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Examining the prevalence, correlates and inequalities of undiagnosed hypertension in Nepal: a population-based study

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Title: Examining the prevalence, correlates and inequalities of undiagnosed hypertension in Nepal: a population-based study

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ABSTRACT

Objective: To examine the prevalence, correlates and socio-demographic inequalities of undiagnosed hypertension in Nepal.

Design: This study used cross-sectional 2016 Nepal Demographic and Health Survey (NDHS) data. We defined a hypertensive patient to remain undiagnosed if the patient had systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg and not once took any prescribed medicine to lower/control blood pressure or told by health professionals to have hypertension. Multiple binary logistic regression analysis was performed and Concentration Index was measured.

Setting: Nepal

Participants: Adult patients with hypertension

Results: Among 3334 hypertensive patients, 50.4% remained undiagnosed during the survey in Nepal. Adjusted model reveals that patients who were male, belonged to households other than richest quintile, and lived in Province 4 and Province 5 were at higher risk and patients who were 65+ years of age and were overweight/obese were at lower risk of remaining undiagnosed for hypertension. The poor-rich gap was 24.6 percentage points (Q1= 64.1% vs Q5= 39.6%) and poor:rich ratio was 1.6 (Q1/Q5= 1.6) in the prevalence of undiagnosed hypertension. Undiagnosed hypertension was disproportionately distributed among socioeconomically worse-off Nepalese patients (Concentration Index, C= -0.18). Inequalities in the prevalence of undiagnosed hypertension further varied across other geographic locations including place of residence, ecological zones and administrative provinces.

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3 **Conclusions:** Among Nepalese hypertensive patients, undiagnosed hypertension was highly
4 prevalent with substantial inequalities that warrants efforts including increasing awareness and
5 enactment of social insurance policy for prevention and control of this burden.
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10 **Keywords:** Undiagnosed hypertension, Inequality, Demographic and Health Survey, Nepal
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14 **Strengths and limitations of this study**

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- 16 • This study determined the prevalence of undiagnosed hypertension in Nepal using the
17 most updated population-based nationally representative data
 - 18 • This study explored the factors that potentially drive the prevalence of hypertensive
19 patients remained undiagnosed
 - 20 • This study measured both absolute and relative inequalities in the prevalence of
21 undiagnosed hypertension at national level as well as across place of residence,
22 ecological zones and administrative provinces
 - 23 • The cross-sectional nature of the data limits us to measure causal association between
24 undiagnosed hypertension and the explanatory variables studied
 - 25 • The association of some potential behavioral or lifestyle factors and family history with
26 undiagnosed hypertension remain unmeasured due to lack of information
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INTRODUCTION

Globally, hypertension -or raised blood pressure is a directing factor for cardiovascular diseases (CVDs), specially heart diseases, myocardial infarctions, kidney failure, strokes, disability and premature deaths [1–3]. Hypertension affects one billion people and kills nine million people every year worldwide [1]. In South-East Asian countries including Nepal, hypertension affects one out of three adults, which accounts for nearly 1.5 million adult deaths annually; and 9.4% of the total deaths [4]. Studies identified, more than 50% people having hypertension remained undiagnosed in South-East Asian region [5]. Among South Asian countries, Nepal has one of the highest prevalence of hypertension [6].

Currently, Nepal is facing an epidemiological transitions with increasing prevalence of hypertension [7]. Several studies have been driven so far to understand the actual prevalence of hypertension in Nepal. A study based on the Nepal Demographic and Health Survey 2016 showed, about 20% Nepalese adults (aged ≥ 18 years) had hypertension [8]. Studies also found, the prevalence of hypertension ranges from 23% to 34% in Nepal [7,9–12]. Furthermore, national NCD risk factor survey in 2013 showed about 25.7% adults aging 15-69 years had hypertension in Nepal [13]. This survey also found that a large number of (42.7%) adults had never measured their blood pressure. For prevention, control and proper treatment of hypertension, it is prior need to correctly diagnose this disease. In addition, failure to early diagnosis and treatment of hypertension may lead to serious health hazards, disability in the later life, or eventually deaths. Number of government, non-government and private health facilities are providing health services including diagnosis, medication and treatment for hypertension. However, the existing health systems of Nepal is not ready for diagnosis, treatment and control of hypertension especially for the mass people at the community level indicating the challenges to tackle this burden [14].

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3 To prevent hypertension, the disease needs to be diagnosed first before any related complications
4 arise. However there is lack of evidence about the prevalence of undiagnosed hypertension in
5 Nepal at national and subnational levels. The estimates of undiagnosed hypertension, and its socio-
6 demographic inequalities at national and subnational level may help the policy makers for
7 formulating effective strategies for screening, treatment and control as well as prevention of such
8 burden by identifying the most vulnerable groups. Therefore, given the importance of this burden,
9 we aimed to examine the prevalence, correlates and socio-demographic inequalities of
10 undiagnosed hypertension in Nepal.
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25 **METHODS**

26 **Data source**

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31 We used the most updated nationally representative cross-sectional data from Nepal Demographic
32 and Health Survey (NDHS). Though the data of Demographic and Health Surveys is managed by
33 Measure Evaluation, the NDHS was conducted from June 2016 to January 2017 by a private
34 research organization named “NEW ERA” under the monitoring and supervision of the Ministry
35 of Health, Nepal. Designed specially to estimate the prevalence of hypertension nationally in
36 Nepal, the NDHS 2016 obtained informed consent from the household head on behalf of all
37 household members of each surveyed households [15]. For academic and scientific purposes, this
38 anonymous dataset without any identifiers was made available by the ICF International, Maryland,
39 United States [15]. We obtained approval with access to use the data to conduct this study.
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Survey procedure

In 2015, Nepal declared some new places to fall under municipalities and some municipalities have been reformed [8]. After these changes, Nepal has been divided into seven administrative provinces comprising several districts under each province and urban-rural areas. These urban and rural areas were divided into small administrative units as wards. Because of having comparatively greater number of households in urban areas, the urban area was further divided into enumeration area (EA). The primary sampling unit (PSU) were wards for both urban and rural areas [15]. Because of some changes in administrative areas, Nepal revised the sampling frame of National Population and Housing Census (NPHC). The 2016 NDHS used this revised sampling frame and applied a multistage survey that respectively conducted in two and three stages in rural and urban areas. NDHS selected the PSUs proportionately to the size in the first stage and then the random selection of EAs from the systematic selection of households from each PSU in second stage. In third stage, the selection of households were by using stratified cluster sampling technique in urban setting. A detailed description about the methodology is available elsewhere [15]. A total of 11490 households were selected from 383 wards, of which 5520 households from 184 wards were from urban settings and 5970 households from 199 wards were from rural settings. From these households, all the residents whose age 15 years or above were eligible for the measurement of blood pressure. With an overall 95% response rate, a total of 14823 individuals participated in the survey.

Outcome variable

To measure hypertension, the 2016 NDHS used the UA-767F/FAC (A&D Medical) automated device to record the blood pressure of the participants. With 5 minutes intervals between each

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3 measurement, the 2016 NDHS recorded the measurements of blood pressure for three times in a
4 sitting position. NDHS considered the last two measures of blood pressure levels and used their
5 mean to detect hypertension. The survey used the World Health Organization (WHO) guidelines
6 to report a participant as hypertensive [15]. This guideline has integrated the 2017 guidelines of
7 the American College of Cardiology/ American Society of Hypertension [16,17]. According to the
8 guideline, a participant with systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure
9 (DBP) ≥ 90 mmHg is diagnosed as a hypertension case. We also considered participants as patients
10 of hypertension if s/he was previously told by health professional to have hypertension or taking
11 medication to control hypertension. Our outcome variable is undiagnosed hypertension. We
12 considered a patient to remain undiagnosed if the patient had SBP ≥ 140 mmHg or DBP ≥ 90 mmHg
13 during blood pressure measurement of biomarker test of the survey and not once took any
14 prescribed medicine to lower/control blood pressure or being told by health professionals to have
15 hypertension prior survey [18,19].
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37 **Explanatory variables**

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39 This study considered a set of socio-demographic and behavioral characteristics as independent
40 variables. Age (in years), sex, Body Mass Index (BMI) measured through dividing the weight by
41 squared height (kg/m^2), education level, household wealth status place of residence, ecological
42 zone, and provinces were considered as socio-demographic characteristics of the patients. Age was
43 categorized as 15-24, 25-34, 35-44, 45-54, 55-64 and ≥ 65 years. Sex had two categories, male and
44 female. The BMI was categorized as thin/underweight ($\text{BMI} < 18.5 \text{ kg}/\text{m}^2$), normal ($18.5 \text{ kg}/\text{m}^2$
45 $\leq \text{BMI} < 25 \text{ kg}/\text{m}^2$) and overweight/obese ($\text{BMI} \geq 25.0 \text{ kg}/\text{m}^2$). Based on the highest class completed
46 by the respondents, level of education was classified as no education, primary, secondary and
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3 higher. NDHS used principal component analysis [15] to construct the wealth index to desegregate
4 the households into five socioeconomic quintiles (poorest, poorer, middle, richer and richest). The
5 place of residence was stratified as urban and rural across all geographic location. Nepal was
6 ecologically divided in Mountain, Hill and Terai. Using 2015 reformation, 7 administrative
7 provinces were considered as Province 1, Province 2, Province 3, Province 4, Province 5, Province
8 6 and Province 7. Three behavioral characteristics of respondents, caffeine, tobacco and alcohol
9 consumption were considered as independent variables each of which contained dichotomous
10 response on whether respondent consume caffeine, tobacco or alcohol.
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25 **Statistical analyses**

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28 We described the prevalence of undiagnosed hypertension and background characteristics of the
29 study patients by using univariate analysis technique. The estimates of each of the categorical
30 variables included in this study were reported with numbers, weighted percentages and 95%
31 confidence intervals (CI) of estimates. The weighted prevalence of undiagnosed hypertension was
32 determined across the background characteristics of the study patients from bivariate analysis.
33 Statistical significance was detected by applying Chi-square test. Then, we conducted simple and
34 multiple binary logistic regression analyses to examine the correlates of undiagnosed hypertension.
35 The results of the regression analysis were presented in terms of odds ratio with respective 95%
36 CI. Variables that were statistically significant in simple logistic regression analysis were entered
37 in the multiple regression model to estimate the adjusted odds ratio (AOR). Notably, the statistical
38 significance was defined at 5% level ($p\text{-value} < 0.05$). Variance inflation factors to detect
39 multicollinearity among the independent variables were assessed before incorporating them into
40 the multiple regression model. Due to hierarchical structure of NDHS data, we considered the
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3 cluster sampling design of the 2016 NDHS to estimate the prevalence and determinants in this
4 study [15]. We excluded cases with missing values for blood pressure measurements.
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8 Proposed by Wagstaff [20] to measure the inequality, we estimated the concentration index (C),
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10 to show the degree and direction of wealth-based inequality in undiagnosed hypertension
11 prevalence. For the purpose of calculating C, the households were ranked from the poorest to the
12 richest according to their socioeconomic characteristics. We plotted a concentration curve to
13 portray the distribution of undiagnosed hypertension. The Y-axis of the concentration curve
14 representing the cumulative proportion of undiagnosed hypertension and the X-axis represents the
15 cumulative proportions of the population across wealth quintiles. When the concentration curve
16 coincide with the diagonal, the prevalence of undiagnosed hypertension is treated as equally
17 distributed across socioeconomic groups. In contrast, the concentration curve typically deviate
18 from the diagonal if there exist inequalities in the prevalence of undiagnosed hypertension. The C
19 is defined as twice the area between the concentration curve and the diagonal [21–23]. The index
20 value can range between -1 and $+1$, a positive value implies prevalence of undiagnosed
21 hypertension is more concentrated among the better-off socioeconomic group and a negative value
22 implies prevalence is more concentrated among less affluent group [22,24]. We repeat the
23 estimation of C across other geographical locations such as place of residence, ecological zones
24 and provinces to detect the group of patients with highest severity of socioeconomic inequalities
25 in the prevalence of undiagnosed hypertension. STATA (version 13) was used to perform all the
26 analyses [25].
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49 **Patient and public involvement**

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53 Patients and publics were not involved in developing the research questions, measuring outcome
54 and designing the study. Information of the participants were anonymous.
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RESULTS

General Characteristics of the Study Participants

Table 1 shows the general characteristics of the study participants. Among the patients studied, the average age of patients was 49.8 years (95% CI 49.1, 50.5) with the lowest percentage of patients belonged to 15-24 years age group (6.6%) and highest percentage of patients belonged to 45-54 years age group (20.9%). Numbers of males (49.5%) and females (50.5%) in the sample were almost equal. Nearly half of the patients were normal in terms of their BMI while more than one third of the patients were overweight/obese. Though two-third of the patients resided in urban area (64.9%), the educational status of the patients were poor. Nearly half of the patients had no education while 24.1% and 11.5% had secondary and higher education respectively. The highest number of patients belonged to richest wealth quintile (28.3%) and the lowest number of patients belonged to the poorest wealth quintile (15.5%). Also, the highest number of patients were from province 3 (26.0%) followed by province 5 (17.8%) and province 1 (17.0%). However, only 5.6% of the patients were from mountain ecological zone.

Prevalence of Undiagnosed Hypertension among Hypertensive Patients

In our study, we found 3334 cases who had hypertension during the survey. More than half of them were detected as remaining undiagnosed (50.4%). The prevalence of undiagnosed hypertension among the patients varied across their age (p -value < 0.001), sex (p -value < 0.001), BMI (p -value < 0.001), wealth quintile (p -value < 0.001) and place of residence (p -value < 0.01). The prevalence of undiagnosed hypertension were higher among patients with 15-24 years age group and steadily decreasing with the increase of age. The prevalence of undiagnosed

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3 hypertension was higher among male patients (54.2%) than female (46.7%). Compare to patients
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5 with normal BMI, the prevalence of undiagnosed hypertension was higher among thin patients
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7 (57.8%) and lower among overweight/obese patients (44.4%). Compare to patients of the richest
8
9 wealth quintile (39.6%), the prevalence of undiagnosed hypertension was higher among patients
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11 of the poorest (64.1%) and poorer (55.8%) quintiles. The rate of undiagnosed hypertension was
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13 higher among rural patients (55.2%) compare to urban (47.8%). No educational, ecological and
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15 provincial variations in the prevalence of undiagnosed hypertension was observed (**Table 1**).
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23 **Determinants of Undiagnosed Hypertension among Hypertensive Patients**

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25 We found that patient's age, sex, BMI, wealth quintile, place of residence and province were
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27 significantly associated with the prevalence of undiagnosed hypertension among hypertensive
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29 patients in unadjusted logistic regression analysis (see **supplementary**).
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33 **Figure 1** represents the results of multiple logistic regression analysis. The multiple binary logistic
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35 regression model showed that patient's age, sex, BMI, wealth quintile and province had significant
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37 association with undiagnosed hypertension. Elderly patients ≥ 65 years of age had a lower
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39 likelihood of being undiagnosed for hypertension than patients with age 15-24 years (Adjusted
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41 Odds Ratio, AOR = 0.65; 95% CI 0.48, 0.91). Male patients were 1.29 times more likely than
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43 female patients to remain undiagnosed for hypertension (AOR = 1.29, 95% CI 1.11, 1.51).
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45 Compare to patients with normal BMI, overweight/obese patients (AOR = 0.80, 95% CI 0.69,
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47 0.93) were less likely to have undiagnosed hypertension.
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52 We found wealth quintiles as potential correlates of undiagnosed hypertension. The risk of
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54 remaining undiagnosed for hypertension was increasing with the decrease of patient's
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3 socioeconomic status. Patients with a poorer socioeconomic status had higher chance of having
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5 undiagnosed hypertension compared to higher socioeconomic quintiles. Patients of poorest and
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7 poorer wealth quintiles were 2.49 (AOR = 2.49; 95% CI 1.90, 3.30) and 1.67 (AOR = 1.67; 95%
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9 CI 1.29, 2.16) times more likely to have an undiagnosed hypertension condition than patients of
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11 richest wealth quintile.
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15 Moreover, significant provincial variation was evident in the prevalence of undiagnosed
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17 hypertension among hypertensive patients. Patients of province 4 (AOR = 1.36, 95% CI 1.04, 1.79)
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19 and province 5 (AOR = 1.43, 95% CI 1.05, 1.95) were more likely to had undiagnosed
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21 hypertension than patients of province 1.
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28 **Socioeconomic Inequalities in Undiagnosed Hypertension among Hypertensive Patients**

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31 **Figure 2** depicts the inequalities in the prevalence of undiagnosed hypertension among
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33 hypertensive patients. The absolute poor (Q1) - rich (Q5) difference in the distribution of
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35 undiagnosed hypertension was 24.6% between poorest and richest, meaning that the prevalence of
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37 undiagnosed hypertension was greater by 24.6 percentage points among the poorest. The relative
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39 measure of inequality in terms of poor (Q1): rich (Q5) ratio was 1.6 for the prevalence of
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41 undiagnosed hypertension among patients, depicting that the prevalence of undiagnosed
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43 hypertension was higher by 1.6 times among the poorest than richest. We found negative value of
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45 the Concentration Index ($C = -0.18$) which represents that the prevalence of undiagnosed
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47 hypertension among hypertensive patients was disproportionately distributed among worse-off
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49 socioeconomic groups.
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3 In addition, patients living in mountain and in province 7 had large gaps in the prevalence of
4 undiagnosed hypertension (**Figure 3**). The higher Q1:Q5 ratio were observed among those who
5 had large Q1-Q5 gaps in the prevalence of undiagnosed hypertension across different geographic
6 locations. We found large negative values of C among those who had higher Q1-Q5 gaps and
7 Q1:Q5 ratio for the prevalence of undiagnosed hypertension. See **Figure 3** for details.
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18 **DISCUSSION**

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21 Undiagnosed hypertension may lead to adverse health consequences, including some organ
22 damages [26]. Utilizing NDHS 2016 data, this study intended to estimate the prevalence of
23 undiagnosed hypertension. In addition, the risk factors and inequalities associated with it among
24 Nepalese hypertensive patients were identified. About half of the biomarker partekars were found
25 hypertension positive who were not screened/ diagnosed before the survey. Patients unwillingness
26 for regular check-up before any health complication arises due to lack of awareness as well as
27 inaccessibility to screening services may direct this high prevalence [27]. Gap in knowledge,
28 attitude and practice of healthy lifestyle as preventive measure to NCDs may also act as a driver
29 of undiagnosed hypertension [27–29]. Community-based awareness on changing lifestyle to
30 address the burden of NCD from the society as a whole might be effective in reducing this gap
31 [30].
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47 Several studies reported higher risk of hypertension among people who were older in age, male,
48 urban dwellers, had higher education level, regular consumer of tobacco and alcohol, and who are
49 overweight [6,8,28,29]. In contrast, we found that patients aged 65+ years and who were
50 overweight/obese were at lower risk of remaining undiagnosed from this disease. However, our
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3 findings depicted greater proportion of undiagnosed patients among those who were young and
4 physically thin. Young or underweight people are less conscious about their health status as they
5 might have the misconception that they are less likely to suffer from non-communicable diseases
6 [31]. None the less, richest are more aware than the poorest people about the health hazards,
7 typically have greater access for screening diseases and can have the ability to afford treatment
8 cost for the diseases in Nepal [28]. This could lead the poor than the rich to be more exposed to
9 undiagnosed hypertension. On the other hand, similar to risk factors of hypertension, undiagnosed
10 hypertension were also more prevalent among males and tobacco users [6,29]. Although difference
11 in lifestyle practice between male and female in Nepal may not be the key factor behind such
12 exposure, research need to be done to identify the actual risk factor [29].
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15 Globally few studies have been conducted on undiagnosed hypertension to date. World Health
16 Organization, mentioning hypertension as a silent killer, stated the prevalence of hypertension is
17 higher in low- and middle-income countries than developed and high income countries [1]. Our
18 results proves this claim and also aligns with findings from Bangladesh and Sub-Saharan Africa
19 [19,32,33]. Although situated in closer geographic region, prevalence of undiagnosed hypertension
20 from this study differs from that of India and China which are more developed and belongs to high
21 income countries with up to date facility setup and health policies for their citizens [34,35].
22 Similarly, findings from studies conducted in countries with more developed health facilities and
23 advanced screening system such as Japan, Korea, England, Ireland, Egypt , Brazil and USA were
24 also found to have lower level of undiagnosed hypertension than Nepal as found in this study [36–
25 42].
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28 In Nepal, despite the detection of risk factors [6,8,29] and inequalities [28], the prevalence of
29 hypertension was well investigated nationally which lead policy makers to successfully steer away
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3 it's progression [43]. However, this effort will be meaningless unless all patients at risk of
4 hypertension are accurately diagnosed and detected. On that account, it is necessary to identify
5 whether unequal distribution of undiagnosed hypertension exists among patients with hypertension
6 across different socioeconomic groups. It will aid in setting priorities and proper allocation of
7 resources. Our study reveals existence of inequalities in the distribution of undiagnosed
8 hypertension due to economic status, with poorest had higher prevalence of undiagnosed
9 hypertension than richest and showed greater degree of wealth-based inequality concentrated
10 among the poorest. These inequalities were more prevalent among patients living in different
11 geographical locations including place of residence, ecological zones and administrative
12 provinces. Such disparity may ascribed to greater awareness and more utilization of healthcare
13 benefits by people who are rich [28]. Such inequality might increase the catastrophic health
14 spending given the rise of catastrophic household expenditure due to non-communicable diseases
15 in Nepal [14,44]. Public health strategies might reduce this gap by concentrating more on
16 implementing social health insurance policies which has to be equitable for all [36,44]. In this
17 aspect, policy makers could take into consideration the disparities in the distribution of
18 undiagnosed hypertension found in this study.

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21 Ignoring the population at risk of hypertention may become a major threat to health outcomes to
22 any nation. This study bestows an immense opportunity to estimate the prevalence of undiagnosed
23 hypertension which had not yet been studied nationally in Nepal. NDHS 2016 through
24 incorporation of biomarker test bears evidence that a substantial proportion of individuals are
25 suffering from blood pressure abnormalities. This in fact emphasise the need of conducting routine
26 screening for hypertension widened with the greatest possible coverage in the population. A
27 routine surveillance system with technology-based screening can aid in tracing disease incidence

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3 as well as people at risk of being undiagnosed [45]. Our study findings will be helpful to initiate
4 policies and programs in capturing the highest domain of underprivileged population and bring
5 them under routine surveillance at community level with optimum cost.
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10 **Strengths and limitations**

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13 We used most updated nationally representative cross-sectional data to determine the prevalence,
14 correlates and inequalities of undiagnosed hypertension in Nepal. We considered complex survey
15 design to capture variations due to designing. However, there may have residuals and unmeasured
16 potential behavioral or lifestyle factors of undiagnosed hypertension that may remain unmeasured
17 due to lack of information. Since our data was corss-sectional, the relationship between
18 undiagnosed hypertension and confounders were probabilistic rather than causal. However,
19 identification of potential correlates through using odds ratio is widely acceptable. This study
20 measured both absolute and relative inequalities in the prevalence of undiagnosed hypertension at
21 national level as well as across place of residence, ecological zones and administrative provinces
22 to further guide policy/decision makers for better allocation of resources to reduce the burden.
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40 **CONCLUSIONS**

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43 This study manifests, in Nepal huge number of respondents with hypertension remained
44 undiagnosed. Initiative for non-communicable disease diagnoses prioritizing those who are down
45 and out requires to be implemented. Community-based awareness should be raised to improve
46 knowledge, attitude and practice of the people particularly those who are young, slender, poor and
47 male given their higher risk of being undiagnosed. Moreover, identification of inequalities among
48 different risk groups will be beneficial in achieving universal health coverage of sustainable
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3 development goal (Goal 3.8.1). Social insurance policies under integrated national NCD policy
4 should be properly enacted to ensure socioeconomically disadvantaged populations covered under
5 the scheme for prevention and control of hypertension from them.
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16

17 18 **Contributors**

19
20 MMH and AAM conceptualized the study. MMH performed the data analysis and interpretation
21 of the findings. MMH, FT, MT and SA contributed to writing. AAM and SA critically reviewed
22 the analysis and final version of the manuscript. All authors made a through review of the final
23 draft and approved it for submission.
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33
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35
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37 38 **Competing interests**

39
40 None declared.
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43 44 **Ethical approval**

45
46 The NDHS survey methodology and questionnaire was reviewed and approved by the ethical
47 review board of Nepal Research Council and ICF Institutional. NDHS obtained informed consent
48 from the respondents before conducting the survey. Therefore, separate ethical approval was not
49 required for this study and we are using publicly available de-identified data.
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Data sharing statement

Data are available in a public, open access repository. All data related to study are included in the manuscript.

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Table 1: Characteristics of the study participants

Variables	Total			Diagnosed hypertension			Undiagnosed hypertension			Chi-Square Statistic (p-value)
	n	%	95% CI	n	%	95% CI	n	%	95% CI	
Overall	3334	--	--	1634	49.6	47.1-52.1	1700	50.4	47.9-52.9	--
Age										29.6317
15-24	237	6.6	5.6-7.8	107	43.1	36.1-50.4	130	56.9	49.6-63.9	0.0008
25-34	449	13.2	11.9-14.5	196	43.8	38.4-49.3	253	56.2	50.7-61.6	
35-44	637	19.6	18-21.3	287	45.2	40.1-50.3	350	54.8	49.7-59.9	
45-54	687	20.9	19.2-22.8	333	49.4	45-53.8	354	50.6	46.2-55	
55-64	643	18.9	17.4-20.5	344	54.7	49.8-59.5	299	45.3	40.5-50.2	
>=65	681	20.8	19-22.7	367	55.1	50.3-59.8	314	44.9	40.2-49.7	
Sex										18.35
Male	1640	49.5	47.7-51.3	746	45.8	42.6-49.1	894	54.2	50.9-57.4	0.0003
Female	1694	50.5	48.7-52.3	888	53.3	50.1-56.4	806	46.7	43.6-49.9	
BMI										29.2511
Normal	1816	53.6	51.2-56.1	841	47.1	44.3-50	975	52.9	50-55.7	0.0001
Thin	361	11.1	9.9-12.5	156	42.2	35.7-49	205	57.8	51-64.3	
Overweight/obese	1120	35.2	32.5-38	620	55.6	51.7-59.5	500	44.4	40.5-48.3	
Education										6.5852
No education	1576	46.5	44.1-48.9	778	50.9	47.5-54.4	798	49.1	45.6-52.5	0.2125
Primary	602	17.8	16.2-19.5	285	46.1	41.1-51.1	317	53.9	48.9-58.9	
Secondary	804	24.1	22.5-25.9	383	48	43.6-52.4	421	52	47.6-56.4	
Higher	350	11.5	9.9-13.5	187	53	46.9-58.9	163	47	41.1-53.1	
Wealth Quintile										90.7085
Poorest	610	15.5	13.3-18	211	35.9	31.9-40	399	64.1	60-68.1	0.0000
Poorer	689	19.2	16.9-21.7	313	44.2	39.8-48.7	376	55.8	51.3-60.2	
Middle	604	17.3	15.2-19.6	301	49.5	44.5-54.5	303	50.5	45.5-55.5	
Richer	667	19.7	17.1-22.6	344	50.2	44.9-55.5	323	49.8	44.5-55.1	
Richest	764	28.3	24-33	465	60.4	55.4-65.2	299	39.6	34.8-44.6	
Place of residence										16.691
Urban	2221	64.9	59.9-69.6	1152	52.2	49-55.4	1069	47.8	44.6-51	0.0057
Rural	1113	35.1	30.4-40.1	482	44.8	40.7-48.9	631	55.2	51.1-59.3	
Ecological zone										3.43
Mountain	200	5.6	3.6-8.6	92	47.1	39.4-54.8	108	52.9	45.2-60.6	0.3721
Hill	1694	49.9	44.2-55.6	788	48.3	45.1-51.5	906	51.7	48.5-54.9	
Terai	1440	44.5	39.2-49.9	754	51.4	47.1-55.6	686	48.6	44.4-52.9	
Province										23.7869
Province 1	490	17	15.2-19	265	53	47.7-58.3	225	47	41.7-52.3	0.0511
Province 2	460	16.2	14.2-18.3	243	53.1	46.5-59.6	217	46.9	40.4-53.5	
Province 3	575	26	21.8-30.6	303	52.7	46.8-58.5	272	47.3	41.5-53.2	

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Province 4	578	13.2	11.5-15.1	273	46.9	42-51.7	305	53.1	48.3-58	
Province 5	553	17.8	15.4-20.4	253	45.4	39-51.9	300	54.6	48.1-61	
Province 6	343	3.9	3.3-4.6	148	39.8	32.9-47.1	195	60.2	52.9-67.1	
Province 7	335	6	5-7.2	149	41.9	33.8-50.5	186	58.1	49.5-66.2	
Caffeine consumption										0.2587
No	2942	88.4	86.7-89.9	1434	49.4	46.9-52.0	1508	50.6	48.0-53.1	0.6895
Yes	392	11.6	10.1-13.3	200	50.8	44.1-57.4	192	49.2	42.6-55.8	
Tobacco use										5.3524
No	2826	84.9	83.2-86.6	1410	50.4	47.8-53.1	1416	49.6	46.9-52.2	0.0338
Yes	508	15.1	13.5-16.8	224	44.8	40.0-49.8	284	55.1	50.2-60.0	
Alcohol consumption										2.4122
No	3249	97.8	97.1-98.4	1600	49.8	47.2-52.8	1649	50.2	47.6-52.8	0.1505
Yes	85	2.2	1.6-2.9	34	40.6	29.4-52.9	51	59.4	47.1-70.6	

Note: n = Number of sample, CI = Confidence interval

Figure 1: Determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

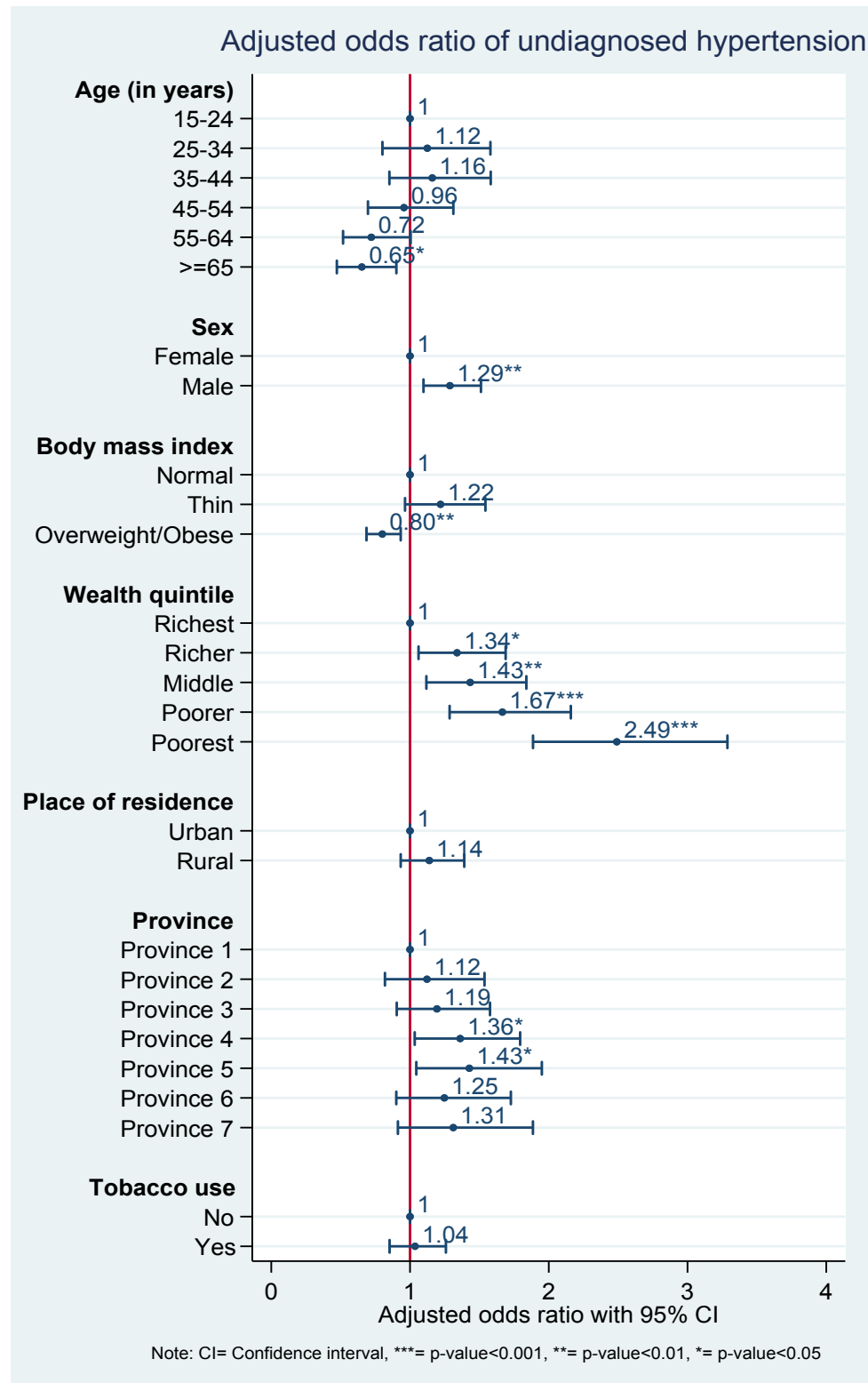


Figure 2: Concentration curve to measure the wealth-based inequality in the prevalence of undiagnosed hypertension among patients with hypertension in Nepal, 2016

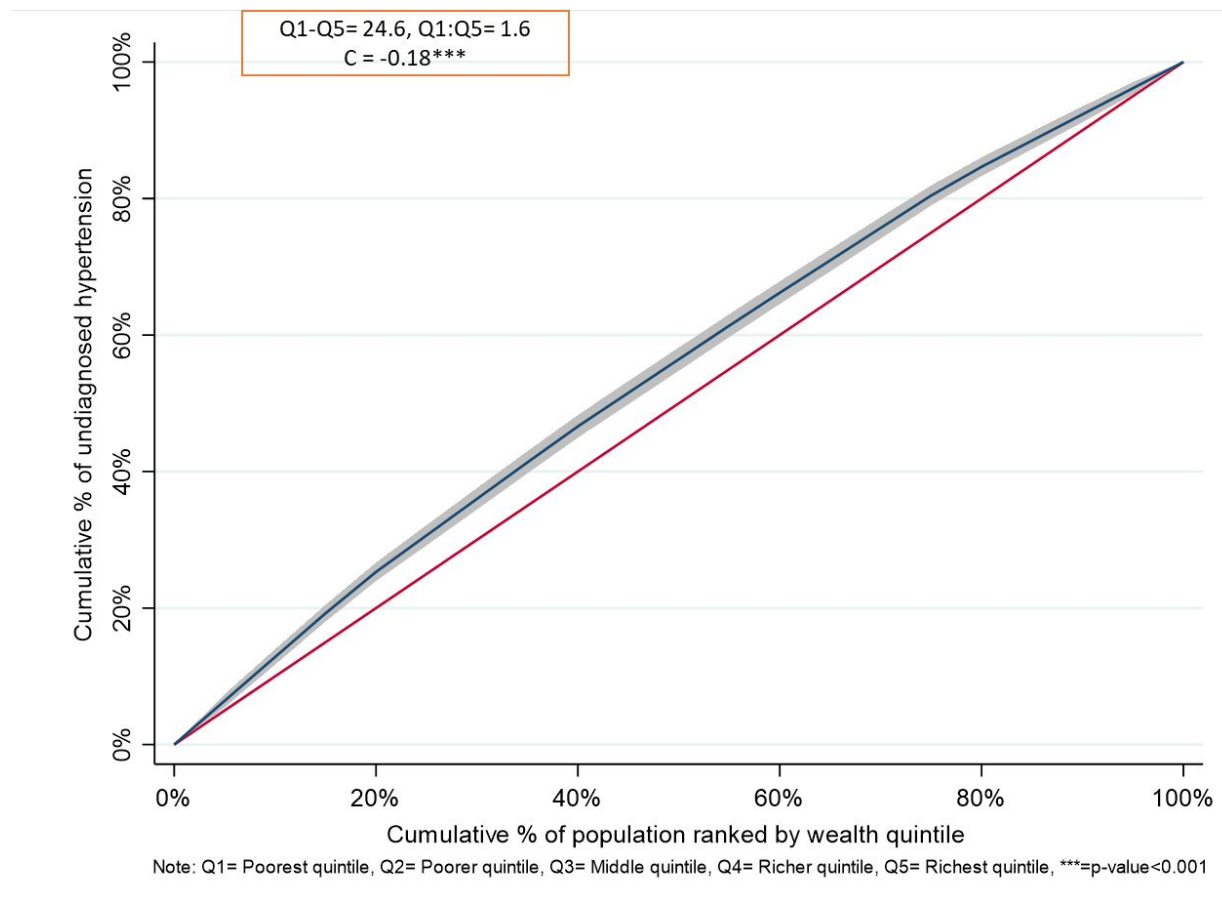
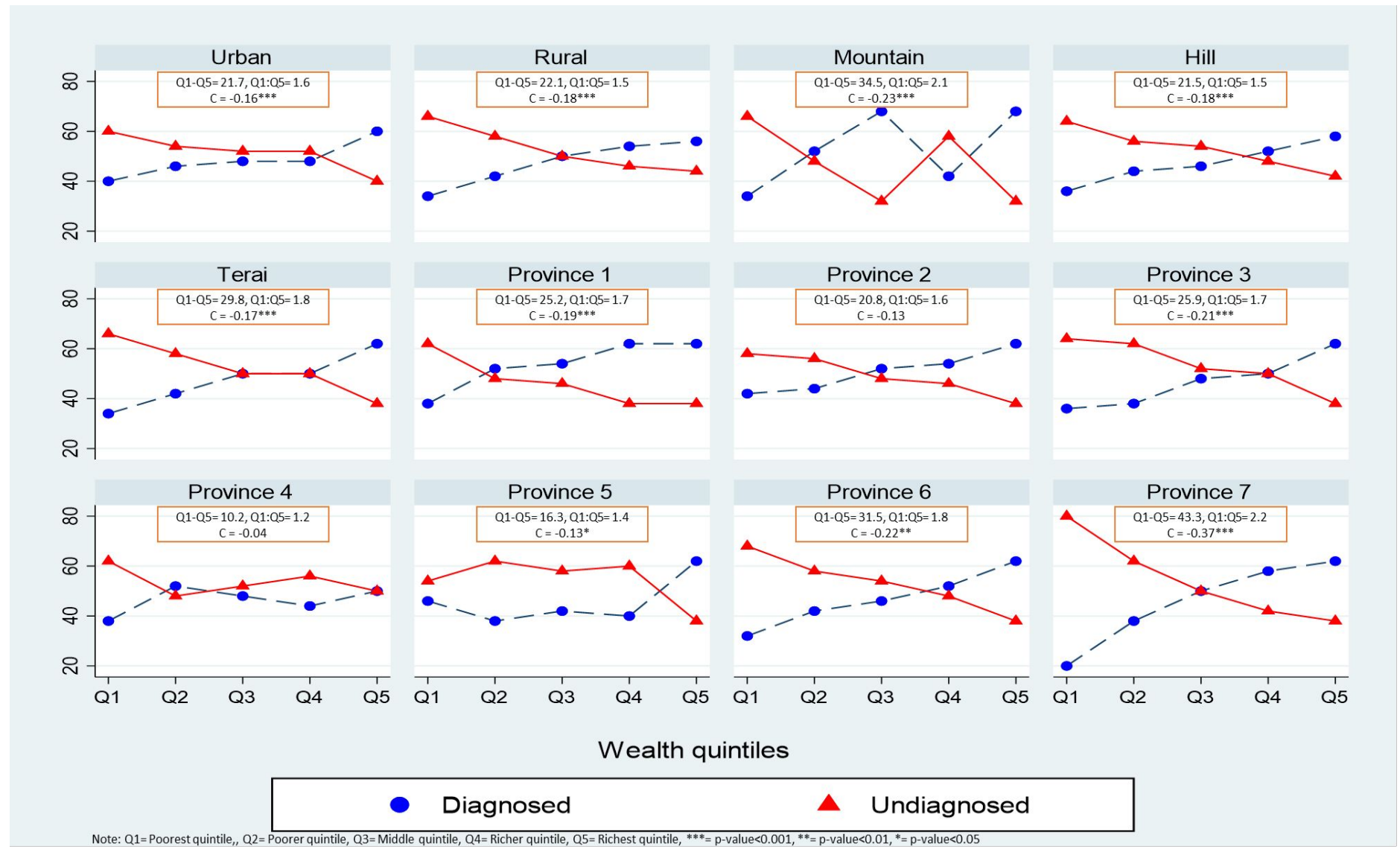


Figure 3: Socioeconomic inequalities in the prevalence of undiagnosed hypertension among patients with hypertension across geographical locations in Nepal, 2016



Supplementary Table 1: Unadjusted determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Variables	COR	95% CI	<i>p</i> -value
Age			
15-24	1		
25-34	1.06	0.77-1.46	0.7090
35-44	1.00	0.75-1.34	0.9800
45-54	0.87	0.65-1.18	0.3760
55-64	0.72	0.52-0.98	0.0400
>=65	0.70	0.52-0.96	0.0250
Sex			
Male	1.32	1.14-1.53	0.0000
Female	1		
BMI			
Normal	1		
Thin	1.13	0.91-1.41	0.2610
Overweight/obese	0.70	0.6-0.8	0.0000
Education			
No education	1		
Primary	1.08	0.9-1.31	0.4010
Secondary	1.07	0.88-1.3	0.4790
Higher	0.85	0.66-1.09	0.2070
Wealth Quintile			
Poorest	2.94	2.29-3.77	0.0000
Poorer	1.87	1.47-2.38	0.0000
Middle	1.57	1.23-1.99	0.0000
Richer	1.46	1.16-1.84	0.0010
Richest	1		
Place of residence			
Urban	1		
Rural	1.41	1.17-1.71	0.0000
Ecological zone			
Mountain	1		
Hill	0.98	0.68-1.41	0.9100
Terai	0.78	0.53-1.12	0.1800
Province			
Province 1	1		
Province 2	1.05	0.77-1.44	0.7540
Province 3	1.06	0.78-1.44	0.7220
Province 4	1.32	1-1.74	0.0530
Province 5	1.40	1.01-1.92	0.0400
Province 6	1.55	1.09-2.2	0.0140

Province 7	1.47	0.99-2.18	0.0550
Caffeine consumption			
No	1.00		
Yes	0.91	0.72-1.15	0.4400
Tobacco consumption			
No	1.00		
Yes	1.26	1.06-1.51	0.0100
Alcohol consumption			
No	1.00		
Yes	1.46	0.91-2.32	0.1140

Note: COR= Crude Odds Ratio, CI= Confidence Interval

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Title: Examining the prevalence, correlates and inequalities of undiagnosed hypertension in Nepal: a population-based cross-sectional study

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ABSTRACT

Objective: To examine the prevalence, correlates and socio-demographic inequalities of undiagnosed hypertension in Nepal.

Design: This study used cross-sectional 2016 Nepal Demographic and Health Survey (NDHS) data. We defined a hypertensive patient to remain undiagnosed if at the survey he/she was diagnosed as hypertensive (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) but never took any prescribed anti-hypertensive medicine to lower/control blood pressure and never told by health professionals to have hypertension prior the survey. Multiple binary logistic regression analysis was performed, and Concentration Index was measured.

Setting: Nepal

Participants: Adult patients with hypertension

Results: Among 3334 hypertensive patients, 50.4% remained undiagnosed during the survey in Nepal. Adjusted model reveals that patients who were male, belonged to households other than richest quintile, and lived in Province 4 and Province 5 were at higher risk and patients who were 65+ years of age and were overweight/obese were at lower risk of remaining undiagnosed for hypertension. The poor-rich gap was 24.6 percentage points (Q1= 64.1% vs Q5= 39.6%) and poor:rich ratio was 1.6 (Q1/Q5= 1.6) in the prevalence of undiagnosed hypertension. Undiagnosed hypertension was disproportionately distributed among socioeconomically worse-off Nepalese patients (Concentration Index, C= -0.18). Inequalities in the prevalence of undiagnosed hypertension further varied across other geographic locations including place of residence, ecological zones and administrative provinces.

Conclusions: Undiagnosed hypertension was highly prevalent in Nepal and there were substantial inequalities by socio-demographics and sub-national levels. Increasing awareness, strengthening

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3 routine screening to diagnose hypertension at primary health service facilities and enactment of
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5 social health insurance policy may help Nepal to prevent and control this burden.
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8 **Keywords:** Undiagnosed hypertension, Inequality, Demographic and Health Survey, Nepal
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11 **Strengths and limitations of this study**

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- 13 • This study determined the prevalence and correlates of undiagnosed hypertension in
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15 Nepal using the most updated population-based nationally representative data.
- 16 • This study measured both wealth-based absolute and relative inequalities in the
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18 prevalence of undiagnosed hypertension at national level as well as across place of
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20 residence, ecological zones and administrative provinces.
- 21 • The cross-sectional nature of the data limits us to measure causal association between
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23 undiagnosed hypertension and the explanatory variables studied.
- 24 • The association of some potential behavioral or lifestyle factors such as physical
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26 activity, dietary patterns and family history with undiagnosed hypertension remain
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28 unmeasured due to lack of information.
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INTRODUCTION

Hypertension or raised blood pressure is recognized as a leading cause of mortality and disability [1], affecting more than one billion people every year worldwide [2]. Globally, hypertension is a directing factor for cardiovascular diseases (CVDs), specially heart diseases, myocardial infarctions, kidney failure, strokes, disability and premature deaths [2,3]. In South-East Asian countries including Nepal, hypertension affects one out of three adults, which accounts for nearly 1.5 million adult deaths annually; and 9.4% of the total deaths [4]. Studies identified, more than 50% people having hypertension remained undiagnosed in South-East Asian region [5]. Among South Asian countries, Nepal has one of the highest prevalence of hypertension [6].

Currently, Nepal is facing an epidemiological transition with increasing prevalence of hypertension [7]. Several studies reported the prevalence of hypertension in Nepal. A study based on the Nepal Demographic and Health Survey 2016 reported about 20% Nepalese adults (aged \geq 18 years) had hypertension [8]. Other studies reported the prevalence of hypertension ranges from 23% to 34% in Nepal [7,9–12]. However, some of these assessments were older and did not represent national scenario. In 2013, the national NCD risk factor survey showed about 25.7% adults aging 15-69 years had hypertension in Nepal [13]. This survey also found that a large number of (42.7%) adults had never measured their blood pressure. For prevention, control and proper treatment of hypertension, it is prior need to correctly diagnose this disease. In addition, failure to early diagnosis and treatment of hypertension may lead to serious health hazards, disability in the later life, or eventually deaths. Number of government, non-government and private health facilities are providing health services including diagnosis, medication and treatment for hypertension. However, the existing health systems of Nepal is not ready for diagnosis,

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3 treatment and control of hypertension especially for the mass people at the community level
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5 indicating the challenges to tackle this burden [14].
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8 To prevent hypertension, the disease needs to be diagnosed first before any related complications
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10 arise. However, there is lack of evidence about the prevalence of undiagnosed hypertension in
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12 Nepal at national and subnational levels. The estimates of undiagnosed hypertension, and its socio-
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14 demographic inequalities at national and subnational level may help the policy makers for
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16 formulating effective strategies for screening, treatment and control as well as prevention of such
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18 burden by identifying the most vulnerable groups. Therefore, given the importance of this burden,
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20 we aimed to examine the prevalence, correlates and socio-demographic inequalities of
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22 undiagnosed hypertension in Nepal.
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30 **METHODS**

31 **Data source**

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34 We used the most updated nationally representative cross-sectional data from Nepal Demographic
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36 and Health Survey (NDHS). Though the data of Demographic and Health Surveys is managed by
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38 Measure Evaluation, the NDHS was conducted from June 2016 to January 2017 by a private
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40 research organization named “NEW ERA” under the monitoring and supervision of the Ministry
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42 of Health, Nepal. To estimate the prevalence of hypertension nationally in Nepal, the NDHS 2016
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44 obtained informed consent from the household head on behalf of all household members of each
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46 surveyed households [15]. For academic and scientific purposes, this anonymous dataset without
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48 any identifiers was made available by the ICF International, Maryland, United States [15]. We
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50 obtained approval with access to use the data to conduct this study.
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Survey procedure and participants

In 2015, Nepal declared some new places to fall under municipalities and some municipalities have been reformed [8]. After these changes, Nepal has been divided into seven administrative provinces comprising several districts under each province and urban-rural areas. These urban and rural areas were divided into small administrative units as wards. Because of having comparatively greater number of households in urban areas, the urban area was further divided into enumeration area (EA). The primary sampling unit (PSU) were wards for both urban and rural areas [15]. Because of some changes in administrative areas, Nepal revised the sampling frame of National Population and Housing Census (NPHC). The 2016 NDHS used this revised sampling frame and applied a multistage survey that respectively conducted in two and three stages in rural and urban areas. NDHS selected the PSUs proportionately to the size in the first stage and then the random selection of EAs from the systematic selection of households from each PSU in second stage. In third stage, the households were selected by using stratified cluster sampling technique in urban setting. A detailed description about the methodology is available elsewhere [15]. A total of 11490 households were selected from 383 wards, of which 5520 households from 184 wards were from urban settings and 5970 households from 199 wards were from rural settings. From these households, all the residents whose age 15 years or above were eligible for the measurement of blood pressure. With an overall 95% response rate, a total of 14823 individuals participated in the survey. The participants of this study were males and females with hypertension of ages 15 years or older. A total of 3334 patients of both sexes were included in this study. A step by step procedure of selecting study sample has shown in Figure 1.

{Figure 1 will be added here}

Outcome variable

To measure hypertension, the 2016 NDHS used the UA-767F/FAC (A&D Medical) automated device to record the blood pressure of the participants. With 5 minutes intervals between each measurement, the 2016 NDHS recorded the measurements of blood pressure for three times in a sitting position. NDHS considered the last two measures of blood pressure levels and used their mean to detect hypertension. The survey used the World Health Organization (WHO) guidelines to report a participant as hypertensive [15]. This guideline has integrated the 2017 guidelines of the American College of Cardiology/ American Society of Hypertension [16,17]. According to the guideline, a participant with systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg is diagnosed as a hypertension case. We also considered participants as patients of hypertension if s/he was previously told by health professional to have hypertension or taking medication to control hypertension. Our outcome variable is undiagnosed hypertension. A patient is considered as undiagnosed for hypertension if at the survey time he/she was diagnosed as hypertensive (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg) but never took any prescribed anti-hypertensive medicine to lower/control blood pressure and never told by health professionals to have hypertension prior the survey [18,19].

Explanatory variables

This study considered a set of socio-demographic and behavioral characteristics as independent variables. Age (in years), sex, Body Mass Index (BMI) measured through dividing the weight by squared height (kg/m^2), education level, household wealth status, place of residence, ecological zone, and provinces were considered as socio-demographic characteristics of the patients. Age was categorized as 15-24, 25-34, 35-44, 45-54, 55-64 and ≥ 65 years. Sex had two categories, male and female. The BMI was categorized as thin/underweight (BMI < 18.5 kg/m^2), normal (18.5 kg/m^2

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3 $\leq \text{BMI} < 25 \text{ kg/m}^2$) and overweight/obese ($\text{BMI} \geq 25.0 \text{ kg/m}^2$) [20]. Based on the highest class
4 completed by the respondents, level of education was classified as no education, primary,
5 secondary and higher. NDHS used principal component analysis [15] to construct the wealth index
6 to desegregate the households into five socioeconomic quintiles (poorest, poorer, middle, richer
7 and richest). The place of residence was stratified as urban and rural across all geographic location.
8 Nepal was ecologically divided in Mountain, Hill and Terai. Using 2015 reformation, 7
9 administrative provinces were considered as Province 1, Province 2, Province 3, Province 4,
10 Province 5, Province 6 and Province 7. Three behavioral characteristics of respondents, caffeine,
11 tobacco and alcohol consumption were considered as independent variables each of which
12 contained dichotomous response on whether respondent consume caffeine, tobacco or alcohol.
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27 **Statistical analyses**

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29 We described the prevalence of undiagnosed hypertension and background characteristics of the
30 study patients by using univariate analysis technique. The estimates of each of the categorical
31 variables included in this study were reported with numbers, weighted percentages and 95%
32 confidence intervals (CIs) of estimates. The weighted prevalence of undiagnosed hypertension was
33 determined across the background characteristics of the study patients from bivariate analysis.
34 Statistical significance was detected by applying Chi-square test. Then, we conducted simple and
35 multiple binary logistic regression analyses to examine the correlates of undiagnosed hypertension.
36 The results of the regression analysis were presented in terms of odds ratio with respective 95%
37 CI. Variables that were statistically significant in simple logistic regression analysis were entered
38 in the multiple regression model to estimate the adjusted odds ratio (AOR). Notably, the statistical
39 significance was defined at 5% level ($p\text{-value} < 0.05$). Variance inflation factors to detect
40 multicollinearity among the independent variables were assessed before incorporating them into
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3 the multiple regression model. Due to hierarchical structure of NDHS data, we considered the
4 cluster sampling design of the 2016 NDHS to estimate the prevalence and determinants in this
5 study [15]. We excluded cases with missing values for blood pressure measurements.
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10 Proposed by Wagstaff [21] to measure the inequality, we estimated the concentration index (C),
11 to show the degree and direction of wealth-based inequality in undiagnosed hypertension
12 prevalence. For the purpose of calculating C, the households were ranked from the poorest to the
13 richest according to their socioeconomic characteristics. We plotted a concentration curve to
14 portray the distribution of undiagnosed hypertension. The Y-axis of the concentration curve
15 representing the cumulative proportion of undiagnosed hypertension and the X-axis represents the
16 cumulative proportions of the population across wealth quintiles. When the concentration curve
17 coincide with the diagonal, the prevalence of undiagnosed hypertension is treated as equally
18 distributed across socioeconomic groups. In contrast, the concentration curve typically deviate
19 from the diagonal if there exist inequalities in the prevalence of undiagnosed hypertension. The C
20 is defined as twice the area between the concentration curve and the diagonal [22–24]. The index
21 value can range between -1 and $+1$, a positive value implies the prevalence of undiagnosed
22 hypertension is more concentrated among the better-off socioeconomic group and a negative value
23 implies the prevalence is more concentrated among less affluent group [23,25]. We repeat the
24 estimation of C across other geographical locations such as place of residence, ecological zones
25 and provinces to detect the group of patients with highest severity of socioeconomic inequalities
26 in the prevalence of undiagnosed hypertension. STATA (version 13) was used to perform all the
27 analyses [26].
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Patient and public involvement

Patients and public were not involved in developing the research questions, measuring outcome and designing the study. Information of the participants were anonymous.

RESULTS

General Characteristics of the Study Participants

Table 1 shows the general characteristics of the study participants. Among the patients studied, the average age of patients was 49.8 years (95% CI 49.1, 50.5) with the lowest percentage of patients belonged to 15-24 years age group (6.6%) and highest percentage of patients belonged to 45-54 years age group (20.9%). Numbers of males (49.5%) and females (50.5%) in the sample were almost equal. Nearly half of the patients were normal in terms of their BMI while more than one third of the patients were overweight/obese. Though two-third of the patients resided in urban area (64.9%), the educational status of the patients were poor. Nearly half of the patients had no education while 24.1% and 11.5% had secondary and higher education respectively. The highest number of patients belonged to richest wealth quintile (28.3%) and the lowest number of patients belonged to the poorest wealth quintile (15.5%). Also, the highest number of patients were from province 3 (26.0%) followed by province 5 (17.8%) and province 1 (17.0%). However, only 5.6% of the patients were from mountain ecological zone.

{Table 1 will be added here}

Prevalence of Undiagnosed Hypertension

Among 3334 participants who had hypertension during the survey, more than half of them were detected as remaining undiagnosed (50.4%). The prevalence of undiagnosed hypertension among the patients varied across their age (p -value < 0.001), sex (p -value < 0.001), BMI (p -value < 0.001), wealth quintile (p -value < 0.001) and place of residence (p -value < 0.01). The prevalence of undiagnosed hypertension were higher among patients with 15-24 years age group and steadily decreasing with the increase of age. The prevalence of undiagnosed hypertension was higher among male patients (54.2%) than female (46.7%). Compare to patients with normal BMI, the prevalence of undiagnosed hypertension was higher among thin patients (57.8%) and lower among overweight/obese patients (44.4%). Compare to patients of the richest wealth quintile (39.6%), the prevalence of undiagnosed hypertension was higher among patients of the poorest (64.1%) and poorer (55.8%) quintiles. The rate of undiagnosed hypertension was higher among rural patients (55.2%) compare to urban (47.8%). No educational, ecological and provincial variations in the prevalence of undiagnosed hypertension was observed (**Table 1**).

Correlates of Undiagnosed Hypertension

We found that patient's age, sex, BMI, wealth quintile, place of residence and province were significantly associated with the prevalence of undiagnosed hypertension among hypertensive patients in unadjusted logistic regression analysis (see **supplementary**).

Figure 2 represents the results of multiple logistic regression analysis. The multiple binary logistic regression model showed that patient's age, sex, BMI, wealth quintile and province had significant association with undiagnosed hypertension. Elderly patients ≥ 65 years of age had a lower

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3 likelihood of being undiagnosed for hypertension than patients with age 15-24 years (Adjusted
4 Odds Ratio, AOR = 0.65; 95% CI 0.48, 0.91). Male patients were 1.29 times more likely than
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6 female patients to remain undiagnosed for hypertension (AOR = 1.29, 95% CI 1.11, 1.51).
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8 Compare to patients with normal BMI, overweight/obese patients (AOR = 0.80, 95% CI 0.69,
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10 0.93) were less likely to have undiagnosed hypertension.
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15 We found wealth quintiles as potential correlates of undiagnosed hypertension. The risk of
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17 remaining undiagnosed for hypertension was increasing with the decrease of patient's
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19 socioeconomic status. Patients with a poorer socioeconomic status had higher chance of having
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21 undiagnosed hypertension compared to higher socioeconomic quintiles. Patients of poorest and
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23 poorer wealth quintiles were 2.49 (AOR = 2.49; 95% CI 1.90, 3.30) and 1.67 (AOR = 1.67; 95%
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25 CI 1.29, 2.16) times more likely to have an undiagnosed hypertension condition than patients of
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27 richest wealth quintile.
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32 Moreover, significant provincial variation was evident in the prevalence of undiagnosed
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34 hypertension among hypertensive patients. Patients of province 4 (AOR = 1.36, 95% CI 1.04, 1.79)
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36 and province 5 (AOR = 1.43, 95% CI 1.05, 1.95) were more likely to had undiagnosed
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38 hypertension than patients of province 1.
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42 {Figure 2 will be added here}
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45 **Socioeconomic Inequalities in Undiagnosed Hypertension**

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48 **Figure 3** depicts the inequalities in the prevalence of undiagnosed hypertension among
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50 hypertensive patients. The absolute poor (Q1) - rich (Q5) difference in the distribution of
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52 undiagnosed hypertension was 24.6% between poorest and richest, meaning that the prevalence of
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54 undiagnosed hypertension was greater by 24.6 percentage points among the poorest. The relative
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3 measure of inequality in terms of poor (Q1): rich (Q5) ratio was 1.6 for the prevalence of
4 undiagnosed hypertension among patients, depicting that the prevalence of undiagnosed
5 hypertension was higher by 1.6 times among the poorest than richest. We found negative value of
6 the Concentration Index ($C = -0.18$) which represents that the prevalence of undiagnosed
7 hypertension among hypertensive patients was disproportionately distributed among worse-off
8 socioeconomic groups.
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18 **{Figure 3 will be added here}**
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20 In addition, patients living in mountain and in province 7 had large gaps in the prevalence of
21 undiagnosed hypertension (**Figure 4**). The higher Q1:Q5 ratio were observed among those who
22 had large Q1-Q5 gaps in the prevalence of undiagnosed hypertension across different geographic
23 locations. We found large negative values of C among those who had higher Q1-Q5 gaps and
24 Q1:Q5 ratio for the prevalence of undiagnosed hypertension. See **Figure 4** for details.
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33 **{Figure 4 will be added here}**
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38 **DISCUSSION**

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40 Globally few studies have been conducted on undiagnosed hypertension to date. Utilizing NDHS
41 2016 data, this study intended to estimate the prevalence of undiagnosed hypertension. In addition,
42 the risk factors and inequalities associated with it among Nepalese hypertensive patients were
43 identified. About half of the biomarker partakers were found hypertension positive who were not
44 screened/diagnosed before the survey. Patients unwillingness for regular check-up before any
45 health complication arises due to lack of awareness as well as inaccessibility to screening services
46 may direct this high prevalence [27]. Gap in knowledge, attitude and practice of healthy lifestyle
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3 as preventive measure to non-communicable diseases (NCDs) may also act as a driver of
4 undiagnosed hypertension [27–29]. Community-based awareness on changing lifestyle to address
5 the burden of NCDs from the society as a whole might be effective in reducing this gap [30].
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10 Several studies reported higher risk of hypertension among people who were older in age, male,
11 urban dwellers, had higher education level, regular consumer of tobacco and alcohol, and who are
12 overweight [6,8,28,29]. In contrast, we found that patients aged 65+ years and who were
13 overweight/obese were at lower risk of remaining undiagnosed from this disease. However, our
14 findings depicted greater proportion of undiagnosed patients among those who were young and
15 physically thin. Young or underweight people are less conscious about their health status as they
16 might have the misconception that they are less likely to suffer from NCDs [31]. Nonetheless,
17 richest are more aware than the poorest people about the health hazards, typically have greater
18 access for screening diseases and can have the ability to afford treatment cost for the diseases in
19 Nepal [28]. This could lead the poor than the rich to be more exposed to undiagnosed hypertension.
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24 On the other hand, similar to risk factors of hypertension, undiagnosed hypertension were also
25 more prevalent among males and tobacco users [6,29]. The higher rate of undiagnosed
26 hypertension among male might be due to their lack of awareness and lower treatment rate than
27 female [32]. Smoking, a main source of using tobacco, is well recognized to have association with
28 increased risk of hypertension in many settings including Nepal [33,34]. However, there is lack of
29 evidence in determining the extent of how tobacco use is affecting patients to remain undiagnosed
30 for hypertension. Our finding demonstrates that in Nepal, factors other than tobacco use played
31 independent role in increasing rate of undiagnosed hypertension. Although difference in lifestyle
32 practices between male and female in Nepal may not be the key factors behind such exposure,
33 research need to be done to identify the actual risk factors [29].
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3 Undiagnosed hypertension may lead to adverse health consequences, including some organ
4 damages [35]. The World Health Organization, mentioning hypertension as a silent killer, stated
5 the prevalence of hypertension is higher in low- and middle-income countries than developed and
6 high income countries [3]. Our results proves this claim and also aligns with findings from
7 Bangladesh and Sub-Saharan Africa [19,36,37]. Although situated in closer geographic region, the
8 prevalence of undiagnosed hypertension from this study differs from more developed and high
9 income countries with up to date facility setup and health policies for their citizens. For example,
10 the prevalence of undiagnosed hypertension was much lower in India and China than Nepal
11 [38,39]. While half of the hypertensive patients remain undiagnosed in Nepal, the recent evidence
12 shows that the prevalence of undiagnosed hypertension was 28.8% in China [40]. The reason
13 behind this difference might be due to the differences in age of study participants. Nepal assessed
14 participants of age 15 years or older while China included older participants (over 45 years) who
15 assumed more aware, because of their ages, about health conditions and were more likely to visit
16 doctors for regular health check-up. Similarly, findings from studies conducted in countries with
17 more developed health facilities and advanced screening system such as Japan, Korea, England,
18 Ireland, Egypt, Brazil and USA were also found to have lower level of undiagnosed hypertension
19 than Nepal as found in this study [41–47]. Being a neighbouring country, the prevalence of
20 undiagnosed hypertension of Nepal is relatively closer with that in Bangladesh [19].
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45 In Nepal, despite the detection of risk factors [6,8,29] and inequalities [28], the prevalence of
46 hypertension was well investigated nationally which lead policy makers to successfully steer away
47 it's progression [48]. However, this effort will be meaningless unless all patients at risk of
48 hypertension are accurately diagnosed and detected. It is necessary to identify whether unequal
49 distribution of undiagnosed hypertension exists among patients with hypertension across different
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3 socioeconomic groups. It will aid in setting priorities and proper allocation of resources. Our study
4 reveals existence of inequalities in the distribution of undiagnosed hypertension due to economic
5 status, with poorest had higher prevalence of undiagnosed hypertension than richest and showed
6 greater degree of wealth-based inequality concentrated among the poorest. These inequalities were
7 more prevalent among patients living in different geographical locations including place of
8 residence, ecological zones and administrative provinces. Such disparity may ascribe to greater
9 awareness and more utilization of healthcare benefits by the people who are rich [28]. Such
10 inequality might increase the catastrophic health spending given the rise of catastrophic household
11 expenditure due to NCDs in Nepal [14,49]. Public health strategies might reduce this gap by
12 concentrating more on implementing social health insurance policies which has to be equitable for
13 all [41,49]. In this aspect, policy makers could take into consideration the disparities in the
14 distribution of undiagnosed hypertension found in this study.

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31 Several initiatives have been taken to control hypertension in Nepal. To address the burden of
32 cardiovascular diseases (CVD), the WHO and partners launched an initiative called “Global
33 Hearts” in 2016 [50]. This initiative took a comprehensive approach to help countries in scaling-
34 up of affordable and adaptable measures to make their health services better able to detect and treat
35 people at risk or suffering from CVD. This initiative comprises of three packages: SHAKE,
36 HEARTS and MPOWER. The package “HEARTS” provides tools to incorporate CVD
37 management best practices at the primary health care level to reduce CVD risk factors such as
38 hypertension and high blood cholesterol. Like many LMICs, Nepal has been under this initiative
39 to tackle the CVD. In addition, the Community-based Management of Hypertension in Nepal
40 (COBIN) is a community-based cost-effective intervention that showed success in reducing
41 hypertension in Nepal [51,52]. However, for designing further programs or interventions, our
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3 findings further provide insights in considering the hypertensive cases that remained undiagnosed
4 and their uneven distributions across a spectrum of sociodemographic characteristics for the
5 prevention of hypertension in Nepal.
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10 Ignoring the population at risk of hypertention may become a major threat to health outcomes to
11 any nation. This study bestows an immense opportunity to estimate the prevalence of undiagnosed
12 hypertension which had not yet been studied nationally in Nepal. NDHS 2016 through
13 incorporation of biomarker test bears evidence that a substantial proportion of individuals are
14 suffering from blood pressure abnormalities. This in fact emphasise the need of conducting routine
15 screening for hypertension widened with the greatest possible coverage in the population. A
16 routine surveillance system with technology-based screening can aid in tracing disease incidence
17 as well as people at risk of being undiagnosed [53]. Our study findings will be helpful to initiate
18 policies and programs in capturing the highest domain of underprivileged population and bring
19 them under routine surveillance at community level with optimum cost.
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34 **Strengths and limitations**

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37 We used most updated nationally representative cross-sectional data to determine the prevalence,
38 correlates and inequalities of undiagnosed hypertension in Nepal. We considered complex survey
39 design to capture variations due to designing. However, there may have residuals and unmeasured
40 potential behavioral or lifestyle factors such as physical activity, dietary patterns and family history
41 of hypertension that remain unmeasured in relating to undiagnosed hypertension due to lack of
42 information. Since our data was corss-sectional, the relationship between undiagnosed
43 hypertension and confounders were probabilistic rather than causal. However, identification of
44 potential correlates through using odds ratio is widely acceptable. This study measured both
45 absolute and relative inequalities in the prevalence of undiagnosed hypertension at national level
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3 as well as across place of residence, ecological zones and administrative provinces to further guide
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5 policy/decision makers for better allocation of resources to reduce the burden.
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10 11 **CONCLUSIONS**

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14 This study manifests, in Nepal huge number of respondents with hypertension remained
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16 undiagnosed. Initiative for NCDs diagnoses prioritizing those who are down and out requires to
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18 be implemented. Community-based awareness should be raised to improve knowledge, attitude
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20 and practice of the people particularly those who are young, slender, poor and male given their
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22 higher risk of being undiagnosed. Routine screening and strengthening diagnosis of hypertension
23
24 in the primary level of health care service facilities may help Nepal in reducing cases with
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26 undiagnosed hypertension. Moreover, identification of inequalities among different risk groups
27
28 will be beneficial in achieving universal health coverage of sustainable development goal (Goal
29
30 3.8.1). Social health insurance policies under integrated national NCD policy should be properly
31
32 enacted to ensure socioeconomically disadvantaged populations covered under the scheme for
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34 prevention and control of hypertension from them.
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48 **Contributors**

49
50 MMH, SA and AAM conceptualized the study. MMH performed the data analysis and
51
52 interpretation of the findings. MMH, FT and MT contributed to writing. AAM and SA critically
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3 reviewed the analysis and final version of the manuscript. All authors made a through review of
4
5 the final draft and approved it for submission.
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16 **Competing interests**

17 None declared.
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22 **Ethical approval**

23 The NDHS survey methodology and questionnaire was reviewed and approved by the ethical
24 review board of Nepal Research Council and ICF Institutional. NDHS obtained informed consent
25 from the respondents before conducting the survey. Therefore, separate ethical approval was not
26 required for this study and we are using publicly available de-identified data.
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34 **Data sharing statement**

35 Data are available in a public, open access repository. All data related to study are included in the
36 manuscript.
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34 **Table 1:** Characteristics of the study participants
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Variables	Total			Diagnosed hypertension			Undiagnosed hypertension			Chi-Square Statistic (p-value)
	n	%	95% CI	n	%	95% CI	n	%	95% CI	
Overall	3334	--	--	1634	49.6	47.1-52.1	1700	50.4	47.9-52.9	--
Age										29.6317
15-24	237	6.6	5.6-7.8	107	43.1	36.1-50.4	130	56.9	49.6-63.9	0.0008
25-34	449	13.2	11.9-14.5	196	43.8	38.4-49.3	253	56.2	50.7-61.6	
35-44	637	19.6	18-21.3	287	45.2	40.1-50.3	350	54.8	49.7-59.9	
45-54	687	20.9	19.2-22.8	333	49.4	45-53.8	354	50.6	46.2-55	
55-64	643	18.9	17.4-20.5	344	54.7	49.8-59.5	299	45.3	40.5-50.2	
>=65	681	20.8	19-22.7	367	55.1	50.3-59.8	314	44.9	40.2-49.7	
Sex										18.35
Male	1640	49.5	47.7-51.3	746	45.8	42.6-49.1	894	54.2	50.9-57.4	0.0003
Female	1694	50.5	48.7-52.3	888	53.3	50.1-56.4	806	46.7	43.6-49.9	
BMI										29.2511
Normal	1816	53.6	51.2-56.1	841	47.1	44.3-50	975	52.9	50-55.7	0.0001

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3											
4	Thin	361	11.1	9.9-12.5	156	42.2	35.7-49	205	57.8	51-64.3	
5	Overweight/obese	1120	35.2	32.5-38	620	55.6	51.7-59.5	500	44.4	40.5-48.3	
6	Education										6.5852
7	No education	1576	46.5	44.1-48.9	778	50.9	47.5-54.4	798	49.1	45.6-52.5	0.2125
8	Primary	602	17.8	16.2-19.5	285	46.1	41.1-51.1	317	53.9	48.9-58.9	
9	Secondary	804	24.1	22.5-25.9	383	48	43.6-52.4	421	52	47.6-56.4	
10	Higher	350	11.5	9.9-13.5	187	53	46.9-58.9	163	47	41.1-53.1	
11											
12	Wealth Quintile										90.7085
13	Poorest	610	15.5	13.3-18	211	35.9	31.9-40	399	64.1	60-68.1	0.0000
14	Poorer	689	19.2	16.9-21.7	313	44.2	39.8-48.7	376	55.8	51.3-60.2	
15	Middle	604	17.3	15.2-19.6	301	49.5	44.5-54.5	303	50.5	45.5-55.5	
16	Richer	667	19.7	17.1-22.6	344	50.2	44.9-55.5	323	49.8	44.5-55.1	
17	Richest	764	28.3	24-33	465	60.4	55.4-65.2	299	39.6	34.8-44.6	
18											
19	Place of residence										16.691
20	Urban	2221	64.9	59.9-69.6	1152	52.2	49-55.4	1069	47.8	44.6-51	0.0057
21	Rural	1113	35.1	30.4-40.1	482	44.8	40.7-48.9	631	55.2	51.1-59.3	
22											
23	Ecological zone										3.43
24	Mountain	200	5.6	3.6-8.6	92	47.1	39.4-54.8	108	52.9	45.2-60.6	0.3721
25	Hill	1694	49.9	44.2-55.6	788	48.3	45.1-51.5	906	51.7	48.5-54.9	
26	Terai	1440	44.5	39.2-49.9	754	51.4	47.1-55.6	686	48.6	44.4-52.9	
27											
28	Province										23.7869
29	Province 1	490	17	15.2-19	265	53	47.7-58.3	225	47	41.7-52.3	0.0511
30	Province 2	460	16.2	14.2-18.3	243	53.1	46.5-59.6	217	46.9	40.4-53.5	
31	Province 3	575	26	21.8-30.6	303	52.7	46.8-58.5	272	47.3	41.5-53.2	
32	Province 4	578	13.2	11.5-15.1	273	46.9	42-51.7	305	53.1	48.3-58	
33	Province 5	553	17.8	15.4-20.4	253	45.4	39-51.9	300	54.6	48.1-61	
34	Province 6	343	3.9	3.3-4.6	148	39.8	32.9-47.1	195	60.2	52.9-67.1	
35	Province 7	335	6	5-7.2	149	41.9	33.8-50.5	186	58.1	49.5-66.2	
36											
37	Caffeine consumption										0.2587
38	No	2942	88.4	86.7-89.9	1434	49.4	46.9-52.0	1508	50.6	48.0-53.1	0.6895
39	Yes	392	11.6	10.1-13.3	200	50.8	44.1-57.4	192	49.2	42.6-55.8	
40											
41	Tobacco use										5.3524
42	No	2826	84.9	83.2-86.6	1410	50.4	47.8-53.1	1416	49.6	46.9-52.2	0.0338
43	Yes	508	15.1	13.5-16.8	224	44.8	40.0-49.8	284	55.1	50.2-60.0	
44											
45	Alcohol consumption										2.4122
46	No	3249	97.8	97.1-98.4	1600	49.8	47.2-52.8	1649	50.2	47.6-52.8	0.1505
47	Yes	85	2.2	1.6-2.9	34	40.6	29.4-52.9	51	59.4	47.1-70.6	

Note: n = Number of sample, CI = Confidence interval

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3 **Figure 1:** Selection of participants
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5 **Figure 2:** Determinants of undiagnosed hypertension among patients with hypertension in
6 Nepal, 2016
7

8 **Figure 3:** Concentration curve to measure the wealth-based inequality in the prevalence of
9 undiagnosed hypertension among patients with hypertension in Nepal, 2016
10

11 **Figure 4:** Socioeconomic inequalities in the prevalence of undiagnosed hypertension among
12 patients with hypertension across geographical locations in Nepal, 2016
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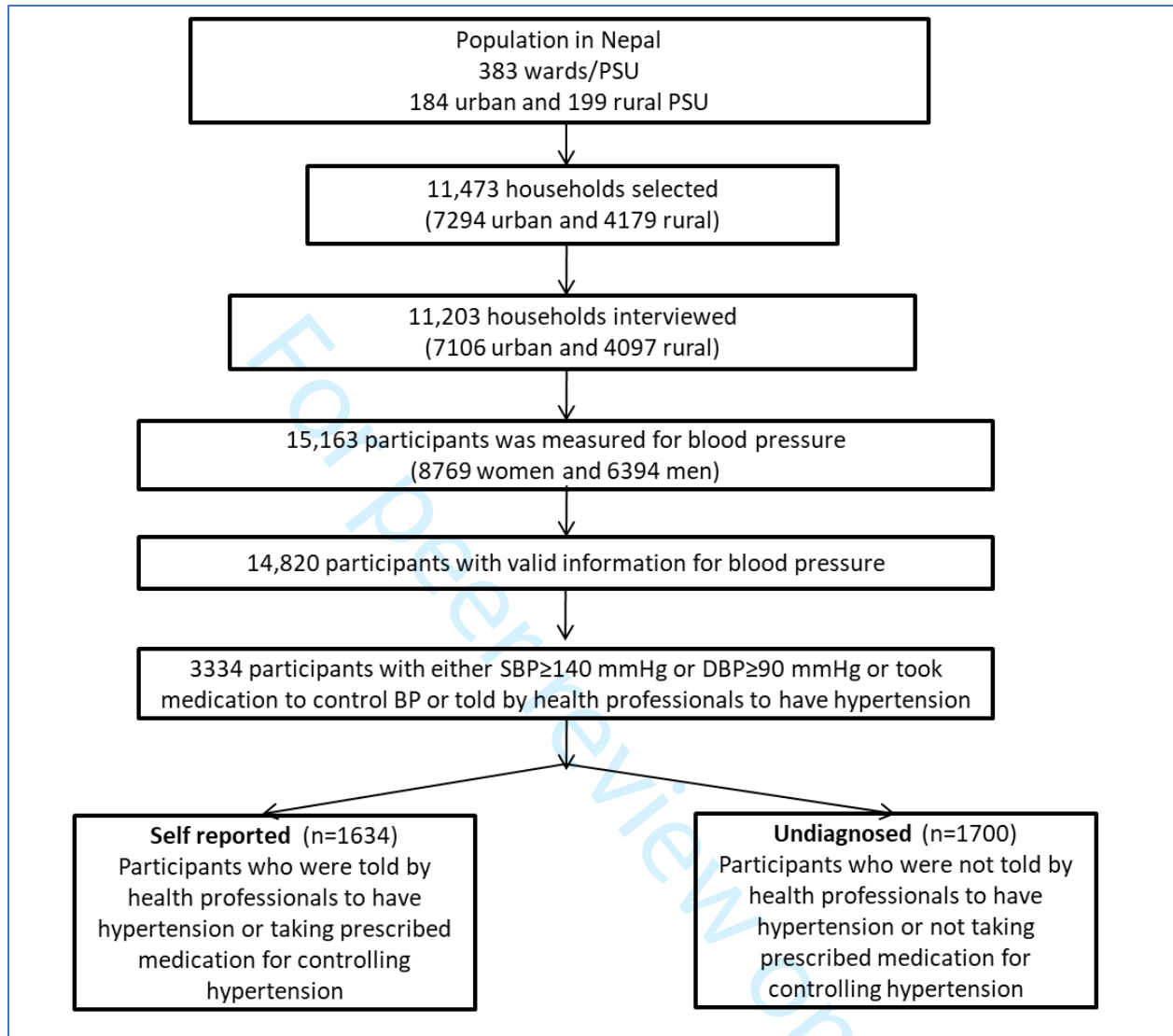
Figure 1: Selection of participants

Figure 2: Determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

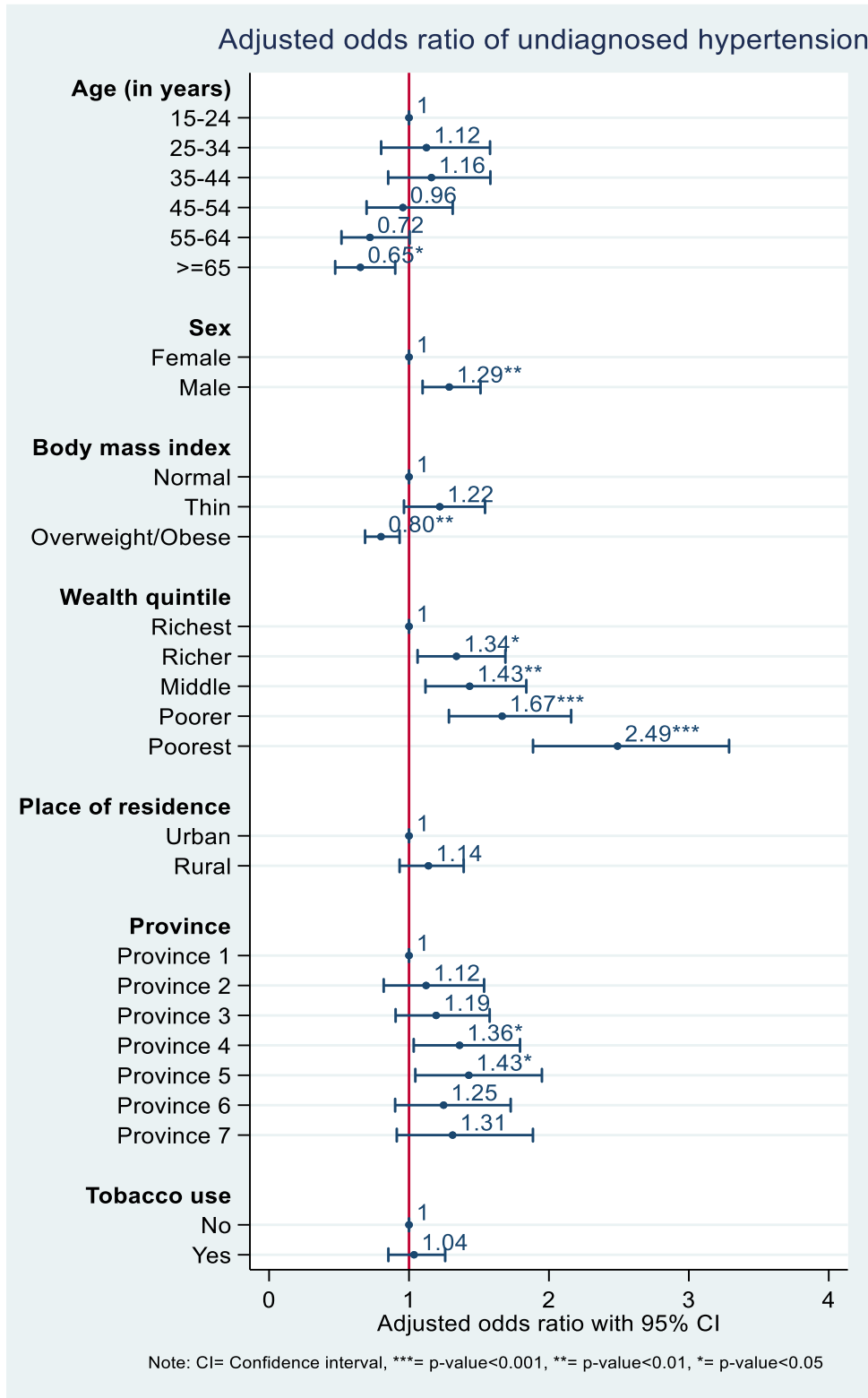


Figure 3: Concentration curve to measure the wealth-based inequality in the prevalence of undiagnosed hypertension among patients with hypertension in Nepal, 2016

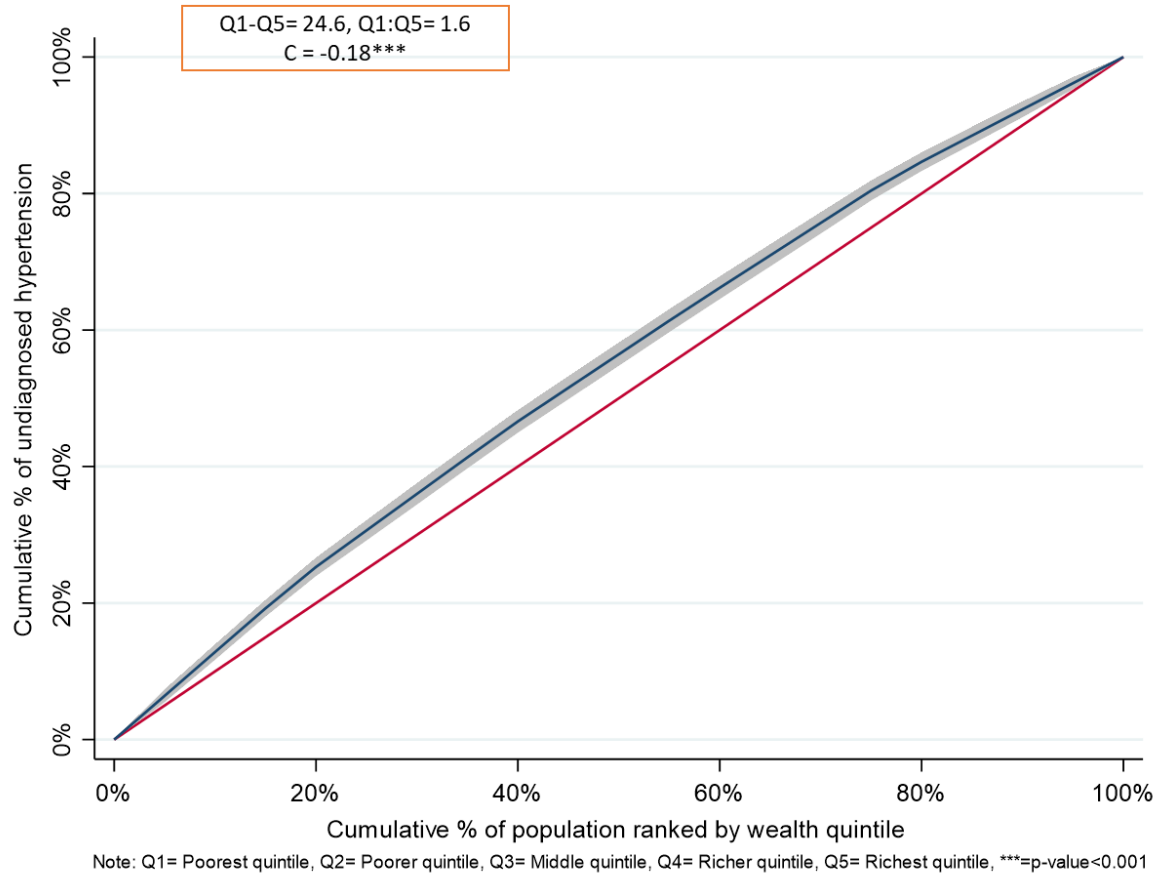
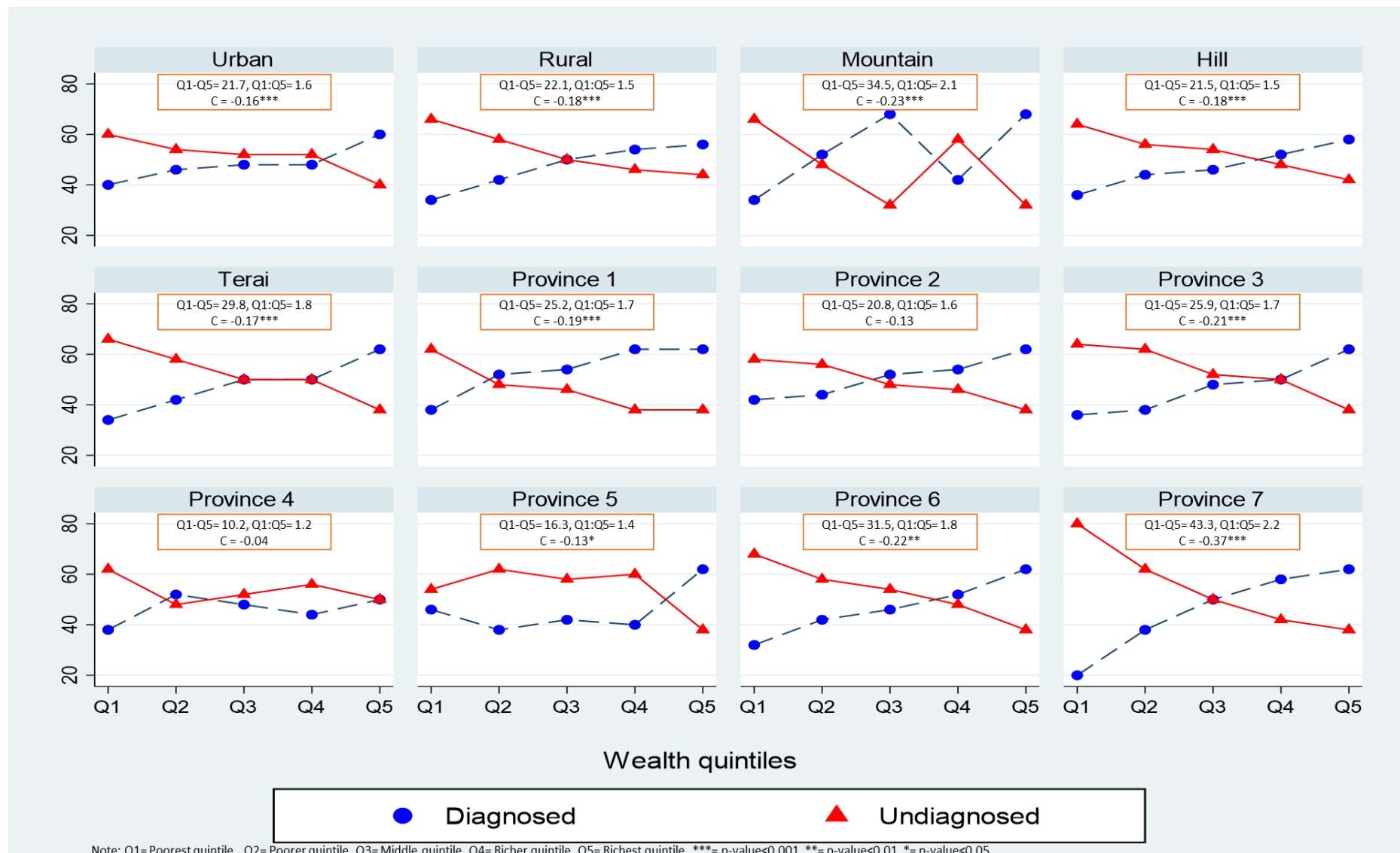


Figure 4: Socioeconomic inequalities in the prevalence of undiagnosed hypertension among patients with hypertension across geographical locations in Nepal, 2016



Note: Q1=Poorest quintile, Q2= Poorer quintile, Q3= Middle quintile, Q4= Richer quintile, Q5= Richest quintile, ***= p-value<0.001, **= p-value<0.01, *= p-value<0.05

Supplementary Table 1: Unadjusted determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Variables	COR	95% CI	p-value
Age			
15-24	1		
25-34	1.06	0.77-1.46	0.7090
35-44	1.00	0.75-1.34	0.9800
45-54	0.87	0.65-1.18	0.3760
55-64	0.72	0.52-0.98	0.0400
>=65	0.70	0.52-0.96	0.0250
Sex			
Male	1.32	1.14-1.53	0.0000
Female	1		
BMI			
Normal	1		
Thin	1.13	0.91-1.41	0.2610
Overweight/obese	0.70	0.6-0.8	0.0000
Education			
No education	1		
Primary	1.08	0.9-1.31	0.4010
Secondary	1.07	0.88-1.3	0.4790
Higher	0.85	0.66-1.09	0.2070
Wealth Quintile			
Poorest	2.94	2.29-3.77	0.0000
Poorer	1.87	1.47-2.38	0.0000
Middle	1.57	1.23-1.99	0.0000
Richer	1.46	1.16-1.84	0.0010
Richest	1		
Place of residence			
Urban	1		
Rural	1.41	1.17-1.71	0.0000
Ecological zone			
Mountain	1		
Hill	0.98	0.68-1.41	0.9100
Terai	0.78	0.53-1.12	0.1800
Province			
Province 1	1		
Province 2	1.05	0.77-1.44	0.7540
Province 3	1.06	0.78-1.44	0.7220
Province 4	1.32	1-1.74	0.0530
Province 5	1.40	1.01-1.92	0.0400
Province 6	1.55	1.09-2.2	0.0140

Province 7	1.47	0.99-2.18	0.0550
Caffeine consumption			
No	1.00		
Yes	0.91	0.72-1.15	0.4400
Tobacco consumption			
No	1.00		
Yes	1.26	1.06-1.51	0.0100
Alcohol consumption			
No	1.00		
Yes	1.46	0.91-2.32	0.1140

Note: COR= Crude Odds Ratio, CI= Confidence Interval

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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Page No	Item No	Recommendation
Title and abstract	1	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
	2-3		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction			
Background/rationale	4-5	2	Explain the scientific background and rationale for the investigation being reported
Objectives	5	3	State specific objectives, including any prespecified hypotheses
Methods			
Study design	5	4	Present key elements of study design early in the paper
Setting	5	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7-8	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	5	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	10	9	Describe any efforts to address potential sources of bias
Study size	6	10	Explain how the study size was arrived at
Quantitative variables	7-8	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	8-9	12	(a) Describe all statistical methods, including those used to control for confounding
	"n/a"		(b) Describe any methods used to examine subgroups and interactions
	"n/a"		(c) Explain how missing data were addressed
	"n/a"		(d) If applicable, describe analytical methods taking account of sampling strategy
	"n/a"		(e) Describe any sensitivity analyses
Results			
Participants	10	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
	"n/a"		(b) Give reasons for non-participation at each stage
	"n/a"		(c) Consider use of a flow diagram
Descriptive data	10	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
	"n/a"		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	11	15*	Report numbers of outcome events or summary measures
Main results	11-13	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

			(b) Report category boundaries when continuous variables were categorized
			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	“n/a”	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion			
Key results	13-14	18	Summarise key results with reference to study objectives
Limitations	17-18	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	14-17	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	18	21	Discuss the generalisability (external validity) of the study results
Other information			
Funding	19	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Examining the prevalence, correlates and inequalities of undiagnosed hypertension in Nepal: a population-based cross-sectional study

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Title: Examining the prevalence, correlates and inequalities of undiagnosed hypertension in Nepal: a population-based cross-sectional study

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ABSTRACT

Objective: To examine the prevalence, correlates and socio-demographic inequalities of undiagnosed hypertension in Nepal.

Design: This study used cross-sectional 2016 Nepal Demographic and Health Survey (NDHS) data. Undiagnosed hypertensive patients were defined as a NDHS respondent who was diagnosed as hypertensive (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) during the survey, but never took any prescribed anti-hypertensive medicine to lower/control blood pressure and was never identified as having hypertension by a health professional prior the survey. Multiple binary logistic regression analysis was performed, and Concentration Index was measured.

Setting: Nepal

Participants: Adult patients with hypertension

Results: Among 3334 hypertensive patients, 50.4% remained undiagnosed during the survey in Nepal. Adjusted model reveals that patients who were male, belonged to households other than the highest wealth quintile, and lived in Province 4 and Province 5 were at higher risk of remaining undiagnosed for hypertension. Patients who were 65+ years of age and were overweight/obese were at lower risk of remaining undiagnosed for hypertension. The poor-rich gap was 24.6 percentage points (Q1= 64.1% vs Q5= 39.6%) and poor:rich ratio was 1.6 (Q1/Q5= 1.6) in the prevalence of undiagnosed hypertension. Undiagnosed hypertension was disproportionately higher among lower socioeconomic status groups (Concentration Index, C= -0.18). Inequalities in the prevalence of undiagnosed hypertension further varied across other geographic locations including place of residence, ecological zones and administrative provinces.

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3 **Conclusions:** Undiagnosed hypertension was highly prevalent in Nepal and there were substantial
4 inequalities by socio-demographics and sub-national levels. Increasing awareness, strengthening
5 routine screening to diagnose hypertension at primary health service facilities and enactment of
6 social health insurance policy may help Nepal to prevent and control this burden.
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13 **Keywords:** Undiagnosed hypertension, Inequality, Demographic and Health Survey, Nepal
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18 **Strengths and limitations of this study**

- 19 • This study determined the prevalence and correlates of undiagnosed hypertension in
20 Nepal using the most updated, population-based, nationally representative data.
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- 23 • This study measured both wealth-based absolute and relative inequalities in the
24 prevalence of undiagnosed hypertension at national level as well as across place of
25 residence, ecological zones and administrative provinces.
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- 28 • The cross-sectional nature of the data limits us to measure causal association between
29 undiagnosed hypertension and the explanatory variables studied.
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- 32 • The association of some potential behavioral or lifestyle factors such as physical
33 activity, dietary patterns and family history with undiagnosed hypertension remain
34 unmeasured due to lack of available data.
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INTRODUCTION

Hypertension, or raised blood pressure, is a leading cause of global mortality and disability [1], affecting over one billion people annually [2]. Hypertension is a directing factor for cardiovascular diseases (CVDs), in particular heart diseases, myocardial infarctions, kidney failure, strokes, disability and premature deaths [2,3]. In South-East Asian countries, hypertension affects approximately one in three adults, accounting for nearly 1.5 million deaths annually and contributing to 9.4% of total deaths [4]. In South-East Asian countries, more than 50% of people with hypertension remain undiagnosed [5]. Nepal has one of the highest prevalence rates of hypertension among South-East Asian countries [6].

Currently, Nepal is facing an epidemiological transition with increasing prevalence of hypertension [7]. A study based on the Nepal Demographic and Health Survey 2016 reported about 20% of Nepalese adults (aged ≥ 18 years) had hypertension [8]. However, other studies have reported that the prevalence of hypertension ranges from 23% to 34% in Nepal [7,9–12], although not all of these studies are representative of the present day Nepalese population. In 2013, the national NCD risk factor survey showed that while 25.7% of adults aged 15-69 years had hypertension in Nepal, a further 42.7% of adults had never measured their blood pressure [13]. Correct diagnoses of hypertension is prerequisite to the prevention, control and proper treatment of this disease. In addition, failure to diagnose and treat hypertension early may lead to serious health hazards, disability in later life, or eventually death. In Nepal, a number of government, non-government and private health facilities are providing health services such as diagnosis, medication and treatment for hypertension. However, owing to challenges with workforce capacity, resourcing of health-care facilities, and out-of-pocket costs incurred by patients, the

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3 current health care system in Nepal is not adequately prepared to support the diagnosis, treatment
4 and control of hypertension [14].
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8 To prevent hypertension, the disease first needs to be diagnosed before any related complications
9 arise. However, there is a lack of evidence about the prevalence of undiagnosed hypertension in
10 Nepal at national and subnational levels. Information on the estimates of undiagnosed
11 hypertension, and its related socio-demographic inequalities, at national and subnational level may
12 assist policy makers in formulating effective strategies for screening, treatment and control as well
13 as prevention of hypertension and associated burdens of disease, particularly among vulnerable
14 groups. As such, we aimed to examine the prevalence, correlates and socio-demographic
15 inequalities of undiagnosed hypertension in Nepal.
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26 27 28 29 30 **METHODS**

31 32 33 **Data source**

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36 We used the most updated nationally representative cross-sectional data from Nepal Demographic
37 and Health Survey (NDHS). While the data of Demographic and Health Surveys is managed by
38 Measure Evaluation, the NDHS was conducted from June 2016 to January 2017 by a private
39 research organization named “NEW ERA” under the monitoring and supervision of the Ministry
40 of Health, Nepal. To estimate the prevalence of hypertension nationally in Nepal, the NDHS 2016
41 obtained informed consent from the household head on behalf of all household members of each
42 surveyed household [15]. For academic and scientific purposes, this anonymous dataset without
43 any identifiers was made available by the ICF International, Maryland, United States [15]. We
44 obtained approval to access and use these data to conduct this study.
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Survey procedure and participants

In 2015, Nepal reformed and restructured municipality boundaries resulting in seven administrative provinces comprising several districts and urban-rural areas with smaller administrative units known as wards [8]. With comparatively greater household numbers, urban areas were further divided into enumeration areas (EA). The primary sampling unit (PSU) were wards, for both urban and rural areas [15]. Because of some changes in administrative areas, Nepal revised the sampling frame of National Population and Housing Census (NPHC). The 2016 NDHS used this revised sampling frame and applied a multistage survey which was conducted in two and three stages across rural and urban areas respectively. NDHS selected the PSUs proportionately to the size in the first stage and then the random selection of EAs from the systematic selection of households from each PSU in the second stage. In the third stage, the households were selected by using a stratified cluster sampling technique in urban areas. A detailed description of the methodology is available elsewhere [15]. A total of 11490 households were selected from 383 wards, of which 5520 households from 184 wards were from urban settings and 5970 households from 199 wards were from rural settings. From these households, all the residents aged 15 years or above were eligible for blood pressure measurement. With an overall response rate of 95%, a total of 14823 individuals participated in the survey. This study uses an analytical sample of adults (> 15 years) with hypertension (n = 3334). Figure 1 illustrates the procedure for selecting the study sample.

{Figure 1 will be added here}

Outcome variable

To measure hypertension, the 2016 NDHS used the UA-767F/FAC (A&D Medical) automated device to record the blood pressure of the participants. With 5 minutes intervals between each measurement, the 2016 NDHS recorded the measurements of blood pressure three times in a sitting position. NDHS considered the last two measures of blood pressure levels and used their mean to detect hypertension. The survey used the World Health Organization (WHO) guidelines to report a participant as hypertensive [15]. The WHO guideline has integrated the 2017 guidelines of the American College of Cardiology/ American Society of Hypertension [16,17]. According to the WHO guideline, a participant with systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg is diagnosed as a hypertension case. We also considered participants as hypertension patients if s/he was previously told by a health professional that they have hypertension or if they were already taking medication to control hypertension. Our outcome variable is undiagnosed hypertension. A patient is considered as undiagnosed for hypertension if, at the time of the survey, s/he was diagnosed as hypertensive (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg) but never took any prescribed anti-hypertensive medicine to lower/control blood pressure and was never told by a health professional that they have hypertension prior the survey [18,19].

Explanatory variables

This study considered a set of socio-demographic and behavioral characteristics as independent variables. Age (in years), sex, Body Mass Index (BMI) measured through dividing the weight by squared height (kg/m^2), education level, household wealth status, place of residence, ecological zone, and provinces were considered as socio-demographic characteristics of the respondents. Age was categorized as 15-24, 25-34, 35-44, 45-54, 55-64 and ≥ 65 years. Sex had two categories, male and female. The BMI was categorized as thin/underweight (BMI < 18.5 kg/m^2), normal (18.5 kg/m^2 \leq BMI < 25 kg/m^2) and overweight/obese (BMI ≥ 25.0 kg/m^2) [20]. Based on the highest class

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3 completed by the respondents, level of education was classified as no education, primary,
4 secondary and higher. NDHS used principal component analysis [15] to construct the wealth index
5 and order households into five socioeconomic quintiles (poorest, poorer, middle, richer and
6 richest). The place of residence was stratified as urban and rural across all geographic locations.
7
8 Nepal was ecologically divided in Mountain, Hill and Terai. The seven administrative provinces
9
10 were identified as Province 1, Province 2, Province 3, Province 4, Province 5, Province 6 and
11 Province 7. Three behavioral characteristics of respondents, caffeine, tobacco and alcohol
12 consumption, were considered as independent variables each of which contained dichotomous
13 response of whether or not the respondent consumed caffeine, tobacco or alcohol.
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24 **Statistical analyses**

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27 Using univariate analysis we described the prevalence of undiagnosed hypertension and
28 background characteristics of the study patients. The estimates of each of the categorical variables
29 included in this study were reported with numbers, weighted percentages and 95% confidence
30 intervals (CIs) of estimates. The weighted prevalence of undiagnosed hypertension was
31 determined across the background characteristics of the study patients from bivariate analysis.
32
33 Statistical significance was detected by applying Chi-square test. Then, we conducted simple and
34 multiple binary logistic regression analyses to examine the correlates of undiagnosed hypertension.
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36 The results of the regression analysis were presented in terms of odds ratio with respective 95%
37 CIs. Variables that were statistically significant in simple logistic regression analysis were entered
38 in the multiple regression model to estimate the adjusted odds ratio (AOR). Notably, the statistical
39 significance was defined at 5% level (p -value < 0.05). Variance inflation factors to detect
40 multicollinearity among the independent variables were assessed before incorporating them into
41 the multiple regression model. Due to hierarchical structure of NDHS data, we considered the
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3 cluster sampling design of the 2016 NDHS to estimate the prevalence and determinants in this
4 study [15]. We excluded cases with missing values for blood pressure measurements.
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8 Proposed by Wagstaff [21] to measure the inequality, we estimated the concentration index (C),
9
10 to show the degree and direction of wealth-based inequality in undiagnosed hypertension
11 prevalence. For the purpose of calculating C, the households were ranked from the poorest to the
12 richest according to their socioeconomic characteristics. We plotted a concentration curve to
13 portray the distribution of undiagnosed hypertension. The Y-axis of the concentration curve
14 representing the cumulative proportion of undiagnosed hypertension and the X-axis represents the
15 cumulative proportions of the population across wealth quintiles. When the concentration curve
16 coincides with the diagonal, the prevalence of undiagnosed hypertension is treated as equally
17 distributed across socioeconomic groups. In contrast, the concentration curve typically deviates
18 from the diagonal if there exists inequalities in the prevalence of undiagnosed hypertension. The
19 C is defined as twice the area between the concentration curve and the diagonal [22–24]. The index
20 value can range between -1 and $+1$, a positive value implies the prevalence of undiagnosed
21 hypertension is more concentrated among higher socioeconomic status groups and a negative value
22 implies the prevalence is more concentrated among lower socioeconomic status groups [23,25].
23
24 We repeated the estimation of C across other geographical locations such as place of residence,
25 ecological zones and provinces to detect the group of patients with highest severity of
26 socioeconomic inequalities in the prevalence of undiagnosed hypertension. STATA (version 13)
27 was used to perform all the analyses [26].
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Patient and public involvement

Patients and public were not involved in developing the research questions, measuring outcome and designing the study. Information of the participants was anonymous.

RESULTS

General Characteristics of the Study Participants

Table 1 shows the general characteristics of the study participants. Among the patients studied, the average age of patients was 49.8 years (95% CI 49.1, 50.5) with the lowest percentage of patients in the 15-24 years age group (6.6%) and highest percentage of patients in the 45-54 years age group (20.9%). The sample was balanced among male (49.5%) and female (50.5%) participant. Nearly half of the patients were normal in terms of their BMI while more than one third of the patients were overweight/obese. Two-thirds of the patients resided in urban area (64.9%). The educational status of the patients were poor with nearly half of the patients having no education while 24.1% and 11.5% had secondary and higher education respectively. The highest number of patients belonged to richest wealth quintile (28.3%) and the lowest number of patients belonged to the poorest wealth quintile (15.5%). Also, the highest number of patients were from province 3 (26.0%) followed by province 5 (17.8%) and province 1 (17.0%). Only 5.6% of patients were from the mountain ecological zone.

{Table 1 will be added here}

Prevalence of Undiagnosed Hypertension

Of the 3334 participants who had hypertension during the survey, more than half of them were detected as remaining undiagnosed (50.4%). The prevalence of undiagnosed hypertension among the patients varied across their age (p -value < 0.001), sex (p -value < 0.001), BMI (p -value < 0.001), wealth quintile (p -value < 0.001) and place of residence (p -value < 0.01). The prevalence of undiagnosed hypertension was higher among younger patients (15-24 years age group) and steadily decreased with the increase of age. The prevalence of undiagnosed hypertension was higher among male patients (54.2%) compared to female patients (46.7%). Compared to patients with normal BMI, the prevalence of undiagnosed hypertension was higher among patients with lower BMI (57.8%) and lower among overweight/obese patients (44.4%). Compared to patients of the richest wealth quintile (39.6%), the prevalence of undiagnosed hypertension was higher among patients of the poorest (64.1%) and poorer (55.8%) quintiles. The rate of undiagnosed hypertension was higher among rural patients (55.2%) compared to urban (47.8%). No educational, ecological and provincial variations in the prevalence of undiagnosed hypertension was observed (**Table 1**).

Correlates of Undiagnosed Hypertension

We found that age, sex, BMI, wealth quintile, place of residence and province were significantly associated with the prevalence of undiagnosed hypertension among hypertensive patients in unadjusted logistic regression analysis (see **supplementary table 1**).

Figure 2 represents the results of multiple logistic regression analysis. The multiple binary logistic regression model showed that age, sex, BMI, wealth quintile and province had significant

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3 association with undiagnosed hypertension. Elderly patients (≥ 65 years of age) had a lower
4 likelihood of being undiagnosed for hypertension than patients aged 15-24 years (AOR = 0.65,
5 95% CI 0.48, 0.91). Male patients were 1.29 times more likely than female patients to remain
6 undiagnosed for hypertension (AOR = 1.29, 95% CI 1.11, 1.51). Compared to patients with normal
7 BMI, overweight/obese patients (AOR = 0.80, 95% CI 0.69, 0.93) were less likely to have
8 undiagnosed hypertension.
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11 We found wealth quintiles as potential correlates of undiagnosed hypertension. The risk of
12 remaining undiagnosed for hypertension increased with decreasing socioeconomic status.
13 Likelihood of having undiagnosed hypertension was greater among poorer socioeconomic status
14 patients compared to higher socioeconomic quintiles. Patients of poorest and poorer wealth
15 quintiles were 2.49 (AOR = 2.49; 95% CI 1.90, 3.30) and 1.67 (AOR = 1.67; 95% CI 1.29, 2.16)
16 times more likely to have an undiagnosed hypertension condition than patients of the wealthiest
17 quintile.
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20 Moreover, significant provincial variation was evident in the prevalence of undiagnosed
21 hypertension among hypertensive patients. Patients of province 4 (AOR = 1.36, 95% CI 1.04, 1.79)
22 and province 5 (AOR = 1.43, 95% CI 1.05, 1.95) were more likely to have undiagnosed
23 hypertension than patients of province 1.
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44 {Figure 2 will be added here}

45 46 47 **Socioeconomic Inequalities in Undiagnosed Hypertension**

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50 **Figure 3** depicts the inequalities in the prevalence of undiagnosed hypertension among
51 hypertensive patients. The difference in the distribution of undiagnosed hypertension was 24.6%
52 between the lowest wealth quintile (Q1) and highest wealth quintile (Q5), meaning that the
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3 prevalence of undiagnosed hypertension was greater by 24.6 percentage points among the poorest
4 patients. The relative measure of inequality in terms of poor (Q1): rich (Q5) ratio was 1.6 for the
5 prevalence of undiagnosed hypertension among patients, depicting that the prevalence of
6 undiagnosed hypertension was 1.6 times higher among the poorest than the richest patients. We
7 found negative value of the Concentration Index ($C = -0.18$) which suggests that the prevalence of
8 undiagnosed hypertension among hypertensive patients was disproportionately distributed among
9 lower socioeconomic status groups.
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20 **{Figure 3 will be added here}**
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23 In addition, patients living in mountain areas and in province 7 had large gaps in the prevalence of
24 undiagnosed hypertension (**Figure 4**). The higher Q1:Q5 ratio were observed among those who
25 had large Q1-Q5 gaps in the prevalence of undiagnosed hypertension across different geographic
26 locations. We found large negative values of C among those who had higher Q1-Q5 gaps and
27 Q1:Q5 ratio for the prevalence of undiagnosed hypertension. See **Figure 4** for details.
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35 **{Figure 4 will be added here}**
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41 **DISCUSSION**

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44 Globally, to date few studies have been conducted on undiagnosed hypertension. For the first time,
45 this study estimated the prevalence of undiagnosed hypertension in Nepal as 50.4% of respondents
46 who tested positive for hypertension in the 2016 NDHS. In addition, this study identified the risk
47 factors and inequalities associated with undiagnosed hypertension in Nepal. The high prevalence
48 of undiagnosed hypertension identified in this study may be due to people's lack of awareness and
49 willingness to partake in regular health check-ups in the absence of health issues, coupled with
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3 accessibility barriers to screening services [27]. Lack of knowledge, attitudes and behaviours that
4 promote healthy lifestyles as preventive measures to non-communicable diseases (NCDs) may
5 also act as a driver of undiagnosed hypertension [27–29]. Community-based awareness raising of
6 changing lifestyles to address the burden of NCDs might be effective in reducing this gap [30].
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13 Several studies have reported higher risks of hypertension among people who are older in age,
14 male, urban dwellers, have higher education level, regularly consume tobacco and/or alcohol, or
15 are overweight [6,8,28,29]. We found that patients aged 65+ years and who were overweight/obese
16 were at lower risk of remaining undiagnosed from hypertension. Our findings depicted a greater
17 proportion of undiagnosed hypertensive patients among those who were young and those with
18 lower BMI. Young or underweight people may be less conscious about their health status as they
19 might have the misconception that they are less likely to suffer from NCDs [31]. In addition, people
20 from lower socioeconomic status groups in Nepal tend to have less knowledge and awareness
21 about health hazards, typically have poorer access to services for screening diseases and lack the
22 capacity to afford treatment costs for diseases [28]. This may contribute to the disproportionate
23 occurrence of undiagnosed hypertension among lower socioeconomic status groups in Nepal.
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39 Similar to risk factors of hypertension, undiagnosed hypertension was also more prevalent among
40 males and tobacco users [6,29]. The higher rate of undiagnosed hypertension among males might
41 be due to their lack of awareness and lower treatment rates than females [32]. Smoking, a main
42 source of using tobacco, is well recognized to be associated with increased risk of hypertension in
43 many settings, including Nepal [33,34]. However, there is lack of evidence to determine the extent
44 to which tobacco use is related to patients remaining undiagnosed for hypertension. Our findings
45 demonstrate that, in Nepal, factors other than tobacco use played independent roles in predicting
46 the rate of undiagnosed hypertension. While differences in lifestyle practices between males and
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3 females in Nepal may be a key factor behind different exposures, further research is needed to
4 identify the actual risk factors [29].
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8 Undiagnosed hypertension may lead to adverse health consequences, including organ damage [35].
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10 The WHO, denoting hypertension as a silent killer, stated that the prevalence of hypertension is
11 higher in low- and middle-income countries compared to developed and high income countries
12 [3]. Our results support this claim and also align with findings from Bangladesh and Sub-Saharan
13 Africa [19,36,37]. Despite being neighbouring countries, the prevalence of undiagnosed
14 hypertension from this study (approximately 50%) is much higher than that of China[38]. For
15 example, recent evidence shows that the prevalence of undiagnosed hypertension in China is
16 28.8% [39]. The reason behind this difference might be due to the differences in age of study
17 participants. Our study assessed participants of age 15 years or older in Nepal, while the Chinese
18 study included older participants (over 45 years) who may be more aware of health conditions and
19 more likely to visit doctors for regular health check-ups. Findings from studies conducted in
20 countries with more developed health care systems and advanced screening processes such as
21 Japan, Korea, England, Ireland, Egypt, Brazil and USA were also found to have lower levels of
22 undiagnosed hypertension than Nepal as found in this study [40–46]. The prevalence of
23 undiagnosed hypertension in Nepal is relatively closer with that of Bangladesh [19]. This might
24 be due to the less advanced health care systems of these two countries with both countries
25 displaying lowHealth Care Index values [38].
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48 In Nepal, despite the detection of risk factors [6,8,29] and inequalities [28], the prevalence of
49 hypertension has been well investigated nationally, resulting in the implementation of new polices
50 to mitigate the rising number of hypertension patients [47]. However, these policy reform efforts
51 will fail to effectively achieve intended hypertension reduction targets if patients remain
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3 undiagnosed, undetected and untreated. It is necessary to identify whether unequal distribution of
4
5 undiagnosed hypertension exists among patients with hypertension across different socioeconomic
6
7 groups. Such information will aid in setting priorities and effective allocation of resources. Our
8
9 study reveals existence of inequalities in the distribution of undiagnosed hypertension due to
10
11 economic status. Lower socioeconomic status groups experienced a higher prevalence of
12
13 undiagnosed hypertension compared to higher socioeconomic groups and a greater degree of
14
15 wealth-based inequality was concentrated among the poorest. These inequalities were more
16
17 prevalent among patients living in different geographical locations including place of residence,
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19 ecological zones and administrative provinces. Such disparities may be owing to greater awareness
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21 of health issues and more utilization of health care services among higher socioeconomic groups
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23 [28]. Such inequality might increase the catastrophic health spending given the rise of catastrophic
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25 household expenditure due to NCDs in Nepal [14,48]. Public health strategies might reduce this
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27 gap by concentrating more on implementing social health insurance policies which are equitable
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29 for all [40,48]. In this respect, policy makers could take into consideration the disparities in the
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31 distribution of undiagnosed hypertension found in this study.
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38 Several initiatives have been taken to control hypertension in Nepal. To address the burden of
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40 cardiovascular diseases (CVD), the WHO and partners launched an initiative called “Global
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42 Hearts” in 2016 [49]. This initiative took a comprehensive approach to help countries in scaling-
43
44 up affordable and adaptable measures to improve capacity of health care services to better detect
45
46 and treat people at risk of or suffering from CVD. This initiative comprises three packages:
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48 SHAKE, HEARTS and MPOWER. The package “HEARTS” provides tools to incorporate CVD
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50 management best practices at the primary healthcare level to reduce CVD risk factors such as
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52 hypertension and high blood cholesterol. Like many low to middle incomes countries, Nepal has
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3 adapted the Global Hearts initiative to address CVD. In addition, the Community-based
4 Management of Hypertension in Nepal (COBIN) is a community-based cost-effective intervention
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6 with demonstrated success in reducing hypertension in Nepal [50,51]. However, for designing
7
8 future programs or interventions for the prevention of hypertension in Nepal, our findings highlight
9
10 the importance of considering undiagnosed hypertensive cases and the uneven distribution of such
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12 cases across a spectrum of socio-demographic characteristics.
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17 Failing to diagnose and detect hypertension among vulnerable populations will have detrimental
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19 health outcomes for any nation. This study, for the first time at a national level, sheds light on the
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21 prevalence of undiagnosed hypertension in Nepal. The NDHS 2016, through incorporation of
22
23 biomarker tests, bears evidence that a substantial proportion of individuals are suffering from
24
25 blood pressure abnormalities. This emphasises the need for conducting routine screening for
26
27 hypertension that ensures access by lower socioeconomic groups and at risk populations. A routine
28
29 surveillance system with technology-based screening can aid in tracing disease incidence including
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31 among people at risk of being undiagnosed [52]. Our study findings will help inform and initiate
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33 policies and programs that capture the highest domain of vulnerable populations and bring them
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35 under routine surveillance at community level with optimal cost.
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41 **Strengths and limitations**

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44 We used the most updated, nationally representative, cross-sectional data to determine the
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46 prevalence, correlates and inequalities of undiagnosed hypertension in Nepal. We considered the
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48 complex survey design in our methods and captured variations. However, there may be residuals
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50 and unmeasured behavioral or lifestyle factors potentially relevant to undiagnosed hypertension,
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52 for example, physical activity, dietary patterns and family history of hypertension, that were not
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54 explored in this study. Since our data was cross-sectional, the relationship between undiagnosed
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3 hypertension and confounders were probabilistic rather than causal. However, identification of
4 potential correlates through using odds ratio is widely acceptable. This study measured both
5 absolute and relative inequalities in the prevalence of undiagnosed hypertension at national level
6 as well as across place of residence, ecological zones and administrative provinces to further guide
7 policy/decision makers for better allocation of resources to reduce hypertension rates.
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18 **CONCLUSIONS**

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21 For the first time on a national level in Nepal, this study estimates the prevalence of undiagnosed
22 hypertension as 50.4% of respondents who tested positive for hypertension in the Nepal
23 Demographic and Health Survey. Furthermore, our results show that prevalence of undiagnosed
24 hypertension is disproportionately higher among lower socioeconomic status groups in Nepal. Our
25 results suggest that efforts should be made to improve the knowledge, attitudes and practices of
26 people around hypertension, particularly among those who are young, slender, poor and male,
27 given their higher risk of being undiagnosed. Routine screening and strengthening diagnosis of
28 hypertension in the primary level of healthcare service facilities may help Nepal in reducing cases
29 with undiagnosed hypertension. Moreover, identification of inequalities among different risk
30 groups will be beneficial in achieving the universal health coverage target of UN Sustainable
31 Development Goals (Goal 3.8.1). Social health insurance policies under an integrated national
32 NCD policy should be properly enacted to ensure socioeconomically disadvantaged populations
33 are adequately covered under the scheme for the prevention and control of hypertension.
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Contributors

MMH, SA and AAM conceptualized the study. MMH performed the data analysis and interpretation of the findings. MMH, FT, MT and AC contributed to writing. AAM and SA critically reviewed the analysis and final version of the manuscript. All authors made a thorough review of the final draft and approved it for submission.

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Competing interests

None declared.

Ethical approval

The NDHS survey methodology and questionnaire was reviewed and approved by the ethical review board of Nepal Research Council and ICF Institutional. NDHS obtained informed consent from the respondents before conducting the survey. Therefore, separate ethical approval was not required for this study and we are using publicly available de-identified data.

Data sharing statement

Data are available in a public, open access repository. All data related to study are included in the manuscript.

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46 **Table 1:** Characteristics of the study participants

Variables	Total			Diagnosed hypertension			Undiagnosed hypertension			Chi-Square Statistic (<i>p</i> -value)
	n	%	95% CI	n	%	95% CI	n	%	95% CI	
Overall	3334	--	--	1634	49.6	47.1-52.1	1700	50.4	47.9-52.9	--
Age										29.6317
15-24	237	6.6	5.6-7.8	107	43.1	36.1-50.4	130	56.9	49.6-63.9	0.0008

1											
2											
3	25-34	449	13.2	11.9-14.5	196	43.8	38.4-49.3	253	56.2	50.7-61.6	
4	35-44	637	19.6	18-21.3	287	45.2	40.1-50.3	350	54.8	49.7-59.9	
5	45-54	687	20.9	19.2-22.8	333	49.4	45-53.8	354	50.6	46.2-55	
6	55-64	643	18.9	17.4-20.5	344	54.7	49.8-59.5	299	45.3	40.5-50.2	
7	>=65	681	20.8	19-22.7	367	55.1	50.3-59.8	314	44.9	40.2-49.7	
8											
9											
10	Sex										18.35
11	Male	1640	49.5	47.7-51.3	746	45.8	42.6-49.1	894	54.2	50.9-57.4	0.0003
12	Female	1694	50.5	48.7-52.3	888	53.3	50.1-56.4	806	46.7	43.6-49.9	
13											
14	BMI										29.2511
15	Normal	1816	53.6	51.2-56.1	841	47.1	44.3-50	975	52.9	50-55.7	0.0001
16	Thin	361	11.1	9.9-12.5	156	42.2	35.7-49	205	57.8	51-64.3	
17	Overweight/obese	1120	35.2	32.5-38	620	55.6	51.7-59.5	500	44.4	40.5-48.3	
18											
19	Education										6.5852
20	No education	1576	46.5	44.1-48.9	778	50.9	47.5-54.4	798	49.1	45.6-52.5	0.2125
21	Primary	602	17.8	16.2-19.5	285	46.1	41.1-51.1	317	53.9	48.9-58.9	
22	Secondary	804	24.1	22.5-25.9	383	48	43.6-52.4	421	52	47.6-56.4	
23	Higher	350	11.5	9.9-13.5	187	53	46.9-58.9	163	47	41.1-53.1	
24											
25	Wealth Quintile										90.7085
26	Poorest	610	15.5	13.3-18	211	35.9	31.9-40	399	64.1	60-68.1	0.0000
27	Poorer	689	19.2	16.9-21.7	313	44.2	39.8-48.7	376	55.8	51.3-60.2	
28	Middle	604	17.3	15.2-19.6	301	49.5	44.5-54.5	303	50.5	45.5-55.5	
29	Richer	667	19.7	17.1-22.6	344	50.2	44.9-55.5	323	49.8	44.5-55.1	
30	Richest	764	28.3	24-33	465	60.4	55.4-65.2	299	39.6	34.8-44.6	
31											
32	Place of residence										16.691
33	Urban	2221	64.9	59.9-69.6	1152	52.2	49-55.4	1069	47.8	44.6-51	0.0057
34	Rural	1113	35.1	30.4-40.1	482	44.8	40.7-48.9	631	55.2	51.1-59.3	
35											
36	Ecological zone										3.43
37	Mountain	200	5.6	3.6-8.6	92	47.1	39.4-54.8	108	52.9	45.2-60.6	0.3721
38	Hill	1694	49.9	44.2-55.6	788	48.3	45.1-51.5	906	51.7	48.5-54.9	
39	Terai	1440	44.5	39.2-49.9	754	51.4	47.1-55.6	686	48.6	44.4-52.9	
40											
41	Province										23.7869
42	Province 1	490	17	15.2-19	265	53	47.7-58.3	225	47	41.7-52.3	0.0511
43	Province 2	460	16.2	14.2-18.3	243	53.1	46.5-59.6	217	46.9	40.4-53.5	
44	Province 3	575	26	21.8-30.6	303	52.7	46.8-58.5	272	47.3	41.5-53.2	
45	Province 4	578	13.2	11.5-15.1	273	46.9	42-51.7	305	53.1	48.3-58	
46	Province 5	553	17.8	15.4-20.4	253	45.4	39-51.9	300	54.6	48.1-61	
47	Province 6	343	3.9	3.3-4.6	148	39.8	32.9-47.1	195	60.2	52.9-67.1	
48	Province 7	335	6	5-7.2	149	41.9	33.8-50.5	186	58.1	49.5-66.2	
49											
50											
51	Caffeine consumption										0.2587
52	No	2942	88.4	86.7-89.9	1434	49.4	46.9-52.0	1508	50.6	48.0-53.1	0.6895
53	Yes	392	11.6	10.1-13.3	200	50.8	44.1-57.4	192	49.2	42.6-55.8	
54											
55	Tobacco use										5.3524
56											
57											
58											
59											
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No	2826	84.9	83.2-86.6	1410	50.4	47.8-53.1	1416	49.6	46.9-52.2	0.0338
Yes	508	15.1	13.5-16.8	224	44.8	40.0-49.8	284	55.1	50.2-60.0	
Alcohol consumption										2.4122
No	3249	97.8	97.1-98.4	1600	49.8	47.2-52.8	1649	50.2	47.6-52.8	0.1505
Yes	85	2.2	1.6-2.9	34	40.6	29.4-52.9	51	59.4	47.1-70.6	

Note: n = Number of sample, CI = Confidence interval

Figure 1: Selection of participants

Figure 2: Determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Figure 3: Concentration curve to measure the wealth-based inequality in the prevalence of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Figure 4: Socioeconomic inequalities in the prevalence of undiagnosed hypertension among patients with hypertension across geographical locations in Nepal, 2016

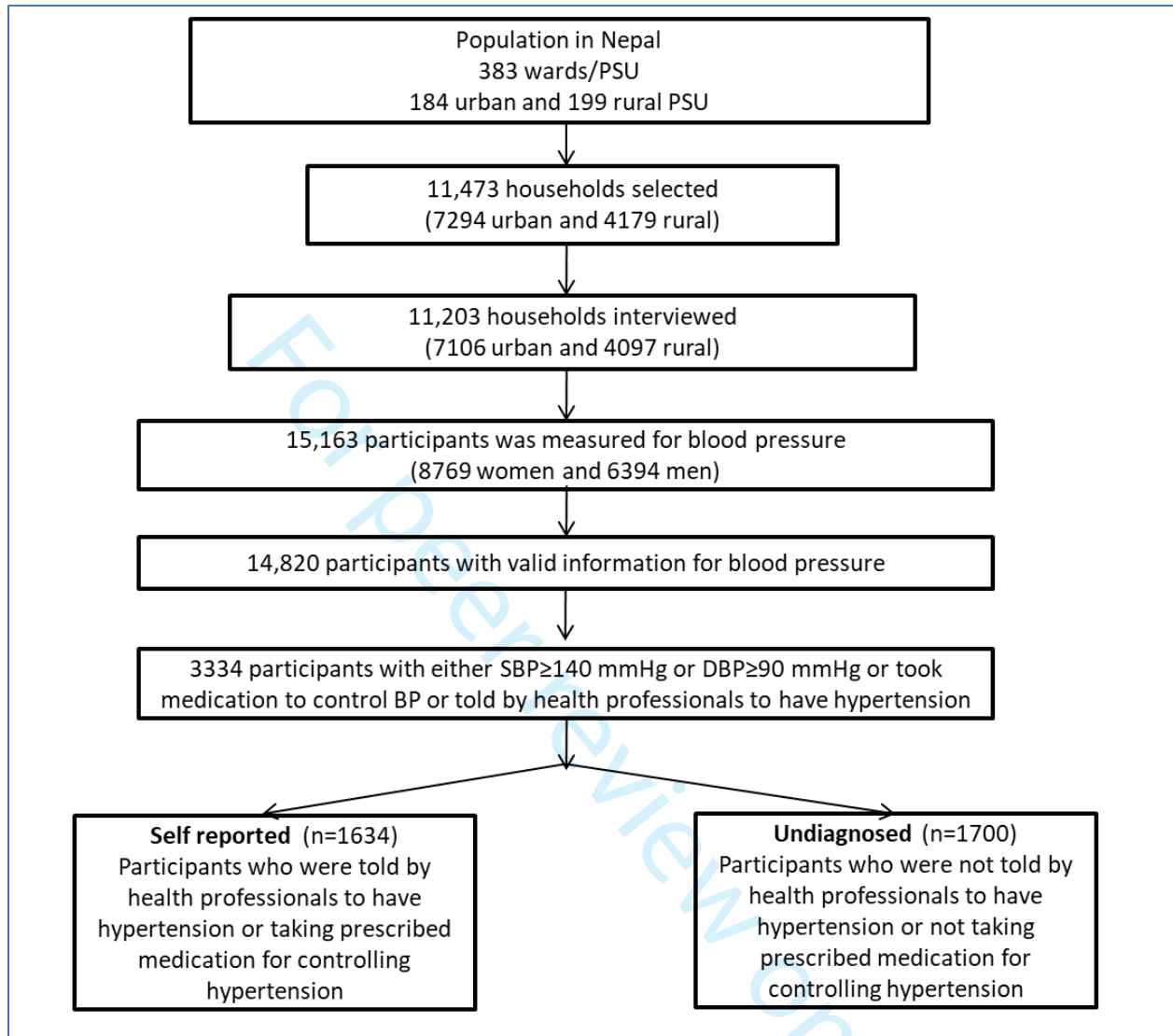
Figure 1: Selection of participants

Figure 2: Determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

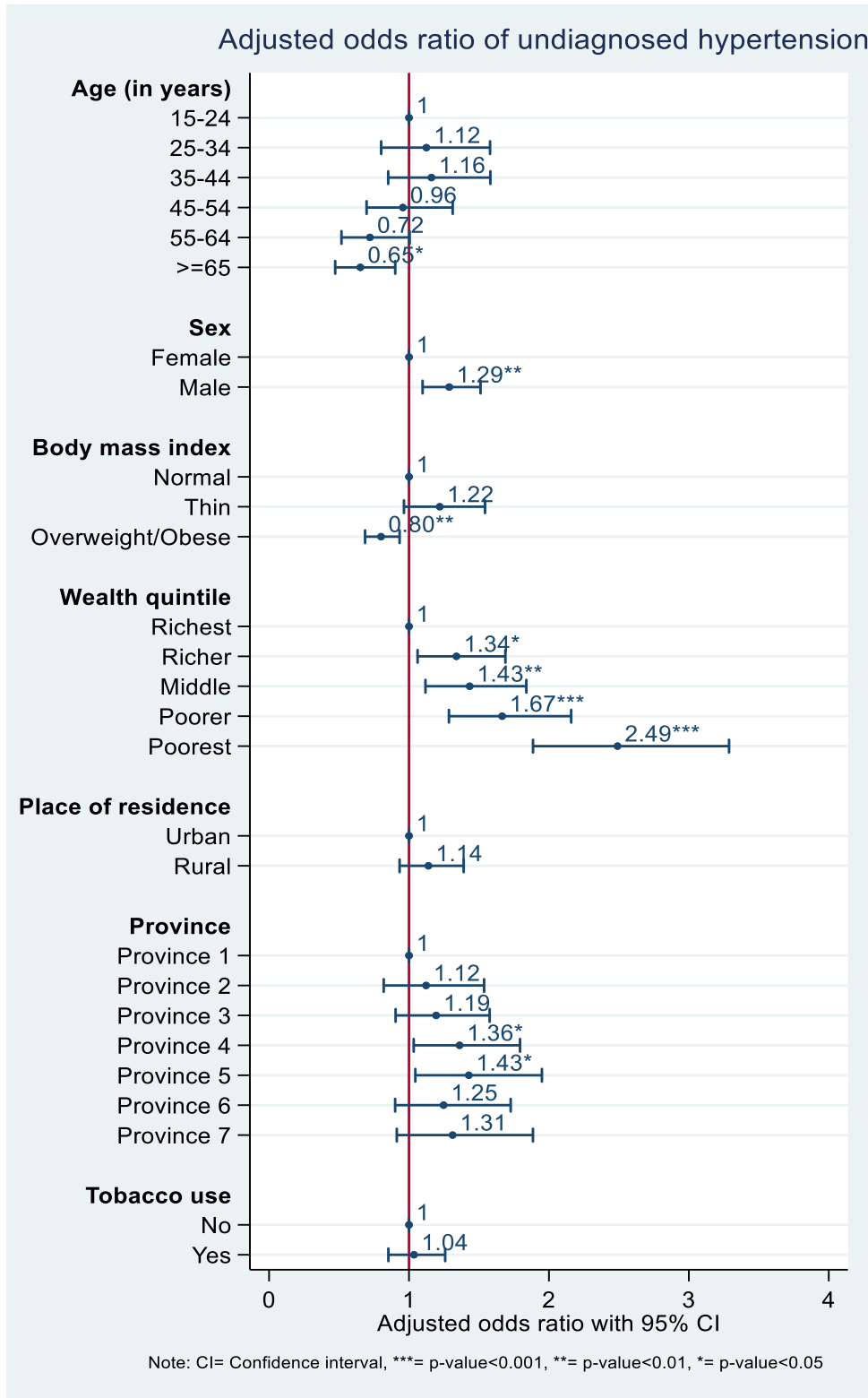
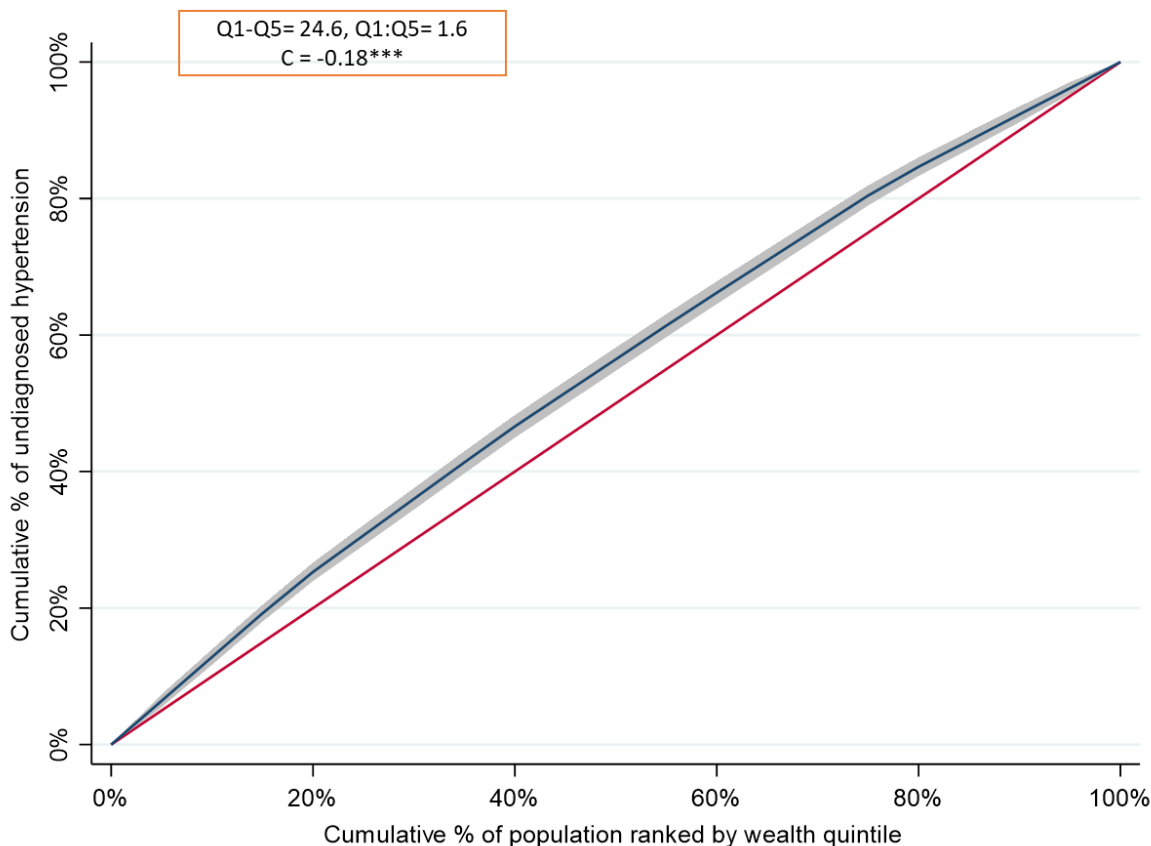


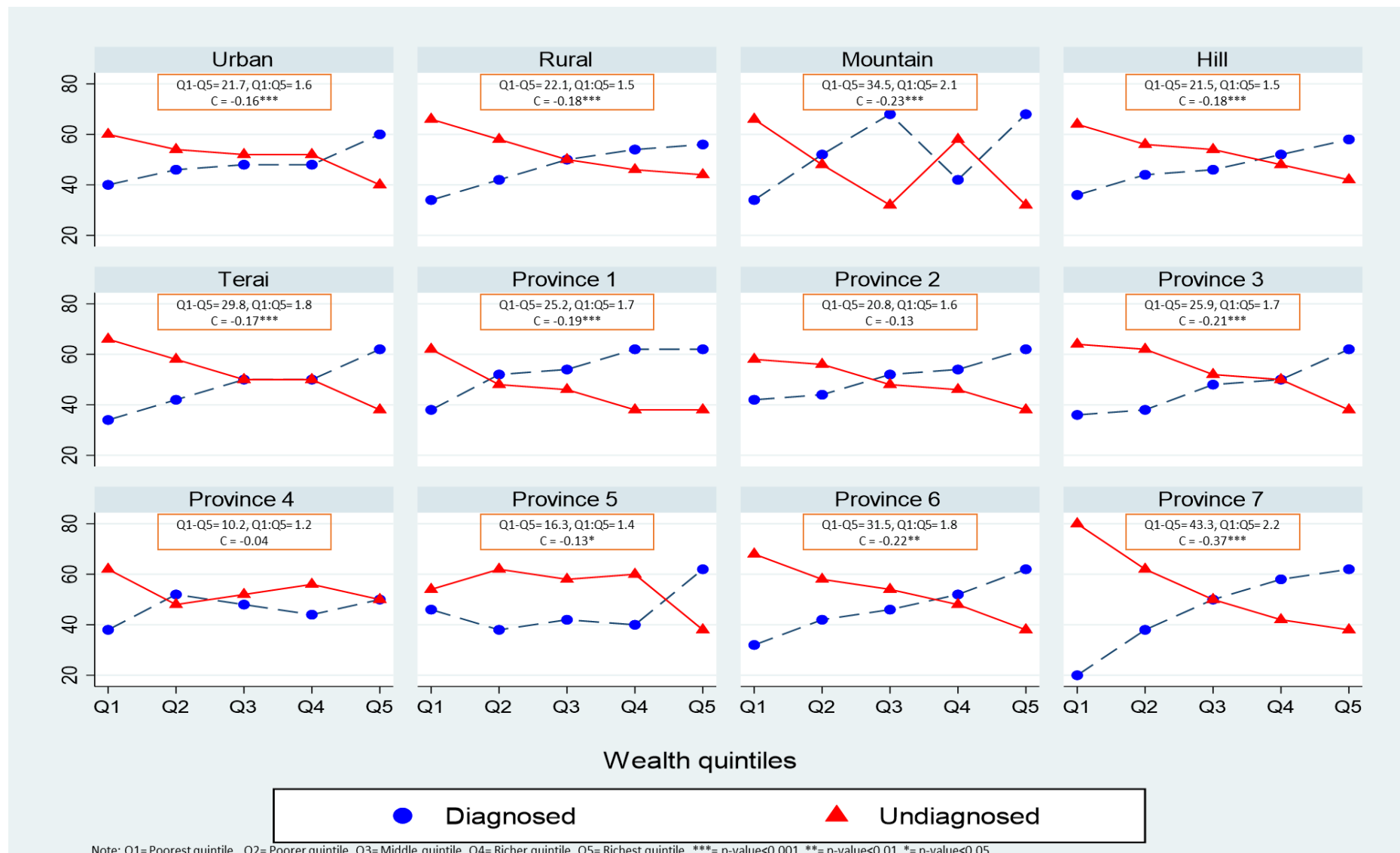
Figure 3: Concentration curve to measure the wealth-based inequality in the prevalence of undiagnosed hypertension among patients with hypertension in Nepal, 2016



Note: Q1= Poorest quintile, Q2= Poorer quintile, Q3= Middle quintile, Q4= Richer quintile, Q5= Richest quintile, ***=p-value<0.001

only

Figure 4: Socioeconomic inequalities in the prevalence of undiagnosed hypertension among patients with hypertension across geographical locations in Nepal, 2016



Note: Q1=Poorest quintile, Q2= Poorer quintile, Q3= Middle quintile, Q4= Richer quintile, Q5= Richest quintile, ***= p-value<0.001, **= p-value<0.01, *= p-value<0.05

Supplementary Table 1: Unadjusted determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Variables	COR	95% CI	<i>p</i> -value
Age			
15-24	1		
25-34	1.06	0.77-1.46	0.7090
35-44	1.00	0.75-1.34	0.9800
45-54	0.87	0.65-1.18	0.3760
55-64	0.72	0.52-0.98	0.0400
>=65	0.70	0.52-0.96	0.0250
Sex			
Male	1.32	1.14-1.53	0.0000
Female	1		
BMI			
Normal	1		
Thin	1.13	0.91-1.41	0.2610
Overweight/obese	0.70	0.6-0.8	0.0000
Education			
No education	1		
Primary	1.08	0.9-1.31	0.4010
Secondary	1.07	0.88-1.3	0.4790
Higher	0.85	0.66-1.09	0.2070
Wealth Quintile			
Poorest	2.94	2.29-3.77	0.0000
Poorer	1.87	1.47-2.38	0.0000
Middle	1.57	1.23-1.99	0.0000
Richer	1.46	1.16-1.84	0.0010
Richest	1		
Place of residence			
Urban	1		
Rural	1.41	1.17-1.71	0.0000
Ecological zone			
Mountain	1		
Hill	0.98	0.68-1.41	0.9100
Terai	0.78	0.53-1.12	0.1800
Province			
Province 1	1		
Province 2	1.05	0.77-1.44	0.7540
Province 3	1.06	0.78-1.44	0.7220
Province 4	1.32	1-1.74	0.0530
Province 5	1.40	1.01-1.92	0.0400
Province 6	1.55	1.09-2.2	0.0140

Province 7	1.47	0.99-2.18	0.0550
Caffeine consumption			
No	1.00		
Yes	0.91	0.72-1.15	0.4400
Tobacco consumption			
No	1.00		
Yes	1.26	1.06-1.51	0.0100
Alcohol consumption			
No	1.00		
Yes	1.46	0.91-2.32	0.1140

Note: COR= Crude Odds Ratio, CI= Confidence Interval

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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Page No	Item No	Recommendation
Title and abstract	1	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
	2-3		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction			
Background/rationale	4-5	2	Explain the scientific background and rationale for the investigation being reported
Objectives	5	3	State specific objectives, including any prespecified hypotheses
Methods			
Study design	5	4	Present key elements of study design early in the paper
Setting	5	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7-8	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	5	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	10	9	Describe any efforts to address potential sources of bias
Study size	6	10	Explain how the study size was arrived at
Quantitative variables	7-8	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	8-9	12	(a) Describe all statistical methods, including those used to control for confounding
	"n/a"		(b) Describe any methods used to examine subgroups and interactions
	"n/a"		(c) Explain how missing data were addressed
	"n/a"		(d) If applicable, describe analytical methods taking account of sampling strategy
	"n/a"		(e) Describe any sensitivity analyses
Results			
Participants	10	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
	"n/a"		(b) Give reasons for non-participation at each stage
	"n/a"		(c) Consider use of a flow diagram
Descriptive data	10	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
	"n/a"		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	11	15*	Report numbers of outcome events or summary measures
Main results	11-13	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

			(b) Report category boundaries when continuous variables were categorized
			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	“n/a”	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion			
Key results	13-14	18	Summarise key results with reference to study objectives
Limitations	17-18	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	14-17	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	18	21	Discuss the generalisability (external validity) of the study results
Other information			
Funding	19	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Examining the prevalence, correlates and inequalities of undiagnosed hypertension in Nepal: a population-based cross-sectional study

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Title: Examining the prevalence, correlates and inequalities of undiagnosed hypertension in Nepal: a population-based cross-sectional study

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ABSTRACT

Objective: To examine the prevalence, correlates and socio-demographic inequalities of undiagnosed hypertension in Nepal.

Design: This study used cross-sectional 2016 Nepal Demographic and Health Survey (NDHS) data. Undiagnosed hypertensive patients were defined as a NDHS respondent who was diagnosed as hypertensive (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) during the survey, but never took any prescribed anti-hypertensive medicine to lower/control blood pressure and was never identified as having hypertension by a health professional prior the survey. Multiple binary logistic regression analysis was performed, and Concentration Index was measured.

Setting: Nepal

Participants: Adult patients with hypertension

Results: Among 3334 hypertensive patients, 50.4% remained undiagnosed during the survey in Nepal. Adjusted model reveals that patients who were male, belonged to households other than the highest wealth quintile, and lived in Province 4 and Province 5 were at higher risk of remaining undiagnosed for hypertension. Patients who were 65+ years of age and were overweight/obese were at lower risk of remaining undiagnosed for hypertension. The poor-rich gap was 24.6 percentage points (Q1= 64.1% vs Q5= 39.6%) and poor:rich ratio was 1.6 (Q1/Q5= 1.6) in the prevalence of undiagnosed hypertension. Undiagnosed hypertension was disproportionately higher among lower socioeconomic status groups (Concentration Index, C= -0.18). Inequalities in the prevalence of undiagnosed hypertension further varied across other geographic locations including place of residence, ecological zones and administrative provinces.

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3 **Conclusions:** Undiagnosed hypertension was highly prevalent in Nepal and there were substantial
4 inequalities by socio-demographics and sub-national levels. Increasing awareness, strengthening
5 routine screening to diagnose hypertension at primary health service facilities and enactment of
6 social health insurance policy may help Nepal to prevent and control this burden.
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13 **Keywords:** Undiagnosed hypertension, Inequality, Demographic and Health Survey, Nepal
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18 **Strengths and limitations of this study**

- 19 • This study determined the prevalence and correlates of undiagnosed hypertension in
20 Nepal using the most updated, population-based, nationally representative data.
21
22
- 23 • This study measured both wealth-based absolute and relative inequalities in the
24 prevalence of undiagnosed hypertension at national level as well as across place of
25 residence, ecological zones and administrative provinces.
26
27
- 28 • The cross-sectional nature of the data limits us to measure causal association between
29 undiagnosed hypertension and the explanatory variables studied.
30
31
- 32 • The association of some potential behavioral or lifestyle factors such as physical
33 activity, dietary patterns and family history with undiagnosed hypertension remain
34 unmeasured due to lack of available data.
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INTRODUCTION

Hypertension, or raised blood pressure, is a leading cause of global mortality and disability [1], affecting over one billion people annually [2]. Hypertension is a directing factor for cardiovascular diseases (CVDs), in particular heart diseases, myocardial infarctions, kidney failure, strokes, disability and premature deaths [2,3]. In South-East Asian countries, hypertension affects approximately one in three adults, accounting for nearly 1.5 million deaths annually and contributing to 9.4% of total deaths [4]. In South-East Asian countries, more than 50% of people with hypertension remain undiagnosed [5]. Nepal has one of the highest prevalence rates of hypertension among South-East Asian countries [6].

Currently, Nepal is facing an epidemiological transition with increasing prevalence of hypertension [7]. A study based on the Nepal Demographic and Health Survey 2016 reported about 20% of Nepalese adults (aged ≥ 18 years) had hypertension [8]. However, other studies have reported that the prevalence of hypertension ranges from 23% to 34% in Nepal [7,9–12], although not all of these studies are representative of the present day Nepalese population. In 2013, the national NCD risk factor survey showed that while 25.7% of adults aged 15-69 years had hypertension in Nepal, a further 42.7% of adults had never measured their blood pressure [13]. Correct diagnoses of hypertension is prerequisite to the prevention, control and proper treatment of this disease. In addition, failure to diagnose and treat hypertension early may lead to serious health hazards, disability in later life, or eventually death. In Nepal, a number of government, non-government and private health facilities are providing health services such as diagnosis, medication and treatment for hypertension. However, owing to challenges with workforce capacity, resourcing of health-care facilities, and out-of-pocket costs incurred by patients, the

1
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3 current health care system in Nepal is not adequately prepared to support the diagnosis, treatment
4 and control of hypertension [14].
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8 To prevent hypertension, the disease first needs to be diagnosed before any related complications
9 arise. However, there is a lack of evidence about the prevalence of undiagnosed hypertension in
10 Nepal at national and subnational levels. Information on the estimates of undiagnosed
11 hypertension, and its related socio-demographic inequalities, at national and subnational level may
12 assist policy makers in formulating effective strategies for screening, treatment and control as well
13 as prevention of hypertension and associated burdens of disease, particularly among vulnerable
14 groups. As such, we aimed to examine the prevalence, correlates and socio-demographic
15 inequalities of undiagnosed hypertension in Nepal.
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26 27 28 29 30 **METHODS**

31 32 33 **Data source**

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35 We used the most updated nationally representative cross-sectional data from Nepal Demographic
36 and Health Survey (NDHS). While the data of Demographic and Health Surveys is managed by
37 Measure Evaluation, the NDHS was conducted from June 2016 to January 2017 by a private
38 research organization named “NEW ERA” under the monitoring and supervision of the Ministry
39 of Health, Nepal. To estimate the prevalence of hypertension nationally in Nepal, the NDHS 2016
40 obtained informed consent from the household head on behalf of all household members of each
41 surveyed household [15]. For academic and scientific purposes, this anonymous dataset without
42 any identifiers was made available by the ICF International, Maryland, United States [15]. We
43 obtained approval to access and use these data to conduct this study.
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Survey procedure and participants

In 2015, Nepal reformed and restructured municipality boundaries resulting in seven administrative provinces comprising several districts and urban-rural areas with smaller administrative units known as wards [8]. With comparatively greater household numbers, urban areas were further divided into enumeration areas (EA). The primary sampling unit (PSU) were wards, for both urban and rural areas [15]. Because of some changes in administrative areas, Nepal revised the sampling frame of National Population and Housing Census (NPHC). The 2016 NDHS used this revised sampling frame and applied a multistage survey which was conducted in two and three stages across rural and urban areas respectively. NDHS selected the PSUs proportionately to the size in the first stage and then the random selection of EAs from the systematic selection of households from each PSU in the second stage. In the third stage, the households were selected by using a stratified cluster sampling technique in urban areas. A detailed description of the methodology is available elsewhere [15]. A total of 11490 households were selected from 383 wards, of which 5520 households from 184 wards were from urban settings and 5970 households from 199 wards were from rural settings. From these households, all the residents aged 15 years or above were eligible for blood pressure measurement. With an overall response rate of 95%, a total of 14823 individuals participated in the survey. This study uses an analytical sample of adults (> 15 years) with hypertension (n = 3334). Figure 1 illustrates the procedure for selecting the study sample.

{Figure 1 will be added here}

Outcome variable

To measure hypertension, the 2016 NDHS used the UA-767F/FAC (A&D Medical) automated device to record the blood pressure of the participants. With 5 minutes intervals between each measurement, the 2016 NDHS recorded the measurements of blood pressure three times in a sitting position. NDHS considered the last two measures of blood pressure levels and used their mean to detect hypertension. The survey used the World Health Organization (WHO) guidelines to report a participant as hypertensive [15]. The WHO guideline has integrated the 2017 guidelines of the American College of Cardiology/ American Society of Hypertension [16,17]. According to the WHO guideline, a participant with systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg is diagnosed as a hypertension case. We also considered participants as hypertension patients if s/he was previously told by a health professional that they have hypertension or if they were already taking medication to control hypertension. Our outcome variable is undiagnosed hypertension. A patient is considered as undiagnosed for hypertension if, at the time of the survey, s/he was diagnosed as hypertensive (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg) but never took any prescribed anti-hypertensive medicine to lower/control blood pressure and was never told by a health professional that they have hypertension prior the survey [18,19].

Explanatory variables

This study considered a set of socio-demographic and behavioral characteristics as independent variables. Age (in years), sex, Body Mass Index (BMI) measured through dividing the weight by squared height (kg/m^2), education level, household wealth status, place of residence, ecological zone, and provinces were considered as socio-demographic characteristics of the respondents. Age was categorized as 15-24, 25-34, 35-44, 45-54, 55-64 and ≥ 65 years. Sex had two categories, male and female. The BMI was categorized as thin/underweight ($\text{BMI} < 18.5 \text{ kg}/\text{m}^2$), normal ($18.5 \text{ kg}/\text{m}^2 \leq \text{BMI} < 25 \text{ kg}/\text{m}^2$) and overweight/obese ($\text{BMI} \geq 25.0 \text{ kg}/\text{m}^2$) [20]. Based on the highest class

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3 completed by the respondents, level of education was classified as no education, primary,
4 secondary and higher. NDHS used principal component analysis [15] to construct the wealth index
5 and order households into five socioeconomic quintiles (poorest, poorer, middle, richer and
6 richest). The place of residence was stratified as urban and rural across all geographic locations.
7
8 Nepal was ecologically divided in Mountain, Hill and Terai. The seven administrative provinces
9
10 were identified as Province 1, Province 2, Province 3, Province 4, Province 5, Province 6 and
11 Province 7. Three behavioral characteristics of respondents, caffeine, tobacco and alcohol
12 consumption, were considered as independent variables each of which contained dichotomous
13 response of whether or not the respondent consumed caffeine, tobacco or alcohol.
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24 **Statistical analyses**

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27 Using univariate analysis we described the prevalence of undiagnosed hypertension and
28 background characteristics of the study patients. The estimates of each of the categorical variables
29 included in this study were reported with numbers, weighted percentages and 95% confidence
30 intervals (CIs) of estimates. The weighted prevalence of undiagnosed hypertension was
31 determined across the background characteristics of the study patients from bivariate analysis.
32
33 Statistical significance was detected by applying Chi-square test. Then, we conducted simple and
34 multiple binary logistic regression analyses to examine the correlates of undiagnosed hypertension.
35
36 The results of the regression analysis were presented in terms of odds ratio with respective 95%
37 CIs. Variables that were statistically significant in simple logistic regression analysis were entered
38 in the multiple regression model to estimate the adjusted odds ratio (AOR). Notably, the statistical
39 significance was defined at 5% level (p -value < 0.05). Variance inflation factors to detect
40 multicollinearity among the independent variables were assessed before incorporating them into
41 the multiple regression model. Due to hierarchical structure of NDHS data, we considered the
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3 cluster sampling design of the 2016 NDHS to estimate the prevalence and determinants in this
4 study [15]. We excluded cases with missing values for blood pressure measurements.
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8 Proposed by Wagstaff [21] to measure the inequality, we estimated the concentration index (C),
9
10 to show the degree and direction of wealth-based inequality in undiagnosed hypertension
11 prevalence. For the purpose of calculating C, the households were ranked from the poorest to the
12 richest according to their socioeconomic characteristics. We plotted a concentration curve to
13 portray the distribution of undiagnosed hypertension. The Y-axis of the concentration curve
14 representing the cumulative proportion of undiagnosed hypertension and the X-axis represents the
15 cumulative proportions of the population across wealth quintiles. When the concentration curve
16 coincides with the diagonal, the prevalence of undiagnosed hypertension is treated as equally
17 distributed across socioeconomic groups. In contrast, the concentration curve typically deviates
18 from the diagonal if there exists inequalities in the prevalence of undiagnosed hypertension. The
19 C is defined as twice the area between the concentration curve and the diagonal [22–24]. The index
20 value can range between -1 and $+1$, a positive value implies the prevalence of undiagnosed
21 hypertension is more concentrated among higher socioeconomic status groups and a negative value
22 implies the prevalence is more concentrated among lower socioeconomic status groups [23,25].
23
24 We repeated the estimation of C across other geographical locations such as place of residence,
25 ecological zones and provinces to detect the group of patients with highest severity of
26 socioeconomic inequalities in the prevalence of undiagnosed hypertension. STATA (version 13)
27 was used to perform all the analyses [26].
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Patient and public involvement

Patients and public were not involved in developing the research questions, measuring outcome and designing the study. Information of the participants was anonymous.

RESULTS

General Characteristics of the Study Participants

Table 1 shows the general characteristics of the study participants. Among the patients studied, the average age of patients was 49.8 years (95% CI 49.1, 50.5) with the lowest percentage of patients in the 15-24 years age group (6.6%) and highest percentage of patients in the 45-54 years age group (20.9%). The sample was balanced among male (49.5%) and female (50.5%) participant. Nearly half of the patients were normal in terms of their BMI while more than one third of the patients were overweight/obese. Two-thirds of the patients resided in urban area (64.9%). The educational status of the patients were poor with nearly half of the patients having no education while 24.1% and 11.5% had secondary and higher education respectively. The highest number of patients belonged to richest wealth quintile (28.3%) and the lowest number of patients belonged to the poorest wealth quintile (15.5%). Also, the highest number of patients were from province 3 (26.0%) followed by province 5 (17.8%) and province 1 (17.0%). Only 5.6% of patients were from the mountain ecological zone.

{Table 1 will be added here}

Prevalence of Undiagnosed Hypertension

Of the 3334 participants who had hypertension during the survey, more than half of them were detected as remaining undiagnosed (50.4%). The prevalence of undiagnosed hypertension among the patients varied across their age (p -value < 0.001), sex (p -value < 0.001), BMI (p -value < 0.001), wealth quintile (p -value < 0.001) and place of residence (p -value < 0.01). The prevalence of undiagnosed hypertension was higher among younger patients (15-24 years age group) and steadily decreased with the increase of age. The prevalence of undiagnosed hypertension was higher among male patients (54.2%) compared to female patients (46.7%). Compared to patients with normal BMI, the prevalence of undiagnosed hypertension was higher among patients with lower BMI (57.8%) and lower among overweight/obese patients (44.4%). Compared to patients of the richest wealth quintile (39.6%), the prevalence of undiagnosed hypertension was higher among patients of the poorest (64.1%) and poorer (55.8%) quintiles. The rate of undiagnosed hypertension was higher among rural patients (55.2%) compared to urban (47.8%). No educational, ecological and provincial variations in the prevalence of undiagnosed hypertension was observed (**Table 1**).

Correlates of Undiagnosed Hypertension

We found that age, sex, BMI, wealth quintile, place of residence and province were significantly associated with the prevalence of undiagnosed hypertension among hypertensive patients in unadjusted logistic regression analysis (see **supplementary table 1**).

Figure 2 represents the results of multiple logistic regression analysis. The multiple binary logistic regression model showed that age, sex, BMI, wealth quintile and province had significant

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3 association with undiagnosed hypertension. Elderly patients (≥ 65 years of age) had a lower
4 likelihood of being undiagnosed for hypertension than patients aged 15-24 years (AOR = 0.65,
5 95% CI 0.48, 0.91). Male patients were 1.29 times more likely than female patients to remain
6 undiagnosed for hypertension (AOR = 1.29, 95% CI 1.11, 1.51). Compared to patients with normal
7 BMI, overweight/obese patients (AOR = 0.80, 95% CI 0.69, 0.93) were less likely to have
8 undiagnosed hypertension.
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10 We found wealth quintiles as potential correlates of undiagnosed hypertension. The risk of
11 remaining undiagnosed for hypertension increased with decreasing socioeconomic status.
12 Likelihood of having undiagnosed hypertension was greater among poorer socioeconomic status
13 patients compared to higher socioeconomic quintiles. Patients of poorest and poorer wealth
14 quintiles were 2.49 (AOR = 2.49; 95% CI 1.90, 3.30) and 1.67 (AOR = 1.67; 95% CI 1.29, 2.16)
15 times more likely to have an undiagnosed hypertension condition than patients of the wealthiest
16 quintile.
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18 Moreover, significant provincial variation was evident in the prevalence of undiagnosed
19 hypertension among hypertensive patients. Patients of province 4 (AOR = 1.36, 95% CI 1.04, 1.79)
20 and province 5 (AOR = 1.43, 95% CI 1.05, 1.95) were more likely to have undiagnosed
21 hypertension than patients of province 1.
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44 {Figure 2 will be added here}

45 46 47 **Socioeconomic Inequalities in Undiagnosed Hypertension**

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50 **Figure 3** depicts the inequalities in the prevalence of undiagnosed hypertension among
51 hypertensive patients. The difference in the distribution of undiagnosed hypertension was 24.6%
52 between the lowest wealth quintile (Q1) and highest wealth quintile (Q5), meaning that the
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3 prevalence of undiagnosed hypertension was greater by 24.6 percentage points among the poorest
4 patients. The relative measure of inequality in terms of poor (Q1): rich (Q5) ratio was 1.6 for the
5 prevalence of undiagnosed hypertension among patients, depicting that the prevalence of
6 undiagnosed hypertension was 1.6 times higher among the poorest than the richest patients. We
7 found negative value of the Concentration Index ($C = -0.18$) which suggests that the prevalence of
8 undiagnosed hypertension among hypertensive patients was disproportionately distributed among
9 lower socioeconomic status groups.
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23 In addition, patients living in mountain areas and in province 7 had large gaps in the prevalence of
24 undiagnosed hypertension (**Figure 4**). The higher Q1:Q5 ratio were observed among those who
25 had large Q1-Q5 gaps in the prevalence of undiagnosed hypertension across different geographic
26 locations. We found large negative values of C among those who had higher Q1-Q5 gaps and
27 Q1:Q5 ratio for the prevalence of undiagnosed hypertension. See **Figure 4** for details.
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41 **DISCUSSION**

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44 Globally, to date few studies have been conducted on undiagnosed hypertension. For the first time,
45 this study estimated the prevalence of undiagnosed hypertension in Nepal as 50.4% of respondents
46 who tested positive for hypertension in the 2016 NDHS. In addition, this study identified the risk
47 factors and inequalities associated with undiagnosed hypertension in Nepal. The high prevalence
48 of undiagnosed hypertension identified in this study may be due to people's lack of awareness and
49 willingness to partake in regular health check-ups in the absence of health issues, coupled with
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3 accessibility barriers to screening services [27]. Lack of knowledge, attitudes and behaviours that
4 promote healthy lifestyles as preventive measures to non-communicable diseases (NCDs) may
5 also act as a driver of undiagnosed hypertension [27–29]. Community-based awareness raising of
6 changing lifestyles to address the burden of NCDs might be effective in reducing this gap [30].
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12 Several studies have reported higher risks of hypertension among people who are older in age,
13 male, urban dwellers, have higher education level, regularly consume tobacco and/or alcohol, or
14 are overweight [6,8,28,29]. We found that patients aged 65+ years and who were overweight/obese
15 were at lower risk of remaining undiagnosed from hypertension. Our findings depicted a greater
16 proportion of undiagnosed hypertensive patients among those who were young and those with
17 lower BMI. Young or underweight people may be less conscious about their health status as they
18 might have the misconception that they are less likely to suffer from NCDs [31]. In addition, people
19 from lower socioeconomic status groups in Nepal tend to have less knowledge and awareness
20 about health hazards, typically have poorer access to services for screening diseases and lack the
21 capacity to afford treatment costs for diseases [28]. This may contribute to the disproportionate
22 occurrence of undiagnosed hypertension among lower socioeconomic status groups in Nepal.
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39 Similar to risk factors of hypertension, undiagnosed hypertension was also more prevalent among
40 males and tobacco users [6,29]. The higher rate of undiagnosed hypertension among males might
41 be due to their lack of awareness and lower treatment rates than females [32]. Smoking, a main
42 source of using tobacco, is well recognized to be associated with increased risk of hypertension in
43 many settings, including Nepal [33,34]. However, there is lack of evidence to determine the extent
44 to which tobacco use is related to patients remaining undiagnosed for hypertension. Our findings
45 demonstrate that, in Nepal, factors other than tobacco use played independent roles in predicting
46 the rate of undiagnosed hypertension. While differences in lifestyle practices between males and
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3 females in Nepal may be a key factor behind different exposures, further research is needed to
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5 identify the actual risk factors [29].
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8 Undiagnosed hypertension may lead to adverse health consequences, including organ damage [35].
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10 The WHO, denoting hypertension as a silent killer, stated that the prevalence of hypertension is
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12 higher in low- and middle-income countries compared to developed and high income countries
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14 [3]. Our results support this claim and also align with findings from Bangladesh and Sub-Saharan
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16 Africa [19,36,37]. Despite being neighbouring countries, the prevalence of undiagnosed
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18 hypertension from this study (approximately 50%) is much higher than that of China[38]. For
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20 example, recent evidence shows that the prevalence of undiagnosed hypertension in China is
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22 28.8% [39]. The reason behind this difference might be due to the differences in age of study
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24 participants. Our study assessed participants of age 15 years or older in Nepal, while the Chinese
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26 study included older participants (over 45 years) who may be more aware of health conditions and
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28 more likely to visit doctors for regular health check-ups. Findings from studies conducted in
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30 countries with more developed health care systems and advanced screening processes such as
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32 Japan, Korea, England, Ireland, Egypt, Brazil and USA were also found to have lower levels of
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34 undiagnosed hypertension than Nepal as found in this study [40–46]. The prevalence of
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36 undiagnosed hypertension in Nepal is relatively closer with that of Bangladesh [19]. This might
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38 be due to the less advanced health care systems of these two countries with both countries
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40 displaying lowHealth Care Index values [38].
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48 In Nepal, despite the detection of risk factors [6,8,29] and inequalities [28], the prevalence of
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50 hypertension has been well investigated nationally, resulting in the implementation of new polices
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52 to mitigate the rising number of hypertension patients [47]. However, these policy reform efforts
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54 will fail to effectively achieve intended hypertension reduction targets if patients remain
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3 undiagnosed, undetected and untreated. It is necessary to identify whether unequal distribution of
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5 undiagnosed hypertension exists among patients with hypertension across different socioeconomic
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7 groups. Such information will aid in setting priorities and effective allocation of resources. Our
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9 study reveals existence of inequalities in the distribution of undiagnosed hypertension due to
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11 economic status. Lower socioeconomic status groups experienced a higher prevalence of
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13 undiagnosed hypertension compared to higher socioeconomic groups and a greater degree of
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15 wealth-based inequality was concentrated among the poorest. These inequalities were more
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17 prevalent among patients living in different geographical locations including place of residence,
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19 ecological zones and administrative provinces. Such disparities may be owing to greater awareness
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21 of health issues and more utilization of health care services among higher socioeconomic groups
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23 [28]. Such inequality might increase the catastrophic health spending given the rise of catastrophic
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25 household expenditure due to NCDs in Nepal [14,48]. Public health strategies might reduce this
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27 gap by concentrating more on implementing social health insurance policies which are equitable
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29 for all [40,48]. In this respect, policy makers could take into consideration the disparities in the
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31 distribution of undiagnosed hypertension found in this study.
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38 Several initiatives have been taken to control hypertension in Nepal. To address the burden of
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40 cardiovascular diseases (CVD), the WHO and partners launched an initiative called “Global
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42 Hearts” in 2016 [49]. This initiative took a comprehensive approach to help countries in scaling-
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44 up affordable and adaptable measures to improve capacity of health care services to better detect
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46 and treat people at risk of or suffering from CVD. This initiative comprises three packages:
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48 SHAKE, HEARTS and MPOWER. The package “HEARTS” provides tools to incorporate CVD
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50 management best practices at the primary healthcare level to reduce CVD risk factors such as
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52 hypertension and high blood cholesterol. Like many low to middle incomes countries, Nepal has
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3 adapted the Global Hearts initiative to address CVD. In addition, the Community-based
4 Management of Hypertension in Nepal (COBIN) is a community-based cost-effective intervention
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6 with demonstrated success in reducing hypertension in Nepal [50,51]. However, for designing
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8 future programs or interventions for the prevention of hypertension in Nepal, our findings highlight
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10 the importance of considering undiagnosed hypertensive cases and the uneven distribution of such
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12 cases across a spectrum of socio-demographic characteristics.
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17 Failing to diagnose and detect hypertension among vulnerable populations will have detrimental
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19 health outcomes for any nation. This study, for the first time at a national level, sheds light on the
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21 prevalence of undiagnosed hypertension in Nepal. The NDHS 2016, through incorporation of
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23 biomarker tests, bears evidence that a substantial proportion of individuals are suffering from
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25 blood pressure abnormalities. This emphasises the need for conducting routine screening for
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27 hypertension that ensures access by lower socioeconomic groups and at risk populations. A routine
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29 surveillance system with technology-based screening can aid in tracing disease incidence including
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31 among people at risk of being undiagnosed [52]. Our study findings will help inform and initiate
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33 policies and programs that capture the highest domain of vulnerable populations and bring them
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35 under routine surveillance at community level with optimal cost.
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41 **Strengths and limitations**

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44 We used the most updated, nationally representative, cross-sectional data to determine the
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46 prevalence, correlates and inequalities of undiagnosed hypertension in Nepal. We considered the
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48 complex survey design in our methods and captured variations. However, there may be residuals
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50 and unmeasured behavioral or lifestyle factors potentially relevant to undiagnosed hypertension,
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52 for example, physical activity, dietary patterns and family history of hypertension, that were not
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54 explored in this study. Since our data was cross-sectional, the relationship between undiagnosed
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3 hypertension and confounders were probabilistic rather than causal. However, identification of
4 potential correlates through using odds ratio is widely acceptable. This study measured both
5 absolute and relative inequalities in the prevalence of undiagnosed hypertension at national level
6 as well as across place of residence, ecological zones and administrative provinces to further guide
7 policy/decision makers for better allocation of resources to reduce hypertension rates.
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18 **CONCLUSIONS**

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21 For the first time on a national level in Nepal, this study estimates the prevalence of undiagnosed
22 hypertension as 50.4% of respondents who tested positive for hypertension in the Nepal
23 Demographic and Health Survey. Furthermore, our results show that prevalence of undiagnosed
24 hypertension is disproportionately higher among lower socioeconomic status groups in Nepal. Our
25 results suggest that efforts should be made to improve the knowledge, attitudes and practices of
26 people around hypertension, particularly among those who are young, slender, poor and male,
27 given their higher risk of being undiagnosed. Routine screening and strengthening diagnosis of
28 hypertension in the primary level of healthcare service facilities may help Nepal in reducing cases
29 with undiagnosed hypertension. Moreover, identification of inequalities among different risk
30 groups will be beneficial in achieving the universal health coverage target of UN Sustainable
31 Development Goals (Goal 3.8.1). Social health insurance policies under an integrated national
32 NCD policy should be properly enacted to ensure socioeconomically disadvantaged populations
33 are adequately covered under the scheme for the prevention and control of hypertension.
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54 **Acknowledgments**

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Contributors

MMH, SA and AAM conceptualized the study. MMH contributed to data acquisition, data analysis, interpretation of the findings and drafting the manuscript. FT, MT and AC helped interpreting the results and contributed to drafting the manuscript. AAM, AC and SA critically reviewed the analysis and final version of the manuscript. All authors made a thorough review of the final draft. All authors read and approved the final manuscript for publication.

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Competing interests

None declared.

Ethical approval

The NDHS survey methodology and questionnaire was reviewed and approved by the ethical review board of Nepal Research Council and ICF Institutional. NDHS obtained informed consent from the respondents before conducting the survey. Therefore, separate ethical approval was not required for this study and we are using publicly available de-identified data.

Data sharing statement

Data are available in a public, open access repository. All data related to study are included in the manuscript.

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Table 1: Characteristics of the study participants

Variables	Total			Diagnosed hypertension			Undiagnosed hypertension			Chi-Square Statistic (p-value)
	n	%	95% CI	n	%	95% CI	n	%	95% CI	
Overall	3334	--	--	1634	49.6	47.1-52.1	1700	50.4	47.9-52.9	--
Age										29.6317

1											
2											
3	15-24	237	6.6	5.6-7.8	107	43.1	36.1-50.4	130	56.9	49.6-63.9	0.0008
4	25-34	449	13.2	11.9-14.5	196	43.8	38.4-49.3	253	56.2	50.7-61.6	
5	35-44	637	19.6	18-21.3	287	45.2	40.1-50.3	350	54.8	49.7-59.9	
6	45-54	687	20.9	19.2-22.8	333	49.4	45-53.8	354	50.6	46.2-55	
7	55-64	643	18.9	17.4-20.5	344	54.7	49.8-59.5	299	45.3	40.5-50.2	
8	>=65	681	20.8	19-22.7	367	55.1	50.3-59.8	314	44.9	40.2-49.7	
9											
10											
11	Sex										18.35
12	Male	1640	49.5	47.7-51.3	746	45.8	42.6-49.1	894	54.2	50.9-57.4	0.0003
13	Female	1694	50.5	48.7-52.3	888	53.3	50.1-56.4	806	46.7	43.6-49.9	
14											
15	BMI										29.2511
16	Normal	1816	53.6	51.2-56.1	841	47.1	44.3-50	975	52.9	50-55.7	0.0001
17	Thin	361	11.1	9.9-12.5	156	42.2	35.7-49	205	57.8	51-64.3	
18	Overweight/obese	1120	35.2	32.5-38	620	55.6	51.7-59.5	500	44.4	40.5-48.3	
19											
20	Education										6.5852
21	No education	1576	46.5	44.1-48.9	778	50.9	47.5-54.4	798	49.1	45.6-52.5	0.2125
22	Primary	602	17.8	16.2-19.5	285	46.1	41.1-51.1	317	53.9	48.9-58.9	
23	Secondary	804	24.1	22.5-25.9	383	48	43.6-52.4	421	52	47.6-56.4	
24	Higher	350	11.5	9.9-13.5	187	53	46.9-58.9	163	47	41.1-53.1	
25											
26	Wealth Quintile										90.7085
27	Poorest	610	15.5	13.3-18	211	35.9	31.9-40	399	64.1	60-68.1	0.0000
28	Poorer	689	19.2	16.9-21.7	313	44.2	39.8-48.7	376	55.8	51.3-60.2	
29	Middle	604	17.3	15.2-19.6	301	49.5	44.5-54.5	303	50.5	45.5-55.5	
30	Richer	667	19.7	17.1-22.6	344	50.2	44.9-55.5	323	49.8	44.5-55.1	
31	Richest	764	28.3	24-33	465	60.4	55.4-65.2	299	39.6	34.8-44.6	
32											
33	Place of residence										16.691
34	Urban	2221	64.9	59.9-69.6	1152	52.2	49-55.4	1069	47.8	44.6-51	0.0057
35	Rural	1113	35.1	30.4-40.1	482	44.8	40.7-48.9	631	55.2	51.1-59.3	
36											
37	Ecological zone										3.43
38	Mountain	200	5.6	3.6-8.6	92	47.1	39.4-54.8	108	52.9	45.2-60.6	0.3721
39	Hill	1694	49.9	44.2-55.6	788	48.3	45.1-51.5	906	51.7	48.5-54.9	
40	Terai	1440	44.5	39.2-49.9	754	51.4	47.1-55.6	686	48.6	44.4-52.9	
41											
42	Province										23.7869
43	Province 1	490	17	15.2-19	265	53	47.7-58.3	225	47	41.7-52.3	0.0511
44	Province 2	460	16.2	14.2-18.3	243	53.1	46.5-59.6	217	46.9	40.4-53.5	
45	Province 3	575	26	21.8-30.6	303	52.7	46.8-58.5	272	47.3	41.5-53.2	
46	Province 4	578	13.2	11.5-15.1	273	46.9	42-51.7	305	53.1	48.3-58	
47	Province 5	553	17.8	15.4-20.4	253	45.4	39-51.9	300	54.6	48.1-61	
48	Province 6	343	3.9	3.3-4.6	148	39.8	32.9-47.1	195	60.2	52.9-67.1	
49	Province 7	335	6	5-7.2	149	41.9	33.8-50.5	186	58.1	49.5-66.2	
50											
51	Caffeine consumption										0.2587
52	No	2942	88.4	86.7-89.9	1434	49.4	46.9-52.0	1508	50.6	48.0-53.1	0.6895
53	Yes	392	11.6	10.1-13.3	200	50.8	44.1-57.4	192	49.2	42.6-55.8	
54											
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Tobacco use										5.3524
No	2826	84.9	83.2-86.6	1410	50.4	47.8-53.1	1416	49.6	46.9-52.2	0.0338
Yes	508	15.1	13.5-16.8	224	44.8	40.0-49.8	284	55.1	50.2-60.0	
Alcohol consumption										2.4122
No	3249	97.8	97.1-98.4	1600	49.8	47.2-52.8	1649	50.2	47.6-52.8	0.1505
Yes	85	2.2	1.6-2.9	34	40.6	29.4-52.9	51	59.4	47.1-70.6	

Note: n = Number of sample, CI = Confidence interval

Figure 1: Selection of participants

Figure 2: Determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Figure 3: Concentration curve to measure the wealth-based inequality in the prevalence of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Figure 4: Socioeconomic inequalities in the prevalence of undiagnosed hypertension among patients with hypertension across geographical locations in Nepal, 2016

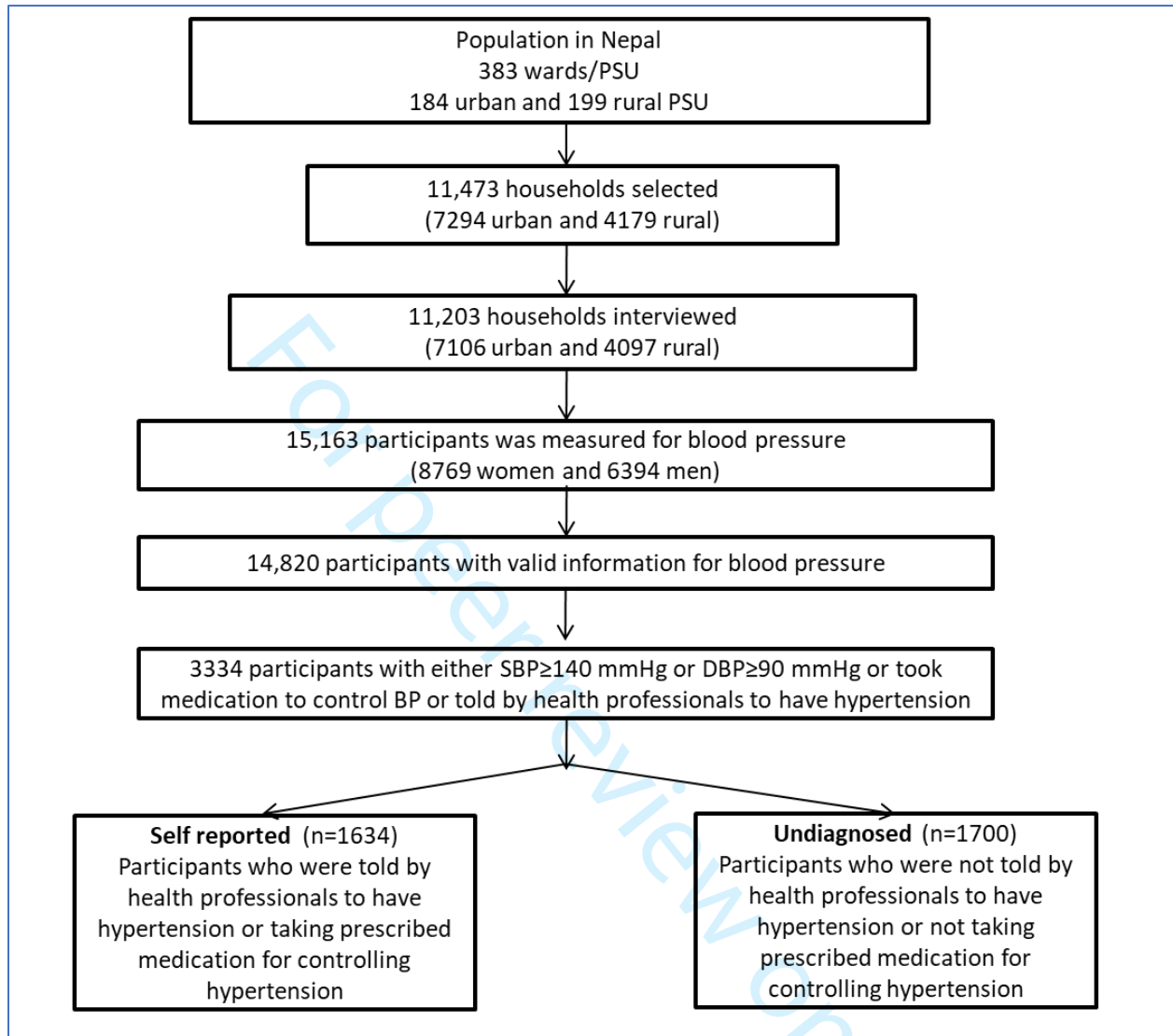
Figure 1: Selection of participants

Figure 2: Determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

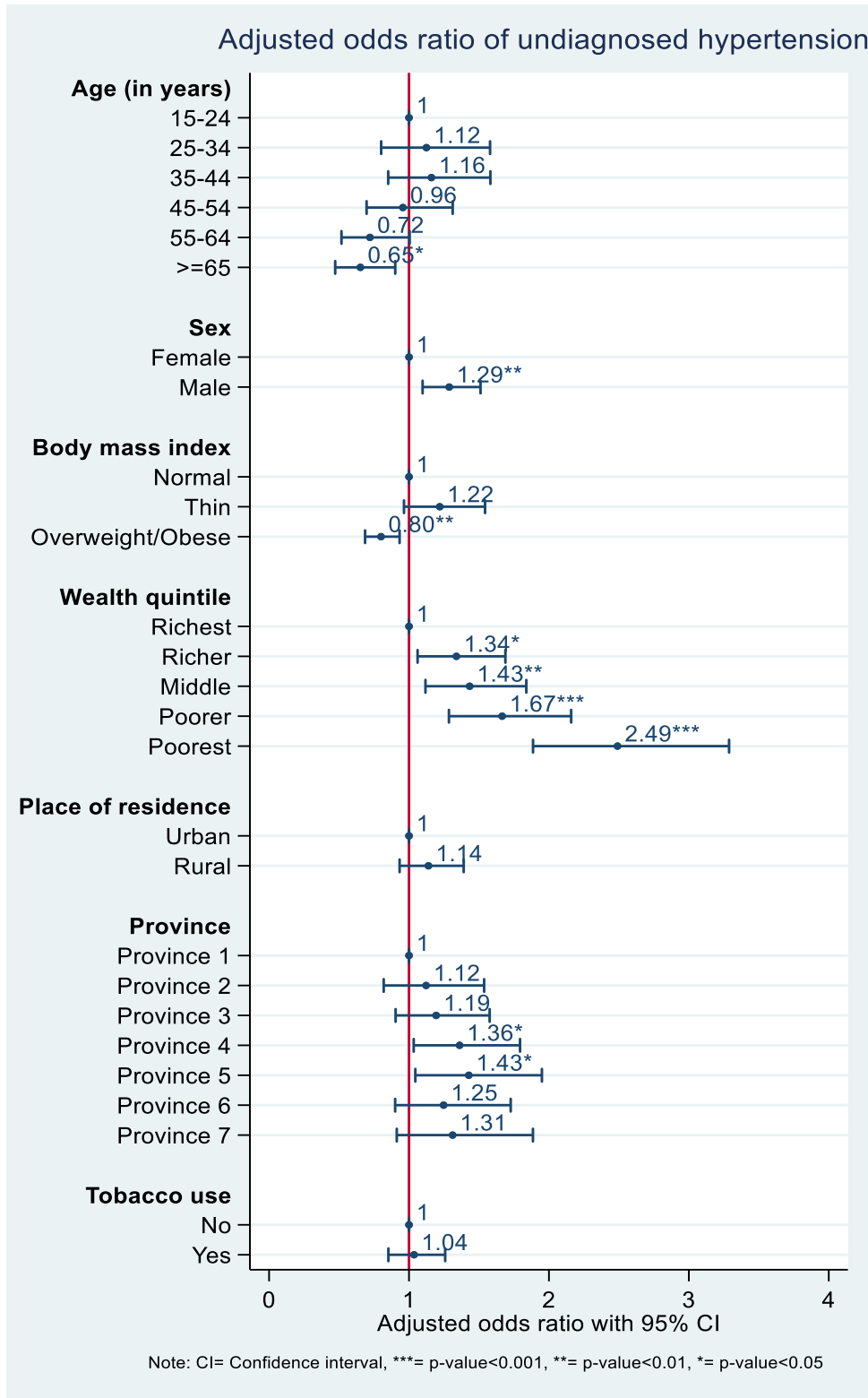


Figure 3: Concentration curve to measure the wealth-based inequality in the prevalence of undiagnosed hypertension among patients with hypertension in Nepal, 2016

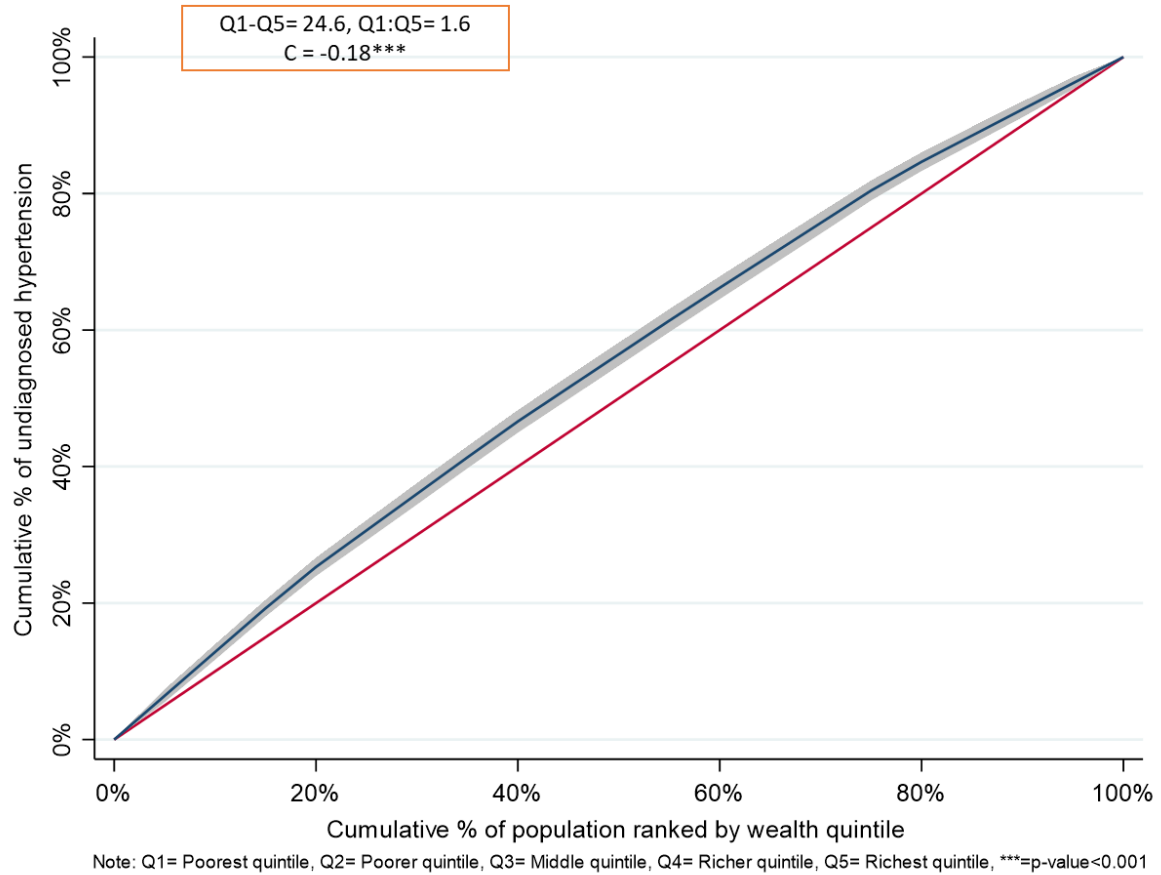
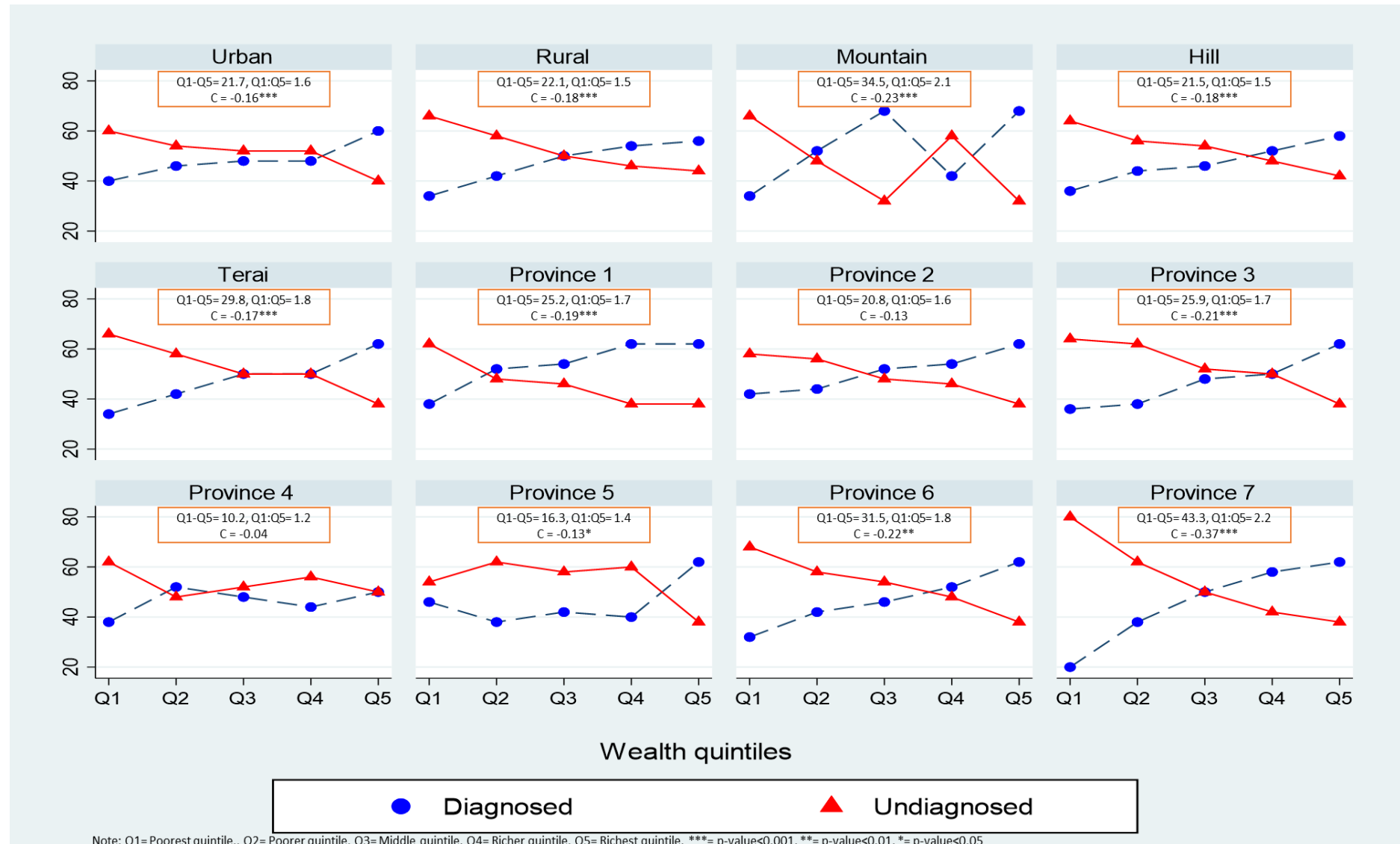


Figure 4: Socioeconomic inequalities in the prevalence of undiagnosed hypertension among patients with hypertension across geographical locations in Nepal, 2016



Note: Q1=Poorest quintile, Q2= Poorer quintile, Q3= Middle quintile, Q4= Richer quintile, Q5= Richest quintile, ***= p-value<0.001, **= p-value<0.01, *= p-value<0.05

Supplementary Table 1: Unadjusted determinants of undiagnosed hypertension among patients with hypertension in Nepal, 2016

Variables	COR	95% CI	p-value
Age			
15-24	1		
25-34	1.06	0.77-1.46	0.7090
35-44	1.00	0.75-1.34	0.9800
45-54	0.87	0.65-1.18	0.3760
55-64	0.72	0.52-0.98	0.0400
>=65	0.70	0.52-0.96	0.0250
Sex			
Male	1.32	1.14-1.53	0.0000
Female	1		
BMI			
Normal	1		
Thin	1.13	0.91-1.41	0.2610
Overweight/obese	0.70	0.6-0.8	0.0000
Education			
No education	1		
Primary	1.08	0.9-1.31	0.4010
Secondary	1.07	0.88-1.3	0.4790
Higher	0.85	0.66-1.09	0.2070
Wealth Quintile			
Poorest	2.94	2.29-3.77	0.0000
Poorer	1.87	1.47-2.38	0.0000
Middle	1.57	1.23-1.99	0.0000
Richer	1.46	1.16-1.84	0.0010
Richest	1		
Place of residence			
Urban	1		
Rural	1.41	1.17-1.71	0.0000
Ecological zone			
Mountain	1		
Hill	0.98	0.68-1.41	0.9100
Terai	0.78	0.53-1.12	0.1800
Province			
Province 1	1		
Province 2	1.05	0.77-1.44	0.7540
Province 3	1.06	0.78-1.44	0.7220
Province 4	1.32	1-1.74	0.0530
Province 5	1.40	1.01-1.92	0.0400
Province 6	1.55	1.09-2.2	0.0140

Province 7	1.47	0.99-2.18	0.0550
Caffeine consumption			
No	1.00		
Yes	0.91	0.72-1.15	0.4400
Tobacco consumption			
No	1.00		
Yes	1.26	1.06-1.51	0.0100
Alcohol consumption			
No	1.00		
Yes	1.46	0.91-2.32	0.1140

Note: COR= Crude Odds Ratio, CI= Confidence Interval

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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Page No	Item No	Recommendation
Title and abstract	1	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
	2-3		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction			
Background/rationale	4-5	2	Explain the scientific background and rationale for the investigation being reported
Objectives	5	3	State specific objectives, including any prespecified hypotheses
Methods			
Study design	5	4	Present key elements of study design early in the paper
Setting	5	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7-8	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	5	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	10	9	Describe any efforts to address potential sources of bias
Study size	6	10	Explain how the study size was arrived at
Quantitative variables	7-8	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	8-9	12	(a) Describe all statistical methods, including those used to control for confounding
	"n/a"		(b) Describe any methods used to examine subgroups and interactions
	"n/a"		(c) Explain how missing data were addressed
	"n/a"		(d) If applicable, describe analytical methods taking account of sampling strategy
	"n/a"		(e) Describe any sensitivity analyses
Results			
Participants	10	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
	"n/a"		(b) Give reasons for non-participation at each stage
	"n/a"		(c) Consider use of a flow diagram
Descriptive data	10	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
	"n/a"		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	11	15*	Report numbers of outcome events or summary measures
Main results	11-13	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

			(b) Report category boundaries when continuous variables were categorized
			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	“n/a”	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion			
Key results	13-14	18	Summarise key results with reference to study objectives
Limitations	17-18	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	14-17	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	18	21	Discuss the generalisability (external validity) of the study results
Other information			
Funding	19	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.