Title: Prevalence and health effects of communicable and non-communicable disease comorbidity in rural KwaZulu Natal, South Africa.

Authors:

Monica Sharman¹, Max Bachmann, Professor²

¹Norwich Medical School, University of East Anglia, Norwich, United Kingdom, ²Department of Population Health and Primary Care, Norwich Medical School, University of East Anglia, Norwich, United Kingdom and School of Nursing and Public Health, University of KwaZulu Natal, Durban, South Africa. **Affiliations**: Africa Health Research Institute

Corresponding author information: Monica Sharman, monica.sharman@uea.ac.uk

Abstract

Objectives

To describe changes in prevalence of hypertension, diabetes, HIV and tuberculosis, and prevalence of comorbidity, and to investigate associations between each condition, and combinations of conditions, with selfreported general health and hospital admission.

Methods

This study utilised data from a longitudinal population-based HIV and health surveillance cohort, conducted by the Africa Health Research Institute (AHRI), based in the Umkhanyakude district of rural KwaZulu-Natal, South Africa.

Results

Prevalence of hypertension, HIV and diabetes increased from 2009-2015, and prevalence of tuberculosis decreased. Among 47,334 participants, 81% were female, hypertension and diabetes were the commonest conditions over age 50 years, whereas HIV was most common under 50 years. Comorbidity of communicable and non-communicable conditions was commonest in 40-60 year olds. The adjusted odd ratios (OR) for better self-reported general health with multimorbidity were 0.53 (95% CI 0.51-0.56), 0.29 (95% CI 0.27-0.29), 0.25 (95% CI 0.21-0.37) and 0.21 (95% CI 0.12-0.37) for one, two three and four conditions, respectively, compared to no conditions. Tuberculosis was most strongly and inversely associated with better general health (OR 0.34 (0.31-0.37) and most strongly associated with hospital admission (OR 3.26 (2.32-2.99)).

Conclusion

The high prevalence of communicable and non-communicable conditions in this rural South African population is giving rise to a burden of multimorbidity, as increased access to antiretroviral treatment has reduced mortality in people with HIV. Health care systems must adapt by working towards integrated primary care for HIV/AIDS and non-communicable diseases.

Conflict of interests: none.

Introduction

The burden of non-communicable diseases (NCDs), including hypertension and type 2 diabetes mellitus is increasing alongside established HIV and tuberculosis epidemics among people in sub-Saharan Africa [1-4]. This is fuelled by increasing urbanisation, changing diet, sedentary lifestyles [5] and, amongst people with HIV, possibly by metabolic side effects of life-long antiretroviral treatment [6]. The World Health Organisation has predicted a 17% increase in global NCD deaths from 2013 to 2020, with low and middle-income countries (LMICs) currently already bearing 86% of the burden of these premature deaths [7]. Prevalence of diabetes in Southern Africa is estimated at 14% amongst older African adults, and the prevalence of hypertension at over 50% of older adults [8]. Community-based epidemiological studies on the prevalence of comorbidities amongst the HIV population in South Africa, Uganda and Tanzania show considerable comorbidity of hypertension in people with HIV, with prevalences of up to 23% [9-14].

Health services are poorly equipped to deal with this newly emerging burden of disease. A national survey of primary care attenders in South Africa found that hypertension was the most common reason for attendance to primary care clinics, and that NCDs accounted for 14% of all visits [15]. This number is thought to be an underestimation [16]. A recent study across six sites in sub-Saharan Africa found that despite South Africa having the highest blood pressure, 60% of men and 46% of women with hypertension in South Africa were unaware of it [17]. Despite evidence of the increasing prevalence of multimorbidity in sub-Saharan Africa, evidence of its impact of multimorbidity on quality of life and hospitalisation is scarce [2]. Secondary analyses from the WHO-SAGE 2007-2010, however, found that healthcare utilisation within the last year increased from 26% for those without any NCDs to 81% for those with multimorbidity, and this was highest in South Africa compared to other LMICs [18]. Another study in South Africa found significant multimorbidity and unmet treatment needs among patients with NCDs [14].

Most evidence of multimorbidity comes from high income countries and little is known about multimorbidity in LMICs, particularly in rural sub-Saharan Africa [19, 20]. More data is needed to further elucidate the prevalence and patterns of multimorbidity in this region, as well as its effects on general health and on healthcare utilisation. Defining this burden of NCDs among people living with HIV will allow a better understanding of multimorbidity, informing future primary healthcare service planning to better manage these co-existing conditions. A 2018 Academy of Medical Sciences report on global multimorbidity research concluded that future research on changing trends and patterns of multimorbidity, and its effects on burden of disease and health care, were priorities [2], which we address in this study.

The Africa Health Research Institute (ARHI), is a demographic surveillance area in a rural socioeconomically deprived area of KwaZulu-Natal, South Africa, with high HIV prevalence. It follows a cohort of about 85,000 adults with annual community-based surveys including questionnaires and HIV testing and has until 2018 focused on HIV and tuberculosis research [21]. Surveys include questions on recent diagnosis and treatment for hypertension, diabetes and tuberculosis. In 2010 the survey also measured blood pressure and found that 26% of participants had hypertension [21]. In the present study we utilised data from population-based surveys of the demographic surveillance area conducted by ARHI from 2009-2015. We investigated a) changes in the prevalence of hypertension (HPT), diabetes (DM), HIV and tuberculosis, b) prevalence of comorbidities, and c) associations between each condition, and combination of conditions, with self-reported general health and hospital admission.

Methods

Study Design and Population

This was a cohort study using data from a longitudinal population-based HIV and health surveillance study, conducted by the Africa Health Research Institute (AHRI previously known as the Africa Centre for Health and Population Studies), based in the Umkhanyakude district of rural KwaZulu-Natal, South Africa [21]. The study population included approximately 85,000 people who were members for around 11,000 households. To be eligible, individuals must be a member of a household within the surveillance area, but not necessarily a permanent resident within it. For this analysis, the study population included all eligible adults aged ≥15 years, who were surveyed annually between 2004 and 2015 and who had been tested for HIV. Non-participation was due to absence or declined consent.

Data Collection

Participants were surveyed at their homes, including interviewer-administered questionnaires and HIV tests. The study aimed to gather data from each eligible individual repeatedly every year, but most individuals did not participate every year because they were absent from their homes at the time of a survey or declined to participate. After providing written informed consent, participants were asked to give finger prick blood samples which were used to prepare dried blood spots (DBS) for HIV testing. HIV status was determined by antibody testing in the AHRI virology laboratory with a broad-based HIV-1/HIV-2 enzyme-linked immunosorbent assay (ELISA) (Vironostika[®] HIV-1 Microelisa System (Biomérieux, Durham, NC, USA) followed by a confirmatory ELISA (Wellcozyme HIV 1 + 2 GACELISA; Murex Diagnostics Benelux B.V., Breukelen, The Netherlands) [21].

Self-reported measurements of the diagnosis or current ongoing treatment of hypertension, diabetes mellitus and tuberculosis within the last 12 months were obtained by interviewer-administered questionnaires. Participants were assumed to have HIV if they had ever testing positive in previous surveys, and to have hypertension or diabetes if they reported to have a diagnosis or treatment for the respective condition currently, during the previous 12 months or in a previous survey. Tuberculosis was only coded as present if reportedly diagnosed or treated during the previous 12 months. Self-reported hospital admission occurring within the last 12 months was also recorded, both as any admission and as number of admissions.

General health status was measured as a single ordered categorical variable by asking one item of the General Health Questionnaire 12, "Describe your general health at present" [22]. Possible responses were excellent, very good, good, fair and poor, with the first three categories were combined into one.

Statistical Analysis

For each annual survey, estimations of the prevalence of each condition, and combinations of conditions were calculated. To investigate associations between these conditions and general health and hospital admission, we used Cuzick's non-parametric test for trend and chi square test, respectively. We constructed random effects ordinal logistic regression, logistic regression and Poisson regression models with general health, at least one hospital admission and number of hospital admissions as outcomes, respectively, with HIV, hypertension, diabetes, tuberculosis, age, age², and year as time-varying covariates, with sex as a timeinvariant covariate, and with individual as a random effect. We constructed an alternative random effects ordinal logistic regression model with general health as outcome and number of conditions as a covariate instead of HIV, hypertension, diabetes, tuberculosis as separate covariates. We also constructed equivalent general estimating equation logistic and Poisson models, with robust adjustment and exchangeable correlation, so as to estimate population average effects [23]. To investigate factors independently associated with missing HIV, hypertension, diabetes, tuberculosis, general health and hospital admission data in any year, we constructed random effects logistic regression models, with missingness of each of these variables as binary outcomes, and with all other outcomes and covariates used in the previous models as covariates. Analyses were done using Stata version 15.0, except for the general estimating equation ordinal logistic model which was done in R []24] A p-value of 0.05 or less was considered statistically significant. Venn diagrams showing prevalence of comorbidities, with each area approximately proportional to prevalence, were constructed using EulerApe 3.0.

Ethics Approval

Ethical approval for the demographic surveillance study and analyses of these data was granted by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa. Participants provided informed consent to participate.

Results

47,334 people were included in the present study, of whom between 14,478 and 17,890 participated each year, and 44,396 participated at least twice. The median age was 32 (interquartile range 20-52) years and 53% were female. The prevalence of hypertension, diabetes and HIV increased over the years from 2009-2015, with the HIV having the highest followed by hypertension, diabetes and tuberculosis, respectively, and with hypertension prevalence approaching that of HIV by 2014. The prevalence of tuberculosis decreased after

2010 (Figure 1). The proportion of participants with two or more conditions increased from 8.4% in 2009 to 13.2% in 2015.

Of the four conditions, HIV had the highest prevalence under 40 years of age, and at ages under 50, HIV was the most common condition in females (Figure 2). Hypertension was the most prevalent condition above 40 years of age in females and above 50 years in males. Hypertension and diabetes were substantially more common in females than in males, whereas tuberculosis was more common in males.

Participants with each condition were significantly less likely to report better general health and more likely to report hospital admission during the past 12 months (Table 1). In ordinal logistic regression analyses, tuberculosis was most strongly and inversely associated with better general health, followed by hypertension, diabetes and HIV respectively (Table 2). In an alternative analysis with number of conditions as covariate, the adjusted odds ratio for better self-reported general health of participants were 0.53 (95% CI 0.51-0.56), 0.29 (95% CI 0.27-0.29), 0.25 (95% CI 0.21-0.37) and 0.21 (95% CI 0.12-0.37) for one disease, two diseases, three diseases and four diseases respectively, compared to having none of these conditions. In logistic regression analyses tuberculosis was most strongly associated with hospital admission, closely followed by diabetes (Table 2). HIV and hypertension were much less strongly, and similarly, associated with hospital admission. Of 5061 occasions when participants reported hospital admission during the last year, 597 (11.8%) reported more than one admission. Associations between covariates and numbers of hospital admissions in the past year were similar to associations with at least one admission (Table 2). General estimating equation models produced similar results to random effects models, except that with hospital admission and number of hospital admissions as outcomes, odds ratios and incidence rate ratio models for HIV, hypertension, diabetes and tuberculosis were slightly smaller with general estimating equation models (Table 2).

Data on HIV, hypertension, diabetes, tuberculosis, general health and hospital admission were missing for 30%, 14%, 10%, 21%, 20% and 20% of interviews, respectively. Data on HIV were more likely to be missing in males and in participants who reported better general health, and were less likely to be missing if they reported hospital admission, hypertension or tuberculosis, and in later survey years (Table 3). Data on tuberculosis were more likely to be missing in participants with HIV or diabetes or who were male, and in later years. In equivalent models, not tabulated, only later survey years were independently associated with missing hypertension data (adjusted odds ratio 1.22 (95% confidence interval 1.14-1.13) per year); only tuberculosis and later years were independently associated with missing diabetes data (adjusted odds ratios 3.74 (2.44-5.76) and 1.11 (1.04-1.19) respectively. Data on general health were more likely to be missing in participants with hypertension and in later survey years (Table 3). No variable independently predicted missing hospital admission data.

Comorbidity was most common amongst those with diabetes, 85.4% of whom also had hypertension, and 12.2% also had hypertension and HIV (Figure 3). Comorbidity was also common in those with tuberculosis, of whom 74.4% also had HIV and 10.3% had HIV and hypertension. 12.1% of those with HIV also had hypertension. Of those aged over 40 years, 66% had at least one condition and 18.4% had at least two, with 11.5% having both diabetes and hypertension.

Discussion

This study described the high burden of NCD and communicable disease comorbidity in this rural South African population, with NCD prevalence comparable to that of data from other South African studies [5, 9, 10].

In this study population, with median age 32 years, HIV had the highest prevalence of the four conditions, with 31.7% being HIV+ in 2015, compared to the national prevalence of HIV in South Africa of 12.5% in the same year [25]. This is very closely followed by hypertension with 27% of participants being affected. This is congruent with emerging studies based on primary care clinic attendants which show that hypertension is the commonest presenting condition across South Africa [5, 15]. Hypertension and HIV comorbidity in this sample was relatively common, with 15.2% of those with hypertension also being HIV+. More people are living longer with HIV, with AIDS-related deaths declining consistently since 2007 because of antiretroviral treatment according to national data [26], and people are hence more likely to develop other chronic conditions. Recent studies show a high prevalence of dysglycaemia, dyslipidaemia and increased visceral adiposity in HIV-infected patients on ART, thereby predisposing to hypertension and diabetes [26, 27]. While efforts to maintain

progress with ART must continue, our findings point to a need to expand our focus to enable effective management of communicable disease and NCD comorbidity particularly among lower socioeconomic groups [6, 10].

Comorbidity was strongly associated with age. Overlap between communicable disease and NCDs is seen especially in the over 40 years age group, where chronic NCD increases alongside HIV. The prevalence of chronic NCD in this age group is notable, with hypertension and diabetes being the most common comorbidity overall, with 70.5% of those with diabetes having hypertension, and with both chronic conditions independently increasing with age. A national study based on over 50-year olds estimated hypertension prevalence to be at 77.3% [28]. A similar study of primary care clinic patients in a peri-urban area of South Africa, found that the most common comorbidity was hypertension and diabetes which increased with increasing age [5]. The presence of these comorbidities as the population ages is likely to complicate management, particularly as more people with HIV survive longer on ART. However, despite this trend, little attention has been paid to HIV and NCDs in the older population [29].

The national South African General Household Survey in 2010 demonstrated that the prevalence of hypertension in women was about twice the prevalence in men, with the gap narrowing for older adults [30]. These results are congruent with our findings. Sociocultural factors may contribute, for example it has been argued that black African women perceive being overweight, a risk factor for hypertension and diabetes, as desirable because it signifies affluence, beauty and being HIV negative [9, 31]. Although being underweight is stigmatised, however, because of its and its association with HIV/AIDS and tuberculosis, a recent study found no association between underweight status and HIV status [31]. Another study pointed to the high levels of tobacco smoking particularly amongst women as a risk factor for hypertension [32].

All four conditions were strongly and independently associated with worse self-reported general health and with hospital admission. The random effects models (estimating subject specific effects) and the generalised estimating equation models (estimating population average effects) produced similar results. The random effects models are arguably preferable in this study, because they are more appropriate for estimating effects of time-varying covariates like comorbidities, and they do not assume that the missingness of data is independent of other variables in the analysis [23].

Tuberculosis was most strongly associated with both outcomes. However, diabetes was almost as strongly associated with hospital admission as tuberculosis was, highlighting the growing burden of illness that diabetes will cause as it becomes more common. A study from Ghana, also a middle-income country, showed increased diabetes admission rates across the last three decades, attributing to complications such as diabetic ketoacidosis, symptomatic hypoglycaemia and end-organ complications [33]. The severity of diagnosed diabetes could explain the strong association between diabetes and hospitalisation. Statistics South Africa reported that in 2016 diabetes was South Africa's second most common cause of death, second only to tuberculosis, and was the most common cause of death in women (7.2%) and the second common cause of death in men (5.5%) [34]. This highlights the importance of improving diabetes prevention and treatment in LMICs, where an estimated 77% of people with diabetes worldwide live [35]. It is surprising that HIV was not more strongly associated with worse general health and hospitalisation than hypertension was, considering that hypertension is usually asymptomatic. This finding suggests that most people with HIV were at early stages of infection or were well controlled on antiretroviral treatment.

Our findings suggest that the impact of multimorbidity on self-reported poor general health outcomes is multiplicative the more conditions suffered. This is consistent with data taken from six LMICs showing a statistically significant negative effect on four quality of life outcomes, and that each outcome showed poorer results the greater the number of chronic conditions suffered [19]. These results contribute to evidence on the nature of disease interactions in multimorbidity.

A strength of the study is that we include a large community-based sample of 47,334 participants which increases the generalisability of the findings. The demographic information system collects information on resident and non-resident members of households, making a distinction between membership and residency. Obtaining information on non-resident members is crucial, as understanding patterns of HIV transmission within rural areas requires knowledge about patterns of circulation and about sexual contacts between

residents and non-resident partners. This longitudinal study contributes to current evidence gaps, allowing a better understanding of the changing prevalence of multimorbidity over time [2].

A limitation of the study was the use of self-reported diagnoses and treatment of hypertension, diabetes and tuberculosis, as well as self-reported measurements of general health and hospital admission, which would less accurate than objective assessment. Furthermore, the consent rates for HIV testing was low, decreasing from 60% in 2003-2004, to 40% in 2005-2006, and almost half did not answer questions about general health and hospital admissions leading to possible selection bias [21]. Non-participation could be explained by migration of healthier individuals in and out of the surveillance area, which could also cause selection bias. The General Health Questionnaire (GHQ-12) was used, which widely validated in general and clinical populations and found to be reliable [36]. However, for this study the responses 'good', 'very good' and 'excellent' were combined, because they could not be clearly distinguished when translated in to Zulu, thereby reducing the instrument's discriminating value. AHRI is currently carrying out community-based tuberculosis, blood pressure and diabetes testing as well as HIV testing in this study population, which will provide more accurate estimates of the prevalence of comorbidity and will allow prospective assessment of the effects of each condition on health outcomes and health care use. Data on HIV were most likely to be missing, because they required additional consent and testing, even though results of previous positive tests had been carried forward to subsequent years. HIV data were less likely to be missing in participants with indicators of worse health and with comorbidities (Table 3), suggesting that their health concerns increased their willingness to be tested. Males were less likely to have been tested for HIV - in keeping with less uptake of HIV testing by men in South Africa nationally - and to have missing tuberculosis data. Missing comorbidity or health outcome data were more likely in later years, but otherwise were not consistently predicted by other covariates or outcomes.

Chronic disease is often underdiagnosed, leading to underestimation of the true prevalence of NCDs in the population. There needs to be a greater priority for chronic disease management, particularly in the context of a rapidly growing burden of communicable and NCD comorbidity. Evidence from the Cape Peninsula, South Africa, found that care for hypertensive and diabetic patients in community health centres was suboptimal, with uncontrolled hypertension in 50% of patients, high prevalence of unrecorded diabetic complications and suboptimal glycaemic control [37]. Issues of access and quality must be taken into consideration, along with culturally-appropriate approaches to behaviour change and chronic disease management.

In line with the WHO Innovative Care for Chronic Conditions report [38], we argue that health care systems must adapt to this rising burden by working towards an integrated model of care for HIV/AIDs and NCDs in the region. The acute care paradigm no longer meets the needs of many patients. Engagement with local communities and healthcare teams must be strengthened to ensure patients are informed, well-educated and empowered to take control of their own health [39].

Acknowledgements We are grateful to the Africa Health Research Institute for providing the data and permitting publication, and in particular to Dickson Gareta for supplying the data, and to Kobus Herbst, Kathy Baisley and Richard Lessells for advice on interpretation of the data. We thank Allan Clark for doing the <u>general</u> <u>estimating equation ordinal logistic</u> analysis in R.

References:

[1] Tollman S.M., Kahn K., Sartorius B., Collinson M.A., Clark S.J., Garenne M.L. (2008). Implications of mortality transition for primary health care in rural South Africa: a population-based surveillance study. *The Lancet.* 372(9642); 893-901.

[2] Multimorbidity: a priority for global health research [PDF file]. Academy of Medical Sciences 2018. Available from: https://acmedsci.ac.uk/file-download/82222577 [accessed 27 May 2018]

[3] Workshop proceedings: Addressing the global challenges of multimorbidity – lessons from South Africa [PDF file]. Academy of Medical Sciences 2018. Available from: https://acmedsci.ac.uk/file-download/68578850 [accessed 16 July 2019]

[4] Lalkhen H., Mash R. (2015). Multimorbidity in non-communicable diseases in South African primary healthcare. *South African Medical Journal*. 105(2):134-138.

[5] Oni T., Youngblood E., Boulle A., McGrath N., Wilkinson R.J., Levitt N.S. (2015). Patterns of HIV, tuberculosis, and non-communicable disease multi-morbidity in peri-urban South Africa – a cross sectional study. *BMC Infectious Disease*. 15(20).

[6] Folb N., Bachmann M.O., Bateman E.D., Steyn K., Levitt N.S., Timmerman V., Lombard C., Gaziano T.A., Fairall L.R. (2016). Socioeconomic and modifiable predictors of blood pressure control for hypertension in primary care attenders in the Western Cape, South Africa. *South African Medical Journal*. 106(12); 1241-1246.

[7] World Health Organisation (2013). Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020. Geneva: World Health Organisation. Available from: http://www.who.int/nmh/events/ncd_action_plan/en/

[8] Manne-Goehler J., Montana L., Gomez-Olive E.X., Rohr J., Harling G., Wagner R.G., Wade A., Kabudula C.W., Gledsetzer P., Kahn K., Tollman S., Berkman L.F., Barnighausen T.W., Gaziano T.A. (2017). The ART Advantage: Health Care Utilisation for Diabetes and Hypertension in Rural South Africa. *Journal of Acquired Immune Deficiency Syndromes.* 75(5); 561-567.

[9] Malaza, A., Mossong, J., Bärnighausen, T. and Newell, M.-L. (2012). Hypertension and obesity in adults living in a high HIV prevalence rural area in South Africa. *PLoS One*. 7(10).

[10] Weimann A., Dai D., Oni T. (2016). A cross-sectional and spatial analysis of the prevalence of multimorbidity and its association with socioeconomic disadvantage in South Africa: A comparison between 2008 and 2012. *Social Science and Medicine*. (163); 144–156.

[11] Stanifer, J.W., Maro, V., Egger, J., Karia, F., Thielman, N., Turner, E.L., Shimbi, D., Kilaweh, H., Matemu, O. and Patel, U.D. (2015) 'The Epidemiology of chronic kidney disease in northern Tanzania: A population-based survey'. *PLoS One*. 10(4).

[12] Kayima, J., Nankabirwa, J., Sinabulya, I., Nakibuuka, J., Zhu, X., Rahman, M., Longenecker, C.T., Katamba, A., Mayanja-Kizza, H. and Kamya, M.R. (2015). 'Determinants of hypertension in a young adult Ugandan population in epidemiological transition—the MEPI-CVD survey'. *BMC Public Health*. 15; 830.

[13] Kwarisiima, D., Balzer, L., Heller, D., Kotwani, P., Chamie, G., Clark, T., Ayieko, J., Mwangwa, F., Jain, V., Byonanebye, D., Petersen, M., Havlir, D. and Kamya, M.R. (2016). Population-based assessment of hypertension Epidemiology and risk factors among HIV-Positive and general populations in rural Uganda. *PLoS One*. 11(5).

[14] Folb N., Timmerman V., Levitt N.S., Bachmann M.O., Lund C., Bateman E.D., Lombard C., Gaziano T.A., Zwarenstein M., Fairall L.R. (2015). Multi-morbidity, control and treatment of non-communicable diseases among primary healthcare attenders in the Western Cape, South Africa. *South African Medical Journal*. 105(8): 642-647.

[15]. Mash B., Fairall L., Adejayan O., Ikpefan O., Kumari J., Mathee S., Okun R. (2012). A morbidity survey of South African primary care. *PLoS One*. 7(5): 10.1371

[16] Rayner B.L. (2010). Hypertension: detection and management in South Africa. *Nephron Clinical Practice*. 116; 269-273.

[17] Gómez-Olivé F. X., Ali S. A., Made F., Kyobutungi C., Nonterah E., Micklesfield L., Alberts M., Boua R., Hazelhurst S., Debpuur C., Mashinya F., Dikotope S., Sorgho H., Cook I., Muthuri S., Soo C., Mukomana F., Agongo G., Wandabwa C., Afolabi A., Oduro A., Tinto H., Wagner R.G., Haregu T., Wade A., Kahn K., Norris S.A., Crowther N.J., Tollman S., Sankoh O., Ramsay M., as members of AWI-Gen and the H3Africa Consortium. (2017). Regional and sex differences in the prevalence and awareness of hypertension across six sites in sub-Saharan Africa: an H3Africa AWI-Gen study. *Global Heart*. 12(2); 81–90.

[18] Lee J.T., Hamid F., Pati S., Atun R., Millett C. (2015). Impact of noncommunicable disease multimorbidity on healthcare utilisation and out-of-pocket expenditures in middle-income countries: cross sectional analysis. *PLoS ONE. 10;7.*

[19] Arokiasamy, P., Uttamacharya, U., Jain, K., Biritwum, R. B., Yawson, A. E., Wu, F., Gwo Y., Maximova T., Espinoza B.M., Rodriguez A.S., Afshar S., Pati S., Ice G., Banerjee S., Liebert M.A., Snodgrass J.J., Naidoo N., Chatterji S., Kowal, P. (2015). The impact of multimorbidity on adult physical and mental health in low- and middle-income countries: what does the study on global ageing and adult health (SAGE) reveal? *BMC Medicine*. 13; 178.

[20] Alaba O., Chola L. (2013). The social determinants of multimorbidity in South Africa. *Journal for Equity in Health*. 12(63).

[21] Tanser F., Hosegood V., Barinighausen T., Herbst K., Nyirenda M., Muhwaya W., Newell C., Vijioen J., Mutevedzi T., Newwell M.L. (2008). Cohort Profile: Africa Centre Demographic Information System (ACDIS) and population-based HIV survey. *International Journal of Epidemiology*. 37(5): 956-962.

[22] Goldberg D.P., Hillier V.F. (1979) A scaled version of the General Health Questionnaire. *Psychol Med*. 9: 139–145.

[23] Szmaragd C, Clarke P, Steele F. (2013) Subject specific and population average models for binary longitudinal data: a tutorial. *Longitudinal and Life Course Studies* 4: 147 – 165.

[24] Touloumis A. (2015) R Package multgee: A generalized estimating equations solver for multinomial responses. *Journal of Statistical Software* 64:1-14. Available from https://www.jstatsoft.org/article/view/v064i08 [accessed 16 July 2019]

[25] Stats SA. (2017). Mid–year population estimates Report P0302. Pretoria: Statistics South Africa. Available from http://www.statssa.gov.za/publications/P0302/P03022017.pdf [accessed 16 July 2019].

[26] Friss-Moller N., Reiss P., Sabin C.A., Weber R., Monfort A., El-Sadr W., Thiebaut R., De Wit S., Kirk O., Fontas E., Law M.G., Phillips A., Lundgren J.D. (2007). Class of antiretroviral drugs and risk of myocardial infarction. *The New England Journal of Medicine*. 356(17); 1723-1735.

[27] Samaras K. (2008). Metabolic consequences and therapeutic options in highly active antiretroviral therapy in human immunodeficiency virus-1 infection. *Journal of Antimicrobial Chemotherapy*. 61(2); 238-245.

[28] Peltzer K., Phaswana-Mafuya. (2013). Hypertension and associated factors in older adults in South Africa. *Cardiovascular Journal of Africa*. 24(3); 66-71.

[29] Negin, J., Mills, E. J., Bärnighausen, T. (2012). Aging with HIV in Africa: the challenges of living longer. *AIDS*. 26(0 1), S1–S5.

[30] Hasumi T., Jacobsen K.H. (2012). Hypertension in South Africa adults: results of a nationwide survey. *Journal of Hypertension*. 30(11); 2098-104.

[31] Heerdan V.A., Barnabas R.V., Norris S.A., Micklesfield L.K., Rooyen H.V., Celum C. (2017). High prevalence of HIV and non-communicable disease (NCD) risk factors in rural KwaZulu-Natal, South Africa. *Journal of the International AIDS Society*. 20:e25012.

[32] Alberts M., Urdal P., Steyn K., Stensvold I., Tverdal A., Nel J.H., Steyn N.P. (2005). Prevalence of cardiovascular diseases and associated risk factors in a rural black population of South Africa. *European Journal of Preventative Cardiology*. 12(4); 347-54.

[33] Sarfo-Kantanka, O., Sarfo, F. S., Oparebea Ansah, E., Eghan, B., Ayisi-Boateng, N. K., Acheamfour-Akowuah, E. (2016). Secular trends in admissions and mortality rates from diabetes mellitus in the Central Belt of Ghana: A 31-Year Review. *PLoS ONE*. 11(11).

[34] Stats SA. Mortality and causes of death in South Africa: Findings from death notification [PDF file], 2016. Report P03093. Pretoria: Statistics South Africa. Available from: http://www.statssa.gov.za/publications/P03093/P030932016.pdf [accessed 16 July 2019].

[35] Pastakia S.D., Pekny C.R., Manyara S.M., Fischer L. (2017). Diabetes in sub-Saharan Africa – from policy to practice to progress: targeting the existing gaps for future care for diabetes. *Diabetes Metabolic Syndrome and Obesity: Targets and Therapy*. 10: 247-263.

[36] Hankins M. (2008). The reliability of the twelve-item general health questionnaire (GHQ-12) under realistic assumptions. *BMC Public Health*. 8:355.

[37] Steyn K., Levitt N.S., Patel M., Fourie J., Lombard C., Everett K. (2008). Hypertension and diabetes: poor care for patients at community health centres. *Journal of Endocrinology, Metabolism and Diabetes of South Africa*. 13(2); 64-70.

[38] Noncommunicable Diseases and Mental Health, World Health Organisation. Innovative care for chronic conditions: building blocks for action: global report. Geneva, Switzerland: World Health Organisation, 2002. Available from:

http://www.who.int/chp/knowledge/publications/icccglobalreport.pdf?ua=1 [accessed 16 July 2019].

[39] Levitt N.S., Steyn K., Dave J., Bradshaw D. (2011). Chronic noncommunicable diseases and HIV/AIDS on a collision course: relevance for health care delivery, particularly in low-resource settings – insights from South Africa. *American Journal of Clinical Nutrition.* 94(suppl); 1690S-6S.

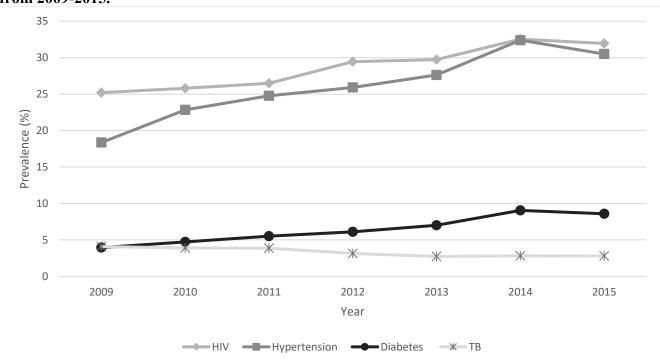


Figure 1: Prevalence (%) of HIV, hypertension, diabetes mellitus and tuberculosis (TB) annually from 2009-2015.

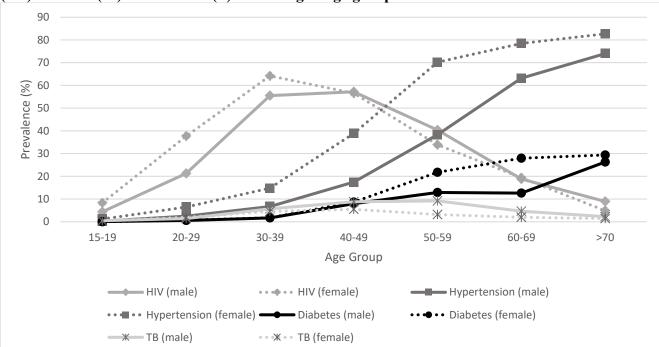


Figure 2: Prevalence (%) of HIV, hypertension (HTN), diabetes mellitus (DM) and tuberculosis (TB) in males (M) and females (F) according to age group in 2015.

	HIV +		HIV -		Hypertension +		Hypertension -		Diabetes +		Diabetes -		Tuberculosis +		Tuberculosis -	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
General Health																
Poor	47	1.2	210	2.4	209	5.9	77	0.7	82	8.6	202	1.4	29	7.0	249	1.7
Fair	1,053	27.8	2,108	24.3	1,800	50.7	1,786	15.6	533	55.6	3,038	21.7	192	46.0	3,370	23.2
Good/Very Good/ Excellent	2,684	70.9	6,359	73.3	1,544	43.5	9,553	83.7	343	35.8	10,768	76.9	196	47.0	10,890	75.1
TOTAL	3,784	100.0	8,677	100.0	3,553	100.0	11,416	100.0	958	100.0	14,008	100.0	417	100.0	14,509	100.0
Hospital Admission																
No	3,668	96.6	8,540	98.0	3,505	97.9	11,160	97.5	925	95.9	13,732	97.7	97.7	381	14,235	97.8
Yes	130	3.4	175	2.0	77	2.1	281	2.5	40	4.1	324	2.3	2.3	35	327	2.2
TOTAL	3,798	100.0	8,715	100.0	3,582	100.0	11,441	100.0	965	100.0	14,056	100.0	100.0	416	14,562	100.0

Table 1: Association between disease and general health score and hospitalisation within the last year in 2015

Associations between each condition and general health tested with Cuzick's non-parametric test for trend. Associations between each condition and hospital admission tested with chi squared rest. P<0.001 for all tests.

Table 2: Association between general health and hospitalisation, and disease and demographic characteristics: regression models

Explanatory variables	Outcome									
		General health*		Hospital	admission in	the last year**	Number of hospital admissions in the last year***			
Random effects models	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value	Incidence rate ratio	95% CI	P value	
HIV	0.72	0.69-0.76	<0.001	1.51	1.36-1.66	<0.001	1.55	1.41-1.71	<0.001	
Hypertension	0.49	0.46-0.52	<0.001	1.45	1.28-1.65	<0.001	1.54	1.36-1.73	< 0.001	
Diabetes	0.64	0.59-0.70	<0.001	2.60	2.18-3.09	<0.001	2.52	2.12-2.99	<0.001	
Tuberculosis	0.34	0.31-0.37	<0.001	3.26	2.80-3.79	<0.001	2.24	1.95-2.58	< 0.001	
Male vs female	1.03	0.98-1.09	0.197	0.77	0.71-0.85	<0.001	0.80	0.73-0.89	<0.001	
Age (years)	0.91	0.91-0.92	<0.001	1.02	1.00-1.03	<0.001	1.02	1.01-1.03	0.002	
Age ²	1.0004	1.0003-1.0004	<0.001	0.9997	0.9996-0.9998	<0.001	0.9997	0.9995-0.9998	<0.001	
Year of survey	1.09	1.08-1.10	<0.001	0.82	0.82	<0.001	0.84	0.81-0.84	<0.001	
Generalised estimating equation models										
HIV	0.74	0.70-0.78	<0.001	1.45	1.33-1.59	<0.001	1.56	1.39-1.75	<0.001	
Hypertension	0.51	0.51-0.48	<0.001	1.40	1.23-0.59	<0.001	1.47	1.24-1.75	<0.001	
Diabetes	0.65	0.60-0.71	<0.001	2.36	2.01-2.78	<0.001	2.36	1.91-2.92	<0.001	
Tuberculosis	0.35	0.32-0.39	<0.001	2.89	2.52-3.31	<0.001	2.43	2.10-2.81	<0.001	
Male vs female	1.04	0.99-1.10	0.112	0.80	0.72-0.88	<0.001	0.82	0.73-0.92	0.001	
Age (years)	0.91	0.91-0.92	<0.001	1.01	1.00-1.03	0.024	1.01	0.99-0.13	0.116	
Age ²	1.0004	1.0003-1.0004	<0.001	0.9997	0.9995-0.9998	<0.001	0.9997	0.80-0.85	<0.001	
Year of survey	1.09	1.08-1.10	<0.001	0.83	0.81-0.85	<0.001	0.83	0.80-0.85	<0.001	

3 * ordinal logistic regression model. ** logistic regression models. *** Poisson regression models

1 2

4 Table 3. Predictors of missing HIV, general health and hospital admission data: random effects logistic regression models

_	
٦.	
2	

Explanatory variables		Outcomes									
		Missing HIV data		Mi	ssing tubercul	osis data	Missing general health data				
	Odds ratio	95% CI	Odds ratio	Odds ratio	Odds ratio	P value	Odds ratio	95% CI	P value		
General health											
• Poor (reference)	1.0			1.0							
• Fair	1.27	1.08-1.50	0.005	0.78	0.49-1.25	0.306					
 Good, very good or excellent 	1.93	1.64-2.29	<0.001	0.71	0.44-1.15	0.166					
Hospital admission in the last year (vs none)	0.83	0.75-0.91	<0.001	1.09	0.72-1.66	0.673	0.75	0.33-1.69	0.485		
HIV				1.35	1.09-1.67	0.005	0.91	0.65-1.26	0.551		
Hypertension	0.85	0.79-0.92	<0.001	1.22	0.94-1.59	0.141	1.61	1.11-2.31	0.011		
Diabetes	1.02	0.91-1.16	0.714	1.02	2.54-1.48	<0.001	1.11	0.69-1.77	0.669		
Tuberculosis	0.70	0.62-0.78	<0.001				0.91	0.42-1.95	0.819		
Male vs female	1.44	1.37-1.52	<0.001	1.37	1.12-1.68	0.002	1.23	0.91-1.65	0.176		
Age (years)	1.01	1.00-1.01	0.041	1.02	1.00-1.00	0.092	1.07	0.974-1.04	0.698		
Age ²	0.9999	0.9998-0.9999	<0.001	0.9999	09996-1.0000	0.204	1.000	0.9997-1.0000	0.951		
Year of survey	0.86	0.86-0.87	<0.001	1.11	1.06-1.16	<0.001	1.33	1.23-1.43	<0.001		

9 Figure 3: Comorbidity between hypertension, diabetes, HIV and tuberculosis in 2015

