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Cardiovascular risk factors among people with drug-resistant tuberculosis in Uganda

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Abstract

Background Tuberculosis (TB) and its risk factors are independently associated with cardiovascular disease (CVD). We determined the prevalence and associations of CVD risk factors among people with drug-resistant tuberculosis (DRTB) in Uganda.

Methods In this cross-sectional study, we enrolled people with microbiologically confirmed DRTB at four treatment sites in Uganda between July to December 2021. The studied CVD risk factors were any history of cigarette smoking, diabetes mellitus (DM) hypertension, high body mass index (BMI), central obesity and dyslipidaemia. We used modified Poisson regression models with robust standard errors to determine factors independently associated with each of dyslipidaemia, hypertension, and central obesity.

Results Among 212 participants, 118 (55.7%) had HIV. Overall, 196 (92.5%, 95% confidence interval (CI) 88.0-95.3) had ≥ 1 CVD risk factor. The prevalence; 95% CI of individual CVD risk factors was: dyslipidaemia (62.5%; 55.4–69.1), hypertension (40.6%; 33.8–47.9), central obesity (39.3%; 32.9–46.1), smoking (36.3%; 30.1–43.1), high BMI (8.0%; 5.0–12.8) and DM (6.5%; 3.7–11.1). Dyslipidaemia was associated with an increase in glycated haemoglobin (adjusted prevalence ratio (aPR) 1.14, 95%CI 1.06–1.22). Hypertension was associated with rural residence (aPR 1.89, 95% CI 1.14–3.14) and previous history of smoking (aPR 0.46, 95% CI 0.21–0.98). Central obesity was associated with increasing age (aPR 1.02, 95%CI 1.00–1.03), and elevated diastolic blood pressure (aPR 1.03 95%CI 1.00–1.06).

Conclusion There is a high prevalence of CVD risk factors among people with DRTB in Uganda, of which dyslipidaemia is the commonest. We recommend integrated services for identification and management of CVD risk factors in DRTB.

Keywords Smoking, Diabetes, Hypertension, Lipids, TB, Cardiovascular, Cholesterol, Obesity, MDR TB

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Background

Africa is undergoing rapid urbanisation which is associated with lifestyles that increase the risk of cardiovascular disease (CVD) [1]. As such, there is an increase in CVD risk factors and consequently CVDs across Africa. Most African countries are unlikely to achieve tobacco control targets by 2025 and a rapid increase in smoking prevalence is projected to occur among men by 2025 [2]. Additionally, an increase in the mean blood pressures was observed between 1975 and 2015 [3]. Further, Africa has seen an explosive increase in the prevalence of high body mass indices. Between 1990 and 2015, there was a 330% increase in the prevalence of "overweight" in Southern Africa, 73% rise in Northern Africa, 70% in West Africa and 9% in East Africa [4]. Lastly, there was a rise in the burden of diabetes mellitus (DM) between 1980 and 2014 from 3.4 to 8.5% in men and 4.1–8.9% in women in Africa [5]. A modelling study projects an exponential increase in DM in Africa between 2017 and 2025 [6]. A recent systematic review reported a high prevalence of several CVD risk factors in sub-Saharan Africa (SSA): hypertension (30%), hyperlipidaemia (25%), physical inactivity (22%), obesity (up to 40% in women and 15% in men), smoking (10%), and DM (3.5%) [7].

At the same time, Africa contributes a quarter of the global tuberculosis (TB) cases [8]. A convergence of CVD and TB is evident in the region [9, 10]. TB independently increases the risk for ischemic stroke [11], acute coronary syndrome [12] and myocardial infarction [13]. Therefore, a high prevalence of CVD among people with TB could synergistically increase the risk of death from major adverse cardiovascular events in these people [14]. However, the prevalence of CVD risk factors is not well established particularly in drug resistant TB (DRTB); which already posts a high mortality rate of 21% in Africa [15]. A study from South Africa reported that 52% of people with DRTB had at least one CVD risk factor, of whom 23% had moderate or severe CVD risk [16]. There is need for more studies to characterise CVD risk factors in DRTB in Africa to inform the need for integrating CVD prevention interventions in TB programs.

Uganda is among the high-burden TB and TB/HIV countries which has enrolled almost 2000 people with DRTB care since the inception of programmatic management of DRTB in 2013 [17–19]. The incidence of rifampicin resistant TB has increased by 20% between 2014 and 2018 [20]. About 10% of premature deaths in Uganda are attributed to CVD and 56% of adults are estimated to have at least two CVD risk factors [21, 22]. In this study, we determined the prevalence of CVD risk factors, and factors associated with selected CVD risk factors among people with DRTB in Uganda.

Methods

Study design, population, and setting

This was a cross sectional study at four DRTB treatment centres in Uganda. We purposively selected a high volume DRTB treatment site from each of the four regions of Uganda due to the geographical variation of hypertension and DM in the country [23, 24]. Between July to December 2021, participants were enrolled from Mulago, Mbarara, Lira, and Mbale referral hospitals in central, western, northern, and eastern Uganda, respectively. Eligible participants were adults (age ≥ 18 years) with bacteriologically confirmed TB, and any form of drug resistance who were receiving treatment at these sites during the period of data collection. We consecutively enrolled participants during the clinic appointment days at the study sites. The programmatic management of DRTB in Uganda has been extensively described recently [19].

Data collection and study measurements

Trained research assistants administered a pretested questionnaire to eligible participants for socio-demographic characteristics, medical history, any history of cigarette smoking and alcohol use. Participants underwent anthropometric measurements of their weight, height and waist/hip ratio using a weighing scale (Seca 760®), stadiometer (Seca 213®) and tape measure respectively. The body mass index (BMI) was calculated using the formula; BMI = weight (kilograms)/height (in metres)^2. Using a battery powered digital blood pressure (BP) machine (Omron®, Hem 7120), the BP was taken on two separate occasions, 20 min apart, at the DRTB treatment centre. The average BP of the two measurements was considered as the participant's BP. A study nurse drew 4 millilitres (mls) of blood which was tested for random blood glucose (RBG), glycated haemoglobin (HbA1c), non-fasting lipid profile, and a complete blood count. The RBG was measured using a point of care glucometer (Accu-Chek®). The HbA1c and blood lipids (triglycerides, total cholesterol, low density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c)) were estimated using the Cobas® 6000 analyzer series (Roche Diagnostics, USA). HIV infection was confirmed using immunochromatographic tests according to the Uganda HIV testing guidelines [25].

Study outcomes

The main study outcome was the prevalence of CVD risk factors. The CVD risk factors of focus were any history of cigarette smoking, DM (HbA1c ≥ 6.5% and/or RBS ≥ 11.1 mmol/l with symptoms and/or use of anti-hyperglycaemic agents) [26], Hypertension (systolic ≥ 140 mmHg and/or diastolic ≥ 90 mmHg and/or use of anti-hypertension medication) [27], central obesity (waist circumference of ≥ 102/88 cm and/or a waist-hip ratio of ≥ 0.90/0.85

in males/females) [27], high BMI (BMI≥25 kg/meters^2), and dyslipidaemia (total cholesterol of >5.0 mmol/l [28] and/or LDL-c of >4.14 mmol/l [29], and/or triglyceride level of ≥1.7 mmol/l, and/or HDL-c of <1.03 mmol/l for men and <1.29 mmol/l for women [30]).

Sample size estimation and statistical analysis

There were approximately 520 people receiving DRTB treatment in 2021. A sample size of 221 would be adequate to determine the prevalence of CVD risk factors, assuming a prevalence of 52.3% of any CVD risk factor and a 95% confidence interval (CI) [16, 31]. We, however, conducted a census of all people with DRTB at the study sites. Data were entered in EpiData 4.4.0 and exported to Stata 16.0 for analysis. Continuous variables were presented as medians with the corresponding interquartile ranges (IQR). Categorical data were presented as proportions. The prevalence of CVD risk factors was calculated as the proportion of people with a given risk factor to the total number of people with DRTB. The corresponding 95% confidence intervals (CI) were also estimated. We used modified Poisson regression models with robust standard errors to determine factors independently associated with each of dyslipidaemia, hypertension, and central obesity. The few counts for DM and high BMI precluded us from performing analyses for factors associated with these risk factors. For all models, we included age, sex, HIV status, residence, BP, blood lipids, HbA1c, alcohol use, smoking, BMI, waist-hip ratio, waist circumference except when the CVD risk factor is measured using one of these variables.

Results

Characteristics of study participants

We enrolled 212 participants of whom 156 (73.6%) were male and 118 (55.7%) had HIV co-infection. The median (IQR) age was 37 (30–46) years (n=211). The median (IQR) BMI was 19.7 (17.7–22.2) Kg/m^2 (n=199) while the systolic and diastolic BPs were 124.0 (116.0–133.5) mmHg and 85.3 (76.5–93.0) mmHg, respectively. The median (IQR) RBG was 4.6 (4.0–5.7) mmol/l while the HbA1c was 4.7% (3.9–5.2). Regarding the blood lipids, the median (IQR) values were as follows: total cholesterol (3.4 [2.7–4.2] mmol/l), LDL-c (1.7 [1.2–2.2] mmol/l), HDL-c (1.2 [0.9–1.7] mmol/l) and triglycerides (1.2 [0.87–1.62] mmol/l). Overall, 77 (78.6%) reported a family history of CVD (including pre-mature CVD death). Table 1 shows the characteristics of the study participants.

Prevalence and distribution of CVD risk factors

Overall, 196 (92.5%, 95% CI: 88.0–95.3) participants had≥1 CVD risk factor. The median (IQR) number of CVD risk factors was 2 (1–2) per participant. Overall, 64 (32.7%) had one CVD risk factor, 87 (44.4%) had two, 36 (18.4%) had three and 9 (4.6%) had≥4. The prevalence; 95% CI of CVD risk factors was: dyslipidaemia (62.5%; 55.4–69.1), hypertension (40.6%; 33.8–47.9), central obesity (39.3%; 32.9–46.1), smoking (36.3%; 30.1–43.1), high BMI (8.0%; 5.0–12.8) and DM (6.5%; 3.7–11.1). The prevalence of the individual CVD risk factors is summarised in Table 2.

Prevalence of CVD risk factors in DRTB by region of Uganda

Table 3 shows the prevalence of CVD risk factors among people with DRTB by region in Uganda. Northern Uganda posted the highest prevalence of hypertension (49.0% [95% CI 36.7–61.8], p=0.003), while Eastern Uganda had the highest prevalence of dyslipidaemia (92.0% [95% CI 71.5–98.1], p=0.003). The prevalence of central obesity was highest in Western Uganda (63.2% [95% CI 38.7–82.3], p=0.052), although the difference across the regions was not statistically significant.

Factors associated with CVD risk factors among people with DRTB in Uganda

Tables 4, 5 and 6 show factors associated with individual CVD risk factors. Dyslipidaemia was associated with an increase in glycated haemoglobin (adjusted prevalence ratio (aPR) 1.14, 95%CI 1.06–1.22, p=0.001). Hypertension was associated with rural residence (aPR 1.89, 95% CI 1.14–3.14, p=0.014) and previous history of smoking (aPR 0.46, 95% CI 0.21–0.98, p=0.045). Central obesity was associated with increasing age (aPR 1.02, 95%CI 1.00–1.03, p=0.040), and elevated diastolic BP (aPR 1.03, 95%CI 1.00–1.06, p=0.043).

Discussion

People with TB have a 51% higher risk of major adverse cardiovascular events [14]. In this multi-center study in Uganda, we determined the prevalence of CVD risk factors and associations of the individual risk factors among people with DRTB. We found that 9 in 10 people with DRTB have at least one CVD risk factor. Dyslipidaemia was the most prevalent (>60%) while hypertension and central obesity were observed in approximately 40% of people. Smoking history was found in more than one-third of the participants. High BMI and DM were the least prevalent and were found in <10%. The prevalence of the CVD risk factors in our study is higher than what is reported in the general population for hypertension (26.4%) [32], central obesity (11.8%) [33], cigarette smoking (9%) [34], and DM (1.4%). However it is lower than what is reported in the general population for high BMI (22.4%) [32] and dyslipidaemia (32–71%) [35, 36]. A high prevalence of CVD risk factors among people with TB is concerning because of their potential to worsen TB treatment outcomes and all-cause mortality even after TB

Table 1 Characteristics of study participants

Characteristic	Frequency (n = 212)	Percentage
DRTB treatment site		
Lira Regional Referral Hospital (Northern region)	85	40.1
Mulago National Referral Hospital (Central region)	83	39.1
Mbale Regional Referral Hospital (Eastern region)	25	11.8
Mbarara Regional Referral Hospital (Western region)	19	9.0
Rural residence	128	60.4
Married	112	52.8
Education (n = 211)		
None	18	8.5
Primary-level education	122	57.8
Secondary-level education	55	26.1
Tertiary-level education	16	7.6
Employment status		
Peasant farmer	92	43.4
Self employed	48	22.6
Unemployed	38	17.9
Formal employment	34	16.0
Family history of cardiovascular disease (n=98)		
Hypertension	55	56.1
Diabetes mellitus	25	25.5
Obesity (n = 97)	8	8.3
Heart failure (n=97)	8	8.3
Kidney disease	7	7.1
Stroke	6	6.1
Premature CVD death in first degree relative**	5	5.1
Any history of alcohol use	148	69.8
Type of DRTB at Baseline (n = 210)		
Rifampicin resistance/multidrug resistant	204	96.2
Pre- XDRTB	3	1.43
Poly resistant tuberculosis	1	0.5
XDR-TB	1	0.5
Mono-resistance	1	0.5
Previous TB episode (n = 210)	112	53.3
Mycobacterial load at treatment initiation* (n = 170)		
High	52	30.6
Medium	35	20.6
Low	28	16.5
Very low	55	32.4
Drugs in the treatment regimen (n = 209)		
Levofloxacin	200	95.7
Cycloserine	197	94.3
Clofazimine	197	94.3
Linezolid	165	79.0
Bedaquiline	157	75.1
Pyrazinamide	39	18.7
Ethionamide	10	4.8
Delamanid	8	3.8
Ethambutol	6	2.9
Moxifloxacin	2	1.0
Amikacin	1	0.5
Time from diagnosis to treatment (days), median (IQR), n= 202	8 (5 – 14)	

*Determined by cycle threshold values of the MTB Xpert/Rif assay. ** (age <55 for male and <65 for female relatives). Abbreviations: DRTB – drug resistant tuberculosis, CVD – cardiovascular disease, XDRTB – extensively drug resistant tuberculosis (defined as resistance to rifampicin, isoniazid, a fluoroquinolone and an injectable aminoglycoside)

Table 2 The prevalence of the CVD risk factors in DRTB

CVD risk factor in DRTB	Number with CVD risk factor	Prevalence (95% confidence interval) (%)
Hypertension (n = 187)[a]	76	40.6 (33.8 – 47.9)
Central obesity (n = 211)	83	39.3 (32.9 – 46.1)
History of smoking (n = 212)**	77	36.3 (30.1 – 43.1)
Dyslipidaemia (n = 192)	120	62.5 (55.4 – 69.1)
High total cholesterol (n = 162)	24	14.8 (10.1 – 21.2)
High LDL-c	25	13.0 (8.9 – 18.6)
Low HDL-c	76	39.6 (32.9 – 46.7)
High triglycerides (n = 190)	41	21.6 (16.3 – 28.0)
High BMI* (n = 199)	16	8.0 (5.0 – 12.8)
Diabetes mellitus (n = 186)[b]	12	6.5 (3.7 – 11.1)

*8 (4.0%) had BMI of ≥ 30 kg/m^2, **9 (4.3%) were current smokers, [a]only 4 were known to have hypertension, [b]only 3 had known diabetes, another 16 (8.7%) had HbA1c ≥5.6% (pre-diabetes). Abbreviations: LDL-c – low density lipoprotein cholesterol, HDL-c – high density lipoprotein cholesterol, CVD – cardiovascular disease, DRTB – drug resistant tuberculosis, BP – blood pressure, BMI – body mass index

Table 3 The prevalence of the CVD risk factors in DRTB

CVD risk factor in DRTB	Number with CVD risk factor (%)	p-value*	Prevalence (95% CI)
At least one CVD risk factor	**196 (100.0)**	**0.839**	**92.5 (88.0 – 95.3)**
Central	76 (38.8)		91.6 (83.2 – 96.0)
Eastern	24 (12.2)		96.0 (74.5 – 99.5)
Western	17 (8.7)		89.5 (63.9 -97.6)
Northern	79 (40.3)		92.9 (85.0 – 96.8)
Hypertension (n = 187)	**76 (100.0)**	**0.003**	**40.6 (33.8 – 47.9)**
Central	39 (51.3)		47.0 (36.4 – 57.9)
Eastern	4 (5.3)		16.0 (63.0 – 94.2)
Western	3 (4.0)		16.7 (5.0 – 43.2)
Northern	30 (39.5)		49.0 (36.7 – 61.8)
Central obesity (n = 211)	**83 (100.0)**	**0.052**	**39.3 (32.9 – 46.1)**
Central	35 (42.2)		42.2 (31.9 – 53.2)
Eastern	6 (7.2)		24.0 (10.7 – 45.4)
Western	12 (14.5)		63.2 (38.7 – 82.3)
Northern	30 (36.1)		35.7 (26.1 – 46.6)
History of smoking (n = 212)	**77 (100.0)**	**0.145**	**36.3 (30.1 – 43.1)**
Central	26 (33.8)		31.3 (22.2 – 42.2)
Eastern	9 (11.7)		36.0 (19.2 – 57.1)
Western	4 (5.2)		21.1 (7.6 – 46.5)
Northern	38 (49.4)		44.7 (34.4 – 55.5)
Dyslipidaemia (n = 192)	**120 (100.0)**	**0.003**	**62.5 (55.4 – 69.1)**
Central	39 (32.5)		51.3 (40.0 – 62.5)
Eastern	23 (19.2)		92.0 (71.5 – 98.1)
Western	11 (9.2)		57.9 (34.1 – 78.5)
Northern	47 (39.2)		65.3 (53.4 – 75.5)
High BMI (n = 199)	**16 (100.0**)	**0.588**	**8.0 (5.0 – 12.8)**
Central	8 (50.0)		9.8 (4.9 – 18.5)
Eastern	3 (18.8)		12.0 (3.7 – 32.7)
Western	1 (6.3)		6.3 (0.7 – 37.6)
Northern	4 (25.0)		5.3 (2.0 – 13.4)
Diabetes mellitus (n = 186)	**12 (100.0)**	**0.150**	**6.5 (3.7 – 11.1)**
Central	2 (16.7)		2.5 (0.6 – 9.5)
Eastern	2 (16.7)		8.0 (1.9 – 28.5)
Western	1 (8.3)		5.9 (0.7 – 35.7)
Northern	7 (58.3)		11.1 (5.3 – 21.8)

*p-value compares the prevalence by regions, Abbreviations: BMI – body mass index, CI – confidence interval, CVD – cardiovascular disease

cure [37]. Our findings, therefore, call for the integration of CVD risk reduction strategies in TB care in Uganda and similar TB high-burden settings. Certain regions posted a higher prevalence of CVD than others. That is, dyslipidaemia was highest in Eastern Uganda, smoking was highest in northern Uganda while high BMI was highest in Western Uganda. This calls for region-specific interventions to reduce CVD among people with DRTB in these settings.

Hypertension in TB has received little attention in literature. However, the prevalence of hypertension is on the rise in SSA [3]. A recent study from Guinea-Bissau has shown that hypertension is associated with poor TB treatment outcomes and a 64% higher risk of death after TB cure [38]. Therefore, BP control is likely to improve TB outcomes and reduce post-TB mortality. This is particularly important in Uganda where only 8% of people with hypertension are aware of their condition [32]. Similar to our findings, a review by Seegert and colleagues reported the prevalence of hypertension of up to 38.3% among people with TB (without DM) [39]. It is unclear why we observed a high prevalence of hypertension. However, inflammation due to chronic infection increases expression of endothelial adhesion molecules, oxidative stress, immune cell activation and infiltration in the kidney and blood vessels that result in vascular resistance and kidney remodelling [40].

Although smoking is an established risk factor for over 30 CVDs, smoking cessation programs are not integrated in TB care [41, 42]. At the same time, smoking adversely affects TB outcomes [43]. Short health workers' training can increase confidence of health workers to elicit smoking history from people with TB and offer smoking cessation support [44]. This might result in BP reduction as suggested by the association between smoking cessation and a lower risk of hypertension in our study. The high prevalence of smoking in TB is likely because smoking increases one's risk for TB. Nicotine in tobacco attenuates innate immune responses against TB by decreasing expression of toll-like receptors and production of cytokines (IL – 6 and 8 and TNFα) and chemokines by lung epithelial cells, macrophages and type 2 pneumocytes

Table 4 Factors associated with hypertension among people with DRTB in Uganda

Variable	Crude prevalence ratio (PR) (95%CI)	p-value	Adjusted PR (95%CI)	p-value
Age	1.00 (0.99 – 1.02)	0.718	1.01 (0.99 – 1.04)	0.197
Sex				
Male	Reference		Reference	
Female	1.10 (0.76 – 1.59)	0.626	0.85 (0.51 – 1.43)	0.550
Residence				
Urban	Reference		Reference	
Rural	1.39 (0.96 – 2.01)	0.084	1.89 (1.14 – 3.14)	0.014
Alcohol use				
Never used alcohol	Reference		Reference	
Former user (≤6 months)	0.84 (0.57 – 1.22)	0.356	1.19 (0.73 – 1.93)	0.485
Current user (>6 months)	0.70 (0.43 – 1.13)	0.147	0.86 (0.44 – 1.66)	0.647
Smoking history				
Never smoked	Reference		Reference	
Former smoker (≤6 months)	0.62 (0.40 – 0.97)	0.036	0.46 (0.21 – 0.98)	0.045
Current smoker (>6 months)	0.53 (0.16 – 1.79)	0.308	0.54 (0.10 – 2.96)	0.477
HIV status				
Positive	Reference		Reference	
Negative	0.84 (0.58 – 1.20)	0.325	1.29 (0.76 – 2.18)	0.338
Total cholesterol	0.98 (0.87 – 1.10)	0.701	1.06 (0.84 – 1.34)	0.607
LDL-c	0.99 (0.86 – 1.13)	0.839	0.79 (0.56 – 1.12)	0.183
HDL-c	0.90 (0.68 – 1.20)	0.469	0.91 (0.52 – 1.57)	0.732
Triglycerides	1.14 (0.89 – 1.45)	0.296	0.93 (0.69 – 1.27)	0.661
Body mass index	0.99 (0.96 – 1.03)	0.736	0.99 (0.95 – 1.04)	0.743
Glycated haemoglobin	0.99 (0.82 – 1.19)	0.876	0.73 (0.51 – 1.05)	0.089
Random blood sugar	1.03 (0.95 – 1.12)	0.427	1.04 (0.96 – 1.13)	0.342
Waist-Hip ratio	0.71 (0.10 – 5.06)	0.731	0.08 (0.002 – 2.25)	0.138
Waist Circumference	1.01 (0.99 – 1.02)	0.295	1.03 (1.00 – 1.06)	0.061

Abbreviations: LDL-c – low density lipoprotein cholesterol, HDL-c – high density lipoprotein cholesterol

Table 5 Factors associated with dyslipidaemia among people with DRTB in Uganda

Variable	Crude prevalence ratio (PR) (95%CI)	p-value	Adjusted PR (95%CI)	p-value
Age	1.00 (0.99 – 1.01)	0.841	1.00 (0.99 – 1.01)	0.921
Sex				
Male	Reference		Reference	
Female	1.27 (1.02 – 1.57)	0.032	1.14 (0.86 – 1.51)	0.361
Residence				
Urban	Reference		Reference	
Rural	1.12 (0.89 – 1.42)	0.318	1.13 (0.87 – 1.46)	0.355
Alcohol use				
Never used alcohol	Reference		Reference	
Former user (≤6 months)	0.85 (0.68 – 1.08)	0.181	0.96 (0.73 – 1.26)	0.757
Current user (>6 months)	0.74 (0.54 – 1.01)	0.060	0.88 (0.59 – 1.30)	0.519
Smoking history				
Never smoked	Reference		Reference	
Former smoker (≤6 months)	0.79 (0.60 – 1.03)	0.078	0.95 (0.68 – 1.32)	0.769
Current smoker (>6 months)	1.17 (0.80 – 1.69)	0.417	1.41 (0.69 – 2.93)	0.346
HIV status				
Positive	Reference		Reference	
Negative	0.98 (0.78 – 1.220	0.823	0.95 (0.75 – 1.20)	0.643
Body mass index	0.99 (0.97 – 1.02)	0.497	0.99 (0.96 – 1.02)	0.412
Glycated haemoglobin	1.10 (1.00 – 1.20)	0.052	1.14 (1.06 – 1.22)	0.001
Random blood sugar	1.02 (0.99 – 1.05)	0.123	1.02 (0.98 – 1.06)	0.332
Waist-Hip ratio	0.43 (0.21 – 0.88)	0.021	0.30 (0.07 – 1.29)	0.106
Waist circumference	1.00 (0.99 – 1.01)	0.806	1.01 (0.99 – 1.02)	0.368
Systolic blood pressure	0.99 (0.98 – 1.00)	0.072	1.00 (0.98 – 1.01)	0.490
Diastolic blood pressure	0.99 (0.99 – 1.00)	0.207	1.00 (0.98 – 1.01)	0.855

[45, 46]. Kirenga and colleagues reported a lower prevalence of smoking of 26% among people with drug sensitive TB in Uganda compared to our study [47]. In comparison, Whitehouse and colleagues reported a prevalence of 31% in DRTB, similar to our study [16]. It is likely that people with DRTB have higher smoking rates than drug sensitive TB [48].

It was interesting to observe a disconnect in the prevalence of obesity as measured by the BMI (4.0%) and waist-hip ratio/waist circumference (39.3%) in our study. In fact, undernutrition, as measured by the BMI is very prevalent among people with DRTB in Uganda [49]. However, similar to our findings, central obesity was prevalent in 33% of people with TB and it correlated with DM better than the BMI in a study from the Philippines [50]. A similar disconnect was observed between

Table 6 Factors associated with central obesity among people with DRTB in Uganda

Variable	Crude prevalence ratio (PR) (95%CI)	p-value	Adjusted PR (95%CI)	p-value
Age	1.02 (1.01 – 1.03)	<0.001	1.02 (1.00 – 1.03)	0.040
Sex				
Male	Reference		Reference	
Female	1.06 (0.73 – 1.54)	0.755	1.54 (0.95 – 2.51)	0.079
Residence				
Urban	Reference		Reference	
Rural	0.95 (0.68 – 1.34)	0.738	0.94 (0.63 – 1.42)	0.786
Alcohol use				
Never used alcohol	Reference		Reference	
Former user (≤6 months)	1.17 (0.79 – 1.73)	0.428	0.89 (0.54 – 1.47)	0.625
Current user (>6 months)	0.87 (0.52 – 1.45)	0.597	0.83 (0.44 – 1.57)	0.573
Smoking history				
Never smoked	Reference		Reference	
Former smoker (≤6 months)	1.16 (0.82 – 1.64)	0.401	1.34 (0.79 – 2.26)	0.278
Current smoker (>6 months)	0.58 (0.17 – 2.03)	0.397	0.91 (0.25 – 3.33)	0.888
HIV status				
Positive	Reference		Reference	
Negative	0.95 (0.68 – 1.34)	0.738	1.00 (0.67 – 1.50)	0.997
Total cholesterol	0.91 (0.80 – 1.03)	0.122	0.89 (0.75 – 1.05)	0.169
LDL-c	0.90 (0.77 – 1.05)	0.186	0.85 (0.69 – 1.04)	0.120
HDL-c	0.87 (0.67 – 1.13)	0.308	1.18 (0.78 – 1.80)	0.425
Triglycerides	1.23 (0.997 – 1.51)	0.053	1.08 (0.81 – 1.44)	0.591
Body mass index	1.02 (0.995 – 1.05)	0.108	1.02 (1.00 – 1.05)	0.234
Glycated haemoglobin	0.99 (0.87 – 1.12)	0.841	0.99 (0.81 – 1.22)	0.957
Random blood sugar	1.06 (1.02 – 1.10)	0.001	1.04 (0.99 – 1.09)	0.112
Systolic blood pressure	1.00 (0.99 – 1.02)	0.407	0.98 (0.96 – 1.01)	0.167
Diastolic blood pressure	1.01 (0.998 – 1.02)	0.096	1.03 (1.00 – 1.06)	0.043

Abbreviations: LDL-c – low density lipoprotein cholesterol, HDL-c – high density lipoprotein cholesterol

the prevalence of obesity by the BMI (3.4%) and waist circumference (13.7%) in Bangladesh [51]. If follows that those measures of central obesity may be better predictors of CVD among people with TB than the BMI, as has been reported in the general population [52]. In support of this, our results showed an association between central obesity with hypertension and increasing age which are predictors of cardiovascular events. Conversely, the BMI was not associated with any of the other CVD risk factors.

Very few studies have evaluated lipid abnormalities among people with TB in Africa. Similar to our study, Lawson and colleagues found that 29% and 50% of people with TB had elevated LDL-c and low HDL-c, respectively, in Nigeria [53]. The effect of high lipids on CVD risk and TB outcomes in people with TB is unclear. However, high lipid levels might favour entry and survival of *Mycobacterium tuberculosis* in the macrophage [54]. Conversely, statins reduce the risk of active TB and this may be by lowering cholesterol; an essential molecule for internalisation of *M. tuberculosis* in host immune cells [55]. Randomised controlled trials are needed to determine the role of statins in CVD prevention in people with active TB and TB survivors. This might be particularly important among people with TB and DM since an association between HbA1c and dyslipidaemia was evident in our study.

The prevalence of DM observed in our study (6.5%) is similar to that reported among people with DRTB in South Africa (5.2%) [16] but lower than the estimated prevalence of DM in TB in Africa (9.0%) [56]. Higher estimates of DM in TB could be due to transient hyperglycaemia that tends to resolve with TB treatment [57]. Our study population was well established on treatment (a median of 8 months into therapy). Our estimate is therefore likely to be reliable. Screening for DM among people with DRTB should be prioritised because DM is a known risk factor for DRTB and predicts TB treatment failure, relapse and death [58, 59].

Our study has some limitations. We did not evaluate the prevalence of physical inactivity among people with DRTB. However, exercise intolerance due to respiratory symptoms would affect assessing this CVD risk factor. We also did not evaluate for hazardous alcohol use to better characterise the effect of alcohol on other CVD risk factors. Nonetheless, estimating the prevalence of hazardous alcohol use is difficult in Africa. This is because the types of alcoholic drinks are varied (often home brewed) and difficult to quantify; while the most common pattern of alcohol consumption is heavy episodic use [60]. Similarly, we did not quantify cigarette smoking, by say the number of pack years. It is, however, important to note that former smokers and people who use as low as one cigarette a day have elevated CVD risk than never smokers [61, 62]. Therefore, using any history of smoking is justified. Lastly, we did not have a control group (people without TB) to compare the prevalence of CVD risk factors. We, however, have compared

our findings with the reported prevalence in the general Ugandan population.

Conclusion

We found a very high prevalence of CVD risk factors among people with DRTB. Dyslipidaemia, hypertension, and smoking were the most prevalent. The prevalence of DM and central obesity were also higher than the estimates in the Ugandan population. There is an urgent need to integrate cost-effective screening strategies for CVD risk factors in DRTB care.

Abbreviations

CVD	Cardiovascular disease
BP	Blood pressure
LDL-c	Low density lipoprotein cholesterol
HDL-c	High density lipoprotein cholesterol
RBG	Random blood glucose
DM	Diabetes mellitus
HbA1c	Glycated haemoglobin
BMI	Body mass index
TB	Tuberculosis
DRTB	Drug resistant tuberculosis
CI	Confidence interval
IQR	Interquartile range
PR	Prevalence ratio

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Author contribution

JBB – conceptualisation, formal analysis, methodology, drafting manuscript, revising manuscript, final approval. MN – formal analysis, methodology, revising manuscript, final approval. JN – methodology, revising manuscript, final approval. WM – methodology, revising manuscript, final approval. WS– methodology, revising manuscript, final approval.IM- methodology, revising manuscript, final approval. LN- methodology, revising manuscript, final approval. RO - methodology, revising manuscript, final approval. FB - methodology, revising manuscript, final approval. IAB - methodology, revising manuscript, final approval. WW - methodology, revising manuscript, final approval.

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Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics committee and consent to participate

All study procedures were conducted in accordance with the Declaration of Helsinki. The study was approved by the Mulago Hospital Research and Ethics Committee (MHREC-2020-23), and the Uganda National Council of Science and Technology (HS1521ES) prior to participant recruitment. Study participants provided written informed consent before study procedures were performed. For participants who couldn't read the consent form, the document was orally presented to them or their legally authorized representative, in the presence of an independent witness.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Bakilo EL, Nkarnkwin DS, Womba L, Atheno V, Kika M, Booto J, et al. Lifestyle and Cardiovascular Risk Factors: Urban Population versus Rural Population in Sub-Saharan Africa [Internet]. Lifestyle and Epidemiology - The Double Burden of Poverty and Cardiovascular Diseases in African Populations. IntechOpen; 2021 [cited 2022 May 15]. Available from: https://www.intechopen.com/chapters/75886.
2. Bilano V, Gilmour S, Moffiet T, d'Espaignet ET, Stevens GA, Commar A, et al. Global trends and projections for tobacco use, 1990–2025: an analysis of smoking indicators from the WHO Comprehensive Information Systems for Tobacco Control. The Lancet. 2015 Mar;14(9972):966–76.
3. Zhou B, Bentham J, Cesare MD, Bixby H, Danaei G, Cowan MJ, et al. Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. The Lancet. 2017 Jan;7(10064):37–55.
4. Agyemang C, Boatemaa S, Frempong GA, Aikins A. Obesity in sub-Saharan Africa. Metab Syndr Switz Springer Int Publ. 2016;1–13.
5. NCD Risk Factor Collaboration (NCD-RisC) – Africa Working Group. Trends in obesity and diabetes across Africa from 1980 to 2014: an analysis of pooled population-based studies. Int J Epidemiol. 2017 Oct 1;46(5):1421–32.
6. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020 Sep;8(1):14790.
7. Yuyun MF, Sliwa K, Kengne AP, Mocumbi AO, Bukhman G. Cardiovascular Diseases in Sub-Saharan Africa Compared to High-Income Countries: An Epidemiological Perspective. Glob Heart. 2020;15(1).
8. World Health Organisation. Global tuberculosis report 2021. Geneva: World Health Organization; 2021.
9. Remais JV, Zeng G, Li G, Tian L, Engelgau MM. Convergence of non-communicable and infectious diseases in low- and middle-income countries. Int J Epidemiol. 2013 Feb;1(1):221–7.
10. Wong EB, Olivier S, Gunda R, Koole O, Surujdeen A, Gareta D, et al. Convergence of infectious and non-communicable disease epidemics in rural South Africa: a cross-sectional, population-based multimorbidity study. Lancet Glob Health. 2021 Jul 1;9(7):e967–76.
11. Sheu JJ, Chiou HY, Kang JH, Chen YH, Lin HC. Tuberculosis and the risk of ischemic stroke: a 3-year follow-up study. Stroke. 2010 Feb;41(2):244–9.
12. Chung WS, Lin CL, Hung CT, Chu YH, Sung FC, Kao CH, et al. Tuberculosis increases the subsequent risk of acute coronary syndrome: a nationwide population-based cohort study. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2014 Jan;18(1):79–83.
13. Huaman MA, Kryscio RJ, Fichtenbaum CJ, Henson D, Salt E, Sterling TR, et al. Tuberculosis and risk of acute myocardial infarction: a propensity score-matched analysis. Epidemiol Infect. 2017;145(7):1363–7.
14. Basham CA, Smith SJ, Romanowski K, Johnston JC. Cardiovascular morbidity and mortality among persons diagnosed with tuberculosis: A systematic review and meta-analysis. PLoS ONE. 2020 Jul;10(7):e0235821.
15. Ismail N, Ismail F, Omar SV, Blows L, Gardee Y, Koornhof H, et al. Drug resistant tuberculosis in Africa: Current status, gaps and opportunities. Afr J Lab Med [Internet]. 2018 Dec 6 [cited 2020 Jan 17];7(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6295755/.
16. Whitehouse ER, Perrin N, Levitt N, Hill M, Farley JE. Cardiovascular risk prevalence in South Africans with drug-resistant tuberculosis: a cross-sectional study. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2019;01(5):587–93.
17. World Health Organisation. WHO global lists of high burden countries for tuberculosis (TB), TB/HIV and multidrug/rifampicin-resistant TB (MDR/RR-TB), 2021–2025. Geneva, Switzerland; 2021 Jun.
18. Ministry of Health. Uganda National TB and Leprosy Annual Report 2020/2021. Kampala, Uganda: Ministry of Health; 2021 Nov.
19. Baluku JB, Nakazibwe B, Naloka J, Nabwana M, Mwanja S, Mulwana R, et al. Treatment outcomes of drug resistant tuberculosis patients with multiple poor prognostic indicators in Uganda: A countrywide 5-year retrospective study. J Clin Tuberc Mycobact Dis. 2021 May 1;23:100221.

20. Bahizi G, Majwala RK, Kisaka S, Nyombi A, Musisi K, Kwesiga B, et al. Epidemiological profile of patients with rifampicin-resistant tuberculosis: an analysis of the Uganda National Tuberculosis Reference Laboratory Surveillance Data, 2014–2018. Antimicrob Resist Infect Control. 2021 May;8(1):76.
21. Wesonga R, Guwatudde D, Bahendeka SK, Mutungi G, Nabugoomu F, Muwonge J. Burden of cumulative risk factors associated with non-communicable diseases among adults in Uganda: evidence from a national baseline survey. Int J Equity Health. 2016 Dec 1;15(1):195.
22. Omagino J, Okello E, Fourie JM, Scholtz W, Nel G. PASCAR and WHF Cardiovascular Diseases Scorecard project. Cardiovasc J Afr. 2020;31(4):s42–8.
23. Lunyera J, Kirenga B, Stanifer JW, Kasozi S, van der Molen T, Katagira W, et al. Geographic differences in the prevalence of hypertension in Uganda: Results of a national epidemiological study. PLoS ONE [Internet]. 2018 Aug 1 [cited 2020 Mar 13];13(8). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6070243/.
24. Bahendeka S, Wesonga R, Mutungi G, Muwonge J, Neema S, Guwatudde D. Prevalence and correlates of diabetes mellitus in Uganda: a population-based national survey. Trop Med Int Health TM IH. 2016 Mar;21(3):405–16.
25. Ministry of Health. National HIV Testing Services Policy and Implementation Guidelines. Ministry of Health of Uganda; 2016.
26. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2019. Diabetes Care. 2019;42(Supplement 1):S13–28.
27. Uganda Ministry of Health. Uganda clinical guidelines 2016. 2010.
28. World Health Organization. WHO STEPS surveillance manual: the WHO STEPwise approach to chronic disease risk factor surveillance. World Health Organization; 2005. p. 9241593830. Report No.
29. World Health Organization. Prevention of Cardiovascular Disease. Pocket Guidelines for Assessment and Management of Cardiovascular Risk. Africa: Who/Ish Cardiovascular Risk Prediction Charts for the African Region. World Health Organization; 2007.
30. Pasternak RC. 2001 National Cholesterol Education Program (NCEP) Guidelines on the Detection, Evaluation and Treatment of Elevated Cholesterol in Adults: Adult Treatment Panel III (ATP III). ACC Curr J Rev. 2002;4(11):37–45.
31. Sullivan KM, Dean A, Soe MM. On academics: OpenEpi: a web-based epidemiologic and statistical calculator for public health. Public Health Rep. 2009;124(3):471–4.
32. Guwatudde D, Mutungi G, Wesonga R, Kajjura R, Kasule H, Muwonge J, et al. The epidemiology of hypertension in Uganda: findings from the national non-communicable diseases risk factor survey. PLoS ONE. 2015;10(9):e0138991.
33. Kabwama SN, Kirunda B, Mutungi G, Wesonga R, Bahendeka SK, Guwatudde D. Prevalence and correlates of abdominal obesity among adults in Uganda: findings from a national cross-sectional, population based survey 2014. BMC Obes. 2018 Dec 3;5(1):40.
34. Kabwama SN, Ndyanabangi S, Mutungi G, Wesonga R, Bahendeka SK, Guwatudde D. Tobacco use and associated factors among Adults in Uganda: Findings from a nationwide survey. Tob Induc Dis [Internet]. 2016 Aug 11 [cited 2022 May 24];14(August). Available from: http://www.tobaccoinduced-diseases.org/Tobacco-use-and-associated-factors-among-Adults-in-Uganda-Findings-from-a-nationwide,67247,0,2.html.
35. Kavishe B, Vanobberghen F, Katende D, Kapiga S, Munderi P, Baisley K, et al. Dyslipidemias and cardiovascular risk scores in urban and rural populations in north-western Tanzania and southern Uganda. PLoS ONE. 2019 Dec;6(12):e0223189.
36. Asiki G, Murphy GA, Baisley K, Nsubuga RN, Karabarinde A, Newton R, et al. Prevalence of dyslipidaemia and associated risk factors in a rural population in South-Western Uganda: a community based survey. PLoS ONE. 2015;10(5):e0126166.
37. Ranzani OT, Rodrigues LC, Bombarda S, Minto CM, Waldman EA, Carvalho CRR. Long-term survival and cause-specific mortality of patients newly diagnosed with tuberculosis in São Paulo state, Brazil, 2010–15: a population-based, longitudinal study. Lancet Infect Dis. 2020 Jan;20(1)(1):123–32.
38. Seegert AB, Patsche CB, Sifna A, Gomes VF, Wejse C, Storgaard M, et al. Hypertension is associated with increased mortality in patients with tuberculosis in Guinea-Bissau. Int J Infect Dis. 2021 Aug 1;109:123–8.
39. Seegert AB, Rudolf F, Wejse C, Neupane D. Tuberculosis and hypertension—a systematic review of the literature. Int J Infect Dis. 2017 Mar 1;56:54–61.
40. Caillon A, Schiffrin EL. Role of Inflammation and Immunity in Hypertension: Recent Epidemiological, Laboratory, and Clinical Evidence. Curr Hypertens Rep. 2016 Feb 4;18(3):21.
41. Banks E, Joshy G, Korda RJ, Stavreski B, Soga K, Egger S, et al. Tobacco smoking and risk of 36 cardiovascular disease subtypes: fatal and non-fatal outcomes in a large prospective Australian study. BMC Med. 2019 Jul;3(1):128.
42. Rutebemberwa E, Nyamurungi K, Joshi S, Olando Y, Mamudu HM, Pack RP. Health workers' perceptions on where and how to integrate tobacco use cessation services into tuberculosis treatment; a qualitative exploratory study in Uganda. BMC Public Health. 2021 Jul 28;21(1):1464.
43. Burusie A, Enquesilassie F, Addissie A, Dessalegn B, Lamaro T. Effect of smoking on tuberculosis treatment outcomes: A systematic review and meta-analysis. PLoS ONE. 2020 Sep;17(9):e0239333.
44. Elsey H, Al Azdi Z, Regmi S, Baral S, Fatima R, Fieroze F, et al. Scaling up tobacco cessation within TB programmes: findings from a multi-country, mixed-methods implementation study. Health Res Policy Syst. 2022 Apr;18(1):43.
45. Valdez-Miramontes CE, Martínez LAT, Torres-Juárez F, Carlos AR, Marin-Luévano SP, Haro-Acosta JP de, et al. Nicotine modulates molecules of the innate immune response in epithelial cells and macrophages during infection with M. tuberculosis. Clin Exp Immunol. 2020;199(2):230–43.
46. O'Leary SM, Coleman MM, Chew WM, Morrow C, McLaughlin AM, Gleeson LE, et al. Cigarette Smoking Impairs Human Pulmonary Immunity to Mycobacterium tuberculosis. Am J Respir Crit Care Med. 2014 Dec;15(12):1430–6.
47. Kirenga BJ, Ssengooba W, Muwonge C, Nakiyingi L, Kyaligonza S, Kasozi S, et al. Tuberculosis risk factors among tuberculosis patients in Kampala, Uganda: implications for tuberculosis control. BMC Public Health [Internet]. 2015 Jan 21 [cited 2020 Jun 22];15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4311451/.
48. Wang MG, Huang WW, Wang Y, Zhang YX, Zhang MM, Wu SQ, et al. Association between tobacco smoking and drug-resistant tuberculosis. Infect Drug Resist. 2018 Jun;12:11:873–87.
49. Baluku JB, Namiiro S, Nabwana M, Muttamba W, Kirenga B. Undernutrition and Treatment Success in Drug-Resistant Tuberculosis in Uganda. Infect Drug Resist. 2021;14:3673–81.
50. White LV, Edwards T, Lee N, Castro MC, Saludar NR, Calapis RW, et al. Patterns and predictors of co-morbidities in Tuberculosis: A cross-sectional study in the Philippines. Sci Rep. 2020 Mar;5:10:4100.
51. Sheuly AH, Arefin SMZH, Barua L, Zaman MS, Chowdhury HA. Prevalence of type 2 diabetes and pre-diabetes among pulmonary and extrapulmonary tuberculosis patients of Bangladesh: A cross-sectional study. Endocrinol Diabetes Metab. 2022;5(3):e00334.
52. Darbandi M. Discriminatory Capacity of Anthropometric Indices for Cardiovascular Disease in Adults: A Systematic Review and Meta-Analysis. Prev Chronic Dis [Internet]. 2020 [cited 2022 May 24];17. Available from: https://www.cdc.gov/pcd/issues/2020/20_0112.htm.
53. Lawson L, Muc M, Oladimeji O, Iweha C, Opoola B, Abdurhaman ST, et al. Tuberculosis and diabetes in Nigerian patients with and without HIV. Int J Infect Dis. 2017 Aug 1;61:121–5.
54. Tahir F, Arif TB, Ahmed J, Shah SR, Khalid M. Anti-tuberculous Effects of Statin Therapy: A Review of Literature. Cureus [Internet]. 2020 Mar 25 [cited 2021 Jun 20];12(3). Available from: https://www.cureus.com/articles/28849-anti-tuberculous-effects-of-statin-therapy-a-review-of-literature.
55. Duan H, Liu T, Zhang X, Yu A, Cao Y. Statin use and risk of tuberculosis: a systemic review of observational studies. Int J Infect Dis. 2020;93:168–74.
56. Alebel A, Wondemagegn AT, Tesema C, Kibret GD, Wagnew F, Petrucka P, et al. Prevalence of diabetes mellitus among tuberculosis patients in Sub-Saharan Africa: a systematic review and meta-analysis of observational studies. BMC Infect Dis. 2019 Mar 13;19(1):254.
57. Boillat-Blanco N, Ramaiya KL, Mganga M, Minja LT, Bovet P, Schindler C, et al. Transient Hyperglycemia in Patients With Tuberculosis in Tanzania: Implications for Diabetes Screening Algorithms. J Infect Dis. 2016 Apr 1;213(7):1163–72.
58. Baker MA, Harries AD, Jeon CY, Hart JE, Kapur A, Lönnroth K, et al. The impact of diabetes on tuberculosis treatment outcomes: A systematic review. BMC Med. 2011 Jul 1;9(1):81.
59. Tegegne BS, Mengesha MM, Teferra AA, Awoke MA, Habtewold TD. Association between diabetes mellitus and multi-drug-resistant tuberculosis: evidence from a systematic review and meta-analysis. Syst Rev. 2018 Oct 15;7(1):161.
60. Ferreira-Borges C, Parry CDH, Babor TF. Harmful Use of Alcohol: A Shadow over Sub-Saharan Africa in Need of Workable Solutions. Int J Environ Res Public Health [Internet]. 2017 Apr [cited 2021 Jun 20];14(4). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5409547/.

61. Hackshaw A, Morris JK, Boniface S, Tang JL, Milenković D. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. The BMJ [Internet]. 2018 Jan 24 [cited 2021 Jun 20];360. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5781309/.
62. Leopold JA, Antman EM. Ideal Cardiovascular Health in Former Smokers. J Clin Med. 2021;10(11):2450.

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