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Prevalence and Risk Factors Associated with Chronic Kidney Disease in Nepal: Evidence from a Nationally Representative Population Based Study

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4 1 **Prevalence and Risk Factors Associated with Chronic Kidney Disease in Nepal: Evidence**
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6 2 **from a Nationally Representative Population Based Study**
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3 **20 Abstract**
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5 **21 Objective:** This study aimed to determine population based prevalence of Chronic Kidney
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8 **22 Disease (CKD) and its associated factors in Nepal.**
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11 **23 Study Design:** The study was a nationwide population-based cross sectional study
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14 **24 Setting & Participants:** nationally representative sample of 12109 adults aged 20 years and
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16 **25 above between 2016 and 2018 in Nepal.**
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19 **26 Primary and secondary outcome measures:** Primary outcome in this study was population
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21 based prevalence of CKD in Nepal. Presence of CKD defined by using Kidney Disease
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23 Outcomes Quality Initiative (KDOQI) clinical practice guideline criteria. A participant was
24
25 considered to have CKD if the Urine Albumin-to-Creatinine Ratio (uACR) was greater than or equal to
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27 30 mg/g and/or estimated Glomerular Filtration Rate (e-GFR) is less than 60 mL/min/1.73 m² at baseline
28
29 and in follow up. The secondary outcome measure was factors associated with CKD in Nepal. The
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31 co-variate adjusted association of risk factors and CKD was calculated using weighted
32
33 multivariable binary logistic regression.
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38 **34 Results:** The overall weighted prevalence of CKD was 6.0%. (95% CI: 5.5-6.6), and was similar
39
40 across provinces. The prevalence of CKD was higher among male, participants with no formal
41
42 education, urban residents and religious minority group. Other factors independently associated
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44 with CKD included older age, hypertension, diabetes, raised total cholesterol and increased
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46 waist-to-hip ratio.
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51 **39 Conclusion:** This nationally representative study shows that the prevalence of CKD in the adult
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53 population of Nepal is substantial, and it is independently associated with several
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3 41 cardiometabolic traits. These findings warrant longitudinal studies to identify the causes of CKD
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5 42 in Nepal and effective strategies to prevent it.
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9 43 **Keywords:** Chronic Kidney Disease, Nepal, adults, prevalence, eGFR, serum creatinine
10

11 **Strengths and limitations of this study**

12

- 13 • This is the first large scale nationwide population-based prevalence of CKD in Nepal.
 - 14 • Strict training processes and vigorous quality assurance programs were used to ensure the
15 quality of data collection
 - 16 • The use of standardized definitions of CKD as per Kidney Disease Outcomes Quality
17 Initiative (KDOQI) clinical practice guideline facilitates international comparisons of
18 CKD prevalence and risk factors.
 - 19 • High overall response rate
 - 20 • Causal inference is unknown
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45 **Background**

46 Chronic Kidney Disease (CKD) is one of the most rapidly growing non-communicable diseases
47 (NCDs) worldwide ¹. According to the Global Burden of Disease (GBD) study, CKD was the
48 11th leading cause of death in 2019, up from 19th in 1990 accounting for 2.53% of total deaths².
49 CKD is also associated with substantial morbidity, mortality, and healthcare costs. Although it is
50 largely preventable, over 9% of the population worldwide is estimated to be affected by the
51 condition, particularly developing countries ^{3,4}, and it is associated with diabetes type II,
52 hypertension and obesity, which are also growing at an alarming rate. The rapid increase of
53 CKD is likely to impose a great socioeconomic and public health burden in resource-poor
54 setting⁵.

55 The evidence on the prevalence of CKD in South East Asia is relatively limited, but it
56 consistently shows a high prevalence of CKD⁶⁻⁸, however data remain poorly characterized due
57 to inconsistent assessment of kidney function and nonstandard approaches which might distort
58 the true estimates of CKD prevalence. There are few studies in Nepal already warned the higher
59 prevalence of CKD⁹⁻¹¹ and reported data largely depends on the population studied (rural/
60 urban/or general/at high risk group) methods and the lack of representativeness from the
61 general population. Nepal has overcome many of the critical health challenges to survive the
62 first five years of life, and that NCDs and burden of potential underlying risk factors such as
63 obesity, hypertension, and diabetes and unhealthy lifestyle habits including poor diets are highly
64 prevalent¹².

65 Understanding the burden and risk factors associated with CKD is important for making health
66 care planning, designing screening strategies, and prevention of these diseases in this resource

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3 67 constrains setting, where access to renal replacement therapy is costly. Therefore, this study
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5 68 aimed to determine the population based prevalence of CKD and its associated factors in Nepal.
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8 9 **Methods**

10 11 **Study design and subjects**

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13 71 The Nepal Health Research Council designed and implemented the “National Population based
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15 72 Prevalence Survey of Selected NCDs in Nepal”. This was a population-based survey to
16
17 73 investigate the prevalence of NCDs including CKD, chronic obstructive pulmonary disease
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19 74 carried out between 2016 and 2018 in adult's ≥ 20 years old from seven provinces of the country.
20
21 75 Full details of the design and protocols of the survey are available elsewhere¹³.
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26 76 The sample size for the survey was calculated taking as reference the prevalence of raised blood
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28 77 glucose ($p=4\%$) from NCD risk factors: STEPwise approach to Surveillance(STEPS) survey
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30 78 2013¹⁴, Z value of 1.96 at 95% confidence level and margin of error (d) of 20%, design effect of
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32 79 2, adjusting the sample across three domains of the Terai, hills and mountains and adding a non-
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34 80 response rate of 20% yielded a sample size of 12,965. With a plan to enroll 33 participants in
35
36 81 each cluster (400), the final sample size was 13,200. A ward (lowest administrative unit of the -
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38 82 then Village Development Committees (VDCs) and Municipalities) was considered as a cluster-
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40 83 Primary Sampling Unit (PSU) of the study design. With the support from Central Bureau of
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42 84 Statistics, a total of 400 clusters were sampled. The survey team members in the field used
43
44 85 official or socially mapped household list to select 33 households (Secondary Sampling Units –
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46 86 SSUs) from each cluster using systematic random sampling. One participant out of the eligible
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48 87 candidates (≥ 20 years and above, resident in the study area at least 6 months and able to provide
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50 88 informed consent) was selected to take part in the survey using the KISH method. Of 13,200
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52 89 participants who were approached for interview, 12,557 responded to the invitation in Day 1,
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3 90 Among 12,557 who accepted the invitation, only 12,148 participants responded in day 2 of
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5 91 clinical setting. For the present study, data from 12,109 subjects were available for analyses, as
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7 92 39 (0.32%) were excluded, because they refused providing blood and urine samples to evaluate
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9 93 renal function in day 2.

13 94 **Data collection and measurements**

15 95 Data collection was performed in 400 clusters within 72 districts of Nepal. Data collection teams
16
17 96 at each site consisted of five member having academic background of nursing, general medicine,
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19 97 Bachelor in medical laboratory technology or public health.

23 98 Participants' appointment for face to face personal interview at convenient and accessible site or
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25 99 at home on two occasions (Day 1 and Day 2): Following written informed consent, from the
26
27 100 participants in Day 1, a structured questionnaire was administered to collect information about
28
29 101 participants' general health and socio-demographic characteristics. Participants self-reported
30
31 102 their health and socio-demographic status, personal and family medical histories and history of
32
33 103 medicine used. Information concerning their lifestyle factors (cigarette smoking, alcohol intake)
34
35 104 was collected, and then physical and clinical measurements were performed. The clinical
36
37 105 examination included measurements of height, weight, waist hip ratio and blood pressure (BP)
38
39 106 following standard protocols. Height was measured in centimeters with a portable Bioplus®
40
41 107 stature meter and weight with a portable digital seca® 874 weighing scale (Seca, Germany) and
42
43 108 recorded in kilograms ensuring that the participant was wearing light clothes and was without
44
45 109 footwear. Waist circumference was measured using Seca tape in cm at the level midway between
46
47 110 the twelfth rib and the uppermost lateral border of the iliac crest during normal expiration. Blood
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49 111 pressure was measured at least three times with a minimum 3 min, and then averaged to be
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51 112 recorded by using an Omron digital automatic blood pressure monitor model HEM-8712 (Omron
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3 113 Health Care Co., Ltd, Japan) with appropriate sized cuffs ¹⁵. Participants were classified as
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5 114 hypertensive when the Raised BP is defined as having systolic BP ≥ 140 mm of Hg and/or
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7 115 diastolic BP ≥ 90 mm of Hg during the study, or being previously diagnosed as having
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9 116 hypertension.

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13 117 We used fasting, at least an 8-hour fast, and two hour post prandial (PP) blood sample to test
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15 118 various biochemical parameters. Following aseptic technique, blood samples were drawn by a
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17 119 trained enumerators using vacutainers to test laboratory parameters such as fasting blood glucose
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19 120 level, PP blood glucose level, serum creatinine, total cholesterol (TC), triglyceride (TG), high
20
21 121 density lipoprotein (HDL) cholesterol, and serum creatinine. The well trained enumerators
22
23 122 collected around 10 ml of blood sample at the fasting state and provided 82 grams of glucose
24
25 123 monohydrate (equivalent to 75 grams of anhydrous glucose) in 250 ml water to drink. Second
26
27 124 blood sample was collected at 2 hours of glucose intake. Fasting blood glucose, TC, TG, HDL
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29 125 cholesterol and serum creatinine were measured with the fasting sample and two hours PP
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31 126 sample was used for measuring PP blood glucose only. We carried out biochemical analysis with
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33 127 Biolyzer® 100 Clinical Chemistry Analyzer (Semi-automatic biochemistry analyzer, Analyticon,
34
35 128 Germany) and used glucose oxidase-peroxidase (GOD-POD) method for blood glucose,
36
37 129 cholesterol oxidase/phenol aminophenazone (CHOD-PAP) for TC, glycerol-3-phosphate
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39 130 oxidase/phenol aminophenazone (GPO-PAP) for TG, HDL cholesterol by poly ethylene glycol/
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41 131 cholesterol oxidase/ phenol aminophenazone (PEG/CHOD-PAP) and serum creatinine measured
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43 132 by Jaffe Reaction method. The laboratory supervisors calculated the low-density lipoprotein
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45 133 (LDL) cholesterol by Freidewald's Formula using TC, TG, and HDL cholesterol.
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134 **Outcome measurements**

135 A spot urine sample was collected from single voided specimen to measure urine albumin and
136 creatinine using the same semi-automatic biochemistry analyzer (AnalyticonBiolyzer® 100
137 Clinical Chemistry Analyzer, Germany). Laboratory supervisors measured urine albumin
138 concentration by Turbidimetric tests and urine creatinine concentration by Jaffe Reaction method
139 and finally albumin-creatinine ration (ACR) was calculated and expressed in mg/g. Renal
140 function was evaluated by using estimated GFR (eGFR), based on the widely used 4-variable
141 Modification of Diet in Renal Disease Study (MDRD) equation. To confirm CKD, we carried
142 out a follow up test after three months of initial data collection of the participants with albumin
143 creatinine ratio ≥ 30 mg/g. Initially the enumerators took written informed consent from the
144 participants. Then they collected 5 ml blood and random urine samples from the participants
145 using similar procedures as mentioned above.

146 A participant was considered to have CKD if the Urine Albumin-to-Creatinine Ratio (uACR)
147 was greater than or equal to 30 mg/g and/or estimated Glomerular Filtration Rate (e-GFR) is less
148 than 60 mL/min/1.73 m² at baseline and in follow up¹⁶. The secondary outcome measure was
149 factors associated with CKD in Nepal

150 **Data management and analysis**

151 We used android mobile phones inbuilt with data collection software (REMO) to collect data
152 digitally. Data cleaning including correction of inconsistencies was performed in SPSS version
153 20.0. We then exported the dataset to STATA version 13 for analysis. To adjust for unequal
154 distribution of selection and to produce estimates that are representative of the general
155 (national) population, all the estimation was based on sampling weight. Results are expressed as
156 a percentage and odds ratio with 95% CI. Bivariate analysis was conducted to analyze the

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3 157 unconditional association between each explanatory variable and CKD status. To be included in
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5 158 multivariable modeling, the level of significance $\alpha=0.25$ was used during bivariate analysis (i.e.,
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7 159 P-value 0.25 was not statistically significant). Independent variables included demographics
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9
10 160 (age, gender, ethnicity, education, province and place of residence), existing comorbidities
11
12 161 (hypertension, diabetes, raised total cholesterol, increased waist hip ratio), any hypertension, any
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14 162 diabetes (self-reported or physician diagnosed [fasting blood glucose ≥ 126 mg/dl]), lifestyles
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16 163 (smoking and alcohol consumption), overweight or obesity (Body Mass Index [BMI] ≥ 25
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18 164 kg/m²).

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22 165 Multicollinearity, the variance inflation factor (VIF) was assessed for all the independent
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24 166 variables found to be statistically significant from the bivariate analysis. Multivariable logistic
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26 167 regression modeling was conducted with CKD as a dependent variable using the independent
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28 168 variables identified as being statistically significant from the bivariate analysis.
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33 34 35 170 **Results**

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38 171 A total of 12,109 subjects aged 20-60 years were included in the analyses. Among them 61.1%
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40 172 were female, two fifth were adults in the age group 20-59 years (41.6%), one third was from
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42 173 upper caste ethnic group (34.2%), and just above half of them were either illiterate or had no
43
44 174 formal schooling (54.6%). Detailed demographic characteristics of the study population
45
46 175 weighted to be representative of the Nepalese adult population are presented in Table 1.
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50 176 **Table 1: Socio-demographic characteristics of the study participants (N=12,109)**

Characteristics	n	%
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Age		
20-39 years	4336	35.8
40-59 years	5034	41.6
60 years and above	2739	22.6
Sex		
Male	4708	38.9
Female	7401	61.1
Ethnicity		
Upper caste group	4144	34.2
Disadvantaged janajati	2546	21.0
Relatively advantaged janajati	2018	16.7
Disadvantaged non-dalit terai caste	1836	15.2
Dalit	1225	10.1
Religious minorities	340	2.8
Education		
Illiterate/No formal schooling	6607	54.6

Below secondary (<10 years)	2742	22.6
Secondary and above (≥ 10 years)	2760	22.8
Province		
Province 1	2049	16.9
Province 2	2003	16.5
Bagmati Province	3096	25.6
Gandaki Province	1315	10.9
Lumbini Province	2030	16.8
Karnali Province	588	4.9
Sudurpashchim Province	1028	8.5
Place of residence		
Rural	6107	50.4
Urban	6002	49.6

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180 **Table 2: Bivariate and multivariable analysis of sociodemographic risk factors for CKD**
 181 **among the study participants (N=12,109)**

Characteristics	Chronic Kidney Disease				
	N	n (%)	COR (95% CI)	AOR (95% CI)	p- value
Age					
20-39 years	4336	118 (2.6)	1(ref)	1	
40-59 years	5034	294 (5.8)	2.3(1.8-3.0)***	1.4(1.0-1.8)**	0.021
60 years and above	2739	316 (11.5)	4.9 (3.8-6.3)***	2.6(1.9-3.6)***	0.001
Sex					
Female	7401	415 (5.7)	1(ref)		
Male	4708	313 (6.5)	1.2(1.0-1.4)	1.2 (0.8-1.6)	0.425
Ethnicity					
Upper caste	4144	212 (5.1)	1(ref)		
Disadvantaged Janajati	2546	138 (5.4)	1.1(0.8-1.4)	1.1(0.9-1.5)	0.339
Dalit	1225	84 (7.1)	1.4 (1.0-1.9)*	1.6 (1.1-2.3)	0.011
Disadvantaged non-Dalit	1836	116 (6.4)	1.3(0.9-1.7)	1.4 (0.9-2.1)	0.114

terai caste						
Religious minorities	340	25 (8.0)	1.6 (1.0-2.7)	1.7(1.0-2.9)	0.060	
Relatively advantaged Janajati	2018	153 (7.4)	1.5(1.1-2.0)**	1.4(1.0-1.9)	0.028	
Education						
Illiterate/No formal schooling	6607	459 (7.0)	1 (ref)			
Below secondary (<10 years)	2742	146 (5.4)	0.8(0.6-0.9)**	1.1 (0.9-1.5)	0.367	
Secondary and above (≥10 years)	2760	123 (4.5)	0.6(0.5-0.8)***	1.1 (0.7-1.4)	0.894	
Province						
Karnali Province	588	30 (4.7)	1 (ref)			
Province 1	2049	100 (5.2)	1.1 (0.7-1.8)	1.1(0.6-2.0)	0.728	
Province 2	2003	133 (6.6)	1.4(0.9-2.3)	1.2 (0.6-2.2)	0.578	
Bagmati Province	3096	196 (6.5)	1.4(0.9-2.2)	1.1 (0.6-1.9)	0.706	
Gandaki Province	1315	93 (6.8)	1.5 (0.9-2.3)	1.2 (0.7-2.0)	0.575	
Lumbini Province	2030	118 (5.7)	1.2(0.7-2.2)	0.9 (0.5-1.6)	0.705	

Sudurpashchim Province	1028	58(5.9)	1.3(0.7-2.2)	1.4 (0.7-2.6)	0.309
Place of residence					
Rural	6107	341 (5.8)	1 (ref)	-	
Urban	6002	387 (6.5)	1.2(1.0-1.4)	1.0(0.8-1.3)	0.894

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184 **Table 3 Bivariate and multivariate analysis of Behavioral and biological characteristics for**
 185 **CKD among the study participants (N=12,109)**

Characteristics	Chronic Kidney Disease				p- value
	N	n (%)	COR (95%CI)	AOR (95%CI)	
Smoking habit					
Non smoker	8305	443 (5.3)	1(ref)	1(ref)	
Smokers	3804	285 (7.6)	1.5(1.2-1.7)***	1.2(1.0-1.5)	0.104
Alcohol consumption					
No	9131	537 (6.0)	1(ref)		
Yes	2978	191 (6.2)	1.0(0.9-1.2)		
Blood pressure					
Normal	7754	256 (3.3)	1(ref)	1(ref)	
Raised	4355	472 (10.8)	3.6 (3.0-4.3) ***	2.4 (2.0-3.0)***	0.001
Body mass index (N=12108)					
Normal	6896	377 (5.5)	1 (ref)	1(ref)	
Underweight	1494	88 (6.2)	1.1(0.9-1.5) *	1.1(0.8-1.6)	0.531

Overweight and obese	3718	263 (6.9)	1.3(1.1-1.5) **	0.9 (0.7-1.1)	0.153
Total cholesterol (N=10861)					
Normal	7741	398 (5.2)	1(ref)	1(ref)	
Raised	3120	254 (8.2)	1.6(1.3-2.0) ***	1.3(1.0-1.6)**	0.032
Waist hip ratio					
Normal	5095	282 (5.4)	ref		
Increased	6884	440 (6.6)	1.2(1.0-1.5)	1.6(1.2-2.3)	0.005
Diabetes Mellitus					
No	10393	506 (4.8)	1(ref)		
Yes	878	172 (19.8)	4.9(3.8-6.2) ***	3.2(2.5-4.1)	0.001

186

187 Factors associated with CKD

188 The multivariable analyses to investigate the association of independent factors and CKD are
189 shown in Table 3.

190 In the bivariate analysis, age, smoking, BMI, ethnicity, education, having diabetes mellitus
191 (DM), being hypertensive and having raised cholesterol were found to be statistically
192 significantly associated with CKD. Therefore, those 8 factors including place of residence and
193 sex of participants (P-value ≤ 0.25) were considered in the multiple logistic models. After

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3 194 adjustment, only six variables: age, ethnicity, diabetes, hypertension, raised TC, and increased
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5 195 waist hip ratio, were found to be significant predictors of CKD. There was a strong positive
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7 196 association between age and CKD, i.e. the odds of having CKD were about 1.4 (95% CI = 1.0-
8
9 1.8) and 2.6(95% CI= 1.9-3.6) times higher for people aged 40–59 years and ≥ 60 years
10
11 197 respectively, compared with people aged 20-39 years. Participants with DM had about 3.2 (95%
12
13 198 CI = 2.5-4.1) times higher odds of occurrence of CKD than non-diabetic participants. Similarly,
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15 199 participants with raised BP had 2.4 (95% CI = 2.0-3.0) higher odds of having CKD than non-
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17 200 hypertensive/normal participants.
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22 202 Participants with raised total cholesterol had 1.3 (95% CI = 1.0-1.6) times higher odds of having
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24 203 CKD relative to participants who had normal cholesterol level, whereas those with raised waist
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26 204 hip ratio had 1.6(95% CI: 1.2-2.3) times higher odds than normal participants to have CKD.
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28 205 Individuals who were classified as Dalit by ethnicity were 1.6 (95% CI: 1.1-2.3) times or
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30 206 relatively advantaged janajati had 1.4 (OR = 95% CI: 1.0-1.9) times higher odds of having CKD
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32 207 when compared to individuals with an upper caste.
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37 208 **Discussion**

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39 209 This is the first large scale nationwide population based representative study to report prevalence
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41 210 of and factors associated with CKD in Nepal among population aged 20 years and above. CKD
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43 211 was prevalent among 6% of the population. Moreover, increased age, diabetes, hypertension,
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45 212 raised TC, increased waist hip ratio, and education were independently associated to it.
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49 213 The findings show that approximately one every sixteen adults in Nepal is affected by CKD.
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51 214 This value is higher than the 4.7% found in Ghana ¹⁷ , similar to 6.8% in South Korea ¹⁸ , but
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53 215 much lower than the prevalence of many south Asian countries with 29.9% in Pakistan ⁸ , 26.2 %
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3 216 in Bangladesh ¹⁹ and 17.2 % in India ²⁰. However, a comparison between studies depends on the
4
5 217 CKD diagnostic criteria, study design, and methodology. It is also lower than the prevalence
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7 218 reported by a community-based study in eastern part of Nepal ¹¹. We hypothesized some reasons
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10 219 for the lower prevalence of CKD noted in our study compared to studies from India, Pakistan
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12 220 and eastern Nepal. Most of these previous studies were restricted to more of urban centric,
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14 221 specific setting (e.g. hospital) , occupations and age where prevalence of risk factors are higher
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17 222 ^{6,19,21-23}.

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20 223 CKD was not found to be associated with gender in our targeted participants. Earlier literature in
21
22 224 this regard has shown different findings. The association between CKD and gender has been
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24 225 reported in some other studies²⁴⁻²⁶.

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28 226 We also could not find significant association between CKD and alcohol consumption, place of
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30 227 residence, and provinces. Compared to rural settings, CKD seems to be more prevalent in urban
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32 228 areas despite the lack of statistical difference as rapid and unplanned urbanization, has
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34 229 contributed to the rise of kidney disease and other NCDs in Nepal which has led to lifestyles
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36 230 characterized by unhealthy nutrition, reduced physical activity and tobacco and alcohol
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38 231 consumption. However, the prevalence of CKD was not much different among provinces of
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40 232 Nepal.

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45 233 In our study, CKD was more common in participants having lower education level and those
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47 234 from Relatively Advantaged Janajati and Dalit; however, the association was not found to be
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49 235 statistically significant. The association between smoking and CKD was supported by evidence
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51 236 of a dose-response relationship^{27,28}. The association between smoking and CKD was reported in
52
53 237 bivariate analysis only in our study and remained marginally significant in multivariable

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3 238 analysis. Our multivariable analysis found that CKD was independently associated with older
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5 239 age, hypertension, diabetes, raised TC and increased waist hip ratio ($p < 0.05$ for each) which are
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7 240 all major NCDs risk factors and consistent with previous findings^{29–33}.

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11 241 Age is a well-established risk factor for development of CKD³⁴. As expected, age was found to
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13 242 be the most strongly associated risk factor in our study, we observed nearly three times higher
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15 243 odds of occurrence of CKD among people aged 60 years or older compared to people aged 20 to
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17 244 39 years. Generally, as a part of the normal physiologic process, renal function (GFR) starts to
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19 245 decline even in a healthy individual by 1 mL /min/1.73 m² per year after the age of 30 years³⁵. A
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21 246 similar steep increase in CKD prevalence by age has also been reported by others^{36–38}.

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25 247 The number of patients with kidney failure treated by dialysis and transplantation has increased
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27 248 dramatically in Nepal. Because of the costs, limited ability to afford dialysis and the complexity
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29 249 of its treatment, very few patients are able to obtain adequate treatment, and CKD places a heavy
30
31 250 financial burden on any individual and society^{39,40}. Furthermore, there are many challenges
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33 251 concerning prevention and management kidney diseases in Nepal, firstly we currently lack
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35 252 population –based epidemiological data and national registry of kidney diseases. In order to
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37 253 reduce the frequency of disease occurrence, project the management needs of those who would
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39 254 acquire the disease, there is need of a data of its prevalence and associated factors to the extent
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41 255 possible and such knowledge only be obtained from population-based epidemiological studies.

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47 256 The increase in prevalence of CKD and its progression to end-stage renal failure worldwide are
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49 257 mainly a result of the rising global diabetes and hypertension pandemic. In line with other
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51 258 surveys in South East Asia, our findings show that the odds of CKD occurrence was significantly
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53 259 and independently higher by around 2-fold with the presence of hypertension; this supports

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3 260 previous reports^{35,41–43} indicating the importance of early detection and treatment of hypertension
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5 261 in Nepal. In our study people with diabetes mellitus had more than three times higher odds of
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7 262 occurrence of CKD than people without diabetes. Almost one fifth of people with diabetes had
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9 263 CKD as well. Supporting findings from our research, studies around the world indicate diabetes
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11 264 is independently associated with development of CKD^{44,45}. A survey across 10 Asian countries
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13 265 showed that the most common cause of End Stage Renal Disease (ESRD) in 9 out of 10
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15 266 countries was diabetic nephropathy⁴⁶. In addition; elevated total cholesterol was substantially
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17 267 associated with higher odds for CKD.
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22 268 Despite finding an association between CKD and several known established risk factors
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24 269 including waist hip ratio, no association was found between CKD and BMI. The correlation
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26 270 between CKD and waist hip ratio and not BMI is plausible since this ratio is a more sensitive
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28 271 marker for central obesity ,metabolic syndrome and potentially less influenced by muscle mass
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30 272 than BMI, this is in agreement with earlier studies^{47–49}.
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35 273 Evidence suggested that the adverse outcomes of CKD can be prevented or altered through
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37 274 therapeutic interventions during early stages, including regular BP control, blood glucose control
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39 275 in diabetic patient, treatment with angiotensin-receptor blockers and angiotensin-converting
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41 276 enzyme inhibitors and, dietary protein restriction. Given the double burden of disease and the
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43 277 early onset of NCDs in the country – at age 40 people are already having CKD and other co-
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45 278 morbidities, as shown in this manuscript, these findings have important medical and public-
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47 279 health implications, in targeting these “high-risk” population subgroup of the population, to
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49 280 reduce progression and delay the onset of cardiovascular complications and ESRD⁵⁰.
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3 281 Our study poses several strengths. To the best of our knowledge, no national survey of CKD has
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5 282 been done in the context of Nepal as per Kidney Disease Outcomes Quality Initiative (KDOQI)
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7 283 clinical practice guideline; using (eGFR $<60\text{mL}/\text{min}/1.73\text{m}^2$, presence of albuminuria $\geq 30\text{mg}/\text{g}$
8
9 284 and chronicity confirmed by repeated testing after three months) to confirm presence of CKD.
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11 285 This is the first study to report prevalence of CKD using a validated standardized estimation of
12
13 286 the glomerular filtration rate by the MDRD study equation which is carried out in a large
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15 287 representative population-based sample of the adult population in Nepal following the strict
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17 288 guideline and protocols, strict training processes and vigorous quality assurance programs were
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19 289 used to ensure the quality of data collection. Additional strengths of the study include a high
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21 290 overall response rate and analyses based on survey weights which ensure geographic
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23 291 representativeness of the study. Thus, our findings would be generalizable to the general
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25 292 population. However, the limitations of our analysis definitely deserve comment; potential
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27 293 limitations include dependency on estimation of GFR, rather than direct measurement using
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29 294 injection of an exogenous marker factors as well as cross-sectional design of the study which
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31 295 does not permit inferences regarding causal relationships.
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38 296 **Conclusions**

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41 297 This is the first population-based epidemiological survey of CKD using the protocols
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43 298 recommended by KDOQI in Nepal. The prevalence of CKD was found to be 6.0%. CKD was
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45 299 independently associated with older age, hypertension, diabetes mellitus, increased waist hip
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47 300 ratio and raised total cholesterol. Our findings highlight the need for early preventive measures
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49 301 to manage predisposing conditions such as diabetes and hypertension which could ultimately
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51 302 lead to CKD and to reduce the prevalence and mortality arising from the associated
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53 303 comorbidities in Nepal.
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56 305 **Declarations**

7
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20
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22
23

24 312 **Competing interests:** The authors declare no conflict of interest.
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26

27 313 **Data sharing statement:** The datasets used and/or analyzed will be made from the
28
29 314 corresponding author on reasonable request
30
31

32 315 **Author's contributions:** KBK, KKA and MD conceived the study. LG and DKC helped in data
33
34 316 entry and management. AP, BB and NS was involved in conducting data analysis. AP wrote the
35
36 317 manuscript. AKJ supported in monitoring overall data quality. PG, VGL, UK, DAG and SKS
37
38 318 revised and edited the manuscript. Each author provided intellectual content during manuscript
39
40 319 drafting and revision, accepts accountability for their contributions.
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45 320 **Ethics statement:** The study protocol was approved by the Ethical Review Board (ERB) of
46
47 321 Nepal Health Research Council, Government of Nepal (Reg.no.110/2016). Written informed
48
49 322 consent was taken from all participants before proceeding for data collection.
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52 323 **Patient and public involvement:** Patients and/or the public were not involved in the design, or
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54 324 conduct, or reporting, or dissemination plans of this research.
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325 **Patient consent for publication:** Not required.

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

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
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	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
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	8
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	8-9
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8-9
		(c) Explain how missing data were addressed	10
		(d) If applicable, describe analytical methods taking account of sampling strategy	5
		(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	5-6
		(b) Give reasons for non-participation at each stage	5-7
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-17
		(b) Indicate number of participants with missing data for each variable of interest	10-17
Outcome data	15*	Report numbers of outcome events or summary measures	10-17
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	10-17

		which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	10-17
		(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	10-17
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
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	21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
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	22

*Give information separately for exposed and unexposed groups.

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

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Prevalence and Risk Factors Associated with Chronic Kidney Disease in Nepal: Evidence from a Nationally Representative Population Based Study

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4 1 **Prevalence and Risk Factors Associated with Chronic Kidney Disease in Nepal: Evidence**
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6 2 **from a Nationally Representative Population Based Cross sectional Study**
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20 Abstract

21 **Objective:** This study aimed to determine population based prevalence of Chronic Kidney Disease
22 (CKD) and its associated factors in Nepal.

23 **Study Design:** The study was a nationwide population-based cross sectional study

24 **Setting & Participants:** Cross-sectional survey conducted in a nationally representative sample
25 of 12109 Nepalese adult from 2016 to 2018 on selected chronic non-communicable diseases were
26 examined. Multistage cluster sampling with a mix of probability proportionate to size (PPS) and
27 systematic random sampling was used for the selection of individuals aged 20 years and above.

28 **Primary and secondary outcome measures:** Primary outcome in this study was population based
29 prevalence of CKD in Nepal. A participant was considered to have CKD if the Urine Albumin-to-
30 Creatinine Ratio (uACR) was greater than or equal to 30 mg/g and/or estimated Glomerular
31 Filtration Rate (e-GFR) is less than 60 mL/min/1.73 m² at baseline and in follow up using
32 modification of diet in renal disease study (MDRD) equations. The secondary outcome measure
33 was factors associated with CKD in Nepal. The co-variate adjusted association of risk factors and
34 CKD was calculated using multivariable binary logistic regression.

35 **Results:** The overall prevalence of CKD in Nepal was 6.0% (95% CI: 5.5-6.6). Factors
36 independently associated with CKD included older age, (adjusted OR (AOR) 2.6, 95% CI: 1.9 to
37 3.6), Dalit caste (AOR 1.6, 95% CI: 1.1 to 2.3), hypertension, (AOR 2.4, 95% CI: 2.0 to 3.0)
38 diabetes mellitus (AOR 3.2, 95% CI: 2.5 to 4.1), raised total cholesterol (AOR 1.3, 95% CI: 1.0 to
39 1.6) and increased waist-to-hip ratio (AOR 1.6, 95% CI: 1.2 to 2.3).

40 **Conclusion:** This nationally representative study shows that the prevalence of CKD in the adult
41 population of Nepal is substantial, and it is independently associated with several cardiometabolic

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3 42 traits. These findings warrant longitudinal studies to identify the causes of CKD in Nepal and
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5 43 effective strategies to prevent it.
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8
9 44 **Keywords:** Chronic Kidney Disease, Nepal, adults, prevalence, eGFR, serum creatinine
10

11 **Strengths and limitations of this study**

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- 13 • This is the first large scale nationwide population-based prevalence of CKD in Nepal.
 - 14 • Strict training processes and vigorous quality assurance programs were used to ensure
15 the quality of data collection
 - 16 • The use of standardized definitions of CKD facilitates international comparisons of CKD
17 prevalence and risk factors.
 - 18 • High overall response rate of 91.7. % in first visit and 86.9% in follow up visit.
 - 19 • Causal inference is unknown
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46 **Background**

47 Chronic Kidney Disease (CKD) is one of the most rapidly growing non-communicable diseases
48 (NCDs) worldwide ¹. According to the Global Burden of Disease (GBD) study, CKD was the
49 11th leading cause of death in 2019, up from 19th in 1990 accounting for 2.53% of total deaths².
50 CKD is also associated with substantial morbidity, mortality, and healthcare costs. Although it is
51 largely preventable, over 9% of the population worldwide is estimated to be affected by the
52 condition, particularly developing countries ^{3,4}, and it is associated with diabetes type II,
53 hypertension and obesity, which are also growing at an alarming rate. The rapid increase of CKD
54 is likely to impose a great socioeconomic and public health burden in in resource-poor setting⁵.
55 The evidence on the prevalence of CKD in South East Asia is relatively limited, but it consistently
56 shows a high prevalence of CKD⁶⁻⁸, however data remain poorly characterized due to inconsistent
57 assessment of kidney function and nonstandard approaches which might distort the true estimates
58 of CKD prevalence. There are few studies in Nepal already warned the higher prevalence of CKD⁹⁻
59 ¹¹ and reported data largely depends on the population studied (rural/ urban/or general/at high risk
60 group) methods and the lack of representativeness from the general population. Nepal has
61 overcome many of the critical health challenges to survive the first five years of life, and that
62 NCDs and burden of potential underlying risk factors such as obesity, hypertension, and diabetes
63 and unhealthy lifestyle habits including poor diets are highly prevalent¹².
64 Understanding the burden and risk factors associated with CKD is important for making health
65 care planning, designing screening strategies, and prevention of these diseases in this resource
66 constrains setting, where access to renal replacement therapy is costly. Therefore, this study aimed
67 to determine the population based prevalence of CKD and its associated factors in Nepal.

68 **Methods**

69 **Study design and subjects**

70 The Nepal Health Research Council designed and implemented the “National Population based
71 Prevalence Survey of Selected NCDs in Nepal”. This was a population-based survey to investigate
72 the prevalence of NCDs including CKD, chronic obstructive pulmonary disease carried out
73 between 2016 and 2018 in adult's ≥ 20 years old from seven provinces of the country. Full details
74 of the design and protocols of the survey are available elsewhere¹³.

75 **Participants, sample size, and study setting**

76 The sample size for the survey was calculated taking as reference the prevalence of raised blood
77 glucose ($p=4\%$) from NCD risk factors: STEPwise approach to Surveillance(STEPS) survey
78 2013¹⁴, Z value of 1.96 at 95% confidence level and margin of error (d) of 20%, design effect of
79 2, adjusting the sample across three domains of the Terai, hills and mountains and adding a non-
80 response rate of 20% yielded a sample size of 12,965. With a plan to enroll 33 participants in each
81 cluster (400), the final sample size was 13,200. A ward (lowest administrative unit of the -then
82 Village Development Committees (VDCs) and Municipalities) was considered as a cluster-
83 Primary Sampling Unit (PSU) of the study design. With the support from Central Bureau of
84 Statistics, a total of 400 clusters were sampled. To select a representative sample of cluster; the
85 rural and urban areas within each region were identified as the main sampling strata and the sample
86 was selected in two stages in which ecological belts (Terai, Hill and Mountains) and five
87 development region (Central, Eastern, Mid-Western, Western and Far western), stratification was
88 taken into account.

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3 89 The survey team members in the field used official or socially mapped household list to select 33
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5 90 households (Secondary Sampling Units – SSUs) from each cluster using systematic random
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8 91 sampling. One participant out of the eligible candidates (≥ 20 years and above, resident in the study
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10 92 area at least 6 months and able to provide informed consent) was selected to take part in the survey
11
12 93 using the KISH method. Of 13,200 participants who were approached for interview, 12,557
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14 94 responded to the invitation in Day 1, Among 12,557 who accepted the invitation, only 12,148
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16 95 participants responded in day 2 of clinical setting. For the present study, data from 12,109 subjects
17
18 96 were available for analyses with a response rate of 91.7%, 39 (0.32%) were excluded, because they
19
20 97 refused providing blood and urine samples to evaluate renal function in day 2.
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23

24 98 Data weighting was carried out to make the sampled population comparable to the national
25
26 99 population. Data weighting was done using sampling weight. Sample weighting was carried out
27
28 100 for probabilities of selection of Primary sampling unit (Ward/cluster), selection of households, and
29
30 101 selection of an individual in a household using 2011 population for Nepal with the support from
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32 102 Central Bureau of Statistics.
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36 37 103 **Data collection and measurements**

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39 104 Data collection was performed in 400 clusters (figure 1) within 72 districts of Nepal. Data
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41 105 collection teams at each site consisted of five member having academic background of nursing,
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43 106 general medicine, Bachelor in medical laboratory technology or public health.
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47 107 Participants' appointment for face to face personal interview at convenient and accessible site or
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49 108 at home on two occasions (Day 1 and Day 2): Following written informed consent, from the
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51 109 participants in Day 1, a structured questionnaire was administered to collect information about
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53 110 participants' general health and socio-demographic characteristics. Participants self-reported their
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3 111 health and socio-demographic status, personal and family medical histories and history of
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5 112 medicine used. Information concerning their lifestyle factors (cigarette smoking, alcohol intake)
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8 113 was collected, and then physical and clinical measurements were performed. The clinical
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10 114 examination included measurements of height, weight, waist hip ratio and blood pressure (BP)
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12 115 following standard protocols. Height was measured in centimeters with a portable Bioplus®
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14 116 stature meter and weight with a portable digital seca® 874 weighing scale (Seca, Germany) and
15
16 117 recorded in kilograms ensuring that the participant was wearing light clothes and was without
17
18 118 footwear. Waist circumference was measured using Seca tape in cm at the level midway between
19
20 119 the twelfth rib and the uppermost lateral border of the iliac crest during normal expiration. Blood
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22 120 pressure was measured at least three times with a minimum 3 min, and then averaged to be
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24 121 recorded by using an Omron digital automatic blood pressure monitor model HEM-8712 (Omron
25
26 122 Health Care Co., Ltd, Japan) with appropriate sized cuffs ¹⁵. Participants were classified as
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28 123 hypertensive when the Raised BP is defined as having systolic BP ≥ 140 mm of Hg and/or diastolic
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30 124 BP ≥ 90 mm of Hg during the study, or being previously diagnosed as having hypertension.
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36 125 We used fasting, at least an 8-hour fast, and two hour post prandial (PP) blood sample to test
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38 126 various biochemical parameters. Following aseptic technique, blood samples were drawn by a
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40 127 trained enumerators using vacutainers to test laboratory parameters such as fasting blood glucose
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42 128 level, PP blood glucose level, serum creatinine, total cholesterol (TC), triglyceride (TG), high
43
44 129 density lipoprotein (HDL) cholesterol, and serum creatinine. The well trained enumerators
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46 130 collected around 10 ml of blood sample at the fasting state and provided 82 grams of glucose
47
48 131 monohydrate (equivalent to 75 grams of anhydrous glucose) in 250 ml water to drink. Second
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50 132 blood sample was collected at 2 hours of glucose intake. Fasting blood glucose, TC, TG, HDL
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52 133 cholesterol and serum creatinine were measured with the fasting sample and two hours PP sample
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3 134 was used for measuring PP blood glucose only. We carried out biochemical analysis with
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5 135 Biolyzer® 100 Clinical Chemistry Analyzer (Semi-automatic biochemistry analyzer, Analyticon,
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7 136 Germany) and used glucose oxidase-peroxidase (GOD-POD) method for blood glucose,
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9 137 cholesterol oxidase/phenol aminophenazone (CHOD-PAP) for TC, glycerol-3-phosphate
10
11 138 oxidase/phenol aminophenazone (GPO-PAP) for TG, HDL cholesterol by poly ethylene glycol/
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13 139 cholesterol oxidase/ phenol aminophenazone (PEG/CHOD-PAP) and serum creatinine measured
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15 140 by Jaffe Reaction method. The laboratory supervisors calculated the low-density lipoprotein
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17 141 (LDL) cholesterol by Freidewald's Formula using TC, TG, and HDL cholesterol.
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22 142 **Outcome measurements**

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24 143 A spot urine sample was collected from single voided specimen to measure urine albumin and
25
26 144 creatinine using the same semi-automatic biochemistry analyzer (AnalyticonBiolyzer® 100
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28 145 Clinical Chemistry Analyzer, Germany). Laboratory supervisors measured urine albumin
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30 146 concentration by Turbidimetric tests and urine creatinine concentration by Jaffe Reaction method
31
32 147 and finally albumin-creatinine ratio (ACR) was calculated and expressed in mg/g. Renal function
33
34 148 was evaluated by using estimated GFR (eGFR), based on the widely used 4-variable Modification
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36 149 of Diet in Renal Disease Study (MDRD) equation. A participant was considered to have CKD if
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38 150 the Urine Albumin-to-Creatinine Ratio (uACR) was greater than or equal to 30 mg/g and/or
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40 151 estimated Glomerular Filtration Rate (e-GFR) was less than 60 mL/min/1.73 m² at baseline and in
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42 152 follow up¹⁶. The secondary outcome measure was factors associated with CKD in Nepal
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49 153 **Follow up of study participants to determine CKD**

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51 154 Participants having albumin-creatinine ratio (ACR) greater than or equal to 30 mg/g in the baseline
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53 155 were revisited again after 3 months in their place of residence to ensure the chronicity of the renal
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3 156 disease. Written consent was taken prior to blood and urine sample collection using similar
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5 157 procedures as mentioned above. Out of 1382 participants having a high ACR ratio in the baseline,
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7 158 1202 gave consent. However, data of ACR was missing for 8 participants making the
8
9 159 availability of complete data for 1194 participants for analysis, with a response rate of 86.9%.

13 160 **Data management and analysis**

15 161 We used android mobile phones inbuilt with data collection software (REMO) to collect data
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17 162 digitally. Data cleaning including correction of inconsistencies was performed in SPSS version
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19 163 20.0. We then exported the dataset to STATA version 13 for analysis. To adjust for unequal
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21 164 probability of selection, appropriate sampling weights with complex sampling analysis were used
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23 165 to provide valid estimates for the relevant Nepalese population which is based on 2011 national
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25 166 population and housing census data. Results are expressed as a percentage and odds ratio with 95%
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27 167 CI. Bivariate analysis was conducted to analyze the unconditional association between each
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29 168 explanatory variable and CKD status. To be included in multivariable modeling, the level of
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31 169 significance $\alpha=0.25$ was used during bivariate analysis (i.e., P-value 0.25 was not statistically
32
33 170 significant). Independent variables included demographics (age, gender, ethnicity, education,
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35 171 province and place of residence), existing comorbidities (hypertension, diabetes, raised total
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37 172 cholesterol, increased waist hip ratio), any hypertension, any diabetes (self-reported or physician
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39 173 diagnosed [fasting blood glucose ≥ 126 mg/dl]), lifestyles (smoking and alcohol consumption),
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41 174 overweight or obesity (Body Mass Index [BMI] ≥ 25 kg/m²).

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43 175 Ethnicity/ caste data were self-reported and categorized into six major groups based on the caste
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45 176 coding by government of Nepal and STEPS survey Nepal, 2013 categorization¹⁷. (1) Upper Caste
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47 177 Groups (population with relatively higher socio economic and education status, mostly Brahmins,
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49 178 Chhetris, Thakuri and Sanyasi);(2) Disadvantaged Janajatis (disadvantaged group of people and

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3 179 also indigenous, with relatively lower socio-economic and education status);(3) Dalit
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5 180 (untouchables, most disadvantaged marginalized group of people, with relatively lower socio-
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7 181 economic and education status); (4) Disadvantaged non Dalit Terai Caste Groups (disadvantaged
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9 182 group of people from the Terai, the lowlands, with relatively lower socio-economic and education
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11 183 status but not the dalit groups); (5)Religious Minorities (Muslim, Christian, etc.); (6) Relatively
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13 184 advantaged Janajatis (indigenous group of people with relatively higher socio-economic status,
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15 185 such as Gurung , Newar and Thakali)
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20 186 Multicollinearity, the variance inflation factor (VIF) was assessed for all the independent variables
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22 187 found to be statistically significant from the bivariate analysis. Multivariable logistic regression
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24 188 modeling was conducted with CKD as a dependent variable using the independent variables
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26 189 identified as being statistically significant from the bivariate analysis.
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33 191 **Results**

34
35 192 A total of 12,109 subjects aged 20 years and above were included in the analyses. Among them
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37 193 61.1% were female, two fifth were adults in the age group 20-59 years (41.6%), one third was
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39 194 from upper caste ethnic group (34.2%), and just above half of them were either illiterate or had no
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41 195 formal schooling (54.6%). Table 1 presents the unweighted numbers and proportions of different
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43 196 demographic characteristics of the study population as measured in the study.
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198 **Table 1: Socio-demographic characteristics of the study participants (N=12,109)**

Characteristics	n	%
Age		
20-39 years	4336	35.8
40-59 years	5034	41.6
60 years and above	2739	22.6
Sex		
Male	4708	38.9
Female	7401	61.1
Ethnicity		
Upper caste group	4144	34.2
Disadvantaged janajati	2546	21.0
Relatively advantaged janajati	2018	16.7
Disadvantaged non-dalit terai caste	1836	15.2
Dalit	1225	10.1
Religious minorities	340	2.8
Education		

Illiterate/No formal schooling	6607	54.6
Below secondary (<10 years)	2742	22.6
Secondary and above (≥ 10 years)	2760	22.8
Province		
Province 1	2049	16.9
Province 2	2003	16.5
Bagmati Province	3096	25.6
Gandaki Province	1315	10.9
Lumbini Province	2030	16.8
Karnali Province	588	4.9
Sudurpaschim Province	1028	8.5
Place of residence		
Rural	6107	50.4
Urban	6002	49.6

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202 **Table 2 Factors associated with chronic kidney disease by univariate and multivariate**
 203 **analysis (N = 12109)**

Characteristics	Count	Chronic Kidney Diseases(CKD)		
	N	CKD prevalence (n %)	COR (95% CI)	AOR(95% CI)
Age				
20-39 years	4336	118 (2.6)	1	1
40-59 years	5034	294 (5.8)	2.3(1.8-3.0)***	1.4(1.0-1.8)*
60 years and above	2739	316 (11.5)	4.9 (3.8-6.3)***	2.6(1.9-3.6)***
Sex				
Female	7401	415 (5.7)	1	1
Male	4708	313 (6.5)	1.2(1.0-1.4)	1.2 (0.8-1.6)
Ethnicity				
Upper caste	4144	212 (5.1)	1	1
Disadvantaged Janajati	2546	138 (5.4)	1.1(0.8-1.4)	1.1(0.9-1.5)
Dalit	1225	84 (7.1)	1.4 (1.0-1.9)*	1.6 (1.1-2.3) **
Disadvantaged non-Dalitterai caste	1836	116 (6.4)	1.3(0.9-1.7)	1.4 (0.9-2.1)
Religious minorities	340	25 (8.0)	1.6 (1.0-2.7)	1.7(1.0-2.9)

1 2 3 4 5 6 7 8	Relatively advantaged Janajati	2018	153 (7.4)	1.5(1.1-2.0)*	1.4(1.0-1.9)*
9	Education				
10 11 12 13 14 15	Illiterate/No formal schooling	6607	459 (7.0)	1	1
16 17 18 19 20	Below secondary (<10 years)	2742	146 (5.4)	0.8(0.6-0.9)**	1.1 (0.9-1.5)
21 22 23 24	Secondary and above (≥10 years)	2760	123 (4.5)	0.6(0.5-0.8)***	1.1 (0.7-1.4)
25	Province				
26 27 28 29 30	Karnali Province	588	30 (4.7)	1	1
31 32 33	Province 1	2049	100 (5.2)	1.1 (0.7-1.8)	1.1(0.6-2.0)
34 35 36	Province 2	2003	133 (6.6)	1.4(0.9-2.3)	1.2 (0.6-2.2)
37 38 39	Bagmati Province	3096	196 (6.5)	1.4(0.9-2.2)	1.1 (0.6-1.9)
40 41 42	Gandaki Province	1315	93 (6.8)	1.5 (0.9-2.3)	1.2 (0.7-2.0)
43 44 45	Lumbini Province	2030	118 (5.7)	1.2(0.7-2.2)	0.9 (0.5-1.6)
46 47 48 49	Sudurpashchim Province	1028	58(5.9)	1.3(0.7-2.2)	1.4 (0.7-2.6)
50	Place of residence				
51 52 53 54 55 56	Rural	6107	341 (5.8)	1	1

Urban	6002	387 (6.5)	1.2(1.0-1.4)	1.0(0.8-1.3)
Smoking habit				
Non smoker	8305	443 (5.3)	1	1
Smokers	3804	285 (7.6)	1.5(1.2-1.7)***	1.2(1.0-1.5)
Alcohol consumption				
No	9131	537 (6.0)	1	1
Yes	2978	191 (6.2)	1.0(0.9-1.2)	
Blood pressure				
Normal	7754	256 (3.3)	1	1
Raised	4355	472 (10.8)	3.6 (3.0-4.3) ***	2.4 (2.0-3.0)***
Body mass index (N=12108)#				
Normal	6896	377 (5.5)	1	1
Underweight	1494	88 (6.2)	1.1(0.9-1.5)	1.1(0.8-1.6)
Overweight and obese	3718	263 (6.9)	1.3(1.1-1.5) **	0.9 (0.7-1.1)
Total cholesterol (N=10861)#				
Normal	7741	398 (5.2)	1	1

Raised	3120	254 (8.2)	1.6(1.3-2.0) ***	1.3(1.0-1.6)*
Waist hip ratio (N=11979)#				
Normal	5095	282 (5.4)	1	1
Increased	6884	440 (6.6)	1.2(1.0-1.5) *	1.6(1.2-2.3) *
Diabetes Mellitus (N=11271)#				
No	10393	506 (4.8)	1	1
Yes	878	172 (19.8)	4.9(3.8-6.2) ***	3.2(2.5-4.1)***
Total	12109	6.0 (95% CI: 5.5 -6.6)		

Definition of chronic kidney disease status: Urinary albumin to creatinine ratio of ≥ 30 mg/g and/or glomerular filtration rate < 60 ml/min/1.73 m² both at baseline and follow up)

OR: odds ratio; CI: Confidence interval; COR: Crude odds ratio; AOR: Adjusted odds ratio. Adjusted OR estimated from the stepwise multivariate logistic regression model with all the above variables added except alcohol consumption.

¹ Reference group.

* Indicated the corresponding variable had significant impact on the occurrence of CKD.

*p value ≤ 0.05 **p value ≤ 0.01 ***p value ≤ 0.0001

Missing value; refusal for blood sample collection led to variation in the sample size

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207 Prevalence of CKD

208 The overall prevalence of CKD based on the eGFR MDRD equation, (urinary albumin to
209 creatinine ratio of ≥ 30 mg/g and/or glomerular filtration rate < 60 both at baseline and follow up)
210 was 6.0% (95% CI: 5.5-6.6). The prevalence was higher in males compared to female (6.5 vs 5.7)
211 though not statistically significant. Prevalence increased with increasing age (11.5% among 60
212 years and above and 2.6 % among 20-39 years age group). (Table 2). The mean (\pm SD) eGFR in
213 baseline was 92.6 (± 22.1) mL/min/1.73 m² for male and 88.2 (± 20.5) mL/min/1.73 m² for female
214 (figure 2) .The mean (\pm SD) eGFR was 88.0 (± 25.7) mL/min/1.73 m² for male and 81.1 (± 23.4)
215 mL/min/1.73 m² for female in follow up (figure 3).

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219 **Factors associated with CKD**

220 The multivariable analyses to investigate the association of independent factors and CKD are
221 shown in Table 2. In the bivariate analysis, age, smoking, BMI, ethnicity, education, having
222 diabetes mellitus (DM), being hypertensive, increased waist hip ratio, and having raised total
223 cholesterol were found to be statistically significantly associated with CKD. Therefore, those 9
224 factors including place of residence, province, and sex of participants (P-value ≤ 0.25) were
225 considered in the multiple logistic models. After adjustment, only six variables: age, ethnicity,
226 diabetes, hypertension, raised TC, and increased waist hip ratio, were found to be significant
227 predictors of CKD. There was a strong positive association between age and CKD, i.e. the odds of
228 having CKD were about 1.4 (95% CI : 1.0-1.8) and 2.6(95% CI: 1.9-3.6) times higher for people
229 aged 40–59 years and ≥ 60 years respectively, compared with people aged 20-39 years. Participants
230 with DM had about 3.2 (95% CI: 2.5-4.1) times higher odds of occurrence of CKD than non-
231 diabetic participants. Similarly, participants with raised BP had 2.4 (95% CI: 2.0-3.0) higher odds
232 of having CKD than non-hypertensive/normal participants.

233 Participants with raised total cholesterol had 1.3 (95% CI: 1.0-1.6) times higher odds of having
234 CKD relative to participants who had normal cholesterol level, whereas those with raised waist
235 hip ratio had 1.6(95% CI: 1.2-2.3) times higher odds than normal participants to have CKD.
236 Individuals who were classified as Dalit by ethnicity were 1.6 (95% CI: 1.1-2.3) times or relatively
237 advantaged janajati had 1.4 (95% CI: 1.0-1.9) times higher odds of having CKD when compared
238 to individuals with an upper caste.

239 Discussion

240 This is the first large scale nationwide population based representative study to report prevalence
241 of and factors associated with CKD in Nepal among population aged 20 years and above. In the
242 absence of population validated e-GFR equation for our population, MDRD equation as done in
243 previous studies was chosen over the CKD-EPI equation to facilitate comparison of results, CKD
244 was prevalent among 6% of the population. The findings show that approximately one every
245 sixteen adults in Nepal is affected by CKD. This value is higher than the population based study
246 conducted in Morocco 5.1%¹⁸ and Vietnam 3.1%¹⁹, almost similar to 6.8% in South Korea²⁰,
247 east African countries including Uganda and Kenya²¹ but much lower than the prevalence of many
248 Asian countries with 10.2% in china²², 17.5% in Thailand²³, 18.9% in Iran²⁴ and 17.2% in India
249²⁵. Prevalence of CKD in Nepal is lower than the global burden of disease study estimated
250 prevalence of 8%–10%³ globally. However, these differences in the prevalence of CKD may be in
251 part due to the differences in CKD diagnostic criteria, study design, laboratory methods and lack
252 of validated measures for eGFR for Nepalese population.

253 Our multivariable analysis found that CKD was independently associated with age, hypertension,
254 diabetes, raised TC, ethnicity and increased waist hip ratio ($p < 0.05$ for each) which are all major
255 NCDs risk factors and consistent with previous findings^{26–30}. Age is a well-established risk factor
256 for development of CKD³¹. As expected, age was found to be the most strongly associated risk
257 factor in our study, we observed nearly three times higher odds of occurrence of CKD among
258 people aged 60 years or older compared to people aged 20 to 39 years. Generally, as a part of the
259 normal physiologic process, renal function (GFR) starts to decline even in a healthy individual by
260 1 mL/min/1.73 m² per year after the age of 30 years³². A similar steep increase in CKD prevalence
261 by age has also been reported by others^{33–35}.

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3 262 In line with other surveys in South East Asia, our findings show that the odds of CKD occurrence
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5 263 was significantly and independently higher by around 2-fold with the presence of hypertension;
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7 264 this supports previous reports^{32,36–38} indicating the importance of early detection and treatment of
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9 265 hypertension in Nepal. In our study people with diabetes mellitus had more than three times higher
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11 266 odds of occurrence of CKD than people without diabetes. Almost one fifth of people with diabetes
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13 267 had CKD as well. Supporting findings from our research, studies around the world indicate
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15 268 diabetes is independently associated with development of CKD^{39,40}. A survey across 10 Asian
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17 269 countries showed that the most common cause of End Stage Renal Disease (ESRD) in 9 out of 10
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19 270 countries was diabetic nephropathy⁴¹. In addition; elevated total cholesterol was substantially
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21 271 associated with higher odds for CKD. Given the double burden of disease and the early onset of
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23 272 NCDs in the country – at age 40 people are already having CKD and other co-morbidities, as
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25 273 shown in this manuscript, these findings have important medical and public-health implications,
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27 274 in targeting these “high-risk” population subgroup of the population, to reduce progression and
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29 275 delay the onset of cardiovascular complications and ESRD⁴².

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31 276 Nepal is an ethnically diverse country with more than 125 castes/ethnic groups. Interestingly
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33 277 ethnicity/ caste was another factor contributing to CKD in our study. Compared with upper caste
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35 278 participants, Dalit participants had a significantly higher prevalence of CKD. The mechanism
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37 279 underlying these differences might be multifactorial, including cultural differences such as
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39 280 smoking and drinking habit, lifestyle and genetic factors. By ethnicity, Dalit group of people are
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41 281 considered as one of the most marginalized in terms of socioeconomic, education, political and
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43 282 health indicators, resulting in decreased access to resources and higher vulnerability to poor
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45 283 health outcomes. This calls for future studies regarding CKD on ethnic differences.
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3 285 Despite finding an association between CKD and several known established risk factors including
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5 286 waist hip ratio, no association was found between CKD and BMI. The correlation between CKD
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8 287 and waist hip ratio and not BMI is plausible since this ratio is a more sensitive marker for central
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10 288 obesity ,metabolic syndrome and potentially less influenced by muscle mass than BMI, this is in
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12 289 agreement with earlier studies^{28,43,44}. The association between smoking and CKD was reported in
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15 290 bivariate analysis only in our study.

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18 291 In general, the prevalence of CKD was higher among women compared to men, and this difference
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20 292 has been demonstrated in the past by several population based cross sectional studies.⁴⁵ However
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22 293 in the present study, though not statistically significant, we found slightly higher prevalence of
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24 294 CKD among male participants. These discrepancies in the prevalence may be due to the traditional
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27 295 risk factors such as hypertension and hyperglycemia being prevalent among male participant in
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29 296 our study. We also could not find significant association between CKD and alcohol consumption,
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31 297 place of residence, and provinces.

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35 298 Traditional risk factors such as diabetes and hypertension are the major cause of CKD in most
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37 299 developed and developing countries^{46,47}, and several other nontraditional and environmental risk
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39 300 factors such as infectious diseases, analgesic abuse, exposure to heavy metal (Lead, Arsenic,
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41 301 Mercury and Uranium), pesticides, herbal medications, and environmental pollution, impose an
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44 302 additionally threat worsening CKD especially in developing countries⁴⁸ including Nepal .
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46 303 However, we lack information about environmental and some of the nontraditional risk factor,
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48 304 which could be used to quantify the effects of these factors on CKD

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52 305 Our study poses several strengths. To the best of our knowledge, no national survey of CKD has
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54 306 been done in the context of Nepal as per Kidney Disease Outcomes Quality Initiative (KDOQI)

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3 307 clinical practice guideline; using (eGFR <60mL/min/1.73m², presence of albuminuria ≥30mg/g
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5 308 and chronicity confirmed by repeated testing after three months) to confirm presence of CKD. This
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7 309 is the first study to report prevalence of CKD using a validated standardized estimation of the
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9 310 glomerular filtration rate by the MDRD study equation which is carried out in a large
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11 311 representative population-based sample of the adult population in Nepal following the strict
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13 312 guideline and protocols, strict training processes and vigorous quality assurance programs were
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15 313 used to ensure the quality of data collection. Additional strengths of the study include a high overall
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17 314 response rate and analyses based on survey weights which ensure geographic representativeness
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19 315 of the study. Thus, our findings would be generalizable to the general population. However, the
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21 316 limitations of our analysis definitely deserve comment; potential limitations include dependency
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23 317 on estimation of GFR, rather than direct measurement using injection of an exogenous marker
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25 318 factors as well as cross-sectional design of the study which does not permit inferences regarding
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27 319 causal relationships.
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34 320 **Conclusions**

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36 321 This is the first population-based epidemiological survey of CKD using the protocols
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38 322 recommended by KDOQI in Nepal. The prevalence of CKD was found to be 6.0%. The prevalence
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40 323 of CKD was higher among male, participants with no formal education, urban residents, smokers
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42 324 and participants with overweight and obese. CKD was independently associated with older age,
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44 325 hypertension, diabetes mellitus, increased waist hip ratio, raised total cholesterol and individual
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46 326 belonging to the Dalit caste by ethnicity. Our findings highlight the need for early preventive
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48 327 measures to manage predisposing conditions such as diabetes and hypertension which could
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50 328 ultimately lead to CKD and to reduce the prevalence and mortality arising from the associated
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52 329 comorbidities in Nepal.
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331 Declarations

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341 entry and management. AP, BB and NS was involved in conducting data analysis. AP wrote the
342 manuscript. AKJ supported in monitoring overall data quality. PG, VGL, UK, DAG and SKS
343 revised and edited the manuscript. Each author provided intellectual content during manuscript
344 drafting and revision, accepts accountability for their contributions.

345 **Ethics statement:** The study protocol was approved by the Ethical Review Board (ERB) of Nepal
346 Health Research Council, Government of Nepal (Reg.no.110/2016). Written informed consent was
347 taken from all participants before proceeding for data collection.

348 **Patient and public involvement:** Patients and/or the public were not involved in the design, or
349 conduct, or reporting, or dissemination plans of this research.

350 **Patient consent for publication:** Not required.

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3 **477 Figure legend**
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6 **478 Figure 1: Map of Nepal showing the study clusters (400 clusters)**
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9 **479 Figure 2: Histogram of estimated glomerular filtration rate (eGFR) distribution among**
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11 **480 12097 participants in baseline by sex**
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14 **481 Figure 3: Histogram of estimated glomerular filtration rate (eGFR) distribution among 1194**
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16 **482 participants in follow up by sex**
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For peer review only

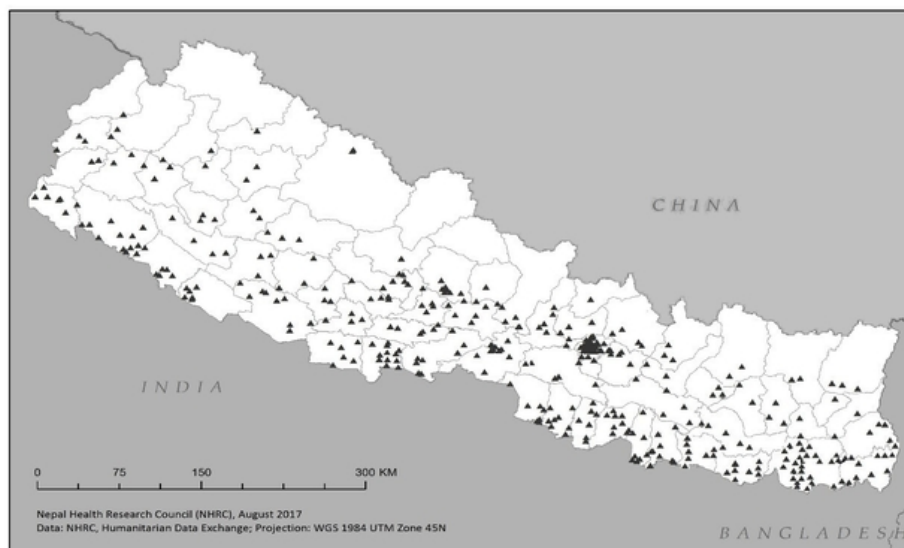


Figure 1: Map of Nepal showing the study clusters (400 clusters)

56x38mm (300 x 300 DPI)

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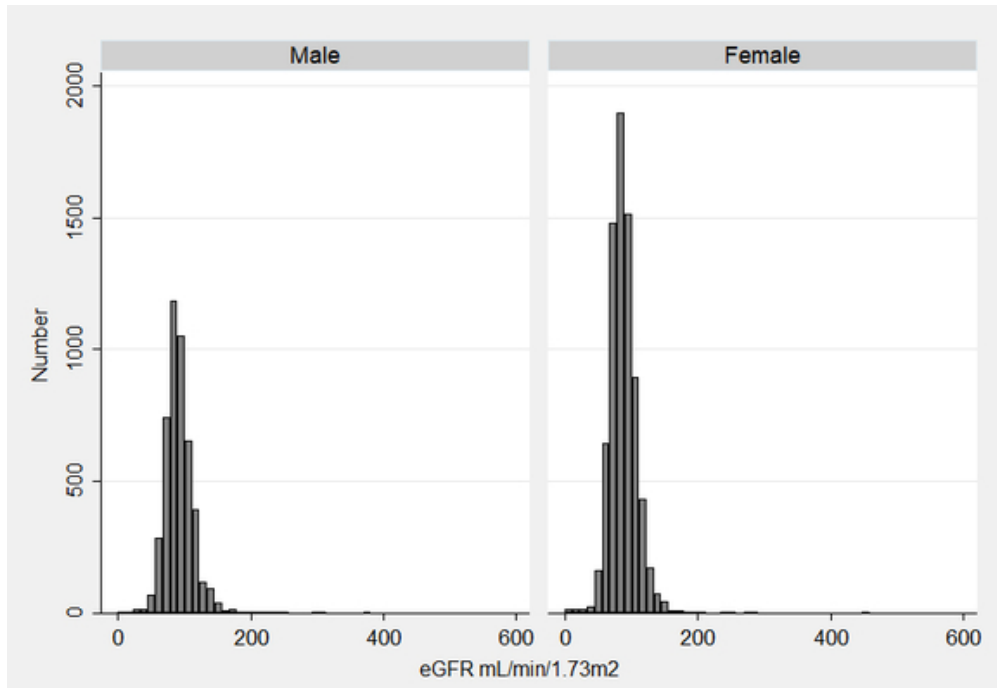


Figure 2: Histogram of estimated glomerular filtration rate (eGFR) distribution among 12097 participants in the baseline by sex

24x16mm (600 x 600 DPI)

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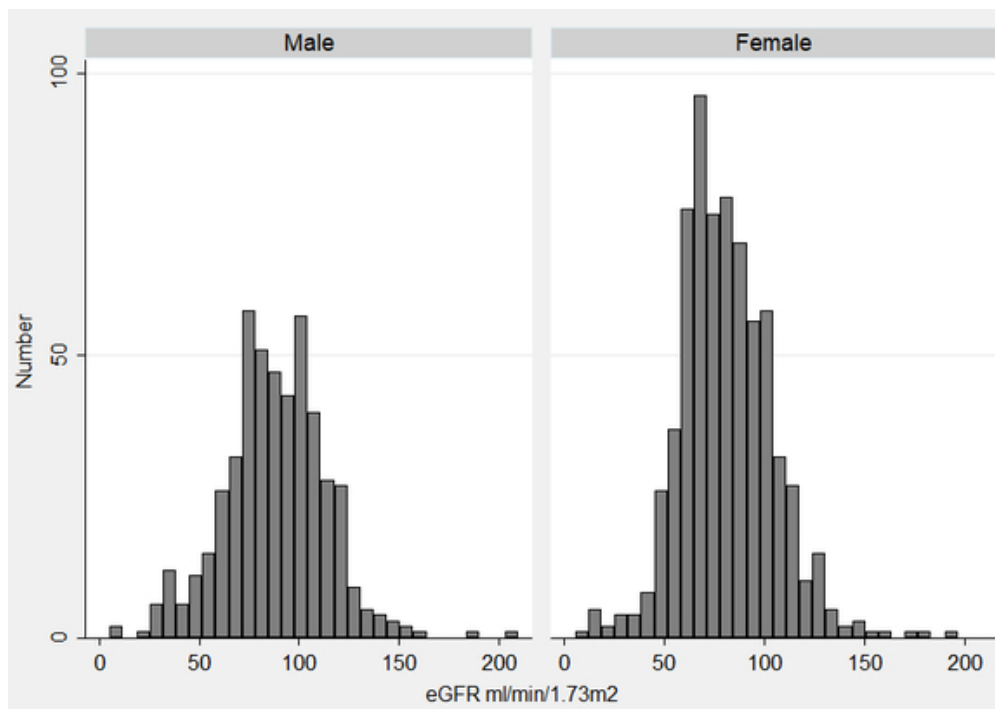


Figure 3: Histogram of estimated glomerular filtration rate (eGFR) distribution among 1194 participants in follow up by sex

24x17mm (600 x 600 DPI)

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

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
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	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
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	8
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	8-9
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8-9
		(c) Explain how missing data were addressed	10
		(d) If applicable, describe analytical methods taking account of sampling strategy	5
		(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	5-6
		(b) Give reasons for non-participation at each stage	5-7
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-17
		(b) Indicate number of participants with missing data for each variable of interest	10-17
Outcome data	15*	Report numbers of outcome events or summary measures	10-17
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	10-17

		which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	10-17
		(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	10-17
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
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	21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
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	22

*Give information separately for exposed and unexposed groups.

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

BMJ Open

Prevalence and Risk Factors Associated with Chronic Kidney Disease in Nepal: Evidence from a Nationally Representative Population-Based cross-sectional Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-057509.R2
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Date Submitted by the Author:	24-Jan-2022
Complete List of Authors:	<p>Poudyal, Anil; Nepal Health Research Council Karki, Khem; Goethe University Frankfurt Institute of Occupational Social and Environmental Medicine; Department of Community Medicine, Maharajgunj Medical Campus, Kathmandu, Nepal Shrestha, Namuna; Public Health Promotion and Development Organization; Aryal, KK; MOMENTUM Country and Global Leadership, Save the Children Nepal, Kathmandu, Nepal, Research Section Mahato, Namra ; Nepal Health Research Council Bista, Bihungum; Nepal Health Research Council, Research Ghimire, Laxmi; Sanjeevani College of Medical Sciences K.C., Dirghayu; Public Health Promotion and Development Organization. Kathmandu, Nepal, Research Gyanwali, Pradip ; Nepal Health Research Council Jha, Anjani; Nepal Health Research Council Garcia Larsen, Vanessa; Johns Hopkins University Bloomberg School of Public Health, International Health Kuch, Ulrich; Goethe University Frankfurt Institute of Occupational Social and Environmental Medicine, Social and Environmental Medicine Groneberg, David; Goethe University Frankfurt Institute of Occupational Social and Environmental Medicine Sharma, Sanjib Kumar; BP Koirala Institute of Health Sciences, Department of Internal Medicine Dhimal, Meghnath; Nepal Health Research Council; Goethe University Frankfurt Institute of Occupational Social and Environmental Medicine</p>
Primary Subject Heading:	Renal medicine
Secondary Subject Heading:	Urology
Keywords:	Chronic renal failure < NEPHROLOGY, Dialysis < NEPHROLOGY, Glomerulonephritis < NEPHROLOGY, Renal transplantation < NEPHROLOGY

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4 1 **Prevalence and Risk Factors Associated with Chronic Kidney Disease in Nepal: Evidence**
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6 2 **from a Nationally Representative Population Based Cross sectional Study**
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20 Abstract

21 **Objective:** This study aimed to determine population based prevalence of Chronic Kidney
22 Disease (CKD) and its associated factors in Nepal.

23 **Study Design:** The study was a nationwide population-based cross sectional study

24 **Setting & Participants:** Cross-sectional survey conducted in a nationally representative sample
25 of 12109 Nepalese adult from 2016 to 2018 on selected chronic non-communicable diseases
26 were examined. Multistage cluster sampling with a mix of probability proportionate to size (PPS)
27 and systematic random sampling was used for the selection of individuals aged 20 years and
28 above. **Primary and secondary outcome measures:** Primary outcome in this study was
29 population based prevalence of CKD in Nepal. A participant was considered to have CKD if the
30 Urine Albumin-to-Creatinine Ratio (uACR) was greater than or equal to 30 mg/g and/or
31 estimated Glomerular Filtration Rate (e-GFR) is less than 60 mL/min/1.73 m² at baseline and in
32 follow up using modification of diet in renal disease study (MDRD) equations. The secondary
33 outcome measure was factors associated with CKD in Nepal. The co-variate adjusted association
34 of risk factors and CKD was calculated using multivariable binary logistic regression.

35 **Results:** The overall prevalence of CKD in Nepal was 6.0% (95% CI: 5.5-6.6). Factors
36 independently associated with CKD included older age, (adjusted OR (AOR) 2.6, 95% CI: 1.9 to
37 3.6), Dalit caste (AOR 1.6, 95% CI: 1.1 to 2.3), hypertension, (AOR 2.4, 95% CI: 2.0 to 3.0)
38 diabetes mellitus (AOR 3.2, 95% CI: 2.5 to 4.1), raised total cholesterol (AOR 1.3, 95% CI: 1.0
39 to 1.6) and increased waist-to-hip ratio (AOR 1.6, 95% CI: 1.2 to 2.3).

40 **Conclusion:** This nationally representative study shows that the prevalence of CKD in the adult
41 population of Nepal is substantial, and it is independently associated with several

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3 42 cardiometabolic traits. These findings warrant longitudinal studies to identify the causes of CKD
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5 43 in Nepal and effective strategies to prevent it.
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9 44 **Keywords:** Chronic Kidney Disease, Nepal, adults, prevalence, eGFR, serum creatinine
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11 **Strengths and limitations of this study**

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- 13 • This is the first large scale nationwide population-based prevalence of CKD in Nepal.
 - 14 • Strict training processes and vigorous quality assurance programs were used to ensure the
15 quality of data collection
 - 16 • The use of standardized definitions of CKD facilitates international comparisons of CKD
17 prevalence and risk factors.
 - 18 • High overall response rate of 91.7. % in first visit and 86.9% in follow up visit.
 - 19 • Causal inference is unknown
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46 **Background**

47 Chronic Kidney Disease (CKD) is one of the most rapidly growing non-communicable diseases
48 (NCDs) worldwide ¹. According to the Global Burden of Disease (GBD) study, CKD was the
49 11th leading cause of death in 2019, up from 19th in 1990 accounting for 2.53% of total deaths².
50 CKD is also associated with substantial morbidity, mortality, and healthcare costs. Although it is
51 largely preventable, over 9% of the population worldwide is estimated to be affected by the
52 condition, particularly developing countries ^{3,4}, and it is associated with diabetes type II,
53 hypertension and obesity, which are also growing at an alarming rate. The rapid increase of
54 CKD is likely to impose a great socioeconomic and public health burden in in resource-poor
55 setting⁵.

56 The evidence on the prevalence of CKD in South East Asia is relatively limited, but it
57 consistently shows a high prevalence of CKD⁶⁻⁸, however data remain poorly characterized due
58 to inconsistent assessment of kidney function and nonstandard approaches which might distort
59 the true estimates of CKD prevalence. There are few studies in Nepal already warned the higher
60 prevalence of CKD⁹⁻¹¹ and reported data largely depends on the population studied (rural/
61 urban/or general/at high risk group) methods and the lack of representativeness from the
62 general population. Nepal has overcome many of the critical health challenges to survive the
63 first five years of life, and that NCDs and burden of potential underlying risk factors such as
64 obesity, hypertension, and diabetes and unhealthy lifestyle habits including poor diets are highly
65 prevalent¹².

66 Understanding the burden and risk factors associated with CKD is important for making health
67 care planning, designing screening strategies, and prevention of these diseases in this resource

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3 68 constrains setting, where access to renal replacement therapy is costly. Therefore, this study
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5 69 aimed to determine the population based prevalence of CKD and its associated factors in Nepal.
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8 9 **Methods**

10 11 **Study design and subjects**

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13 72 The Nepal Health Research Council designed and implemented the “National Population based
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15 73 Prevalence Survey of Selected NCDs in Nepal”. This was a population-based survey to
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17 74 investigate the prevalence of NCDs including CKD, chronic obstructive pulmonary disease
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19 75 carried out between 2016 and 2018 in adult's ≥ 20 years old from seven provinces of the country.
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21 76 Full details of the design and protocols of the survey are available elsewhere¹³.
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26 27 **Participants, sample size, and study setting**

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29 78 The sample size for the survey was calculated taking as reference the prevalence of raised blood
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31 79 glucose ($p=4\%$) from NCD risk factors: STEPwise approach to Surveillance(STEPS) survey
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33 80 2013¹⁴, Z value of 1.96 at 95% confidence level and margin of error (d) of 20%, design effect of
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35 81 2, adjusting the sample across three domains of the Terai, hills and mountains and adding a non-
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37 82 response rate of 20% yielded a sample size of 12,965. With a plan to enroll 33 participants in
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39 83 each cluster (400), the final sample size was 13,200. A ward (lowest administrative unit of the -
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41 84 then Village Development Committees (VDCs) and Municipalities) was considered as a cluster-
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43 85 Primary Sampling Unit (PSU) of the study design. With the support from Central Bureau of
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45 86 Statistics, a total of 400 clusters were sampled. To select a representative sample of cluster; the
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47 87 rural and urban areas within each region were identified as the main sampling strata and the
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49 88 sample was selected in two stages in which ecological belts (Terai, Hill and Mountains) and five
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3 89 development region (Central, Eastern, Mid-Western, Western and Far western , stratification was
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5 90 taken into account.
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9 91 The survey team members in the field used official or socially mapped household list to select 33
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11 92 households (Secondary Sampling Units – SSUs) from each cluster using systematic random
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13 93 sampling. One participant out of the eligible candidates (≥ 20 years and above, resident in the
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15 94 study area at least 6 months and able to provide informed consent) was selected to take part in
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17 95 the survey using the KISH method. Of 13,200 participants who were approached for interview,
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19 96 12,557 responded to the invitation in Day 1, Among 12,557 who accepted the invitation, only
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21 97 12,148 participants responded in day 2 of clinical setting. For the present study, data from 12,109
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23 98 subjects were available for analyses with a response rate of 91.7%, 39 (0.32%) were excluded,
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25 99 because they refused providing blood and urine samples to evaluate renal function in day 2.
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30 100 Data weighting was carried out to make the sampled population comparable to the national
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32 101 population. Data weighting was done using sampling weight. Sample weighting was carried out
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34 102 for probabilities of selection of Primary sampling unit (Ward/cluster), selection of households,
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36 103 and selection of an individual in a household using 2011 population for Nepal with the support
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38 104 from Central Bureau of Statistics.
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42 105 **Data collection and measurements**

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45 106 Data collection was performed in 400 clusters (figure 1) within 72 districts of Nepal. Data
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47 107 collection teams at each site consisted of five member having academic background of nursing,
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49 108 general medicine, Bachelor in medical laboratory technology or public health.
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53 109 Participants' appointment for face to face personal interview at convenient and accessible site or
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55 110 at home on two occasions (Day 1 and Day 2): Following written informed consent, from the
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3 111 participants in Day 1, a structured questionnaire was administered to collect information about
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5 112 participants' general health and socio-demographic characteristics. Participants self-reported
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7 113 their health and socio-demographic status, personal and family medical histories and history of
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9 114 medicine used. Information concerning their lifestyle factors (cigarette smoking, alcohol intake)
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11 115 was collected, and then physical and clinical measurements were performed. The clinical
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13 116 examination included measurements of height, weight, waist hip ratio and blood pressure (BP)
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15 117 following standard protocols. Height was measured in centimeters with a portable Bioplus®
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17 118 stature meter and weight with a portable digital seca® 874 weighing scale (Seca, Germany) and
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19 119 recorded in kilograms ensuring that the participant was wearing light clothes and was without
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21 120 footwear. Waist circumference was measured using Seca tape in cm at the level midway between
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23 121 the twelfth rib and the uppermost lateral border of the iliac crest during normal expiration. Blood
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25 122 pressure was measured at least three times with a minimum 3 min, and then averaged to be
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27 123 recorded by using an Omron digital automatic blood pressure monitor model HEM-8712 (Omron
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29 124 Health Care Co., Ltd, Japan) with appropriate sized cuffs ¹⁵. Participants were classified as
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31 125 hypertensive when the Raised BP is defined as having systolic BP ≥ 140 mm of Hg and/or
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33 126 diastolic BP ≥ 90 mm of Hg during the study, or being previously diagnosed as having
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35 127 hypertension.
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43 128 We used fasting, at least an 8-hour fast, and two hour post prandial (PP) blood sample to test
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45 129 various biochemical parameters. Following aseptic technique, blood samples were drawn by a
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47 130 trained enumerators using vacutainers to test laboratory parameters such as fasting blood glucose
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49 131 level, PP blood glucose level, serum creatinine, total cholesterol (TC), triglyceride (TG), high
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51 132 density lipoprotein (HDL) cholesterol, and serum creatinine. The well trained enumerators
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53 133 collected around 10 ml of blood sample at the fasting state and provided 82 grams of glucose
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3 134 monohydrate (equivalent to 75 grams of anhydrous glucose) in 250 ml water to drink. Second
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5 135 blood sample was collected at 2 hours of glucose intake. Fasting blood glucose, TC, TG, HDL
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7 136 cholesterol and serum creatinine were measured with the fasting sample and two hours PP
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9 137 sample was used for measuring PP blood glucose only. We carried out biochemical analysis with
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11 138 Biolyzer® 100 Clinical Chemistry Analyzer (Semi-automatic biochemistry analyzer, Analyticon,
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13 139 Germany) and used glucose oxidase-peroxidase (GOD-POD) method for blood glucose,
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15 140 cholesterol oxidase/phenol aminophenazone (CHOD-PAP) for TC, glycerol-3-phosphate
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17 141 oxidase/phenol aminophenazone (GPO-PAP) for TG, HDL cholesterol by poly ethylene glycol/
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19 142 cholesterol oxidase/ phenol aminophenazone (PEG/CHOD-PAP) and serum creatinine measured
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21 143 by Jaffe Reaction method. The laboratory supervisors calculated the low-density lipoprotein
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23 144 (LDL) cholesterol by Freidewald's Formula using TC, TG, and HDL cholesterol.
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29 145 **Outcome measurements**

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31 146 A spot urine sample was collected from single voided specimen to measure urine albumin and
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33 147 creatinine using the same semi-automatic biochemistry analyzer (AnalyticonBiolyzer® 100
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35 148 Clinical Chemistry Analyzer, Germany). Laboratory supervisors measured urine albumin
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37 149 concentration by Turbidimetric tests and urine creatinine concentration by Jaffe Reaction method
38
39 150 and finally albumin-creatinine ration (ACR) was calculated and expressed in mg/g. Renal
40
41 151 function was evaluated by using estimated GFR (eGFR), based on the widely used 4-variable
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43 152 Modification of Diet in Renal Disease Study (MDRD) equation. A participant was considered to
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45 153 have CKD if the Urine Albumin-to-Creatinine Ratio (uACR) was greater than or equal to 30
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47 154 mg/g and/or estimated Glomerular Filtration Rate (e-GFR) was less than 60 mL/min/1.73 m² at
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49 155 baseline and in follow up¹⁶. The secondary outcome measure was factors associated with CKD in
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157 **Follow up of study participants to determine CKD**

158 Participants having either albumin-creatinine ratio (ACR) greater than or equal to 30 mg/g in the
159 baseline and/or decreased eGFR (<60 mL/min/1.73 m²) were revisited again after 3 months in
160 their place of residence to ensure the chronicity of the renal disease. Written consent was taken
161 prior to blood and urine sample collection using similar procedures as mentioned above. Out of
162 1382 participants having a high ACR ratio and/or decreased eGFR, 1202 gave consent. However,
163 data of ACR was missing for 8 participants making the availability of complete data for 1194
164 participants for analysis, with a response rate of 86.9%.

165 **Data management and analysis**

166 We used android mobile phones inbuilt with data collection software (REMO) to collect data
167 digitally. Data cleaning including correction of inconsistencies was performed in SPSS version
168 20.0. We then exported the dataset to STATA version 13 for analysis. To adjust for unequal
169 probability of selection, appropriate sampling weights with complex sampling analysis were
170 used to provide valid estimates for the relevant Nepalese population which is based on 2011
171 national population and housing census data. Results are expressed as a percentage and odds
172 ratio with 95% CI. Bivariate analysis was conducted to analyze the unconditional association
173 between each explanatory variable and CKD status. To be included in multivariable modeling,
174 the level of significance $\alpha=0.05$ was used during bivariate analysis (i.e., P-value 0.05 was not
175 statistically significant). Independent variables included demographics (age, gender, ethnicity,
176 education, province and place of residence), existing comorbidities (hypertension, diabetes,
177 raised total cholesterol, increased waist hip ratio), any hypertension, any diabetes (self-reported
178 or physician diagnosed [fasting blood glucose ≥ 126 mg/dl]), lifestyles (smoking and alcohol
179 consumption), overweight or obesity (Body Mass Index [BMI] ≥ 25 kg/m²).

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3 180 Ethnicity/ caste data were self-reported and categorized into six major groups based on the caste
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5 181 coding by government of Nepal and STEPS survey Nepal, 2013 categorization¹⁷. (1) Upper
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7 182 Caste Groups (population with relatively higher socio economic and education status, mostly
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9 183 Brahmins, Chhetris, Thakuri and Sanyasi);(2) Disadvantaged Janajatis (disadvantaged group of
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11 184 people and also indigenous, with relatively lower socio-economic and education status);(3) Dalit
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13 185 (untouchables, most disadvantaged marginalized group of people, with relatively lower socio-
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15 186 economic and education status); (4) Disadvantaged non Dalit Terai Caste Groups (disadvantaged
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17 187 group of people from the Terai, the lowlands, with relatively lower socio-economic and
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19 188 education status but not the dalit groups); (5)Religious Minorities (Muslim, Christian, etc.); (6)
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21 189 Relatively advantaged Janajatis (indigenous group of people with relatively higher socio-
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23 190 economic status, such as Gurung , Newar and Thakali)
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29 191 Multicollinearity, the variance inflation factor (VIF) was assessed for all the independent
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31 192 variables found to be statistically significant from the bivariate analysis. Multivariable logistic
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33 193 regression modeling was conducted with CKD as a dependent variable using the independent
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35 194 variables identified as being statistically significant from the bivariate analysis.
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196 **Results**

45 197 A total of 12,109 subjects aged 20 years and above were included in the analyses. Among them
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47 198 61.1% were female, two fifth were adults in the age group 20-59 years (41.6%), one third was
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49 199 from upper caste ethnic group (34.2%), and just above half of them were either illiterate or had
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51 200 no formal schooling (54.6%). Table 1 presents the unweighted numbers and proportions of
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53 201 different demographic characteristics of the study population as measured in the study.
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202 **Table 1: Socio-demographic characteristics of the study participants (N=12,109)**

Characteristics	n	%
Age		
20-39 years	4336	35.8
40-59 years	5034	41.6
60 years and above	2739	22.6
Sex		
Male	4708	38.9
Female	7401	61.1
Ethnicity		
Upper caste group	4144	34.2
Disadvantaged janajati	2546	21.0
Relatively advantaged janajati	2018	16.7
Disadvantaged non-dalit terai caste	1836	15.2
Dalit	1225	10.1
Religious minorities	340	2.8
Education		

Illiterate/No formal schooling	6607	54.6
Below secondary (<10 years)	2742	22.6
Secondary and above (≥ 10 years)	2760	22.8
Province		
Province 1	2049	16.9
Province 2	2003	16.5
Bagmati Province	3096	25.6
Gandaki Province	1315	10.9
Lumbini Province	2030	16.8
Karnali Province	588	4.9
Sudurpaschim Province	1028	8.5
Place of residence		
Rural	6107	50.4
Urban	6002	49.6

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207**Table 2 Factors associated with chronic kidney disease by univariate and multivariate analysis (N = 12109)**

Characteristics	Count	Chronic Kidney Diseases(CKD)		
	N	CKD prevalence (n %)	COR (95% CI)	AOR(95% CI)
Age				
20-39 years	4336	118 (2.6)	1	1
40-59 years	5034	294 (5.8)	2.3(1.8-3.0)***	1.4(1.0-1.8)*
60 years and above	2739	316 (11.5)	4.9 (3.8-6.3)***	2.6(1.9-3.6)***
Sex				
Female	7401	415 (5.7)	1	1
Male	4708	313 (6.5)	1.2(1.0-1.4)	1.2 (0.8-1.6)
Ethnicity				
Upper caste	4144	212 (5.1)	1	1
Disadvantaged Janajati	2546	138 (5.4)	1.1(0.8-1.4)	1.1(0.9-1.5)
Dalit	1225	84 (7.1)	1.4 (1.0-1.9)*	1.6 (1.1-2.3) **
Disadvantaged non-Dalitterai caste	1836	116 (6.4)	1.3(0.9-1.7)	1.4 (0.9-2.1)
Religious minorities	340	25 (8.0)	1.6 (1.0-2.7)	1.7(1.0-2.9)
Relatively	2018	153 (7.4)	1.5(1.1-2.0)*	1.4(1.0-1.9)*

advantaged Janajati				
Education				
Illiterate/No formal schooling	6607	459 (7.0)	1	1
Below secondary (<10 years)	2742	146 (5.4)	0.8(0.6-0.9)**	1.1 (0.9-1.5)
Secondary and above (≥10 years)	2760	123 (4.5)	0.6(0.5-0.8)***	1.1 (0.7-1.4)
Province				
Karnali Province	588	30 (4.7)	1	1
Province 1	2049	100 (5.2)	1.1 (0.7-1.8)	1.1(0.6-2.0)
Province 2	2003	133 (6.6)	1.4(0.9-2.3)	1.2 (0.6-2.2)
Bagmati Province	3096	196 (6.5)	1.4(0.9-2.2)	1.1 (0.6-1.9)
Gandaki Province	1315	93 (6.8)	1.5 (0.9-2.3)	1.2 (0.7-2.0)
Lumbini Province	2030	118 (5.7)	1.2(0.7-2.2)	0.9 (0.5-1.6)
Sudurpashchim Province	1028	58(5.9)	1.3(0.7-2.2)	1.4 (0.7-2.6)
Place of residence				
Rural	6107	341 (5.8)	1	1
Urban	6002	387 (6.5)	1.2(1.0-1.4)	1.0(0.8-1.3)

Smoking habit				
Non smoker	8305	443 (5.3)	1	1
Smokers	3804	285 (7.6)	1.5(1.2-1.7)***	1.2(1.0-1.5)
Alcohol consumption				
No	9131	537 (6.0)	1	1
Yes	2978	191 (6.2)	1.0(0.9-1.2)	
Blood pressure				
Normal	7754	256 (3.3)	1	1
Raised	4355	472 (10.8)	3.6 (3.0-4.3) ***	2.4 (2.0-3.0)***
Body mass index (N=12108)#				
Normal	6896	377 (5.5)	1	1
Underweight	1494	88 (6.2)	1.1(0.9-1.5)	1.1(0.8-1.6)
Overweight and obese	3718	263 (6.9)	1.3(1.1-1.5) **	0.9 (0.7-1.1)
Total cholesterol (N=10861)#				
Normal	7741	398 (5.2)	1	1
Raised	3120	254 (8.2)	1.6(1.3-2.0) ***	1.3(1.0-1.6)*

Waist hip ratio (N=11979)#				
Normal	5095	282 (5.4)	1	1
Increased	6884	440 (6.6)	1.2(1.0-1.5) *	1.6(1.2-2.3) *
Diabetes Mellitus (N=11271)#				
No	10393	506 (4.8)	1	1
Yes	878	172 (19.8)	4.9(3.8-6.2) ***	3.2(2.5-4.1) ***
Total	12109	6.0 (95% CI: 5.5 -6.6)		

Definition of chronic kidney disease status: Urinary albumin to creatinine ratio of ≥ 30 mg/g and/or glomerular filtration rate < 60 ml/min/1.73 m² both at baseline and follow up)

OR: odds ratio; CI: Confidence interval; COR: Crude odds ratio; AOR: Adjusted odds ratio. Adjusted OR estimated from the stepwise multivariate logistic regression model with all the above variables added except alcohol consumption.

¹ Reference group.

* Indicated the corresponding variable had significant impact on the occurrence of CKD.

*p value ≤ 0.05 **p value ≤ 0.01 ***p value ≤ 0.0001

Missing value; refusal for blood sample collection led to variation in the sample size

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4 **211 Prevalence of CKD**

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6 212 The overall prevalence of CKD based on the eGFR MDRD equation, (urinary albumin to
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8 213 creatinine ratio of ≥ 30 mg/g and/or glomerular filtration rate < 60 both at baseline and follow up)
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10 214 was 6.0% (95% CI: 5.5-6.6). The prevalence was higher in males compared to female (6.5 vs
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12 215 5.7) though not statistically significant. Prevalence increased with increasing age (11.5% among
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14 216 60 years and above and 2.6 % among 20-39 years age group). (Table 2). The mean (\pm SD) eGFR
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16 217 in baseline was 92.6 (\pm 22.1) mL/min/1.73 m² for male and 88.2 (\pm 20.5) mL/min/1.73 m² for
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18 218 female (figure 2) .The mean (\pm SD) eGFR was 88.0 (\pm 25.7) mL/min/1.73 m² for male and 81.1
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20 219 (\pm 23.4) mL/min/1.73 m² for female in follow up(figure 3).
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223 **Factors associated with CKD**

224 The multivariable analyses to investigate the association of independent factors and CKD are
225 shown in Table 2. In the bivariate analysis, age, smoking, BMI, ethnicity, education, having
226 diabetes mellitus (DM), being hypertensive, increased waist hip ratio, and having raised total
227 cholesterol were found to be statistically significantly associated with CKD. Therefore, those 9
228 factors including place of residence, province, and sex of participants (P-value ≤ 0.25) were
229 considered in the multiple logistic models. After adjustment, only six variables: age, ethnicity,
230 diabetes, hypertension, raised TC, and increased waist hip ratio, were found to be significant
231 predictors of CKD. There was a strong positive association between age and CKD, i.e. the odds
232 of having CKD were about 1.4 (95% CI : 1.0-1.8) and 2.6(95% CI: 1.9-3.6) times higher for
233 people aged 40–59 years and ≥ 60 years respectively, compared with people aged 20-39 years.
234 Participants with DM had about 3.2 (95% CI: 2.5-4.1) times higher odds of occurrence of CKD
235 than non-diabetic participants. Similarly, participants with raised BP had 2.4 (95% CI: 2.0-3.0)
236 higher odds of having CKD than non-hypertensive/normal participants.
237 Participants with raised total cholesterol had 1.3 (95% CI: 1.0-1.6) times higher odds of having
238 CKD relative to participants who had normal cholesterol level, whereas those with raised waist
239 hip ratio had 1.6(95% CI: 1.2-2.3) times higher odds than normal participants to have CKD.
240 Individuals who were classified as Dalit by ethnicity were 1.6 (95% CI: 1.1-2.3) times or
241 relatively advantaged janajati had 1.4 (95% CI: 1.0-1.9) times higher odds of having CKD when
242 compared to individuals with an upper caste.

243 Discussion

244 This is the first large scale nationwide population based representative study to report prevalence
245 of and factors associated with CKD in Nepal among population aged 20 years and above. In the
246 absence of population validated e-GFR equation for our population, MDRD equation as done in
247 previous studies was chosen over the CKD-EPI equation to facilitate comparison of results. The
248 findings show that approximately one in every sixteen adults (6%) is affected by CKD in Nepal.
249 This value is higher than the population based study conducted in Morocco 5.1%¹⁸ and Vietnam
250 3.1%¹⁹, almost similar to 6.8% in South Korea ²⁰, east African countries including Uganda and
251 Kenya²¹ but much lower than the prevalence of many Asian countries with 10.2% in
252 china²², 17.5% in Thailand²³, 18.9% in Iran²⁴ and 17.2 % in India ²⁵. Prevalence of CKD in
253 Nepal is lower than the global burden of disease study estimated prevalence of 8%–10%³
254 globally. However, these differences in the prevalence of CKD may be in part due to the
255 differences in CKD diagnostic criteria, study design, laboratory methods and lack of validated
256 measures for eGFR for Nepalese population.

257 Our multivariable analysis found that CKD was independently associated with older age,
258 hypertension, diabetes, raised TC, dalit and relatively advantaged janajati ethnicity and increased
259 waist hip ratio ($p < 0.05$ for each) which are all major NCDs risk factors and consistent with
260 previous findings^{26–30}. Age is a well-established risk factor for development of CKD³¹. As
261 expected, age was found to be the most strongly associated risk factor in our study, we observed
262 nearly three times higher odds of occurrence of CKD among people aged 60 years or older
263 compared to people aged 20 to 39 years.

264 In line with other surveys in South East Asia, our findings show that the odds of CKD
265 occurrence was significantly and independently higher by around 2-fold with the presence of

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3 266 hypertension; this supports previous reports^{32–35} indicating the importance of early detection and
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5 267 treatment of hypertension in Nepal. Similarly, people with diabetes mellitus had more than three
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7 268 times higher odds of occurrence of CKD. Studies around the world show diabetes to be
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9 269 independently associated with development of CKD^{36,37}. A survey across 10 Asian countries
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11 270 showed that the most common cause of End Stage Renal Disease (ESRD) in 9 out of 10
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13 271 countries was diabetic nephropathy³⁸. In addition; elevated total cholesterol though marginal was
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15 272 associated with higher odds of CKD.
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20 273 Nepal is an ethnically diverse country with more than 125 castes/ethnic groups. Interestingly
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22 274 ethnicity/caste was another factor associated with CKD in our study. Compared with upper caste
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24 275 participants, Dalit participants had a significantly higher prevalence of CKD. The mechanism
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26 276 underlying these differences might be multifactorial, including cultural differences such as
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28 277 smoking and drinking habit, lifestyle and genetic factors. By ethnicity, Dalit group of people are
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30 278 considered as one of the most marginalized in terms of socioeconomic, education, political and
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32 279 health indicators, resulting in decreased access to resources and higher vulnerability to poor
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34 280 health outcomes. This calls for future studies regarding CKD on ethnic differences.
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41 282 Despite finding an association between CKD and several known established risk factors
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43 283 including waist hip ratio, no association was found between CKD and BMI. The correlation
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45 284 between CKD and waist hip ratio and not BMI is plausible since this ratio is a more sensitive
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47 285 marker for central obesity, metabolic syndrome and potentially less influenced by muscle mass
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49 286 than BMI, this is in agreement with earlier studies^{28,39,40}. The association between smoking and
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51 287 CKD was reported in bivariate analysis only in our study.
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3 288 In general, the prevalence of CKD was higher among women compared to men, and this
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5 289 difference has been demonstrated in the past by several population based cross sectional
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7 290 studies.⁴¹ However in the present study, though not statistically significant, we found slightly
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9 291 higher prevalence of CKD among male participants. These discrepancies in the prevalence may
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11 292 be due to the traditional risk factors such as hypertension and hyperglycemia being prevalent
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13 293 among male participant in our study. We also could not find significant association between
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15 294 CKD and alcohol consumption, place of residence, and provinces.
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20 295 Traditional risk factors such as diabetes and hypertension are the major cause of CKD in most
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22 296 developed and developing countries^{42,43}, and several other nontraditional and environmental risk
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24 297 factors such as infectious diseases, analgesic abuse, exposure to heavy metal (Lead, Arsenic,
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26 298 Mercury and Uranium), pesticides, herbal medications, and environmental pollution, impose an
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28 299 additionally threat worsening CKD especially in developing countries⁴⁴ including Nepal .
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30 300 However, we lack information about environmental and some of the nontraditional risk factor,
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32 301 which could be used to quantify the effects of these factors on CKD
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37 302 Our study poses several strengths. To the best of our knowledge, this is the first national survey
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39 303 with a large representative population-based sample of the adult population to report prevalence
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41 304 of CKD in Nepal as per Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice
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43 305 guideline; using (eGFR <60mL/min/1.73m², presence of albuminuria \geq 30mg/g and chronicity
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45 306 confirmed by repeated testing after three months) to confirm presence of CKD. The study has
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47 307 used a validated standardized estimation of the glomerular filtration rate by the MDRD equation
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49 308 and all necessary protocols, standard operating procedures and quality assurance mechanism
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51 309 were followed to ensure the quality of data collection. Additional strengths of the study include a
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53 310 high overall response rate and analyses based on survey weights which ensure geographic
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3 311 representativeness of the study making the study findings generalizable to the general
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5 312 population. At the same time, potential limitations include dependency on estimation of GFR,
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8 313 rather than direct measurement using injection of an exogenous marker factors as well as cross-
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10 314 sectional design of the study which does not permit inferences regarding causal relationships.
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13 315 **Conclusions**

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15 316 This is the first population-based epidemiological survey of CKD using the protocols
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17 317 recommended by KDOQI in Nepal. The prevalence of CKD was found to be 6.0% with higher
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19 318 prevalence among male, participants with no formal education, urban residents, smokers and
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21 319 participants with overweight and obese. CKD was independently associated with older age,
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23 320 hypertension, diabetes mellitus, increased waist hip ratio, raised total cholesterol and individual
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25 321 belonging to the Dalit caste by ethnicity. Our findings highlight the need for early preventive
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27 322 measures to manage predisposing conditions such as diabetes and hypertension which could
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29 323 ultimately lead to CKD and to reduce the prevalence and mortality arising from the associated
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31 324 comorbidities in Nepal.
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40 326 **Declarations**

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55 332 **Competing interests:** The authors declare no conflict of interest.
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3 333 **Data sharing statement:** The datasets used and/or analyzed will be made from the
4
5 334 corresponding author on reasonable request
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8 335 **Author's contributions:** KBK, MD, KKA and AKJ were involved with conception ,design and
9
10 336 implemented the study. AP, NS and NKM, implemented the study on the field, completed data
11
12 337 collection, overall supervision of the study. AP drafted the manuscript and conducted data
13
14 338 analysis with input from NS, BB, LG, NKM and DK. SKS, PG, VGL, UK, DAG all contributed
15
16 339 to critical revision of the manuscript, provided feedback on the initial draft and approved the
17
18 340 final version. SKS, KKA, NS, PG, and MD were also involved responding to the comments
19
20 341 raised by BMJ Open Journal reviewers; each authors reviewed the reversed manuscript critically
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22 342 and provided improvements, accepts accountability for their contributions. The corresponding
23
24 343 author attests that all listed authors meet the authorship criteria.
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30 344 **Ethics statement:** The study protocol was approved by the Ethical Review Board (ERB) of
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32 345 Nepal Health Research Council, Government of Nepal (Reg.no.110/2016). Written informed
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34 346 consent was taken from all participants before proceeding for data collection.
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38 347 **Patient and public involvement:** Patients and/or the public were not involved in the design, or
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40 348 conduct, or reporting, or dissemination plans of this research.
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43 349 **Patient consent for publication:** Not required.
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33 466 **Figure legend**

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36 467 **Figure 1: Map of Nepal showing the study clusters (400 clusters)**

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39 468 **Figure 2: Histogram of estimated glomerular filtration rate (eGFR) distribution among**
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41 469 **12097 participants in baseline by sex**

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44 470 **Figure 3: Histogram of estimated glomerular filtration rate (eGFR) distribution among**
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46 471 **1194 participants in follow up by sex**

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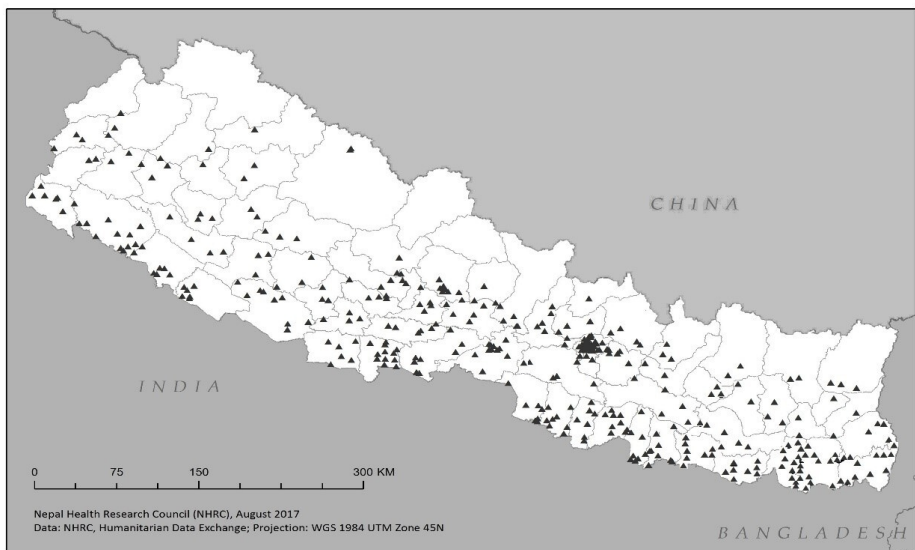


Figure 1: Map of Nepal showing the study clusters (400 clusters)

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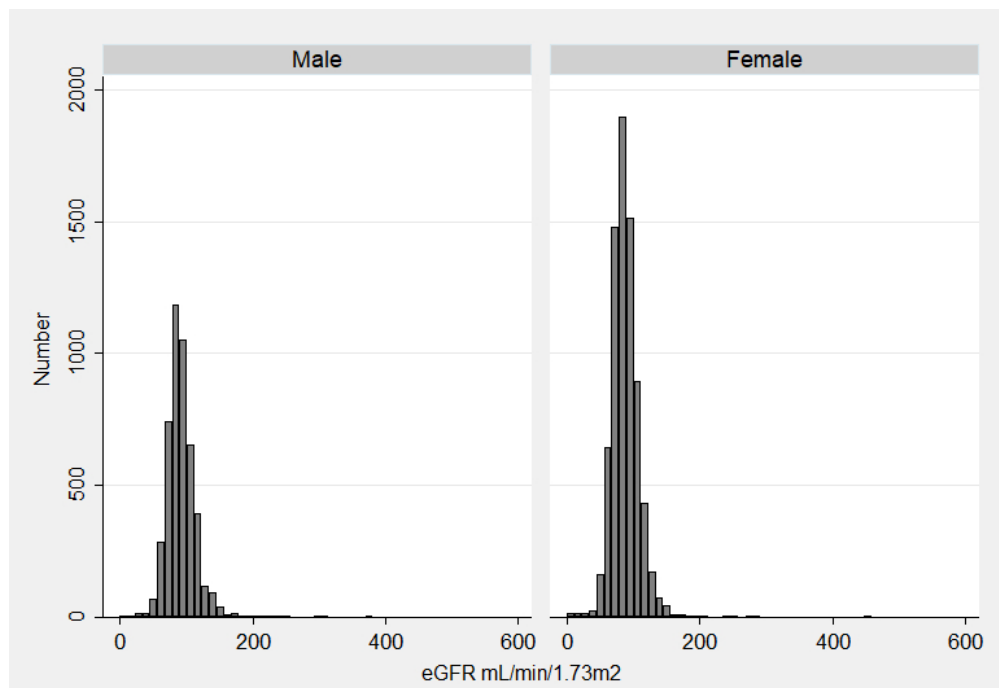


Figure 2: Histogram of estimated glomerular filtration rate (eGFR) distribution among 12097 participants in the baseline by sex

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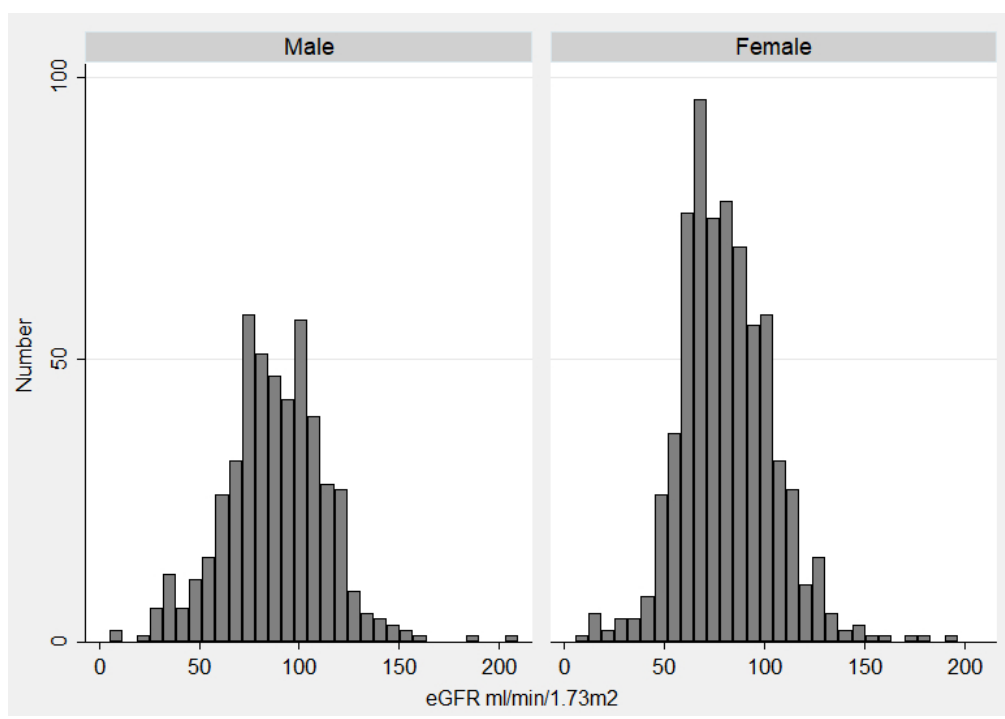


Figure 3: Histogram of estimated glomerular filtration rate (eGFR) distribution among 1194 participants in follow up by sex

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

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
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	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
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	8
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	8-9
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8-9
		(c) Explain how missing data were addressed	10
		(d) If applicable, describe analytical methods taking account of sampling strategy	5
		(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	5-6
		(b) Give reasons for non-participation at each stage	5-7
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-17
		(b) Indicate number of participants with missing data for each variable of interest	10-17
Outcome data	15*	Report numbers of outcome events or summary measures	10-17
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	10-17

		which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	10-17
		(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	10-17
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
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	21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
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	22

*Give information separately for exposed and unexposed groups.

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