

## Original Research Article

# A community based cross sectional study to estimate total cardiovascular risk in rural Punjab

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## ABSTRACT

**Background:** Cardiovascular diseases (CVD) are leading cause of non communicable deaths in India. CVD risk prediction charts by World Health Organization/International Society of Hypertension (WHO/ISH) are designed for implementing timely preventive measures. The objective of the study was to assess the prevalence of CVD risk parameters and to estimate total CVD risk among adults aged  $\geq 40$  years, using the WHO/ISH risk charts alone and also to assess the effect of the inclusion of additional criteria on CVD risk.

**Methods:** A community based cross sectional study was conducted in fifteen villages of Ludhiana district under rural health training centre of Department of Community Medicine, Dayanand Medical College & Hospital, Ludhiana, Punjab. Desired information was obtained using WHO STEPS survey (STEP wise approach to surveillance) from 324 adults aged  $\geq 40$  years. Anthropometric, clinical and laboratory measurements were also performed. WHO/ISH risk prediction chart for South East Asian region (SEAR-D) was used to assess the cardiovascular risk among the subjects.

**Results:** WHO/ISH risk prediction charts identified 16.0% of the subjects with high risk ( $\geq 20\%$ ) of developing a cardiovascular event. The study population showed higher prevalence of physical inactivity, obesity, abdominal obesity, hypertension and diabetes. Amongst high risk CVD group, maximum prevalence was of hypertension and high perceived stress level. However, the proportion of high CVD risk ( $\geq 20\%$ ) increased to 33.6% when subjects with blood pressure  $\geq 160/100$  mmHg and /or on hypertension medication were added as high risk.

**Conclusions:** A substantial proportion of this community is at high risk of developing cardiovascular diseases.

**Keywords:** Cardiovascular disease, Risk prediction charts, Hypertension, India

## INTRODUCTION

Non-communicable diseases (NCD) burden has increased considerably due to ongoing demographic and nutrition transition. Globally cardiovascular diseases are responsible for close to half of NCD deaths. Cardiovascular disease (CVD) & stroke are among the top three causes of life lost due to premature deaths worldwide. Currently over 80.0% of the cardiovascular deaths occur in low- and middle income countries and CVD accounts for one quarter of all deaths in India.<sup>1,2</sup>

Total CVD risk is defined as the probability of an individual experiencing a CVD event over a given period of time and is determined by combined effect of cardiovascular risk factors, which commonly co-exist and act multiplicatively.<sup>3</sup> The findings of INTERHEART study revealed that together current smoking, hypertension and diabetes increase the odds of developing acute myocardial infarction (MI) and with each added risk factor, increase in the risk shows multiplicative effect rather than additive effect.<sup>4</sup>

Estimation of risks for developing cardiovascular events in apparently healthy adults will be useful for stratification of risk and targeting preventive measures based on individual's predicted risk. These timely and sustained lifestyle interventions will reduce the risk of CVD events in people with a high total CVD risk.<sup>3</sup> Risk stratification assists in making logical management decisions and may help to avoid both under and overtreatment and is particularly suitable to setting with limited resources.<sup>5</sup> Thus, an approach that addresses total CVD risk is more cost effective approach than treatment decisions based on individual risk factors threshold only.<sup>3</sup>

World Health Organization (WHO)/International Society of Hypertension (ISH) risk prediction charts have been developed for 14 different WHO sub-regions and are primarily intended to be used in areas where cohort data and resources are not readily available for development of population-specific charts. These charts present ten year risk of major cardiovascular event.<sup>6,7</sup> A comprehensive Risk Stratification Model is yet to be developed for Indians and it is prudent to follow WHO risk score for South East Asian Region (SEAR-D)<sup>9</sup>, which is the only prescribed algorithm for CVD risk assessment in India. Thus the present study was conducted in rural community with an aim to assess the prevalence of CVD risk parameters and to estimate the total CVD risk among adults aged  $\geq 40$  years, using the WHO/ISH risk charts alone and also to assess the effect of the inclusion of additional criteria on CVD risk.

## METHODS

### Study design

A community based cross sectional study was carried out in fifteen villages comprising a population of 31,615 under rural health training centre of Department of Community Medicine, Dayanand Medical College and Hospital, Ludhiana, Punjab, India from March 2015 to Feb 2016. As data on prevalence of diabetes mellitus (one of the CVD risk factor) was not available for rural Punjab, therefore assuming a diabetes prevalence of 50% (which gives the maximum sample size for doing prevalence study) with 5% absolute precision, minimum sample size of 384 eligible subjects was required. Allowing for a non-response rate of 10%, the study was expanded to include 425 subjects.<sup>8</sup>

### Methodology

The selection of the participants was done by systematic random sampling. First subject was selected randomly by currency note method considering the last digit of the currency note. Subsequent subjects were selected as per sampling interval. Study participants were interviewed after obtaining written informed consent and the information was collected using WHO STEPS Instrument. The WHO STEPS tool uses standardized questionnaires and measurement protocols to collect data

and measure non communicable disease risk factors.<sup>9,10</sup> Height, weight, waist circumference, pulse rate and blood pressure were also measured.

Weight was measured in kilogram (kg) by using a standard manual weighing scale with the subject standing on machine without shoes and minimum clothes at the centre of the platform.<sup>10</sup> Height was measured to the nearest centimeter by using a narrow, flexible, non-stretchable measuring tape with subject standing along the wall without shoes with feet parallel to each other.<sup>10</sup> Waist circumference was measured to the nearest cm at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest, using a stretch resistant measuring tape with subject in relaxed state at the end of a normal expiration.<sup>11</sup> One Touch Johnson and Johnson glucometer with application of capillary finger prick method was used to measure plasma glucose levels. Blood pressure was measured on the right arm in a sitting posture, with the subject in a relaxed state using standardized aneroid sphygmomanometer (Diamond deluxe BP apparatus, Pune, India) with adult size cuff as mean of the two readings taken ten minutes apart.<sup>10</sup>

WHO/ISH cardiovascular risk prediction chart for South-East Asian region (SEAR-D) was used to assess the cardiovascular risk among the sampled participants. As measurement of serum cholesterol level was not feasible in the current settings, SEAR-D risk prediction chart without blood cholesterol was used.<sup>7</sup> As WHO/ISH risk prediction charts are designed for population 40 years and older, therefore for this study we included only 324 adults who were aged 40 years and above for further analysis. The predictor variables for risk prediction were age, gender, smoking, systolic blood pressure, presence or absence of diabetes. Ethics clearance for the study was duly obtained from the institutional ethics committee.

### Operational definitions

Education of the subject as self-reported was considered in classifying them into educational groups. Primary occupation of the subject was considered in classifying them into occupational groups. Non-workers included retired, homemaker, unemployed (able to work) and unemployed (unable to work). The socio-economic status was determined by modified Udai Pareek scale.<sup>12</sup> Smoking was defined as the use of any smoke form of tobacco product in the last one year.<sup>10</sup> Subjects were classified as physically active if they followed at least 150 minutes moderate-intensity physical activity in a week.<sup>13</sup> Alcohol use was defined as consumption of any type of alcohol in the last one year.<sup>10</sup> Stress was measured using cohen perceived stress scale (PSS) and was categorized as low to average (score  $< 16$ ) and high to very high (score  $\geq 16$ ) perceived stress level.<sup>14</sup>

Diabetes was defined by physician diagnosis of diabetes and current use of medications for diabetes (insulin or oral hypoglycemic agents) and/or capillary fasting plasma

glucose  $\geq 126$  mg/dl or 2 h capillary post-glucose value  $\geq 200$  mg/dl.<sup>15</sup> A person was considered to be hypertensive if he/ she were already diagnosed case of hypertension and / or on treatment or with a current systolic blood pressure (SBP) of  $\geq 140$  mmHg or diastolic blood pressure (DBP)  $\geq 90$  mmHg.<sup>16</sup> Body

Mass Index (BMI) was calculated from the ratio of Weight (kg)/ Height<sup>2</sup> (m). Obesity was defined as BMI of  $\geq 23$  kg/m<sup>2</sup> as per Asian classification of obesity.<sup>17</sup> Presence of abdominal obesity was considered as waist circumference in men  $\geq 102$  cm and in women  $\geq 88$  cm.<sup>11</sup>

**Table 1: Characteristics of study participants.**

Study Variables	Male (%)	Female (%)	Total (%)	p-value
<b>Total</b>	161 (49.7)	163 (50.3)	324 (100.0)	-
<b>Age in years</b>				<0.001
40-49	54 (33.5)	52 (31.9)	106 (32.7)	
50-59	25 (15.5)	52 (31.9)	77 (23.8)	
60-69	37 (23.0)	36 (22.1)	73 (22.5)	
$\geq 70$	45 (28.0)	23 (14.1)	68 (21.0)	
<b>Educational Status</b>				<0.001
No formal schooling	29 (18.0)	63 (38.6)	92 (28.4)	
Below Matric	63 (39.1)	66 (40.5)	129 (39.8)	
Matric and above	69 (42.9)	34 (20.9)	103 (31.8)	
<b>Occupational Status</b>				<0.001
Non-workers	47 (29.2)	154 (94.5)	201 (62.0)	
Workers	114 (70.8)	09 (5.5)	123 (38.0)	
<b>Socio-economic Status</b>				0.135
Low & low-middle	58 (36.0)	72 (44.2)	130 (40.1)	
High & high-middle	103 (64.0)	91 (55.8)	194 (59.9)	
<b>Tobacco Use</b>				-
Absent	150 (93.2)	163(100.0)	313 (96.6)	
Present	11 (6.8)	-	11 (3.4)	
<b>Alcohol intake</b>				-
Absent	83 (51.6)	163 (100.0)	246 (75.9)	
Present	78(48.4)	-	78 (24.1)	
<b>Physical Activity</b>				0.317
Inactive	75 (46.6)	85(52.1)	160(49.4)	
Active	86(53.4)	78(47.9)	164(50.6)	
<b>BMI (kg/m<sup>2</sup>)</b>				0.138
<23	62(38.5)	50(30.7)	112(34.6)	
$\geq 23$	99(61.5)	113(69.3)	212(65.4)	
<b>Abdominal obesity*</b>				<0.001
Absent	97(60.2)	33(20.2)	130(40.1)	
Present	64(39.8)	130(79.8)	194(59.9)	
<b>Hypertension<sup>†</sup></b>				<0.01
Absent	50 (31.1)	76 (46.6)	126 (38.9)	
Present	111 (68.9)	87 (53.4)	198 (61.1)	
<b>Diabetes<sup>^</sup></b>				0.773
Absent	141 (87.6)	141 (86.5)	282 (87.0)	
Present	20 (12.4)	22 (13.5)	42 (13.0)	
<b>Perceived Stress Health Risk level</b>				<0.01
Low to average	102 (63.4)	79 (48.5)	181 (55.9)	
High	59 (36.6)	84 (51.5)	143 (44.1)	

\*Normal (waist circumference <102 cm for males and <88 cm for females).

<sup>†</sup>High (systolic blood pressure  $\geq 140$  mm Hg and diastolic blood pressure  $\geq 90$  mm Hg).

<sup>^</sup>Present (fasting blood sugar  $\geq 126$  mg/dl and/or postprandial blood sugar ( $\geq 200$  mg/dl).

**Table 2: Distribution of study population into low, moderate and high CVD risk categories as per age and gender.**

Age (Years)	Male (n=161)			Female (n=163)		
	CVD risk (%)					
	Low (<10%)	Moderate (10% to <20%)	High (≥20%)	Low (<10%)	Moderate (10% to <20%)	High (≥20%)
40-49	96.4 (87.2-99.5)	1.8 (0.1-9.9)	1.8 (0.1-9.9)	96.2 (86.8-99.5)	-	3.8 (0.5-13.2)
50-59	88.0 (68.8-97.5)	8.0 (0.98-26.0)	4.0 (0.1-20.3)	76.9 (63.2-87.5)	17.3 (8.2-30.3)	5.8 (1.2-15.9)
60-69	32.4 (18.0-49.8)	35.2 (20.2-52.5)	32.4 (18.0-49.8)	41.7 (25.5-59.2)	27.8 (14.2-45.2)	30.5 (16.3-48.1)
>69	42.2 (27.7-57.8)	28.9 (16.4-44.3)	28.9 (16.4-44.3)	-	60.9 (38.3-80.3)	39.1 (19.7-61.5)
<b>Total</b>	65.2 (57.3-72.5)	18.0 (12.4-24.8)	16.8 (11.3-23.4)	64.4 (56.5-71.7)	20.3 (14.4-27.2)	15.3 (10.2-21.8)

Figures in parenthesis indicate 95% confidence interval  
CVD=Cardiovascular Disease.

**Table 3: Prevalence of risk factors (not included in WHO/ISH chart CVD risk estimation) in the CVD risk groups.**

Risk factors	CVD risk (%)			
	Low (<10%)	Moderate (10% and <20%)	High (≥20%)	Total
<b>Total (n)</b>	<b>210</b>	<b>62</b>	<b>52</b>	<b>324</b>
<b>Physical inactivity</b>	44.8 (37.9-51.8)	53.2 (40.1-66.0)	63.5 (49.0-76.4)	49.4 (43.8-54.9)
<b>BMI (≥23kg/m<sup>2</sup>)</b>	66.7 (59.8-73.0)	66.1 (53.0-77.7)	59.6 (45.1-73.0)	65.4 (59.9-70.5)
<b>Abdominal obesity</b>	61.4 (54.5-68.1)	58.1 (44.8-70.5)	55.8 (41.3-69.5)	59.9 (54.3-65.2)
<b>Smoking</b>	2.4 (0.8-5.5)	3.2 (0.4-11.2)	7.7 (2.1-18.5)	3.4 (1.8-6.2)
<b>Alcohol usage</b>	25.7 (19.9-32.2)	11.3 (4.7-21.9)	32.7 (20.3-47.1)	24.1 (19.6-29.2)
<b>High perceived stress health risk</b>	31.9 (25.7-38.7)	50.0 (37.0-63.0)	86.5 (74.2-94.4)	44.1 (38.7-49.7)
<b>Hypertension</b>	46.7 (39.8-53.7)	77.4 (65.0-87.1)	100.0	61.1 (55.6-66.4)
<b>Diabetes</b>	6.7 (3.7-10.9)	16.1 (8.0-27.7)	34.6 (21.9-49.1)	13.0 (9.6-17.2)
<b>Currently on HT treatment</b>	14.8 (10.3-20.3)	29.0 (18.2-42.0)	44.2 (30.5-58.7)	22.2 (17.9-27.2)
<b>High Pulse Rate</b>	8.6 (5.2-13.2)	8.1 (2.7-17.8)	5.8 (1.2-15.9)	22.2 (17.9-27.2)

Figures in parenthesis indicate 95% confidence interval  
CVD= Cardiovascular Disease.

**Table 4: CVD risk categories with different inclusion criteria for the risk factors.**

Inclusion criteria (N=324)	CVD risk (%)		
	Low (<10%)	Moderate (10% and <20%)	High (≥20%)
<b>Simple application of chart</b>	64.8 (59.3-69.9)	19.2 (15.1-23.9)	16.0(12.3-20.6)
<b>Chart + BP ≥160/100</b>	60.8 (55.2-66.1)	14.5 (10.9-18.9)	24.7(20.2-29.8)
<b>Chart + BP ≥ 160/100 + on HT treatment</b>	54.0 (48.4-59.5)	12.4 (9.1-16.5)	33.6(28.3-39.1)

Figures in parenthesis indicate 95% confidence interval  
CVD= Cardiovascular Disease

The risk level for 10-year risk of a fatal or non-fatal CVD event were classified as low risk (<10%), moderate risk (10% to <20%), high risk ( $\geq 20\%$ ). Association of WHO practice points like subjects who are already on antihypertensive therapy, with obesity including central obesity, sedentary lifestyle and raised pulse rate ( $>90$  per minute)<sup>18</sup> with CVD risk were also studied, as CVD risk may be higher in the presence of some of these additional risk factors.<sup>6,7</sup> Study participants with blood pressure  $\geq 160/100$  mmHg and participants on self-reported hypertension medication (based on receipt of medication) and blood pressure measurements below recommended hypertensive thresholds were also considered in high risk category and association with CVD risk was analyzed.<sup>7,18</sup>

### Statistical Analysis

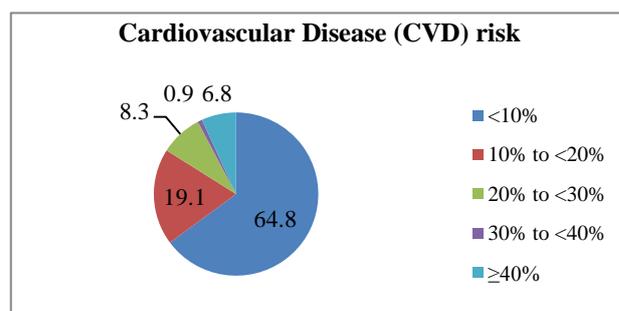
Analysis was performed using Statistical Package for Social Sciences (SPSS package), version 20 (IBM SPSS statistics 20.0.0, 2011) and Epi info™ version 7.1.4.0 (2014). Descriptive statistics are presented in percentages and mean $\pm$ standard deviation. 95% Confidence intervals around prevalence estimates were also computed. Chi-square test was used to examine the association between various categorical variables and gender. All tests were two-tailed and  $p < 0.05$  was considered to be statistically significant.

## RESULTS

There were total of 324 adults aged 40 years and above. Of them, 161 (49.7%) were males. Mean age of males and females was  $59.1 \pm 13.2$  and  $56.3 \pm 11.4$  years respectively ( $p < 0.05$ ). Table 1 reveals the association between different socio-demographic/study variables and the gender of the study subjects. One thirds (32.7%) of the participants were from the age group of 40–49 years and 21% of subjects were aged 70 years and above. A higher proportion of women did not attend the school and were non-workers as compared to the men ( $< 0.001$ ). Most of the study participants belonged to high middle and high socio-economic status among both the sexes ( $p = 0.135$ ). Amongst the study subjects only 3.4% were smokers as almost all subjects were followers of Sikh religion and smoking is prohibited in Sikh religion. Nearly half of the men were alcohol drinkers with none of the women being alcohol drinker. Two third of both the male and female subjects had BMI  $\geq 23$  kg/m<sup>2</sup> ( $p = 0.138$ ), however, prevalence of abdominal obesity was significantly higher among females (79.8%) in comparison to males (39.8%) ( $p < 0.001$ ). Higher proportion of males were hypertensive as compared to females ( $p < 0.01$ ). Females had slightly higher prevalence of physical inactivity and diabetes than males. However, the observed difference was found to be statistically non-significant as shown in Table 1.

WHO/ISH risk prediction charts identified two third of the study participants having low (<10.0%), followed by

19.1% and 16.0% of them having moderate (10% to <20%) and high risk ( $\geq 20\%$ ) of developing cardiovascular event over 10 years respectively (Figure 1). The prevalence of low, moderate and high CVD risk was 65.2%, 18.0% and 16.8% among males and 64.4%, 20.3% and 15.3% among female subjects respectively. Males in the age group of 60–69 years and females aged 70 years and above had maximum prevalence of high CVD risk and it increased significantly in males and females with age as shown in Table 2.



**Figure 1: Distribution of study subjects with 10 year total cardiovascular disease risk using WHO/ISH chart.**

The study population showed higher prevalence of physical inactivity (49.4%), obesity (65.4%), abdominal obesity (39.9%), high perceived stress level (44.1%), hypertension (61.1%) and diabetes (13.0%). When further analyzed, it was observed that in the moderate CVD risk category, maximum prevalence was of had obesity (66.1%) and hypertension (77.4%). Amongst high risk CVD group, all the study participants had hypertension followed by high perceived stress level (86.5%) and physical inactivity (63.5%) as shown in Table 3.

After application of additional criteria, when the proportion of subjects with blood pressure ( $\geq 160/100$  mmHg) were added to chart calculated proportions and were classified as high risk as per WHO practice notes, thereafter the subjects with low risk of CVD were reduced to 60.8% from 64.8% and those with high risk increased from 16.0% to 24.7%. The proportions with high CVD risk rose further to 33.6% if self-reported treatment for raised blood pressure was also taken into account as shown in Table 4.

## DISCUSSION

Current study presented the CVD risk factors burden and assessment of CVD risk prediction in rural community of North India. It was observed that among the socio-demographic variables, both the sexes had significant difference in age, educational, occupational and socio-economic status. Overall, both males and females had relatively high BMI with mean BMI of  $25.1 \pm 5.1$  kg/m<sup>2</sup>. However, females had significantly higher abdominal

obesity as majority of the females were housemakers (88.4%) and half of them were physically inactive. Prevalence of hypertension was significantly higher in males than females. Ghorpade et al in a cross sectional study conducted in rural Pondicherry also observed that level of education, employment status and waist circumference was statistically associated with gender.<sup>19</sup> Other studies conducted in rural India and abroad observed similar association.<sup>20-23</sup> However Herath et al in southern Sri Lanka observed that males and females were not significantly different in BMI, waist circumference, SBP and DBP.<sup>24</sup>

Use of risk prediction charts to estimate total cardiovascular risk is a major advance on the older practice of identifying and treating individual risk factors.<sup>3</sup> Risk for CVD appears to vary substantially across the geographical areas in different countries. Current study identified 64.8% of the subjects having low risk and an alarming 16.0% of participants having high risk of developing CVD in a decade. In a similar study conducted in the same field practice area among the adults attending a health examination camp, Bansal et al. observed that 44.4% subjects had more than 10% risk for fatal or non fatal myocardial infarction or stroke in 10 years.<sup>25</sup> In another community based cross sectional study in Karnataka, Norman et al observed that over 15% of the population had a high risk of CVD (>30%).<sup>21</sup> Reason behind these variations could be attributed to difference in lifestyle and diet between north and south India. Bansal et al in a hospital based study done in Haryana among patients with first myocardial infarction without prior cardiovascular disease predicted high risk of CVD (13.4%) for them, if they had presented prior to suffering the acute myocardial infarction.<sup>26</sup>

Prevalence of high CVD risk varied in studies conducted in Cambodia (1.3%),<sup>18</sup> Sri Lanka (1.9%-8.2%),<sup>23,24</sup> Malaysia (2.3%),<sup>18</sup> Cuba (4.6%),<sup>22</sup> rural Nepal (5.6%),<sup>27</sup> Mongolia (6%)<sup>18</sup>, Latin America (14.7%)<sup>28</sup> and Oman (36.3%)<sup>29</sup>. The observed difference in CVD risk may be due to usage of different inclusion criteria whether blood cholesterol charts were used or not used and these studies were conducted in different healthcare settings. The proportion of high risk study participants increased with age and CVD risk was marginally higher among males than in females. It is consistent with the other studies where CVD risk was higher in males and increased with age.<sup>19,21,22,30</sup> However, Ranawaka et al in Sri Lanka observed that high risk of CVD was commoner among females.<sup>23</sup>

Obesity, abdominal obesity, physical inactivity, socioeconomic status and a family history of premature cardiovascular disease can all modify cardiovascular risk. WHO/ISH charts are also accompanied by practice notes for clinicians to aid interpretation and adjustment of individual risk when these risk factors are present but are not included in the risk score calculations, which may therefore underestimate actual risk in people with these

characteristics.<sup>3</sup> Prevalence of physical inactivity, obesity, abdominal obesity, high perceived stress level and hypertension was higher in the present study and in the high CVD risk group; the prevalence was higher for physical inactivity, high perceived stress level and hypertension. This is also corroborated by the results of Ghorpade et al where in the high risk group; prevalence was higher for salt intake (70.7%) and hypertension (86.2%).<sup>19</sup> Selavarajah et al also reported that there was high prevalence of obesity (32%), hypertension (55%) and diabetes mellitus (18%) in Asian population.<sup>30</sup> This is also in agreement with the results of Otgontuya et al, who in their study conducted in low to middle income countries: Malaysia, Mongolia and Cambodia observed that if these risk factors proportions were added outside the charts proportions, CVD risk increased considerably and prevalence of low physical activity and high pulse rate was higher among high CVD risk group.<sup>18</sup> Other studies also reported similar findings.<sup>21,28</sup>

Application of WHO/ISH risk charts alone at community level may underestimate the population with high total CVD risk and hence actual treatment needs.<sup>6</sup> Thus with the application of additional criteria of high blood pressure ( $\geq 160/100$  mmHg) to WHO/ISH charts criteria, high risk of CVD was considerably increased (16.0% to 24.7%). Similar finding was observed by Ghorpade et al in rural India.<sup>19</sup> Application of risk score charts to cross-sectional population data may also underestimate the risk if persons already on treatment are not taken into account. Simple application of WHO/ISH chart classified sizeable number of study participants currently on hypertension medication with controlled blood pressure levels as low-risk. With the inclusion of additional criteria (subjects on hypertension medication), proportions of subjects with high risk increased markedly. It is in concordance with the results by Otgontuya et al which revealed that underestimation of the high risk was likely to be greater in Malaysia than in Mongolia because of higher proportion of individuals on hypertension treatment.<sup>18</sup>

## CONCLUSION

Present study shows high proportion of CVD risk in rural North India. WHO/ISH CVD risk charts can be used as a simple screening tool for risk stratification in the community by peripheral health workers. In spite of underestimation of CVD risk by using these charts alone, the great strength of risk scoring approach is that it provides a rational means of making decisions about intervening in a targeted way, thereby making best use of resources available to reduce CVD risk. This can help in providing individual as well as population based interventions, including treatment and health education.

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