhejiang CDC, Jiangsu CDC, Sichuan CDC, Beijing CDC, Shanghai CDC, Tianjin CDC, Qinghai CDC, and Harbin Medical University. Professor Liming Li from Peking University is the principle investigator. The cohort study on environmental epidemiology in China project started in July 2010 and will continue until June 2013.

The CNTR's History

At the very beginning of the CNTR, according to the data from Gan's study (Figure 1; Gan & Zheng, 2002), Shandong Province has the largest number of twins in China and that is why Qingdao was selected as one of the first four cities/regions from which twins were recruited. Apart from Qingdao, the CNTR also selected Beijing, Shanghai, and Lishui as the other first three cities to recruit twins. Twins from these cities are located in northern urban, southern urban, and southern rural areas of China, whereas twins from Qingdao are located in a northern rural area. The CNTR is a voluntary registry, although different areas use different methods to collect twins. The twins are mainly recruited through local CDCs, which collaborate with the residence registry in local public security bureaus and communities, and through public media. By the end of 2005, 7,423 twin pairs were enrolled and twin registration was in progress in Shanghai at that time (Figure 1; Li et al., 2006). For those twin pairs who were only registered, a questionnaire was given to the members and used for zygosity assessment (Gao et al., 2006). For twins where both members consented to a detailed assessment (1,613 pairs), gender, ABO blood type, and DNA comparison were used step by step to determine zygosity. Based on the CNTR, a series of scientific research projects have been conducted, such as the evaluation of methods of zygosity determination, secular trends, and associated factors of twinning in Qingdao, studies on the intermediate phenotypes of cardiovascular and cerebrovascular diseases in adult twins, psychological studies of adult twins, and studies on growth and development in adolescent twins. In 2009, the epidemiological study in adult twins was awarded the second Science and Technology prize by the Chinese Preventive Medicine Association Science and Technology.

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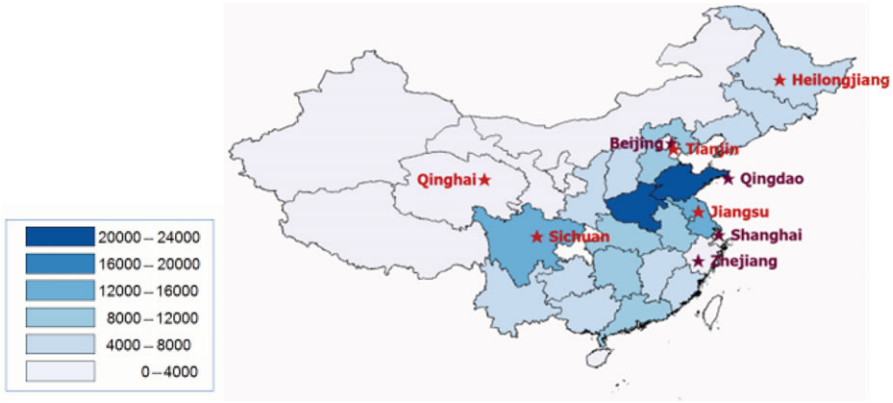

FIGURE 1

(Colour online) The distribution of the CNTR.
Note: The legend indicates the number of new twin pairs in 1989, China (Gan & Zheng, 2002).

Aims of the Twin Cohort

The twin cohort aims to collect 35,000 twin pairs, based at the CNTR, with the goal of collecting data on health and lifestyle, behavior, physical characteristics, and fasting blood sample. Longitudinal follow-ups and a surveillance of major chronic diseases are also planned. In addition, health-related environmental information, such as accessibility to unhealthy food, smoking, and twins' subjective feelings on environment will be collected. The cohort will look for the disease-discordant twins and exposure-discordant twins to determine the causal relationship between environmental risk factors and chronic diseases.

The study protocol for the Cohort Study on Environmental Epidemiology in China — Twin Cohort was reviewed and approved by the Ethics Committee for Human Subject Studies of the Peking University Health Science Center in 2011 (ID: IRB00001052-11029).

Advances of the Twin Cohort

The cohort study on environmental epidemiology in China started in 2011. In addition to the first four cities in the CNTR, another five cities or provinces — Tianjin City, Jiangsu Province, Sichuan Province, Qinghai Province, and Heilongjiang Province — have joined the twin cohort (Figure 1). The nine cities/provinces together covered the areas that have a large (Qingdao, Jiangsu, and Sichuan), moderate (Heilongjiang and Qinghai), and low (Zhejiang, Shanghai, Beijing, and Tianjin) number of twins. Also, these nine cities/provinces geographically covered western (Qinghai and Sichuan), eastern (Qingdao, Jiangsu, Shanghai, and Zhejiang), northern (Heilongjiang), and southern areas (Shanghai and Zhejiang) in China.

Twins were asked to complete one of the three questionnaires. The first questionnaire was developed for twins aged below 18 years. In the first questionnaire, twins were asked to provide their demographic information, parents' names, contact details, birth weight, current weight, current height, medical history (obesity, hypertension, diabetes, asthma, and genetic disease history), and zygosity. Adult twins who were aged 18 years and over were asked to select one of the two questionnaires: the second and the third questionnaires. The second questionnaire included questions on demographic information, contact details and zygosity questions, waist circumference, and medical history (e.g., hypertension, hyperlipidemia, diabetes, coronary heart disease, stroke, chronic bronchitis/emphysema, and cancer); 6,176 twins who were aged 18 and over completed this questionnaire (Table 1). The third questionnaire was developed later and is more complex. Twins who accepted the third questionnaire needed to provide information on an alternate person who could help update future contact details. In addition, the third questionnaire included questions on demographic information, socioeconomic status (SES), birth weight, birth defects, birth place, whether reared apart, current height, weight, waist circumference, zygosity, smoking, drinking, fruit and vegetable consumption, physical activity, medical history (hypertension, hyperlipidemia, diabetes, coronary heart disease, stroke, chronic bronchitis/emphysema, and cancer), allergic history, family medical history (hypertension, hyperlipidemia, diabetes, coronary heart disease, stroke, chronic bronchitis/emphysema, and cancer); 12,611 twins who were aged 25 and over completed the third questionnaire (Table 1). Twins are currently tracked and updated on their contact information, height, weight, waist, and the onset of new chronic diseases, when possible. The age and gender distribution of the twins recruited so far is presented in Table 1.

From the recruited twins, disease-discordant twin pairs have been found and are shown in Tables 2–4. As our zygosity assessment was not completed, concordance/discordance status in Tables 2–4 is based on combined samples of monozygotic and dizygotic twins. In the

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TABLE 1

The Age and Gender Distribution of the Twins Recruited

		Twin pairs			Triplet–Quadruplet sets		
Questionnaire	Age	M/M	M/F*	F/F	Same sex	Opposite sex	Total
First	0–	2,326	1,379	2,071	26	20	5,822
	5–	1,656	852	1,541	20	16	4,085
	10–	1,298	656	1,243	17	13	3,227
	15–	783	381	776	8	5	1,953
Second	18–	2,320	1,233	2,098	18	7	5,676
	25–	83	46	65	0	0	194
	30–	72	31	39	0	0	142
	40–	69	29	31	0	0	129
	50–	14	6	4	0	0	24
	60–	8	1	2	0	0	11
Third	25–	1,284	676	1,144	3	7	3,114
	30–	2,012	816	1,282	3	6	4,119
	40–	1,903	580	867	5	3	3,358
	50–	800	209	261	1	1	1,272
	60–	274	56	80	1	0	411
	70–	202	51	82	2	0	337
Total		15,104	7,002	11,586	104	78	33,874

Note: *M/M: twin pairs who are both male; F/F: twin pairs who are both female; M/F: twin pairs with opposite sex.

TABLE 2

Disease-Discordant Twin Pairs Found From the First Questionnaire (Age < 18 years)

	Y/Y		Y/N		N/N		Total	
Disease	Twin pairs	%	Twin pairs	%	Twin pairs	%	Twin pairs	%
1 Obesity	25	0.2%	28	0.3%	10,767	99.5%	10,820	100.0%
2 Hypertension	25	0.4%	13	0.2%	6,126	99.4%	6,164	100.0%
3 Diabetes	22	0.2%	10	0.1%	14,582	99.7%	14,614	100.0%
4 Asthma	37	0.3%	50	0.5%	10,735	99.2%	10,822	100.0%
5 Genetic diseases	37	0.3%	26	0.2%	14,545	99.5%	14,608	100.0%

Note: Y = disease present, N = disease absent.

TABLE 3

Disease-Discordant Twin Pairs Found From the Second Questionnaire (Age ≥ 18 years)

	Y/Y		Y/N		N/N		Total	
Disease	Twin pairs	%	Twin pairs	%	Twin pairs	%	Twin pairs	%
1 Diabetes	3	0.0%	4	0.1%	6,027	99.9%	6,034	100.0%
2 Coronary heart disease	2	0.0%	3	0.1%	6,027	99.9%	6,032	100.0%
3 Stroke	2	0.0%	4	0.1%	6,027	99.9%	6,033	100.0%
4 Hypertension	7	0.1%	8	0.1%	6,017	99.8%	6,032	100.0%
5 Hyperlipidemia	5	0.1%	11	0.2%	6,015	99.7%	6,031	100.0%
6 Chronic bronchitis/emphysema	2	0.0%	9	0.1%	6,023	99.9%	6,034	100.0%
7 Cancer (breast, stomach, or colorectal cancer)	2	0.0%	6	0.1%	5,217	99.9%	5,225	100.0%
8 Cancer (lung, oral, or esophagus cancer)	3	0.1%	9	0.2%	5,210	99.7%	5,222	100.0%

Note: Y = disease present, N = disease absent.

TABLE 4

Diseases-Discordant Twin Pairs Found From the Third Questionnaire (Age ≥ 25 years)

	Y/Y		Y/N		N/N		Total	
Disease	Twin pairs	%	Twin pairs	%	Twin pairs	%	Twin pairs	%
1 Diabetes	76	0.6%	213	1.7%	12,127	97.7%	12,416	100.0%
2 Coronary heart disease	45	0.4%	144	1.2%	12,222	98.4%	12,411	100.0%
3 Stroke	12	0.1%	66	0.5%	12,332	99.4%	12,410	100.0%
4 Hypertension	250	2.0%	455	3.7%	11,702	94.3%	12,407	100.0%
5 Hyperlipidemia	89	0.7%	251	2.0%	12,056	97.3%	12,396	100.0%
6 Chronic bronchitis/emphysema	45	0.4%	150	1.2%	12,212	98.4%	12,407	100.0%
7 Cancer (breast, stomach, or colorectal cancer)	11	0.1%	79	0.7%	10,826	99.2%	10,916	100.0%
8 Cancer (lung, oral, or esophagus cancer)	8	0.1%	45	0.4%	10,861	99.5%	10,914	100.0%

Note: Y = disease present, N = disease absent.

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TABLE 5

Exposure-Discordant Twin Pairs Found in the Third Questionnaire (Age ≥ 25 years)

	Y/Y		Y/N		N/N		Total	
Exposure	Twin pairs	%	Twin pairs	%	Twin pairs	%	Twin pairs	%
Smoking[1]	2,650	21.5%	2,154	17.6%	7,494	60.9%	12,298	100.0%
Alcohol drinking	2,071	16.9%	1,625	13.2%	8,588	69.9%	12,284	100.0%
Fruit and vegetable consumption[2]	5,837	63.1%	477	5.2%	2,930	31.7%	9,244	100.0%
Physical activity[3]	4,931	46.7%	850	8.1%	4,773	45.2%	10,554	100.0%

Note: [1]Y = current smoker/drinker or ex-smoker/drinker; N = never smoker/drinker. A current smoker is defined as anyone who, self-reportedly, smokes one or more cigarettes (or cigars, pipes, or any other smoked tobacco products) daily in the past year. The definition of a current drinker is anyone who self-reportedly consumes >50 g of liquor with 52% alcohol by volume daily in the past year.
[2]Y = those who eat at least three servings of vegetables and two servings of fruit per day.
[3]Y = those who do moderate or vigorous physical activity for at least 30 minutes at a time on at least 5 days/week. Moderate activities refer to activities that take moderate physical effort and make breathing somewhat harder than normal. Vigorous physical activities refer to activities that take hard physical effort and make breathing much harder than normal.

third questionnaire, behaviors such as smoking, alcohol drinking, fruit and vegetable consumption, and physical activity have been investigated. This questionnaire enabled us to determine exposure-discordant twin pairs (Table 5).

Environmental Scan

The cohort study on environmental epidemiology has conducted an 'environmental scan' in 12 cities of China, and aims to objectively describe the environment related to four main risk behaviors: physical inactivity, an unhealthy diet, and tobacco and alcohol use. Street blocks were systematically sampled from all communities of chosen districts in these cities. The tools were developed following a review of existing auditing tools and modified according to the results of a prior similar study in Hangzhou, which also investigated the relationship between these four behaviors and built environment (Du et al., 2012; Gong et al., 2011; Lv et al., 2011; Wong et al., 2011). The survey assessed five kinds of public places of interest: streets, stores and restaurants, recreational facilities, schools, and hospitals. Through the survey, we hope to obtain a description of the distribution of these places of interest, as well as their health behaviors, such as safety, accessibility to unhealthy food, and non-smoking information.

From an extensive and comprehensive collection of urban built environments and comparisons between cities, our study attempts to establish the relationship between health behaviors and environment. The survey also takes a further step in providing evidence for macro-level chronic diseases prevention strategies due to the causal relationship between unhealthy behaviors and chronic disease, which has been recommended in WHO reports (WHO, 2004, 2011). However, there is still a lack of proof in China. Furthermore, the survey can also be the foundation for future studies in which we can add to the population data.

The New Face of the CNTR

The new logo of the CNTR was designed and used for this project (Figure 2). The inspiration for this logo came from the Chinese character of the 'double (双)', which was designed with the shape of two dancing people. The green color implies healthy and cheerful twins in China. It is strongly recognizable. The CNTR now has its own website at http://cntr.bjmu.edu.cn. Twins can register themselves, and research assistants can input the twin information on the Internet. The Internet also helps data managers to manage twin data in a timely fashion, although face-to-face interview questionnaires printed on paper are currently still preferred by most research assistants.

FIGURE 2

(Colour online) Logo of the CNTR.

Future Plans

In the next step, fasting blood samples will be collected in the disease/exposure-discordant twins, who will undergo a detailed physical examination. Matched case control and cohort studies focusing on one kind of disease or one kind of exposure will be conducted in these twins. The epigenetic mark of DNA methylation will be analyzed in cardiovascular disease-discordant MZ twins.

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