**Total cardiovascular risk for next 10 years among rural population of Nepal using WHO/ISH risk prediction chart**

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**Abstract**

**Background:** Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality globally. Primary prevention of CVD based on total CVD risk approach using WHO/ISH risk prediction chart would be more effective to stratify population under different risk levels, prioritize and utilize the scarce resources of low and middle-income countries. This study estimated total 10-year CVD risk and determined the proportion of population who need immediate drug therapy among the rural population of Nepal.

**Methods:** A community based cross-sectional study conducted among 345 participants aged 40–80 years in rural villages of Lamjung District of Nepal. They were selected randomly from total eighteen wards. Data were collected using WHO STEPS questionnaires. WHO/ISH risk prediction chart for SEAR D was used to estimate total cardiovascular risk. Chi-square and independent t-test were used to test significance at the level of p < 0.05 in SPSS version 16.0.

**Results:** Of the total participants, 55.4% were female. The mean age (standard deviation) of the participants was 53.5 ± 10.1 years. According to WHO/ISH chart proportions of low, moderate and high CVD risk were 86.4%, 9.3%, and 4.3%, respectively. Eleven percent of participants were in need of immediate pharmacotherapy. Age (p = 0.001), level of education (p = 0.01) and occupation (p = 0.001) were significantly associated with elevated CVD risk.

**Conclusion:** A large proportion of Nepalese rural population is at moderate and high CVD risk. Immediate pharmacological interventions are warranted for at least one in every ten individuals along with lifestyle interventions. Both population-wise and high-risk approaches are required to minimize CVD burden in the future.

**Keywords:** Cardiovascular diseases, WHO/ISH chart, Risk prediction, Total 10-year CVD risk, Rural population

**Background**

Cardiovascular diseases (CVD) are the major public health problem globally with disproportionately higher occurrence and consequences in developing countries. Data of 2012 showed estimated deaths due to CVD was 17.5 million (31% of total death) with 37% of premature deaths below the age of 70, globally. Almost 80% of such death occurred in low and middle-income countries (LMIC) with the high disparity of premature deaths among such LMIC [1]. In another way, it has been projected that 23.3 million people would die by 2030 only due to CVD [2]. Even in South–East Asia Region (SEAR), CVD accounted for a quarter (25%) of all deaths due to Noncommunicable Diseases (NCD) [3]. Likewise, in Nepal, the prevalence of CVD was 40% among all NCD in-patients in non-specialty hospitals [4].

Population-wise strategies and high-risk strategies are two important methods for prevention of CVD complementing each other [5]. The high-risk strategy identifies individuals who need immediate and sustained care to prevent the development of CVD [5]. The high-risk strategy can be applied through two distinct approaches, first one is targeting and managing each of the single risk factors like hypertension, hyper-cholesterol separately.
Another is accounting the total risk of CVD by measuring the cumulative effect of relative risk of all risk factors [6]. However, later one seems to be accurate for identifying a high-risk individual and can enable to guide limited healthcare resources of LMIC cost-effectively [7–9]. Established tools to estimate the total CVD risk are Framingham, SCORE, QRISK, ASSIGN. These tools were developed considering the specific population and might not be applicable to others [10–15]. However, World Health Organization/International Society of Hypertension (WHO/ISH) risk prediction charts have been developed using information on the population distribution of risk factors from WHO Comparative Risk Assessment study of different sub-regions focusing non western developing countries [16, 17]. The chart estimates the total risk of developing fatal and non-fatal cardiovascular diseases (coronary artery disease and stroke) in following 10 years among those people whose CVD were not manifested clinically, categorizes an individual in different risk groups so that the person can be managed only by lifestyle modification or need drug therapy also [16]. The chart is easy to utilize by all physicians and other health workers at all levels of health care. This tool not only helps to make a clinical decision but also estimates and monitor population distribution of total CVD risk [16, 18]. However, there is paucity of evidence on the use of WHO/ISH risk prediction chart in Nepal. Therefore, this study aimed to estimate total 10-year CVD risk and to determine the proportion of population who need immediate drug therapy among the rural community of Nepal using WHO/ISH chart.

**Methods**

**Study design and settings**

This was a community-based cross-sectional study conducted at Bhotewodar and Sunderbazar Village Development Committee (VDC) of Lamjung between October and November 2014. These villages are about 200 km west from capital city Kathmandu of Nepal and consist of 14,275 population living in 3,869 households. These are the hilly rural areas where agriculture is the main source of livelihood. The sites are the inhabitants of culturally rich people like Gurung, Tamang, Magar, Newar and Dalit, most of them are socially deprived [19]. All eligible men and women were included as the study population. Eligible criteria were age 40–80 years, without having self-reported angina, myocardial infarction, stroke, and intermittent claudication. Pregnant women, mentally retarded and bed-ridden patients were excluded from the study.

**Sample size and sampling technique**

The sample size was calculated by using the formula for estimation of proportion for one sample situation. To detect prevalence of 9.5% of moderate and high CVD risk population, as determined by a study conducted in suburban municipalities of Nepal [20], the minimum sample size required was 292 with allowable error of 4% and a design effect of 1.5. Taking into consideration a non-response rate of 15%, we decided to select 343 subjects from all male and female population aged 40–80 years (N = 3712).

A cluster sampling technique was used to recruit the required number of participants for the study. Firstly, four wards were selected out of 18 wards using probability proportion to size (PPS). In each ward, we selected the first household from a randomly selected point at the entry of the main road. Then, every 6th household was taken as the study household. All eligible members of each household were listed and one subject was selected randomly for interview by using Kish Table [21].

**Data collection**

Five health professionals who had at least intermediate level of health-related education were trained for one week on study protocol, tools and data collection techniques of the study. Data were collected using standard STEPS instrument version 2.2 [21]. The survey tool encompassed questions related to demography and socio-economy, tobacco and alcohol use, dietary intake, physical activity level, and history of high blood pressure and diabetes. The questionnaires were translated into Nepali language and revised after conducting a pilot survey among 20 participants. Blood pressure was measured using doctor’s aneroid sphygmomanometer and stethoscope with an appropriately sized cuff on the unclothed left arm. First reading was taken after 15 min rest-crossing leg and second and third readings were recorded at 5 min interval. Trained technical person collected venous blood, after conforming overnight 12 h fasting to measure blood sugar and lipid profile. All biochemical measurements were done using semi-automated machine of Erba Mannheim (Germany), chem5 v3 model.

**WHO/ISH risk prediction chart**

WHO/ISH chart for SEAR D of WHO epidemiological sub-region [22] was used to estimate the total 10-year risk of CVD of all participants. Age, gender, smoking status, systolic blood pressure, presence or absence of diabetes and total serum cholesterol in millimole/liter (mmol/l) were used to compute the total CVD risk. The chart can
stratify an individual into low (<10%), moderate (10% to <20%), high (20% to <30%), and very high (>30%) risk groups [16].

Definitions of variables
A smoker was the one who has smoked currently and who quit smoking less than one year before the assessment [23]. Systolic blood pressure was mean of last two readings. A respondent with diabetes mellitus was defined as the one who had fasting venous blood sugar level 7 mmol/l or who was taking oral hypoglycemic drug or insulin [23, 24]. Caste was categorized into upper caste (Bramhan and Kshetri), Janajati (Gurung, Tamang, Newar, Magar and Thakali) and Dalit (low caste). For occupation, respondent working in paid governmental and nongovernmental organization was labeled as employed, running own business as self-employed, and student or housemaker or non-paid worker as unemployed. Economic status was categorized as poor (<8498) and medium to high (≥8498) economic status according to family income per person per month in Nepalese Rupees (NR) [25].

Statistical analysis
Data were compiled and entered in Epidata version 3.1. Duplication and omissions of data were checked and edited before coding and exporting into SPSS V.16.0 for further analysis. Descriptive statistics were used to compute different risk categories with 95% confidence interval (CI) for proportion. Mean was calculated with standard deviation (SD) for continuous variables. Chi-square and independent t-tests were conducted to compare categorical and continuous variables, respectively. All tests were two-tail test and p < 0.05 was considered statistically significant.

Ethical consideration
Ethical clearance was obtained from ethical review committee of Nepal Health Research Council. Written informed consent or thumb impression (if unable to write) were taken from all participants. Study objectives, data collection procedures, benefits and risks of the study, confidentiality, and anticipated use of the results were explained to all participants in detail before taking consent.

Results
Socio-demographic characteristics
Total 345 participants were attended in the study. Mean age of study participants was 53.5 ± 10.1 years. The majority of participants were female (55.4%). Forty percent of respondents were in the lowest age group of 40–49 years. Almost all study participants were married (91.3%). More than half of participants (53.6%) did not have formal education. The majority of participants were janajati (55.4%), unemployed (58%). Almost all participants (91.5%) had poor economic status (Table 1).

| Table 1 Socio-demographic characteristics of respondents |
| --- |
| Characteristics | Male, n (%) | Female, n (%) | Total, n (%) | p value |
| --- | --- | --- | --- | --- |
| Age in years | | | | |
| 40–49 | 65 (42.2) | 72 (37.7) | 137 (39.7) | 0.6 |
| 50–59 | 46 (29.9) | 59 (30.9) | 105 (30.4) | |
| 60–69 | 32 (20.8) | 39 (20.4) | 71 (20.6) | |
| 70–79 | 11 (7.1) | 21 (11) | 32 (9.3) | |
| Mean ± SD | 53.3 ± 9.9 | 53.7 ± 10.3 | 53.5 ± 10.1 | 0.68 |
| Marital status | | | | |
| Married | 152 (98.7) | 163 (98.3) | 315 (91.3) | 0.001* |
| Widow or widower | 2 (1.2) | 28 (14.6) | 30 (8.6) | |
| Level of education | | | | |
| No formal education | 30 (19.5) | 155 (81.2) | 185 (53.6) | 0.001* |
| Primary school | 49 (31.1) | 21 (11) | 70 (20.3) | |
| ≥ Secondary school | 75 (48.7) | 15 (7.9) | 90 (26.1) | |
| Caste | | | | |
| Upper caste | 67 (43.5) | 66 (34.6) | 133 (38.6) | 0.03* |
| Janajati | 74 (48.1) | 117 (61.3) | 191 (55.4) | |
| Dalit | 13 (8.4) | 8 (4.2) | 21 (6.1) | |
| Occupation | | | | |
| Employed | 33 (21.4) | 7 (3.7) | 40 (11.6) | 0.001* |
| Self-employed | 54 (35.1) | 24 (12.6) | 78 (22.6) | |
| Unemployed | 42 (27.3) | 158 (82.7) | 200 (58) | |
| Retired | 25 (16.2) | 2 (1) | 27 (7.8) | |
| Economic status | | | | |
| Poor | 135 (39.2) | 179 (52.3) | 314 (91.5) | 0.05* |
| Medium and high | 19 (12.3) | 12 (6.3) | 31 (9.0) | |

Chi square test was done
* Is significant
a Fischer-exact test
b Independent t test for mean difference

Total 10-year CVD risk using WHO/ISH chart
The majority of people had low (<10%) 10-year CVD risk [86.4% (CI 82.8–90)]. Moderate and high risk were 9.3% (CI 6.2–12.4) and 4.3% (CI 2.2–6.4), respectively. More female (10.5%) than male (7.8%) had moderate risk. However, more men (4.5%) than women (4.2%) were at high CVD risk (Table 2). Of total study participants, 6 (1.7%) were at >30% CVD risk (Table 3). As expected, total CVD risk was increasing with age. The highest risk was observed among 70–79 years where almost 44% were at moderate risk and 15.6% were at high risk. While only 0.7% were at moderate and high risk at the age of forties (Table 2).
Socio-demographic factors associated with elevated 10-year CVD risk
CVD risk was significantly \(p = 0.01\) associated with the level of education. Of participants without formal education, 18.4% had elevated CVD risk. However, it was 10% and 6.7% of participants who had a primary and secondary level of education. Elevated CVD risk was higher among Janajati and Dalit (14.7% and 14.3%) in comparison to upper caste participants (12%). Participants whose partner was not alive (30%) had higher CVD risk compared to married (12.1%). Occupation was significantly \(p = 0.001\) associated with CVD risk. Of students, homemaker or non-paid workers, 16% had elevated CVD risk. Similarly, among retired participants, 37% had more than 10% CVD risk. However, the elevated risk was only 1.3% and 10% among self-employed and employed participants, respectively (Table 3).

Proportion of population who need immediate drug therapy
The estimated proportion of population who need drug therapy was 8.6% using threshold of >30% risk and while it was 11% at threshold level of >20% risk. However, such estimated proportion was more than threefold (36%) using single risk factor approach. Proportion of men who required drug intervention was 11.7% and 14.3% at threshold of >30% and >20% CVD risk, respectively. While proportion of women was 6.3% and 8.4% at same threshold level (Table 4).

### Table 2 Distribution of study population into low, moderate and high cardiovascular risk categories, n (%)

| Sex        | Age (years) | Risk categories | Low risk | Moderate risk | High risk |
|------------|-------------|-----------------|----------|---------------|-----------|
| Male       | 40–49       | 64 (98.5)       | 1 (1.5)  | 0 (0.0)       |
|            | 50–59       | 43 (93.5)       | 2 (4.3)  | 1 (2.2)       |
|            | 60–69       | 24 (75.0)       | 4 (12.5) | 4 (12.5)      |
|            | 70–79       | 4 (36.4)        | 5 (45.5) | 2 (18.2)      |
|            | Total       | 135 (87.7)      | 12 (7.8) | 7 (4.5)       |
| Female     | 40–49       | 71 (98.6)       | 0 (0)    | 1 (1.4)       |
|            | 50–59       | 56 (94.9)       | 2 (3.4)  | 1 (1.7)       |
|            | 60–69       | 27 (69.2)       | 9 (23.1) | 3 (7.7)       |
|            | 70–79       | 9 (42.9)        | 9 (42.9) | 3 (14.3)      |
|            | Total       | 163 (85.3)      | 20 (10.5) | 8 (4.2)       |
| Male and Female | 40–49 | 135 (98.5) | 1 (0.7) | 1 (0.7) |
|            | 50–59       | 99 (94.9)       | 4 (3.8)  | 2 (1.9)       |
|            | 60–69       | 51 (71.8)       | 13 (18.3) | 7 (9.9) |
|            | 70–79       | 13 (40.6)       | 14 (43.8) | 5 (15.6) |
|            | Total       | 298 (86.4)      | 32 (9.3) | 15 (4.3)      |

### Table 3 Socio-demographic factors associated with elevated 10-year CVD risk, n (%)

| Variables | <10% risk (low) | >10% risk (elevated) | p value |
|-----------|-----------------|----------------------|---------|
| Gender    |                 |                      |         |
| Male      | 135 (87.7)      | 19 (12.3)            | 0.53    |
| Female    | 163 (85.3)      | 28 (14.7)            |         |
| Age       |                 |                      |         |
| 40–49     | 135 (98.5)      | 2 (1.5)              | 0.001*  |
| 50–59     | 99 (94.3)       | 6 (5.7)              |         |
| 60–69     | 51 (71.8)       | 19 (29.2)            |         |
| 70–79     | 13 (40.6)       | 19 (59.4)            |         |
| Level of education |              |                      |         |
| No formal education | 151 (81.6) | 34 (18.4) | 0.01* |
| Primary   | 63 (90.0)       | 7 (10.0)             |         |
| ≥Secondary | 84 (93.3) | 6 (6.7)              |         |
| Caste/ethnicity |         |                      |         |
| Upper cast | 117 (88.0) | 16 (12.0)            | 0.46    |
| Janajati  | 163 (85.3)      | 28 (14.7)            |         |
| Dalit     | 18 (85.7)       | 3 (14.3)             |         |
| Marital status |       |                      |         |
| Married   | 277 (87.9)      | 38 (12.1)            | 0.006*  |
| Widower or widower | 21 (70.0) | 9 (30.0)              |         |
| Occupationa |             |                      |         |
| Employ   | 36 (90.0)       | 4 (10.0)             | 0.001*  |
| Self employed | 77 (98.7) | 1 (1.3)              |         |
| Unemployed | 168 (84.0) | 32 (16.0)            |         |
| Retired   | 17 (63.0)       | 10 (37.0)            |         |
| Economic status |         |                      |         |
| Poor (<NRs 8498) | 271 (86.3) | 43 (13.7)            | 0.9     |
| Higher (>NRs 8498) | 27 (87.1) | 4 (12.9)              |         |

* Chi square test was done
* Is significant
* Fischer exact test

### Discussion
Our study had an objective to estimate total 10-year CVD risk among study population. This study found that large proportion of study participants had moderate to high risk (13.6%) which was consistent with the findings reported in national and international studies conducted in similar settings. This proportion of population at elevated risk of CVD was almost same in one sample of Nepal (13.4%) reported by Mendis et al. [7], while higher than the finding of another study conducted in a suburban population of Nepal (9.5%) [20]. However, the proportion of raised risk in current study was slightly lower than that of Kathmandu (14.6%) [26] and rural India (16%) [27]. Regarding the proportion of population under high risk of CVD, it was slightly higher in our study...
(4.3%) than that of study conducted in Malaysia (2.3%) and Cambodia (1.3%) and lower than that of Mangu-lian study (6%) [12]. Similar heterogeneous results were observed in different countries (China 1.1%, Iran 1.7%, Sri Lanka 2.2%, Cuba 2.8%, Nigeria 5.0%, Georgia 9.6%, Pakistan 10.0%) [7]. Very high-risk (>30%) was 1.7% in our study, which was slightly lower than the estimated for age 40–65 years throughout the country of Nepal (3.2%) [28]. These different data revealed that the population under risk for development of stroke and coronary heart disease were high even in a rural community of Nepal. Application of WHO/ISH chart helps to categorize population into different risk levels. Population-based lifestyle modification strategy can be applied to low-risk population while individual counseling and frequent follow-up assessment need to be added for moderate risk population. However, more rigorous treatment strategies would be needed for the population at high and very high-risk category [16].

CVD risk was significantly associated with the level of education. A study conducted in Vienna echoed the same finding that education is associated with the level of understanding on risk factors [29]. Evidence also suggests that increasing knowledge on risk factors can substantially motivate people for changing risk behaviors [30]. This fact suggests that we need to improve awareness and knowledge about prevention of cardiovascular diseases. Occupation was significantly associated with elevated CVD risk. A higher proportion of unemployed and retired participants had raised risk. One study of Mauritius also proved the association of occupation and cardiovascular risk, mostly related to physical activities and economic status [31]. These findings provide the evidence that we should target unemployed population for early prevention of cardiovascular disease. As expected, age-related increase in CVD risk was associated with an increase in risk factor level [32].

As explained in the WHO guideline for assessment and management of cardiovascular disease [16], individuals who have blood pressure of ≥160/100 mm Hg need appropriate drug therapy even though they are in low and moderate CVD risk category. However, there is still no universal consensus for appropriate threshold (30% vs 20%) of total CVD risk at which drug treatment are initiated [7, 16]. It depends on the availability of resource of a country and impact of the specific intervention. Current data reveals that we can prevent large numbers of ischemic heart disease and stroke incidence if threshold is reduced from >30 to >20% risk. Our result demonstrated that about 11% would be treated by drug if >20% risk was taken as threshold while about 8.6% would need drug at threshold of >30% risk. However, about threefold more individual would require pharmacotherapy if we target single risk factors like hypertension and raised cholesterol. Our estimation of proportion of the population in need of drug therapy was slightly lower than that of Bangladesh at same threshold level (8.3% and 4%). However, as in our study, population who require drug were almost threefold higher by targeting single risk factors (28.2%) [33]. Our estimation was comparable to another study conducted at Cuba [34], where sample population requiring drug at aforementioned threshold level were 12.5% and 11.5% with total risk approach restricting about threefold of the population from over prescription of the drug than single risk factor approach (43.8%). Similar result was found in a study in Africa [7, 9]. Therefore, high proportion of the population were in need of pharmacotherapy and it would prevent over prescription of the drug if total CVD risk approach applied to prevent CVD.

### Table 4 Study population requiring pharmacotherapy using WHO/ISH chart at different threshold levels and single risk factors approach, n (%)

| Approach | Variants | Persons requiring drugs | | | |
| --- | --- | --- | --- | --- | --- |
| | | Threshold CV risk >30% | | | |
| | | Male | Female | Total | Male | Female | Total |
| WHO/ISH chart | Chart | 2 (1.3) | 4 (2.0) | 6 (1.8) | 7 (4.5) | 8 (4.2) | 15 (4.3) |
| | Chart + BPa | 16 (10.6) | 8 (4.2) | 24 (6.9) | 15 (9.7) | 8 (4.2) | 23 (6.6) |
| | Total | 18 (11.7) | 12 (6.3) | 30 (8.6)b | 22 (14.3) | 16 (8.4) | 38 (11)c |
| Single risk factor | BP ≥ 140/90 | 58 (38.7) | 52 (27.2) | 110 (31.9) | 58 (38.7) | 52 (27.2) | 110 (31.9) |
| | TC ≥ 6 | 8 (5.3) | 6 (3.1) | 14 (4.1) | 8 (5.2) | 6 (3.1) | 14 (4.1) |
| | Total | 64 (43.9) | 58 (30.3) | 124 (36) | 64 (43.9) | 58 (30.3) | 124 (36) |

a BP ≥ 160/100 mmHg
b Chart with BP ≥ 160/100 mmHg vs single risk factor, at >30% threshold, χ² = 64, p = 0.001
c Chart with BP ≥ 160/100 mmHg vs single risk factor, at >20% threshold, χ² = 64.5, p = 0.001
Due to lack of data related to cardiovascular morbidity and mortality, WHO/ISH charts have not validated yet in Nepal. The chart might have underestimated the total CVD risk, as it did not include the individual with anti-hypertensive therapy, raised triglyceride, low HDL, family history of CVD and obesity. Higher number of janajati participants were involved in the study. Therefore, findings of the study should cautiously be generalized to other rural population of Nepal.

Conclusion
A large proportion of Nepalese rural population is at moderate and high CVD risk. Immediate pharmacological interventions are warranted for at least one in every ten individuals along with lifestyle interventions. This situation underlines the importance of immediate designing and implementation of both population-wise and high-risk approaches to minimize CVD burden in the future. Total risk approach would be more effective for initiation of preventive pharmacotherapy compared to the single risk factor approach to allocate the limited resources more efficiently.

Abbreviations
CVD: Cardiovascular Diseases; LMIC: Low and Middle Income Countries; NCD: Noncommunicable Diseases; WHO/ISH: World Health Organization/International Society for Hypertension; STEPS: Stepwise Approach to Surveillance; SEAR: South East Asia Region.

Authors' contributions
MKK designed the main thesis, trained field enumerators, analysed data, interpreted data and drafted the manuscript; MSAMA oversaw the quality of the main thesis and reviewed the manuscript; MZ interpreted results critically, conceptualized the manuscript and critically reviewed it; PCB and PB collected, compiled, analyzed the data and involved in drafting the main thesis and reviewed the manuscript; MZ interpreted results critically and involved in drafting the manuscript; MSAMA oversaw the quality of the main thesis and revision; MKK designed the main thesis, trained field enumerators, analysed data, interpreted data and drafted the manuscript; MSAMA oversaw the quality of the main thesis and reviewed the manuscript; MZ interpreted results critically and involved in drafting the manuscript; MSAMA oversaw the quality of the main thesis and reviewed the manuscript; MZ interpreted results critically and involved in drafting the manuscript.

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Competing interests
The authors declare that they have no competing interests.

Availability of data and materials
The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate
Ethical clearance was obtained from the ethical review committee of Nepal Health Research Council. Written informed consent (or thumb impression if unable to write) were taken using a consent form in Nepali language from all participants.

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