

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Millions Persons Project-Pilot
AUTHORS	Lu, Jiapeng; Xuan, Si; Downing, Nicholas; Wu, Chaoqun; Li, Li; Krumholz, Harlan; Jiang, Lixin

VERSION 1 - REVIEW

REVIEWER	Dong Zhao Capital Medical University Beijing Anzhen Hospital, Beijing Institute of Heart, Lung & Blood Vessel Diseases. Beijing, China
REVIEW RETURNED	14-Oct-2015

GENERAL COMMENTS	<p>This manuscript is well written with focus on methodology and feasibility of a very large national screening program for high CVD risk population in China. The authors of this manuscript have a profound understanding and original vision for advantages of such a big data collection.</p> <p>I have two minor revision suggestions</p> <p>1 Authors estimated the nonfasting LDL-C using Friedewald equation. And the LDL-C ≥ 160mg/dL based on this estimation will be used as cutting point of high risk. I suggest to use or add TC cutting point for high risk assessment in initial screening because LDL-C estimation by Friedewald equation should be based on fasting TC, TG and HDL-C. And this equation can't be used to people with TG > 400mg/dL. If the Nonfasting TG is used as component of calculation, more people can't have LDL-C level for risk assessment.</p> <p>2. Patients with diabetes should be considered as high risk because diabetes has much higher CVD risk than dyslipidemia either elevated LDL-C or low HDL-C.</p>
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REVIEWER	Andrew Moran Columbia University, United States of America
REVIEW RETURNED	15-Oct-2015

GENERAL COMMENTS	<p>Lu et al. report on the pilot stage of a very ambitious large scale population based cardiovascular disease and risk factor screening program planned for China. The paper is well written, the quality of study measures is high, and steps taken to ensure protections of human subjects are described. I recommend some minor revisions to this study protocol manuscript:</p> <p>1) Response rate: On page 16 (Results), the authors report a response rate of 32%. Given that they report selecting</p>
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	<p>districts/counties with “local capacity”, it is concerning that the response rate was so low. What will the investigators find when they recruit participants in “low capacity” areas? The low response rate should be mentioned in the Limitations section, along with proposed approach to improving response rate in the main study.</p> <p>2) Uniqueness of the survey: On page 19, the authors state that this study “may serve as a model for development of similar projects in other countries”. Despite the ambition of this survey and its proposed large scale, I don’t see what distinguishes this survey from others (for example the surveys mentioned on page 20). Is it the efficiency and sparseness of the interview phase? Mass storage of blood samples? The authors should elaborate on what makes this survey special.</p> <p>3) “Precision Medicine” approach: The term “precision medicine” is in vogue and is mentioned throughout the paper. Yet, just how this study will allow for a precision medicine approach is not made clear. Is it the banking of blood samples? I would think that detailed family medical history would be an important part of a precision medicine approach, but it appears that family history data collection is minimal (aside from in the high risk group).</p> <p>4) Identification of high risk: On page 18, the authors state that prior studies did not assess CVD risk in participants. It is not difficult to calculate an estimated 10-year CVD risk for survey study participants with measured risk factors—InterASIA was able to do this. I think the authors may mean that their study was unique in using risk stratification in order to reach out to and bring back high risk participants. If this is the case, it should be stated more clearly.</p> <p>5) Follow up of high risk participants: The one month follow up time of high risk participants is not explained. It seems like a short time. Was the purpose to assess how participants responded to lifestyle change advice? Or was the objective to simply prove, in this pilot study, that a high rate of follow up could be achieved by the investigators?</p>
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REVIEWER	Professor Gorm Boje Jensen MD, DMSc The Copenhagen City Heart Study, Frederiksberg Hospital Nordre Fasanvej 57 opg. 5 2000 Frederiksberg C, Denmark
REVIEW RETURNED	20-Oct-2015

GENERAL COMMENTS	<p>Post-war chronic disease epidemiology has focussed on the identification of risk factors for ischemic heart disease (IHD). Subsequent modification of these risk factors by individual or population strategies have been very successful in reducing the incidence and mortality of IHD by at least 50% in most developed countries. In contrast and mainly due to increased affluence, IHD is increasing in a catastrophic way in China and other countries previously having low incidence and prevalence rates of IHD. This manuscript describes the findings in the pilot phase of a nationwide epidemiological study planned in China, the PEACE study (the acronym by the way is fine, but the wording of the title itself is unclear: what is meant by "Patientcentered evaluative</p>
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	<p>assessment" ...?).</p> <p>The pilot study is carried out in a convenience sample of 100.000 individuals, assessed by traditional epidemiological parameters like blood pressure, cholesterol, smoking, diabetes, prevalent IHD. Subjects in a high risk subgroup defined by risk factors and health behaviour are further examined by ECG and ultrasound. High risk individuals are advised in regard of smoking cessation, healthy eating Follow-up is planned at 30 days. A biobank of blood and other biological material is planned.</p> <p>Regarding preliminary results: the prevalences of hypertension and diabetes are very high. This is to be expected with the sampling method used.</p> <p>The study is of obvious importance, the methods are well described, and the (very) preliminary results clearly presented.</p> <p>I find it difficult to understand the stated aims in the introduction in relation to e.g. individual approach and precision medicine and the machinery of a classical epidemiological cohort study. The phrasing: many risk factors are undiagnosed, is unclear. It would be better to write: Many patients with risk factors are undiagnosed....</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1:

1. Authors estimated the nonfasting LDL-C using Friedewald equation. And the LDL-C ≥ 160 mg/dL based on this estimation will be used as cutting point of high risk. I suggest to use or add TC cutting point for high risk assessment in initial screening because LDL-C estimation by Friedewald equation should be based on fasting TC, TG and HDL-C. And this equation can't be used to people with TG > 400mg/dL. If the Nonfasting TG is used as component of calculation, more people can't have LDL-C level for risk assessment.

Response: We appreciate this comment. This study is in the field so we do not have an option of changing our screening approach. The interest was having specific criteria to identify high-risk patients. In our study design, the fourth criteria for identifying the high CVD risk subject (page 10), TC is included to estimate the risk of CVD in 10 years. It is possible that some people will have high TG and seemingly not have a high LDL, but we do not expect many people to be in that group. That would result in a false negative for high risk.

2. Patients with diabetes should be considered as high risk because diabetes has much higher CVD risk than dyslipidemia either elevated LDL-C or low HDL-C.

Response: In our study design, the fourth criteria for identifying the high CVD risk subject (page 10), the presence of diabetes has been included to estimate the risk of CVD in 10 years. We did not use it as a singular criterion as there is controversy about whether it is a CVD equivalent and studies have shown marked heterogeneity of risk among diabetics. Moreover, as a sole criterion it would have markedly increased the number of people identified as high-risk, making the study primarily about diabetics.

Reviewer #2:

1. Response rate: On page 16 (Results), the authors report a response rate of 32%. Given that they report selecting districts/counties with "local capacity", it is concerning that the response rate was so low. What will the investigators find when they recruit participants in "low capacity" areas? The low response rate should be mentioned in the Limitations section, along with proposed approach to improving response rate in the main study.

Response: We appreciate this comment.

1) Inclusion criteria: one of the inclusion criteria for eligible participants is that the Hukou (a record officially identifying a person as a resident of a particular area) of subjects needs to be registered in the selected study region. However, many participants between 40 and 60 years of age do not work in their hometowns, and this is especially true for participants who come from rural areas. According to the Sixth National Population Census conducted in 2010, Beijing is 35.9% internal migrants, whereas in Shanghai the same figure is 40%. Nationwide, there are roughly 230 million migrants in urban areas, or 16.7% of the total population. These numbers are likely to have increased over the past 5 years. Although we do not know the exact extent to which this lowered our response rate, given China's well-documented high internal migration rates, we suspect that this may have played an important role in driving our response rate down. Unfortunately we did not collect the information for the reason why people were ineligible or did not participate.

2) Recruitment methods: as we described in the manuscript, potential participants were identified in each community or village through official residential records, and then invited by local community workers via extensive publicity campaigns on television and in local newspapers. This makes our 'contact rate' (members contacted/total local population) very high. However, we stopped enrolling subjects once we reached 20,000 enrollees at a site. This means that many people did not refuse to participate but were not able to participate because of the cap. The response rate that we reported was calculated with the number of people who enrolled in our study in the numerator, over the number of people contacted in the denominator. Hence, the rate is likely lower than would have been the case if there were no fixed cap on enrollees at each site.

3) Voluntary enrollment: as mentioned in the manuscript, our cohort was comprised of volunteer subjects from 4 provinces across China. It is well documented that large voluntary cohorts can have low response rates. The MONICA study in Europe (41 – 90%) and InterAsia Study (83.3%) in China, both of which used more targeted random sampling recruitment techniques, had much higher response rates than their voluntary counterparts the UK Biobank Study (5-10%) and China Kadoorie Biobank (CKB, 30%). Our response rate is consistent with and a modest improvement over that seen in the CKB, a blood-based prospective study of 0.5 million people in China that employed similar recruitment strategies. And it is a significant improvement over the low responses seen in Europe for similar studies: the UK Biobank Study (5-10%) and a study that constructed a nationwide biobank in Estonia (~5%).

We mention these response rate considerations with other Limitations.

In response to this comment, we have now explained potential reasons for the low response rate seen for our study:

DISCUSSION (Page 21, Lines 3 - 12)

The pilot is limited in three ways. First, the response rate for the pilot was not high –about 32%. The response rate may have been driven down by the fact that many of the participants with a rural Hukou (about half of the total sample of people) live and work in cities, which might makes it more difficult for them to participate in the study. In addition, participation was entirely voluntary, which may also have driven down the response rate. However, because of its large size, we believe that our sample is large enough to capture the full diversity of the Chinese population. Our response rate is also consistent with and a modest improvement over that seen in the China Kadoorie Biobank, a study that employed similar recruitment strategies. And it is a significant improvement over the low response

rates seen in Europe for similar studies, such as the UK Biobank Study (5-10%) and a study that constructed a nationwide biobank in Estonia (~5%).

2. Uniqueness of the survey: On page 19, the authors state that this study “may serve as a model for development of similar projects in other countries”. Despite the ambition of this survey and its proposed large scale, I don’t see what distinguishes this survey from others (for example the surveys mentioned on page 20). Is it the efficiency and sparseness of the interview phase? Mass storage of blood samples? The authors should elaborate on what makes this survey special.

Response: Compared with previous large-scale population-based CVD studies in China, our study is distinctive because it 1) recruited 0.4 million individuals in the pilot and are expanding to 4 million in the main study, which is the larger than any prior study; 2) uses risk stratification to detect and conduct comprehensive health assessment for a high-risk population; 3) employed standardized and efficient electronic data entry and collection on a wide range of information relevant to cardiovascular health and other diseases; 4) involved the mass storage of biospecimens; and 5) included large-scale follow up employing clinical trial methodology.

Thus, our pilot is unique in its ability to provide original and accurate data for characterizing high CVD risk populations through a highly efficient process. It is designed to answer research questions related to socio-demographics, biology, health behaviors, health trajectories, and the relationship between CVD risk factors and outcomes in high-risk populations. It will allow policymakers and academics to produce evidence-based research to inform future approaches to CVD prevention and intervention.

In response to this comment, we now state how our study is unique in the manuscript:

DISCUSSION (Page 18 – 19, Lines 22 – 37)

Previous large-scale, Chinese-population-based CVD studies have been limited to determining the prevalence of CVD risk factors without actually identifying high-risk subjects and comprehensively assessing their cardiovascular health.^{35 37 40 41} Only one prior CVD study has identified a high-risk CVD population, but this study was hindered by the fact that it was cross-sectional and limited to rural residents in only one province.³⁰ Therefore, outside of this pilot project, there have been no other longitudinal, large-scale studies that use risk stratification to detect high-risk populations in China, and then conduct detailed health assessments and follow-up on them. In addition to its large scale, our pilot employed standardized, efficient and self-monitoring electronic data collection on a wide range of information relevant to cardiovascular health and other diseases; involved the mass storage of biospecimens; and included large-scale follow up employing clinical trial methodology. Thus, our pilot is unique in its ability to provide original and accurate data for characterizing high CVD risk populations through a highly efficient process. It is designed to answer research questions related to socio-demographics, biology, health behaviors, health trajectories, and the relationship between CVD risk factors and outcomes in high-risk populations. It will allow policymakers and academics to produce evidence-based research to inform future approaches to CVD prevention and intervention and may serve as a possible model for the development of similar projects in other countries.

3. “Precision Medicine” approach: The term “precision medicine” is in vogue and is mentioned throughout the paper. Yet, just how this study will allow for a precision medicine approach is not made clear. Is it the banking of blood samples? I would think that detailed family medical history would be an important part of a precision medicine approach, but it appears that family history data collection is minimal (aside from in the high risk group).

Response: In this pilot, we collected detailed information on socio-demographics, disease history,

extreme phenotypes, biospecimens, lifestyle, and health behaviors for 0.4 million people. Using this information, researchers will be able investigate individual differences in genes, behaviors, and lifestyles to advance the emerging field of precision medicine. Through this, we hope to make important insights into developing and informing more individualized approaches for CVD prevention and intervention.

Additionally, our work is similar in spirit to the Precision Medicine Initiative (PMI) launched in the US in January 2015, which aims to recruit 1 million Americans and “will encourage and support the next generation of scientists to develop creative new approaches for detecting, measuring, and analyzing a wide range of biomedical information — including molecular, genomic, cellular, clinical, behavioral, physiological, and environmental parameters.” Our study has a similar approach and objective, and more importantly, will create a platform for putting precision medicine into practice.

In response to this comment, we now state how our study allows for a precision medicine approach in the manuscript:

INTRODUCTION (Page 5, Lines 10 – 24)

Consequently, the Chinese government has committed to the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Millions Persons Project (MPP), whose pilot protocol we report here. The China PEACE MPP is a patient-centered national screening initiative to detect populations at high-risk for CVD. It will collect biospecimens and detailed information on socio-demographics, disease histories, extreme phenotypes, lifestyles, and behaviors for millions of persons. Our work is similar in spirit to the Precision Medicine Initiative (PMI) launched in the US in January 2015, which aims to recruit 1 million Americans and “will encourage and support the next generation of scientists to develop creative new approaches for detecting, measuring, and analyzing a wide range of biomedical information — including molecular, genomic, cellular, clinical, behavioral, physiological, and environmental parameters.”³¹ Like the PMI, our national screening initiative will collect biological samples, behaviors, and lifestyle information from a voluntary national research cohort to create a platform for precision medicine studies. Using collected information, researchers will be able investigate individual differences in genes, behaviors, and lifestyles to advance the emerging field of precision medicine. The US PMI will put a near-term focus on supporting more and better cancer treatments, whereas our study will focus on cardiovascular health. Further investigating cardiovascular health is especially important in a country like China, which is both newly old and increasingly urbanized. Our initiative should, in the long run, provide important insights in informing future efforts to develop more individualized approaches for CVD prevention and intervention. In the near-term, the public health component of this initiative seeks to address the nation’s pressing needs to identify high-risk CVD subjects, characterize population risk factors, and define the relationship between risk factors and CVD outcomes in high-risk populations.

This effort, funded by the Ministry of Finance (MOF) and the National Health and Family Planning Commission (NHFP) of China, is initially planned to screen 0.4 million people across four provinces, with the potential for expansion to 4 million people across the entire country. Thus, the China PEACE MPP Pilot was designed to determine if a much-needed and large-scale public health effort could be effectively paired with a high quality research program to amass a database capable of supporting and advancing precision medicine research in China.

4. Identification of high risk: On page 18, the authors state that prior studies did not assess CVD risk in participants. It is not difficult to calculate an estimated 10-year CVD risk for survey study participants with measured risk factors—InterASIA was able to do this. I think the authors may mean that their study was unique in using risk stratification in order to reach out to and bring back high-risk participants. If this is the case, it should be stated more clearly.

Response: Our study is distinctive because it uses risk stratification to detect subjects at high-risk for

CVD, and then includes comprehensive health assessments and follow-up for this high-risk population.

In response to this comment, we now state in the manuscript (this revision is on part of the excerpt from comment 2):

DISCUSSION (Page 18 – 19, Lines 22 – 37)

Previous large-scale, Chinese-population-based CVD studies have been limited to determining the prevalence of CVD risk factors without actually identifying high-risk subjects and comprehensively assessing their cardiovascular health.^{35 37 40 41} Only one prior CVD study has identified a high-risk CVD population, but this study was hindered by the fact that it was cross-sectional and limited to rural residents in only one province.³⁰ Therefore, outside of this pilot project, there have been no other longitudinal, large-scale studies that use risk stratification to detect high-risk populations in China, and then conduct detailed health assessments and follow-up on them.

5. Follow up of high-risk participants: The one-month follow up time of high risk participants is not explained. It seems like a short time. Was the purpose to assess how participants responded to lifestyle change advice? Or was the objective to simply prove, in this pilot study, that a high rate of follow up could be achieved by the investigators?

Response: Since the pilot was conducted primarily to test the feasibility of a large-scale screening program, the reason we chose a one-month follow up was to test if a high rate of follow-up could be achieved. The relatively high 70% follow-up rate in our volunteer population is an encouraging sign for our main study, which will have a one-year follow-up interval.

In response to this comment, we now explained in the manuscript:

METHODS

Design Overview (Page 7, Lines 5 – 9)

Follow-up on high-risk subjects was done either in a return clinic visit or through a telephone interview. In the pilot, we conducted a one-month follow-up to test if a high-rate for such a large-scale follow-up could be achieved. The follow-up assessment consists of blood pressure and weight measurements, an ECG, and a questionnaire assessing cardiovascular health status.

Reviewer #3:

1. This manuscript describes the findings in the pilot phase of a nationwide epidemiological study planned in China, the PEACE study (the acronym by the way is fine, but the wording of the title itself is unclear: what is meant by "Patient-centered evaluative assessment"...?).

Response: We appreciate this comment and the opportunity it presents to elaborate on our China PEACE initiative.

The China National Center for Cardiovascular Disease (NCCD), the Yale-New Haven Hospital Center for Outcomes Research and Evaluation (CORE), the Chinese government and over 200 Chinese hospitals have partnered to create a research collaborative called the China Patient-centered Evaluative Assessment of Cardiac Events (China PEACE). The central feature of China PEACE is a nationwide sample of Chinese hospitals that can facilitate efficient knowledge generation about the quality and outcomes of the care provided in Chinese hospitals through observational and interventional studies.

It is patient-centered, in that we seek to understand individual differences and collect patient-reported outcomes (PROs). Many of its component studies also evaluate patients by assessing various aspects of their person, health and care including socio-demographics, clinical outcomes, in-hospital treatments/prescribed medications, bio-samples, behaviors, and lifestyle.

The goal of the network is to generate new knowledge relevant to practice and policy and to translate this knowledge into action to improve care and outcomes for patients with cardiovascular disease. We aspire to share this new knowledge with the world and contribute to harmony among nations.

2. I find it difficult to understand the stated aims in the introduction in relation to e.g. individual approach and precision medicine and the machinery of a classical epidemiological cohort study.

Response:

We appreciate this comment. Like the US Precision Medicine Initiative (PMI) this study seeks to collect genetic data, biological samples and lifestyle information on a massive number of people to investigate individual differences in people's genes, environments, and lifestyles. This precision medicine approach will give clinicians the tools to better understand the complex mechanisms underlying a patient's health, disease, or condition, and to better predict which treatments will be most effective. In the US, the PMI will place its near-term focus on cancer, whereas our study in China will focus on cardiovascular health, a more pressing public health concern in a country that is newly old and urbanized.

In response to this comment we have revised the manuscript to more clearly state our study's aims in relation to precision medicine and how our approach differs from classical epidemiological cohort studies:

Consequently, the Chinese government has committed to the China PEACE Millions Persons Project (MPP), whose pilot protocol we report here. The China PEACE MPP is a patient-centered national screening initiative to detect populations at high-risk for CVD. It will collect biospecimens and detailed information on socio-demographics, disease histories, extreme phenotypes, lifestyles, and behaviors for millions of persons. Our work is similar in spirit to the Precision Medicine Initiative (PMI) launched in the US in January 2015, which aims to recruit 1 million Americans and "will encourage and support the next generation of scientists to develop creative new approaches for detecting, measuring, and analyzing a wide range of biomedical information — including molecular, genomic, cellular, clinical, behavioral, physiological, and environmental parameters."³¹ Like the PMI, our national screening initiative will collect genetic data, biological samples and lifestyle information from a voluntary national research cohort to create a platform for precision medicine studies. Using collected information, researchers will be able investigate individual differences in genes, behaviors, and lifestyles to advance the emerging field of precision medicine. This approach transcends the classical epidemiological cohort study in both size and scope and will yield powerful new discoveries and several new treatments that are tailored to specific characteristics of individuals. The US PMI will put a near-term focus on supporting more and better cancer treatments whereas our study will focus on cardiovascular health, which is especially important in a country like China that is both newly old and increasingly urbanized. Our initiative should, in the long run, provide important insights in informing future efforts to develop more individualized approaches for CVD prevention and intervention. In the near-term, the public health component of this initiative seeks to address the nation's pressing needs to identify high-risk CVD subjects, characterize population risk factors, and define the relationship between risk factors and CVD outcomes in high-risk populations.

This effort, funded by the Ministry of Finance (MOF) and the National Health and Family Planning Commission (NHFPC) of China, is initially planned to screen 0.4 million people across four provinces, with the potential for expansion to 4 million people across the entire country. Thus, the China PEACE MPP Pilot was designed to determine if a much-needed and large-scale public health effort could be effectively paired with a high quality research program to amass a database capable of supporting and advancing precision medicine research in China.

3. The phrasing: many risk factors are undiagnosed, is unclear. It would be better to write: Many patients with risk factors are undiagnosed....

Response: in response to this comment, we now state in the manuscript:

INTRODUCTION (Page 5, Lines 2 – 3)

Unfortunately, many patients in China have CVD risk factors that remain undiagnosed and uncontrolled.

VERSION 2 – REVIEW

REVIEWER	Andrew Moran Columbia University, USA
REVIEW RETURNED	14-Nov-2015

GENERAL COMMENTS	I am satisfied with the authors' responses to my comments. The responses and corresponding changes to the paper were thorough and sophisticated.
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Erratum: Protocol for the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Million Persons Project pilot

Lu J, Xuan S, Downing NS, *et al.* Protocol for the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Million Persons Project pilot. *BMJ Open* 2015;5:e010200. There is an error in the last two rows of table 3. The number and percent of haemorrhage stroke and ischaemic stroke were reversed in total and gender subgroups. The correct table 3 is given below.

Table 3 Anthropometric parameters and medical history of screening subjects in four provinces

	Male (N=42469)		Female (N=57531)		Total (N=10000)	
	N or mean	% or SD	N or mean	N or mean	% or SD	N or mean
Height (cm)	166.81	6.91	156.22	6.42	160.72	8.45
Weight (kg)	68.22	10.34	59.21	9.39	63.03	10.77
BMI (kg/m²)	24.46	3.05	24.23	3.36	24.33	3.24
<18.5	583	1.37%	1449	2.52%	2032	2.03%
18.5–24.9	25237	59.42%	34903	60.67%	60140	60.14%
25.0–29.9	14656	34.51%	17984	31.26%	32640	32.64%
≥30.0	1974	4.65%	3195	5.55%	5169	5.17%
SBP (mm Hg)	140.53	19.33	138.96	20.54	139.63	20.05
DBP (mm Hg)	82.91	10.78	80.10	10.80	81.29	10.88
High blood pressure*	20193	47.55%	25275	43.93%	45468	45.47%
TC (mmol/L)	4.65	1.02	5.01	1.12	4.86	1.09
TG (mmol/L)	1.88	1.17	2.02	1.19	1.96	1.18
HDL (mmol/L)	1.44	0.46	1.58	0.45	1.52	0.46
LDL (mmol/L)	2.50	0.84	2.65	0.90	2.58	0.88
Medical history						
Hypertension	8254	19.44%	12602	21.90%	20856	20.86%
Diabetes	2197	5.17%	3536	6.15%	5733	5.73%
Myocardial infarction	512	1.21%	486	0.84%	998	1.00%
PCI	272	0.64%	143	0.25%	415	0.42%
CABG	39	0.09%	31	0.05%	70	0.07%
Stroke	2031	4.78%	2466	4.29%	4497	4.50%
<i>Hemorrhage stroke</i>	194	0.46%	161	0.28%	355	0.36%
<i>Ischemic stroke</i>	1604	3.78%	2016	3.50%	3620	3.62%

Values are n (%) or mean (SD) as indicated.

* χ^2 test for proportion and two-tailed t test (or t' test if equal variances not assumed) for means, $\alpha=0.05$.

†High blood pressure: SBP \geq 140 mm Hg or DBP \geq 90 mm Hg.

BMI, body mass index; CABG, coronary artery bypass grafting; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

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