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Qingdao Port Cardiovascular Health Study: a prospective cohort study

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ABSTRACT

Purpose: In China, efforts are underway to respond to rapidly increasing rates of heart disease and stroke. Yet the epidemiology of cardiovascular disease in China may be different from that of other populations. Thus, there is a critical need for population-based studies that provide insight into the risk factors, incidence and outcomes of cardiovascular disease in China. The Qingdao Port Cardiovascular Health Study is designed to investigate the burden of cardiovascular disease and the sociodemographic, biological, environmental and clinical risk factors associated with disease onset and outcomes.

Participants: For this study, from 2000 through 2013, 32 404 employees aged 18 years or older were recruited from the Qingdao Port Group in China, contributing 221 923 annual health assessments. The mean age at recruitment was 43.4 (SD=12.9); 79% were male. In this ongoing study, annual health assessments, governed by extensive quality control mechanisms, include a questionnaire (capturing demographic and employment information, medical history, medication use, health behaviours and health outcomes), physical examination, ECG, and blood and urine analysis. Additional non-annual assessments include an X-ray, echocardiogram and carotid ultrasound; bio-samples will be collected for future genetic and proteomic analyses. Cardiovascular outcomes are accessed via self-report and are actively being verified with medical insurance claims; efforts are underway to adjudicate outcomes with hospital medical records.

Findings to date: Early findings reveal a significant increase in cardiovascular risk factors from 2000 to 2010 (hypertension: 26.4–39.4%; diabetes: 3.3–8.9%; hyperlipidaemia: 5.0–33.6%; body mass index >28 m/kg^2: 14.1–18.6%).

Future Plans: We aim to generate novel insights about the epidemiology and outcomes of cardiovascular disease in China, with specific emphasis on the potentially unique risk factor profiles of this Chinese population. Knowledge generated will be disseminated in the peer-reviewed literature, and will inform population-based strategies to improve cardiovascular health in China.

Trial registration number: NCT02329886.

Strengths and limitations of this study

- This is a prospective cohort study conducted for over 10 years.
- The study collected a variety of information including cardiovascular risk factors, clinical outcomes and bio-samples, allowing a wide ranging assessment of risk factors and genetic factors related to cardiovascular disease onset and cardiovascular outcomes.
- Findings will have broad implications for China's workforce and for employer-based healthcare.
- Participants are limited to a single company and may not be representative of the larger population of China.

INTRODUCTION

Epidemiological studies are the cornerstone for understanding cardiovascular risk factors and disease. Decades of research extending from the Framingham Heart Study and other cardiovascular studies (eg, Atherosclerosis Risk in Communities Study) provide insight into the complex interplay between biology, behaviour, environment and genes, on the risk of cardiovascular disease (CVD) and stroke.[1–4] However, existing studies of the epidemiology of CVD may have limited relevance to other populations, particularly in countries with different health behaviours and environments.

The relationships between risk factors and CVD outcomes differ between populations. As demonstrated in the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project, along with other studies, metabolic, dietary and other lifestyle factors do not consistently portend the same cardiovascular risk across populations.[5–11] The graded relationship between higher cholesterol levels and mortality from coronary heart disease varies among Western countries[12] and may differ in China.[13] [14] Studies also demonstrate

differences in the epidemiology of stroke, with the slope of the relationship between blood pressure and stroke steeper among Asian populations as compared with Australian populations,[15] and haemorrhagic stroke occurring more frequently in Chinese populations than in Western populations.[16] In summary, the epidemiology of heart disease and stroke in China, and its associated risk factors, may be different from that of other populations, and thus may have different implications for intervention and prognosis. Understanding potential differences in the epidemiology and outcomes of CVD in China requires population-based studies.

Well-conducted, population-based prospective studies focused on CVD are critical, especially as China is experiencing remarkable changes in the cardiovascular risk of its population.[17–20] Similar to other developing countries undergoing an epidemiological transition, there has been a dramatic rise in the prevalence of non-communicable diseases such as CVD.[13 21] Approximately 1 in 5 Chinese adults aged 18 years or older (approximately 230 million people) have CVD, the prevalence of which is expected to double in the next decade.[22 23] Beyond the expected rise in CVD associated with longer life expectancy,[24] other factors such as urbanisation,[25] environmental pollutants[26–28] and sociocultural shifts,[29] have been associated with the increasing prevalence of obesity,[30] hypertension,[31] diabetes[32] and smoking,[33] though their relationship with CVD in China has not been well described.[34 35] To date, there are few contemporary, prospective, population-based studies to identify factors associated with heart disease and stroke in the Chinese population.[36 37]

Accordingly, the Qingdao Port Group and its affiliated hospital, Qingdao Fuwai Hospital, established the Qingdao Port Cardiovascular Health Study in 2000, a prospective cohort study of employees of the Group, with the aims of monitoring the incidence of CVD and associated risk factors, and identifying risk factors associated with the incidence of CVD and cardiovascular outcomes. Knowledge gained from this study will be used to guide China's efforts in preventing and managing heart disease and stroke. In this paper, we describe the design, cohort and investigational priorities of the Qingdao Port Cardiovascular Health Study.

COHORT DESCRIPTION
Study design and investigational priorities
The Qingdao Port Cardiovascular Health Study was started in 2000. The study is designed to monitor CVD trends and to understand risk factors contributing to chronic conditions with a focus on heart disease and stroke.[38 39] Specifically, the main investigational priorities are: (1) surveillance of cardiovascular risk factors, disease and outcomes; (2) investigation of sociocultural, biological, behavioural, social and environmental factors on work productivity, CVD onset and CVD health outcomes; (3) development and validation of risk models to predict cardiovascular events; and (4) genetic and proteomic analysis of biological samples to elucidate disease mechanisms and inherited risk profiles.

Setting, recruitment and eligibility
The Qingdao Port Group of the Shandong province in China is one of the oldest and largest shipping and trade companies in the world (figure 1). The workforce is diverse, with administrative personnel, technical personnel (eg, pilots, computer analysts and information technology

Figure 1 Examination sites for the Qingdao Port Cardiovascular Health Study.
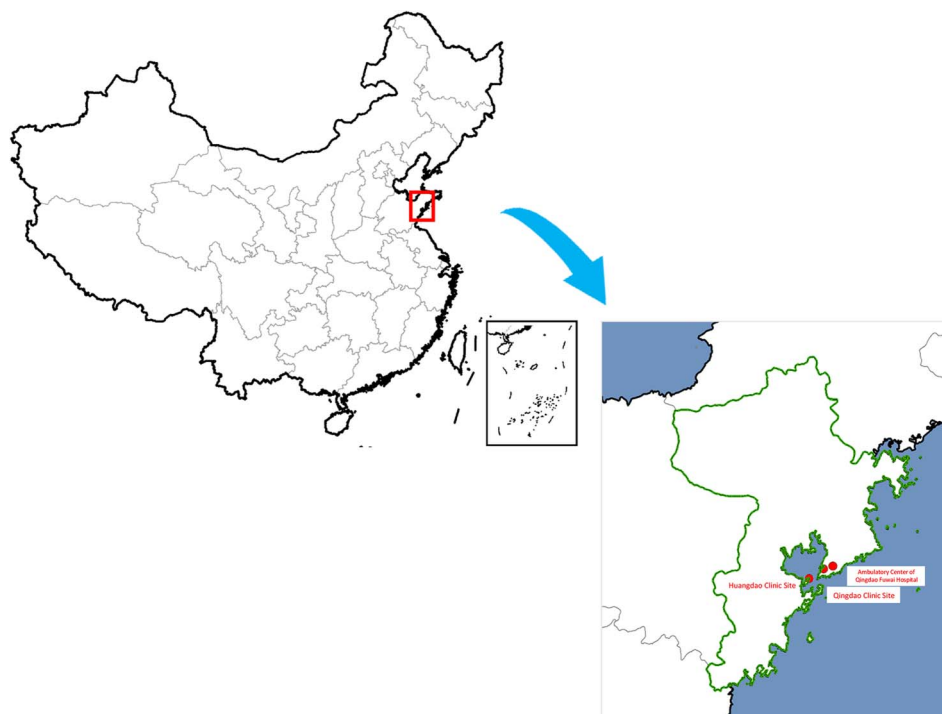
specialists, police, teachers, physicians, nurses and other hospitals staff), production operators, ship workers, dock-workers and drivers. Among them, ship workers and dock-workers account for the majority of all staff.

The company contributes to each employee's health insurance plan, which is administered by the Qingdao Medical Insurance Bureau. The plan covers annual health assessments, on-site ambulatory medical care and coverage of inpatient services rendered at the Qingdao Fuwai Hospital—the local hospital and partner in this study—as well as other public hospitals in Qingdao city. All employees aged 18 years or older, who present for an annual health assessment, are eligible for study participation. The only exclusion is workers who are migrant, as they are not covered by the local health insurance and do not receive annual health examinations, effectively rejecting them from study participation.

Prior to 2013, employees were verbally asked to participate. Since then, however, employees sign an informed consent document prior to enrolment (see online supplementary appendix 1: translated informed consent document). Among the employees who present for a health assessment, almost all (98%) agreed to participate in the study. At each annual visit, employees renew their agreement to participate. Participants are informed that the data are confidential.

The annual health assessments, offered at the three work sites, serve as the platform for data collection. The organisational structure for the study is presented in figure 2.

Health assessment components

Annual health assessments, which are performed by 35 trained physicians and nurses, consist of a questionnaire, physical examination, ECG, laboratory testing and bio-sampling. In 2013, echocardiography and carotid ultrasound were additionally performed, and bio-samples were collected for future analysis. Currently, there are 466 unique variables summarised by domain in online supplementary appendix 2.
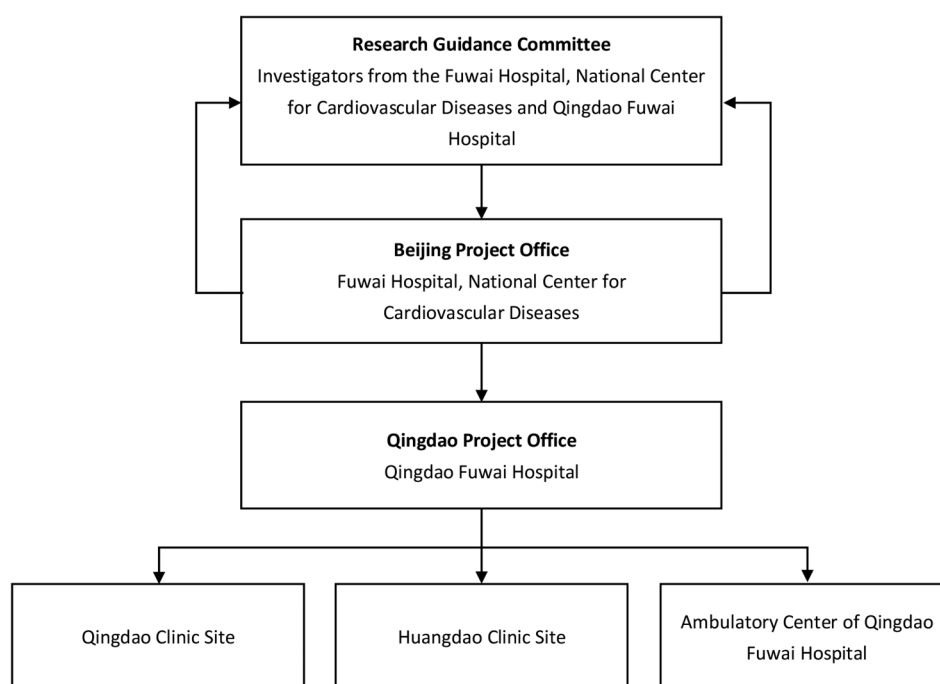
Questionnaire

A standardised questionnaire is administered by trained personnel during a face-to-face annual health assessment (see online supplementary appendix 3). Questions are adapted from prior epidemiological studies[40] and, when available, questionnaires validated in Chinese are used.[41] The following domains are assessed: demographics (eg, income, education, family structure); personal medical history (eg, medical history, medication use and adherence); family history; health behaviours (eg, nutritional intake; physical activity;[42] smoking; alcohol use/abuse); healthcare utilisation (eg, hospitalisations; use of traditional Chinese medicine); menopause (including hormone use); emotional health (eg, anxiety, stress); and employment structure (eg, physical labour; shift-work).

Physical examination

A detailed, comprehensive physical examination is conducted at baseline by trained medical staff. Nurses measure height, weight, waist circumference, hip circumference, blood pressure and heart rate. Physicians perform a detailed eye and ear examination, dental assessment, thyroid palpation, cardiopulmonary auscultation and abdominal examination. Nurses and physicians follow standardised protocols for measurement and examination. Height (cm), weight (kg), and waste and hip circumferences are measured using sonographic

Figure 2 Organisational structure of the Qingdao Port Cardiovascular Health Study.

Research Guidance Committee
Investigators from the Fuwai Hospital, National Center for Cardiovascular Diseases and Qingdao Fuwai Hospital

Beijing Project Office
Fuwai Hospital, National Center for Cardiovascular Diseases

Qingdao Project Office
Qingdao Fuwai Hospital

Qingdao Clinic Site

Huangdao Clinic Site

Ambulatory Center of Qingdao Fuwai Hospital

technology (Ultrasound Height & Weight Machine, TCS-160D-W/H, Shenzhen Sonka Electronic Technology Co, Ltd, Guangdong, China), averaged to the nearest 0.1 unit. Instruments are calibrated weekly with phantom mannequins. Blood pressure and heart rate are measured after the patient has been seated for 5 min, using a calibrated electronic sphygmomanometer. Blood pressure measurement is performed by placing the cuff on the dominant arm, at the level of the heart, and taking the average of three measurements spaced 1 min apart. Heart rate is recorded contemporaneously with each blood pressure measurement.

Laboratory tests
Venipuncture, performed by trained nurses, is obtained annually. Some blood chemistries are repeated each year (eg, fasting glucose, lipid profile, creatinine). Tests performed intermittently include liver and thyroid function.

Bio-samples for future analysis
Since 2013, participants have been invited to submit bio-samples, including blood, urine and saliva samples, for storage, to be used for future DNA, RNA and biochemical analysis. Over 90% of study participants have consented to date. Whole blood samples are drawn into EDTA, serum gel, heparin lithium and Tempus blood RNA tubes (Applied Biosystems, Foster City, California, USA) for future gene expression analysis. When stored in Tempus tubes at −80°C, the whole blood RNA retains high integrity and purity for over a 6-year period.[43] To collect saliva, participants are asked to chew a cotton roll for 45 s; the cotton roll is placed into a Salivette tube (Sarstedt AG & Co, Nümbrecht, Germany). Within 24 h, trained nurses centrifuge blood and saliva samples, and divide and transfer the samples into cryovials, according to standard protocol. Urine is transferred directly into

cryovials. All samples are immediately stored at −80°C, and are transported to Fuwai Hospital, National Center for Cardiovascular Diseases (NCCD), for long-term storage, within 2 months.

Additional testing
ECG is performed every year. Additionally, specific cardiovascular screening tests were conducted during different years including: chest X-ray, echocardiogram and carotid ultrasound. All imaging tests are conducted by certified technologists in accordance with standards set forth by the Ministry of Health.

Follow-up
Follow-up health assessments are performed annually. While the employee population is dynamic, among the 32 404 study participants from 2000 to 2013, more than half (18 111; 55.9%) have 5 or more years of follow-up; 11 537 (35.6%) participants have 10 or more years of follow-up (figure 3). Of the original cohort of 11 201 people who started in 2000, 7433 were not participating in annual follow-up as of 2013. For example, among 22 128 study participants who enrolled between 2000 and 2010, 3280 (14.8%) had no follow-up visit after 2011 and before the end of the 2013 measurement period. These employees may have left the company or declined further participation; it is also possible, though less likely, that they missed three consecutive visits and will return in 2014. Distinguishing individuals with interrupted visits from permanent drop-outs is a goal for the future (table 1).

The components of the follow-up visit are the same as the baseline assessment and include a face-to-face interview, physical examination, laboratory testing and imaging examinations specified for that year. New participants are recruited each year (figure 4) and, since
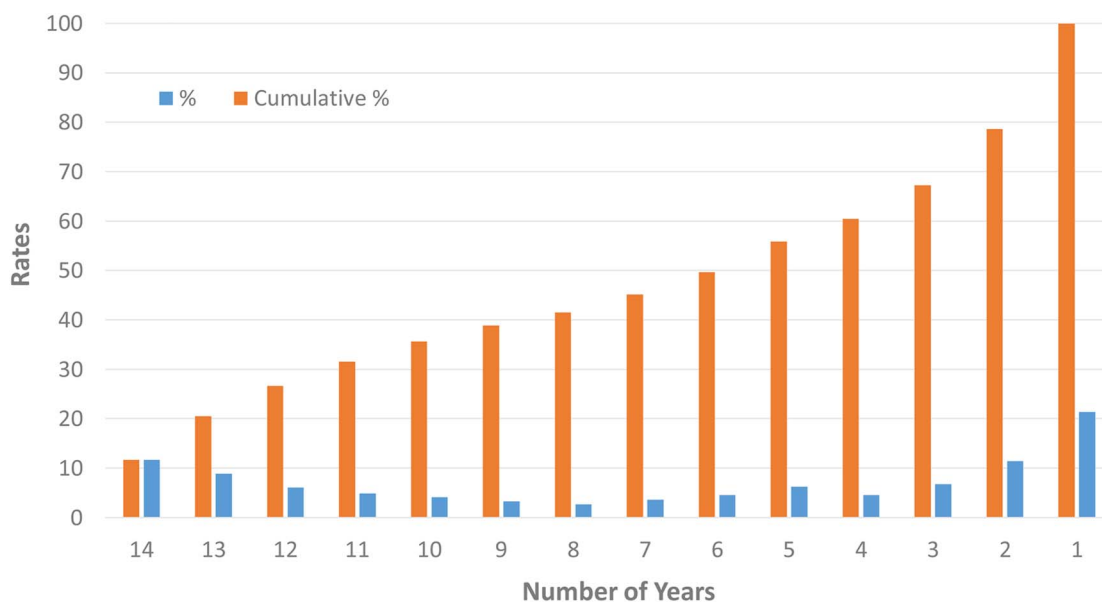

Figure 3 Distribution of frequency of study participant follow-up.

Table 1 Follow-up among study participants

Description	Total cohort	Returning participants	Non-returning participants	
			N	**Percent**
2000 to 2001–2013	11 201	11 201	0	0.00
2000–2001 to 2002–2013	12 363	12 260	103	0.83
2000–2002 to 2003–2013	13 474	13 291	183	1.36
2000–2003 to 2004–2013	15 849	15 212	637	4.02
2000–2005 to 2006–2013	16 614	15 637	977	5.88
2000–2006 to 2007–2013	17 136	15 838	1298	7.57
2000–2007 to 2008–2013	17 963	16 263	1700	9.46
2000–2008 to 2009–2013	18 947	16 833	2114	11.16
2000–2009 to 2010–2013	20 221	17 476	2745	13.57
2000–2010 to 2011–2013	22 128	18 848	3280	14.82
2000–2011 to 2012–2013	22 670	18 775	3895	17.18
2000–2012 to 2013	24 636	18 521	6115	24.82

2003, participants have or are being followed into retirement, up until death. In China, the statutory retirement age for general workers is 60 years for men and 50–55 years for women, depending on their job position. Among heavy labourers, the retirement age is 55 years for men and 45 years for women. Senior professionals may work until the age of 65–70 years. Since 2003, retirees account for approximately one-quarter of all annual health assessments each year, with approximately 7000 retirees in the study.

Outcomes

The following cardiovascular outcomes are collected: unstable angina; acute myocardial infarction; revascularisation with either percutaneous coronary intervention or coronary artery bypass grafting; heart failure; stroke; and all-cause death. As part of the annual health questionnaire, participants are asked to report information on newly diagnosed diseases, hospitalisations and treatments that occurred in the previous year. Self-reported health outcomes are actively being linked with medical claims data; since all employees have the same insurance plan, complete insurance claims data are available for all years except 2000 and 2001, years in which not all employees were insured with the same plan. Additionally, since 2013, medical claims have been linked with health assessment data every 3 months, independent of whether participants self-reported a clinical outcome. From the medical claims, the following information is abstracted: admission date, discharge date, discharge diagnoses and corresponding International Classification of Disease (ICD) codes; and discharge status. Deaths are monitored by the insurance plan and shared with the Qingdao Port Company and study
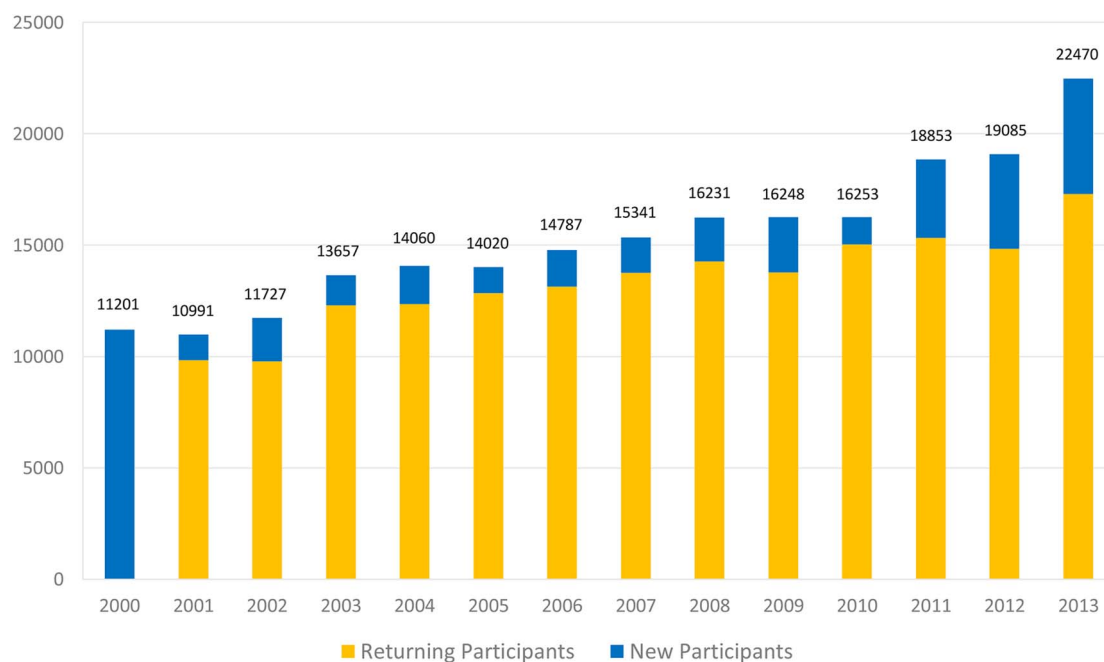
Figure 4 Distribution of new and returning study participants per year.

group, which prompts the collection of death certificates and autopsy reports to elucidate the cause of death. Hospital medical records are also assessed to verify cause of death. If hospitalisation records or other supportive records are not available, interviews with the person's relatives and physicians are conducted to acquire the date and cause of death.

Efforts are underway to adjudicate a subset of outcomes using hospital medical records. In 2013, 855 participants reported hospitalisations, 300 of which were reported to have occurred at Qingdao Fuwai Hospital, all of which were verified. Among patients who reported being hospitalised outside of Qingdao Fuwai Hospital (n=555), medical records from 246 participants were obtained. These records came directly from participants, though there are efforts to develop a process that will enable the direct collection of study participants' medical records from outside hospitals. Consistent with other cardiovascular research protocols,[44] adjudicators will review the clinical diagnosis and the claims-based ICD code, and compare them with self-reported data. Discrepancies between the medical record and claims data are resolved by the research guidance committee in Fuwai Hospital, NCCD.

Quality assurance and control

All research staff participate in 2 days of intensive training focused on administering the questionnaire and learning the protocols for blood pressure measurements, anthropometry, blood collection and sample processing, ECG and data entry. Further operational training is conducted at the study sites. Each year, all equipment, including the biochemical analyser, ultrasound machine, X-ray machine, electronic sphygmomanometer and ultrasound stadiometers are tested and calibrated by the Qingdao Institute of Measurement and Testing and the Qingdao Institute of Weighing Apparatus Management; annual calibration certificates by these two institutes are required. The validity of all measurements is checked monthly by examination of data outliers and missing fields. Additionally, site monitoring is conducted by two trained research staff members from Fuwai Hospital, NCCD, every 3–6 months, assessing: (1) the completeness of the documentation and (2) fidelity to protocol for recruitment, health screening, physical examination, and sample collection and processing. Finally, annual meetings are held to discuss problems with measurement and data entry, and to optimise study processes.

To improve the validity and reliability of the measurement of cardiovascular risk factors, questions were adapted from prior epidemiological studies in China, such as questions assessing smoking and dietary patterns.[40] In 2013, questionnaires that were previously validated in Chinese were incorporated. We used the Alcohol Use Disorders Identification Test (AUDIT) questionnaire to identify persons with hazardous and harmful patterns of alcohol consumption,[41] the International Physical Activity Questionnaire (IPAQ) to

assess physical activity[42] and the EuroQoL (EQ-5D) to measure health status.[45]

The definition of hyperlipidaemia changed from earlier years in accordance with the level of data available. For example, in some prior years, no blood lipid tests were performed; in these years, only self-report and medication use were used to define hyperlipidaemia. Since 2010, hyperlipidaemia has been defined as: either self-report of high cholesterol or dyslipidaemia (either: total cholesterol ≥5.2 mmol/L or low-density lipoprotein ≥3.4 mmol/L or high-density lipoprotein <1.0 mmol/L or triglycerides ≥1.7 mmol/L) or use of a lipid-lowering medication.

From 2000 to 2012, data were collected on paper and double-entered by two different researchers into a computer-based system, to reduce error. Since 2013, results from the questionnaire, physical examination, laboratory testing and other examinations have been collected electronically with an internet-based data management system developed specifically for the study. To increase the validity and reliability of the data, this system includes predefined data formats, predetermined data ranges for quantitative data, and required fields. After research personnel enter the data, internal data checks are performed to confirm that the data are correctly entered. Finally, prior to the beginning of each measurement year, all personal information is verified (name, sex, ID number, work ID, company, department, contact telephone number and address); these steps improve the accuracy of participants' information, decrease the duration of face-to-face interview time and facilitate linkage with medical insurance records.

Data security and management

All data are treated as protected health information, and are securely stored in an encrypted and password-protected database. Laptops are password protected, and all research personnel have individual passwords to login to the system. All data between the three sites are independent, which means research personnel only have access to the data collected at their own site.

All source data, including questionnaires, health assessment results, hospitalisation and clinical medical records, are securely stored in the three clinic sites of the Qingdao Fuwai Hospital. The electronic version of the files as well as the image files of ECG and chest X-rays are securely stored on the servers of Qingdao Fuwai Hospital. The Research Guidance Committee, comprised of investigators from the Fuwai Hospital, NCCD, and Qingdao Fuwai Hospital, make the ultimate decisions on the usage of the data, governed by institutional review board approval.

Cohort

From 2000 through 2013, a total of 32 404 study participants contributed 221 923 health assessments. In this cohort, the mean age was 43.4 (SD=12.9); 79% were male, consistent with the demographics of the company.

Participants ranged in occupation: loading/unloading (9.7%); warehouse clerk (8.0%); ship crew (18.8%); other shipping and dockworkers (29.9%); management (19.9%); other (13.7%).

Findings to date

Table 2 compares cardiovascular risk factors across three time periods (2000 to 2005 to 2010), demonstrating an increased prevalence of hypertension (26.4% to 38.6% to 39.4%) and diabetes (3.3% to 5.9% to 8.9%), respectively. The 2005 estimates for hypertension and diabetes are similar to those observed in the 2005 International Collaborative Study of CVD in Asia (InterAsia).[46] Rates

of hyperlipidaemia increased from 5% to 12.4% to 33.6% across study years; however, full blood lipid panels were not conducted between 2001 and 2006. These rates are lower than those observed in a meta-analysis in which 41% of community-residing adults had dyslipidaemia.[47]

Strengths and limitations

The Qingdao Port Cardiovascular Health Study is uniquely positioned to measure disease incidence and trends, characterise the complex relationships between biology, environment, culture and behaviour with disease onset, trajectories and outcomes, and ultimately

Table 2 Trends in characteristics of study participants (2000–2010)

Description	2000		2005		2010	
	n	Percent	n	Percent	n	Percent
Total participants	12 023		14 152		16 378	
Retirees	NA	NA	3369	23.8	4594	28.1
Demographics						
Age (mean; SD)	39	8.7	45	12.0	45	13.7
Gender						
Male	9227	76.7	10 945	77.3	13 076	79.8
Female	2796	23.3	3207	22.7	3302	20.2
Cardiovascular profile						
High blood pressure*						
Yes	3176	26.4	5457	38.6	6451	39.4
Missing	0	0	4	<0.1	4	<0.1
Diabetes†						
Yes	396	3.3	838	5.9	1458	8.9
Missing	0	0	0	0	4	<0.1
Hyperlipidaemia‡						
Yes	600	5.0	1749	12.4	5499	33.6‡
Missing	0	0	565	4.0	4	<0.1
Acute myocardial infarction						
Yes	NA	NA	66	0.5	128	0.8
			50	0.4	301	1.8
Stroke						
Yes	66	0.5	130	0.9	188	1.1
Missing	3	<0.1	49	0.4	320	2.0
Anthropometrics						
Waist (cm)						
Mean (SD)	81.6	11.2	83.9	9.6	86.6	12.3
Missing	0	0	292	2.1	215	1.3
BMI (cm/kg^2)						
Missing	25	0.2	277	2.0	190	1.2
Normal body weight (<24)	5852	48.7	5317	37.6	6313	38.6
Overweight (24 to <28)	4456	37.1	5972	42.2	6831	41.7
Obese (≥28)	1690	14.1	2586	18.3	3044	18.6
Systolic blood pressure						
Missing	0	0	58	0.4	63	0.4
Mean (SD)	121	17.1	122	18.3	125	20.9
Diastolic blood pressure						
Mean (SD)	80	12.1	82	11.6	82	11.2

*Self-report or mean blood pressure ≥140 systolic or ≥90 mm Hg diastolic or antihypertensive medication therapy.
†Self-report or fasting glucose ≥7.0 mmol/L or glucose-lowering medication.
‡Self-report or lipid-lowering therapy for year 2000; self-report only for year 2005; self-report or dyslipidaemia (either: total cholesterol ≥5.2 mmol/L or low-density lipoprotein ≥3.4 mmol/L or high-density lipoprotein <1.0 mmol/L or triglycerides ≥1.7 mmol/L) or lipid lowering medication therapy for year 2010.
BMI, body mass index; NA, not available.

inform the approach to CVD prevention and population health, especially among China's urban, working population. Knowledge generated from the population of the Qingdao Port Cardiovascular Health Study will have broad implications for China's workforce and for employer-based healthcare, where large employers contract with health systems to provide comprehensive healthcare services to their employees, including health screenings, outpatient medical care and inpatient services. In 2006, approximately 160 million people (about 28% of the urban population) were covered by employer-based health insurance.[48] This study, which aligns research objectives with current health challenges, is embedded in the employer-based health services model, and can thereby foster knowledge dissemination and translation among such employers. Importantly, the rigorous methodological design and health data collection, follow-up into retirement, and linkage of health screening data with insurance claims and medical records, will provide a rich opportunity to investigate disease trajectories and outcomes, and inform approaches to population-based healthcare delivery. Other Chinese population-based studies, such as the China National Diabetes and Metabolic Disorders Study (2007–2008), while nationally representative, are cross-sectional and less comprehensive.[18 47] The Singapore Chinese Health Study[49] and the Chinese Health and Retirement Longitudinal Study (CHARLS)[50] provide data on older populations, though they are not focused on CVD and have limited follow-up data. To date, there are no longitudinal, population-based cardiovascular studies of the urban, working population of China. The study is supported by the Fuwai Hospital, NCCD—a clinical research group with longstanding expertise in standardised data abstraction, cataloguing and linkage, ensuring excellent quality control, and organisation for scientific investigation.[51–53]

There are some limitations to this study. The population represents a single company and may not be representative of the larger population of China. Additionally, employed individuals may be healthier than the general population, which may influence the relationship between risk factors and disease onset. However, the study subjects from the Qingdao Port Company are from diverse sectors of the workplace; moreover, the data set is rich with health behaviours and socioeconomic information, which may account for variation in associations within the population. The focus on an employee population is consistent with new models of knowledge discovery and health promotion.[54] Additionally, longitudinal follow-up of a stable population has the advantage of allowing for insights into risk trajectories and outcomes. Second, participants are recruited from an annual health screening, and so we lack information about employees who are eligible but do not participate in the health screening. However, very few employees decline participation; nonetheless, processes for collecting this information are being developed. Related to

this, it is possible that, in some cases, responses to the interview questions might be influenced by the participants' perceptions that their answers might affect their employment status. Third, the collection of outcomes for any longitudinal study is a challenge. The current mechanisms, including self-report and claims data of services rendered through the Qingdao Medical Insurance Bureau are already more advanced than most population-based studies. In the first year of attempting to obtain medical records, over half were successfully obtained. Further efforts are needed to improve this proportion, though this can be accomplished. Additionally, the ascertainment of claims data allows for extensive utilisation and cost analyses, which are unique to this study.

Collaboration

The Qingdao Port Cardiovascular Study is ongoing, with increasing capacity to adjudicate cardiovascular outcomes, enhancing self-reported outcomes with insurance claims data and hospital medical records. The publications committee and data analytic centre are comprised of researchers from the NCCD, Fuwai Hospital, Beijing, and from Yale University—two institutions with a long-standing partnership and commitment to improving cardiovascular health in China. At this time, all research will be conducted in collaboration with the study investigators. Prospective collaborators are encouraged to contact either JLu (jiapeng.lu@fwoxford.org) or ESS (Erica.spatz@yale.edu).

China's unique position of being a low-income to middle-income country with significant intellectual resources—as well as shared goals between academic, private and public domains—can provide important lessons to the world on the effects of globalisation and the tools needed to protect the health of the public. Longitudinal, population-based studies play an important part in this learning. The Qingdao Port Cardiovascular Health Study is designed to fill these knowledge gaps, and to provide important insights for the public and healthcare system at large.

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The Qingdao Port Cardiovascular Health Study

Consent Form

Name: _____   ID Number:_____   Employee ID:_____

Date of birth: _____Year____Month___Day   Gender: ○ Male   ○ Female

- ➤ I understand the objective and contents of the study. I understand the study does not involve any intervention to me.
- ➤ I have asked questions and these have been answered satisfactorily. I have had enough time to consider whether I will take part in the study.
- ➤ I understand that I have the opportunity to ask questions during the study at any time.
- ➤ I understand that my participation is voluntary and that I am not required to take part in the study and that I am free to quit at any time for any reason without my legal rights being affected. If I quit the study, I understand that I will not receive questionnaire surveys or provide bio-samples in the future.
- ➤ I understand I will receive questionnaire surveys and will give blood, urine and saliva bio-sample over the course of the study.
- ➤ I provide permission that my blood and urine samples be taken for long-term storage, and not be tested immediately. I agree to that these bio-samples can be tested for genetics and other kinds of analyses in the future. I understand these analyses are being conducted for medical research, and the results will be kept confidential.
- ➤ I understand that the information collected about me for this study will be kept secure and confidential. It will be stored on encrypted databases at Qingdao Fuwai Hospital and the National Center for Cardiovascular Diseases, Fuwai Hospital.
- ➤ I understand that authorized researchers from the research management committee may review sections of my medical records and other health related information. I give permission for these individuals to have access to my records on the understanding that this will be done in confidence.

I am delighted to take part in the Qingdao Port Cardiovascular Health Study

_____   _____   _____
Printed name of employee   Signature   Today's date

_____   _____   _____
Printed name of person providing consent   Signature   Today's date

The Questionnaire of the Qingdao Port Cardiovascular Health Study

A.	NIGHT SHIFT

A.1 Do you always have a night shift?
○ Yes
○ No

A.2 [If A1 "yes"] How many times per month? ____

A.3 [If A1 "yes"] The average time of each night shift? ____

A.4 Whether attend the health check clinic right after a night shift?
○ Yes
○ No

B.	SOCIAL ECONOMIC STATUS

B.1 Your highest achieved education is:
○ Illiteracy/semi-illiteracy
○ Primary school
○ Junior high school
○ Senior high school (technical school or technical secondary school)
○ College (junior college)
○ Postgraduate
○ Unknown
○ Refuse to answer

B.2 What is/was your primary occupation:
○ Workers (Docker, driver, sailor, etc.)
○ Administrators or managers (middle-senior manager in government or company)
○ Professionals or technicians (financial staff, engineer, doctors, etc.)
○ Administrative clerk
○ Service personnel (Sailor, chef, etc.)
○ Soldier
○ Retiree

B.3	Have you sent text messages using a cell phone? ○ Yes ○ No ○ Unknown ○ Refuse to answer
B.4	Do you browse the web? ○ Yes ○ No ○ Unknown ○ Refuse to answer
B.5	What's your primary way to gain health-related knowledge? ○ TV ○ Internet ○ Broadcast ○ Newspapers or magazines ○ Books or pamphlets ○ Posters ○ Lectures or lessons ○ Talking with others ○ None or unknown ○ Refuse to answer
B.6	Who's your primary source of health-related knowledge? ○ Health professionals ○ Families ○ Friends ○ Others ○ Unknown ○ Refuse to answer
B.7	Current marital status: ○ Married ○ Divorced /Separated ○ Widowed ○ Single ○ Refuse to answer
B.8	Including you, there are currently _ _ people living together in your family (sharing the household income in the last year)
B.9	What was your total household income in the last year? ○ < ¥10000 ○ ¥10000 - 29999 ○¥ 30000 - 49999 ○ ¥50000 - 69999 ○ ¥70000 - 99999 ○≥ ¥100000 ○ Unknown ○ Refuse to answer
C.	**MEDICAL HISTORY**
C.1	Main reason for admission during the past year*[one by one]*

C.2	Which of the following diseases have you been diagnosed as? *[Check all that apply]* □ Angina, the year of diagnosis____ □ MI, the year of diagnosis____ □ Heart Failure, the year of diagnosis____ □ Valve diseases, the year of diagnosis____ □ Arrhythmias, the year of diagnosis____ □ Ischemic stroke, the year of diagnosis____ □ Hemorrhagic stroke, the year of diagnosis____ □ Diabetes, the year of diagnosis____ □ Hypertension, the year of diagnosis____ □ Dyslipidemia, the year of diagnosis____ □ Chronic kidney diseases, the year of diagnosis____ □ Chronic lung diseases, the year of diagnosis____ □ PCI, the year of latest intervention ____ □ CABG, the year of latest operation ____ □ Other cardiac surgery ____
D.	**SECONDARY PREVENTION**
D.1	Secondary prevention medications of CVD during the past year (name, daily dosage) *[one by one]*
D.2	In the past month, how often did you miss a dose of the medication? ○ Never ○ Once ○ 2-3 times ○ Once per week ○ 2-5 times per week ○ Everyday or nearly everyday ○ Unknown ○ Refuse to answer
E.	**TCM USE**
E.1	During the past year, have you ever been to TCM clinics or seen TCM doctors? ○ No **[JUMP TO E3]** ○ Yes ○ Unknown **[JUMP TO E3]** ○ Refuse to answer **[JUMP TO E3]**

E.2   Which ones do you agree to? *[Check all that apply]*
□ The TCM doctors are easier to see
□ My family has always used TCM
□ Explanations from the TCM doctor are more satisfactory
□ The TCM approaches are more effective
□ The TCM approaches are safer
□ The TCM approaches are less expensive
□ I see TCM doctors just to recuperate
□ I go to TCM clinics in addition to western medicine clinics, not instead of them
□ None above

E.3   During the past year, have you ever taken TCM medications?
○ No **[JUMP TO E5]**   ○ Yes   ○ Unknown **[JUMP TO E5]**   ○ Refuse to answer **[JUMP TO E5]**

E.4   **[IF E3 "YES"]** Have you ever taken TCM medications for specific health problems?
○ No   ○ Yes, please specify: _____   ○ Unknown   ○ Refuse to answer

E.5   During the past year, have you ever accepted TCM physiotherapy (acupuncture, massage, cupping, etc.)?
○ No **[JUMP TO F1]**   ○ Yes   ○ Unknown **[JUMP TO F1]**   ○ Refuse to answer **[JUMP TO F1]**

E.6   **[IF E5 "YES"]** Have you ever accepted TCM physiotherapy (acupuncture, massage, cupping, etc.) for specific health problems?
○ No   ○ Yes, please specify: _____   ○ Unknown   ○ Refuse to answer

E.7   **[IF E3 or E5 "YES"]** Have you ever decided to stop or skip medications because you are using TCM medications and interventions instead?
○ No   ○ Yes   ○ Unknown   ○ Refuse to answer

F.   FAMILY HISTORY

F.1   In your father and brothers, did anyone have any of the following diseases before his 55? *[Check all that apply]*
□ CHD
□ Stroke
□ Diabetes
□ Cancers
□ None above

F.2	In your mother and sisters, did anyone have any of the following diseases before his 65? *[Check all that apply]*
	□ CHD
	□ Stroke
	□ Diabetes
	□ Cancers
	□ None above

G. DIETARY

During the past year, how often did you have the following food?

	Food	Daily	4-6 d/w	1-3 d/w	1-3 d/m	<1 d/m
G.1	Rice: including rice, rice porridge and rice noodle	o	o	o	o	o
G.2	Wheaten food: wheat flour produced or processed into various types of food, such as noodles, steamed buns, bread, and pie	o	o	o	o	o
G.3	Grains: all other food crops except wheat and rice, including millet, maize, sorghum	o	o	o	o	o
G.4	Meat and meat products	o	o	o	o	o
G.5	Poultry and poultry products	o	o	o	o	o
G.6	Aquatic/seafood and the products: including freshwater fish, shrimp, crab, and saltwater fish, shrimp, crab, and a variety of shellfish (fresh, frozen or processed)	o	o	o	o	o
G.7	Eggs: fresh eggs or egg products (such as preserved eggs, salted eggs)	o	o	o	o	o
G.8	Fresh vegetables	o	o	o	o	o
G.9	Pickles, sauerkraut, preserved vegetables, pickled vegetables	o	o	o	o	o
G.10	Fresh fruit	o	o	o	o	o
G.11	Soy foods: various types of soy products (including tofu) and beverages (including soy milk) with soybean as raw material	o	o	o	o	o

G.12	Milk and dairy food: milk, goat's milk, yogurt, cheese, milk powder and pure dairy products	○	○	○	○	○

G.13	During the past year, have you ever taken the following types of nutritional supplements for at least a month? *[Check all that apply]* □ Cod liver oil / fish oil □ Vitamins □ Calcium / iron / zinc preparations □ Traditional Chinese health products □ None of the above

H. SMOKING

H.1	Which of the following best describes your current cigarette smoking status? ○ Never smoked **[go to H4]** ○ I stopped smoking more than 1 year ago **[go to H4]** ○ I stopped smoking between 1 month and 1 year ago **[go to H4]** ○ Smoked in the past 30 days ○ Unknown **[go to H4]** ○ Refuse to answer **[go to H4]**
H.2	**[If smoked in the past 30 days or stopped smoking more than 1 month ago]** On average you smoke _ _ cigarettes per day in the last month. ○ Unknown ○ Refuse to answer
H.3	**[If smoked in the past 30 days or stopped smoking more than 1 month ago]** How old were you when you began smoking regularly? _ _ ○ Unknown ○ Refuse to answer
H.4	_ _ _ hours per week are you exposed to others' tobacco smoke on average in the past month. ○ Unknown ○ Refuse to answer
H.5	Is there remarkable change in the amount of the cigarettes you smoked compared to 1 year before? ○ Significantly more ○ Significantly less ○ no changes ○ unknown

I. ALCOHOL DRINKING

I.1	During the past 1 year, How often do you have a drink containing alcohol? ○ Never **[go to I9]** ○ Monthly or less ○ 2 to 4 times a month ○ 2 to 3 times a week ○ 4 or more times a week ○ Unknown ○ Refuse to answer **1 DRINK is 17ml pure alcohol, which equals to 120ml wine, or 360ml beer (half a bottle or 1 tin), or 45ml liquor (1 LIANG)**

I.2	How many drinks containing alcohol do you have on a typical day when you are drinking?
	○ 1 or 2 ○ 3 or 4 ○ 5 or 6 ○ 7, 8, or 9 ○ 10 or more ○ Unknown ○ Refuse to answer

I.3   How often do you have six or more drinks on one occasion?

○ Never   ○ Less than monthly   ○ Monthly   ○ Weekly   ○ Daily or almost daily   ○ Unknown   ○ Refuse to answer   **[Skip to Questions I9 if I2 "1 or 2" AND I3 "Never"]**

How often during the last year have you found

		Never	Less than monthly	Monthly	Weekly	Daily or almost daily
I.4	not able to stop drinking once you had started?	○	○	○	○	○
I.5	failed to do what was normally expected from you because of drinking?	○	○	○	○	○
I.6	Needed a first drink in the morning to get yourself going after a heavy drinking session?	○	○	○	○	○
I.7	had a feeling of guilt or remorse after drinking?	○	○	○	○	○
I.8	unable to remember what happened the night before because of your drinking?	○	○	○	○	○

I.9   Have you or someone else been injured as a result of your drinking?

○ No   ○ Yes, but not in the last year   ○ Yes, during the last year   ○ Unknown   ○ Refuse to answer

I.10   Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?

○ No   ○ Yes, but not in the last year   ○ Yes, during the last year   ○ Unknown   ○ Refuse to answer

I.11   Is there remarkable change in the amount of the alcohol you drank compared to 1 year before?

○ Significantly more   ○ Significantly less   ○ no changes   ○ unknown

J.   PHYSICAL ACTIVITIES

J.1	***Vigorous*** *physical activities refer to activities that take hard physical effort and make you breathe much harder that normal.* During the last 7 days, on how many days did you do <u>**vigorous**</u> physical activities like heavy lifting, digging, aerobics, or fast bicycling,? Think about *only* those physical activities that you did for at least 10 minutes at a time ○ none [go to J3]　　○ 1 day　　○ 2 day　　○ 3 day　　○ 4 day　　○ 5 day　　○ 6 day　　○ 7 day
J.2	How much time in total did you usually spend on one of those days doing **vigorous** physical activities? ____hours____minutes
J.3	***Moderate*** *activities refer to activities that take moderate physical effort and make you breathe somewhat harder that normal.* Again, think *only* about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do <u>**moderate**</u> physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking. ○ none [go to J5]　　○ 1 day　　○ 2 day　　○ 3 day　　○ 4 day　　○ 5 day　　○ 6 day　　○ 7 day
J.4	How much time in total did you usually spend on one of those days doing **moderate** physical activities?○ Yes　　____hours____minutes
J.5	During the last 7 days, on how many days did you <u>**walk**</u> for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did solely for recreation, sport, exercise or leisure. ○ none [go to J7]　　○ 1 day　　○ 2 day　　○ 3 day　　○ 4 day　　○ 5 day　　○ 6 day　　○ 7 day
J.6	How much time in total did you usually spend **walking** on one of those days? ____hours____minutes
J.7	The last question is about the time you spent **sitting** on weekdays while at work, at home, while doing course work and during leisure time. This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television. During the last 7 days, how much time in total did you usually spend **sitting** on a **week day**? ____hours____minutes
J.8	Is there remarkable change in your weight compared to 1 year before? ○ Significantly more　　　○ Significantly less　　　○ no changes　　　○ unknown
J.9	During the past year, have you ever tried to control your weight by dieting or taking medicine? ○ Yes　　○ No　　○ Unknown　　○ Refuse to answer
J.10	When you were about 25 years old, what was your weight? _ _ _ kg　　○ unknown
K.	**MENSTRUAL HISTORY**
K.1	**[If female]** Menopause？ ○ Yes　　○ No　○ Unknown　　○ Refuse to answer

K.2	**[If K1 "Yes"]** The age of menopause _ _ _ yr o unknown
K.3	**[If K1 "Yes"]** Estrogen replacement treatment? o Yes o No o Unknown o Refuse to answer

L.	**HEALTH-RELATED QUALITY OF LIFE (EQ-5D)**
	The following questions ask about your current health state. In each of the following categories, please indicate which statement best describes your own health state today.
L.1	Mobility o I have **no** problems in walking about. o I have **some** problems in walking about. o I am **confined to bed**.
L.2	Self-care o I have **no** problems with self-care. o I have **some** problems washing or dressing myself. o I am **unable to wash or dress myself**.
L.3	Usual activities (e.g., work, study, housework, family or leisure activities) o I have **no** problems with performing my usual activities. o I have **some** problems with performing my usual activities. o I am **unable to perform my usual activities**.
L.4	Pain/discomfort o I have **no** pain or discomfort. o I have **moderate** pain or discomfort. o I have **extreme** pain or discomfort.
L.5	Anxiety/depression o I am **not** anxious or depressed. o I am **moderately** anxious or depressed. o I am **extremely** anxious or depressed.
L.6	Please **score** how good or bad your own health is the week before this admission. The best state you can imagine is 100 and the worst health state you can imagine is 0. Overall, how would you score your own health today between 0 and 100? Enter value between 0 and 100: _ _ _

Table 2. Overview of variables collected at health screening exams: 2000-2013

Domains	Variable Overview	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
	Cohort (n)	12023	11193	12884	14314	14335	14152	14857	15383	16322	16381	16378	19081	21319	23301
Demographics	Age, sex	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Education, Occupation	√	√	√	√										√
	Income				√										√
Health Behaviors	Smoking	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Alcohol Use	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Physical Activity	√	√												√
	Nutrition	√	√	√											√
	Reproductive History	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Family History	√	√	√	√	√	√		√	√	√	√	√	√	√
Medical History	High Blood Pressure	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Antihypertensive Medication	√		√	√	√	√	√	√	√	√	√	√ +	√ +	√ +
	Hyperlipidemia	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Hyperlipidemia Medication	√	√	√	√										√
	Diabetes	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Diabetes Medication	√	√	√	√	√	√	√	√	√	√	√	√ +	√ +	√ +
	Stroke	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Coronary Heart Disease	√	√	√	√										
	Angina, AMI				√	√	√	√	√	√	√	√	√	√	√
	Kidney Disease	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Liver Disease	√	√	√	√	√	√	√	√	√	√	√	√	√	
	PCI														√

Category	Item	1	2	3	4	5	6	7	8	9	10	11	12	13	14
	CABG														√
	Other Cardiac Surgery														√
	Stroke or AMI Hospitalization	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Health Status, Sleep, Stress, Anxiety, Depression		√												√
Chinese Medicine Use		√	√	√	√	√	√	√	√	√	√	√	√	√	√
Quality of Life															√
Laboratory Analysis	Cell Blood Count							√	√	√	√	√	√		
	Triglyceride/Total Cholesterol	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	HDL and LDL							√	√	√	√	√	√	√	√
	Fasting glucose	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Creatinine	√	√			√	√	√	√	√	√	√	√	√	√
Physical Examination	Vital Signs; Anthropometrics	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Cardiopulmonary Auscultation					√	√	√	√	√	√	√	√	√	√
	Thyroid Palpation					√	√	√	√	√	√				
ECG		√	√	√	√	√	√	√	√	√	√	√	√	√	√
Diagnostic Imaging	Chest X-ray	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	Liver/Gallbladder Ultrasound					√	√	√	√	√	√	√	√	√	√
	Carotid Ultrasound													√	√
	Thyroid Ultrasound										√	√	√	√	√
	Echocardiogram													√	√

√ + = Medication list abstracted