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Research paper

Validating World Health Organization cardiovascular disease risk charts and optimizing risk assessment in China

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ABSTRACT

Background: World Health Organization (WHO) released region-specific cardiovascular disease (CVD) risk prediction charts recently, but the extent to which the charts can apply to Chinese population is unknown. We aimed to validate the WHO CVD risk charts for East Asia, and evaluate their practicability combining with China-PAR (Prediction for Atherosclerotic Cardiovascular Disease Risk in China) equations among Chinese adults.

Methods: The China-PAR cohort with 93,234 participants aged 40–80 years was followed up during 1992–2015, including 29,337 participants from three sub-cohorts with follow-up period of over 10 years. We validated the WHO CVD risk charts using the China-PAR cohort by assessment of the predicted number of events, C index, calibration χ^2, and calibration plots, further elaborated the concordance between the China-PAR equations and the WHO risk charts.

Findings: During an average follow-up of 13•64 years, 1849 incident CVD cases were identified from 29,337 participants. Both the laboratory-based and non-laboratory-based charts overestimated CVD events by 59% and 58% in men, and by 72% and 85% in women, respectively. However, 92% of participants identified as high risk by the China-PAR equations could be successfully detected by the laboratory-based charts at the cut-off point of 10%. We also observed that the non-laboratory-based charts demonstrated the poor performance for diabetic population, with high proportion of high-risk individuals (17% for men, 31% for women) would be missed.

Interpretation: Although the WHO CVD risk charts for East Asia apparently overestimated CVD risk among Chinese population, they could be pragmatic pre-selection tools, as potential supplement to the China-PAR equations. The widespread use of the WHO risk charts along with the China-PAR equations might facilitate the implementation of the risk-based CVD prevention in China.

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Research in context

Evidence before this study

We aimed to validate the WHO cardiovascular disease risk charts published online on Sep 2, 2019 as applied to East Asian population. We searched PubMed to identify articles on validation of the WHO risk charts by East Asian cohorts using the following strategy: (World Health Organization) AND (cardiovascular disease) AND (risk chart OR risk score OR risk equation OR risk algorithm OR risk prediction) AND (East Asia), published in any language after Sep 2, 2019. No study was found to evaluate the performance of the WHO risk charts in East Asia. Therefore, uncertainties still exist as applied the WHO risk charts to East Asian population, especially to Chinese population. It needs to be validated and evaluated in Chinese national cohorts.

Added value of this study

WHO has developed simple and practical region-specific cardiovascular disease risk prediction charts, and mainly aimed to the low- and middle-income countries. As the largest developing country, China has most enormous burden of cardiovascular diseases. Therefore, it is critical to validate the WHO risk charts and evaluate their practicability in China. The current study provided powerful evidence from a large, contemporary, Chinese national, population-based prospective cohort. It indicated that the WHO risk charts could detect most individuals at high risk of cardiovascular disease, despite existing apparent overestimation of cardiovascular risk in China. Consequently, they could be considered as pragmatic pre-selection tools, which are potential supplement to the China-PAR (Prediction for Atherosclerotic Cardiovascular Disease Risk in China) equations.

Implications of all the available evidence

The WHO risk charts removed major obstacles in implementing risk-based prevention strategies in China. Their widespread use in combination with the China-PAR equations might promote risk assessment and risk factor management, and reduce the burden of cardiovascular diseases in China.

1. Introduction

Cardiovascular disease (CVD) has resulted in enormous global disease burden and deaths worldwide, especially in developing countries, such as China [1,2]. Guidelines have emphasized that assessment of CVD risk is the foundation of primary prevention, and can assist in identifying individuals at high risk and making logical management decisions [3-5]. Considering lack of models for CVD risk assessment, particularly in developing regions, World Health Organization (WHO) released CVD risk prediction charts for all WHO regions in 2007 [6]. However, the validity issues still existed when applied them to different countries [7]. Therefore, WHO developed new CVD risk prediction models recently, revised them more tailored to low- and middle-income countries, and simplified to 21 region-specific CVD risk charts [8].

The WHO risk models enhanced the accuracy, validity, generalizability and practicability of CVD risk prediction in 21 regions using powerful, extensive, and complementary global datasets [8]. However, some limitations should be noted. First, the original WHO risk models were derived from 85 prospective cohorts mostly in high-income countries, but not in developing countries, e.g. China. Second, WHO declaimed that the risk models might overestimate or underestimate CVD risk, because of insufficient consideration on recurrent CVD events and prevention therapies when they were recalibrated to 21 global regions [8]. Third, the WHO risk models for East Asia mainly aimed at Chinese adults, while no external validation was conducted comprehensively from Chinese nationally representative cohorts. In addition, aside from the WHO laboratory-based models, the non-laboratory-based models were also developed for the resource-constrained regions, where laboratory measurements were unavailable. It indicated the poor performance among individuals with diabetes [8]. In brief, some uncertainties should exist as applied the WHO risk models for East Asia to Chinese population directly. Therefore, it is urgent to evaluate the performance and practicability of the charts in Chinese national cohort.

The China-PAR (Prediction for Atherosclerotic Cardiovascular Disease Risk in China) equations were derived and validated using the China-PAR project, which is a large, population-based Chinese prospective cohort study [9]. The equations have excellent performance on CVD risk prediction, and their accuracy has been confirmed by other Chinese cohorts [10,11]. They have been adopted by the American College of Cardiology/American Heart Association guideline and the Chinese guideline as pragmatic tools to facilitate CVD risk assessment and risk factor management [3,12].

In this article, we aimed to validate the WHO CVD risk charts for East Asia using the China-PAR cohort, and explore the practicability of the charts in combination with the China-PAR equations.

2. Methods

2.1. Study design and participants

Study participants were selected from the China-PAR project, including the China Multi-Center Collaborative Study of Cardiovascular Epidemiology (China MUCA) (1992–1994), the China MUCA (1998), the International Collaborative Study of Cardiovascular Disease in Asia (InterASIA), and the Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study (CIMIC). The China MUCA (1992–1994) and the China MUCA (1998) selected 14,392 (9 clusters) and 11,480 participants (11 clusters) aged 35–59 years using cluster random sampling method in 1992–1994 and 1998, respectively. Each cluster contained nearly 1000 or 2000 participants. The InterASIA used a 4-stage stratified sampling method to enroll 15,540 participants aged 35–74 years from 10 provinces as nationally representative sample of China in 2000–2001. The CIMIC is a large community-based study, which recruited 86,428 participants aged $\geq$18 years by a 3-stage cluster random sampling method in 2007–2008. The study design, methods of the China-PAR project have been previously described in detail [9]. In brief, four sub-cohorts of the China-PAR project were established during 1992–2008. The follow-up surveys of the China MUCA (1992–1994) were conducted every two years during 1996–2004. The China MUCA (1998) and the InterASIA were followed up between 2007 and 2008. All four sub-cohorts were followed up together during 2012–2015. The China-PAR project was approved by the Institutional Review Board at Fuwai Hospital in Beijing. Written informed consent was signed by each participant before examination.

In summary, among 127,840 participants aged $\geq$18 years, 119,388 participants (93•4%) completed the follow-up survey successfully. After excluding 1704 participants with CVD at baseline, 23,222 participants aged $<$40 or $>$80 years (the WHO risk charts were available for participants aged 40–80 years), and 1228 participants without complete data for the WHO CVD risk non-laboratory-based charts, 93,234 participants entered into the final analysis. Of which, 29,337 participants from three sub-cohorts with follow-up period over 10 years were used for external validation of the WHO risk charts, including the China MUCA (1992–1994), the China MUCA (1998), and the InterASIA (Fig. 1).

2.2. Procedures

In baseline survey of each sub-cohort, demographic characteristics, lifestyle information, medical history, family history, and an-

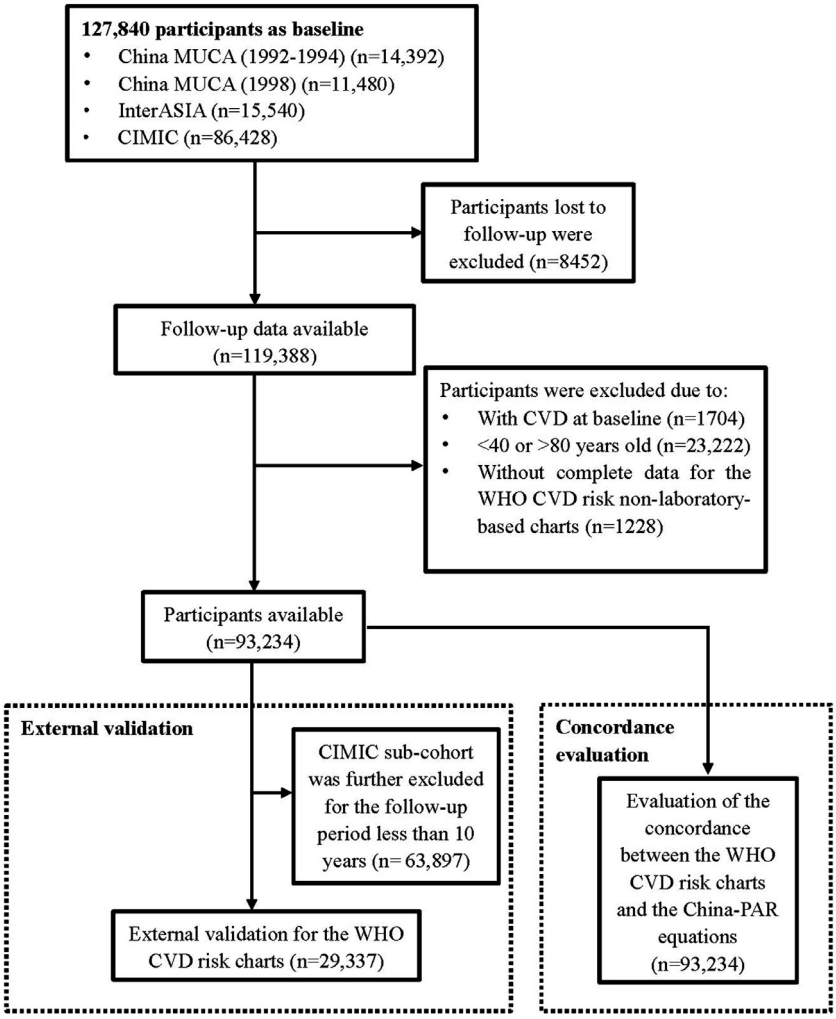

Fig. 1. Flowchart of study participants included and excluded in the analysis.
China MUCA=China Multi-Center Collaborative Study of Cardiovascular Epidemiology. InterASIA=International Collaborative Study of Cardiovascular Disease in Asia. CIMIC=Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study. China-PAR=Prediction for Atherosclerotic Cardiovascular Disease Risk in China. WHO=World Health Organization. CVD=cardiovascular disease.

thropometric measurements were collected by well-trained health-care staffs using the standard protocol and questionnaires with stringent quality control. Smoking was self-reported, and defined as having smoked at least 400 cigarettes, or at least 1 cigarette per day for 1 year, or 500-g tobacco leaves. Smoking was further categorized into former and current smoking. Family history of CVD referred to participants having at least one relative (parent or sibling) with myocardial infarction or stroke. Anthropometric measurements, including body height, weight and waist circumference (at 1 cm above the navel with minimal respiration) were obtained from participants in light indoor clothing without shoes. Body mass index was calculated as weight (kg) divided by height (m^2). Blood pressures were measured three times for participants with an interval of 30 s after they had rested for at least 5 min. The average of the three readings was used for this analysis. Ten-hour fasting venous blood samples were drawn from participants by venipuncture to measure serum glucose and lipids levels. Diabetes was diagnosed as fasting blood glucose 7•0 mmol/L or above, or self-reported current antidiabetic treatment.

2.3. Outcomes

Follow-up surveys were conducted using standard protocol and questionnaires. The disease and vital information were obtained through 1) tracking study participants or their proxies to acquire their hospital records or death certificates by well-trained interviewers; 2) integrating local routine monitoring data of disease and death. All endpoint events were ascertained by a study-wide endpoint assessment committee established at Fuwai Hospital in Beijing. Two committee members independently determined the final endpoint events by reviewing incidence and death information according to the pre-specified criteria, and discrepancies were adjudicated by an additional committee member.

CVD included acute myocardial infarction, fatal coronary heart disease, and nonfatal or fatal stroke. To ensure the accuracy and consistency of CVD definition, we identified CVD events during the follow-up period using standard pre-specified criteria as below. Acute myocardial infarction was defined as changed biochemical markers of myocardial necrosis with at least one of the 4 symptoms (ischemic symptoms, pathological Q waves, ST-segment elevation or depression, or coronary intervention). Fatal coronary heart disease included fatal myocardial infarction and other coronary deaths. Stroke defined as clinical signs and symptoms of subarachnoid or intracerebral hemorrhage or cerebral infarction, with signs of focal (or global) disturbances in cerebral function for 24 h and above, excluding apparent nonvascular causes [9].

Table 1
Baseline characteristics of the study participants stratified by sex.

Variable	Men	Women
N	38,537	54,697
Age (years)	54•29 (47•22–61•08)	53•74 (46•62–60•42)
Northern China	18,115 (47%)	25,588 (47%)
Urban	5647 (15%)	5925 (11%)
Current Smoker	20,876 (54%)	1669 (3%)
Body mass index (kg/m^2)	23•05 (20•82–25•48)	23•84 (21•48–26•44)
Waist circumference (cm)	81•00 (74•00–88•75)	80•00 (73•00–87•00)
Systolic blood pressure (mm Hg)	126•67 (115•33–141•00)	126•33 (113•33–142•67)
Diastolic blood pressure (mm Hg)	80•00 (72•33–88•00)	78•00 (70•67–86•00)
Diabetes	2152 (6%)	3451 (7%)
Total Cholesterol (mmol/L)	4•45 (3•90–5•05)	4•62 (4•06–5•24)
Family history of CVD	4417 (11%)	5911 (11%)
The 10-year CVD risk (%) according to:		
WHO CVD risk laboratory-based charts for East Asia	8•00 (5•00–14•00)	5•00 (3•00–9•00)
WHO CVD risk non-laboratory-based charts for East Asia	8•00 (5•00–14•00)	5•00 (3•00–10•00)
China-PAR equations	5•22 (2•60–9•74)	3•24 (1•45–6•59)

Data are median (25–75th centiles) or n (%).
WHO=World Health Organization. CVD=cardiovascular disease. China-PAR=Prediction for Atherosclerotic Cardiovascular Disease Risk in China.

2.4. CVD risk prediction models

We used three models to assess the CVD risk: the China-PAR equations including sex, age, geographic region (Northern China/Southern China), urbanization (urban/rural), waist circumference, treated or untreated systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, current smoking (yes/no), diabetes mellitus (yes/no), and family history of CVD (yes/no); the WHO CVD risk laboratory-based charts for East Asia including sex, age, current smoking, systolic blood pressure, diabetes mellitus, and total cholesterol; and the WHO CVD risk non-laboratory-based charts for East Asia including sex, age, current smoking, systolic blood pressure, and body mass index [8,9].

2.5. Statistical analysis

The 10-year CVD risk was estimated for each participant according to the WHO CVD risk laboratory-based, non-laboratory-based charts for East Asia, and the China-PAR equations. Sex-specific baseline characteristics of study participants were presented as medians with 25–75th centiles for continuous variables, and numbers with percentages for categorical variables.

We applied the WHO risk charts for East Asia to three China-PAR sub-cohorts with follow-up period over 10 years, and calculated predicted number of events, discrimination C index, and calibration χ^2 to assess their performance [13-15]. We also illustrated prediction ability of these models using calibration plots by deciles of the predicted CVD risk. Based on the cut-off points in Chinese guideline [12], participants were divided into three categories (low risk [<5%], moderate risk [5%–9•9%], and high risk [≥10%]) according to the predicted 10-year CVD risk, the observed CVD event rates were obtained by the Kaplan-Meier methods[14], and compared with the predicted event rates in each category.

WHO CVD risk was classified into 5 levels using cut-off points of 5%, 10%, 20%, and 30%. A proper cut-off point for detecting high-risk individuals should be selected based on social realities in different countries. Therefore, we categorized participants into low-moderate risk group (<10%) and high risk group (≥10%) according to the China-PAR equations, and elaborated the concordance between the China-PAR equations and the WHO CVD risk charts for East Asia using the cut-off points pre-specified by WHO among four China-PAR sub-cohorts. Due to the poor discrimination ability for the cut-off points of 5% and 30%, only 10% and 20% were used. Furthermore, considering WHO statement of poor performance in the WHO CVD risk non-laboratory-based charts for diabetic patients, the concordance between the WHO CVD risk laboratory-based charts and the non-laboratory-based charts in identifying individuals at high risk was further estimated among participants with or without diabetes.

All analyses were performed using SAS 9•4 (SAS Institute Inc., Cary, NC).

2.6. Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

3. Results

Sex-specific baseline characteristics of study participants are presented in Table 1. Of all 93,234 participants, the median age was 53•95 years old, and 38,537 (41%) of them were men. Compared with women, men had higher waist circumference, diastolic blood pressure, prevalence of smoking, and the 10-year predicted CVD risk, as well as lower body mass index, total cholesterol, and prevalence of diabetes.

Among 29,337 participants from three China-PAR sub-cohorts with follow-up period of over 10 years, 1849 incident CVD cases (1073 in men and 776 in women) were identified during an average follow-up of 13•64 years, with an incidence of 462•12/100,000 person-year (574•40/100,000 person-year in men and 363•79/100,000 person-year in women). We applied the WHO CVD risk charts for East Asia to the China-PAR cohort and estimated their performance (Table 2). The WHO CVD risk charts apparently overestimated CVD risk in China. After adjusted by the Kaplan-Meier method, the observed CVD events within the 10-year period were 640•3 and 449•9 in men and women, respectively. However, the WHO CVD risk laboratory-based charts overestimated CVD events by 59% with predicted events of 1017•6 in men, and by 72% with predicted events of 775•8 in women, respectively. Similarly, the WHO CVD risk non-laboratory-based charts also over-predicted CVD events by 58% and 85% in men and women, respectively. In addition, the WHO CVD risk charts, both laboratory-based charts and non-laboratory-based charts had good discrimination ability, with all C indices of 0•75 and above. However, their calibration χ^2 values of greater than 280, which suggested a poor ability of calibration.

Table 2
Validation of WHO CVD risk charts for East Asia as applied to the China-PAR cohort*.

	Men		Women	
	WHO CVD risk laboratory-based charts	WHO CVD risk non-laboratory-based charts	WHO CVD risk laboratory-based charts	WHO CVD risk non-laboratory-based charts
Total N	12,958	13,962	14,363	15,375
Actual events	610	642	435	449
KM-adjusted events	640•3	674•3	449•9	464•6
Predicted events	1017•6	1064•2	775•8	860•9
C index	0•759	0•762	0•752	0•754
95% confidence interval	0•740–0•779	0•744–0•781	0•728–0•777	0•731–0•777
P Value	<0•001	<0•001	<0•001	<0•001
Calibration χ^2	321•55	386•18	280•69	439•99
P Value	<0•001	<0•001	<0•001	<0•001

* Involved three China-PAR sub-cohorts with follow-up period over 10 years, including the China MUCA (1992–1994), the China MUCA (1998), and the InterASIA.Actual events: actual number of events through 10-year follow-up period.KM-adjusted events: observed number of events after Kaplan-Meier adjustment through 10-year follow-up period.Predicted events: expected number of events through 10-year follow-up period based on the WHO CVD risk charts or the China-PAR equations.WHO=World Health Organization. CVD=cardiovascular disease. China-PAR=Prediction for Atherosclerotic Cardiovascular Disease Risk in China. China MUCA=China Multi-Center Collaborative Study of Cardiovascular Epidemiology. InterASIA=International Collaborative Study of Cardiovascular Disease in Asia.

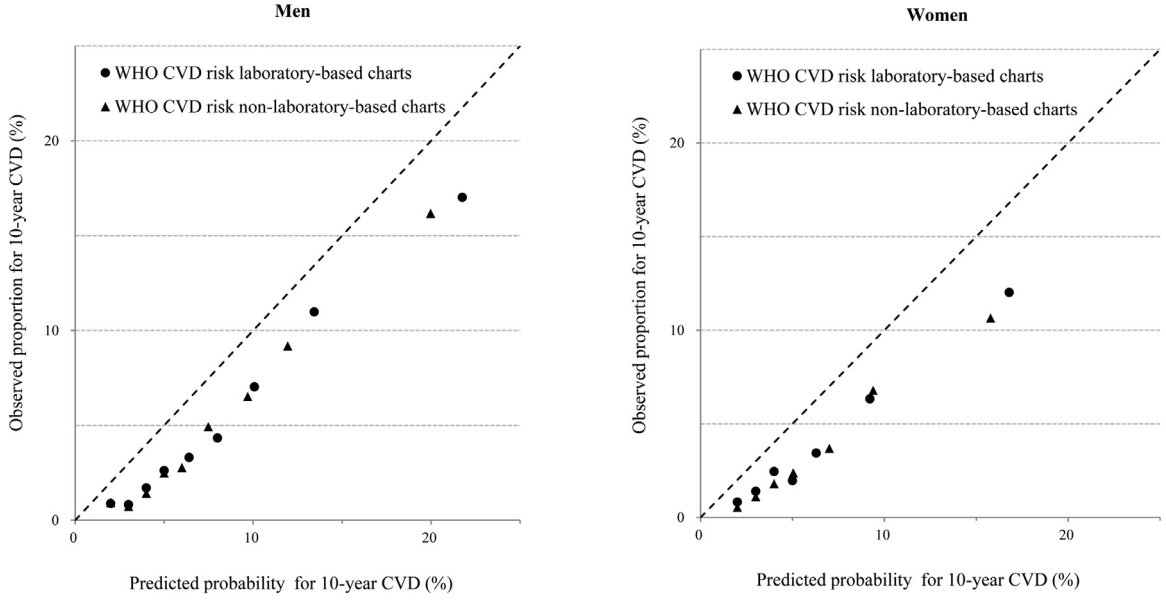

Fig. 2. Calibration plots for the China-PAR cohort* using the WHO CVD risk charts for East Asia.
* Involved three China-PAR sub-cohorts with follow-up period over 10 years, including the China MUCA (1992–1994), the China MUCA (1998), and the InterASIA.
WHO=World Health Organization. CVD=cardiovascular disease. China-PAR=Prediction for Atherosclerotic Cardiovascular Disease Risk in China. China MUCA=China Multi-Center Collaborative Study of Cardiovascular Epidemiology. InterASIA=International Collaborative Study of Cardiovascular Disease in Asia.

Calibration plots were drawn by deciles or three risk categories of the predicted CVD risk (Figs. 2 and 3). Substantial differences were found between the observations and the predictions using either the WHO CVD risk laboratory-based or non-laboratory-based charts for East Asia. The two WHO CVD risk charts notably overestimated the CVD event rates across all risk categories. For example, according to the WHO CVD risk laboratory-based charts, the predicted 10-year CVD event rates in the China-PAR cohort were 3%, 6%, and 16% among men at low, moderate, and high risk, respectively, while the corresponding observed event rates were only 1%, 4%, and 12%, respectively. The predicted event rates were also much higher than the observed rates in low (3% vs. 1%), moderate (6% vs. 4%), and high risk categories (15% vs. 10%) among women. In addition, Bland-Altman plots indicated the WHO CVD risk charts predicted higher CVD risk than the China-PAR equations and the funnel-shaped form suggested that the differences became more apparent especially among participants with higher CVD risk (Supplementary Fig. S1).

We further assessed the concordance of identifying high-risk individuals between the China-PAR equations and the two WHO CVD risk charts for East Asia using different cut-off points among 93,234 participants in all four China-PAR sub-cohorts (Table 3). Generally, more high-risk individuals identified by the China-PAR equations would be detected when WHO CVD risk cut-off point was set at 10% rather than 20%, no matter using the laboratory-based or non-laboratory-based charts. For example, among men at China-PAR high risk, 92% (22%/24%) had the risk of ≥10% based on the WHO CVD risk laboratory-based charts, while only 38% (9%/24%) had the risk of ≥20%. Among women at China-PAR high risk, 92% (12%/13%) and 31% (4%/13%) were over the cut-off point of 10% and 20%, respectively. We also conducted risk reclassification analysis for participants with and without 10-year CVD event

Table 3
Concordance between the China-PAR equations and the WHO CVD risk charts for East Asia with different cut-off points.

Distribution (%)	China-PAR equations			
	Men		Women	
	Low-moderate risk	High risk	Low-moderate risk	High risk
N	27,397	8688	44,403	6880
Total	76%	24%	87%	13%
WHO CVD risk laboratory-based charts for East Asia				
<10%	56%	2%	74%	1%
≥10%	20%	22%	13%	12%
<20%	75%	15%	86%	9%
≥20%	1%	9%	1%	4%
WHO CVD risk non-laboratory-based charts for East Asia				
<10%	56%	2%	73%	2%
≥10%	20%	22%	14%	11%
<20%	75%	15%	86%	9%
≥20%	1%	9%	1%	4%

According to the China-PAR equations, low-moderate risk refers to the predicted 10-year CVD risk <10%, and high risk refers to the predicted risk ≥10%.
WHO=World Health Organization. CVD=cardiovascular disease. China-PAR=Prediction for Atherosclerotic Cardiovascular Disease Risk in China.

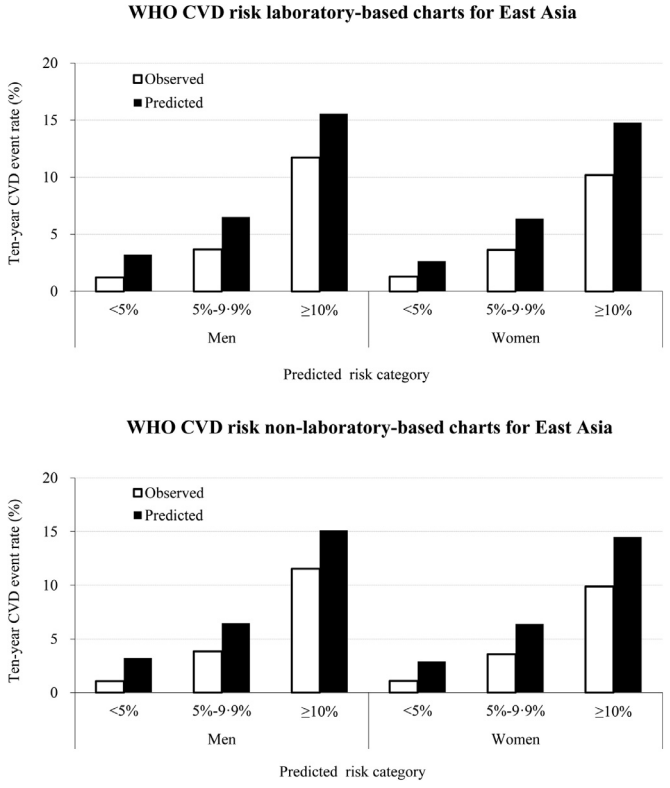

Fig. 3. The observed and predicted 10-year CVD event rates among participants in different risk categories.
WHO=World Health Organization. CVD=cardiovascular disease.

to determine the proper cut-off points using the net reclassification improvement and evaluate the concordance, after excluding the CIMIC sub-cohort for its shorter follow-up time (Supplementary Table S1). We observed consistent results with the concordance analysis.

Furthermore, we observed the poor performance of the WHO non-laboratory-based chart for diabetic patients (Table 4). The vast majority of diabetic patients with high China-PAR risk could be detected by the laboratory-based chart at the cut-off point of 10% (98% [52%/53%] for men, 98% [51%/52%] for women), whereas a high proportion of high-risk diabetic participants would be left out when using the non-laboratory-based chart, especially in women, with nearly one third of high-risk individuals (31% [16%/52%]) being missed.

In addition, the non-laboratory-based chart could efficiently screen out most low-moderate-risk individuals without diabetes (57% for men, 75% for women), and the laboratory-based chart could screen out nearly 20% diabetic patients without high risk (18% for men, 28% for women) (Table 4). Therefore, the WHO CVD risk charts could be used as pre-selection tools prior to the China-PAR equations.

4. Discussion

Using a large population-based prospective cohort, we validated the WHO CVD risk charts for East Asia, and suggested that both the laboratory-based and the non-laboratory-based charts apparently overestimated 10-year CVD risk for Chinese population. However, they had good discrimination ability, and could screen most individuals at high CVD risk correctly at the cut-off point of 10%. Hence the WHO CVD risk charts can be used as pre-selection tools to identify potential high-risk population with less variables, and further ascertainment should be done using the China-PAR equations among Chinese adults. Combining the China-PAR equations with the WHO risk charts might optimize CVD risk assessment in China. In addition, the non-laboratory-based charts were not applicable to diabetic patients.

The current study demonstrated that the WHO CVD risk charts for East Asia overestimated 10-year CVD events by more than 50% among Chinese population with poor calibration. Consequently, they would exaggerate the costs of risk-based CVD primary prevention in China. The apparent risk overestimation by the WHO risk charts existed in both sexes and across all risk categories. As is known, all derivation cohorts of the original WHO models were from developed countries, where strikingly different risk factors pattern and CVD profile from China [1,2,16-18]. In addition, high incidence and significant upward trend of recurrent CVD in past two decades were observed in China [19-21], but recurrent CVD events could not be excluded completely when the models were further recalibrated based on region-specific incidence at the population level from the Global Burden of Disease studies [8]. There-

Table 4
Concordance between the WHO CVD risk laboratory-based and non-laboratory-based charts among participants with or without diabetes.

Distribution (%)	China-PAR equations			
	Men		Women	
	Low-moderate risk	High risk	Low-moderate risk	High risk
Participants without diabetes				
N	26,400	7556	42,782	5094
Total	78%	22%	89%	11%
WHO CVD risk laboratory-based charts for East Asia				
<10%	59%	2%	77%	1%
≥10%	19%	20%	12%	10%
WHO CVD risk non-laboratory-based charts for East Asia				
<10%	57%	1%	75%	1%
≥10%	21%	21%	14%	10%
Participants with diabetes				
N	997	1132	1621	1786
Total	47%	53%	48%	52%
WHO CVD risk laboratory-based charts for East Asia				
<10%	18%	1%	28%	1%
≥10%	29%	52%	20%	51%
WHO CVD risk non-laboratory-based charts for East Asia				
<10%	39%	9%	44%	16%
≥10%	8%	44%	4%	36%

According to the China-PAR equations, low-moderate risk refers to the predicted 10-year CVD risk <10%, and high risk refers to the predicted risk ≥10%.
WHO=World Health Organization. CVD=cardiovascular disease. China-PAR=Prediction for Atherosclerotic Cardiovascular Disease Risk in China.

fore, the WHO models would inevitably overestimate the CVD risk of Chinese population, as other models from Western countries [9,22-24].

WHO stated that the cut-off point of the CVD risk charts should be set according to economic and social realities of each country [25], and did not provide the region-specific cut-off points for the risk charts [8]. In reference to the China-PAR equations, we explored the appropriate cut-off point of the WHO CVD risk charts among Chinese adults. The WHO risk charts at the cut-off point of 10% could identify most of individuals at high risk indeed, although including nearly half of false high-risk individuals. More than 60% of high-risk individuals were left out if the cut-off point of 20% was used. Hence, some uncertainty should exist in the results of a most recent study, which assessed the prevalence of high CVD risk in China using the WHO CVD risk charts with the cut-off point of 20% [26]. In brief, our findings indicated that the WHO risk charts at cut-off point of 10% rather than 20% showed greater advantage for screening individuals at high risk in China.

In consideration of the impractical laboratory measurements in some poor resource settings, the WHO CVD risk non-laboratory-based charts were developed, with body mass index instead of serum glucose and total cholesterol level [8]. Our study compared the non-laboratory-based charts with the laboratory-based charts, and indicated similar performance among individuals without diabetes. Thus, the non-laboratory-based charts are simple and optimal pre-selection tools for population without diabetes, especially taking account of the imbalance of Chinese economic and social development. In resource scarcity settings, the CVD risk could be assessed under the limited costs and inconvenience of laboratory measurements [27]. Meanwhile, the poor performance of the non-laboratory-based charts among diabetic population should be noted, as declaimed by WHO [8]. As an important risk factor, diabetes increased CVD risk significantly, [28,29] and most diabetes patients had moderate or high CVD risk [3]. However, the non-laboratory-based charts tended to underestimate the CVD risk among Chinese diabetic patients. Therefore, the laboratory-based charts should be given priority when implementing screening in individuals with diabetes. Nowadays, the community-based screening of diabetic patients in the Chinese National Essential Public Health Services made it available for selecting the suitable tools for CVD risk assessment. It also improved the applicability of the China-PAR equations in Chinese adults. Meanwhile, the WHO CVD risk non-laboratory-based charts would be optional tools when lack of lipid measurements for the China-PAR equations, considering the low awareness of lipid abnormalities in China [30].

The WHO CVD risk charts removed major obstacles for global implementation of risk-based prevention [31], and they are easy to be used in developing countries, particularly the non-laboratory-based charts. It makes sense for an initial screening to be done with a more parsimonious set of variables, before proceeding with a more accurate model that requires more variables to be collected. Therefore, in combination with the China-PAR equations, the risk charts could help screen people who would benefit most from intervention with the lower cost, inform individuals about their CVD risk level, promote self-management, guide doctor therapeutic decision-making, and consequently improve CVD prevention and treatment [8,25,32,33]. Accurate and practical risk assessment and management would enable limited healthcare resources to be focused on the population most in need, promote both individualized and community-based CVD prevention, and further reduce the burden of CVD in China [8,12,25].

Due to large burden of high CVD risk and the low implementation of risk reduction intervention in China [34], it makes urgent the need to provide the practical and feasible tool for CVD risk assessment. Our findings implied that the China-PAR equations in combination with the WHO risk charts might be optimal tools. First, the WHO risk laboratory-based chart at the cut-off point of 10% could be used as a preferable pre-selection tool with less assessing variables in China, and the non-laboratory-based chart was an optional tool for non-diabetic population. It would be helpful to narrow the target population for further accurate risk assessment. More accurate CVD risk assessment should be conducted subsequently by the China-PAR equations to identify high-risk individuals most in need for intervention. Furthermore, lifestyle modification, risk factors management, and drug treatment should be implemented among identified people according to the related guidelines. The effectiveness of risk factors control needs to be further evaluated at individual and population

level by integrating the WHO CVD risk charts and the China-PAR equations.

There are several strengths in the current study. For the first time, we comprehensively evaluated the accuracy and practicability of the WHO CVD risk charts using the China-PAR project, which is a large, Chinese national, contemporary, population-based prospective cohort. This research could provide insights to guide application of the WHO CVD risk charts along with the China-PAR equations to Chinese population. The China-PAR project has a high rate of follow-up (93•4%) and high-quality data for its standard protocol and stringent quality control. The well-validated China-PAR equations have been established based on this project and been recommended to be used in China [3,12,35]. It also provided us an opportunity to estimate the concordance of the WHO CVD risk charts with the China-PAR equations sufficiently. Inevitably, our study also has several potential limitations. Using the China-PAR CVD risk, but not actual risk, as the reference might induce misclassification bias, while the effect should be slight due to the excellent performance of the China-PAR equations. We validated the WHO CVD risk charts excluding the CIMIC sub-cohort. It might affect the generalizability of our findings in China. However, the impact might be slight because the CIMIC had no apparently systematical difference from other 3 sub-cohorts considering their similar good performance in the China-PAR equations [9]. Moreover, the concordance analysis was conducted subsequently using all four sub-cohorts. In addition, the China-PAR cohort came from Chinese population, which could not reflect the whole East Asia region, and further researches from the other countries of the East Asia region are needed.

In conclusion, despite the WHO CVD risk charts for East Asia apparently overestimated CVD risk in China, they could still be considered as pragmatic pre-selection tools for identifying high-risk population with less variables. In addition, the non-laboratory-based charts are applicable to the non-diabetic population, while diabetic patients should use the laboratory-based charts. Combining the China-PAR equations with the WHO risk charts might optimize the process of CVD risk assessment. The widespread use of the two tools could perhaps enhance the generalizability, practicability and accuracy of efforts to implement risk-based CVD prevention, and further reduce the disease burden in China.

Author Contributions

XLu contributed to the concept and design of the study. JL, FL, YX, JCao, SC, JCh, KH, CS, XLiu, LY, YZ, XiaW, LZ, XigW, YL, DH and JH collected the survey data. JL did the statistical analysis and drafted the article. All authors contributed to the interpretation of results and critically revised the draft.

Data sharing statement

Deidentified participant data generated for this Article will be available after approval by Fuwai Hospital (Beijing, China). Please email the corresponding author for more information.

Declaration of Interests

We declare no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2021.100096.

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