


BMJ Open Prevalence and risk factors of lower extremity disease in high risk groups in Malawi: a stratified cross-sectional study

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ABSTRACT

Objective Low/middle-income countries face a disproportionate burden of cardiovascular diseases. However, among cardiovascular diseases, burden of and associations with lower extremity disease (LED) (peripheral arterial disease and/or neuropathy) is neglected. We investigated the prevalence and factors associated with LED among individuals known to have cardiovascular disease risk factors (CVDRFs) in Malawi, a low-income country with a significant prevalence of CVDRFs.

Design This was a stratified cross-sectional study.

Setting This study was conducted in urban Lilongwe Area 25, and the rural Karonga Health and Demographic Surveillance Site.

Participants Participants were at least 18 years old and had been identified to have two or more known CVDRFs.

Main outcome measures LED—determined by the presence of one of the following: neuropathy (as assessed by a 10 g monofilament), arterial disease (absent peripheral pulses, claudication as assessed by the Edinburgh claudication questionnaire or Ankle Brachial Pulse Index (ABPI) <0.9), previous amputation or ulceration of the lower limbs.

Results There were 806 individuals enrolled into the study. Mean age was 52.5 years; 53.5% of participants were men (n=431) and 56.7% (n=457) were from the rural site. Nearly a quarter (24.1%; 95% CI: 21.2 to 27.2) of the participants had at least one symptom or sign of LED. 12.8% had neuropathy, 6.7% had absent pulses, 10.0% had claudication, 1.9% had ABPI <0.9, 0.9% had an amputation and 1.1% had lower limb ulcers. LED had statistically significant association with increasing age, urban residence and use of indoor fires.

Conclusions This study demonstrated that a quarter of individuals with two or more CVDRFs have evidence of LED and 2.4% have an amputation or signs of limb threatening ulceration or amputation. Further epidemiological and health systems research is warranted to prevent LED and limb loss.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study is the first attempt in Malawi to determine the prevalence of lower extremity disease (LED).
- ⇒ This study used multiple parameters to ensure accurate estimation of the prevalence of LED.
- ⇒ This study included both rural and urban populations to provide a comprehensive picture of LED prevalence.
- ⇒ Some participants with vascular calcification may have had false negative Ankle Brachial Pulse Index results.

and hypercholesterolaemia. Infectious agents, particularly HIV, also contribute to an increased risk of peripheral vascular disease.¹ Resources required to optimise preventative strategies, treat complications and offer rehabilitation after surgery for peripheral vascular disease and peripheral neuropathies disease are largely the same whether the underlying disease process was predominantly ischaemic or neuropathic. As such, we have considered these conditions as one entity representing a spectrum of problems under the term 'lower extremity disease' (LED). Individuals with LED are at risk of lower limb amputation, particularly in cases where there is significant ischaemic necrosis and infection. Amputation can be a life-saving procedure, relieving pain and sepsis, but may also be associated with negative physical, psychological, social and economic consequences.^{2,3}

With increasing prevalence of CVDRF in low/middle-income countries (LMICs) superimposed on a background of chronic infections, it is strongly suspected that the associated risk of lower limb amputation will become increasingly important for individuals, families, health systems, and economies.⁴ Evidence from LMICs is lacking but suggestive that burden of amputations related to LED conditions will grow. Almost 70% of people with peripheral arterial disease live in LMICs; African countries in particular



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INTRODUCTION

Peripheral vascular disease and peripheral neuropathies (including the spectrum of diabetic foot disease) share a common group of overlapping risk factors, namely cardiovascular disease risk factors (CVDRFs) such as hypertension, diabetes, smoking, obesity

show a high population-prevalence of peripheral arterial disease (e.g., 33% in a population of people >65 years old in Central Africa).⁵⁻⁷ Studies in people who have managed to access CVDRF clinics in referral hospitals also show that a large number of people have peripheral artery disease; for example, in Ghana, 27% of nearly 1000 people with diabetes had clinically measurable peripheral arterial disease.⁸ In our pilot study of 191 patients attending a hospital clinic in Blantyre, Malawi, peripheral arterial disease was seen in 8.5% of 45–64 year olds and 17% of people aged 65 and over.⁹ Reliable data on population prevalence of diabetic foot ulceration are lacking, however, studies show that in people with diabetes who have accessed services, the prevalence ranged from 4.0% to 9.9%; it could be far higher if people who had not accessed services were included.¹⁰

To develop health systems to manage and prevent LED and its consequences requires knowledge of its prevalence. The aim of this study was to investigate the population prevalence of LED among high risk individuals in rural and urban Malawi.

METHODS

Study setting

The study was conducted in Area 25 in urban Lilongwe, and the rural Karonga Health and Demographic Surveillance Site (HDSS). The Karonga site has a population of approximately 45 000, and the economy is mainly subsistence farming. Area 25 (Lilongwe) has an approximate total population of 65 000 with a mixed economy.

Study design and participants

We conducted a stratified cross-sectional study of the prevalence of LED, defined as neuropathy and/or vasculopathy, in all adults of at least 18 years age with two or more CVDRFs. This population was selected to ensure a reasonable sample size of people at the highest risk of LED.

Identification of participants

We included all eligible participants who were at least 18 years old and had been identified to have two or more known risk factors for LED during a population wide survey of cardiometabolic conditions conducted between 2013 and 2017 in the study areas.¹¹ Presence of hypertension, diabetes mellitus, HIV, tobacco smoking, obesity, and age at least 40 years were used to characterise high risk individuals.

Data collection and definitions

Data on participant sociodemographic characteristics (sex, date of birth, marital status, highest attained education, use of indoor fire, and household wealth) and presence of CVDRFs (history of smoking, diabetes mellitus, hypertension, dyslipidaemia, and HIV status using previous laboratory diagnosis) were extracted from the initial baseline study. Methods used to capture data

and definitions used in that baseline survey have been published elsewhere.¹¹ In brief, diabetes mellitus was defined as a fasting blood glucose of at least 7.0 mmol/L (as determined by a Beckman Coulter AU480 Chemistry Analyser) or self-report of a previous diagnosis of the condition by a health professional regardless of the drug history. Hypertension was defined as a blood pressure of at least 140/90 mm Hg or current use of antihypertensive medication for blood pressure control. Participants with a body mass index of at least 30 kg/m² were classified as having obesity. Participants were defined as smokers if they reported smoking at least one cigarette per day in the immediate past 6 months preceding the survey. Participants were defined as HIV-positive if they had previously been tested antibody positive by the study team or self-reported HIV positivity.

For the current study, participants were interviewed and examined in their own homes, and data collectors were blind to the participant's previous medical history. In cases where the potential participant was missed during the first visit, and it was established that they had neither left the study area nor died, the household was visited at least three times before declaring the potential participant as 'missed'. All participants were interviewed to determine if they had any changes in cardiovascular disease risk profile. The Edinburgh claudication questionnaire was used to determine the presence of claudication and participants who reported the presence of clinical CVDRFs were asked additional questions regarding access to care for the relevant conditions they had.

Participants were examined to determine the presence of leg or foot ulcers, palpable peripheral pulses (brachial, posterior tibial, and dorsalis pedis) or lower limb amputations in both extremities. Neuropen 10 g monofilaments were used to test for the presence of peripheral neuropathy on the plantar surfaces of the great toe and over the metatarsal heads of the great, 3rd and 5th toes of both feet. Portable sphygmomanometers (Welch Allyn DS55 Durashock hand aneroid model) and handheld continuous wave Doppler ultrasound devices (Bistos Hi.dop BT-200 vascular Doppler with 8 MHz probe) were used to determine the Ankle Brachial Pressure Index (ABPI). The ABPI for each participant was determined according to the methods recommended by Aboyans *et al.*^{12 13} A low ABPI reading suggests peripheral arterial disease, with the blood pressure reduced at the ankle compared with the arm, which implies stenosis within the arterial tree supplying the lower limbs. Each participant was considered to have low ABPI if they had ABPI <0.9 on any or both sides.

Outcomes

The primary outcome of interest was the presence of any symptom or sign suggestive of LED, termed 'LED prevalence' (history of claudication, limb ulcers, loss of sensation on the plantar surfaces of feet, ABPI <0.9, limb amputation, or absent peripheral pulses). Secondary outcomes were these as individual outcomes.

Statistical analysis

Given the dearth of information on the prevalence of LED in the local setting, we based our sample size calculation on pilot data from a study of 90 people with diabetes living in the Malawi HDSS, which suggested that the prevalence of LED was around 10%. Considering people with diabetes to be at high risk and similar to those chosen for our study, we calculated a sample of 912 people would be required to detect a prevalence of LED of 10% with a CI of 6% to 14%.

Prevalence of the primary and secondary outcomes, sociodemographic characteristics of the study participants and CVDRFs are described as mean (SD) and count (%). Logistic regression and likelihood ratio tests were done to determine associations between the primary outcome and independent variables. Sociodemographic characteristics and the presence of CVDRFs were considered as a priori independent variables of interest in our analysis. The association between the number of CVDRFs and the crude prevalence of the outcome of interest was also investigated.

All variables of interest were added to the regression model, and likelihood ratio testing was done to determine the presence of interactions between the independent variables. Stratified analyses of the full regression model were done for all variables that were identified as having statistically significant interactions. All statistical analysis was done using Stata V.15 statistical package.

Role of the funding source

The funders had no role in the study design; collection, analysis and interpretation of data; or report writing. The corresponding author had full access to the data and the final responsibility to submit for publication.

Patient and public involvement

There was no patient and public involvement in this study.

RESULTS

A total of 829 people were visited, of whom 806 (97.2%) consented to be recruited (figure 1). Most of the participants were at least 50 years old (mean age 52.5; 95% CI: 51.7 to 53.3), male (53.5%; n=431), from the rural site (56.7%; n=457), employed (70.6%; n=569), married (74.1%; n=597) and had no more than primary education (61.1%; n=493). Cooking with biomass fuel was reported by 94.8% (n=764) of the participants (table 1). The majority, 88.1% (n=710), of participants, had at least two clinical risk factors for LED (hypertension, obesity, HIV, diabetes, and dyslipidaemia), and the remaining 96 participants were aged at least 40 years and had a history of smoking tobacco (figure 2 and table 1). The mean age of the rural participants was higher than that of the urban participants (53.5 years (95% CI: 52.4 to 54.6) compared with 51.2 years (95% CI: 50.1 to 52.3); p=0.005). Missing data accounted for not more than 6.1% of all the data on any variable.

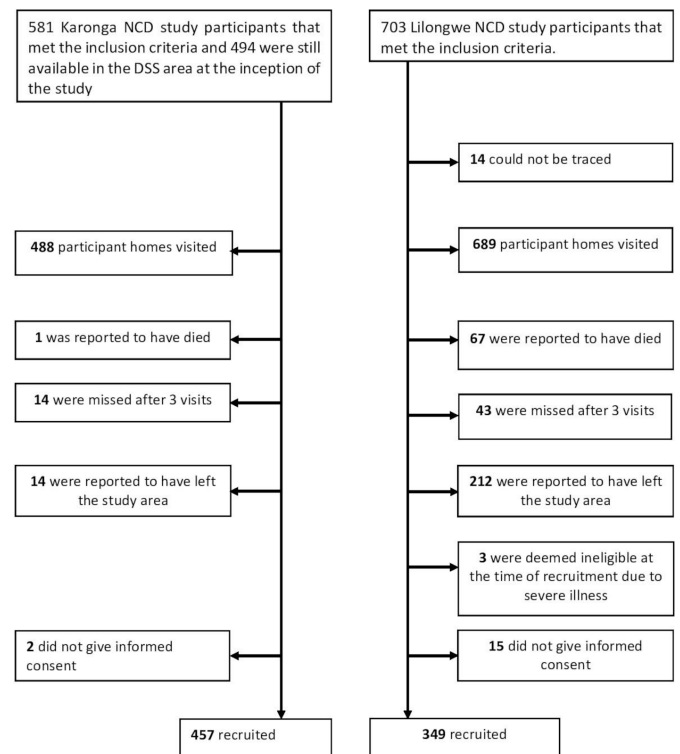


Figure 1 Flowcharts of study participation by site. DSS, Demographic Surveillance Site; NCD, Non-Communicable Diseases.

Nearly a quarter (24.1%; 95% CI: 21.2 to 27.2) of the participants had at least one symptom or sign of LED (table 2). Peripheral neuropathy (n=103; 12.8%) and claudication (n=81; 10%) were the most common features of LED, and signs of limb threatening disease (ie, ulcers (n=13; 1.1%) and lower limb amputations (n=7; 0.9%)) were the least prevalent, affecting 2.4% (n=19) of participants. ABPI <0.9 was recorded among 15 (1.9%) participants, and 391 (48.5%) had ABPI >1.2. (online supplemental table 1). Four participants had ABPI <0.9 on one side and ABPI >1.2 on the contralateral side. In view of the reduced ABPI <0.9, which is more likely to be a true positive, these individuals were categorised as having low ABPI. Those with ABPI >1.2 on both sides were grouped with participants with ABPI between 0.9 and 1.2. At least 25% of participants with each CVDRF, apart from smoking, had LED. LED prevalence rates of over 30% were recorded among participants who were urban residents, women, aged over 50 years, single, indoor users of biomass fuel or homemakers. The prevalence of LED was directly proportional to the number of CVDRFs with the highest prevalence of LED (35.6%; 95% CI: 23.6 to 49.1) being recorded among participants that had five or more risk factors (table 2).

In the full regression model (figure 3), statistically significantly increased odds of LED were found in participants aged at least 50 years ((OR: 1.19; 95% CI: 1.22 to 2.99) among those aged 50–60, and (OR: 2.33; 95% CI: 1.43 to 3.8) among those over 60 years old) and urban residents (OR: 1.76; 95% CI: 1.05 to 2.94) (online

Table 1 Summary of participant characteristics

Variables	n (%)	Both sites		Karonga (rural)		Lilongwe (urban)	
		Men	Women	Men	Women	Men	Women
Total		431	375	303	154	128	221
Age							
Under 50	346 (42.9)	199 (46.2)	147 (39.2)	138 (45.5)	51 (33.1)	61 (47.7)	96 (43.4)
50–60	239 (29.7)	113 (26.2)	126 (33.6)	80 (26.4)	49 (31.8)	33 (25.8)	77 (34.8)
Over 60	221 (27.4)	119 (27.6)	102 (27.2)	85 (28.1)	54 (35.1)	34 (26.6)	48 (21.7)
Wealth quintiles							
Poorest	108 (13.4)	41 (9.5)	67 (17.9)	34 (11.2)	51 (33.1)	7 (5.5)	16 (7.2)
Second	150 (18.6)	83 (19.3)	67 (17.9)	80 (26.4)	46 (29.9)	3 (2.3)	21 (9.5)
Third	139 (17.3)	85 (19.7)	54 (14.4)	77 (25.4)	29 (18.8)	8 (6.3)	25 (11.3)
Fourth	191 (23.7)	103 (23.9)	88 (23.5)	66 (21.8)	18 (11.7)	37 (28.9)	70 (31.7)
Wealthiest	218 (27.1)	119 (27.6)	99 (26.4)	46 (15.2)	10 (6.5)	73 (57)	89 (40.3)
Marital status							
Single	209 (25.9)	54 (12.5)	155 (41.3)	36 (11.9)	82 (53.3)	18 (14.1)	73 (33.0)
Married	597 (74.1)	377 (87.5)	220 (58.7)	267 (88.1)	72 (46.8)	110 (85.9)	148 (67.0)
Highest attained education							
0–5 years primary education	164 (20.4)	59 (13.7)	105 (28)	48 (15.8)	66 (42.9)	11 (8.6)	39 (17.7)
Standard 6–8	329 (40.8)	184 (42.7)	145 (38.7)	156 (51.5)	65 (42.2)	28 (21.9)	80 (36.2)
Secondary	230 (28.5)	141 (32.7)	89 (23.7)	94 (31.0)	21 (13.6)	47 (36.7)	68 (30.8)
Post-secondary	83 (10.3)	47 (10.9)	36 (9.6)	5 (1.7)	2 (1.3)	42 (32.8)	34 (15.4)
Occupation							
Homemaker	237 (29.4)	74 (17.2)	163 (43.5)	32 (10.6)	34 (22.1)	42 (32.8)	129 (58.4)
Farming/fishing	296 (36.7)	209 (48.5)	87 (23.2)	208 (68.7)	84 (54.6)	1 (0.8)	3 (1.36)
Employed	273 (33.9)	148 (34.3)	125 (33.3)	63 (20.8)	36 (23.4)	85 (66.4)	89 (40.3)
Indoor fire							
No	42 (5.2)	26 (6.0)	16 (4.3)	17 (5.6)	6 (3.9)	9 (7.0)	10 (4.5)
Yes, inside the house	39 (4.8)	19 (4.4)	20 (5.3)	5 (1.7)	3 (2.0)	14 (10.9)	17 (7.7)
Yes, but in a separate kitchen	725 (90.0)	386 (89.6)	339 (90.4)	281 (92.7)	145 (94.2)	105 (82)	194 (87.8)
Smoking history							
Non-smokers	487 (60.4)	130 (30.2)	357 (95.2)	72 (23.8)	142 (92.2)	58 (45.3)	215 (97.3)
Smokers	319 (39.6)	301 (69.8)	18 (4.8)	231 (76.2)	12 (7.8)	70 (54.7)	6 (2.7)
Diabetes							
Non-diabetic	502 (62.3)	324 (75.2)	324 (75.2)	251 (82.8)	88 (57.1)	73 (57)	90 (40.7)
Diabetic	273 (33.9)	87 (20.2)	87 (20.2)	42 (13.9)	62 (40.3)	45 (35.2)	124 (56.1)
Missing data	31 (3.9)	20 (4.6)	20 (4.6)	10 (3.3)	4 (2.6)	10 (7.8)	7 (3.2)
Dyslipidaemia							
Yes	344 (42.7)	238 (55.2)	175 (46.7)	177 (58.4)	73 (47.4)	61 (47.7)	102 (46.2)
No	413 (51.2)	165 (38.3)	179 (47.7)	114 (37.6)	74 (48.1)	51 (39.8)	105 (47.5)
Missing data	49 (6.1)	28 (6.5)	21 (5.6)	12 (4.0)	7 (4.6)	16 (12.5)	14 (6.3)
Hypertension							
Hypertensive	482 (59.8)	220 (51.0)	104 (27.7)	171 (56.4)	40 (26.0)	49 (38.3)	64 (29.0)
Not hypertensive	324 (40.2)	211 (49.0)	271 (72.3)	132 (43.6)	114 (74.0)	79 (61.7)	157 (71.0)
Mean blood pressure (SD)	139.1 (38.2)	136 (41.6)	142.6 (33.7)	137 (47)	149.1 (43.6)	133.7 (24.1)	138.1 (23.6)
HIV							
Negative	413 (51.2)	237 (55.0)	176 (46.9)	170 (56.1)	80 (52.0)	67 (52.3)	96 (43.4)

Continued

Table 1 Continued

Variables	n (%)	Both sites		Karonga (rural)		Lilongwe (urban)	
		Men	Women	Men	Women	Men	Women
Positive	247 (30.7)	107 (24.8)	140 (37.3)	78 (25.7)	57 (37.0)	29 (22.7)	83 (37.6)
Unknown	146 (18.1)	87 (20.2)	59 (15.7)	55 (18.2)	17 (11.0)	32 (25)	42 (19)
Obesity							
No	634 (78.7)	402 (93.3)	232 (61.9)	292 (96.4)	113 (73.4)	110 (85.9)	119 (53.9)
Yes	172 (21.3)	29 (6.7)	143 (38.1)	11 (3.6)	41 (26.6)	18 (14.1)	102 (46.2)

supplemental table 2). Cooking with methods other than biomass burning was negatively associated with LED (OR: 0.19; 95% CI: 0.05 to 0.69). The following sets of variables had some statistically significant interactions that affected the odds of the LED: (1) sex and history of smoking, (2) obesity and highest attained education and (3) obesity and participant's wealth quintile, as computed in the full model. The results of these interactions are presented in online supplemental tables 3–6.

DISCUSSION

This study aimed to describe the prevalence of LED among individuals with known CVDRFs in rural and urban Malawi. Of the 806 individuals studied, a large proportion had at least one sign of LED, with claudication and peripheral neuropathy being the most common. The prevalence of LED was directly related to the number of risk factors with advancing age, urban living, and poverty demonstrating the greatest association. Although amputations and active ulceration were less frequently seen, 2.4% of individuals in this study had these conditions which are indicative of active or previous limb threatening disease.

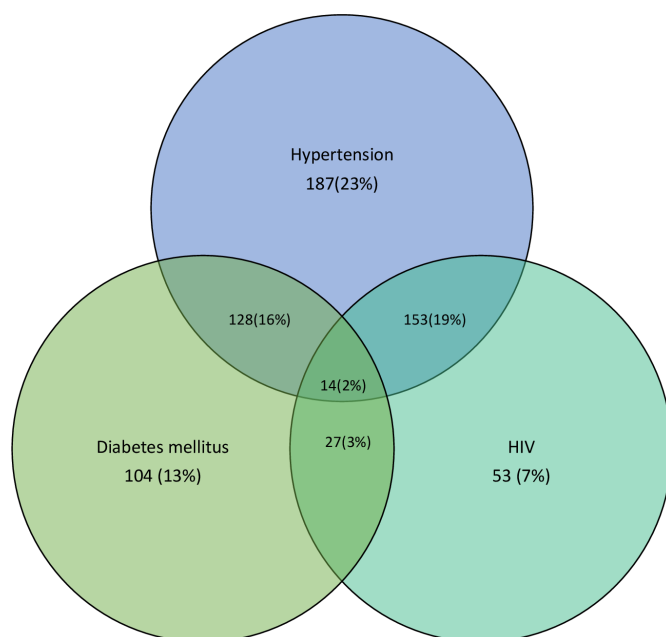


Figure 2 Three major risk factors and multimorbidity across the study population.

Provision of healthcare services to manage CVDRFs or care for patients with LED is limited in Malawi and tends to be focused around large urban centres.¹⁴ Health literacy also tends to be poor among those living with chronic conditions, with patients and families often understanding little about their condition or the longer term consequences of inadequate management.¹⁵ Provision of surgical services for the management of LED (eg, vascular reconstructive techniques, amputation, and rehabilitation services) is limited throughout southern Africa, and this field has not been viewed as a priority among competing healthcare development needs.^{16 17}

In poorly resourced health systems where people present late with disease, amputation rates and subsequent mortality is high. For example, a small study in Tanzania showed that 33% of people admitted to hospital with diabetic foot disease were managed by amputation and mortality was nearly 50%.¹⁸ By comparison, in the UK 17% of people presenting with disease underwent amputation within 1 year of presentation with no reported mortality.¹⁹ After limb loss, poor postoperative care and the dearth of services for rehabilitation, prostheses, and mobility aids result in further mortality and morbidity.²⁰ The devastating effects are tragic given there are simple and cheap strategies—including preventing and treating CVDRFs and regular monitoring for signs of LED in high risk individuals with early referral to specialist services—to reduce deleterious outcomes.

Although this is one of the few studies to look at the population prevalence of LED,⁷ the findings of this study are in keeping with previously published work.^{8 21} For example, population prevalence of vascular disease has been reported at over 30% in those over 65 years.⁷

An interesting 'U' shaped association between LED and wealth was observed, with the greatest prevalence of disease being in the poorest and the wealthiest groups. The prevalence of hypertension and diabetes in these groups was also significantly higher at the extremes of wealth than in the middle three quintiles, which may go some way to explain the observations. There may be other factors, beyond the scope of this study to characterise, such as lack of access to skilled healthcare services for optimum management of these comorbidities in the poorer communities,²² and potentially other social drivers towards worse ill-health such as sedentary lifestyle and westernised dietary habits among the wealthier group,

Table 2 Prevalence of led in total and by participant characteristics

Variables	n	LED prevalence (95% CI) n=194
Total	806	24.1 (21.2 to 27.2)
Age		
<50	346	15.9 (12.2 to 20.2)
50–60	239	27.6 (22.0 to 33.7)
>60	221	33.0 (26.9 to 39.7)
Sex		
Male	431	15.8 (12.5 to 19.6)
Female	375	33.6 (28.8 to 38.6)
Residence		
Rural	457	17.5 (14.1 to 21.3)
Urban	349	32.7 (27.8 to 37.9)
Wealth quintiles		
Poorest	108	32.4 (16.2 to 30.2)
Second	150	22.7 (16.2 to 30.2)
Third	139	15.8 (10.2 to 23.0)
Fourth	191	24.1 (18.2 to 30.8)
Wealthiest	218	26.1 (20.4 to 32.5)
Marital status		
Single	209	34.0 (27.6 to 40.8)
Married	587	20.6 (17.4 to 24.1)
Educational achievement		
0–5 years primary education	164	25 (18.6 to 32.3)
Standard 6–8	329	25.5 (20.9 to 30.6)
Secondary	230	21.7 (16.6 to 27.6)
Post-secondary	83	22.9 (14.4 to 33.4)
Occupation		
Homemaker	237	37.1 (31.0 to 43.6)
Farming/fishing	296	15.5 (11.6 to 20.2)
Employed	273	22.0 (17.2 to 27.4)
Indoor fire		
None	42	7.1 (1.5 to 19.5)
Fire usually lit Inside the house	39	30.8 (17.0 to 47.6)
Fire usually lit in a separate kitchen area	725	24.7 (21.6 to 28.0)
Any smoking history		
No	487	29.4 (25.4 to 33.6)
Yes	319	16.0 (12.1 to 20.5)
Diabetes		
Non-diabetic	502	19.7 (16.3 to 23.5)
Diabetic	273	33.7 (28.1 to 39.6)
Missing data	31	9.7 (2.0 to 25.8)
Dyslipidaemia		

Continued

Table 2 Continued

Variables	n	LED prevalence (95% CI) n=194
No	413	22.8 (18.8 to 27.1)
Yes	344	26.5 (21.9 to 31.5)
Missing data	49	18.4 (8.8 to 32.0)
HIV		
Negative	413	23.0 (19.0 to 27.4)
Positive	247	23.9 (18.7 to 29.7)
Unknown	146	27.4 (20.3 to 35.4)
Hypertension		
Not-hypertensive	324	21.9 (17.6 to 26.8)
Hypertensive	482	25.5 (21.7 to 29.7)
Obesity		
No	634	20.8 (17.7 to 24.2)
Yes	172	36.0 (28.9 to 43.7)
Number of risk factors		
2	201	14.9 (10.3 to 20.6)
3	342	23.1 (18.7 to 27.9)
4	204	32.4 (26.0 to 39.2)
≥5	59	32.2 (20.6 to 45.6)
Prevalence of outcomes by risk factors		
No diabetes and no hypertension	193	14.0 (25.6 to 42.4)
Diabetes but no hypertension	131	33.6 (25.6 to 42.4)
Hypertension but no diabetes	340	22.1 (17.8 to 26.8)
Hypertension and diabetes	142	33.8 (26.1 to 42.2)

LED, lower extremity disease.

which somewhat negate improved access to healthcare for those who are more wealthy.^{23–25} It will be important to fully understand these associations in future work to understand which interventions may be the most effective in preventing LED among different population groups.

Smoking status in this study was not shown to be a significant factor associated with LED, in contrast to a well-established body of evidence from high-income countries.²⁶ The reasons for this are not clear, however, smoking is not as common in Malawi as in some high-income countries and the cut-off for being defined as a smoker in this study was more than six cigarettes per week, which is a relatively low level of consumption.

This was a large-scale population-based study, highlighting those at risk of limb loss among a group with known CVDRE. In focusing on population level data, the study reduces the potential for bias towards those who have already engaged with healthcare services. This is an advantage over much of the published literature to date,

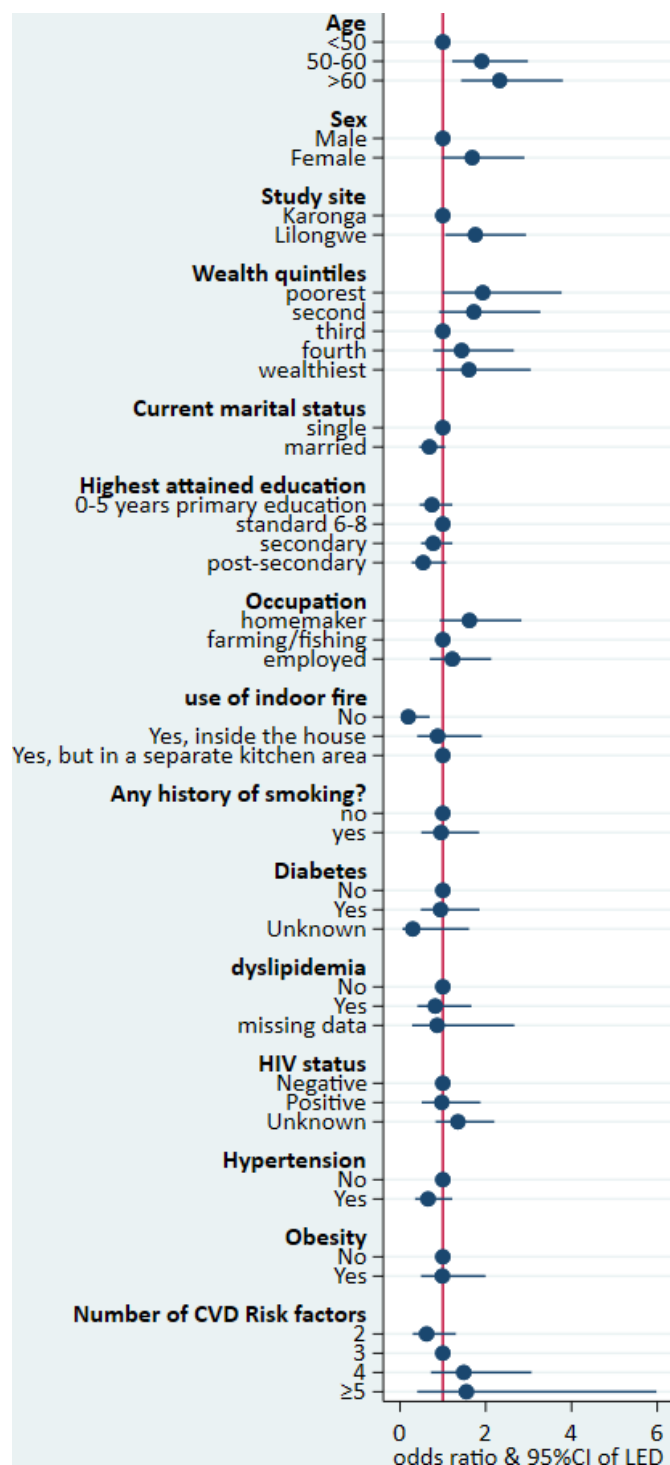


Figure 3 Coefficient plot of factors associated with lower extremity disease. CVD, cardiovascular disease; LED, lower extremity disease.

and provides a greater understanding of the scale of LED across different population groups in Malawi. The use of multiple approaches to evaluate the presence of LED is also a strength of this study, recognising that no single assessment is either sensitive or specific in isolation.⁴

There are potential limitations to the conclusions to be drawn from this study. The use of ABPI and the Edinburgh Claudication Questionnaire as surrogate markers

for peripheral vascular disease, while both validated techniques, do have drawbacks. Claudication, in itself, may never progress to represent a limb-threatening condition, however, can be a good marker of more generalised cardiovascular ill-health and therefore highlight opportunities for optimisation of best medical therapy in order to reduce cardiovascular mortality.²⁷ ABPI may be confounded by calcification in vessels, resulting in falsely elevated ratios; this is particularly seen among diabetic individuals. The inclusion of those with ABPI >1.2 into the group with ABPI 0.9–1.2 may have resulted in some false negative results, neglecting to report arterial disease which was in fact present. While Toe Brachial Pressure Index (TBPI) may be a more reliable observation in this group,²⁸ there is little published data on TBPI studies in Sub-Saharan Africa and therefore interpretation of the findings from this study in the context of previously published work would have been more limited had this technique been used. We also did not enquire about the aetiology of ulcers hence it is not possible to establish the aetiology of the ulcers. Finally, we failed to achieve the sample size for this study, however, the proportion of participants affected by LED was far greater than we had estimated and would have required a lower number of participants to reliably detect. In a retrospective calculation, 460 participants would have been required to detect a prevalence of LED of 24% with the same width of CI as in our initial power calculation.

In conclusion, this study demonstrated that 1 in 4 individuals with two or more CVDRFs have evidence of LED and 2.4% already had active signs of limb threatening ulceration or previous amputation. An interesting U-shaped association with wealth was observed. Future work will need to explore the social determinants of health in relation to LED in order to guide health system interventions appropriately; the solutions may be complex and it is likely that there will not be a 'one size fits all' approach to preventing limb loss in this region. It is likely that both therapeutic and preventive services will have to be developed in parallel.

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REFERENCES

- Pillay B, Ramdial PK, Naidoo DP. Hiv-Associated large-vessel vasculopathy: a review of the current and emerging clinicopathological spectrum in vascular surgical practice. *Cardiovasc J Afr* 2015;26:70–81.
- Madsen UR, Baath C, Berthelsen CB, et al. Age and health-related quality of life, general self-efficacy, and functional level 12 months following dysvascular major lower limb amputation: a prospective longitudinal study. *Disabil Rehabil* 2019;41:2900–9.
- Taghipour H, Moharamzad Y, Mafi AR, et al. Quality of life among veterans with war-related unilateral lower extremity amputation: a long-term survey in a prosthesis center in Iran. *J Orthop Trauma* 2009;23:525–30.
- Johnston LE, Stewart BT, Yangni-Angate H, et al. Peripheral arterial disease in sub-Saharan Africa: a review. *JAMA Surg* 2016;151:564.
- Fowkes FGR, Rudan D, Rudan I, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet* 2013;382:1329–40.
- Joshi R, Jan S, Wu Y, et al. Global inequalities in access to cardiovascular health care: our greatest challenge. *J Am Coll Cardiol* 2008;52:1817–25.
- Guerchet M, Aboyans V, Mbelesso P, et al. Epidemiology of peripheral artery disease in elder general population of two cities of central Africa: Bangui and Brazzaville. *Eur J Vasc Endovasc Surg* 2012;44:164–9.
- Yeboah K, Puiampu P, Ainuson J, et al. Peripheral artery disease and exertional leg symptoms in diabetes patients in Ghana. *BMC Cardiovasc Disord* 2016;16:1–9.
- Chisala P, Sandford B. Peripheral arterial disease among high-risk patients at a tertiary hospital in Blantyre, Malawi: a 2-phase observational study. *East Cent Afr J Surg* 2020;25.
- Okello S, Millard A, Owori R, et al. Prevalence of lower extremity peripheral artery disease among adult diabetes patients in southwestern Uganda. *BMC Cardiovasc Disord* 2014;14:75.
- Price AJ, Crampin AC, Amberbir A, et al. Prevalence of obesity, hypertension, and diabetes, and cascade of care in sub-Saharan Africa: a cross-sectional, population-based study in rural and urban Malawi. *Lancet Diabetes Endocrinol* 2018;6:208–22.
- Aboyans V, Lacroix P, Lebourdon A, et al. The intra- and interobserver variability of ankle-arm blood pressure index according to its mode of calculation. *J Clin Epidemiol* 2003;56:215–20.
- Aboyans V, Criqui MH, Abraham P, et al. Measurement and interpretation of the Ankle-brachial index: a scientific statement from the American heart association. *Circulation* 2012;126:2890–909.
- Chikowe I, Mwapasa V, Kengne AP. Analysis of rural health centres preparedness for the management of diabetic patients in Malawi. *BMC Res Notes* 2018;11:267.
- Assayed AA, Muula AS, Nyirenda MJ. The quality of care of diabetic patients in rural Malawi: a case of Mangochi district. *Malawi Med J* 2014;26:109–14.
- Veller MG. Education in vascular surgery-critical issues: a southern African perspective. *J Vasc Surg* 2008;48:84S–6.
- Magnusson L, Ahlström G, Ramstrand N, et al. Malawian prosthetic and orthotic users' mobility and satisfaction with their lower limb assistive device. *J Rehabil Med* 2013;45:385–91.
- Gulam-Abbas Z, Lutale JK, Morbach S, et al. Clinical outcome of diabetes patients hospitalized with foot ulcers, Dar ES Salaam, Tanzania. *Diabet Med* 2002;19:575–9.
- Paisey RB, Abbott A, Levenson R, et al. Diabetes-Related major lower limb amputation incidence is strongly related to diabetic foot service provision and improves with enhancement of services: peer review of the south-west of England. *Diabet Med* 2018;35:53–62.
- Guest JF, Fuller GW, Vowden P. Diabetic foot ulcer management in clinical practice in the UK: costs and outcomes. *Int Wound J* 2018;15:43–52.
- Zhang P, Lu J, Jing Y, et al. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. *Ann Med* 2017;49:106–16.
- Angwenyi V, Aantjes C, Kajumi M, et al. Patients experiences of self-management and strategies for dealing with chronic conditions in rural Malawi. *PLoS One* 2018;13:e0199977.
- Geldsetzer P, Manne-Goehler J, Marcus M-E, et al. The state of hypertension care in 44 low-income and middle-income countries: a cross-sectional study of nationally representative individual-level data from 1.1 million adults. *The Lancet* 2019;394:652–62.
- Manne-Goehler J, Geldsetzer P, Agoudavi K, et al. Health system performance for people with diabetes in 28 low- and middle-income countries: a cross-sectional study of nationally representative surveys. *PLoS Med* 2019;16:e1002751.
- Kreatsoulas C, Anand SS, Frcpc SSA. The impact of social determinants on cardiovascular disease. *Canadian Journal of Cardiology* 2010;26:8C–13.
- U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. *How tobacco smoke causes disease: the biology and behavioral basis for Smoking-Attributable disease*, 2010.
- Bevan GH, White Solaru KT. Evidence-Based medical management of peripheral artery disease. *Arterioscler Thromb Vasc Biol* 2020;40:541–53.
- Williams DT, Harding KG, Price P. An evaluation of the efficacy of methods used in screening for lower-limb arterial disease in diabetes. *Diabetes Care* 2005;28:2206–10.

Appendix

Appendix table 1: Crude prevalence of factors associated with LED

		OUTCOME						
	N	LED prevalence (95% CI) n=194	Absent pulse prevalence (95% CI) n=54	Amputation Prevalence (95% CI) n=7	Ulcer Prevalence (95% CI) n=13	Claudication Prevalence (95% CI) n=81	Neuropathy Prevalence (95% CI) n=103	ABPI<0.9 Prevalence (95% CI) n=15
Total								
	806	24.1 (21.2—27.2)	6.7 (5.1—8.7)	0.9 (0.3—1.8)	1.1 (0.4— 1.8)	10 (8.1—12.3)	12.8 (10.6—15.3)	1.9 (1.0—3.1)
Age								
<50	346	15.9 (12.2—20.2)	4.9 (2.9—7.8)	0.3 (0.0—1.6)	2.3 (1.0—4.5)	9.0 (6.2—12.5)	6.1 (3.8—9.1)	0.3 (0.0—1.6)
50-60	239	27.6 (22.0—33.7)	6.7 (3.9—10.6)	2.1 (0.7—4.8)	0.8 (0.1—3.0)	12.6 (8.6—17.4)	15.1 (10.8—20.2)	0.8 (0.1—3.0)
>60	221	33.0 (26.9—39.7)	9.5 (6.0—14.2)	0.5 (0.0—2.5)	1.4 (0.3—3.9)	9.0 (5.6—13.6)	20.8 (15.7—26.8)	5.4 (2.8—9.3)
Sex								
Male	431	15.8 (12.5—19.6)	5.8 (3.8—8.4)	0.5 (0.1—1.7)	1.4 (0.5—3.0)	4.2 (2.5—6.5)	10.2 (7.5—13.5)	0.9 (0.3—2.4)
Female	375	33.6 (28.8— 38.6)	7.7 (5.2—10.9)	1.3 (0.4—3.1)	1.9 (0.8— 3.8)	16.8 (13.2—21.0)	15.7 (12.2—19.8)	2.9 (1.5—5.2)
Residence								
Rural	457	17.5 (14.1—21.3)	9.0 (6.5—12.0)	1.1 (0.4—2.5)	1.8 (0.8—3.4)	2.2 (1.1— 4.0)	13.8 (10.8—17.3)	1.8 (0.8—3.4)
Urban	349	32.7 (27.8—37.9)	3.7 (2.0—6.3)	0.6 (0.1— 2.1)	1.4 (0.5—3.3)	20.3 (16.2—25.0)	11.5 (8.3—15.3)	2.0 (0.8—4.1)
Wealth quintiles								
poorest	108	32.4 (16.2—30.2)	13.0 (7.3—20.8)	0.9 (0.02—5.1)	0.9 (0.02—5.1)	7.5 (2.6—12.9)	25 (17.2—34.3)	5.6 (2.1—11.7)

second	150	22.7 (16.2—30.2)	5.3 (2.3—10.2)	0.0 (0—2.4)	0.6 (0.02—3.7)	7.3 (3.7—12.7)	14.0 (8.9—20.6)	2.0 (0.4—5.7)
third	139	15.8 (10.2—23.0)	6.5 (3.0—11.9)	0.0 (0—2.6)	1.4 (0.2—5.1)	6.5 (3.0—11.9)	8.6 (4.5—14.6)	0.7 (0.0—3.9)
fourth	191	24.1 (18.2—30.8)	4.7 (2.2—8.8)	2.1 (0.6—5.3)	0.5 (0.0—2.9)	13.1 (8.7—18.7)	11.0 (6.9—16.3)	1.6 (0.3—4.5)
wealthiest	218	26.1 (20.4—32.5)	6.4 (3.6—10.5)	0.9 (0.1—3.3)	3.7 (1.6—7.1)	13.3 (9.1—18.5)	10.1 (6.4—15.9)	0.9 (0.1—3.3)
Marital status								
Single	209	34.0 (27.6—40.8)	10.0 (6.3—15.0)	1.0 (0.1—3.4)	1.9 (0.5—4.8)	12.4 (8.2—17.7)	18.7 (13.6—24.6)	3.8 (1.7—7.4)
married	587	20.6 (17.4—24.1)	5.5 (3.8—7.7)	0.8 (0.3—1.9)	1.5 (0.7—2.8)	9.2 (7.0—11.8)	10.7 (8.4—13.5)	1.2 (0.5—2.4)
Educational achievement								
0-5 years primary education	164	25 (18.6—32.3)	7.9 (4.3—13.2)	0 (0.0—2.2)	1.2 (0.1—4.3)	6.7 (3.4—11.7)	16.5 (11.1—23.0)	4.3 (1.7—8.6)
Standard 6-8	329	25.5 (20.9—30.6)	6.7 (4.2—9.9)	0.6 (0.1—2.2)	1.5 (0.5—3.5)	11.9 (8.6—15.8)	12.5 (9.1—16.5)	2.1 (0.9—4.3)
Secondary	230	21.7 (16.6—27.6)	6.1 (3.4—10.0)	1.7 (0.5—4.4)	2.6 (1.0—5.6)	8.2 (5.0—12.6)	12.2 (8.2—17.1)	0.4 (0.0—2.4)
Post-secondary	83	22.9 (14.4—33.4)	6.0 (2.0—13.5)	1.2 (0.0—6.5)	0.0 (0—4.3)	14.5 (7.7—23.9)	8.4 (3.5—16.6)	0.0 (0.0—4.3)
occupation								
homemaker	237	37.1 (31.0—43.6)	7.2 (4.2—11.2)	1.7 (0.5—4.3)	2.5 (0.9—5.4)	18.6 (13.8—24.1)	15.6 (11.2—20.9)	4.2 (2.0—7.6)
Farming/ fishing	296	15.5 (11.6—20.2)	9.1 (6.1—13.0)	0.3 (0.0—1.9)	1.0 (0.2—2.9)	1.7 (0.6—3.9)	12.8 (9.2—17.9)	1.7 (0.6—3.9)
employed	273	22.0 (17.2—27.4)	3.7 (1.8—6.6)	0.7 (0.0—2.6)	1.5 (0.4—3.7)	11.7 (8.2—16.1)	10.3 (6.9—14.5)	0.0 (0—1.3)
Indoor fire								
none	42	7.1 (1.5—19.5)	4.8 (0.6—16.2)	0.0 (0—8.4)	2.4 (0.0—12.6)	4.8 (0.6—16.2)	0.0 (0—8.4)	0.0 (0—8.4)
Fire usually lit Inside the house	39	30.8 (17.0—47.6)	7.7 (1.6—20.9)	0.0 (0—9.0)	2.6 (0.0—13.5)	17.9 (7.5—33.5)	12.8 (4.3—27.4)	0.0 (0—9.0)
Fire usually lit in a separate	725	24.7 (21.6—28.0)	6.8 (5.0—8.8)	1.0 (0.4—2.0)	1.5 (0.8—2.7)	9.9 (7.9—12.3)	13.5 (11.1—16.2)	2.1 (1.2—3.4)

kitchen area								
Any Smoking history								
no	487	29.4 (25.4—33.6)	7.6 (5.4—10.3)	1.2 (0.5—2.7)	1.8 (0.8—3.5)	14.0 (11.0—17.4)	14.4 (11.4—17.8)	2.1 (1.0—3.7)
yes	319	16.0 (12.1—20.5)	5.3 (3.1—8.4)	0.3 (0.0—1.7)	1.3 (0.3—3.2)	4.1 (2.2—6.9)	10.3 (7.2—14.2)	1.6 (0.5—3.6)
Diabetes								
Non-diabetic	502	19.7 (16.3—23.5)	6.2 (4.2—8.7)	0 (0—0.7)	1.2 (0.4—2.6)	8.2 (5.9—10.9)	10.2 (7.7—13.1)	1.4 (0.6—2.9)
diabetic	273	33.7 (28.1—39.6)	7.7 (4.8—11.5)	2.6 (1.0—5.2)	2.2 (0.8—4.7)	13.9 (10.0—18.6)	18.7 (14.2—23.8)	2.9 (1.3—5.7)
Missing data	31	9.7 (2.0—25.8)	6.5 (0.8—21.4)	0.0 (0—11.2)	3.2 (0.0—16.7)	6.5 (0.8—21.4)	3.2 (0.1—16.7)	0.0 (0.0—11.2)
Dyslipidaemia								
no	413	22.8 (18.8—27.1)	6.5 (4.4—9.4)	0.7 (0.2—2.1)	1.2 (0.4—2.8)	10.4 (7.6—13.8)	10.7 (7.8—14.0)	2.4 (1.2—4.4)
yes	344	26.5 (21.9—31.5)	7.0 (4.5—10.2)	1.2 (0.3—3.0)	1.7 (0.6—3.8)	10.2 (7.2—13.9)	15.7 (12.0—20.0)	1.5 (0.5—3.4)
Missing data	49	18.4 (8.8—32.0)	6.1 (1.3—16.9)	0.0 (0.0—7.3)	4.1 (0.5—14.0)	6.1 (1.3—16.9)	10.2 (3.4—22.2)	0.0 (0.0—7.3)
HIV								
negative	413	23.0 (19.0—27.4)	7.5 (5.2—10.5)	0.7 (0.2—2.1)	1.2 (0.4—2.8)	10.0 (7.2—13.2)	12.1 (9.1—15.6)	2.4 (1.2—4.4)
positive	247	23.9 (18.7—29.7)	6.1 (3.4—9.8)	0.4 (0.0—2.2)	2.0 (0.7—4.7)	10.1 (6.7—14.6)	12.6 (8.7—17.3)	0.8 (0.1—2.9)
unknown	146	27.4 (20.3—35.4)	5.5 (2.4—10.5)	0.0 (0—2.5)	0.7 (0.0—3.8)	10.3 (5.9—16.4)	15.1 (9.7—21.9)	2.7 (0.8—6.9)
hypertension								
Not-hypertensive	324	21.9 (17.6—26.8)	4.6 (2.6—7.5)	0.9 (0.2—2.7)	2.2 (0.9—4.4)	9.3 (6.3—13.0)	12.7 (9.2—16.8)	0.6 (0.1—2.2)
hypertensive	482	25.5 (21.7—29.7)	8.1 (5.8—10.9)	0.8 (0.2—2.1)	1.2 (0.5—2.7)	10.6 (8.0—13.7)	12.9 (10.0—16.2)	2.7 (1.4—4.6)
obesity								

no	634	20.8 (17.7—24.2)	5.8 (4.1—8.0)	0.6 (0.2—1.6)	1.6 (0.8—2.9)	7.3 (5.4—9.6)	11.8 (9.4—14.6)	1.9 (1.0—3.3)
yes	172	36.0 (28.9—43.7)	9.9 (5.9—15.4)	1.7 (0.4—5.0)	1.7 (0.4—5.0)	20.3 (14.6—27.1)	16.3 (11.1—22.7)	1.7 (0.4—5.0)
Number of risk factors								
2	201	14.9 (10.3—20.6)	3.0 (1.1—6.4)	1.0 (0.1—3.5)	1.1 (0.1—3.5)	7.5 (4.2—12.0)	6.5 (3.4—10.8)	0.5 (0.0—2.7)
3	342	23.1 (18.7—27.9)	6.7 (4.3—9.9)	0.3 (0.0—1.6)	2.0 (0.8—4.2)	8.8 (6.0—12.3)	12.0 (8.7—15.9)	2.6 (1.2—4.9)
4	204	32.4 (26.0—39.2)	9.3 (5.7—14.2)	0.5 (0.0—2.7)	1.0 (0.5—4.9)	14.7 (10.1—20.3)	18.1 (13.1—24.1)	2.0 (0.5—4.9)
≥5	59	32.2 (20.6—45.6)	10.2 (3.8—20.8)	5.1 (1.1—14.1)	0.0 (0.0—6.1)	10.2 (3.8—20.8)	20.3 (11.0—32.8)	1.7 (0.0—9.1)
Prevalence of outcomes by risk factors								
No diabetes and no hypertension	193	14.0 (25.6—42.4)	4.1 (1.8—8.0)	0.0 (0.0—1.9)	1.6 (0.3—4.4)	4.7 (2.2—8.7)	9.3 (5.6—14.3)	0.0 (0.0—1.9)
Diabetes but no hypertension	131	33.6 (25.6—42.4)	5.3 (2.2—10.7)	2.3 (0.5—6.5)	3.1 (0.8—7.6)	16.0 (10.2—23.5)	17.6 (11.5—25.2)	1.5 (0.2—5.4)
Hypertension but no diabetes	340	22.1 (17.8—26.8)	7.4 (4.8—10.7)	0.0 (0.0—1.1)	1.2 (0.3—3.0)	10 (7.0—13.7)	10.0 (7.0—13.7)	2.1 (0.8—4.2)
Hypertension and diabetes	142	33.8 (26.1—42.2)	9.9 (5.5—16.0)	2.8 (0.8—7.1)	1.4 (0.2—5.0)	12.0 (7.1—18.5)	19.7 (13.5—27.2)	4.2 (1.6—9.0)

Appendix table 2: full regression model of factors associated with Lower extremity disease

	Odds Ratio	Std. Err.	z	P>z	95% confidence interval	Lr test p value
Age						
<50	1	ref.				0.0012
50-60	1.91	0.4	2.8	0.0	1.22—2.99	
>60	2.33	0.6	3.4	0.0	1.43—3.8	
sex						
Male	1.0	ref.				0.0574
Female	1.69	0.5	1.9	0.1	0.98—2.9	
site						
Karonga	1.0	ref.				0.0296
Lilongwe	1.76	0.5	2.2	0.0	1.05—2.94	
Wealth quintiles						
poorest	1.93	0.7	1.9	0.1	0.99—3.77	0.3322
second	1.72	0.6	1.7	0.1	0.91—3.27	
third	1.0	ref.				
fourth	1.43	0.4	1.2	0.2	0.78—2.66	
wealthiest	1.61	0.5	1.5	0.1	0.85—3.05	
Marital status						
single	1.0	ref.				0.0862
married	0.69	0.1	-1.7	0.1	0.45—1.05	
Highest attained education						
years primary education	0.75	0.2	-1.2	0.2	0.46—1.22	0.2630
standard 6-8	1.0	ref.				
secondary	0.78	0.2	-1.1	0.3	0.49—1.22	
post-secondary	0.54	0.2	-1.7	0.1	0.27—1.08	
Occupation						
homemaker	1.62	0.5	1.7	0.1	0.93—2.83	0.2026
farming/fishing	1.0	ref.				
employed	1.22	0.3	0.7	0.5	0.7—2.13	
Indoor smoke						
No	0.19	0.1	-2.5	0.0	0.05—0.69	0.0105
Yes, inside the house	0.88	0.3	-0.3	0.7	0.4—1.91	
Yes, in a separate kitchen area	1.0	ref.				
any history of smoking						
no	1.0	ref.				0.8995
yes	0.96	0.3	-0.1	0.9	0.5—1.84	
Diabetes						
No	1.0	ref.				0.3532
Yes	0.95	0.3	-0.2	0.9	0.48—1.86	

Unknown	0.3	0.3	-1.4	0.2	0.06—1.61	
Dyslipidaemia						
No	1.0	ref.				0.8425
Yes	0.82	0.3	-0.5	0.6	0.41—1.66	
missing data	0.87	0.5	-0.3	0.8	0.28—2.67	
HIV status						
Negative	1.0	ref.				0.4490
Positive	0.98	0.3	-0.1	0.9	0.51—1.88	
Unknown	1.35	0.3	1.2	0.2	0.83—2.2	
hypertension						
No	1.0	ref.				0.1768
Yes	0.65	0.2	-1.3	0.2	0.35—1.22	
obesity						
No	1.0	ref.				0.9754
Yes	0.99	0.4	0.0	1.0	0.49—2.0	
CVDRF						
2	0.62	0.2	-1.3	0.2	0.3—1.3	0.4812
3	1.0	ref.				
4	1.49	0.5	1.1	0.3	0.72—3.07	
≥5	1.54	1.1	0.6	0.5	0.4—5.98	

Stratified analysis for lower extremity disease

Appendix table 3: stratification by sex

	Male	Female
Age		
<50	(ref)	(ref)
50-60	1.96 (0.91—4.22)	1.97 (1.08—3.6)
>60	2.41 (1.08—5.37)	2 (1.0 [*] —4.01)
site		
Karonga	(ref)	(ref)
Lilongwe	1.84 (0.79—4.31)	1.65 (0.82—3.34)
Wealth quintiles		
poorest	1.92 (0.6—6.19)	2.04 (0.86—4.88)
second	2.32 (0.87—6.18)	1.4 (0.58—3.39)
third	(ref)	(ref)
fourth	1.74 (0.65—4.64)	1.51 (0.66—3.46)
wealthiest	1.23 (0.42—3.6)	2.03 (0.87—4.72)
Marital status		
single	(ref)	(ref)
married	0.39 (0.18—0.86)	0.81 (0.47—1.39)
Highest attained education		
0-5 years prima..	1.01 (0.41—2.48)	0.69 (0.36—1.3)
standard 6-8	(ref)	(ref)
secondary	0.86 (0.42—1.73)	0.68 (0.36—1.28)
post-secondary	0.62 (0.19—2.06)	0.43 (0.17—1.09)
Occupation		
homemaker	1.09 (0.44—2.72)	2.19 (0.98—4.89)
farming/fishing	(ref)	(ref)
employed	0.91 (0.4—2.06)	1.87 (0.8—4.38)
Indoor fire		
No	(empty)	0.28 (0.07—1.17)
Yes, inside the house	0.66 (0.17—2.59)	1.06 (0.39—2.92)
Yes, but in a separate kitchen area.	(ref)	(ref)
History of smoking		
no	(ref)	(ref)
yes	0.79 (0.34—1.8)	1.83 (0.52—6.47)
Diabetes		
No	(ref)	(ref)
Yes	1.89 (0.71—5.01)	0.38 (0.13—1.18)
Unknown	0.48 (0.05—5.04)	0.18 (0.01—2.69)
Dyslipidaemia		

* Rounded up from .9989416

No	(ref)	(ref)
Yes	0.91 (0.32—2.59)	0.48 (0.16—1.49)
missing data	1.05 (0.18—6.21)	0.6 (0.12—2.97)
HIV status		
Negative	(ref)	(ref)
Positive	1.81 (0.74—4.41)	0.38 (0.13—1.13)
Unknown	1.69 (0.8—3.58)	0.93 (0.46—1.85)
hypertension		
No	(ref)	(ref)
Yes	0.52 (0.22—1.24)	0.39 (0.13—1.19)
obesity		
No	(ref)	(ref)
Yes	2.13 (0.64—7.07)	0.5 (0.17—1.48)
CVDRF		
2	0.68 (0.23—1.97)	0.45 (0.14—1.47)
3	(ref)	(ref)
4	1.37 (0.48—3.94)	2.59 (0.82—8.2)
≥5	0.76 (0.09—6.61)	6.48 (0.73—57.42)

Appendix table 4: Stratification by Sex and history of smoking

Variables and variable categories	Male non-smoker	Male smoker	Female non-smoker	Female current smokers [†]
Age				
<50	(ref)	(ref)	(ref)	
50-60	2.74 (0.5—14.91)	1.43 (0.53—3.85)	2.1 (1.15—3.85)	
>60	4.53 (0.62—32.88)	1.86 (0.68—5.06)	1.95 (0.96—3.94)	
Site				
Karonga	(ref)	(ref)	(ref)	
Lilongwe	0.63 (0.12—3.41)	3.38 (1.07—10.62)	1.82 (0.88—3.78)	
Wealth Quintile				
poorest	6.26 (0.26—150.93)	1.58 (0.35—7.09)	1.71 (0.7—4.18)	
second	4.03 (0.18—89)	2.85 (0.9—9.05)	1.38 (0.56—3.43)	
third	(ref)	(ref)	(ref)	
fourth	4.67 (0.28—76.66)	1.27 (0.41—3.99)	1.24 (0.54—2.87)	
wealthiest	14.33 (0.91—225.09)	0.72 (0.16—3.21)	1.62 (0.69—3.81)	
Marital status				
single	(ref)	(ref)	(ref)	
married	0.04 (0.0—0.56)	0.58 (0.21—1.58)	0.91 (0.52—1.58)	
Education				
years primary education	4.93 (0.17—139.91)	0.88 (0.33—2.35)	0.64 (0.33—1.24)	
standard 6-8	(ref)	(ref)	(ref)	
secondary	3.02 (0.57—15.97)	0.62 (0.24—1.57)	0.78 (0.41—1.49)	
post-secondary	1.35 (0.19—9.71)	0.75 (0.07—8.19)	0.47 (0.19—1.18)	
Occupation				
homemaker	1.82 (0.29—11.26)	0.72 (0.2—2.6)	2.09 (0.9—4.88)	
farming/fishing	(ref)	(ref)	(ref)	
employed	0.43 (0.07—2.8)	1.1 (0.38—3.23)	1.68 (0.69—4.08)	
Indoor smoke				
No	(empty)	(empty)	(empty)	
Yes, inside the house	(empty)	0.82 (0.17—3.98)	1.02 (0.37—2.8)	
a separate kitchen area	(ref)	(ref)	(ref)	
diabetes				
No	(ref)	(ref)	(ref)	
Yes	1.57 (0.11—22.08)	3.79 (0.94—15.32)	0.35 (0.1—1.22)	
Unknown	(empty)	0.58 (0.02—16.66)	0.24 (0.02—3.85)	
Dyslipidaemia				
No	(ref)	(ref)	(ref)	
Yes	0.17 (0.01—3.9)	0.79 (0.2—3.14)	0.45 (0.13—1.53)	
missing data	0.28 (0.01—5.91)	0.7 (0.03—14.21)	0.57 (0.1—3.22)	
HIV status				

[†] No observations

Negative	(ref)	(ref)	(ref)	
Positive	1.82 (0.12—28.15)	2 (0.65—6.15)	0.41 (0.13—1.33)	
Unknown	2.01 (0.41—9.92)	1.74 (0.65—4.71)	0.99 (0.48—2.02)	
hypertension				
No	(ref)	(ref)	(ref)	
Yes	0.65 (0.06—6.93)	0.35 (0.1—1.15)	0.37 (0.11—1.25)	
obesity				
No	(ref)	(ref)	(ref)	
Yes	0.59 (0.04—9.2)	6.62 (1.06—41.46)	0.52 (0.16—1.72)	
CVDRF				
2	0.66 (0.04—11.7)	0.46 (0.11—1.85)	0.41 (0.11—1.49)	
3	(ref)	(ref)	(ref)	
4	20.29 (0.76—539.61)	0.51 (0.11—2.41)	2.67 (0.76—9.37)	
5	62.07 (0.17—22604.06)	0.26 (0.01—7.99)	6.71 (0.61—73.19)	

Appendix table 5: Stratification by obesity and wealth quintiles

Variables and variable categories	non obese WQ1	Non obese wq2	Non obese wq3	Non obese WQ4	Non obese WQ5	Obese WQ1 [‡]	Obese WQ2 [§]	Obese WQ3	Obese WQ4	Obese WQ5
Age										
<50	(ref)	(ref)	(ref)	(ref)	(ref)			1.45E-31 (.—.)	(ref)	(ref)
50-60	43.49 (1.51—1248.98)	4.57 (1.07—19.58)	0.8 (0.11—6.03)	2.63 (0.77—8.93)	0.85 (0.23—3.06)			5.54E-47 (.—.)	1.44 (0.07—30.58)	3.48 (0.5—24.14)
>60	12.11 (0.89—164.53)	4.43 (1.03—19.09)	0.42 (0.04—4.69)	3.82 (1.03—14.23)	2.18 (0.49—9.74)				1.91 (0.06—57.17)	2.65 (0.33—21.42)
sex										
Male	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(empty)	(ref)
Female	3.29 (0.44—24.85)	4.32 (0.64—28.94)	0.62 (0.03—13.88)	1.26 (0.32—4.93)	1.67 (0.45—6.18)			8.6E+107 (.—.)	(omitted)	1.9 (0.19—18.76)
site										
Karonga	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(empty)	(ref)
Lilongwe	12.72 (0.89—182.11)	3.95 (0.65—24.04)	2.64 (0.35—19.71)	2.49 (0.73—8.5)	0.53 (0.11—2.43)			2.6E+15 (.—.)	(omitted)	5.05 (0.13—202.03)
Marital status										
single	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
married	1.39 (0.29—6.64)	0.95 (0.28—3.28)	0.29 (0.04—2.15)	0.5 (0.14—1.7)	0.64 (0.14—2.9)			8.6E+107 (.—.)	0.53 (0.03—8.15)	0.14 (0.02—1.04)
Highest attained education										
0—5 years primary education	11.09 (1.5—82.05)	0.89 (0.28—2.81)	0.34 (0.02—4.67)	0.76 (0.15—3.75)	2.09 (0.21—21.31)			8.1E-78 (.—.)	0.26 (0.0—16.1)	0.3 (0.02—5.47)
standard 6-8	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
secondary	57.88 (1.61—2080.34)	1.4 (0.3—6.59)	1.42 (0.27—7.35)	0.71 (0.24—2.11)	2.24 (0.63—7.94)			(empty)	0.34 (0.01—8.42)	0.49 (0.07—3.34)
post-secondary	42.93 (0.52—3528.5)	(empty)	(empty)	1.37 (0.08—24.48)	1.35 (0.27—6.7)				(empty)	0.37 (0.06—2.51)

[‡] No observations

[§] No observations

occupation										
homemaker	0.8 (0.11—5.7)	0.61 (0.12—3.13)	21.78 (0.94—504.37)	0.79 (0.15—4.1)	5.97 (0.83—42.82)			4.7E+61 (.—.)	2.00 (0.04—100.23)	0.73 (0.0—155.92)
farming/fishing	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(empty)	(ref)
employed	2.15 (0.29—16.04)	1.43 (0.23—9.04)	13.15 (0.9—192.03)	0.66 (0.17—2.58)	1.33 (0.23—7.83)			1.5E+154 (.—.)	(omitted)	0.19 (0.0—34.71)
Indoor smoke										
No	(empty)	0.26 (0.02—3.55)	(empty)	(empty)	(empty)				(empty)	0.75 (0.04—15.21)
Yes, inside the house	(empty)	2.91 (0.27—30.92)	(empty)	3.89 (0.65—23.19)	0.12 (0.01—1.5)				(empty)	1.64 (0.18—15.18)
Yes, in a separate kitchen area	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
History of Smoke										
no	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
yes	0.29 (0.0—17.25)	3.07 (0.33—28.35)	0.12 (0.0—4.39)	0.94 (0.17—5.11)	0.26 (0.04—1.65)			4.1E+169 (.—.)	(empty)	0.54 (0.01—23.36)
Diabetes										
No	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
Yes	0.13 (0—16.29)	2.43 (0.29—20.13)	0.17 (0.0—9.5)	2.54 (0.54—12)	1.15 (0.19—7.16)			1.8E+46 (.—.)	0.07 (0.0—14.48)	1.15 (0.09—14.87)
Unknown	(empty)	(empty)	2.1E-08 (0.1—22.1)	7.2E+05 (0.0—.)	(empty)				(empty)	
Dyslipidaemia										
No	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
Yes	0.06 (0.0—4.64)	0.58 (0.07—4.84)	0.06 (0.0—1.92)	3.03 (0.53—17.14)	0.06 (0.0—1.19)			2.6E+07 (.—.)	0.31 (0.0—22.6)	0.93 (0.03—26.3)
missing data	(empty)	(empty)	7.7E+07 (0.0—.)	2.0E-06 (0.0—.)	0.18 (0.02—2.11)			(empty)	(empty)	0.48 (0—64.61)
HIV status										
Negative	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
Positive	0.08 (0.0—6.74)	1.15 (0.17—7.63)	0.12 (0.0—4.26)	1.94 (0.37—10.03)	1.41 (0.24—8.31)			1.45E-31 (.—.)	0.24 (0—22.56)	1.98 (0.14—27.98)
Unknown	2.1 (0.33—13.38)	1.66 (0.4—6.81)	1.33 (0.08—22.1)	2.04 (0.5—8.3)	1.63 (0.27—9.77)			1.45E-31 (.—.)	0.39 (0.02—7.7)	1.79 (0.23—13.66)

Hypertension										
No	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
Yes	0.11 (0.0—9.9)	0.7 (0.1—4.87)	0.03 (0.0—0.91)	0.85 (0.21—3.47)	0.6 (0.09—4.13)			1.81E+46 (.—.)	0.33 (0.01—19.43)	1.41 (0.14—14.27)
CVDRF										
2	0.03 (0.0—1.88)	0.8 (0.1—6.22)	0.0 (0.0—0.29)	1.59 (0.28—9.08)	1.29 (0.17—9.96)					
3	(ref)	(ref)	(ref)	(ref)	(ref)			(ref)	(ref)	(ref)
4	49.06 (0.47—5153.28)	1.87 (0.18—18.98)	2.7 (0.06—112.27)	0.92 (0.18—4.78)	16.97 (1.14—253.16)			1.81E+46 (.—.)	1.17 (0.0—154.19)	0.58 (0.02—18.29)
≥5	(empty)	(empty)	(empty)	(empty)	(empty)			(omitted)	6.75 (0.0—24323.16)	0.48 (0.0—105.76)

Appendix table 6: Stratification by highest attained education and obesity

Variables and variable categories	Non-obese & 0-5 years elementary education	Non-obese & 6-8 elementary education	Non obese & secondary education	Non-obese & post-secondary education**	Obese & 0-5 years elementary education ^{††}	Obese & 6-8 years elementary education	Obese & secondary education	Obese & post-secondary education ^{††§§}
Age								
<50	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
50-60	10.76 (1.45—79.81)	1.33 (0.57—3.15)	2.18 (0.66—7.22)	.	2.07e+19 (.—.)	2.96 (0.6—14.49)	12.52 (0.3—525.67)	1.14E-57 (.—.)
>60	5.85 (0.9—38)	1.65 (0.63—4.29)	6.74 (1.83—24.92)	.	264.2 (.—.)	3.12 (0.43—22.52)	5.03 (0.02—1686.17)	1.64E+56 (.—.)
Sex								
Male	(ref)	(ref)	(ref)	(ref)	(omitted)	(ref)	(ref)	(ref)
Female	7.38 (0.9—60.6)	2.73 (0.77—9.71)	1.28 (0.35—4.69)	.		0.47 (0.03—8.69)	0.84 (0.02—45.4)	4.96E+56 (.—.)
Site								
Karonga	(ref)	(ref)	(ref)	(empty)	(ref)	(ref)	(ref)	(ref)
Lilongwe	5.38 (0.91—31.62)	3.06 (1.12—8.35)	0.88 (0.26—3.04)	(omitted)	3.6E+22 (.—.)	2.01 (0.23—17.74)	1.06 (0.01—97.43)	3.8E+107 (.—.)
Wealth quintiles								
poorest	25.05 (1.9—330.22)	1.59 (0.42—6.0)	1.72 (0.23—12.74)	.	1.8E+21 (.—.)	0.3 (0.03—3.47)	(empty)	(empty)
second	7.82 (0.71—86.4)	3.3 (1.02—10.68)	1.56 (0.28—8.67)		3.1E+42 (.—.)	0.37 (0.03—4.01)	13.09 (0.03—5949.07)	(empty)
third	(ref)	(ref)	(ref)	(empty)	(ref)	(ref)	(ref)	(empty)
fourth	2.4 (0.15—37.21)	1.85 (0.64—5.37)	1.96 (0.49—7.89)	(empty)	3.9E-21 (.—.)	0.22 (0.02—2.3)	0.24 (0—38.03)	(empty)
wealthiest	2.09 (0.1—42.23)	0.84 (0.24—2.92)	3.39 (0.75—15.3)	(omitted)	7.8 (.—.)	0.44 (0.04—4.71)	11.69 (0.09—1444.24)	(omitted)
Marital status								

** Site, wealth quintiles and occupation omitted because of collinearity

†† Sex, occupation and history of smoking omitted because of collinearity

†† Wealth and occupation have no observations

§§ History of smoking and CVDRF omitted because of collinearity

single	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
married	1.11 (0.28—4.43)	1.32 (0.54—3.23)	0.31 (0.11—0.91)	0.0 (.—.)	4.6E-22 (.—.)	0.69 (0.11—4.38)	0.13 (0.01—2.61)	7.38E+17
occupation								
homemaker	2.51 (0.56—11.17)	1.66 (0.54—5.08)	0.69 (0.17—2.84)	0.0 (.—.)	4.0 e+19 (.—.)	2.78 (0.29—26.69)	0.3 (0.01—12.69)	1.04E+95 (.—.)
farming/fishing	(ref)	(ref)	(ref)	(empty)	(empty)	(ref)	(empty)	(empty)
employed	1.87 (0.27—12.76)	1.83 (0.67—4.99)	0.5 (0.12—2.03)	1 (omitted)	1 (omitted)	1.71 (0.15—19.93)	1 (omitted)	(omitted)
Indoor smoke								
No	0.96 (0.04—21.49)	(Empty)	(Empty)	(empty)	(empty)	(empty)	(empty)	4.62E+74 (.—.)
Yes, inside the house	1.93 (0.21—17.91)	1.88 (0.42—8.4)	0.11 (0.01—1.59)	(empty)		0.93 (0.05—18.44)	5.99 (0.04—988.69)	4.72E+94 (.—.)
Yes, in a separate kitchen area	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Smoking history								
no	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
yes	10.25 (0.96—109.45)	1.29 (0.29—5.66)	0.25 (0.05—1.3)	0.0 (.—.)	(empty)	0.35 (0.01—14.51)	9.43E+07 (0.0—.)	(empty)
Diabetes								
No	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Yes	1.06 (0.1—11.91)	0.88 (0.21—3.71)	1.28 (0.26—6.33)	0.0 (.—.)	1.2E-20 (.—.)	0.53 (0.05—5.5)	1.4e+07 (0.0—.)	2.0E+163 (.—.)
Unknown	(empty)	0.22 (0.01—5.99)	(empty)	(empty)		(empty)	(empty)	
Dyslipidaemia								
No	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Yes	1.05 (0.12—9.23)	0.43 (0.11—1.75)	2.43 (0.38—15.56)	0.0 (.—.)	1.4E+23 (.—.)	1 (0.05—21.22)	32.63 (0.17—6363.24)	1.5E-127 (.—.)
missing data	0.41 (0.02—7.53)	3.39 (0.18—65.18)	0.14 (0.01—2.05)	(empty)		(empty)	109.64 (0.06—205197.3)	(empty)
HIV status								
Negative	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Positive	0.85 (0.08—9.02)	0.6 (0.14—2.55)	2.5 (0.62—10.07)	.	5.5E+23 (.—.)	0.88 (0.05—17.25)	24.16 (0.59—992.53)	1.6E+105 (.—.)

Unknown	0.87 (0.15—5.16)	1.34 (0.52—3.45)	2.37 (0.6—9.4)	.	(empty)	0.75 (0.14—3.89)	157.01 (0.5—49479.48)	8.25E-77 (.—.)
Hypertension								
No	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Yes	1.58 (0.23—10.99)	0.51 (0.13—1.97)	0.68 (0.13—3.57)	0.0 (.—.)	4.4E-38 (.—.)	0.44 (0.04—5.13)	2.37 (0.06—95.27)	6.1E+132 (.—.)
CVDRF								
2	0.53 (0.05—5.26)	0.18 (0.04—0.8)	2.39 (0.45—12.74)	.				(ref)
3	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	2.43E+94 (.—.)
4	2.88 (0.28—29.86)	2.42 (0.57—10.31)	0.62 (0.1—3.8)	.	1.4E-22 (.—.)	0.99 (0.04—23.46)	27.92 (0.04—17774.42)	(omitted)
≥5		(empty)	21.02 (0.37—1193.6)	(empty)	4.4e-07 (.—.)	1.95 (0.01—423.84)	1.44 (0.0—2718.99)	1.14E-57 (.—.)