




BMJ Open Absolute cardiovascular risk scores and medication use in rural India: a cross-sectional study

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ABSTRACT

Objectives We compared the performance of laboratory-based cardiovascular risk prediction tools in a low-income and middle-income country setting, and estimated the use of antihypertensive and lipid-lowering medications in those deemed at high risk of a cardiovascular event.

Design A cross-sectional study.

Setting The study population comprised adult residents (aged ≥ 18 years) of the Rishi Valley region located in Chittoor District, south-western Andhra Pradesh, India.

Participants 7935 participants were surveyed between 2012 and 2015. We computed the 10-year cardiovascular risk and undertook pair-to-pair analyses between various risk tools used to predict a fatal or non-fatal cardiovascular event (Framingham Risk Score (FRS), World Health Organization Risk Score (WHO-RS) and Australian Risk Score (ARS)), or a fatal cardiovascular event (Systematic COronary Risk Evaluation (SCORE-high and SCORE-low)). Concordance was assessed by ordinary least-products (OLP) regression (for risk score) and quadratic weighted kappa (κ_w , for risk category).

Results Of participants aged 35–74 years, 3.5% had prior cardiovascular disease. The relationships between risk scores were quasi-linear with good agreement between the FRS and ARS (OLP slope=0.96, κ_w =0.89). However, the WHO-RS underestimated cardiovascular risk compared with all other tools. Twenty per cent of participants had $\geq 20\%$ risk of an event using the ARS; 5% greater than the FRS and nearly threefold greater than the WHO-RS. Similarly, 16% of participants had a risk score $\geq 5\%$ using SCORE-high which was 6% greater than for SCORE-low. Overall, absolute cardiovascular risk increased with age and was greater in men than women. Only 9%–12% of those deemed ‘high risk’ were taking lipid-lowering or antihypertensive medication.

Conclusions Cardiovascular risk prediction tools perform disparately in this setting of disadvantage. Few deemed at high risk were receiving the recommended treatment.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death globally.¹ While communicable, maternal and nutritional diseases remain important causes of death in low-income and middle-income countries (LMICs),² deaths from CVD are on the rise.³

Strengths and limitations of this study

- This study is the first comprehensive assessment of multiple risk prediction tools and use of medications in a large sample in a rural low-income and middle-income country setting.
- The study was conducted using a large sample, standardised methods of data collection and comprehensive measures of cardiovascular risk factors.
- Due to the cross-sectional study design, we have not been able to fully resolve which risk prediction tool works best in this setting.

Indeed, approximately 80% of all deaths from CVD occur in LMICs.³ Therefore, an important strategy to tackle the growing burden of CVD in LMICs is promotion and expansion of CVD prevention strategies that have been successful in high-income countries (HICs).^{4,5}

In HICs, growth in the burden of CVD has been curbed through a strategy combining reduction in risk factors at the population level and by targeting high-risk groups.⁶ Various cardiovascular risk prediction tools have been developed which are now a core feature of many clinical guidelines.^{7–9} Tools commonly used in HICs include the Framingham Risk Score (FRS),¹⁰ the Australian Risk Score (ARS)⁷ and the Systematic COronary Risk Evaluation (SCORE) risk tools: SCORE-high and SCORE-low.¹¹

Critically, there are no well-validated tools for use in LMICs¹² such as India.¹³ Furthermore, due to setting-dependent differences in both the prevalence and impact of various risk factors,¹⁴ the available tools may not be suitable in LMICs. The presence of multiple tools also creates uncertainty among policy-makers and clinicians about which cardiovascular risk tool to choose for their setting.¹⁵ To resolve this concern, the World Health Organization (WHO) recently developed



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region-specific risk tools,¹⁶ but these have not been externally validated in disadvantaged settings such as rural India.

We hypothesised that cardiovascular risk prediction tools perform disparately in rural India, but regardless of which risk tool is used, medication use is inadequate in this disadvantaged population. Therefore, we first aimed to compare laboratory-based tools, to estimate 10-year CVD risk, among a cross-section of adults in a rural region of southern India. Our secondary aim was to estimate the use of antihypertensive and lipid-lowering medication in those deemed at high risk of a cardiovascular event by these tools.

METHODS

Study design

Cross-sectional.

Setting

The study population comprised adult residents (aged ≥ 18 years) of the Rishi Valley region located in the Chittoor District, south-western Andhra Pradesh, India (see online supplemental methods).

Participants

Following exclusion of one hamlet which comprised a wealthy school and four small hamlets with no residents, 216 hamlets were available for sampling. These were categorised into small, medium and large hamlets and a similar number of hamlets from each group were randomly sampled (online supplemental figure 1). Among the 133 hamlets sampled, there were 13 077 eligible residents, of whom 5142 either refused or were otherwise unavailable for participation. This left 7935 who participated in a baseline survey between August 2012 and December 2015. Among these, 6472 had comprehensive data, while 1463 had some data available (online supplemental figure 1). There were some differences in the characteristics of the two samples (see online supplemental methods and online supplemental table 1).

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Data collection techniques and procedures

Using standardised questionnaires, field-workers collected data on the following variables: (1) sociodemographic factors: age, sex, marital status, education and income; (2) lifestyle factors: smoking and alcohol consumption (3) self-reported conditions: diabetes mellitus, hypertension, stroke, high cholesterol and cardiac disease; (4) standard clinical measures: blood pressure (BP), height and weight; and (5) lipid status: total cholesterol and high-density lipoprotein (HDL).

Arterial BP was measured in the seated position using a calibrated digital automatic BP monitor (OMRON

HEM-907, OMRON Health-care, Kyoto, Japan), after 15 min at rest. Three measurements were taken at 3 min intervals using the appropriate cuff size, according to the WHO-STEPS protocol.¹⁷ Measurements continued until two consecutive readings differed by <10 mm Hg systolic and <6 mm Hg diastolic, with a maximum of 5 measurements. The mean of the last two consecutive measurements was considered the participant's BP. Hypertension was defined as systolic BP (SBP)/diastolic BP $\geq 140/90$ mm Hg and/or prescription of antihypertensive medication.

We measured height (within 0.1 cm) using a portable stadiometer (213, Seca, Hamburg, Germany) and weight (within 0.1 kg) using a portable digital weighting scale (9000SV3R, Salter, Kent, UK). Blood cholesterol concentration was measured using an Accutrend GCT device (Roche Diagnostics, Mannheim, Germany). Hypercholesterolaemia was defined as total cholesterol ≥ 214 mg/dL and/or prescription of lipid-lowering agents. Diabetes status was confirmed when participants self-reported having diabetes. Details of these measurements have been described previously.^{18–20}

Cardiovascular risk prediction tools

'Absolute risk' is a term used to describe the probability that an individual will have a cardiovascular event within a given time period.⁷ Risk prediction tools are variously referred to as risk tools, risk scores, risk equations, risk algorithms and risk functions. Herein, the term 'tool' refers to the specific algorithm used to generate an estimate of absolute risk, the term 'score' refers to the resulting estimate of absolute risk, and the term 'band' refers to absolute risk categories. We assessed absolute risk using five different risk prediction tools: the FRS,¹⁰ the ARS,⁷ the WHO Risk Score (WHO-RS),¹⁶ the SCORE-low and the SCORE-high.¹¹ FRS, ARS and WHO-RS provide estimates for any cardiovascular event (fatal or non-fatal) whereas SCORE-low and SCORE-high predict a fatal cardiovascular event. For more details of the tools, see online supplemental methods, online supplemental figure 2 and online supplemental tables 2–4.

Calculation of cardiovascular risk score

The variables used to assess absolute risk included age, sex, smoking status, SBP, serum HDL, serum total cholesterol, and diabetes status. The individual-level risk scores were calculated using each of the five sex-specific risk tools. Then, for all people without a self-reported prior history of CVD (heart disease or coronary bypass surgery or angioplasty or stent inserted or stroke), the individual's estimated 10-year absolute risk scores for a fatal or non-fatal cardiovascular event were categorised in risk bands ($<10\%$, 10% – 20% or $\geq 20\%$; see online supplemental methods). Similarly, the scores for a fatal cardiovascular event were categorised as $<1\%$, 1% – 5% or $\geq 5\%$.

Statistical analyses

Statistical analyses were performed in Stata V.15 (STATA IC/15, StataCorp) or SYSTAT (V.13). The WHO

cardiovascular risk package in Stata was used to estimate WHO-RS.²¹ A two-tailed $p \leq 0.05$ was considered statistically significant.

Frequencies within categorical variables are presented as percentages with 95% confidence intervals (95% CI). Mean and 95% CI were calculated for data that were distributed in an approximately normal fashion. We first assessed normality using the Shapiro-Wilk test and then manually inspected the distributions using histograms and Q-Q plots. Most variables failed the Shapiro-Wilk test, but visual inspection revealed that their distribution approximated normality. Dichotomous comparisons were made using the χ^2 test for categorical variables and Student's unpaired t-test for continuous variables.

Among participants without self-reported history of CVD, we estimated the distribution of risk scores across various age categories. The various risk tools are specific for people within various age ranges (online supplemental table 2 and online supplemental figure 2). To allow direct comparison of the scores between tools, we applied each tool to those aged 35–74 years in all instances. Moreover, for some of the participants (n=1463) some data were not available (online supplemental figure 1). Thus, we used complete case analysis to minimise bias and optimise precision.²² Ordinary least-products regression analysis was used to determine the relationships between the risk scores generated by the five risk prediction tools.²³

Because qualitative risk bands can be used to make clinical decisions, we also compared these across the various tools. Risk bands were classified based on the established cut-offs in various guidelines^{7 8 24 25} with a slight modification for the ARS. For example, in the ARS guidelines, the 5-year risk of a fatal or non-fatal cardiovascular event is categorised as 'high risk' if the score is $>15\%$.⁷ But, in our study, we applied a 10-year prediction horizon. Thus, to make the ARS cut-off comparable to the cut-offs for the FRS²⁵ and WHO-RS,²⁴ we considered 'high risk' when the

score was $\geq 20\%$ as has been suggested and used in prior studies.^{26 27} Similarly, for SCORE-high and SCORE-low, the 10-year risk of a fatal cardiovascular event was categorised 'high risk' if the score was $\geq 5\%$.⁸ Comparisons were made only among tools with the same endpoint (fatal event only (SCORE-high and SCORE-low) and fatal or non-fatal event (FRS, ARS, and WHO-RS)). The concordance level in pair-to-pair analyses of risk bands was assessed using quadratic weighted kappa (κ_w).^{28 29} The agreement level was classified as poor (<0.2), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80) or very good (0.81–1.00).³⁰ Spearman's rank correlation (r_s) was computed to assess the relationships between the various risk bands.³¹

RESULTS

Sociodemographic characteristics and disease status of participants

Of the 7935 adults surveyed, 57% were women and the mean age was 44.9 years (SD ± 16.2). In total, 3.5% of the participants had self-reported history of CVD, defined as self-reported heart disease (2%) or coronary bypass surgery (0.2%) or angioplasty or stent inserted (0.4%) or stroke (1%) and 84% were aged between 35 and 74 years (online supplemental table 5).

In subsequent analyses, participants were restricted to those without a self-reported history of CVD and aged between 35 and 74 years (n=4202). Compared with women (4%), men had a greater prevalence of diabetes (6.1%). Similarly, the prevalence of smoking was greater in men (35.9%) than in women (0.4%). But, the prevalence of hypercholesterolaemia and hypertension was similar in men and women (table 1). For qualitative risk band comparisons, only participants with complete data required for all tools were included (n=3444).

Table 1 Baseline risk factors for cardiovascular disease (CVD) among adults without a self-reported history of CVD and aged 35–74 years in the Rishi Valley, Andhra Pradesh, India

Characteristics	Men		Women		P value
	n=1466	95% CI	n=1978	95% CI	
Age, years	51.8	51.2 to 52.3	50.5	50.0 to 51.0	<0.001
BMI, kg/m ²	21.0	20.8 to 21.2	20.7	20.5 to 20.9	0.05
Hypercholesterolaemia, n (%)	178 (12.1)	155 to 204	270 (13.7)	241 to 301	0.19
Hypertension, n (%)	398 (27.1)	365 to 432	493 (24.9)	456 to 532	0.14
Current smoker, n (%)	527 (35.9)	492 to 564	8 (0.4)	4 to 16	<0.001
Diabetes, n (%)	89 (6.1)	73 to 109	80 (4.0)	64 to 99	0.01

Values are presented as mean (age, BMI) and frequency (%).

P values for continuous variables were calculated according to independent sample t-test, while categorical variables were calculated using χ^2 .

Hypertension was defined as SBP/DBP $\geq 140/90$ mm Hg and/or prescription of antihypertensive medication. Hypercholesterolaemia was defined as total cholesterol ≥ 214 mg/dL and/or prescription of lipid-lowering medication. Current smoker refers to use of any tobacco products such as bidis, cigarettes and cheroot. Diabetes refers to a self-report of the condition.

BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

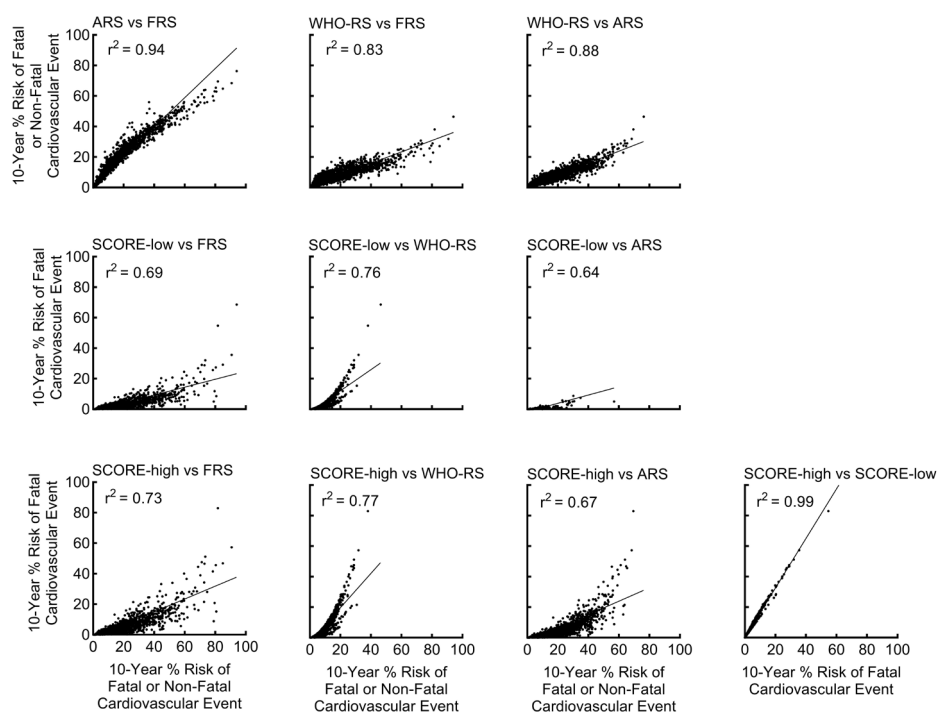


Figure 1 Relationships between risk prediction scores among participants without self-reported history of CVD and aged 35–74 years. The scatterplots show the individual coordinates of pair of risk scores. The lines of best fit were determined by ordinary least-products regression. All comparisons are for the dependent variable (y-axis) versus the independent variable (x-axis). For example, FRS is the independent variable for all three of the left-most panels. ARS, Australian Risk Score; CVD, cardiovascular disease; FRS, Framingham Risk Score; high, regions of high cardiovascular risk; low, regions of low cardiovascular risk; SCORE, Systematic COronary Risk Evaluation; WHO-RS, WHO Risk Score.

Quantitative analysis of agreement between risk scores generated by the various risk tools

All relationships between risk tools were quasi-linear, with straight-line relationships explaining 64%–99% of the variance (figure 1, online supplemental table 6). The calculated regression equations allow approximate inter-conversion between each pair of scores. In all comparisons, the 95% confidence limits of the Y-intercept of the regression equations did not include zero (online supplemental table 6). However, the divergence of the intercept from zero was relatively small, being the greatest for the comparison between WHO-RS and SCORE-high (–2.88%). In all comparisons, the 95% confidence limits of the slope did not include unity. There was good agreement between the FRS and ARS in predicting the 10-year risk of a fatal or non-fatal cardiovascular event (slope=0.96). However, the WHO-RS systematically underestimated this risk compared with both the FRS (slope=0.37) and ARS (slope=0.39). The absolute 10-year risk of a fatal or non-fatal cardiovascular event determined by the WHO-RS tool more closely aligned with the 10-year risk of a fatal cardiovascular event determined by either SCORE-low (slope=0.69) or SCORE-high (slope=1.13) than with the FRS or ARS. SCORE-high systematically generated greater scores of absolute risk of a fatal cardiovascular event than SCORE-low (slope=1.62).

Qualitative analysis of agreement between risk bands generated by the various risk tools

In line with the observed quantitative relationships between the various risk scores, with regard to qualitative risk bands, there was good agreement between the FRS and ARS in predicting the 10-year risk of a fatal or non-fatal cardiovascular event, but poor agreement between the WHO-RS and both the FRS and ARS (table 2). The pairwise agreement between the WHO-RS and both the FRS and ARS was poor, particularly in those with high total cholesterol, high SBP, high body mass index or who had diabetes mellitus (online supplemental table 7). SCORE-high and SCORE-low showed good agreement in predicting the 10-year risk of a fatal cardiovascular event (percentage agreement=83.36; $\kappa_w=0.84$, $r_s=0.86$; table 2). Agreement between the risk bands for the various tools was mostly greater for women than men, except for the comparison between the FRS and ARS (table 2 and online supplemental figure 3). In most cases, percentage agreement between scores declined with age, although this pattern was not evident for the quadratic weighted kappa (online supplemental figure 4).

Ten-year absolute risk of a cardiovascular event

The proportion of people categorised within each risk band differed for each of the five risk tools (table 3). For example, the proportion of individuals deemed at low risk

Table 2 Concordance between categories* of absolute risk in cardiovascular risk prediction tools among adults without self-reported history of cardiovascular disease at baseline and aged 35–74 years

Comparison of cardiovascular risk prediction tools	Men (n=1466)			Women (n=1978)			Total (n=3444)		
	Agreement (%)	Quadratic weighted kappa	Spearman's r (r _s)	Agreement (%)	Quadratic weighted kappa	Spearman's r (r _s)	Agreement (%)	Quadratic weighted kappa	Spearman's r (r _s)
FRS versus ARS	91.81	0.94	0.95	84.13	0.76	0.77	87.40	0.89	0.89
FRS versus WHO-RS	52.93	0.48	0.66	86.70	0.70	0.70	72.33	0.58	0.65
ARS versus WHO-RS	49.59	0.44	0.64	76.29	0.60	0.59	64.92	0.52	0.63
SCORE-low versus SCORE-high	74.28	0.80	0.85	90.09	0.86	0.85	83.36	0.84	0.86

Agreement was measured by using risk bands generated by the various risk tools.

*The category of risk bands are: <10%, 10% to <20%, or ≥20% risk for FRS, ARS and WHO-RS and <1%, 1% to <5%, or ≥5% risk for SCORE-high and SCORE-low.

ARS, Australian Risk Score; FRS, Framingham Risk Score; high, regions of high cardiovascular risk; low, regions of low cardiovascular risk; r_s, Spearman's r; SCORE, Systematic COronary Risk Evaluation; WHO-RS, WHO Risk Score.

(<10% risk of a fatal or non-fatal cardiovascular event) was 83% using the WHO-RS, 24% greater than that for the ARS. In contrast, one-fifth of the participants were deemed at high risk (≥20% risk of fatal or non-fatal cardiovascular event) when using the ARS, 5% greater than that for the FRS and 12% greater than that for the WHO-RS. Across all risk prediction tools, the proportion of men deemed at high risk (≥20% risk of a fatal or non-fatal cardiovascular event or ≥5% risk of a fatal cardiovascular event) was greater than for women (table 3).

The proportion of participants deemed at high risk of a fatal or non-fatal cardiovascular event were progressively greater with age (figure 2, online supplemental table 8). Among those aged 35–54 years, less than 2.0% were in the high-risk category (≥5% risk) for a fatal cardiovascular event using the SCORE-high or SCORE-low. In addition, when using the ARS, 5% of participants were deemed at high risk (≥20%) of a fatal or non-fatal cardiovascular event, nearly 2% greater than that for the FRS and WHO-RS. In all risk prediction tools, across all age groups, more men were in the high-risk category than women (figure 2, online supplemental table 8).

Antihypertensive and lipid-lowering medications

Among the 189 individuals aged 35–74 years with self-reported history of CVD, over one third were taking either antihypertensive or lipid-lowering medications (online supplemental figure 5). More details are provided in online supplemental results and online supplemental table 9.

Of those without self-reported history of CVD but at high risk of a cardiovascular event, 9%–12% of individuals reported taking either antihypertensive or lipid-lowering therapy, and this was similar between risk prediction tools (table 4). When limiting this analysis to those with a diagnosis of hypertension or hypercholesterolaemia, between 10% and 17% of those categorised as being at high risk were taking either antihypertensive or lipid-lowering medication (table 4). Among those with hypertension, 546 (61.3%) were unaware of their hypertensive status (online supplemental table 10). Similarly, among those with hypertension who were also at high risk of a cardiovascular event, approximately 60% were unaware of their hypertensive status. In addition, 194 (24.4%) had never had their BP measured prior to the survey, so were newly defined as having hypertension as a result of the survey.

DISCUSSION

Our analysis provides two novel and important findings. First, we found that cardiovascular risk prediction tools performed disparately in a resource-constrained rural setting in a LMIC. Thus, only some, but not all, are likely valid in such settings. Their relative merits can only be assessed by prospective follow-up, which is currently underway. Our other important finding was that, regardless of the risk prediction tool used, few individuals deemed at high risk (≥20% risk of a fatal or non-fatal

Table 3 Category of 10-year risk bands of a cardiovascular event among adults without a self-reported history of cardiovascular disease at baseline and aged 35–74 years

Risk prediction tools and risk bands	Men (n=1466)	Women (n=1978)	Total (n=3444)
FRS			
<10%	665 (45.4)	1635 (82.7)	2300 (66.8)
10%–20%	364 (24.8)	250 (12.6)	614 (17.8)
≥20%	437 (29.8)	93 (4.7)	530 (15.4)
ARS			
<10%	610 (41.6)	1411 (71.3)	2021 (58.7)
10%–20%	357 (24.4)	378 (19.1)	735 (21.3)
≥20%	499 (34.0)	189 (9.6)	688 (20.0)
WHO-RS			
<10%	1104 (75.3)	1757 (88.8)	2861 (83.1)
10%–20%	231 (15.8)	84 (4.3)	315 (9.2)
≥20%	131 (8.9)	137 (6.9)	268 (7.8)
SCORE-low			
<1%	761 (51.9)	1481 (74.9)	2242 (65.1)
1%–5%	457 (31.2)	417 (21.1)	874 (25.4)
≥5%	248 (16.9)	80 (4.0)	328 (9.5)
SCORE-high			
<1%	546 (37.2)	1335 (67.5)	1881 (54.6)
1%–5%	510 (34.8)	513 (25.9)	1023 (29.7)
≥5%	410 (28.0)	130 (6.6)	540 (15.7)

All values are reported as frequencies (percentages). Due to rounding, percentages may not add up to 100%.

ARS, Australian Risk Score; FRS, Framingham Risk Score; high, regions of high cardiovascular risk; low, regions of low cardiovascular risk; SCORE, Systematic COronary Risk Evaluation; WHO-RS, WHO Risk Score.

event or ≥5% risk of a fatal event) were receiving antihypertensive or lipid-lowering therapy. Thus, there remains a considerable treatment-gap in those at risk of a cardiovascular event in this setting.

Performance of the risk prediction tools

We found substantial variation in the absolute cardiovascular risk estimates of various risk prediction tools, as has been reported by others.¹⁵ The lack of well-developed and validated risk prediction tools in LMICs^{12 13} and the presence of multiple tools with varied predictive performance^{13 15 32–34} creates a lack of certainty regarding which tool to choose in clinical practice in settings of disadvantage in LMICs. Notably, the current WHO-RS showed lower estimated absolute risk levels and moderate agreement compared with the ARS and FRS which is consistent with findings based on the previous version of this risk prediction tool.³⁴ While risk prediction tools have the potential to identify those at high risk of a cardiovascular event in LMICs,^{15 33 34} the disparities in categorisation likely mean that some are invalid in such a setting. Prospective follow-up will enable assessment of their validity.

Gender and age

Predicted risk of a fatal or non-fatal cardiovascular event in rural south India was greater in men than women.

This observation is consistent with prior work in both LMICs^{15 35} and HICs.³⁶ It likely reflects the better risk factor profile in women than men, such as lesser prevalence of diabetes and tobacco use. In accordance with our findings, another plausible explanation could be use of antihypertensive or lipid-lowering treatments which is greater in women than men.³⁷ Previous investigators have also suggested that this could be biological³⁵ and related to sex hormones.³⁸

Fatal or non-fatal cardiovascular events have been reported to occur at younger ages in an LMIC setting than in an HIC setting.⁴ Our finding that only 3%–5% of the participants aged 35–54 years were deemed at high risk of a fatal or non-fatal cardiovascular event does not really accord with this prior finding, so potentially these risk tools may underestimate risk in these settings.⁴ Thus, it may be beneficial to target primary prevention strategies in disadvantaged settings to those of a younger age. Such strategies could include screening for risk factors and assessment of cardiovascular risk, counselling and treatment. Indeed, in a recent consensus statement for Aboriginal and Torres Strait Islander populations in Australia, a significantly disadvantaged community, it was recommended that cardiovascular risk assessment commences at the age of 18 years, and at 30 years at the

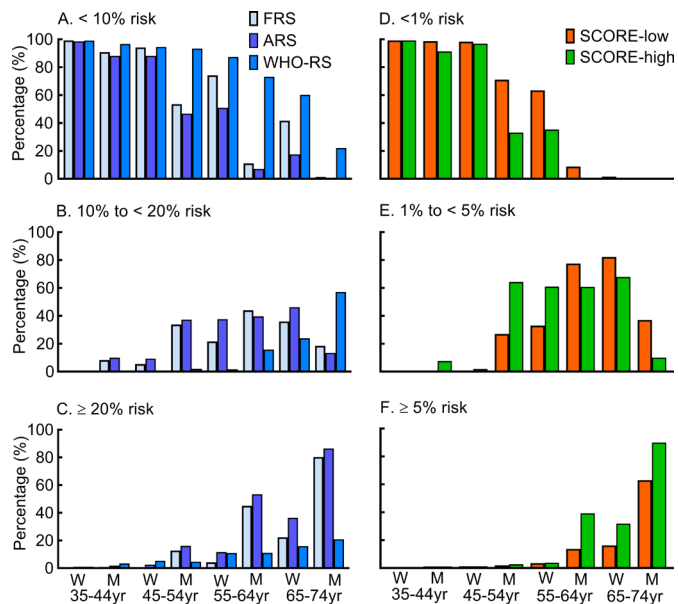


Figure 2 The proportion of adults in various risk bands for a fatal or non-fatal cardiovascular event by sex and age. Proportion of adults categorised in each of (A) <10%, (B) 10%–20%, and (C) \geq 20% risk bands of a fatal or non-fatal cardiovascular event at 10 years; (D) <1%, (E) 1%–5%, and (F) \geq 5% risk bands of a fatal cardiovascular event at 10 years, according to age and sex. Risk bands were categorised based on laboratory-based FRS, ARS, WHO-RS, SCORE-low and SCORE-high risk scores. ARS, Australian Risk Score; FRS, Framingham Risk Score; high, regions of high cardiovascular risk; low, regions of low cardiovascular risk; M, men; SCORE, Systematic COronary Risk Evaluation; W, women; WHO-RS, WHO Risk Score; yr, years.

latest.³⁹ Therefore, targeting at-risk populations at an earlier age (35–54 years) in these settings could be an effective strategy to reduce the impact of cardiovascular risk factors.⁴

Antihypertensive and lipid-lowering medication

Regardless of the risk prediction tool used, few individuals deemed at high risk were receiving antihypertensive or lipid-lowering therapy in a resource-limited rural setting in an LMIC. With less than 18% of individuals with hypertension or hypercholesterolaemia deemed at high-risk taking any antihypertensive or lipid-lowering therapies, there is clearly a considerable treatment-gap in those at risk of a cardiovascular event in this setting. Similarly, low levels of medication use have been found in other Indian settings.^{40 41} Moreover, medication use in India appears to be considerably less than in Australian Aboriginal and Torres Strait Islander communities, where 4 in 10 people at high risk were found to be taking lipid-lowering medication.³²

The WHO's Global Action Plan includes a target that, by 2025, at least 50% of eligible people receive drug therapy and counselling to prevent CVD.⁴² Medication use among those deemed at high risk of a cardiovascular event in the cohort we studied was significantly lower than this target. Drug utilisation varies between

countries according to economic status.⁴³ For example, it has been estimated that over 80% of eligible patients from low-income countries, 45% in upper-middle-income countries, and 11% in HICs do not receive their recommended treatment. Affordability of medications makes a major contribution to these discrepancies. In India, for example, 65% of households could not afford the monthly cost (US\$30) of the two lowest cost antihypertensives plus the lowest cost statin medication.⁴⁴ Some of the treatment-gap in LMICs is probably a consequence of lack of awareness.^{45–50} Indeed, approximately 60% of those with hypertension were unaware of their hypertensive status and about a quarter had never previously had their BP measured. These observations may indicate missed opportunities for diagnosis of hypertension or missed opportunities for educating the patient about their BP and treatment options. Thus, enhanced screening, together with education about hypertension, should go some way to improving uptake of medications. But, other factors such as under-diagnosis, limited access to healthcare, lack of prescription, contraindications, cost, resistance/refusal by the patient and cultural beliefs are likely also important.^{32 40 41 45} Use of cardiovascular risk prediction tools, to manage primary prevention, that are relevant to the population, may help overcome at least one of these barriers, as they enable strategies that are more cost-effective and efficient than targeting single risk factors.^{40 51 52} Facilitating treatment in those at high risk of CVD may then assist LMICs to meet the WHO target. In addition, investment in prevention and treatment of CVDs could help to avert the vicious cycle of poverty and non-communicable diseases in LMICs.^{53 54}

For people identified as being at high risk of a cardiovascular event, national and international guidelines recommend various lifestyle behaviour changes alone or in combination with pharmacotherapy.^{13 42} However, given the difference in the risk performance of the risk prediction tools, in our study region and similar LMICs,^{15 33} well-validated tools with appropriate cut-offs are required to better target high-risk groups for early prevention and treatment in LMICs.

Strengths and limitations

To the best of our knowledge, ours is the first comprehensive assessment of multiple risk prediction tools and use of medications in a large sample in a rural LMIC setting. We used rigorous training of all data collectors and research staff to ensure standardisation of methods for data collection, validity and generalisability of our findings. In addition, we used comprehensive measures of cardiovascular risk factors. Our community-based findings provide evidence for policy-makers and clinicians for optimising prevention at the population level and for treatment at an individual level.

A limitation of our study was the large proportion of people who refused to participate. However, the socio-demographics of the screened participants were similar to those of participants included in the analysis, so this

Table 4 Use of antihypertensive and/or lipid-lowering medications among adults, aged 35–74 years, without a self-reported history of CVD at baseline

Risk prediction tools and risk bands	Lipid-lowering medication		Antihypertensive medication		Either antihypertensive or lipid-lowering medication	
	All (n=3444) Freq (%)	Hypercholesterolaemic (n=448) Freq (%)	All (n=3444) Freq (%)	Hypertensive (n=891) Freq (%)	All (n=3444) Freq (%)	Hypercholesterolaemic and/or hypertensive (n=1152) Freq (%)
FRS						
<10%	4 (0.2)	4 (2.1)	45 (2.0)	45 (15.6)	46 (2.0)	46 (10.4)
10%–20%	0 (0.0)	0 (0.0)	29 (4.7)	29 (10.7)	29 (4.7)	29 (8.7)
≥20%	4 (0.8)	4 (3.1)	64 (12.1)	64 (19.3)	65 (12.3)	65 (17.4)
ARS						
<10%	2 (0.1)	2 (1.4)	31 (1.5)	31 (15.4)	31 (1.5)	31 (9.6)
10%–20%	2 (0.3)	2 (1.5)	39 (5.3)	39 (14.7)	40 (5.4)	40 (11.7)
≥20%	4 (0.6)	4 (2.4)	68 (9.9)	68 (16.0)	69 (10.0)	69 (14.2)
WHO-RS						
<10%	5 (0.2)	5 (1.7)	80 (2.8)	80 (17.1)	81 (2.8)	81 (11.8)
10%–20%	2 (0.6)	2 (2.6)	31 (9.8)	31 (18.7)	32 (10.2)	32 (16.1)
≥20%	1 (0.4)	1 (1.4)	27 (10.1)	27 (10.5)	27 (10.1)	27 (10.2)
SCORE-low						
<1%	3 (0.1)	3 (1.5)	54 (2.4)	54 (17.4)	54 (2.4)	54 (11.7)
1%–5%	3 (0.3)	3 (1.9)	54 (6.2)	54 (15.8)	56 (6.4)	56 (13.0)
≥5%	2 (0.6)	2 (2.4)	30 (9.2)	30 (12.6)	30 (9.2)	30 (11.5)
SCORE-high						
<1%	3 (0.2)	3 (1.9)	41 (2.2)	41 (17.6)	41 (2.2)	41 (11.7)
1%–5%	1 (0.1)	1 (0.6)	46 (4.5)	46 (14.5)	47 (4.6)	47 (11.2)
≥5%	4 (0.7)	4 (3.1)	51 (9.4)	51 (15.0)	52 (9.6)	52 (13.6)

Hypertension was defined as SBP/DBP ≥140/90 mm Hg and/or prescription of antihypertensive medication.

Hypercholesterolaemia was defined as total cholesterol ≥214 mg/dL and/or prescription of lipid-lowering agents.

This table shows the number (%) of patients receiving these medications both with respect to the entire cohort and with respect to the subset of participants with hypercholesterolaemia, hypertension and either hypercholesterolaemia or hypertension.

All values are reported as frequencies (row percentages).

, ; ARS, Australian Risk Score; DBP, diastolic blood pressure; FRS, Framingham Risk Score; high, regions of high cardiovascular risk; low, regions of low cardiovascular risk; SBP, systolic blood pressure; SCORE, Systematic COronary Risk Evaluation; WHO-RS, WHO Risk Score.

may not have reduced the generalisability of our findings. In addition, we were unable to fully resolve which risk prediction tool works best in our setting. Further prospective data are required to answer this question.

CONCLUSIONS

In a disadvantaged rural setting in a LMIC, cardiovascular risk prediction tools performed disparately, resulting in uncertainties regarding the best choice of tool for this setting. Our findings indicate that absolute cardiovascular risk is higher in men than women and increases markedly with age. These laboratory-based tools have the potential to help identify individuals at high risk of a cardiovascular event in such settings. But, first, their validity must be established using hard outcomes. Importantly, few individuals deemed at high risk were receiving

antihypertensive or lipid-lowering therapy. Thus, there remains a considerable treatment gap in those at risk of a cardiovascular event in this setting.

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Ethics approval Ethical approval was obtained from the Rishi Valley Education Centre (RVEC), the Health Ministry's Screening Committee of the Indian Council of Medical Research (58/4/1F/CHR/2013/NCD II), and Monash University (CF13/2516-2013001327). After explaining the purpose of the study, field workers sought informed consent from each study participant. Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available on reasonable request. The Rishi Valley Study is an ongoing cohort among disadvantaged communities in rural India. We have a successful history of conducting collaborative research and we welcome specific proposals for new collaborations. Deidentified and restricted data are available on reasonable request. Initial enquiries should be made to the principal investigator AGT (Amanda.Thrift@monash.edu).

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