Large-Scale Epidemiologic Studies of Cardiovascular Diseases in China



Need for Improved Data Collection, Methods, Transparency, and Documentation

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ABSTRACT

With the advent of international precision medicine initiatives, it is important to evaluate existing large-scale studies to inform future investigation. This study sought to review, describe, and evaluate all large-scale cardiovascular disease (CVD) studies completed in China. We undertook a review of all large-scale CVD studies completed in China to describe and evaluate their design, implementation, and dissemination in published medical reports. Seventeen studies met the inclusion criteria. There were substantial variations in study design, geographic location, and data collection. Most studies lacked standard study names, did not publish their methods, and provided no publicly available data. Few studies included underdeveloped regions or minority groups. Most published articles contained only descriptions of the average population at risk of CVD, and no study predicted individual CVD risk or identified people at high risk. Future CVD studies in China may need to incorporate stronger systematic data collection methods, increased data transparency, clearer documentation, and standard study names to most gain from China's burgeoning field of CVD research.

The widespread availability of electronic data collection and processing facilitates the undertaking of increasingly large cohort studies. Global biobanks and precision medicine initiatives have been established in anticipation of expanding study capacities [1]. As such, it is important to assess past efforts to conduct large-scale public health studies that can inform the design, administration, and evaluation of future investigations.

Cardiovascular disease (CVD) is the global leading cause of death [2], and thus is a field that can benefit enormously from potentially high-impact, large-scale studies. Indeed, China's large population and central government organization can facilitate large-scale studies, many of which have already been undertaken [3,4]. To better inform the design and implementation of such studies, it is important to evaluate and critique prior efforts. However, prior studies have not systematically identified all large-scale, epidemiologic studies on CVD in China, nor have they described study approaches, designs, implementations, transparency, and publications. Such information, particularly regarding ways in which studies succeed or fail in collecting and reporting meaningful data, could inform future CVD research initiatives both in China and abroad, especially given that much information remains inaccessible to researchers outside of China. In addition, CVD information on the prevalence and incidence of cardiovascular risk factors and patients' knowledge and attitudes would be especially useful in designing future interventions.

We conducted a review of published reports to identify large-scale studies in China that addressed cardiovascular risk factors such as diabetes, hypertension, obesity, dyslipidemia, smoking, inactivity, and diet. We focused on studies that enrolled \geq 100,000 participants to parallel the magnitude of other well-established large-scale epidemiologic studies [5-7], and to inform the design and implementation of China's PEACE MPP (Patient-centered Evaluative Assessment of Cardiac Events Million Persons Project), which is among the largest ongoing populationbased studies, that aims to enroll 5 million people in China [8]. We described study characteristics and assessed studies based on study design, demographic characteristics, geographic location, funding sources, and data collection methods. We further evaluated studies' statistical analyses and resulting publications in high-impact journals. We sought to understand the methodological approaches and publications of large-scale CVD research in China, and to use our findings to formulate recommendations for how future epidemiologic CVD studies might best be conducted and reported.

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MATERIALS AND METHODS

Search strategy and selection criteria

A standardized review protocol, including eligibility criteria and data extraction methods, was designed to form a detailed search strategy for papers. The protocol is described in detail in Figure 1. A systematic literature search was performed in OvidSP MEDLINE and PubMed using the combined text, acronyms and MeSH heading search strategy (["hypertension" OR "diabetes", "obesity" OR "dyslipidemia" OR "smoking" OR "physical activity" OR "diet"] AND ["China"] AND ["incidence" OR "prevalence" OR "epidemiology" OR "population"]). Reference lists of review articles identified in the search process were also considered. Additionally, the annual National Reports on Cardiovascular Diseases in China (published by the National Center for Cardiovascular Diseases in China) were reviewed. After excluding duplicate articles, 2 reviewers (H.Q. and S.X.) independently screened all the remaining articles' titles and abstracts to determine whether the studies met the eligibility criteria. Discordant assessments were adjudicated by a third reviewer (E.B.), who made the final decision. After identifying eligible studies, the number of publications from each study was systematically searched on PubMed using the study names. We also supplemented our findings by searching 2 Chinese research databases (Wanfang and China National Knowledge Infrastructure). For each study, in order to expand studies' designs and outcomes for more accurate data



FIGURE 1. Flow diagram of included studies. Though 2 studies (the Kailuan Study and the 2010 China NCD [Non-communicable Disease Survey]) included slightly <100,000 people, they studied all 7 cardiovascular risk factors.

extraction, we searched both databases for any published papers and reviewed any such articles conducted on the Chinese population in China.

Our eligibility criteria included all studies that: (1) were conducted in mainland China; (2) reported prevalence/incidence of CVD or ≥ 1 cardiovascular risk factor (smoking, obesity, diet, physical activity, hypertension, diabetes, or dyslipidemia) in adults; (3) were population-based; and (4) had a total sample of $\geq 100,000$ participants. Studies were excluded if they discussed the association between risk factors and CVD, biomedical mechanisms, or treatment responses in animal models. Interventional studies were not excluded. No restrictions were placed on studies' publication dates, eligibilities, or languages. In this study, we focused mainly on but were not limited to coronary heart disease and stroke.

Data extraction and analysis

For all included studies, we extracted the following information based on a modified version of the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) Checklist (Online Appendix 1): study name; name of the method paper (if available); first author; publication year; screening year; funding source; collaborating organizations; study aims/hypotheses; study design; eligibility criteria; sample size; population characteristics; sample selection method; sample source; diagnostic criteria; cardiovascular risk factors measured; method of measurement; data validation/quality assurance methods; and potential biases. We began each abstraction by reviewing the methods paper, then supplemented with details from other manuscripts of the same study. When the same study population was used in multiple articles, we selected the article with the most recent publication date or the longest follow-up. Three investigators (H.Q., S.X., E.G.) independently extracted the necessary information from all included studies. Disagreements were discussed and resolved to reach a consensus among all 3 investigators.

The characteristics of each study were summarized. Each study was assessed on the basis of study design, sampling strategies, number of cardiovascular risk factors studied, demographic characteristics, response rate, method of measurement, method of data validation, or quality assurance, as well as result information to analyze the methodological quality and transparency. To evaluate how successful these studies were in publishing their findings in high-profile journals, we selected articles published in journals of an impact factor (IF) >10 in the public health or cardiovascular realm (Online Appendix 2).

RESULTS

Study characteristics

In total, 17 studies satisfied our inclusion criteria (Figure 1). Two studies (the Kailuan Study and the 2010 China NCD [Non-Communicable Disease Surveillance]

study) were included because they had only slightly <100,000 people and studied all 7 cardiovascular risk factors. Of the 17 studies, 9 were cross-sectional and 8 were longitudinal with follow-up periods ranging from 4 to 23 years. Of all the longitudinal studies included, 5 (the SHWS & SHMS [Shanghai Men and Women Study], the 1991 Hypertension and Follow-up study, China Kadoorie Biobank, the Da Qing IGT and DM [Impaired Glucose Tolerance and Diabetes Mellitus] Study, and Chinese Prospective Smoking Study) reported a response rate. The sample size for the included studies ranged from 92,562 to approximately 5 million people. The mean age of participants was between 35 to 58 years. The sex ratio (menwomen) ranged from 1:0.88 to 1:1.94, with the exception of the Kailuan Study [9], whose ratio was approximately 1:0.25 as most of its study subjects were coal miners. More than one-half of the studies (n = 9) were nationally representative, and 5 focused exclusively in 1 geographical location (the Kailuan Study in Tangshan, the SHWS & SHMS in Shanghai, the Da Qing IGT and DM Study in Daqing, the rural Yuhuan Health Population Cohort in Yuhuan, and the Tianjin Study in Tianjin). The study years of all included studies ranged from 1979 to 2012, as shown in Figure 2.

All studies were initiated or at least given partial financial support by the central government. Many received academic assistance in design, data processing, and interpretation from abroad. For most, local Centers for Disease Control, local hospitals, grassroots physicians, and local public health officials were all involved in the data collection processes. Eleven studies were partially or fully supported by international funding agencies, and 13 involved collaboration with foreign institutions (Tables 1 and 2) [10-29].

Transparency, methodology, and quality

Eight studies either had no official study name or did not publish a methods paper. The lack of official study name may prohibit a systematic identification of all published articles, and the lack of methods paper may hinder a comprehensive evaluation of study quality and methodology. Only the Kailuan Study, the 1991 Hypertension Study follow-up, China Kadoorie Biobank, Sino-MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) [14], the REACTION (Risk Evaluation of cAncers in Chinese diabeTic Individuals: a lONgitudinal study), the 2002 China National Nutrition and Health Survey, the SHWS & SHMS, and 2010 NCD study published user manuals or methods papers with detailed descriptions of the study design, methodology, and evaluation.

All studies, except the 1994 Diabetes Study, clearly reported their sampling strategies. Two studies (Yuhuan Study and Tianjin Study) were whole-population studies [28,29]. Among the 9 nationally representative studies, 3 used the Chinese DSP (Disease Surveillance Points) [18,21,27], a surveillance network created by the Chinese

Center for Disease Control and Prevention that covers $\sim 1\%$ of the population and includes 145 nationally representative regions using stratified cluster random sampling [30]. The other 6 national studies did not report whether they shared the same sampling strategy. Very few studies recruited participants from underdeveloped regions such as Tibet and Xinjiang. For all studies, sampling was based on socioeconomic status and geographic location, with no mentions of minority groups. In addition, all data were gathered using the Hukou system (residence) or longtime (≥ 6 months) residence data, thereby excluding migrant workers whose numbers have been increasing since 1980 and reached nearly 36% of the total workforce in 2015 [31]. Lastly, several studies found that their sample populations did not include enough young people as many had already left home for work and were therefore unavailable at the time of research [32].

All studies reported how they collected participant questionnaires or conducted standardized interviews, except for the 1979 National Hypertension survey and the 1984 People's Republic of China smoking survey, although only 2 studies (China Kadoorie Biobank and the SHWS & SHMS) have made the Case Report Form publicly available (Online Appendix 3).

In terms of data quality, many studies did not report essential design and result information such as follow-up rate, sample size calculation, or demographics. For example, only 5 of the cohort studies reported a response rate: SHWS & SHMS (men: 91.9% [17], women: 92.7% [18]); the 1991 Hypertension and Follow-up study (93% for 13 of 19 provinces [33]); China Kadoorie Biobank (80% at resurvey [4]); the Da Qing IGT and DM Study (94% for the initial screening [26]); and the Chinese Prospective Smoking Study ($\sim 80\%$ [23]). Despite these high response rates, none included information on how these rates were calculated. Additionally, for all studies except the China National Nutrition and Health Survey and Sino-MONICA, there were no explanations for how the sample size was chosen. Nevertheless, all studies used at least some method of data validation or quality assurance, such as the application of standardized protocols, the creation of pilot studies, or the implementation of quality control surveys.

In-depth information was also lacking with regard to the collection of CVD information. Most studies only collected data on demographic variables and some cardiovascular risk factors. Before 2000, studies focused primarily on the prevalence and incidence of a single cardiovascular risk factor and the related morbidity and mortality. Few studies have assessed multiple cardiovascular risk factors simultaneously and little emphasis has been made on patients' knowledge of CVD, attitudes, beliefs, or behavior [21,23,24,26,34]. In recent years, studies have incorporated more cardiovascular risk factors and now include associated behaviors and demographic details, as well as more comprehensive study designs and better data validation methods, such as SHWS & SHMS and the China Kadoorie Biobank study. In general, few studies collected a wide range of detailed information on biological, behavioral, demographic, socioeconomic, and genetic factors. Furthermore, whereas most studies collected information using objective methods such as clinical examinations and hospital records, 3 studies used only in-person interviews and/or questionnaires. Ten studies obtained biospecimen samples from the participants. The extent to which studies researched cardiovascular risk factors varied greatly. Six studies covered all 7 major cardiovascular risk factors, namely diet, obesity, hypertension, dyslipidemia, diabetes, smoking, and inactivity, and 4 studies focused only on 1 risk factor. Smoking, hypertension, and obesity were the most commonly covered risk factors. Lastly, most studies reported averaged results across the population and no study quantified individual CVD risk. The Da Qing IGT and DM Study was the only study to identify high-risk (impaired glucose tolerance) subjects and perform interventions based on subjects' risk factors (diet and/or physical activity) after a massive population-based diabetes screening. The lifestyle intervention of this study lasted 6 years and the diabetes incidence reduction persisted for 2 decades [35]. Nevertheless, this study was a randomized controlled clinical trial designed to investigate the effect of lifestyle interventions on the development of type 2 diabetes rather than to reduce individual CVD risk and associated mortality.

No study conducted before 2000 has publicly available data, partly because computer storage was not accessible to underdeveloped areas until the late 1990s and early 2000s. Nevertheless, even for those studies conducted after 2000, only the China Kadoorie Biobank and the SHWS & SHMS willingly share data with other investigators via direct online or application-based access.

Publications

While all studies have successfully published ≥ 1 paper in a peer-reviewed journal, it nevertheless proved difficult to identify the exact number of publications for all studies due to the lack of standardized official study names. To focus primarily on the most important publications, we further evaluated articles of each study published in journals with IF >10. In total, 38 articles from 11 studies were published in 16 journals with IF >10 (Online Appendix 4), including 16 articles from the SHWS & SHMS; 4 studies had no publications in journals with an IF >10. Of note, although the SHWS & SHMS official website lists 45 high-profile papers [36], only 16 of these publications were found on PubMed by searching the study name. The 29 papers that were not identified by PubMed's search engine were either systematic reviews or regional genetic analyses and therefore were judged to provide little to no new information on CVD and risk factors.

Of the 38 high-profile articles, 2 were descriptive articles that only reported demographics, distribution, and prevalence of CVD and its associated risk factors; 28 used traditional epidemiology methods and examined the associations among risk factors, outcomes, and attributable risks; 3 used more advanced statistical analyses, such as simulations or the introduction of new models; and 5 focused on genetic analysis. Most identified articles were descriptive, with no sophisticated statistical analysis. In addition, all of the identified publications characterized only the prevalence and incidence of risk factors and their relationships with cardiovascular outcomes for the general population.

DISCUSSION

We identified 17 large-scale, published studies in China that focused on CVD and risk factors, with study populations of approximately 100,000 or more. These studies varied substantially with respect to study design, geographic location, follow-up length, funding sources, and data collection methods. Most lacked standard study names, did not publish methods papers, and few provided publicly available data. All studies received at least partial support from the central and local government, but few enrolled participants from underdeveloped regions, migrant workers, young people, or minority groups. Most of the published articles contained only descriptions of the average population at risk of CVD, and no study predicted individual CVD risk or identified people at high risk (Table 3).

Our findings have several important implications for the implementation of future CVD studies. First, the lack of official study names, method papers, and easily obtainable data sources has hindered the systematic collection of accurate information regarding study design and methodology. In addition, it prohibited combining different studies that shared the same data collection strategies and used the same definitions to improve power. Therefore, there is a need for researchers to more consistently document and disseminate their study information. For example, a study should have a unique study name that can be clearly identified by database search engines. Studies should also ensure any published method papers are searchable, and include Case Report Forms in the appendix so that all variables and measurements are publicly available. Published papers should contain comprehensive information regarding their study designs and results. In addition, since 2003, the US National Institute of Health has issued a detailed data-sharing policy for studies receiving its grant of >\$500,000 to open data for the replication and translation of research [37,38]. The Chinese National Natural Science Foundation and other funding agencies may also require all its funded studies to follow the same way. Lastly, open databases, such as a website with detailed information on the approaches, designs, implementations, and publications of the study as well as data acquisition procedures, would greatly inform future CVD research initiatives, as well as promote academic cooperation.

Second, few of the identified studies collected enough information on cardiovascular risk factors or enrolled participants from underprivileged population, such as rural participants, migrant workers, young people, or minority groups. These limitations may confound the generalizability of the studies' final conclusions, especially considering that migrant workers and minority groups are frequently overlooked high-risk populations for CVD [39,40]. In addition, China is uniquely positioned to conduct mega studies given its enormous endorsements from the central and local governments. Therefore, future studies should make use of the pre-existing mega epidemiology foundations, such as the well-established DSP. Future efforts would also do well to collect information on the above-listed overlooked groups when studying CVD. In addition, electronic data collection will facilitate more timely and personalized predictions and interventions.



FIGURE 2. Timeline of included studies. Blue line: cross-sectional study; dashed blue line: repetitive cross sectional study; green line: cohort study. Da Qing IGT and DM, Impaired Glucose Tolerance and Diabetes Mellitus; NHSS, National Health Services Surveys; REACTION, Risk Evaluation of cAncers in Chinese diabeTic Individuals: a IONgitudinal study.

TABLE 1. Characteristics of cohort studies

Study Name [Ref. #]	CVD Risk Factors	Study Design	Sample Population Size	Screening Year(s)	Length and Frequency of Follow-Up (yrs)	Follow-Up Rate
Kailuan [10]	7	Cohort; prospective	92,562	2006—2010	4, every 2	N/A
China Kadoorie Biobank [11]	7	Cohort; prospective	512,891	2004—2024	20, every 4—5	Ongoing
1991 Hypertension and Follow-Up Study [12,13]	Hypertension (baseline); hypertension, smoking, physical activity, obesity, diabetes (follow-up)	Cohort	Baseline: 950,356; follow-up: 169,871	1991—2000	8.3, once	17 of 30 provinces
Sino-MONICA [14]	Hypertension, obesity, dyslipidemia, smoking	Cohort; prospective	~5 million	1985—1993	7, once	N/A
REACTION [15,16]	Diabetes, smoking, physical activity, obesity, dyslipidemia, hypertension	Cohort; prospective	259,657	2011–2021	10, once	N/A
Shanghai Health Study [17,18]	7	Cohort; prospective	Men: 61,480; women: 74,942	Men: 2001—2012; women: 1996—2000	men: 12, every 3–4 s; women: 4, every 2	>90%
The Da Qing IGT and DM Study [19]	Diabetes (for all); diabetes, blood pressure, obesity, dyslipidemia, diet, physical activity (for OGTT people)	Cohort, prospective	110,660	1986—2009	6 (for intervention) /23 (for death rates), every 2	Intervention: 99.8% death rates: 94.1%
Chinese Prospective Smoking Study [20]	Smoking, blood pressure, obesity, drinking, diet	Cohort, prospective	219,893	1990 (ongoing)	Every year/decade	~97%

Evaluation of cAncers in Chinese diabeTic Individuals: a IONgitudinal study; Sino-MONICA, Monitoring Trends and Determinants in Cardiovascular Disease in China. *Some studies are ongoing or have produced multiple main findings, therefore the list may not be comprehensive.

> Data generated in the course of clinical care from hospital information systems and those from surveillance systems and portable health devices could all serve as data sources for conducting future mega studies. In this way, we may further refine the prevention and treatment of complex medical conditions based on real-world data. However, these approaches remain aspirational due to high costs, provider and individual concerns about data privacy, incompatible health information systems, and limited data standardization across platforms.

> Third, no identified large-scale study applied advanced statistical methods to take advantage of the large data resources, which could have been used to

identify high CVD risk subjects, assess their cardiovascular health, and design individualized treatment strategies. Most published articles from these studies focused on "average" population health and lacked strategic evaluation of individual CVD risk. In order to decrease population-level CVD risk, it is important to first identify and reduce individual patients' risks. To further decrease CVD-related mortality, better-personalized predictions and interventions are urgently needed. Several public health efforts have begun to promote such lines of thought, including the UK Biobank, which has enrolled approximately 0.5 million people in order to study the pathogenesis and development of various diseases [5].

Data Collection		Geographic		
Methodology	Funding	Locations	Outcome	Main Findings*
Interview and	China	Kailuan Community	First occurrence of CVD	Elevated resting heart
clinical examination				rate might be a risk marker
				for myocardial infarction in
				general populations
Questionnaire and	China, United	10 regions	Deaths and disease incidence	Genetic and nongenetic risk
clinical examination	Kingdom		for stroke, ischemic heart	factors can cause many common
			disease, cancers, and diabetes	chronic diseases
Interview, questionnaire,	United States,	Baseline: national;	Hypertension, death	Increased blood pressure is the
clinical examination,	China	follow-up:		leading preventable risk
and hospital records		17 provinces		factor for premature mortality
				in the Chinese general population
Reports from grassroots	China, World	16 provinces	All acute coronary and	Established the feasibility of long-term
health station personnel,	Health		stroke events	monitoring of CVD events and
hospital records, and	Organization			risk factors with standardized methods
death certificates		25		
Interview and clinical	China, Europe	25 communities	Newly diagnosed cancer,	Identified factors that modify the risk
examination		across mainland	diabetes, and cardiovascular	of cancer among individuals with
		China	diseases; sociodemographic	diabetes and pre-diabetes
			status; mestyles	
Questionnaire interview	United States	Shanghai	Death cancer cardiovascular	Determined lifestule factors, environmental
and clinical examination	United States	Shanghai	disease stroke hone fracture	evocures and biomarkers for the risk
			and other chronic diseases	of cancer and other chronic diseases
				of cancer and other enronic discuses
Questionnaire and	World Bank. China	Da Qing	CVD (mvocardial infarction.	Diet and/or exercise interventions led
clinical examination	,		sudden death, or congestive	to a significant decrease of diabetes
			heart failure), stroke, or	over a 6-year period among
			noncardiovascular causes	those with IGT
Questionnaire and	China, United Kingdom,	National	Chronic obstructive pulmonary	The tobacco-attributed proportion is
clinical examination	World Bank, Canada		disease-related death	increasing in men, but low, and
				decreasing, in women

Therefore, in this new era of precision medicine, carefully designed protocols and advanced statistical analyses should be used to both identify and inform public health interventions for individuals at high risk of CVD.

Our study is the first that identifies and describes the characteristics of large-scale epidemiology studies on CVD in China. Using rigorous methodological design and standardized review methods, we comprehensively identified large-scale studies on cardiovascular risk factors in China and analyzed their qualities of transparency, study design, and publications. The findings of our study have already informed the China PEACE MPP study, a national CVD prevention and intervention initiative in China [8].

The limitations of this review reflect, to a large extent, the limitations of the data available in studies to this point in China. Due to the lack of standard study names or public data acquisition procedures, we may have missed some of the large-scale epidemiology studies, their method papers, or other important information. In addition, the information we extracted was usually from an individual paper, rather than from the original study protocol or database. Our results may therefore be biased by inadequate details in the publications, protocol violations, and undocumented patient compliance. However, we exhausted all available searching methods, including the use of systematic database reviews, comprehensive identification of all reference lists, systematic reviews, Chinese databases and the official websites of studies if available, pre-designed standardized review protocol, comparison with other reviews, and bilingual team members in order to overcome the above-mentioned limitations.

Study Name	CVD Risk	Sample Population	Screening	Geographic		
[Ref. #]	Factors*	Size	Year(s)	Locations	Main Findings [†]	Funding
1996 Smoking Survey [21]	Smoking	120,298	1996	National	High rates of smoking in men found in this study signal an urgent need for smoking prevention and cessation.	United States
National Health Service Survey [22]	Smoking	1993: 215,163; 1998: 216,101; 2003: 193,698	1993, 1998, 2003	National	Smoking prevalence declined in China over the study period, perhaps due to the combined effect of smoking cessation, reduced uptake in women and selective mortality among men >40 yrs of age.	Canada; China
1979 Hypertension study [23]	Hypertension	4,012,128	1979	National	Hypertension in China has higher rate in northern/northeastern provinces and larger/industrialized cities, than in the southern provinces/rural areas.	N/A
1984 Smoking Survey [24]	Smoking	519,600	1984	National	Most Chinese smokers start smoking in their youth; hard to quit when started; prevention should be focused to keep young people from starting.	United Kingdom, China, World Health Organization
Nutrition and Health Survey [25]	7	141,892	2002	National	Limited dietary diversity and intake of high-energy-dense foods were notably observed among stunted overweight children.	China
1994 Diabetes study [26]	7	224,251	1994	19 provinces	The prevalence of diabetes in China is increasing with economic development and changes from traditional to modernized lifestyle, especially where people had lower level of education and socioeconomic development.	N/A
2010 China NCD Surveillance [27]	7	98,258	2010	National	Described prevalence of noncommunicable diseases and associated laboratory test results, such as HbA _{1c} .	China
Rural Yuhuan Health Population Cohort [28]	Hypertension, smoking, diabetes, and physical activity	118,274	2009	Yuhuan	Hyperglycemia was common in adults \geq 35 yrs old who were living in rural China.	N/A
Tianjin Diabetes Study [29]	Diabetes, smoking	769,792	2004	Tianjin	The prevalence of impaired fasting glucose and diabetes is relatively high in the rural population in Tianjin, and it has become an important public health problem in China.	China, Finland
HbA _{1c} , glycosylated hemoglo *The 7 CVD risk factors stud [†] Some studies are ongoing c	bin; NCD, noncommunicable diseas ied are diet, obesity, hypertension, or have produced multiple main fin	ses; other abbreviations dyslipidemia, diabetes, s dings, therefore the liste	as in Table 1. smoking, and inact d may not be com	ivity. prehensive.		

TABLE 3. Summary of the main results

Study Characteristics
17 studies were included: Sample size ranged from 92,562 to approximately 5 million people 9 were cross-sectional and 8 were longitudinal with follow-up periods ranging from 4 to 23 yrs
Transparency, Methodology, and Quality
8 studies did not have study names making them difficult to search or did not publish method papers Data from 15 studies are not publicly available Among the 9 nationally representative studies, only 3 described the use of established data collection systems Two studies (SHWS & SHMS and China Kadoorie Biobank) collected a wide range of detailed information on biological, behavioral, sociodemographic, and genetic factors
Publications
38 articles from 11 studies were published in 16 journals with an impact factor $>$ 10 No identified large-scale study applied advanced statistical methods to take advantage of the large data resources
SHWS & SHMS, Shanghai Men and Women Study.

SUMMARY

Our findings suggest that with the immense resources devoted and the contributions of both researchers and participants, stronger systematic data collection methods might be incorporated along with increased data transparency, clearer documentation, and standard study names in order to gain the most from China's burgeoning field of CVD research.

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APPENDIX

ONLINE APPENDIX 1. Modified version of the STROBE Checklist

Study number		
Study name		
Type of cardiovascular risk factors		
Region		
Funding source		
Collaborating organizations		
Method paper? (Yes or no)		
Name of the method paper (if available)		
Author		
Publication year		
Screening year		
Study aims/hypotheses		
Study design		
	Cohort/case control/cross-sectional study?	
	Prospective/retrospective	
	Periods of recruitment	
	Follow-up years	
	Methods of follow-up	
	Sample size calculation performed	
	Total number	
	Describe number of individuals at each stag	e of study
		Number screened
		Number eligible
		Number included
		Number completed follow-up
	Eligibility criteria	
	Data source (hospital-based/regional)	
	Setting and locations where data were colle	ected
	Sources and methods of selection of partici	pants
	Measurement/assessment of variables of in	terest
	Biospecimens	
	Endpoint	
Demulation Chamataniation	Data validation/quality assurance methods	
Population Characteristics	Manage and and any second	
	Read age and age range	
	Demographics (ago, cox, marital status, omr	loumont minority groups)
	Sov ratio	boyment, minority groups)
	Cardiovascular risk factors moasured	
	Missing to follow-up and reasons (at each s	tage ie at 1 vr 2 vrs etc)
	Open data?	tage, i.e., at 1 yi, 2 yis, etc.)
Others		
oticis	Number of articles evaluating CV risk factor	s using data from study
	Potential biases?	
		Sample size
		Sampling method
		Measurement of variables
		Measurement of follow-up
		Analyses
STROBE, STrengthening the Reporting of OBservational	studies in Epidemiology.	

ONLINE APPENDIX 2. LIST OF HIGH IMPACT JOURNALS (IMPACT FACTOR >10)

Cancer Journal for Clinicians (CA Cancer J Clin) 115.840 NEJM (N Engl J Med) 55.873 Lancet 45.217 Nature 41.456 Nature Reviews Molecular Cell Biology (Nat Rev Mol Cell Biol) 37.806 Nature Reviews Cancer (Nat Rev Cancer) 37.400 Nature Reviews Genetics (Nat Rev Genet) 36.978 IAMA 35.289 Nature Reviews Immunology (Nat Rev Immunol) 34.985 Science 33.611 Cell 32.242 Nature Reviews Neuroscience (Nat Rev Neurol) 31.427 Nature Genetics (Nat Genet) 29.352 Nature Medicine (Nat Med) 28.223 Lancet Oncology (Lancet Oncol) 24.725 Cancer Cell 23.523 Lancet Neurology 21.896 Endocrine Reviews (Endocr Rev) 20.833 Nature Immunology (Nat Immunol) 20.004 Cancer Discovery (Cancer Discov) 19.453 Annual Review of Neuroscience (Annu Rev Neurosci) 19 320 Journal of Clinical Oncology (J Clin Oncol) 18.443 Annals of Internal Medicine (Ann Intern Med) 17.737 Archives of Internal Medicine (Arch Intern Med) 17.333 BMJ 17.445 Nature Neuroscience (Nat Neurosci) 16.095 Journal of the American College of Cardiology (J Am Coll Cardiol) 16,503 Science Translational Medicine (Sci Transl Med) 15.843 Annual Review of Genetics (Annu Rev Genet) 15.724 Nature Reviews Neurology (Nat Rev Neurol) 15.358 European Heart Journal (Eur Heart J) 15.203 Circulation 15.073 JAMA Internal Medicine 15.04 PLoS Medicine 14.429 Systematic Biology (Syst Biol) 14.387

Nature Reviews Clinical Oncology (Nat Rev Clin Oncol) 14.180 Nature Reviews Endocrinology (Nat Rev Endocrinol) 13.281 Journal of Clinical Investigation (J Clin Invest) 13.262 Annual Review of Medicine (Annu Rev Med) 12.928 Journal of the National Cancer Institute (J Natl Cancer Inst) 12.583 Journal of Experimental Medicine (J Exp Med) 12.515 Nature Communications (Nat Commun) 11.47 Trends in Biochemical Sciences (Trends Biochem Sci) 11 227 Circulation Research (Circ Res) 11.019 American Journal of Human Genetics (Am J Hum Genet) 10.931 Genome Biology (Genome Biol) 10.810 Genes & Development (Genes Dev) 10.798 EMBO Journal (EMBO J) 10.434 Molecular Aspects of Medicine (Mol Aspects Med) 10.238 Lancet Global Health (Lancet Glob Health) 10.042 Note: Some of the journals listed above are not cardiovascular disease-specific. However, we listed the journals as comprehensively as possible because the objectives of studies greatly varied in scope.

ONLINE APPENDIX 3. CASE REPORT FORM SOURCES FOR CHINA KADOORIE BIOBANK AND SHWS & SHMS (SHANGHAI MEN AND WOMEN STUDY)

- 1. Vanderbilt Epidemiology Center. Shanghai Women's and Men's Health Studies: Cohort Resources. 2016. Available at: http://staging.mc.vanderbilt.edu/swhssmhs/DAS_smhs/DAS_smhs_page2.html. Accessed May 20, 2016.
- 2. International Coordinating Center—China Kadoorie Biobank. China Kadoorie Biobank: Overview and Study Resources. 2015. Available at: http://www.ckbiobank. org/site/Study+Resources. Accessed May 16, 2016.

ONLINE APPENDIX 4. List of articles	published in journals with IF > 10
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Study Name	Number of Publications	Publications in Journals With IF >10
National Health Service Survey	1	Meng Q, Xu L, Zhang Y, et al. Trends in access to health services and financial protection in China between 2003 and 2011: a cross-sectional study. Lancet 2012;379:805–14.
1984 Smoking Survey	1	Yu JJ, Mattson ME, Boyd GM, et al. A comparison of smoking patterns in the People's Republic of China with the United States: an impending health catastrophe in the Middle Kingdom. JAMA 1990;264:1575–9.
Nutrition and Health Survey	1	Wu Y, Huxley R, Li L, et al. Prevalence, awareness, treatment, and control of hypertension in China: data from the China National Nutrition and Health Survey 2002. Circulation 2008;118:2679–86.
The Da Qing IGT and DM study	1	Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008;371:1783–9.
Chinese Prospective Smoking Study	2	 Chen Z, Peto R, Zhou M, et al., for the CKB Collaborative Group. Contrasting male and female trends in tobacco-attributed mortality in China: evidence from successive nationwide prospective cohort studies. Lancet 2015;386:1447–56. Niu SR, Yang GH, Chen ZM, et al. Emerging tobacco hazards in China: 2. Early mortality results from a prospective study. BMJ 1998:317:1423–4.
1996 Smoking Study	2	 Yang G, Fan L, Tan J, et al. Smoking in China: findings of the 1996 National Prevalence Survey. JAMA 1999;282:1247–53. Levy D, Rodríguez-Buño RL, Hu TW, Moran AE. The potential effects of tobacco control in China: projections from the China SimSmoke simulation model. BMJ 2014;348:g1134.
Sino-MONICA	2	 Critchley J, Liu J, Zhao D, Wei W, Capewell S. Explaining the increase in coronary heart disease mortality in Beijing between 1984 and 1999. Circulation 2004;110:1236–44. Wu Z, Yao C, Zhao D, et al. Sino-MONICA project: a collaborative study on trends and determinants in cardiovascular diseases in China, Part I: morbidity and mortality monitoring. Circulation 2001;103:462–8.
2010 China Non-Communicable Disease Surveillance Study	2	 Bi Y, Jiang Y, He J, et al., for the 2010 China Non-Communicable Disease Surveillance Group. Status of cardiovascular health in Chinese adults. J Am Coll Cardiol 2015;65:1013–25. Xu Y, Wang L, He J, et al., for the 2010 China Non-Communicable Disease Surveillance Group. Prevalence and control of diabetes in Chinese adults. JAMA 2013;310:948–59.
1991 Hypertension and Follow-Up Study	4	 He J, Gu D, Wu X, et al. Major causes of death among men and women in China. N Engl J Med 2005;353:1124-34. Gu D, He J, Duan X, et al. Body weight and mortality among men and women in China. JAMA 2006;295:776-83. Kelly TN, Gu D, Chen J, et al. Hypertension subtype and risk of cardiovascular disease in Chinese adults. Circulation 2008;118:1558-66. Gu D, Kelly TN, Wu X, et al. Mortality attributable to smoking in China. N Engl J Med 2009;360:150-9. He J, Gu D, Chen J, et al. Premature deaths attributable to blood pressure in China: a prospective cohort study. Lancet 2009;374:1765-72.
China Kadoorie Biobank	5	 Chen Z, Peto R, Zhou M, et al., for the CKB Collaborative Group. Contrasting male and female trends in tobacco-attributed mortality in China: evidence from successive nationwide prospective cohort studies. Lancet 2015;386:1447–56. Lewington S, Lacey B, Clarke R, et al. The Burden of Hypertension and Associated Risk for Cardiovascular Mortality in China. JAMA Intern Med 2016;176:524–32. Lv J, Qi L, Yu C, et al., for the CKB Collaborative Group. Consumption of spicy foods and total and cause specific mortality: population based cohort study. BMJ 2015;351: h3942.

ONLINE APPENDIX 4. Continued

Study Name	Number of Publications	Publications in Journals With IF >10
		 Millwood IY, Bennett DA, Walters RG, et al., for the CKB Collaborative Group. Lipoprotein-associated phospholipase A2 loss-of-function variant and risk of vascular diseases in 90,000 Chinese adults. J Am Coll Cardiol 2016;67:230–1. Yang L, Li L, Lewington S, et al., for the CKB Collaborative Group. Outdoor temperature, blood pressure, and cardiovascular disease mortality among 23,000 individuals with diagnosed cardiovascular diseases from China. Eur Heart J 2015;36:1178–85.
Shanghai Women and Men's Health Study		 J 2015;36:11/8–85. Luu HN, Blot WJ, Xiang YB, et al. Prospective evaluation of the association of nut/peanut consumption with total and cause-specific mortality. JAMA Intern Med 2015;175:755–66. Shungin D, Winkler TW, Croteau-Chonka DC, et al. New genetic loci link adipose and insulin biology to body fat distribution. Nature 2015;518:187–96. Day FR, Ruth KS, Thompson DJ, et al. Large-scale genomic analyses link reproductive aging to hypothalamic signaling, breast cancer susceptibility and BRCA1-mediated DNA repair. Nat Genet 2015;47:1294–303. Cai Q, Zhang B, Sung H, et al. Genome-wide association analysis in East Asians identifies breast cancer susceptibility loci at 1q32. 1, 5q14. 3 and 15q26. 1. Nat Genet 2014;46:886–90. Yang G, Shu XO, Li HL, et al. Prediagnosis soy food consumption and lung cancer survival in women. J Clin Oncol 2013;31:1548–53. Chen X, Lu W, Zheng Y, et al. Exercise, tea consumption, and depression among breast cancer survivors. J Clin Oncol 2010;28:991–8. Dai Q, Gao YT, Shu XO, et al. Oxidative stress, obesity, and breast cancer risk: results from the Shanghai Women's Health Study. J Clin Oncol 2009;27:2482–8. Cai Q, Gao YT, Chow WH, et al. Prospective study of urinary prostaglandin E2 metabolite and colorectal cancer risk. J Clin Oncol 2006;24:5010–6. Zhang X, Shu XO, Yang G, et al. Abdominal adiposity and mortality in Chinese women. Arch Intern Med 2007;167:886–92. Zhang X, Shu XO, Gao YT, et al. Environmental tobacco smoke and mortality in Chinese women who have never smoked: prospective cohort study. BMJ 2006;33:376. Nechuta SJ, Shu XO, Li HL, et al. Combined impact of lifestyle-related factors on total and cause-specific mortality among Chinese women: prospective cohort study. PLoS Med 2010;7:e1000339. Zhang W, Shu XO, Li HL, et al. Combined impact of lifestyle-related factors on total and cause-specific mortality among Chinese women: prospective cohort study. PLoS Med
		French JD, Ghoussaini M, Edwards SL, et al. Functional variants at the 11q13 risk locus for breast cancer regulate cyclin D1 expression through long-range enhancers. Am J Human Genet 2013;92:489–503.

Da Qing IGT and DM, Impaired Glucose Tolerance and Diabetes Mellitus; IF, impact factor.

Note: No articles in journals with IF >10 were detected for the 1994 Diabetes Study, REACTION (Risk Evaluation of Cancers in Chinese Diabetic Individuals: A Longitudinal study), the 1979 Hypertension Study, nor the Kailuan study.