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Factors affecting anaemia among women of reproductive age in Nepal: a multilevel and spatial analysis

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1 **Factors affecting anaemia among women of reproductive** 2 **age in Nepal: a multilevel and spatial analysis**

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14
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16 **ABSTRACT**

17 **Objective:** The main objective of this study was to explore the factors affecting anemia among
18 women of reproductive age (WRA) in Nepal using spatial and multilevel epidemiological
19 analysis.

20 **Design:** This cross-sectional study analyzed the data from the 2016 Nepal demographic and
21 health survey (NDHS 2016). The spatial analysis was performed using ArcGIS software V.10.8
22 to identify the hot and cold spots of anaemia among WRA (15 to 49 years). Data were analyzed
23 using multilevel mixed-effect logistic regression analysis.

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2
3 24 **Setting:** Nepal
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6 25 **Participants:** A total of 6,414 WRA were included in the analysis.
7

8
9 26 **Main outcome measure:** Anaemia defined by World Health Organization (WHO) as
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11
12 27 hemoglobin level less than 12g/dL in non-pregnant women and less than 11g/dL in pregnant
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14 28 women.
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16
17 29 **Results:** The spatial analysis showed that statistically significant hotspots of anaemia were in
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19
20 30 the southern Terai region (4 districts in Province-1, 8 districts in Province-2, 1 district in
21
22 31 Bagmati province, and 3 districts in Province-5) of Nepal. At the individual level, women with
23
24 32 no education (aOR: 2.07 95% CI: 1.21-3.54), and from middle socio-economic class families
25
26 33 (aOR: 1.66, 95% CI: 1.02-2.68) were more likely to be anemic, whereas, older women (≥ 35
27
28 34 years) (aOR: 0.48, 95% CI: 0.26-0.91), and those women who were using hormonal
29
30 35 contraceptives (aOR: 0.57, 95% CI: 0.39-0.84) were less likely to be anaemic. At the community
31
32 36 level, women from Province-2 (aOR: 3.12, 95% CI: 1.58-6.14) had higher odds of being
33
34 37 anaemic.
35
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37

38 38 **Conclusion:** WRA had higher odds of developing anemia and it varied by the geographical
39
40 39 regions. High prevalence of anaemia were observed in the southern Terai. The multi-pronged
41
42 40 approaches including nutritional, and non-nutritional anaemia prevention and control strategies
43
44 41 can benefit by tailoring the programs to the high risk provinces and districts with high burden of
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46 42 anemia.
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Strengths and limitations of this study

- Used comprehensive, nationally representative data with haemoglobin level.
- The combined statistical methods including multilevel and spatial analysis were applied, which takes into account the role of geographical risk profile and determinants of anaemia among WRA in Nepal.
- Due to the cross-sectional design, it was difficult to determine the cause-and-effect relationships between the predictors and outcome variable (anaemia).
- Other potential confounding factors of anaemia such as nutrient intake, worm infestations, malaria and other non-modifiable risk factors were beyond the scope of this study.
- This study could not distinguish the types of anaemia such as nutritional, genetic and infectious.

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46 INTRODUCTION

47 Anaemia remains a significant public health problem in developing countries despite advances in
48 health science.[1] Approximately one-third of the population is affected by anaemia
49 globally.[2,3] South Asian accounts for the largest burden of anaemia with estimated prevalence
50 of 49% in 2016 among women of reproductive age (WRA).[4] The highest prevalence over the
51 past 26 years was 55.2% in 1990.[4] Despite the implementation of a ‘1000 days nutrition
52 program’ among various other programs, targeted to a mother with newborn babies in South
53 Asia, the reduction in anemia among pregnant women has not been significant.[5] To accelerate
54 reduction of anaemia, the World Health Assembly has set a target of achieving a 50% reduction
55 of anaemia among WRA by 2025 relative to 2010.[6] However, not a single South Asian country
56 is on the way to achieve the 2025 targets.[7] Despite the historic efforts in preventing anaemia
57 through the implementation of national nutrition programs and policies including iron-folic acid
58 supplementation across the country, the prevalence of anaemia among WRA has been steadily
59 increasing from 35% in 2011 to 41% in 2016.[8,9] These figures suggest that anaemia continues
60 to be a severe public health problem in Nepal where the prevalence rate is $\geq 40\%$.[10]

61 Anaemia in WRA is associated with multiple conditions and consequences such as preterm
62 delivery,[11] miscarriage,[12] low birth weight,[13] child growth faltering, impairment of
63 cognitive function, increased susceptibility to infection, and poverty.[14,15] It is also associated
64 with increased risk of prenatal and maternal mortality.[13,16] Approximately 20% of maternal
65 deaths are caused by anaemia and it is also considered as an additional risk factor for 50% of all
66 maternal deaths.[17,18]

67 Contributing factors and distribution of anaemia include a complex interplay of political,
68 ecological, social, and biological factors.[19] In Nepal, anaemia among WRA is associated with

1
2
3 69 various socio-ecological factors. In the southern Terai of Nepal, low community education
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5 70 status, gender based-inequality, poor health seeking behavior,[20–22] inadequate dietary intake
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7 71 during pregnancy,[23–25] lack of diversified diet,[9,24,26] high burden of hookworm infection
8
9 72 and malaria,[27–29] and high amount of arsenic in potable water[30] were identified as factors
10
11 73 contributing to anaemia. On the other hand, high prevalence of anaemia in the mountainous
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13 74 region were attributed to among others, food insecurity, and low dietary diversity,[9,24,31] poor
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15 75 health services,[22] illiteracy, and gender based-inequality.[20,21]
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20 76 To the best of our knowledge, this is the first study to explore the geographical regions with
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22 77 hotspots (high prevalence rate) and factors affecting anaemia among WRA using cluster
23
24 78 sampling of the nationally representative data of Nepal. Exploring spatial patterns and factors
25
26 79 affecting anaemia by geographical region is crucial to inform the planning for targeted anaemia
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28 80 control and prevention programs.[32] The main objective of this study was to explore the spatial
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30 81 distribution and contributing factors of anaemia among WRA in Nepal.
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35 82 **METHODS**

36 83 **Patient and public involvement**

37 84 This study utilized a publicly available data set (NDHS); therefore, there was no patient
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39 85 involved.
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44 86 **Data source**

45 87 This study was based on the data from Nepal Demographic and Health Survey (NDHS) 2016, a
46
47 88 nationally representative cross-sectional survey. This survey was carried out as part of the DHS
48
49 89 program by New ERA under the guidance of the Ministry of Health, Government of Nepal and
50
51 90 was supported by ICF international and United States Agency for International Development
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91 (USAID). The study population for this study was WRA from the Nepal Demographic and
92 Health Survey 2016.

93 **Sampling strategy**

94 The NDHS 2016 utilized a stratified, two-stage cluster sampling design to provide representative
95 estimates for seven provinces, three ecological zones, and urban and rural areas. The survey used
96 enumeration areas (EAs) which is a primary sampling unit (PSU) and was selected from 383
97 wards in both rural (n=199) and urban (n=184) areas with probability proportional to size
98 method. In the second stage, 30 households on average within EAs were selected using a
99 systematic sampling technique. A more detailed methodology of the NDHS has been published
100 elsewhere.[9] All WRA (pregnant and non-pregnant) with available data on anaemia, complete
101 socio-demographic and nutritional characteristics who were resident or who had slept in the
102 selected households on the night before the survey were eligible for the survey. The details of the
103 sample size and exclusion criteria for the selection of the samples are presented in Figure 1.

104 **Study variables**

105 **Outcome variables**

106 Haemoglobin level was measured using capillary blood by a battery-operated portable HemoCue
107 rapid testing machine and was adjusted for altitude and smoking status.[9] According to the
108 WHO, for non-pregnant and pregnant women aged 15-49 years, any form of anaemia is defined
109 as haemoglobin concentration <12.0g/dL and 11g/dL respectively.[33] The categories of
110 anaemia were further dichotomized into 'anaemic' and 'not anaemic'.

111 **Predictor's variables**

112 Predictors of anaemia were selected based on the literature review.[14,34–36] The wide range of
113 socio-demographic, individual, household and community factors were hypothesized to increase

1
2
3 114 the likelihood of anaemia. The predictors of anaemia including both individual-level and
4
5 115 community-level factors were included in the analysis. The coding strategy of individual-level
6
7
8 116 and community-level factors are presented in online supplementary Table 1.
9

10 11 117 **Individual-level factors**

12 118 A total of 11 individual-level factors were identified, and that included for example, respondent's
13
14 119 age, education level, occupation, wealth index, nutritional status, pregnancy status, and minimum
15
16 120 dietary diversity for WRA (MDD-W). The minimum Dietary Diversity for Women of
17
18 121 Reproductive age (MDD-W) was calculated using the guideline of the modified FANTA III tool
19
20 122 developed by the Food and Agriculture Organization (FAO) of the United Nations.[37]
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24 123 **Community-level factors**

25 124 The six different factors were included in the community-level factors that included place of
26
27 125 residence, province, community wealth, community female education, community safe water
28
29 126 access, and community toilet facility. The selection of community-level factors were based on
30
31 127 the group of women living in similar settings.[32] If more women have shared features such as
32
33 128 place of residence, province, type of water source, and toilet facility; it was considered to have
34
35 129 the same effect on anaemia among WRA.[32] For community level wealth and female education,
36
37 130 we constructed the aggregate continuous community-level predictor-variables by aggregating
38
39 131 individual-level characteristics at the community (cluster) level. We dichotomized the aggregate
40
41 132 variables into "high" or "low" based on the distribution of the proportion values calculated for
42
43 133 each community.[38] The mean value was used as a cut-off point of the proportion values for the
44
45 134 categorization of community-level variables. The community wealth was categorized as 'high' if
46
47 135 the proportion of women from richest (rich, richest) households in the community was above
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49 136 21% and 'low' if the proportion was 0 to 21%. Community female education was defined as the
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3 137 mean percentage of women in the community with at least primary education and above.[39]
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5 138 Water supply and sanitation guidelines based on the WHO and UNICEF Joint Monitoring
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7
8 139 Programme (JMP) were used to define improved toilet facility and improved water source.[40]
9

10 11 140 **Data analysis**

12 13 141 **Statistical analysis**

14
15 142 Data were analyzed using Stata/MP version 14.1 (StataCorp LP, College Station, Texas). Data
16
17 143 were adjusted for enumeration areas (EAs) and disproportionate sampling and non-response.

18
19 144 Weighted frequencies, weighted percentage, mean and SD were used for the descriptive analysis.

20
21 145 The multilevel mixed-effect logistic regression analysis was performed to estimate the adjusted
22
23 146 odds ratio and to estimate the extent of random variations between communities.

24
25
26
27 147 Four models were created and were fitted. Model 1 (empty model) was fitted without predictor
28
29 148 variable to test random variability in the intercept and to estimate the intra-class correlation

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31 149 (ICC).[41] Model 2 examined the effects of individual-level characteristics, model 3 examined

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33 150 the effects of community-level variables, and model 4 examined the effects of both individual

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35 151 and community-level characteristics simultaneously. In the multilevel mixed-effect logistic

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37 152 regression models, the fixed effects estimated the association between the likelihood of anaemia

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39 153 among WRA and the individual-level and community-level factors, and the findings are reported

40
41 154 in terms of adjusted odds ratio (aOR) with p-values <0.05 and 95% confidence intervals (CIs).

42
43 155 To prevent statistical bias in the multilevel logistic regression model, we examined and reported

44
45 156 multicollinearity among the predictor variables using variation inflation factors (VIF). In this

46
47 157 study, we used "10" as a cut-off value for the maximum level of VIF.[42] The random effects are

48
49 158 expressed as ICC,[41] and proportional change in variance (PCV).[43] The ICC was calculated

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51 159 to evaluate the cluster variability; and PCV can measure the total variation due to factors at the

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3 160 individual- and community- levels.[41] Models fit were assessed using Akaike information
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5 161 criterion (AIC) and the Bayesian information criterion (BIC). Considering the nested structure of
6
7 162 the survey data, a multilevel model is considered to be appropriate than ordinary single-level
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9 163 regression model because it provides correct parameter estimates by handling the cluster
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11 164 data.[44,45]
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15 165 **Spatial analysis**

16 166 Spatial analysis were performed using ArcGIS software V.10.8, and base files of the
17
18 167 administrative provinces and districts of Nepal were obtained from Government of Nepal,
19
20 168 Ministry of Land Management, [46] and Natural Earth.[47] The global positioning system (GPS)
21
22 169 data set for NDHS was obtained from the DHS website after receiving the approval letter. The
23
24 170 prevalence of anaemia and standardized prevalence ratio were computed for both the districts
25
26 171 and provinces in Stata/MP version 14.1 software and were later transferred to Excel spreadsheet.
27
28 172 These data were imported into the ArcGIS software to link the reported anaemia prevalence for
29
30 173 each cluster to the corresponding geographical location (survey cluster data). The spatial
31
32 174 variations of the prevalence of anaemia among WRA by both districts and provinces were
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34 175 visualized. Similarly, the standardized prevalence ratio of anaemia among WRA (normalized to
35
36 176 the national prevalence of 41%) for both districts and provinces were visualized.
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43 177 The spatial analysis was performed to explore the clustering of anaemia among WRA using the
44
45 178 Getis-Ord G-statistic tool in ArcGIS software. The Getis-Ord G-statistics identifies statistically
46
47 179 significant spatial clusters of high values (hot spots) and low values (cold spots).[48] The
48
49 180 statistical significance of autocorrelation was determined by z-scores and p-value ≤ 0.05 with a
50
51 181 95% Confidence Intervals (CIs).[32,48] An autocorrelation can be categorized into positive and
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53 182 negative using Getis-Ord G-statistics. For statistically significant positive autocorrelation, larger
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3 183 z-score, meant more intense clustering of high values (hot spots) and for statistically significant
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5 184 negative autocorrelation, smaller z-score meant more intense clustering of low values (cold spot)
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7
8 185 which allowed us to identify the spatial variability of anaemia among WRA.[9] An anaemia hot
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10 186 spot was defined as the occurrence of high prevalence rates of anaemia clustered together on the
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12 187 map. Anaemia cold spot was referred to the occurrence of low prevalence rates of anaemia
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14
15 188 clustered together on the map.[32,48] The spatial pattern and distribution of anaemia prevalence
16
17 189 rates among WRA in Nepal are visualized on the map (Figure 2)

190 **Ethical consideration**

21
22 191 The DHS survey protocols were approved by the institutional review boards of ICF, the DHS
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24 192 program, and the Nepal Health Research Council (NHRC). The details on ethical procedures
25
26
27 193 used in this survey have been published elsewhere.[9] We registered and requested for access to
28
29 194 both main data and GPS data from the DHS website[49] and received an approval to access and
30
31 195 download the DHS data file. DHS program collected data following a written informed consent
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33 196 from each individual. All individual identifiers were precluded from the final dataset in this
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36 197 study.

39 **RESULTS**

41 **Socio-demographic characteristics of study participants**

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43 200 In this study, a total of 6,414 WRA were included in the analysis (Table 1). The mean (\pm SD) age
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45
46 201 of the study participants was 29 (\pm 9.7) years. More than one third (38.1%) of the participants
47
48 202 from age group 15-24 years, and women (35.5%) had attended secondary level of education.
49
50 203 Nearly one quarter (22.4%) of study participants were from richer wealth quintiles and more than
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52 204 half (59.7%) of the women were not using any contraceptive methods, and a half (50.6%) of the
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55 205 participants consumed more than five food types. High proportion of women (68.8%) belonged

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3 206 to urban areas, and were from Bagmati province (21.9%). More than half (54.2%) of the women
4
5 207 had the highest percentage of community female education, whilst, nearly two-thirds (64%) of
6
7 208 the women belonged to a low percentage of community female wealth index. Majority of the
8
9
10 209 participants had improved sources of drinking water (91%) and type of toilet facility (84.1%).
11
12 210 (Table 1)

211 **Prevalence of anaemia among women of reproductive age**

212 In the current study, the overall prevalence of any anaemia across Nepal was 41% (95% CI:
213 38.5-42.9%). At the individual level, the prevalence of anaemia was higher among younger age
214 groups (43.5%), and women who attended at least secondary level education (42.6%). The
215 higher cases of anaemia were found in middle socio-economic class families (48.9%). The
216 prevalence of anaemia was more in who used various contraceptive methods (43.1%), and those
217 who consumed less than five food groups (51%). At the community-level, the prevalence of
218 anaemia was higher in women who came from Province-2 (57.7%). The high proportion of
219 anaemia was found in community with low female education (47.8%), female wealth index
220 (44.3%), and who did not have improved toilet facility (51.4%) (Table 1).

222 **Factors affecting anemia among women of reproductive age**

223 The fixed effects (a measure of association) and the random-effects for the risk of developing
224 anaemia among WRA are presented in Table 2. The results of the empty model (model 1)
225 showed that there was statistically significant variability in the odds of anaemia between
226 communities ($\tau=0.627$, $p<0.001$). The ICC in the empty model implied that 16% of the total
227 variance for the risk of developing anaemia was attributed to differences between the
228 communities. In individual-level factors (model 2), women who did not have formal education
229 (aOR=2.23, 95% CI: 1.35-3.67) compared to those with higher education, and who belonged to

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2
3 230 middle-class families (aOR=1.81, 95% CI: 1.17-2.75) compared to the family from poorest
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5 231 families were found to have higher odds of anemia. Older women had 54% lower (aOR=0.46,
6
7 232 95% CI: 0.24-0.88) odds of developing anaemia compared to younger women. Women who used
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9 233 hormonal contraceptive methods had 39% lower (aOR=0.61, 95% CI: 0.42-0.86) odds of
10
11 234 anaemia compared to who did not use contraceptive methods. The ICC in model 2 indicated that
12
13 235 13.9% of the variation in WRA anaemia was attributable to differences across communities. The
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15 236 PCV indicated that 15.3% of the variance in WRA anaemia across communities was explained
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17 237 by the individual-level characteristics.

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21
22 238 The community-level (model 3) showed that women from Province-2 had 2.5 times higher
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24 239 (aOR=2.51, 95% CI: 1.79-3.53) odds of anaemia compared to women from Bagmati province.
25
26 240 Women who belonged to communities with a high percentage of the wealthy households had
27
28 241 1.48 times higher (aOR=1.48, 95% CI: 1.21-1.80) odds of anaemia compared to those coming
29
30 242 from low percentage of the wealthy household; and women residing in communities with a high
31
32 243 percentage of community female education had 1.39 times higher (aOR=1.39, 95% CI: 1.15-
33
34 244 1.68) odds of anaemia compared to those coming from the communities with a low percentage of
35
36 245 education. The ICC in model 3 showed that differences between communities accounted for
37
38 246 about 11.1% of the variation in anaemia among WRA. In addition, the PCV indicated that 33.9%
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40 247 of the variation in WRA anaemia between communities was explained by community-level
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42 248 characteristics.

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49 249 In model 4, women who had no formal education were found to have 2 times higher (aOR=2.07,
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51 250 95% CI: 1.21-3.54) odds of anaemia compared to women who had higher education. Women
52
53 251 from middle socio-economic family had higher (aOR=1.66, 95% CI: 1.02-2.68) odds of anaemia
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55 252 compared to poorest counterparts. Women who came from Province-2 (aOR=3.12, 95% CI:

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3 253 1.1.58-6.14) had higher odds of anaemia compared to Bagmati province. The older women had
4
5 254 52% lower (aOR=0.48, 95% CI: 0.26-0.91) odds of anaemia compared to younger women, and
6
7
8 255 women who used hormonal contraceptive methods had 43% lower (aOR=0.57, 95% CI: 0.39-
9
10 256 0.84) odds of anaemia compared to who did not use contraceptive methods. After the inclusion
11
12 257 of both the individual and community-level variables in model 4, the ICC indicated that 10% of
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14
15 258 the variability in anaemia among WRA was attributable to the difference between communities.
16
17 259 Furthermore, the PCV indicated that 39.5% of the variation in anaemia among WRA between
18
19 260 communities was explained by both individual and community-level characteristics (Table 2).
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21

22 261 **Spatial data analysis**

23
24 262 Figure 3(a) shows the prevalence of anaemia among WRA across provinces in Nepal. A severe
25
26 263 anaemia prevalence ($\geq 40\%$) among WRA was seen in Province-2, followed by Province-1 and 5.
27
28
29 264 The prevalence of moderate anaemia (20-39.9%) was observed in Bagmati, Gandaki, Karnali,
30
31 265 and Sudurpaschim province. Mild anaemia (prevalence $<19.9\%$) was not found in any provinces.
32
33 266 Figure 3(b) shows the prevalence of anaemia among WRA across 75 districts in Nepal. The
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35 267 prevalence rate of severe anaemia was observed in 29 out of 75 districts, and mild anaemia was
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37
38 268 found in only eight districts (Figure 3).
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41 269 The standardized prevalence ratio by provinces (standardized to the national mean prevalence of
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43 270 41%) are shown in Figure 4 (a), and ranged from 0.68 to 1.4. The higher prevalence ratio of
44
45 271 anaemia was found in Province-2, whereas a lower prevalence ratio was observed in Bagmati,
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48 272 Gandaki, and Karnali province. Figure 4 (b) shows the standardized prevalence ratio across the
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50 273 75 districts, and ranged from 0.76 to 1.59. The higher standardized prevalence ratio of anaemia
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52 274 was observed in 17 out of 75 districts across the country (Figure 4).
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3 275 The spatial pattern and distribution of anaemia among WRA at the cluster level are displayed in
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5 276 Figure 5. The spatial analysis at the cluster level showed that statistically significant high
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8 277 hotspots of anaemia were observed in the southern Terai of the country bordering India:
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10 278 Province-2 (8 districts), Province-1 (4 districts), southern plain of the Bagmati province (1
11
12 279 district), and southwestern region of Province-5 (3 districts). Whilst, cold spots of anaemia were
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15 280 observed in most of the hilly regions of the country (Figure 5).
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18 281 **DISCUSSION**

19 282 **Overall findings**

20 283 In this study, more than 40% of WRA were anaemic which implies that anaemia is still a serious
21
22 284 public health problem in Nepal.[33] Geographical pattern showed that anaemia is a serious
23
24 285 public health problem in three of the seven provinces and 29 out of the 75 districts in Nepal. The
25
26 286 higher prevalence of anaemia was observed in the southern Terai bordering India particularly in
27
28 287 Province-2, and the upper Himalayan region of the country. The spatial analysis at the cluster
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31 288 level showed that high hot spots of anaemia were observed in Terai region especially in
32
33 289 Province-1, 2 and 5. A possible reason could be that WRA from Terai region and high
34
35 290 mountainous regions are more likely to be of a lower socioeconomic status and thus can afford
36
37 291 less diversified diet compared to other provinces and districts.[9,26]
38
39 292 In the southern Terai of Nepal, despite ecological richness, people have long suffered from a
40
41 293 deficiency of micronutrients such as Vitamin A, iron and zinc,[23] and a high burden of
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43 294 hookworm infestation and a high prevalence of malaria which are established to contribute to
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45 295 anemia.[27] Diet of women in the Terai lack diversity and, nutrient adequacy which pose an
46
47 296 increased risk of anaemia.[24] Furthermore, the Terai region of Nepal is considered to be high
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49 297 malaria-endemic region,[28,29,50] and higher risk of malaria is associated with a higher risk of
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3 298 anaemia.[27] The majority (90%) of the population from Terai region rely on groundwater
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5 299 especially shallow tube well for domestic purposes including drinking.[30] Higher arsenic
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7 300 concentration can inhibit haem iron metabolism and increase erythrocyte hemolysis.[51]
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9 301 Consequently, drinking arsenic-containing water poses an increased risk of anaemia among
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11 302 women.[52] Arsenic exposure was more likely to cause anemia among women in
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13 303 Bangladesh.[53]
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15 304 The spatial analysis at the cluster level found that high hotspots of anaemia were also observed in
16
17 305 southwestern region (Province-5), particularly Banke, Bardiya and Kanchanpur district. A
18
19 306 previous study highlighted that Glucose 6 phosphate dehydrogenase deficiency (G6PDd), sickle
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21 307 cell trait (SCT), and sickle cell anaemia (SCA) as the most common disorder in Tharu
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23 308 community living in southwestern Province-5.[54,55] G6PDd and haemoglobinopathies are
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25 309 established to cause anaemia among WRA.[36]
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27 310 The geographical variance of high cases of anaemia across the high mountainous region could be
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29 311 attributed to food insecurity, low dietary diversity, [9,24,31] less calorie diet,[24] poor health
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31 312 service coverage,[22] high illiteracy, gender based-inequality, and poor health seeking
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33 313 behaviour.[20,21]
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40 **Socio-demographic characteristic among women and anaemia**

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42 315 Women who had no formal education, and those who came from middle socio-economic
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44 316 households, and from younger age group were at increased risk of anaemia. These findings
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46 317 corroborate with previous studies from low and middle-income countries (LMICs) including
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48 318 Ethiopia,[32] India,[56] Tanzania,[57] Rwanda,[58] Timor-Leste,[59] and Bangladesh.[60]
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50 319 Studies from Ethiopia and Tanzania suggest that higher-level education might enable women to
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52 320 gain knowledge and improve attitude which in turn can promote them to adopt healthier lifestyle
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3 321 including good nutrition habits, better health-seeking behavior, and good hygiene practices that
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5 322 can prevent anaemia.[32,57]
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8 323 Anaemia is a multifaceted problem where nutrition and household economic status are
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10 324 considered to have a synergistic association.[58] Women belonging to poorer households are
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12 325 more likely to be anaemic compared to those living in middle or richer households in most of the
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14 326 countries.[14,32,58] Contrastingly, this study revealed that poorer Nepalese women were less
15
16 327 likely to be anaemic. In this study, prevalence of anaemia was 32.3% in poorest, 41.5% in
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18 328 poorer, 48.9% in middle, 43.4% in richer, and 35.9% in richest households. These results are in
19
20 329 agreement with a previous study that used the data from the 2016 Nepal National Micronutrient
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22 330 Status Survey (NNMSS).[36] The possible reason could be Nepal is an agrarian-based country
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24 331 and the staple diet may be similar for most of the households.[61] Most of the Nepalese people
25
26 332 consume iron-rich staple foods including cereal, grains, lentils and animal source food regardless
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28 333 of wealth status.[61] Future research are critical to explore the association of household
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30 334 economic status and anaemia among WRA in Nepal.

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36 335 In this study, the prevalence of anaemia was found to decrease with increasing age. These
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38 336 findings are consistent with studies from Ethiopia,[32] Demographic Republic of Congo,[62] and
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40 337 Benin.[52] The possible reason could be that the low fertility rates are high among older
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42 338 women.[32] Relatively higher prevalence of anaemia in a younger age could be because of lower
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44 339 dietary iron intake and the additional demand for iron to compensate iron loss during
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46 340 menstruation, pregnancy, and lactation.[1] High prevalence of anaemia among younger women
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48 341 could also be attributed to teenage pregnancy.[35]
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53 342 **Effect of contraceptive use on anaemia**

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3 343 In this study, the use of hormonal contraceptive methods was less likely to be associated with
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5 344 anaemia among WRA which is consistent with previous studies conducted in Nepal,[35]
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7 345 Rwanda,[58] Tanzania,[57] and Ethiopia.[63] This could be due to multiple reasons. For
8
9 346 instance, the plausible primary mechanism could be the use of hormonal contraceptive lead to
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11 347 less blood loss during the menstruation.[64,65] Almost 100-150 mg of iron is lost during
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13 348 menstrual bleeding.[66] Subsequently, this may directly or indirectly furnish iron loss among
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15 349 women at high risk for iron-deficiency anaemia.[65,66] A previous study also suggested that
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17 350 Depo-Provera injections were more likely to increase haemoglobin concentration among WRA
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19 351 in Nepal.[67]
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24 352 **Community-level factors and anaemia**

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26 353 In this study, estimated intra-class correlation (ICC) shows that about 10.3% of the community
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28 354 level variability was attributable to the difference between communities among WRA. The PCV
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30 355 indicated that 39.5% of the variation in WRA anaemia between communities was explained by
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32 356 both individual and community-level characteristics. This finding is in line with the study
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34 357 conducted in Ethiopia, where both individual- and community-level factors accounted for about
35
36 358 43% of the variability of anaemia among WRA.[32] Women who came from Province-2 had
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38 359 more than three times higher odds of anaemia compared to Bagmati province. A possible reason
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40 360 could be due to the fact that WRA from Province-2 are more likely to be of a lower
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42 361 socioeconomic status and are less likely to afford a diverse diet.[9,26] In addition, compliance
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44 362 rate of recommended dose of iron tablets amongst the pregnant mothers in Province-2 was also
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46 363 low (28%) compared to other provinces.[9] This study showed that promoting community
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48 364 female education has a potential role in lowering the likelihood of anaemia which echoes with a
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50 365 study from Malawi.[38] This could be explained by the fact that higher community education
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3 366 provides a context where women are enabled to gain nutritional knowledge and material
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5 367 resources[25] that can increase consumption of iron absorption enhancers such as vitamin C,
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7 368 phytates (whole grains, legumes), and calcium (dairy products). With increase knowledge,
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9 369 women may also reduce the intake of tea, coffee, and some spices which are known to inhibit the
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11 iron absorption.[68]
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14 15 371 **Strength and limitation**

16 372 This is the first study to explore the spatial pattern and multilevel analysis of anaemia among
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18 373 WRA in Nepal using stringent cluster sampling of a comprehensive nationally representative
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20 374 data. The combined statistical methods including multilevel and spatial analysis used in this
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22 375 study provides important insights on the role of contextual factors and geographical patterns in
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24 376 the occurrences of anaemia among WRA in Nepal. This study has some limitations. The cross-
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26 377 sectional design of the study does not allow us to establish the causality. This study relied on
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28 378 haemoglobin as the measure of anaemia; further studies should consider other indices that
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30 379 include total ferritin and total iron binding capacity to differentiate the types of anemia. Since
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32 380 this study is based on the secondary data analysis, we are unable to incorporate potential
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34 381 confounding factors of anaemia such as nutrient intake, worm infestations, malaria and other
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36 382 non-modifiable risk factors.
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43 383 **CONCLUSION**

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45 384 This study highlighted a high prevalence of anaemia among WRA across Nepal. At an individual
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47 385 level, women who had no formal education, those who came from middle socio-economic class
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49 386 families were more likely to be anaemic, whereas, older women, and those who used hormonal
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51 387 contraceptive were less likely to be anaemic. At the community level, low community female
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53 388 education, and women living in Province-2 were associated with increased odds of anaemia. In
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3 389 the spatial analysis, our study found statistically significant hot spots in the southern Terai region
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5 390 particularly in Province-1 (4 districts), Province-2 (8 districts), Bagmati province (1 district), and
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7 391 Province-5 (3 districts). Multi-pronged approaches including nutritional, and non-nutritional
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9 392 anaemia prevention and control strategies can benefit by tailoring the programs to the high risk
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11 393 provinces and districts with high burden of anemia.
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28
29 400 DR Su designed, conceptualized the study, data extraction and analysis, interpreted the results,
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31 401 generate the map, writing an original draft, reviewing, editing, and overall supervision of the
32
33 402 research. SS generate the map, and writing an original draft. DR Si, BA, and PMSP writing an
34
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37 404 approved the final manuscript.
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50 408 **Competing interests**

51
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55 410 **Patient consent for publication**

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3 411 Not required
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7 412 **Ethical approval**

8 413 The NDHS 2016 was approved by the Nepal Health Research Council (NHRC) and ICF Macro.
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12 414 **Data sharing statement**

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14 415 Dataset used in this study is publicly available from the DHS website (URL:

15
16 416 <https://www.dhsprogram.com/data/available-datasets.cfm>).
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49 620 **Figure 1 Flow chart for sample size selection**

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52 621 **Figure 2 Study area map and observed anaemia prevalence among women of reproductive**
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55 622 **age for the NDHS survey clusters**

623 **Table 1 Socio-demographic characteristics and prevalence of anaemia among women of**
 624 **reproductive age by determining factors (n=6,414)**

625 **Table 2 Multilevel mixed-effects logistic regression for individual and community-level**
 626 **factors affecting anaemia among women of reproductive age (n=6,414)**

627 **Figure 3 (a) Prevalence of anaemia among women of reproductive age across provinces. 3**
 628 **(b) Prevalence of anaemia among women of reproductive age across districts**

629 **Figure 4 (a) Standardized prevalence ratio of anaemia among women of reproductive age**
 630 **across provinces. 4 (b) Standardized prevalence ratio of anaemia among women of**
 631 **reproductive age across districts (standardized to the national mean prevalence of 41%)**

632 **Figure 5 Spatial pattern and distribution of hot and cold spots of anaemia among women of**
 633 **reproductive age at cluster level in Nepal**

634
 635 **Table 1 Socio-demographic characteristics and prevalence of anaemia among women of**
 636 **reproductive age by determining factors (n=6,414)**

Variables	Total sample	Prevalence of any anemia		p-value ^{1,2}
		Frequency (%)	Frequency (%)	
Overall prevalence	6414	2614 (40.7)	[38.5-42.9]	
Severe anemia	17 (0.3)			
Moderate anemia	450 (7)			
Mild anemia	2147 (33.4)			
Hemoglobin level, mean (\pmSD)	12.3 \pm 1.5	10.8 \pm 1.1		<0.001*
Individual-level factors				
Age in years, mean (\pmSD)	29.1 \pm 9.7	28.4 \pm 9.5		<0.001*
Age				<0.001*
15-24	2443 (38.1)	1065 (43.5)	[40.6-46.5]	
25-34	1971(30.7)	814 (41.3)	[38.4-44.2]	
\geq 35	2000(31.1)	735 (36.7)	[34-39.6]	
Education				0.086
No education	2144 (33.4)	892 (41.5)	[38.2-44.9]	

Primary	1069 (16.6)	411 (38.4)	[34.2-42.8]	
Secondary	2277 (35.5)	972 (42.6)	[39.6-45.7]	
Higher	924 (14.4)	339 (36.7)	[32.3-41.3]	
Occupation				0.084
Not working	2096 (32.6)	899 (42.9)	[39.6-46.2]	
Working	4318 (67.3)	1715 (39.7)	[37.2-42.2]	
Wealth index				<0.001*
Poorest	1093 (17)	353 (32.3)	[28.7-36.1]	
Poorer	1225 (19.1)	508 (41.5)	[37.9-45.2]	
Middle	1317 (20.5)	645 (48.9)	[45.1-52.8]	
Richer	1441 (22.4)	626 (43.4)	[38.8-48.1]	
Richest	1338 (20.8)	482 (35.9)	[32.1-40.1]	
BMI, mean (\pmSD)	22 \pm 3.8	21.4 \pm 3.6		<0.001*
BMI (n=6411)				<0.001*
Normal	3925 (61.2)	1673 (42.6)	[39.7-45.5]	
Underweight	1077 (16.8)	518 (48.1)	[44.6-51.6]	
Overweight/obesity	1408 (21.9)	423 (30)	[26.7-33.4]	
Currently pregnant				
No	6124 (95.4)	2481 (40.5)	[38.3-42.7]	0.081
Yes	290(4.5)	133 (46)	[39.4-52.7]	
Currently breastfeeding				
No	4988 (77.7)	1961 (39.3)	[37.1-41.6]	<0.001*
Yes	1426 (22.2)	653 (45.8)	[42.2-49.3]	
Total children ever born				0.612
No child	1842 (28.7)	770 (41.8)	[38.2-45.4]	
1-3 child	3386 (52.8)	1358 (40.1)	[37.7-42.5]	
4+ child	1186 (18.4)	487 (41)	[37.2-44.8]	
Current contraceptive use				<0.001*
Not using	3832 (59.7)	1625 (42.4)	[39.8-45]	
Natural/barrier/permanent	1676 (26.1)	723 (43.1)	[40.1-46.1]	
Hormonal	829 (12.9)	241 (29.1)	[25.2-33.3]	
IUD	77 (1.2)	25 (33)	[20.8-47.9]	
Cigarette/smoking				<0.001*
Smoking	573 (8.9)	156 (28.9)	[24.7-33.4]	
Not smoking	5841 (91.1)	2449 (41.9)	[39.7-44.1]	
MDD-W (n=1131)				0.025*
Not diverse	558 (49.3)	284 (51)	[45.8-56.1]	
Diverse	573 (50.6)	248 (43.1)	[38.2-48.2]	
Community-level factors				

Place of residence				0.202
Urban	4029 (68.8)	1596 (39.6)	[36.8-42.4]	
Rural	2385 (37.1)	1018 (42.6)	[39-46.3]	
Province				<0.001*
Province-1	1073 (16.7)	464 (43.2)	[37.9-48.7]	
Province-2	1285 (20)	742 (57.7)	[52.7-62.6]	
Bagmati	1408 (21.9)	409 (29)	[24.8-33.5]	
Gandaki	627 (9.7)	176 (28)	[23-33.6]	
Province-5	1086 (16.9)	472 (43.4)	[39.4-47.5]	
Karnali	369 (5.7)	129 (34.9)	[29.9-40.2]	
Sudurpaschim	566 (8.8)	222 (39.3)	[33.6-45.2]	
Community female education^a				<0.001*
Low	2936 (45.7)	1406 (47.8)	[44.8-50.9]	
High	3478 (54.2)	1208 (34.7)	[31.9-37.6]	
Community female wealth index^b				<0.001*
Low	4107 (64)	1820 (44.3)	[41.2-47.3]	
High	2307 (35.9)	795 (34.45)	[31.1-37.8]	
Source of drinking water (n=6084)				0.004*
Improved	5537 (91)	2286 (41.2)	[38.9-43.6]	
Not improved	547 (8.9)	184 (33.7)	[29.2-38.5]	
Type of toilet facility (n=6084)				<0.001*
Improved	5117 (84.1)	1972 (38.5)	[36.3-40.7]	
Not improved	967 (16)	498 (51.4)	[46-56.8]	
Frequency and percentage (%) are weighted				
^{1, 2} denotes Pearson Chi-Square test for categorical variables and independent t-test for continuous variables				
*denotes statistically significant at p<0.05				
^a mean percent of households wealth quintiles categorized richer and richest and above				
^b mean percent of women with primary education level and above				
BMI: Body Mass Index				
MDD-W: Minimum Dietary Diversity for Women				

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639 **Table 2 Multilevel mixed-effects logistic regression analysis for individual and community-**
 640 **level factors affecting anemia among women of reproductive age (n=6,414)**

Variables	Model 1 Empty model	Model 2 Individual-level factors	Model 3 community-level factors	Model 4 Individual and community-level factors
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Fixed-effects model				
Individual-level factors				
Age				
15-24		0.76 (0.56-1.04)		0.73 (0.54-1.01)
25-34		Ref		Ref
≥35		0.46 (0.24-0.88)*		0.48 (0.26-0.91)*
Education				
No education		2.23 (1.35-3.67)**		2.07 (1.21-3.54)*
Primary		1.56 (0.96-2.56)		1.41 (0.84-2.38)
Secondary		1.63 (1.06-2.49)*		1.52 (0.96-2.38)
Higher		Ref		Ref
Occupation				
Not working		Ref		Ref
Working		1.01 (0.75-1.36)		0.91 (0.66-1.25)
Wealth index				
Poorest		Ref		Ref
Poorer		1.50 (1.00-2.24)		1.49 (0.97-2.29)
Middle		1.81 (1.18-2.78)**		1.66 (1.02-2.68)*
Richer		1.46 (0.92-2.30)		1.39 (0.84-2.32)
Richest		1.61 (0.90-2.87)		1.32 (0.69-2.52)
BMI (n=6411)				
Normal		Ref		Ref
Underweight		1.16 (0.82-1.64)		1.08 (0.74-1.56)
Overweight/obesity		0.90 (0.59-1.37)		1.03 (0.66-1.61)
Currently pregnant				
No		0.82 (0.42-1.62)		1.08 (0.53-2.20)
Yes		Ref		Ref
Currently breastfeeding				
No		Ref		Ref
Yes		1.38 (0.65-2.91)		1.59 (0.71-3.60)
Total children ever born				
No child		Ref		Ref

1-3 child		-		-
4+ child		1.18 (0.74-1.86)		1.02 (0.63-1.63)
Current contraceptive use				
Not using		Ref		Ref
Natural/barrier/permanent		1.26 (0.87-1.82)		1.26 (0.85-1.85)
Hormonal		0.61 (0.42-0.86)*		0.57 (0.39-0.84)*
IUD		2.54 (0.69-9.32)		2.07 (0.68-10.61)
Cigarette/smoking				
Smoking		0.81 (0.44-1.50)		1.21 (0.63-2.33)
Not smoking		Ref		Ref
MDD-W (n=1131)				
Not diverse		1.24 (0.93-1.64)		1.03 (0.76-1.40)
Diverse		Ref		Ref
Community-level factors				
Place of residence				
Urban			Ref	Ref
Rural			1.01 (0.83-1.21)	0.89 (0.64-1.24)
Province				
Province-1			1.70 (1.23-2.34)**	3.04 (1.59-5.82)**
Province-2			2.51 (1.79-3.53)***	3.12 (1.58-6.14)**
Bagmati			Ref	Ref
Gandaki			0.90 (0.64-1.26)	0.77 (0.39-1.51)
Province-5			1.60 (1.16-2.21)**	2.43 (1.31-4.55)**
Karnali			1.19 (0.85-1.66)	1.69 (0.88-3.19)
Sudurpaschim			1.54 (1.11-2.15)*	1.64 (0.84-3.17)
Community female education^a				
Low			1.39 (1.15-1.68)***	-
High			Ref	-
Community wealth index^b				
Low			1.48 (1.21-1.80)***	-
High			Ref	-
Source of drinking water (n=6084)				
Improved			Ref	Ref
Not improved			1.05 (0.84-1.30)	1.13 (0.68-1.86)

Type of toilet facility (n=6084)				
Improved			Ref	Ref
Not improved			1.03 (0.84-1.24)	0.95 (0.63-1.45)
Random-effects model				
Community-level variance (τ) (SE)	0.627 (0.073)***	0.531 (0.207)***	0.414 (0.056)***	0.379 (0.201)**
ICC (%)	16	13.9	11.1	10.3
PCV (%)	Ref	15.3	33.9	39.5
Model fit statistics				
AIC	8322.6	1558.6	7838.4	1397.9
BIC	8336.1	1669.6	7925.8	1551.4
Log-likelihood	4159.3	757.3	3906.2	667.9
<p>Model 1 (empty model): without adjusted predictors variables; model 2: adjusted for individual-level factors; model 3: adjusted for community-level factors; model 4: adjusted for both individual-level and community-level factors.</p> <p>*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$,</p> <p>aOR=adjusted odds ratio, CI: confidence interval, Ref: reference category, SE: standard error, ICC: intra-class correlation, PCV: percentage change in variation, AIC: Akaike information criterion, BIC: Bayesian information criterion</p> <p>^a mean percent of households wealth quintiles categorized richer and richest and above</p> <p>^b mean percent of women with primary education level and above</p> <p>community female education and community wealth index is omitted in Model 4 due to collinearity</p>				

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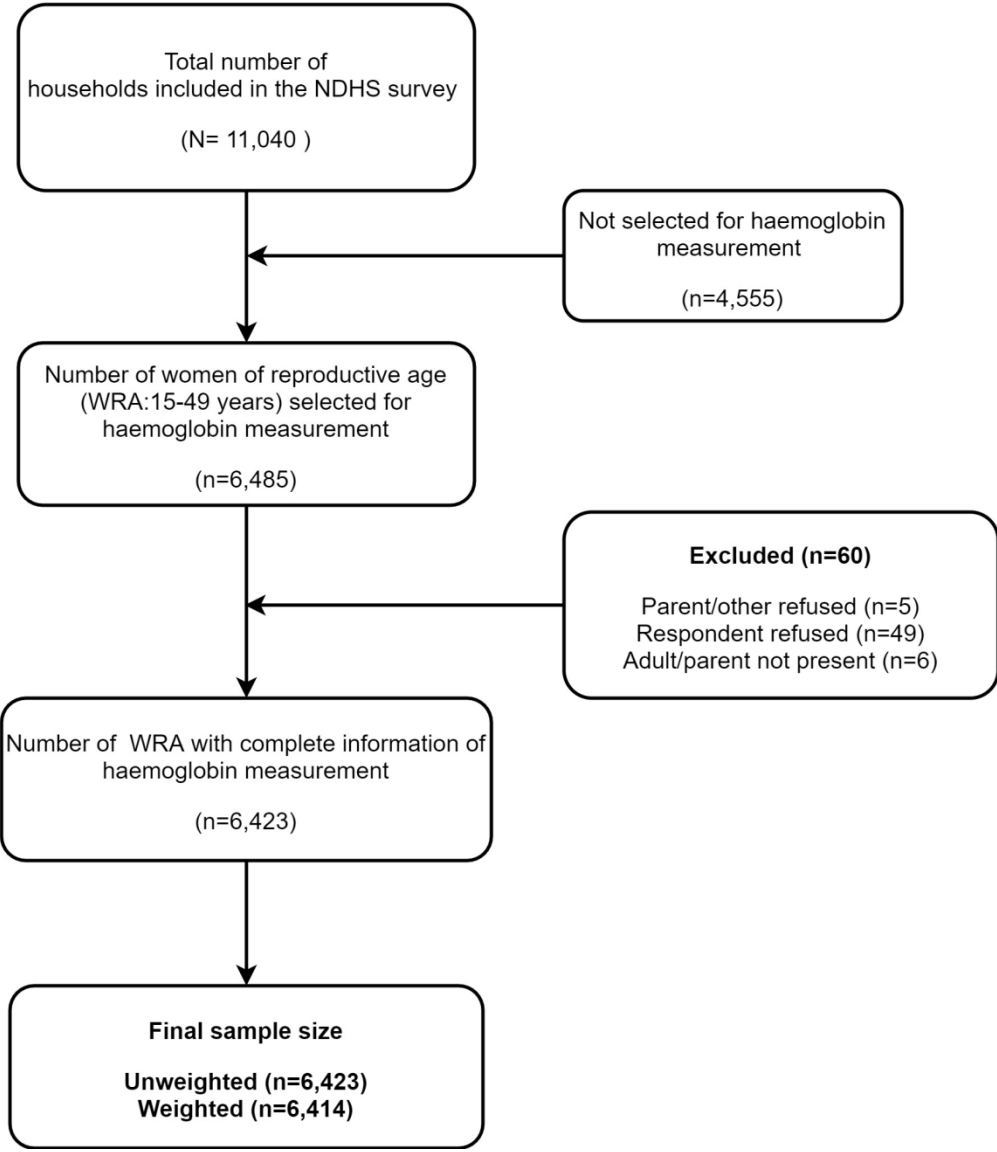


Figure 1 Flow chart for sample size selection

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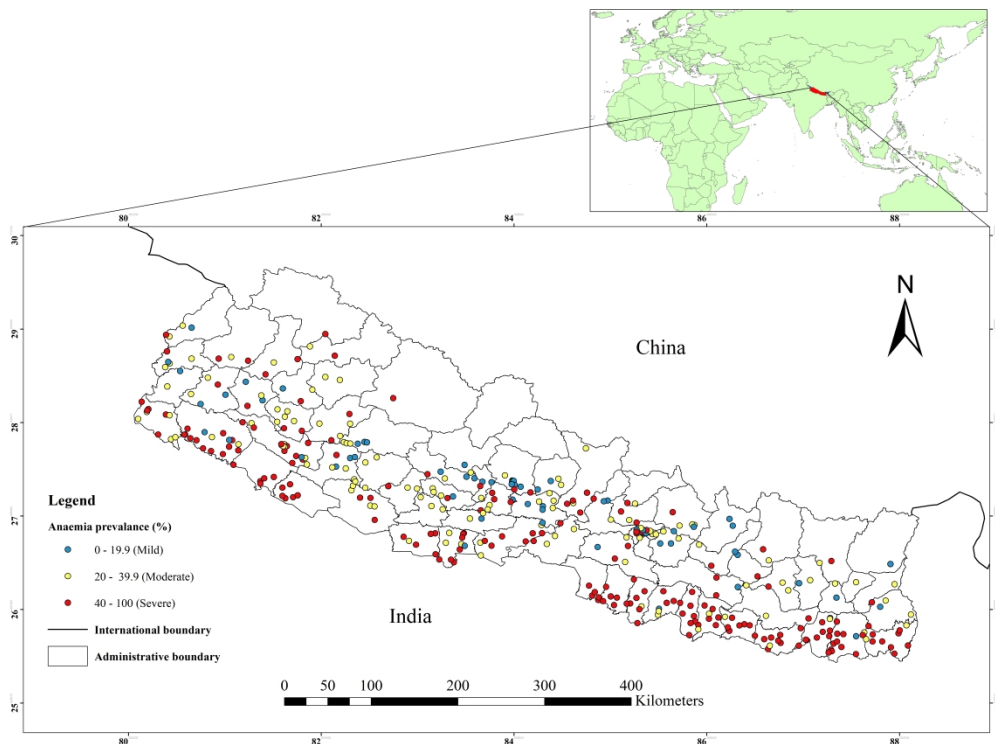
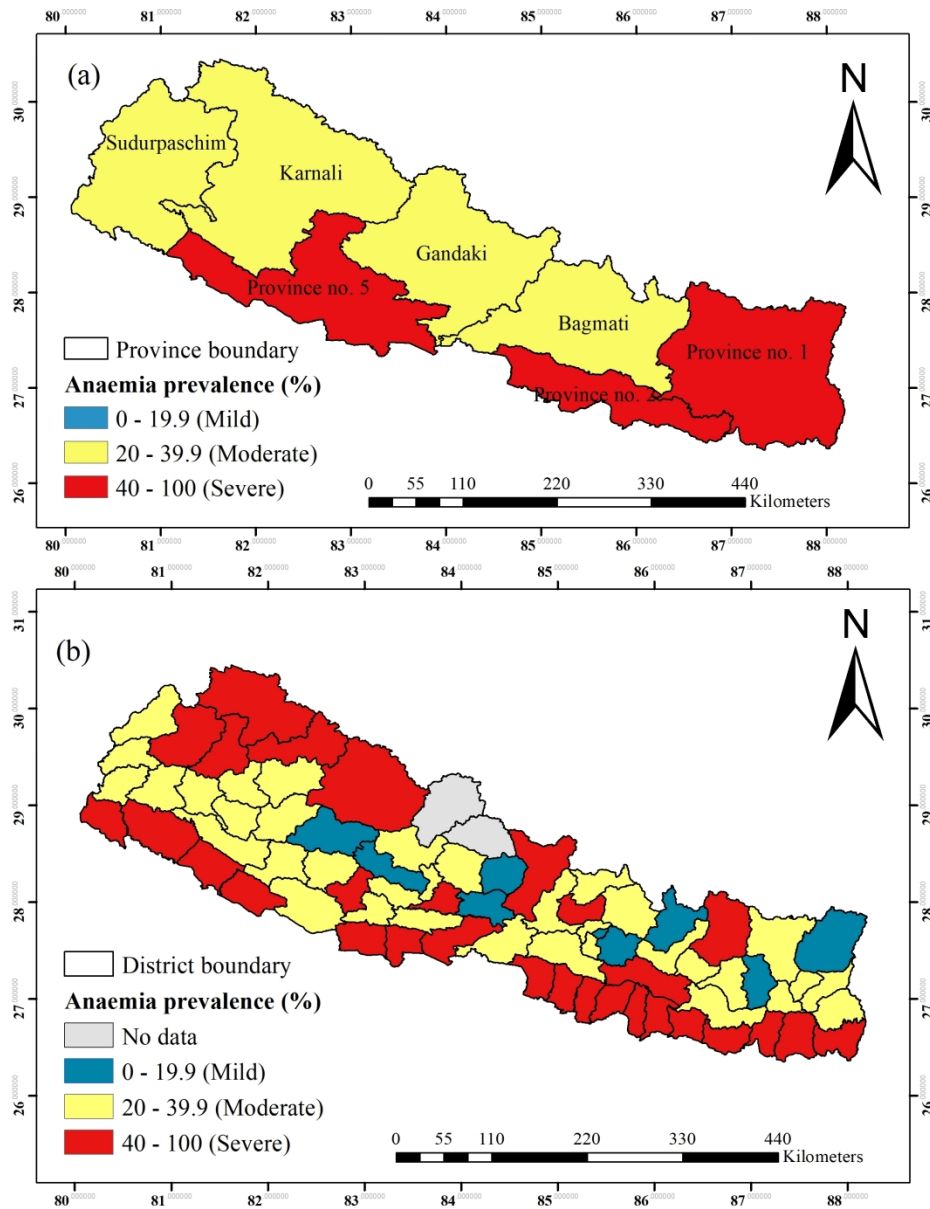


Figure 2 Study area map and observed anaemia prevalence among women of reproductive age for the NDHS survey clusters

609x457mm (300 x 300 DPI)



45 Figure 3 (a) Prevalence of anaemia among women of reproductive age across provinces. 3 (b) Prevalence of
46 anaemia among women of reproductive age across districts

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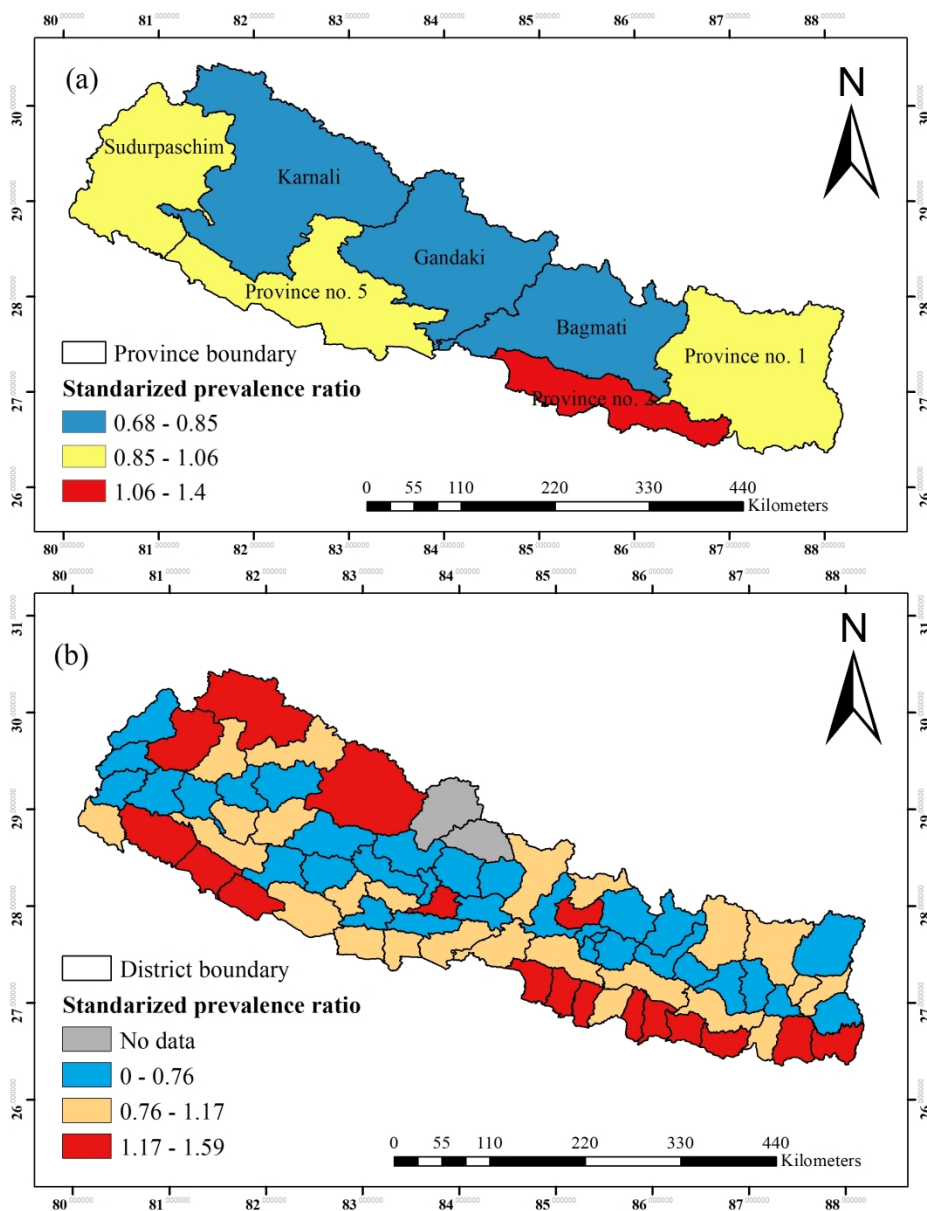


Figure 4 (a) Standardized prevalence ratio of anaemia among women of reproductive age across provinces.
 4 (b) Standardized prevalence ratio of anaemia among women of reproductive age across districts
 (standardized to the national mean prevalence of 41%)

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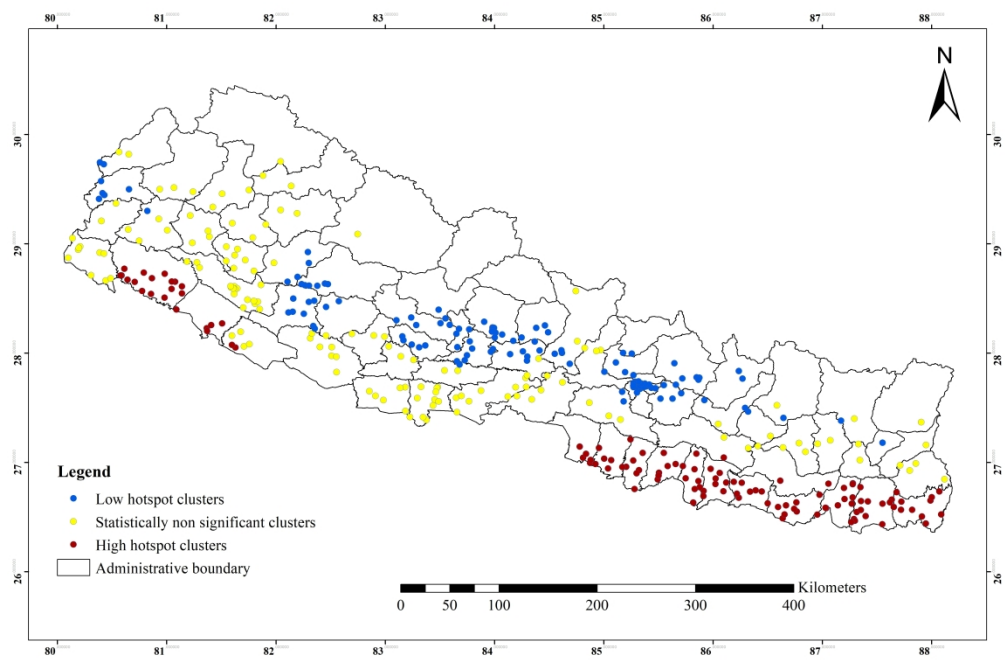


Figure 5 Spatial pattern and distribution of hot and cold spots of anaemia among women of reproductive age at cluster level in Nepal

457x304mm (300 x 300 DPI)

S1 Table Plan for data coding and description of the study variables

Study variables	Coding category for analysis
Age in years	1=15-24; 2=25-34; 3=35-49
Education	1=No education; 2=Primary; 3=Secondary; 4=Higher
Occupation	1= Not working; 2=Working (professional/technical/managerial, clerical, sales/services, agriculture-self-employed, skilled manual, unskilled manual, others)
Wealth index	1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest
Body mass index (BMI)	1=Normal (18.5-24.99); 2=Underweight(<18.5); 3=Overweight/Obesity(≥ 25)
Currently pregnant	1=No; 2=Yes
Currently breastfeeding	1=No; 2=Yes
Total children ever born	1= No child; 2=1-3 child; 3=4+ child
Current contraceptive use	1=Not using; 2=Natural/barrier/permanent (Male condom, female sterilization, male sterilization, periodic abstinence, withdrawal, other traditional, lactation amenorrhea); 3=Hormonal (Pill, Injections, Implants/Norplant's, Emergency contraception); 4=IUD
Cigarette/smoking	1= Smoking; 2=Not smoking
Minimum dietary diversity for women (MDD-W)	1=Not diverse (consume <5 food groups); 2=Diverse (Consume ≥ 5 food groups)
Residence	1=Urban; 2=Rural
Province	1=Province-1; 2=Province-2, 3=Bagmati Province; 4=Gandaki Province; 5=Province-5; 6=Karnali Province; 7=Sudurpaschim Province
Community female education	1=Low (mean percent of women with lower primary education level was 0-25%); 2=High (mean percent of women with primary education level above 25%)
Community wealth index	1=Low (mean proportion of women from richest (rich, richest) households in the community was 0-21%); 2=High (mean

	proportion of women from richest (rich, richest) households in the community was above 21%)
Source of drinking water	1=Improved (piped water into dwelling, piped water to yard/plot, public tap or standpipe, tube well or borehole, protected dug well-protected spring and rainwater); 2=Not improved (Piped to neighbor, unprotected well, river, dam ponds, lake, and rainwater)
Type of toilet facility	1=Improved facility (flush toilet, piped sewer system, septic tank, flush/pour flush to pit latrine, ventilated improved pit latrine, pit latrine with slab, and composting toilet); 2=Not improved (flush to somewhere, flush don't know where, pit latrine without slab/open pit, and no facility/bush/field)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	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	8-10
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-10
		(b) Describe any methods used to examine subgroups and interactions	8-10
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA
Results			

Participants	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	10
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	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	11-14
		(b) Report category boundaries when continuous variables were categorized	6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	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	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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1 **Factors affecting anaemia among women of reproductive** 2 **age in Nepal: a multilevel and spatial analysis**

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15 **ABSTRACT**

16 **Objective:** The main objective of this study was to explore the factors affecting anaemia
17 among women of reproductive age (WRA) in Nepal using spatial and multilevel epidemiological
18 analysis.

19 **Design:** This cross-sectional study analyzed the data from the 2016 Nepal demographic and
20 health survey (NDHS 2016). The spatial analysis was performed using ArcGIS software V.10.8
21 to identify the hot and cold spots of anaemia among WRA (15 to 49 years). Data were analyzed
22 using multilevel mixed-effect logistic regression analysis.

23 **Setting:** Nepal

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4 24 **Participants:** A total of 6,414 WRA were included in the analysis.
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7 25 **Main outcome measure:** Anaemia defined by World Health Organization (WHO) as
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9 26 hemoglobin level less than 12g/dL in non-pregnant women and less than 11g/dL in pregnant
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11 27 women.
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15 28 **Results:** The spatial analysis showed that statistically significant hotspots of anaemia were in
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17 29 the southern Terai region (4 districts in Province-1, 8 districts in Province-2, 1 district in
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19 30 Bagmati province, and 3 districts in Province-5) of Nepal. At the individual level, women who
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21 31 underwent female sterilization (aOR: 3.61, 95% CI: 1.10-11.84), with no education (aOR: 1.99,
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23 32 95% CI: 1.17-3.39), and from middle socio-economic class families (aOR: 1.65, 95% CI: 1.02-
24
25 33 2.68) were more likely to be anemic, whereas, older women (≥ 35 years) (aOR: 0.51, 95% CI:
26
27 34 0.26-0.97), and those women who were using hormonal contraceptives (aOR: 0.63, 95% CI:
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29 35 0.43-0.90) were less likely to be anaemic. At the community level, women from Province-2
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31 36 (aOR=2.97, 95% CI: 1.52-5.82) had higher odds of being anaemic.
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37 37 **Conclusion:** WRA had higher odds of developing anaemia, and it varied by the geographical
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39 38 regions. Nutrition specific and nutrition sensitive interventions can tailor the interventions based
40
41 39 on the factors identified in this study to curb the high burden of anaemia.
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Strengths and limitations of this study

- This study utilizes comprehensive, and nationally representative data with haemoglobin level.
- The combined statistical methods including multilevel and spatial analysis were applied, which takes into account the role of geographical risk profile and determinants of anaemia among WRA in Nepal.
- Due to the cross-sectional design, it was difficult to determine the cause-and-effect relationships between the predictors and outcome variable (anaemia).
- Other potential confounding factors of anaemia such as nutrient intake, worm infestations, other non-modifiable risk factors, and other qualitative factors were beyond the scope of this study.
- This study could not distinguish the types of anaemia such as nutritional, genetic and infectious.

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43 INTRODUCTION

44 Anaemia remains a significant public health problem in developing countries despite advances in
45 health science.[1] Approximately one-third of the population is affected by anaemia
46 globally.[2,3] South and Southeast Asian countries account for the largest burden of anaemia
47 with estimated prevalence of 52.5% among women of reproductive age (WRA).[4] The highest
48 prevalence over the past 26 years was 55.2% in 1990.[5] Despite the implementation of a ‘1000
49 days nutrition program’ among various other programs, targeted to a mother with newborn
50 babies in South Asia, the reduction in anaemia among pregnant women has not been
51 significant.[6] To accelerate reduction of anaemia, the World Health Assembly has set a target of
52 achieving a 50% reduction of anaemia among WRA by 2025 relative to 2010.[7] However, not a
53 single South Asian country is on the way to achieve the 2025 targets.[8]

54 The Government of Nepal has set targets in line with various global and national indicators such
55 as Multi-Sectoral Nutrition Plan II (2018–2022), and Sustainable Development Goals (SDGs)
56 2030 for the reduction of anaemia. [9,10] Despite the historic efforts in preventing anaemia
57 through the implementation of national nutrition programs and policies including iron-folic acid
58 supplementation across the country, the prevalence of anaemia among WRA has been increasing
59 steadily from 35% in 2011 to 41% in 2016.[11,12] These figures suggest that anaemia continues
60 to be a serious public health problem in Nepal.[13]

61 Anaemia in WRA is associated with multiple conditions and consequences such as preterm
62 delivery,[14] miscarriage,[15] low birth weight,[16] child growth faltering, impairment of
63 cognitive function, increased susceptibility to infection, and poverty.[17,18] It is also associated
64 with increased risk of prenatal and maternal mortality.[16,19] Approximately 20% of maternal

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3 65 deaths are caused by anaemia and it is also considered as an additional risk factor for 50% of all
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5 66 maternal deaths.[20,21]
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8 67 Contributing factors and distribution of anaemia include a complex interplay of political,
9
10 68 ecological, social, and biological factors.[22] In Nepal, anaemia among WRA is associated with
11
12 69 various socio-ecological factors. In the southern Terai of Nepal, low community education
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14 70 status, gender based-inequality, poor health seeking behavior,[23–25] inadequate dietary intake
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16 71 during pregnancy,[26–28] lack of diversified diet,[12,27,29] high burden of hookworm infection
17
18 72 and malaria,[30–32] and high amount of arsenic in potable water[33] were identified as factors
19
20 73 contributing to anaemia. On the other hand, high prevalence of anaemia in the mountainous
21
22 74 region were attributed to among others, food insecurity, and low dietary diversity,[12,27,34]
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24 75 poor health services,[25] illiteracy, and gender based-inequality.[23,24]
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30 76 To decrease the burden of anaemia, it is necessary to generate adequate evidence in terms of the
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32 77 role and contribution of individual, household and the community level factors along with the
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34 78 geographical risk profile of anaemia. Only a few studies in the past have explored factors
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36 79 affecting anaemia among WRA using nationally representative Nepal Demographic and Health
37
38 80 Survey (NDHS) [35–37]. Till date, no studies have used spatial data to explore the geographical
39
40 81 hotspots (high prevalence) of anaemia among WRA using cluster sampling of the NDHS data. In
41
42 82 addition, population in Nepal has diverse characteristics in terms of their culture, ethnicity and
43
44 83 geographical locations. Within the latitude of 193km (North to South), Nepal bears tropical/sub-
45
46 84 tropical landscape on the south and temperate to alpine in the North, with an elevation ranging
47
48 85 from 70m to the summit of Mount Everest (8848m).[38] The distinct characteristics such as
49
50 86 dietary habit, lifestyle and socio-economic status linked to the geographical regions of Nepal are
51
52 87 unique and pose risk of developing anaemia. Exploring spatial patterns and factors affecting
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3 88 anaemia by geographical region is therefore critical to inform the plans and policies for targeted
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5 89 anaemia control and prevention programs.[39] The main objective of this study was to explore
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8 90 the spatial distribution and contributing factors of anaemia among WRA in Nepal.
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11 91 **METHODS**

12 92 **Patient and public involvement**

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15 93 This study utilized a publicly available data set (NDHS); therefore, there were no patients
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17 94 involved.
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20 95 **Data source**

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22 96 This study was based on the data from Nepal Demographic and Health Survey (NDHS) 2016, a
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24
25 97 nationally representative cross-sectional survey. This survey was carried out as part of the DHS
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27 98 program by New ERA (a private non-profit research organization based in Kathmandu) under
28
29 99 the guidance of the Ministry of Health, Government of Nepal and was supported by ICF
30
31
32 100 international and United States Agency for International Development (USAID). The study
33
34 101 population for this study was WRA from the Nepal Demographic and Health Survey 2016.
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37 102 **Study settings and Sampling strategy**

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39 103 The sample for the 2016 NDHS was designed to provide estimates of population health, and
40
41 104 nutrition indicators including fertility and mortality rates for the overall country, provinces,
42
43 105 development regions, urban and rural municipalities, and for the ecological zones: Terai, Hills,
44
45
46 106 and Mountains. The NDHS 2016 utilized a stratified, two-stage cluster sampling design. The
47
48 107 survey used enumeration areas (EAs) which is a primary sampling unit (PSU) and was selected
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50
51 108 from 383 wards in both rural (n=199) and urban (n=184) areas with probability proportional to
52
53 109 size method. In the second stage, 30 households on average within EAs were selected using a
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55 110 systematic sampling technique. A more detailed methodology of the NDHS has been published
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3 111 elsewhere.[12] All WRA (pregnant and non-pregnant) with complete socio-demographic and
4
5 112 nutritional characteristics who were residents or who had slept in the selected households on the
6
7 113 night before the survey were eligible for the survey. The details of the sample size selection in
8
9 114 the NDHS 2016 are presented in Figure 1.

13 115 **Study variables**

15 116 **Outcome variables**

17 117 Haemoglobin level was measured using capillary blood by a battery-operated portable HemoCue
18
19 118 rapid testing machine and was adjusted for altitude and smoking status.[12] According to the
20
21 119 WHO, for non-pregnant and pregnant women aged 15-49 years, any form of anaemia is defined
22
23 120 as haemoglobin concentration <12 g/dL and <11g/dL respectively.[40] The categories of
24
25 121 anaemia were further dichotomized into 'anaemic' and 'not anaemic'.

29 122 **Predictor's variables**

31 123 Predictors of anaemia were selected based on the literature review. [4,35–37,39] The wide range
32
33 124 of socio-demographic, individual, household and community factors were hypothesized to
34
35 125 increase the likelihood of anaemia. The predictors of anaemia including both individual-level
36
37 126 and community-level factors were included in the analysis. The coding strategy of individual-
38
39 127 level and community-level factors are presented in online supplementary Table 1.

43 128 **Individual-level factors**

45 129 A total of 11 individual-level factors were identified, and that included for example, respondent's
46
47 130 age, education level, occupation, wealth index, nutritional status, pregnancy status, and minimum
48
49 131 dietary diversity for WRA (MDD-W). The minimum dietary diversity for women of
50
51 132 reproductive age (MDD-W) was calculated using the guideline of the modified FANTA III tool
52
53 133 developed by the Food and Agriculture Organization (FAO) of the United Nations.[41]

134 **Community-level factors**

135 The six different factors were included in the community-level factors that included place of
136 residence, province, community wealth, community female education, community safe water
137 access, and community toilet facility. The selection of community-level factors were based on
138 the group of women living in similar settings.[39] If more women have shared features such as
139 place of residence, province, type of water source, and toilet facility; it was considered to have
140 the same effect on anaemia among WRA.[39] For community level wealth and female education,
141 we constructed the aggregate continuous community-level predictor-variables by aggregating
142 individual-level characteristics at the community (cluster) level. We dichotomized the aggregate
143 variables into "high" or "low" based on the distribution of the proportion values calculated for
144 each community[42], but it was not applicable for the provinces and place of residence. Based on
145 distribution of the aggregate variable (normal or non-normal), mean and median was used as a
146 cut off point for the categorization of community-level variables respectively. The community
147 wealth was categorized as 'high' if the proportion of women from richest (rich, richest)
148 households in the community was above 21% and 'low' if the proportion was 0 to 21%.
149 Community female education was defined as the mean percentage of women in the community
150 with at least primary education and above.[43] Water supply and sanitation guidelines based on
151 the WHO and UNICEF Joint Monitoring Programme (JMP) were used to define improved toilet
152 facility and improved water source.[44]

153 **Data analysis**

154 **Statistical analysis**

155 Data were analyzed using Stata/MP version 14.1 (StataCorp LP, College Station, Texas). The
156 'svy' command was used to account for sampling weights, clustering, and stratification in
157 complex survey data. Weighted frequencies, weighted percentage, mean and SD were used for

1
2
3 158 the descriptive analysis. Pearson Chi-Square test for categorical variables and independent t-test
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5 159 for continuous variables were used. The multilevel mixed-effect logistic regression analysis was
6
7 160 performed to estimate the adjusted odds ratio and to estimate the extent of random variations
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9 161 between communities.
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13 162 Four models were created and were fitted. Model 1 (empty model) was fitted without predictor
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15 163 variable to test random variability in the intercept and to estimate the intra-class correlation
16
17 164 (ICC).[45] Model 2 examined the effects of individual-level characteristics, model 3 examined
18
19 165 the effects of community-level variables, and model 4 examined the effects of both individual
20
21 166 and community-level characteristics simultaneously. In the multilevel mixed-effect logistic
22
23 167 regression models, the fixed effects estimated the association between the likelihood of anaemia
24
25 168 among WRA and the individual-level and community-level factors, and the findings are reported
26
27 169 in terms of adjusted odds ratio (aOR), and 95% confidence intervals (CIs). To prevent statistical
28
29 170 bias in the multilevel logistic regression model, we examined and reported multicollinearity
30
31 171 among the predictor variables using variation inflation factors (VIF). In this study, we used "10"
32
33 172 as a cut-off value for the maximum level of VIF.[46] The random effects are expressed as
34
35 173 ICC,[45] and proportional change in variance (PCV).[47] The ICC was calculated to evaluate the
36
37 174 cluster variability; and PCV can measure the total variation due to factors at the individual- and
38
39 175 community- levels.[45] Models fit were assessed using Akaike information criterion (AIC) and
40
41 176 the Bayesian information criterion (BIC). Considering the nested structure of the survey data, a
42
43 177 multilevel model is considered to be appropriate than ordinary single-level regression model
44
45 178 because it provides correct parameter estimates by handling the cluster data.[48,49]
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53 179 **Spatial analysis**

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3 180 Spatial analysis were performed using ArcGIS software V.10.8, and base files of the
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5 181 administrative provinces and districts of Nepal were obtained from Government of Nepal,
6
7 182 Ministry of Land Management, [50] and Natural Earth.[51] The global positioning system (GPS)
8
9 183 data set for NDHS was obtained from the DHS website after receiving the approval letter. The
10
11 184 prevalence of anaemia and standardized prevalence ratio were computed for both the districts
12
13 185 and provinces in Stata/MP version 14.1 software and were later transferred to Excel spreadsheet.
14
15 186 These data were imported into the ArcGIS software to link the reported anaemia prevalence for
16
17 187 each cluster to the corresponding geographical location (survey cluster data). The spatial
18
19 188 variations of the prevalence of anaemia among WRA by both districts and provinces were
20
21 189 visualized. To estimate the standardized prevalence ratio (SPR; ratio of observed prevalence to
22
23 190 expected prevalence)[52] of anaemia among WRA, we first determined the prevalence of
24
25 191 anaemia for both districts and provinces. District and province wise prevalence rate of anaemia
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27 192 among WRA was multiplied by the national prevalence rate of 41% (normalized to the national
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29 193 prevalence of 41%).
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36 194 The Local Moran's I, Gettis-Ord G-statistics tool in ArcGIS software was used to compute to
37
38 195 measure how spatial autocorrelation of anaemia among WRA varies across different locations in
39
40 196 Nepal. The Getis-Ord G-statistics identifies statistically significant spatial clusters of hotspot
41
42 197 clusters (High-High), and cold spot clusters (Low-Low).[53,54] Hotspot analysis computes Z-
43
44 198 score and p-value to determine the statistical significance of the clustering of anaemia over the
45
46 199 study area at different significance levels simultaneously. [54,55] The statistical significance of
47
48 200 autocorrelation was determined by z-scores and p-value ≤ 0.05 with a 95% Confidence Intervals
49
50 201 (CIs).[39,55] An anaemia hot spot was defined as the occurrence of high prevalence rates of
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52 202 anaemia clustered together on the map. Anaemia cold spot was referred to the occurrence of low
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3 203 prevalence rates of anaemia clustered together on the map.[39,55] The spatial pattern and
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5 204 distribution of anaemia prevalence rates among WRA in Nepal are visualized on the map (Figure
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8 205 2)
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10 206 **Ethical consideration**

11 207 The DHS survey protocols were approved by the institutional review boards of ICF, the DHS
12
13 208 program, and the Nepal Health Research Council (NHRC). The details on ethical procedures
14
15 209 used in this survey have been published elsewhere.[12] We registered and requested for access to
16
17 210 both main data and GPS data from the DHS website [56] and received an approval to access and
18
19 211 download the DHS data file. DHS program collected data following a written informed consent
20
21 212 from each individual. All individual identifiers were precluded from the final dataset in this
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23 213 study.
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30 214 **RESULTS**

31 215 **Socio-demographic characteristics of study participants**

32 216 In this study, a total of 6,414 WRA were included in the analysis (Table 1). The mean (\pm SD) age
33
34 217 of the study participants was 29 (\pm 9.7) years. More than one third (38.1%) of the participants
35
36 218 were from age group 15-24 years, and women (35.5%) had attended secondary level of
37
38 219 education. Nearly one quarter (22.4%) of study participants were from richer wealth quintiles
39
40 220 and more than half (59.7%) of the women were not using any contraceptive methods, and a half
41
42 221 (50.6%) of the participants consumed more than five food types. More than three quarters
43
44 222 (77.1%) of participants had mosquitoes bed nets for sleeping. High proportion of women
45
46 223 (68.8%) belonged to urban areas, and were from Bagmati province (21.9%). More than half
47
48 224 (54.2%) of the women had the highest percentage of community female education, whilst, nearly
49
50 225 two-thirds (64%) of the women belonged to a low percentage of community female wealth
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226 index. Majority of the participants had improved sources of drinking water (91%) and type of
227 toilet facility (84.1%). (Table 1)

228 **Prevalence of anaemia among women of reproductive age**

229 In the current study, the overall prevalence of any anaemia across Nepal was 41% (95% CI:
230 38.5-42.9%). At the individual level, the prevalence of anaemia was higher among younger age
231 groups (43.6 %), and women who attended at least secondary level education (42.7 %). The
232 higher prevalence of anaemia were found in middle socio-economic class families (48.9%). The
233 prevalence of anaemia was more among women who had undergone female sterilization
234 (53.7%), and those who consumed less than five food groups (51%). At the community-level, the
235 prevalence of anaemia was higher in women who came from Province-2 (57.7%). The high
236 prevalence of anaemia was found in community with low female education (47.9 %), female
237 wealth index (44.3%), and who did not have improved toilet facility (51.5 %) (Table 1).

239 **Factors affecting anaemia among women of reproductive age**

240 The fixed effects (a measure of association) and the random-effects for the risk of developing
241 anaemia among WRA are presented in Table 2. The results of the empty model (model 1)
242 showed that there was statistically significant variability in the odds of anaemia between
243 communities ($\tau=0.627$, $p<0.001$). The ICC in the empty model implied that 16% of the total
244 variance for the risk of developing anaemia was attributed to differences between the
245 communities. In individual-level factors (model 2), women who did not have formal education
246 (aOR=2.22, 95% CI: 1.35-3.82) compared to those with higher education, and who belonged to
247 middle-class families (aOR=1.38, 95% CI: 0.86-2.20) compared to the family from poorest
248 families were found to have higher odds of anaemia. Older women had 52% lower (aOR=0.48,
249 95% CI: 0.24-0.83) odds of developing anaemia compared to younger women. Women who used

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3 250 hormonal contraceptive methods had 35% lower (aOR=0.65, 95% CI: 0.46-0.92) odds of
4
5 251 anaemia compared to who did not use contraceptive methods. The ICC in model 2 indicated that
6
7 252 11.8% of the variation in WRA anaemia was attributable to differences across communities. The
8
9 253 PCV indicated that 29.3% of the variance in WRA anaemia across communities was explained
10
11 254 by the individual-level characteristics.
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14

15 255 The community-level (model 3) showed that women from Province-2 had 2.5 times higher
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17 256 (aOR=2.51, 95% CI: 1.79-3.53) odds of anaemia compared to women from Bagmati province.
18
19 257 Women who belonged to communities with a low percentage of the wealthy households had 1.48
20
21 258 times higher (aOR=1.48, 95% CI: 1.21-1.80) odds of anaemia compared to those coming from
22
23 259 high percentage of the wealthy household; and women residing in communities with a low
24
25 260 percentage of community female education had 1.39 times higher (aOR=1.39, 95% CI: 1.15-
26
27 261 1.68) odds of anaemia compared to those coming from the communities with a high percentage
28
29 262 of education. The ICC in model 3 showed that differences between communities accounted for
30
31 263 about 11.1% of the variation in anaemia among WRA. In addition, the PCV indicated that 33.9%
32
33 264 of the variation in WRA anaemia between communities was explained by community-level
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35 265 characteristics.
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42 266 In model 4, women who had undergone female sterilization were at higher (aOR: 3.61, 95% CI:
43
44 267 1.10-11.84) odds of anaemia compared to those who did not use contraceptive methods. Women
45
46 268 with no formal education were found to have 2 times higher (aOR=1.99, 95% CI: 1.17-3.39)
47
48 269 odds of anaemia compared to women who had higher education. Women from middle socio-
49
50 270 economic family had higher (aOR=1.65, 95% CI: 1.02-2.68) odds of anaemia compared to
51
52 271 poorest counterparts. Women who came from Province-2 (aOR=2.97, 95% CI: 1.52-5.82) had
53
54 272 higher odds of anaemia compared to Bagmati province. The older women had 49% lower
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273 (aOR=0.51, 95% CI: 0.26-0.97) odds of anaemia compared to younger women, and women who
274 used hormonal contraceptive methods had 37% lower (aOR=0.63, 95% CI: 0.43-0.90) odds of
275 anaemia compared to who did not use contraceptive methods. After the inclusion of both the
276 individual and community-level variables in model 4, the ICC indicated that 9.5% of the
277 variability in anaemia among WRA was attributable to the difference between communities.
278 Furthermore, the PCV indicated that 44.6% of the variation in anaemia among WRA between
279 communities was explained by both individual and community-level characteristics (Table 2).

280 **Spatial data analysis**

281 Figure 3(a) shows the prevalence of anaemia among WRA across provinces in Nepal. A severe
282 anaemia prevalence ($\geq 40\%$) among WRA was seen in Province-2, followed by Province-1 and 5.
283 The prevalence of moderate anaemia (20-39.9%) was observed in Bagmati, Gandaki, Karnali,
284 and Sudurpaschim province. Mild anaemia (prevalence $<19.9\%$) was not found in any provinces.
285 Figure 3(b) shows the prevalence of anaemia among WRA across 75 districts in Nepal. The
286 prevalence rate of severe anaemia was observed in 29 out of 75 districts, and mild anaemia was
287 found in only eight districts (Figure 3).

288 The standardized prevalence ratio by provinces (standardized to the national mean prevalence of
289 41%) are shown in Figure 4 (a), and ranged from 0.68 to 1.4. The higher prevalence ratio of
290 anaemia was found in Province-2, whereas a lower prevalence ratio was observed in Bagmati,
291 Gandaki, and Karnali province. Figure 4 (b) shows the standardized prevalence ratio across the
292 75 districts, and ranged from 0.76 to 1.59. The higher standardized prevalence ratio of anaemia
293 was observed in 17 out of 75 districts across the country (Figure 4).

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2
3 294 The spatial pattern and distribution of anaemia among WRA at the cluster level are displayed in
4
5 295 Figure 5. The spatial analysis at the cluster level showed that statistically significant high
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7
8 296 hotspots of anaemia were observed in the southern Terai of the country bordering India:
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10 297 Province-2 (8 districts), Province-1 (4 districts), southern plain of the Bagmati province (1
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12 298 district), and southwestern region of Province-5 (3 districts). Whilst, cold spots of anaemia were
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15 299 observed in most of the Hilly regions of the country (Figure 5).
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18 300 **DISCUSSION**

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20 301 In this study, more than 40% of WRA were anaemic which implies that anaemia is still an
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22 302 important public health problem in Nepal.[40] Geographical pattern showed that anaemia is an
23
24 303 important public health problem in three of the seven provinces and 29 out of the 75 districts in
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27 304 Nepal. The higher prevalence of anaemia was observed in the southern Terai bordering India
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29 305 particularly in Province-2, and the upper Himalayan region of the country. The spatial analysis at
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31 306 the cluster level showed that high hot spots of anaemia were observed in Terai region especially
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34 307 in Province 1, 2 and 5. These findings are consistent with a previous study [57] which was based
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36 308 on the analysis of Nepal National Micronutrient Status Survey 2016 and found WRA living in
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38 309 the Terai ecological zone had higher odds of anaemia relative to women living in the Mountain
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40 310 and Hill regions. A possible reason could be that in the Terai region, there is a shortage of safe
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43 311 and adequate drinking water supply and the risks of malaria and hookworm infestation are high.
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48 313 In the southern Terai of Nepal, despite ecological richness, people have long suffered from a
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50 314 deficiency of micronutrients such as Vitamin A, iron and zinc,[26] and a high burden of
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52 315 hookworm infestation and malaria which can contribute to development of anaemia.[30] Diet of
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55 316 women in the Terai lack diversity and, nutrient adequacy which pose an increased risk of
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3 317 anaemia.[27] Terai region of Nepal is endemic to malaria in contrast to Hill and Mountain region
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5 318 of Nepal, [31,32,58] and thus poses higher risk of anaemia.[30] The majority (90%) of the
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7 319 population from Terai region rely on groundwater especially shallow tube well for domestic
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9 320 purposes including drinking whereas most of the people from Mountain and Hill region rely on
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11 321 municipal taps, spring water source, and stone spouts as drinking water sources. Terai region is
12
13 322 the most densely populated region compared to Hill and Mountain regions of Nepal. The
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15 323 population of Terai increased dramatically after the 1970s because people from the Mountains
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17 324 and Hills migrated to Terai for permanent settlement. [33] Most of the water wells were
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19 325 installed to meet the growing population demand. However, well water in the Terai consists of
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21 326 high arsenic concentrations ($>10 \mu\text{g}/\text{L}$) beyond the WHO recommendation. [33] A previous
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23 327 study also explained the high burden of anaemia might be due to chronic exposure to arsenic
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25 328 through contaminated groundwater in Terai region. [57] Higher arsenic concentration can inhibit
26
27 329 haem iron metabolism and increase erythrocyte hemolysis.[59] Consequently, drinking arsenic-
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29 330 containing water poses an increased risk of anaemia among women.[60] Arsenic exposure was
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31 331 more likely to cause anaemia among women in Bangladesh.[61] The spatial analysis at the
32
33 332 cluster level found that high hotspots of anaemia were also observed in southwestern region
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35 333 (Province-5, and southern plain of Sudurpaschim province), particularly Banke, Bardiya and
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37 334 Kanchanpur district. A previous study highlighted that Glucose 6 phosphate dehydrogenase
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39 335 deficiency (G6PDd), sickle cell trait (SCT), and sickle cell anaemia (SCA) as the most common
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41 336 disorder in Tharu communities living in southwestern province-5, and sudurpaschim province
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43 337 [62,63]. Study based on the Nepal National Micronutrient Status Survey 2016 also found the
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45 338 G6PD and haemoglobinopathies had strong association with anaemia among WRA.[57]
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3 339 The geographical variance of high cases of anaemia across the high Mountainous region could be
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5 340 attributed to food insecurity, low dietary diversity, [12,27,34] less calorie diet,[27] poor health
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7 341 service coverage,[25] high illiteracy, gender based-inequality, and poor health seeking
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10 342 behaviour.[23,24]

11 343 **Socio-demographic characteristic among women and anaemia**

12 344 Women who had no formal education, and those who came from middle socio-economic
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14 345 households, and from younger age group were at increased risk of anaemia. These findings are in
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16 346 line with previous studies from low and middle-income countries (LMICs) including
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18 347 Ethiopia,[39] India,[64] Tanzania,[65] Rwanda,[66] Timor-Leste,[67] and Bangladesh.[68]
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20 348 Studies from Ethiopia and Tanzania suggest that higher-level education might enable women to
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22 349 gain knowledge and improve attitude which in turn can promote them to adopt healthier lifestyle
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24 350 including good nutrition habits, better health-seeking behavior, and good hygiene practices that
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26 351 can prevent anaemia.[39,65]

27
28 352 Anaemia is a multifaceted problem where nutrition and household economic status are
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30 353 considered to have a synergistic association.[66] Women belonging to poorer households are
31
32 354 more likely to be anaemic compared to those living in middle or richer households in most of the
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34 355 countries.[17,39,66]. Contrastingly, this study revealed that poorer Nepalese women were less
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36 356 likely to be anaemic. Similar findings were reported by a previous study which was based on the
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38 357 analysis of the 2016 NDHS dataset.[36] The possible reason could be first, Nepal is an agrarian-
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40 358 based country and the staple diet may be similar for most of the households.[69] Second, poorer
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42 359 Nepalese women being at lower risk of anaemia might be due to the nationwide open defecation
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44 360 free (ODF) campaign initiated after 2011, which was targeted at poor households which
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46 361 contributed to the reduction of anaemia through the reduction in prevalence of helminthiasis.
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3 362 [36] Third, there was various ongoing health and nutrition intervention program targeted at
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5 363 poorer households. For instance, consumption of iron-rich dark green leafy vegetables available
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7 364 from their kitchen garden,[70] consumption of animal source foods, and dietary iron
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9 365 consumption. Interventions such as Suaahara-I (from 2011 to 2016), and Sunaula Hazar Din
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11 366 (from 2014 to 2017), which provided financial and technical support to poor households for
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13 367 poultry farming, and contributed to increased consumption of meat and eggs among
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15 368 WRA.[71,72] Future studies are critical to explore the association of household economic status
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17 369 and anaemia among WRA in Nepal.

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22 370 In this study, the prevalence of anaemia was found to be decreasing with increasing age. These
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24 371 findings are consistent with studies from Nepal, [36] Ethiopia,[39] Demographic Republic of
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26 372 Congo,[73] and Benin.[60] The possible reason could be that the low fertility rates are high
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28 373 among older women.[39] Also, it might be due to young girls being under-represented in the
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30 374 public health programs that aim to prevent anaemia in Nepalese context. [36] However,
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32 375 Government of Nepal has started weekly iron folic acid supplementation to adolescent girls aged
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34 376 10–19 years only after 2016.[74] In contrast, few studies from Nepal did not show any
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36 377 association of age with anaemia.[35,37] The discrepancies might be due to the nature of
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38 378 statistical model used in the analysis.

379 **Effect of contraceptive use on anaemia**

380 In this study, those using hormonal contraceptive were less likely to be anaemic among WRA
381 which is consistent with previous studies conducted in Nepal,[35,36] Rwanda,[66] Tanzania,[65]
382 and Ethiopia.[75] This could be due to multiple reasons. For instance, use of hormonal
383 contraceptive can reduce the blood loss during the menstruation.[76,77] Almost 100-150 mg of
384 iron is lost during menstrual bleeding.[78] Subsequently, this may directly or indirectly furnish

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3 385 iron loss among women at high risk for iron-deficiency anaemia.[77,78] A previous study also
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5 386 suggested that Depo-Provera injections were more likely to increase haemoglobin concentration
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7 387 among WRA in Nepal.[79] Interestingly, in this study women who had undergone female
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9 388 sterilization were at increased risk of anaemia. These findings are in line with the similar study
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11 389 conducted in Nepal.[36,80]
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15 390 **Community-level factors and anaemia**

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17 391 In this study, estimated intra-class correlation (ICC) shows that about 9.5% of the community
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19 392 level variability was attributable to the difference between communities among WRA. The PCV
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21 393 indicated that 44.6% of the variation in WRA anaemia between communities was explained by
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23 394 both individual and community-level characteristics. This finding is in line with the study
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25 395 conducted in Ethiopia, where both individual- and community-level factors accounted for about
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27 396 43% of the variability of anaemia among WRA.[39] Women who came from Province-2 had
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29 397 more than two times higher odds of anaemia compared to Bagmati province. Previous studies
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31 398 reported that women from province number 2 were more likely to be coming from lower
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33 399 socioeconomic status and less diverse diet (an estimated 29% of minimum dietary diversity
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35 400 (MDD)). [12,29] Other evidence from Nepal also suggested that women in Province 2 have poor
36
37 401 nutritional status.[81] In addition, compliance rate of recommended dose of iron tablets amongst
38
39 402 the pregnant mothers in Province-2 was also low (28%) compared to other provinces.[12] This
40
41 403 study showed that promoting community female education has a potential role in lowering the
42
43 404 likelihood of anaemia which echoes with a study from Malawi.[42] This could be explained by
44
45 405 the fact that higher community education provides a context where women are enabled to gain
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47 406 nutritional knowledge and material resources [28] that can increase consumption of iron-
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49 407 absorption-enhancers such as vitamin C, phytates (whole grains, legumes), and calcium (dairy
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3 408 products). Increasing community level education can play an important role in promoting
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5 409 knowledge and attitude which in turn can incite them to adopt healthier lifestyle including good
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7 410 nutrition habits that can ultimately prevent anaemia.[39,65,70]
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10 411 **Strength and limitation**

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12 412 This study is conducted based on the spatial pattern and multilevel epidemiological analysis of
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14 413 anaemia among WRA in Nepal using cluster sampling of nationally representative data. The
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16 414 combined statistical methods including multilevel and spatial analysis used in this study provides
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18 415 important insights on the role of contextual factors and geographical patterns in the occurrences
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20 416 of anaemia among WRA in Nepal. This study has some limitations. The cross-sectional design of
21
22 417 the study does not allow us to establish the causality. This study relied on haemoglobin as the
23
24 418 measure of anaemia; further studies should consider other indices that include total ferritin and
25
26 419 total iron binding capacity to differentiate the types of anaemia. Since this study is based on the
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28 420 secondary data analysis, we are unable to incorporate potential confounding factors of anaemia
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30 421 such as nutrient intake, worm infestations, and other non-modifiable risk factors.
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36 422 **CONCLUSION**

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38 423 This study highlighted a high prevalence of anaemia among WRA across Nepal. At an individual
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40 424 level, women who had no formal education, those who came from middle socio-economic class
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42 425 families were more likely to be anaemic, whereas, older women, and those who used hormonal
43
44 426 contraceptive were less likely to be anaemic. At the community level, low community female
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46 427 education, and women living in Province-2 were associated with increased odds of anaemia. In
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48 428 the spatial analysis, our study found statistically significant hot spots in the southern Terai region
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50 429 particularly in Province-1 (4 districts), Province-2 (8 districts), Bagmati province (1 district), and
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52 430 Province-5 (3 districts). Both nutrition specific and nutrition sensitive interventions such as
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3 431 social and behavioral programs can tailor their strategies based on the factors identified in this
4
5 432 study to reduce the high burden of anaemia.
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19

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26
27 441 extraction and analysis, interpreted the results, generate the map, writing an original draft,
28
29 442 reviewing, editing, and overall supervision of the research. SS generate the map, and writing an
30
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32
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43
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46
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50 450 **Patient consent for publication**

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52 451 Not required
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55 452 **Ethical approval**

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3 453 The NDHS 2016 was approved by the Nepal Health Research Council (NHRC) and ICF Macro.
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6 454 **Data sharing statement**

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8 455 Dataset used in this study is publicly available from the DHS website (URL:

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11 456 <https://www.dhsprogram.com/data/available-datasets.cfm>).
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33 699 **Figure 1 Flow chart for sample size selection**

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36 700 **Figure 2 Study area map and observed anaemia prevalence among women of reproductive**
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38 701 **age for the NDHS survey clusters**

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40 702 **Table 1 Socio-demographic characteristics and prevalence of anaemia among women of**
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42 703 **reproductive age by determining factors (n=6,414)**

43 704 **Table 2 Multilevel mixed-effects logistic regression for individual and community-level**
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45 705 **factors affecting anaemia among women of reproductive age (n=6,414)**

46 706 **Figure 3 (a) Prevalence of anaemia among women of reproductive age across provinces.**

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48 707 **3 (b) Prevalence of anaemia among women of reproductive age across districts**
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708 **Figure 4 (a) Standardized prevalence ratio of anaemia among women of reproductive age**
 709 **across provinces. 4 (b) Standardized prevalence ratio of anaemia among women of**
 710 **reproductive age across districts (standardized to the national mean prevalence of 41%)**
 711 **Figure 5 Spatial pattern and distribution of hot and cold spots of anaemia among women of**
 712 **reproductive age at cluster level in Nepal**

713
 714 **Table 1 Socio-demographic characteristics and prevalence of anaemia among women of**
 715 **reproductive age by determining factors (n=6,414)**

Variables	Total sample Frequency (%)	Anaemia status % (95% CI)		p-value ^{1,2}
		Not anaemic	Anaemic	
Overall prevalence	6414	59.3 (57.0-61.4)	40.7 (38.5-42.9)	
Severe anaemia	17 (0.3)			
Moderate anaemia	450 (7)			
Mild anaemia	2147 (33.4)			
Hemoglobin level, mean (±SD)	12.3 ± 1.5	13.2 ± 0.9	10.8 ± 1.1	<0.001*
Individual-level factors				
Age in years, mean (±SD)	29.1 ± 9.7	29.5 ± 9.7	28.4 ± 9.5	<0.001*
Age				<0.001*
15-24	2443 (38.1)	56.4 (53.4-59.3)	43.6 (40.6-46.5)	
25-34	1971 (30.7)	58.7 (55.7-61.5)	41.3 (38.4-44.2)	
≥35	2000 (31.1)	63.2 (60.3-66)	36.8 (34-39.6)	
Education				0.086
No education	2144 (33.4)	58.4 (55-61.7)	41.6 (38.2-44.9)	
Primary	1069 (16.6)	61.5 (57.1-65.7)	38.5 (34.2-42.8)	
Secondary	2277 (35.5)	57.3 (54.2-60.3)	42.7 (39.6-45.7)	

Higher	924 (14.4)	63.3 (58.7-67.6)	36.7 (32.3-41.3)	
Occupation				0.084
Not working	2096 (32.6)	57.1 (53.7-60.3)	42.9 (39.6-46.2)	
Working	4318 (67.3)	60.3 (57.7-62.7)	39.7 (37.2-42.2)	
Wealth index				<0.001*
Poorest	1093 (17)	67.7 (63.8-71.2)	32.3 (28.7-36.1)	
Poorer	1225 (19.1)	58.5 (54.8-62.1)	41.5 (37.9-45.2)	
Middle	1317 (20.5)	51.1 (47.2-54.8)	48.9 (45.1-52.8)	
Richer	1441 (22.4)	56.6 (51.8-61.1)	43.4 (38.8-48.1)	
Richest	1338 (20.8)	64.1 (59.9-67.9)	35.9 (32.1-40.1)	
BMI, mean (\pmSD)	22 \pm 3.8	22.4 \pm 3.9	21.4 \pm 3.6	<0.001*
BMI (n=6411)				<0.001*
Normal	3925 (61.2)	57.4 (54.4-60.2)	42.6 (39.7-45.5)	
Underweight	1077 (16.8)	51.9 (48.3-55.4)	48.1 (44.6-51.6)	
Overweight/obesity	1408 (21.9)	69.9 (66.5-73.2)	30.1 (26.7-33.4)	
Currently pregnant				0.081
No	6124 (95.4)	59.5 (57.3-61.6)	40.5 (38.3-42.7)	
Yes	290 (4.5)	53.9 (47.2-60.5)	46.1 (39.4-52.7)	
Currently breastfeeding				<0.001*
No	4988 (77.7)	60.7 (58.4-62.9)	39.3 (37.1-41.6)	
Yes	1426 (22.2)	54.2 (50.6-57.7)	45.8 (42.2-49.3)	
Total children ever born				0.612
No child	1842 (28.7)	58.2 (54.5-61.7)	41.8 (38.2-45.4)	
1-3 child	3386 (52.8)	59.9	40.1	

		(57.4-62.2)	(37.7-42.5)	
4+ child	1186 (18.4)	58.9 (55.1-62.7)	41.1 (37.2-44.8)	
Current contraceptive use				<0.001*
Not using	3832 (59.7)	57.6 (54.9-60.1)	42.4 (39.8-45.1)	
Hormonal	905 (14.1)	70.5 (66.5-74.2)	29.5 (25.7-33.4)	
Female sterilization	730 (11.4)	46.3 (41.8-50.8)	53.7 (49.1-58.2)	
Male contraception	268 (4.2)	71.7 (61.9-79.8)	28.3 (20.1-38.1)	
Traditional	679 (10.6)	62.4 (58.1-61.4)	37.6 (33.3-41.9)	
Cigarette/smoking				<0.001*
Smoking	573 (8.9)	71.1 (66.5-75.2)	28.9 (24.7-33.4)	
Not smoking	5841 (91.1)	58.1 (55.8-60.3)	41.9 (39.7-44.1)	
MDD-W (n=1131)				0.025*
Not diverse	558 (49.3)	49 (43.8-54.1)	51 (45.8-56.1)	
Diverse	573 (50.6)	56.8 (51.7-61.7)	43.2 (38.2-48.2)	
Mosquitoes bed net for sleeping				0.024*
No	1412 (22.1)	68.9 (65.6-72.1)	31.1 (27.9-34.3)	
Yes	5002 (77.1)	56.5 (53.9-59)	43.5 (41-46.1)	
Place of residence				0.202
Urban	4029 (68.8)	60.4 (57.5-63.1)	39.6 (36.8-42.4)	
Rural	2385 (37.1)	57.3 (53.6-60.9)	42.7 (39.1-46.3)	
Province				<0.001*
Province-1	1073 (16.7)	56.7 (51.2-62.1)	43.3 (37.9-48.7)	
Province-2	1285 (20)	42.2	57.7	

		(37.3-47.2)	(52.7-62.6)	
Bagmati	1408 (21.9)	70.9 (66.4-75.1)	29.1 (24.8-33.5)	
Gandaki	627 (9.7)	71.9 (66.3-76.9)	28.1 (23.1-33.6)	
Province-5	1086 (16.9)	56.5 (52.5-60.5)	43.5 (39.4-47.5)	
Karnali	369 (5.7)	65.1 (59.7-70.1)	34.9 (29.9-40.2)	
Sudurpaschim	566 (8.8)	60.7 (54.7-66.3)	39.3 (33.6-45.2)	
Community female education^a				<0.001*
Low	2936 (45.7)	52.1 (49.1-55.2)	47.9 (44.8-50.9)	
High	3478 (54.2)	65.3 (62.3-68.1)	34.7 (31.9-37.6)	
Community female wealth index^b				<0.001*
Low	4107 (64)	55.7 (52.6-58.7)	44.3 (41.2-47.3)	
High	2307 (35.9)	65.5 (62.1-68.8)	34.5 (31.1-37.8)	
Source of drinking water (n=6084)				0.004*
Improved	5537 (91)	58.7 (56.3-61.1)	41.3 (38.9-43.6)	
Not improved	547 (8.9)	66.3 (61.4-70.8)	33.7 (29.2-38.5)	
Type of toilet facility (n=6084)				<0.001*
Improved	5117 (84.1)	61.5 (59.3-63.6)	38.5 (36.3-40.7)	
Not improved	967 (16)	48.5 (43.1-53.9)	51.5 (46.1-56.8)	
Frequency and percentage (%) are weighted				
^{1, 2} denotes Pearson Chi-Square test for categorical variables and independent t-test for continuous variables				
*denotes statistically significant at p<0.05				
^a mean percent of households wealth quintiles categorized richer and richest and above				

^bmean percent of women with primary education level and above
 BMI: Body Mass Index
 MDD-W: Minimum Dietary Diversity for Women

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717 **Table 2 Multilevel mixed-effects logistic regression analysis for individual and community-**
 718 **level factors affecting anaemia among women of reproductive age (n=6,414)**

Variables	Model 1 Empty model	Model 2 Individual-level factors	Model 3 community-level factors	Model 4 Individual and community-level factors
		aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Fixed-effects model				
Individual-level factors				
Age				
15-24		0.80 (0.57-1.08)		0.75 (0.54-1.04)
25-34		Ref		Ref
≥35		0.48 (0.24-0.83)*		0.51 (0.26-0.97)*
Education				
No education		2.22 (1.35-3.82)**		1.99 (1.17-3.39)*
Primary		1.52 (0.99-2.63)		1.33 (0.79-2.23)
Secondary		1.61 (1.08-2.54)*		1.46 (0.93-2.29)
Higher		Ref		Ref
Occupation				
Not working		Ref		
Working		0.98 (0.73-1.32)		
Wealth index				
Poorest		Ref		Ref
Poorer		1.20 (0.79-1.86)		1.46 (0.95-2.25)
Middle		1.38 (0.86-2.20)**		1.65 (1.02-2.68)*
Richer		1.13 (0.68-1.82)		1.39 (0.84-2.32)
Richest		1.28 (0.69-2.30)		1.33 (0.70-2.52)
BMI (n=6411)				
Normal		Ref		Ref
Underweight		1.10 (0.80-1.60)		1.05 (0.72-1.51)
Overweight/obesity		0.89 (0.59-1.35)		1.03 (0.65-1.58)
Currently pregnant				
No		0.81 (0.42-1.58)		1.08 (0.53-2.19)
Yes		Ref		Ref
Currently breastfeeding				

No		Ref		Ref
Yes		1.34 (0.63-2.82)		1.60 (0.71-3.59)
Total children ever born				
No child		Ref		Ref
1-3 child		-		-
4+ child		1.15 (0.75-1.87)		1.02 (0.63-1.63)
Current contraceptive use				
Not using		Ref		Ref
Hormonal		0.65 (0.46-0.92)*		0.63 (0.43-0.90)*
Female sterilization		3.55 (1.21-10.44)*		3.61 (1.10-11.84)*
Male contraception		0.92 (0.17-4.79)		0.74 (0.14-3.77)
Traditional		1.10 (0.74-1.63)		1.12 (0.74-1.69)
Cigarette/smoking				
Smoking		0.89 (0.48-1.66)		1.21 (0.63-2.33)
Not smoking		Ref		Ref
MDD-W (n=1131)				
Not diverse		1.20 (0.91-1.59)		1.03 (0.76-1.40)
Diverse		Ref		Ref
Mosquitoes bed net for sleeping				
No		0.57 (0.38-0.86)		
Yes		Ref		
Community-level factors				
Place of residence				
Urban			Ref	Ref
Rural			1.01 (0.83-1.21)	0.89 (0.64-1.24)
Province				
Province-1			1.70 (1.23-2.34)**	2.07 (1.57-5.64)**
Province-2			2.51 (1.79-3.53)***	2.97 (1.52-5.82)**
Bagmati			Ref	Ref
Gandaki			0.90 (0.64-1.26)	0.76 (0.39-1.49)
Province-5			1.60 (1.16-2.21)**	2.42 (1.31-4.50)**
Karnali			1.19 (0.85-1.66)	1.66 (0.88-3.14)
Sudurpaschim			1.54 (1.11-2.15)*	1.62 (0.84-3.10)
Community female education^a				
Low			1.39 (1.15-1.68)***	-
High			Ref	-

Community wealth index^b				
Low			1.48 (1.21-1.80) ^{***}	-
High			Ref	-
Source of drinking water (n=6084)				
Improved			Ref	Ref
Not improved			1.05 (0.84-1.30)	1.13 (0.68-1.86)
Type of toilet facility (n=6084)				
Improved			Ref	Ref
Not improved			1.03 (0.84-1.24)	0.96 (0.63-1.45)
Random-effects model				
Community-level variance (τ) (SE)	0.627 (0.073) ^{***}	0.443 (0.192) ^{***}	0.414 (0.056) ^{***}	0.347 (0.194) ^{**}
ICC (%)	16	11.8	11.1	9.5
PCV (%)	Ref	29.3	33.9	44.6
Model fit statistics				
AIC	8322.6	1554.7	7838.4	1400.6
BIC	8336.1	1675.8	7925.8	1559.1
Model 1 (empty model): without adjusted predictors variables; model 2: adjusted for individual-level factors; model 3: adjusted for community-level factors; model 4: adjusted for both individual-level and community-level factors.				
*p<0.05, **p<0.01, ***p<0.001,				
aOR=adjusted odds ratio, CI: confidence interval, Ref: reference category, SE: standard error,				
ICC: intra-class correlation, PCV: percentage change in variation, AIC: Akaike information criterion, BIC: Bayesian information criterion				
^a mean percent of households wealth quintiles categorized richer and richest and above				
^b mean percent of women with primary education level and above				
community female education and community wealth index is omitted in Model 4 due to collinearity				

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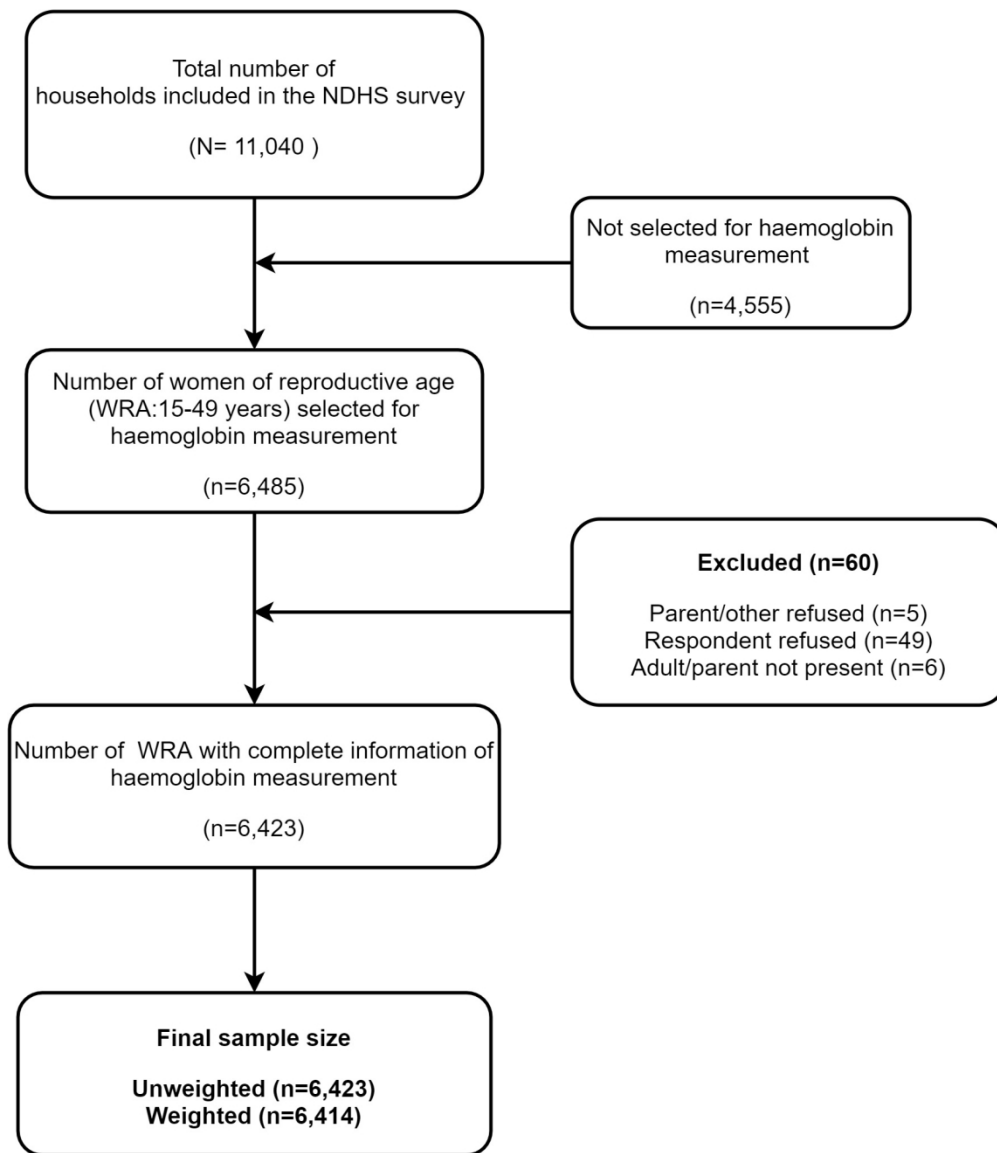


Figure 1 Flow chart for sample size selection

626x717mm (72 x 72 DPI)

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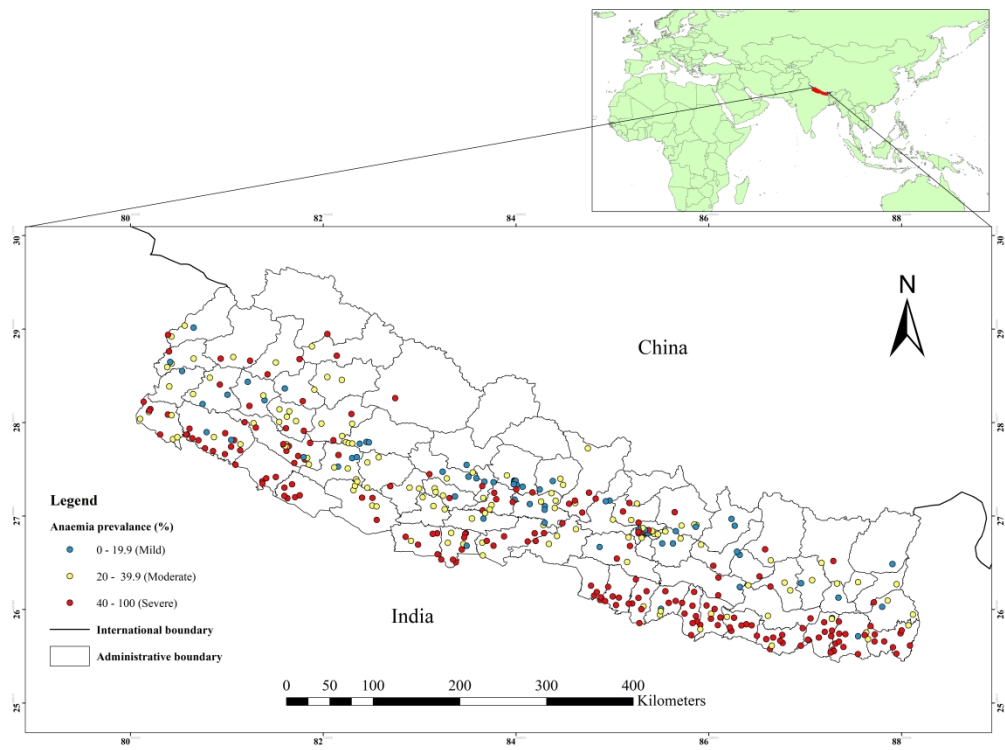


Figure 2 Study area map and observed anaemia prevalence among women of reproductive age for the NDHS survey clusters

609x457mm (300 x 300 DPI)

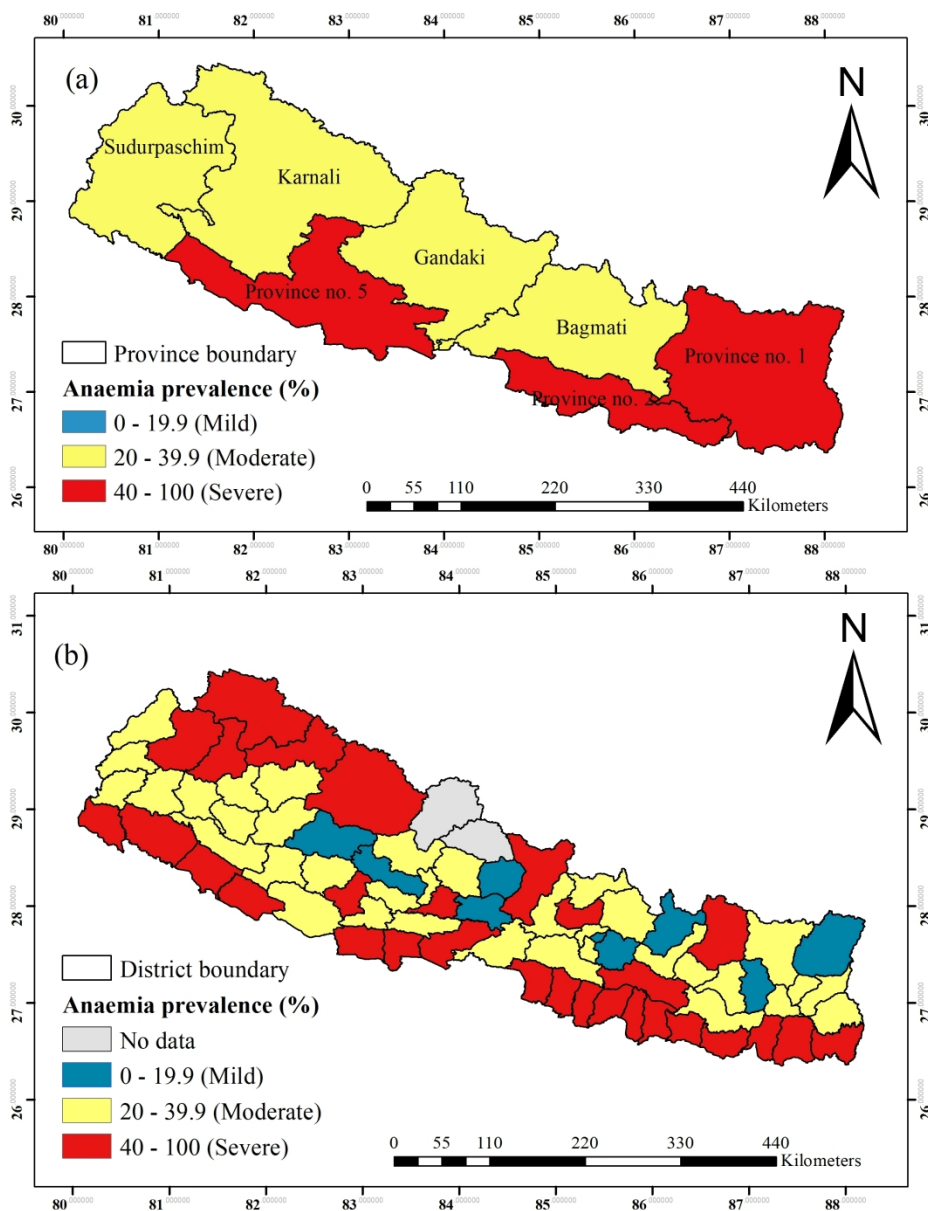


Figure 3 (a) Prevalence of anaemia among women of reproductive age across provinces. 3 (b) Prevalence of anaemia among women of reproductive age across districts

215x279mm (300 x 300 DPI)

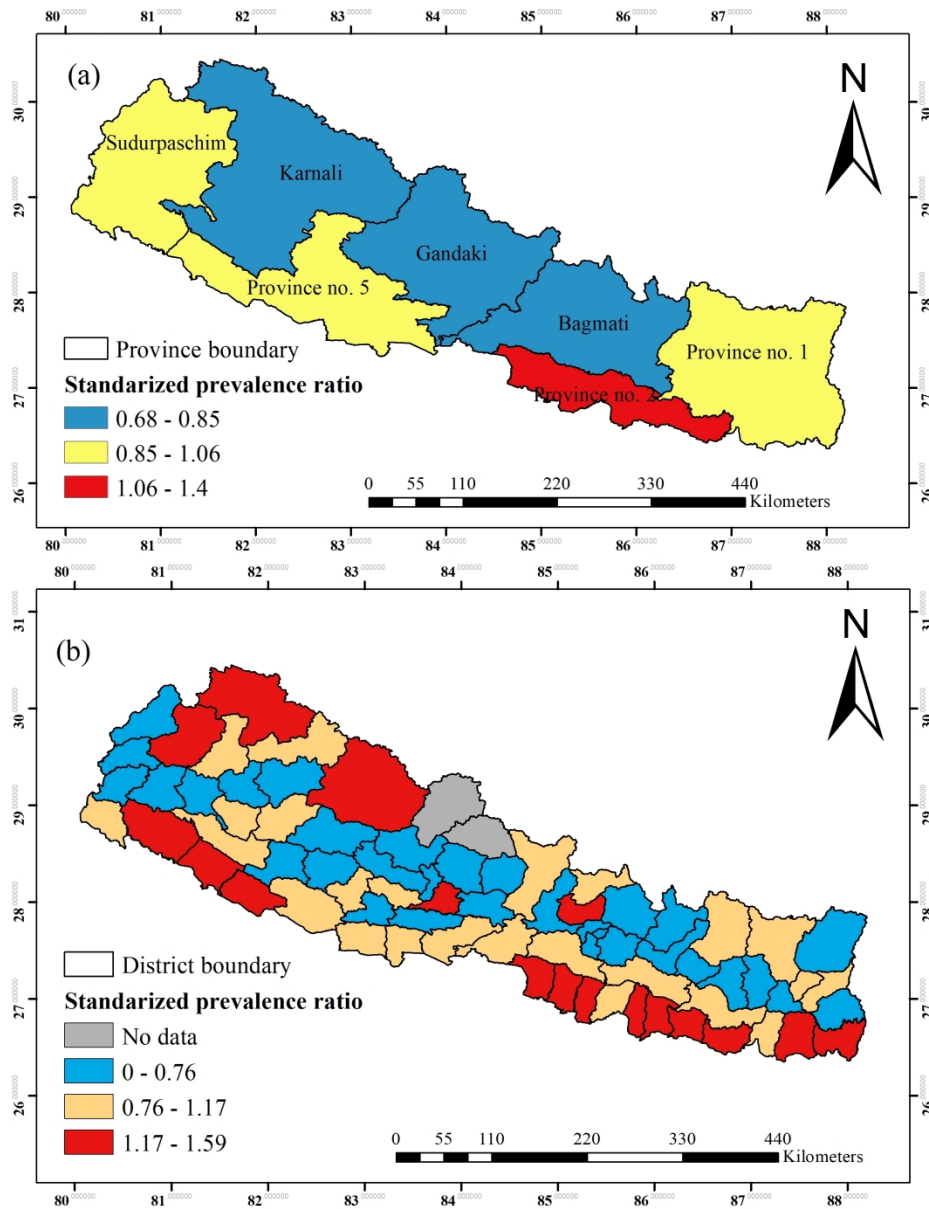


Figure 4 (a) Standardized prevalence ratio of anaemia among women of reproductive age across provinces.
 4 (b) Standardized prevalence ratio of anaemia among women of reproductive age across districts
 (standardized to the national mean prevalence of 41%)

215x279mm (300 x 300 DPI)

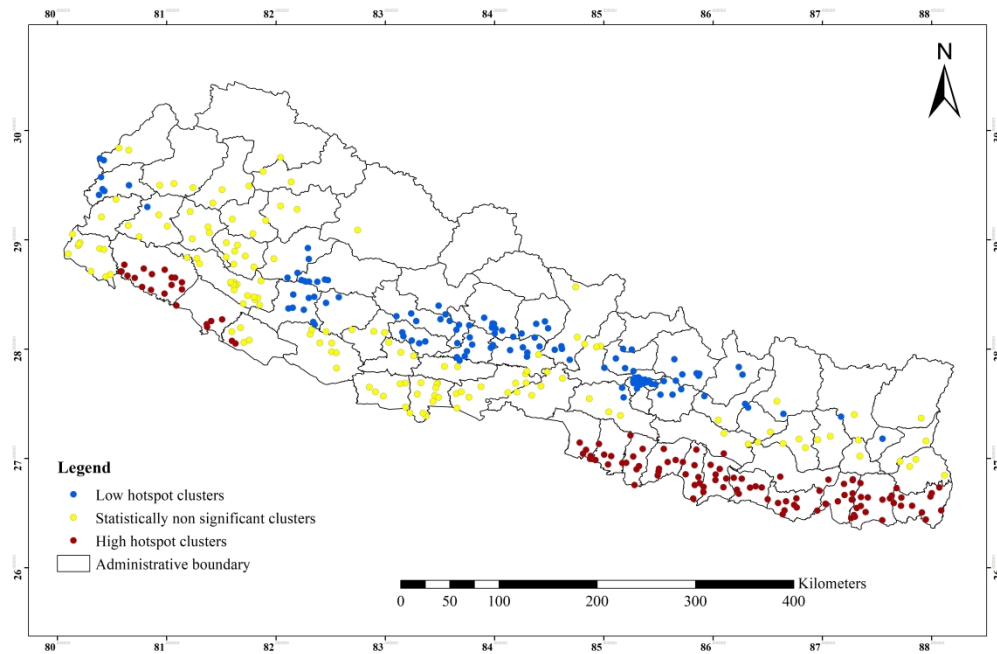


Figure 5 Spatial pattern and distribution of hot and cold spots of anaemia among women of reproductive age at cluster level in Nepal

457x304mm (300 x 300 DPI)

S1 Table Plan for data coding and description of the study variables

Study variables	Coding category for analysis
Age in years	1=15-24; 2=25-34; 3=35-49
Education	1=No education; 2=Primary; 3=Secondary; 4=Higher
Occupation	1= Not working; 2=Working (professional/technical/managerial, clerical, sales/services, agriculture-self-employed, skilled manual, unskilled manual, others)
Wealth index	1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest
Body mass index (BMI)	1=Normal (18.5-24.99); 2=Underweight(<18.5); 3=Overweight/Obesity(≥ 25)
Currently pregnant	1=No; 2=Yes
Currently breastfeeding	1=No; 2=Yes
Total children ever born	1= No child; 2=1-3 child; 3=4+ child
Current contraceptive use	1=Not using; 2=Hormonal (Pill, Injections, Implants/Norplant's, Emergency contraception); 3=Female sterilization; 4=Male contraception; 5= Traditional (Male condom, periodic abstinence, withdrawal, other traditional, lactational amenorrhea)
Cigarette/smoking	1= Smoking; 2=Not smoking
Minimum dietary diversity for women (MDD-W)	1=Not met (consume <5 food groups); 2= Met (Consume ≥ 5 food groups)
Mosquitoes bed net for sleeping	1= No; 2= Yes
Residence	1=Urban; 2=Rural
Province	1=Province-1; 2=Province-2, 3=Bagmati Province; 4=Gandaki Province; 5=Province-5; 6=Karnali Province; 7=Sudurpaschim Province
Community female education	1=Low (mean percent of women with lower primary education level was 0-25%); 2=High (mean percent of women with primary education level above 25%)
Community wealth index	1=Low (mean proportion of women from richest (rich, richest) households in the community was 0-21%); 2=High (mean

	proportion of women from richest (rich, richest) households in the community was above 21%)
Source of drinking water	1=Improved (piped water into dwelling, piped water to yard/plot, public tap or standpipe, tube well or borehole, protected dug well-protected spring and rainwater); 2=Not improved (Piped to neighbor, unprotected well, river, dam ponds, lake, and rainwater)
Type of toilet facility	1=Improved facility (flush toilet, piped sewer system, septic tank, flush/pour flush to pit latrine, ventilated improved pit latrine, pit latrine with slab, and composting toilet); 2=Not improved (flush to somewhere, flush don't know where, pit latrine without slab/open pit, and no facility/bush/field)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	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	8-10
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-10
		(b) Describe any methods used to examine subgroups and interactions	8-10
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA
Results			

Participants	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	10
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	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	11-14
		(b) Report category boundaries when continuous variables were categorized	6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	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	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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.