Temporal changes in cause of death among adolescents and adults in six countries in eastern and southern Africa in 1995–2019: a multi-country surveillance study of verbal autopsy data

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Summary

Background The absence of high-quality comprehensive civil registration and vital statistics systems across many settings in Africa has led to little empirical data on causes of death in the region. We aimed to use verbal autopsy data to provide comparative, population-based estimates of cause-specific mortality among adolescents and adults in eastern and southern Africa.

Methods In this surveillance study, we harmonised verbal autopsy and residency data from nine health and demographic surveillance system (HDSS) sites in Kenya, Malawi, Tanzania, South Africa, Uganda, and Zimbabwe, each with variable coverage from Jan 1, 1995, to Dec 31, 2019. We included all deaths to adolescents and adults aged 12 or over that were residents of the study sites and had a verbal autopsy conducted. InSilicoVA, a probabilistic model, was used to assign cause of death on the basis of the signs and symptoms reported in the verbal autopsy. Levels and trends in all-cause and cause-specific mortality rates and cause-specific mortality fractions were calculated, stratified by HDSS site, sex, age, and calendar periods.

Findings 52 484 deaths and 5 157 802 person-years were reported among 1 071 913 individuals across the nine sites during the study period. 47 961 (91·4%) deaths had a verbal autopsy, of which 46 570 (97·1%) were assigned a cause of death. All-cause mortality generally decreased across the HDSS sites during this period, particularly for adults aged 20–59 years. In many of the HDSS sites, these decreases were driven by reductions in HIV and tuberculosis-related deaths. In 2010–14, the top causes of death were: road traffic accidents, HIV or tuberculosis, and meningitis or sepsis in adolescents (12–19 years); HIV or tuberculosis in adults aged 20–59 years; and neoplasms and cardiovascular disease in adults aged 60 years and older. There was greater between-HDSS and between-sex variation in causes of death for adolescents compared with adults.

Interpretation This study shows progress in reducing mortality across eastern and southern Africa but also highlights age, sex, within-HDSS, and between-HDSS differences in causes of adolescent and adult deaths. These findings highlight the importance of detailed local data to inform health needs to ensure continued improvements in survival.

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Introduction

Despite substantial declines in mortality since 2000, many countries in sub-Saharan Africa still face high rates of premature mortality across all age groups.[1] For example, in 2016, the adult (15–60 years) mortality rate was 277 per 1000 population, which was almost twice the global average.[2] Understanding which causes of death drive this high mortality is essential to inform policy and programme priorities with the aim of reducing this burden.

Tracking causes of death in sub-Saharan Africa is particularly challenging because few countries have comprehensive civil registration and vital statistics systems.[3] Some studies have relied on cause of death data from health facilities; however, these data are often of poor quality, incomplete, and unlikely to be representative of deaths occurring in the community.[4,5] Verbal autopsy, in which relatives or close caregivers of someone who recently died are asked to provide details on the signs, symptoms, and circumstances preceding the death, presents a unique opportunity to explore cause of death. Historically, cause of death was assigned from verbal autopsies by physicians but, increasingly, automated methods are applied because they are cheaper, faster, and produce reproducible results.[6]

Published papers that report cause of death among adults using verbal autopsy in sub-Saharan Africa have

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See Online for appendix 1

Research in context

Evidence before this study

Existing evidence on the cause of death distribution among adolescents and adults by age, sex, and calendar period with cross-country comparisons in Africa is limited. We identified peer-reviewed articles by searching PubMed and Embase on Feb 21, 2023, and included any relevant studies published in English from Jan 1, 2013, to Dec 31, 2022, using search terms related to adolescent or adult, cause of death, and sub-Saharan African countries (appendix 1 pp 2–4). We identified 97 papers investigating one or multiple causes of death in at least one sub-Saharan African country. Two major studies contributed to multi-country reporting of the full spectrum of cause of death profiles across six of the papers. The first set of papers (three papers) were derived from the Global Burden of Disease study, and provided cause of death distributions by sex, age, calendar period, and country; however, these findings were largely derived from modelled estimates rather than empirical data and so need to be interpreted cautiously. The second set of papers (three papers) were derived from the INDEPTH network of health and demographic surveillance system (HDSS) sites, in which the automated algorithm InterVA-4 was used to assign cause of death for pooled verbal autopsy data; however, these studies only covered time periods up to 2012. Other papers were either focused on specific causes of death (72 papers) or focused on a single geographical area or country (19 papers).

Added value of this study

We were able to provide comparative empirical data on cause of death by drawing together data from nine HDSS sites in six countries in eastern and southern Africa. These HDSS sites are all members of the Analysing Longitudinal Population-Based HIV/AIDS Data on Africa network. The study populations all have a high prevalence of HIV. The study describes the leading causes of death and trends in cause-specific and all-cause mortality by age, sex, and geographical area over a 25-year period.

Implications of all the available evidence

This study provides the most up-to-date empirical adolescent and adult cause of death estimates across eastern and southern Africa. Reductions in the number of HIV and tuberculosis deaths have contributed to improvement in survival across the region. There are notable age, sex, and country-specific differences in the main causes of death, which reinforces the importance of empirical, local-level data to inform priority setting to improve adolescent and adult survival. The study also shows how the most recently developed computer algorithm, InSilicoVA, can be used to assign causes of death with data from verbal autopsies.

generally covered small populations with different methods that make comparison across settings challenging.[7–11] In this study, we used verbal autopsy data from the Analysing Longitudinal Population-Based HIV/AIDS Data on Africa (ALPHA) network,[12] harmonising data from nine independent health and demographic surveillance system (HDSS) sites across eastern and southern Africa to provide comparative, population-based estimates of cause-specific mortality among adolescents and adults aged 12 years and older.

Methods

Study settings

For more on the **ALPHA network** see https://alpha.lshtm.ac.uk

Data from nine HDSS sites that are members of the ALPHA network were used for this prospective surveillance study: Nairobi (Kenya),[13] Karonga (Malawi),[14] Kisesa[15] and Ifakara[16] (Tanzania), uMkhanyakude[17] and Agincourt[18] (South Africa), Masaka and Rakai (Uganda),[19] and Manicaland (Zimbabwe).[20] Although every HDSS site is independently managed with their own tailored data collection protocol, survey instruments, and data management processes, they are similar in methodological approaches and types of data collected.[12] More specifically, these HDSS sites have collected information on births, deaths, and migrations of all people living in geographically defined study areas at regular intervals.[12] When a death was identified, a verbal autopsy was conducted, after allowing for a period of mourning of at least 2–3 weeks. The one exception was Manicaland, which is not set up as a HDSS site but as a cohort study. Although all deaths in households in the Manicaland study area were routinely identified, only two-thirds of household members were randomly selected into a cohort that included follow-up verbal autopsy, which was restricted to adults aged 15–54 years for most study rounds. Detailed descriptions of each HDSS population are provided in appendix 1 (pp 5–8). Differences between the HDSS sites (table 1) include: the timing and frequency of data collection; the languages used for interview (appendix 1 p 8); and the verbal autopsy questionnaires used, particularly for data collected before the introduction of standardised verbal autopsy questionnaires from WHO, which were first released in 2007 and adopted at varying times in different settings. Ethical approval for this analysis was granted by the London School of Hygiene & Tropical Medicine ethics committee. Each HDSS site used their own consent procedure and materials appropriate to the local context to obtain informed consent from participants.[13–20] Each site also had their own protocol for inclusion and exclusion criteria, although the core princples were similar.

Data preparation

Data analysts and managers at each HDSS site prepared residency and verbal autopsy data according to standard specifications. The residency data included dates of entry into the study (due to birth or in-migration) and dates of exit (due to death or out-migration). Verbal autopsy data included the signs and symptoms reported during the

verbal autopsy interview for each death. Verbal autopsy data were harmonised and mapped to the input format required by InSilicoVA[21,22] (appendix 1 pp 9–13). If a specific sign or symptom was not available for a given verbal autopsy questionnaire then it was included in the InSilicoVA input as missing for all verbal autopsies collected with that questionnaire. Data were only included from Jan 1, 1995, to Dec 31, 2019. In Manicaland, data were restricted to only adults aged 20–54 years, excluding adolescents aged 15–19 years due to small numbers (on average fewer than two deaths with a verbal autopsy per year). Verbal autopsies were only retained for analysis if they could be linked to a death recorded in the HDSS.

Data analysis

We calculated verbal autopsy coverage as the percentage of HDSS deaths that had a verbal autopsy across HDSS sites and over time. We calculated all-cause mortality rates from the total number of deaths and person-years of observation among all residents in each HDSS stratified by sex, age group (adolescents aged 12–19 years; adults aged 20–59 years; and adults aged 60 years and older), and 5-year calendar periods (1995–99, 2000–04, 2005–09, 2010–14, and 2015–19). Mortality rates were calculated from aggregated total number of deaths and aggregated person-years within the respective periods.

We used the openVA software[23] to run the InSilicoVA algorithm to automate cause of death assignment.[22] InSilicoVA identifies the joint distribution of individual causes of death and population-level cause-specific mortality fractions (CSMFs) that is most consistent with the verbal autopsy signs and symptoms recorded for a group of deaths. Using that result, InSilicoVA produces a probability distribution for each cause for each death and a probability distribution for each CSMF. McCormick and colleagues provide a full description of InSilicoVA and present a validation study.[22] The CSMFs describe the percentage of deaths attributable to each cause in a defined group of deaths.[21,22] InSilicoVA was run for each HDSS site separately, with subpopulations specified by sex, age groups, and 5-year calendar periods. Cases missing key inputs, such as sex or age group, or all key symptoms, could not be assigned a cause of death and were excluded from further analyses.

InSilicoVA reports CSMFs using the WHO standard verbal autopsy cause list of 61 causes of death (level 3). Notably, InSilicoVA causes categorised as other and unspecified (eg, other and unspecified infections) included deaths without enough information for the algorithm to identify a more specific cause within the standard verbal autopsy cause list. Causes were then grouped into nine categories (level 2) and four broad categories (level 1) for visualisation in this paper (appendix 1 pp 14–15). The 95% credible intervals (CrIs) of

	Study setting	Years of data included in this analysis*	Frequency of demographic data collection	Population size for the latest year included	Questionnaire
Nairobi, Kenya	Urban, informal settlements	2002–18	Every 6 months	98 500	Adapted INDEPTH questionnaire†
Karonga, Malawi	Rural	2003–17	Continuous (village informants)	43 600	Locally developed questionnaire
Agincourt, South Africa	Rural	1995–2019	Annual	113 700	Locally developed questionnaire (1992–2012); WHO 2012 questionnaire (2012–16); WHO 2016 verbal autopsy questionnaire (2016–19)
uMkhanyakude, South Africa	Rural	2000–18	Every 6 months	112 200	Locally developed questionnaire, with revisions introduced in 2003 and 2011 (2000–16); WHO 2016 questionnaire (2017–18)
Ifakara, Tanzania	Urban, small urban settlement	2008–14	Triannual up to 2012; biannual after 2012	35 400	WHO 2007 questionnaire (2008–14)
Kisesa, Tanzania	Rural	1995–2019	Variable (between 4 months and 1 year)	39 900	Locally developed questionnaire (1994–2002); INDEPTH questionnaire (2003–07); WHO 2007 questionnaire (2008–19)
Masaka, Uganda	Rural	2008–19	Annual	14 200	Locally developed questionnaire (2008–14); WHO 2012 questionnaire (2014–16); WHO 2016 questionnaire (2017–19)
Rakai, Uganda	Rural	1999–2019	Every 12–16 months	23 500	Locally developed questionnaire (1999–2013); WHO 2012 questionnaire (2014–19)
Manicaland, Zimbabwe	Rural	1999–2013	Every 2–3 years	7700	Locally developed questionnaire

HDSS=health and demographic surveillance system. *Calendar periods are determined by the inclusion of only years with at least ten deaths identified in the demographic surveillance that had a verbal autopsy, from 1995 up to 2019. †INDEPTH questionnaire was a standardised verbal autopsy questionnaire used in the International Network for the Demographic Evaluation of Populations and Their Health.

Table 1: **Verbal autopsy data availability by HDSS site**

For more on the **INDEPTH questionnaire** see http://www.indepth-network.org/resources/tools

	HDSS deaths	Number of HDSS deaths with a verbal autopsy	Verbal autopsy coverage among total HDSS deaths	Number of deaths with a verbal autopsy assigned cause of death by InSilicoVA			
				Total	Adolescent (12–19 years)	Adult (20–59 years)	Older adult (≥60 years)
Nairobi, Kenya							
Total	4442	3923	88·3%	3835	210	3186	439
Women	1813	1595	88·0%	1559	74	1282	203
Men	2629	2328	88·6%	2276	136	1904	236
Karonga, Malawi							
Total	2461	2461	100%	2461	113	1252	1096
Women	1234	1234	100%	1234	56	574	604
Men	1227	1227	100%	1227	57	678	492
Agincourt, South Africa							
Total	15 194	14 948	98·4%	14 823	446	8852	5525
Women	7403	7267	98·2%	7203	230	4010	2963
Men	7791	7681	98·6%	7620	216	4842	2562
uMkhanyakude, South Africa							
Total	18 735	18 683	99·7%	17 754	556	12 161	5037
Women	9281	9250	99·7%	8784	276	5666	2842
Men	9454	9433	99·8%	8970	280	6495	2195
Ifakara, Tanzania							
Total	1705	1011	59·3%	1007	31	402	574
Women	940	553	58·8%	551	19	212	320
Men	765	458	59·9%	456	12	190	254
Kisesa, Tanzania							
Total	3528	2369	67·1%	2135	152	1276	707
Women	1679	1116	66·5%	994	68	593	333
Men	1849	1253	67·8%	1141	84	683	374
Masaka, Uganda							
Total	1228	971	79·1%	968	37	405	526
Women	582	448	77·0%	448	17	184	247
Men	646	523	81·0%	520	20	221	279
Rakai, Uganda							
Total	3210	2529	78·8%	2525	138	1492	895
Women	1629	1296	79·6%	1295	66	720	509
Men	1581	1233	78·0%	1230	72	772	386
Manicaland*, Zimbabwe							
Total	1981	1066	53·8%	1062	..	1062	..
Women	1230	658	53·5%	656	..	656	..
Men	751	408	54·3%	406	..	406	..

HDSS=health and demographic surveillance system. *In Manicaland, HDSS deaths were identified for all household residents in the study area; however, only approximately two-thirds of household residents (with restriction to adults aged 15–54 years for most survey rounds) were randomly selected for inclusion to a cohort for more detailed follow-up including verbal autopsy, leading to lower verbal autopsy coverage by design. All analyses of Manicaland data were restricted to adults aged 20–54 years.

Table 2: **Verbal autopsy deaths by HDSS site**

For more on the **analysis codes** see https://github.com/sinafala/alpha-network-va

CSMFs were the 2·5% and 97·5% percentiles of the CSMF distributions. Injuries were an exception. If an injury was reported, InSilicoVA assigned this as the cause of death with exact probability of 1·0 (no uncertainty). Cause-specific mortality rates (CSMRs) were derived by applying CSMFs to all-cause mortality rates. Results from any subgroups with fewer than ten deaths with verbal autopsy were not presented due to concerns about the stability of estimates. Comparative analyses between HDSS sites focused on the period 2010–14, the most recent calendar period when all HDSS sites were able to contribute. Additional data were presented for earlier and later periods for HDSS sites if they were available.

Data harmonisation and cleaning was conducted with Stata 15.1, and the analysis was conducted in R (version 4.2.0) with the openVA package (version 1.1.1).[23] Analysis codes are publicly available on GitHub. The reporting of methods and results follows GATHER guideline (appendix 1 p 16).

Role of the funding source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of this manuscript.

Results

A total of 52 484 deaths and 5 157 802 person-years from 1 071 913 individuals were reported across the nine HDSS sites. Of 52 484 deaths, 47 961 (91·4%) had a verbal autopsy, and of those with a verbal autopsy, 46 570 (97·1%) were assigned a cause of death by InSilicoVA. The population sizes and the total numbers of deaths varied substantially between the HDSS sites, with nearly two-thirds of deaths occurring in uMkhanyakude and Agincourt due to large population sizes under surveillance (table 2). Agincourt, Karonga, and uMkhanyakude had full or nearly full verbal autopsy coverage for all identified deaths (table 2; appendix 1 pp 17–18). Ifakara, Kisesa, Manicaland, Masaka, Nairobi, and Rakai had moderate coverage with fluctuations over time.

Trends in all-cause mortality rates over time by age group, sex, and HDSS site are shown in figure 1 (appendix 1 pp 19–20). Across all age groups, there was a tendency toward declining mortality rates over time, with the most notable declines from the period 2005–09 and among adults aged 20–59 years. Compared with other HDSS sites, the mortality declines started later in Agincourt and Manicaland. The most rapid decreases among adults were observed between the periods 2005–09 and 2010–14 in uMkhanyakude and Manicaland, and between 2000–04 and 2005–09 for Rakai. Over time, we found a convergence of the mortality rates across the HDSS sites. Men had slightly higher or similar mortality compared with women in 2010–14 and 2015–19, except for older adults in Nairobi. Between-HDSS site differences in mortality rates were greater among men compared with women, especially for adults aged 60 years and older.

The CSMFs varied by HDSS sites, age group, and sex for the 2010–14 period. The 2010–14 period was the most recent period for which all HDSS sites had data (appendix 1 p 21).

Among adolescent girls, the percentage of deaths attributed to communicable diseases ranged from 26·0% (95% CrI 12·2–42·5) in Nairobi to 55·7% (44·8–65·2) in uMkhanyakude. For most HDSS sites, communicable diseases were mainly attributable to HIV or tuberculosis, meningitis or sepsis, and pneumonia. The CSMF for maternal causes was high in Rakai (20·7% [95% CrI 2·3–57·8]) and Agincourt (14·3% [5·5–25·4]). There was a high percentage of injury-related deaths among men, particularly in Nairobi (87·8%), uMkhanyakude (55·9%), and Kisesa (50·0%). HIV or tuberculosis was among the leading causes of death in adolescent boys in all HDSS sites, with a CSMF of 5·8% (95% CrI 1·3–9·9) in Nairobi and up to 30·2% (21·9–37·3) in uMkhanyakude. In Rakai, although HIV or tuberculosis was less than 2% in the adolescent age group, a high percentage of deaths were attributed to other and unspecified infectious diseases in both adolescents and adults, potentially including HIV/AIDS deaths with inadequate information for more specific classification (appendix 1 pp 24–25).

Among adults aged 20–59 years, infectious diseases including HIV and tuberculosis accounted for the highest percentage of deaths in all HDSS sites, with assigned HIV and tuberculosis being the dominant cause of death for women and men, except in Rakai and Manicaland where other or unspecified communicable diseases made up the largest percentage of deaths. Non-communicable diseases generally accounted for a similar or slightly higher percentage of deaths for adults compared with adolescents. In Nairobi, for example, the percentage of deaths assigned to non-communicable disease in all adolescents and adults aged 12 and older in 2010–14 was 29·9% (95% CrI 27·8–32·2), in adolescents it was 10·3% (95% CrI 4·1–17·8), and in adults aged 20–49 it was 25·8% (95% CrI 22·5–29·3). The percentage of deaths attributed to maternal causes was lower in adults than in adolescents. For example, in uMkhanyakude, 2·0% (95% CrI 1·1–3·2) of deaths were attributed to maternal causes among adults compared with 8·7% (3·1–16·2) among adolescents. Among men, injuries were still among the leading causes, although this was a lower percentage than observed among adolescents, ranging from 12·9% in Rakai to 45·8% in Nairobi for adult men.

Differences between men and women among adults aged 60 years and older were less notable than those among adolescents and adults (appendix p 21). Non-communicable diseases accounted for more than half of older adult deaths for all the HDSS sites except for Rakai, ranging from 56·3% (95% CrI 47·5–64·9) among men in Masaka to 77·8% (71·4–83·2) among women in Karonga, with some variation in the relative contribution of neoplasms and cardiovascular disease. With the exception of uMkhanyakude and Kisesa, HIV and tuberculosis only accounted for a small fraction of deaths due to specified communicable disease among adults aged 60 years and older, with other communicable diseases, such as pneumonia, accounting for a greater percentage of these deaths. Among adults aged 60 years and older, a lower percentage of deaths were attributed to injuries compared with adults and adolescents. The highest fraction of deaths attributed to injuries among adults aged 60 years and older was for men in Nairobi (13·5%) and for women in Kisesa (11·5%).

Figure 2 shows the CSMFs and figure 3 shows the CSMRs for each available calendar period from 1995 to 2019 for the total study population aged 12 years and older in each HDSS site (with further breakdown by age group and sex provided in appendix 1 pp 22–23).

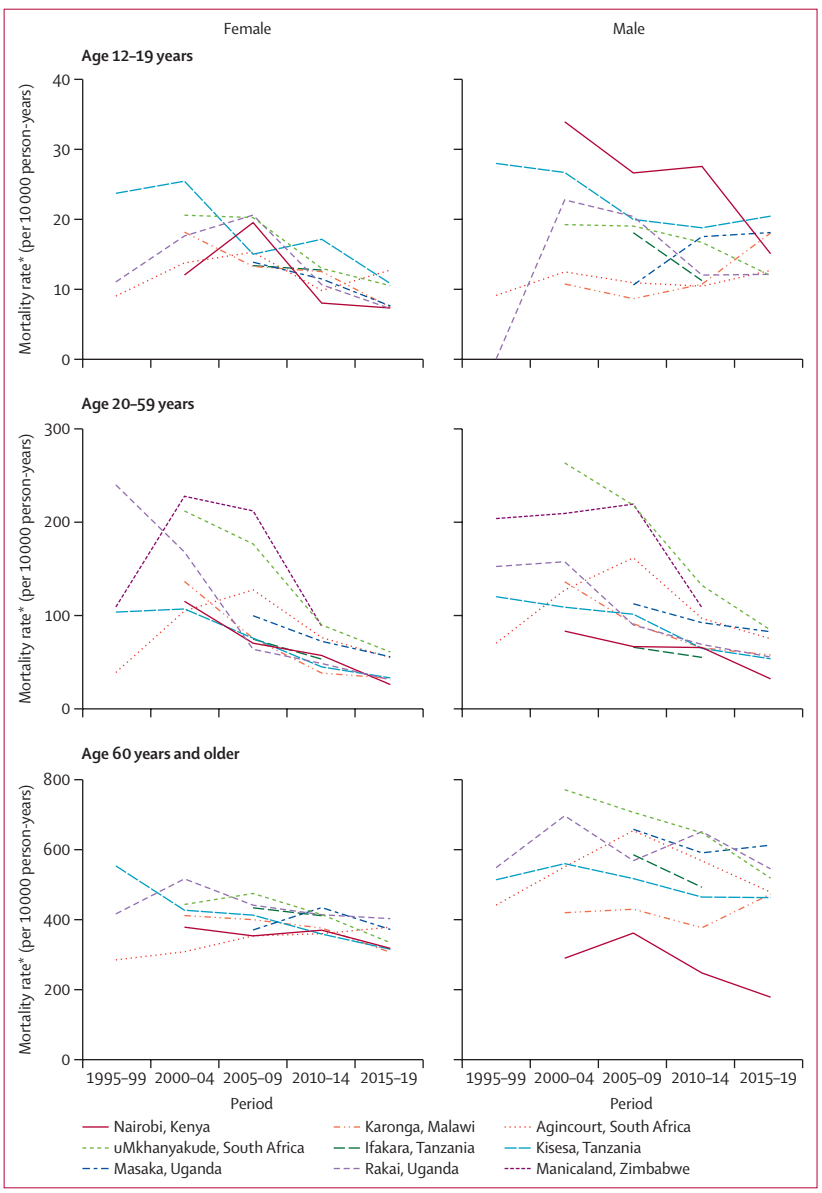

Figure 1: **All-cause mortality rates by sex and age group, by HDSS site**
HDSS=health and demographic surveillance system. *The y-axis scale (ie, mortality rates per 10 000 person-years) varies by age group.

The CSMFs and CSMRs for three levels of cause of death (appendix pp 14–15), by sex, age group, HDSS site, and calendar period, are available on GitHub (appendix 1 p 24).

The percentage of deaths attributed to HIV or tuberculosis changed substantially among adults aged 20–59 years in some of the HDSS sites (eg, Agincourt, Ifakara, women in Masaka, and men in Nairobi), whereas other HDSS sites showed no substantial changes (eg, Karonga and Kisesa). Specifically in Agincourt, there was an increasing percentage of deaths attributed to HIV/AIDS from 1990–94 up to varying periods between 2000 and 2009 depending on sex, followed by declines in more recent calendar periods (figure 2; appendix 1 p 22). We did, however, find slightly different trends over time when looking at the CSMRs. For men in Agincourt, there was a drop in the percentage of deaths attributed to HIV and tuberculosis from 50·1% (95% CrI 46·8–53·4) in 2000–04 to 45·9% (43·3–48·5) in 2005–09; however, due to mortality rates increasing between these periods, there was an increase in the HIV and tuberculosis mortality rate from 63·7 (59·5–67·9) per 10 000 person-years in 2000–04 to 74·1 (69·9–78·3) per

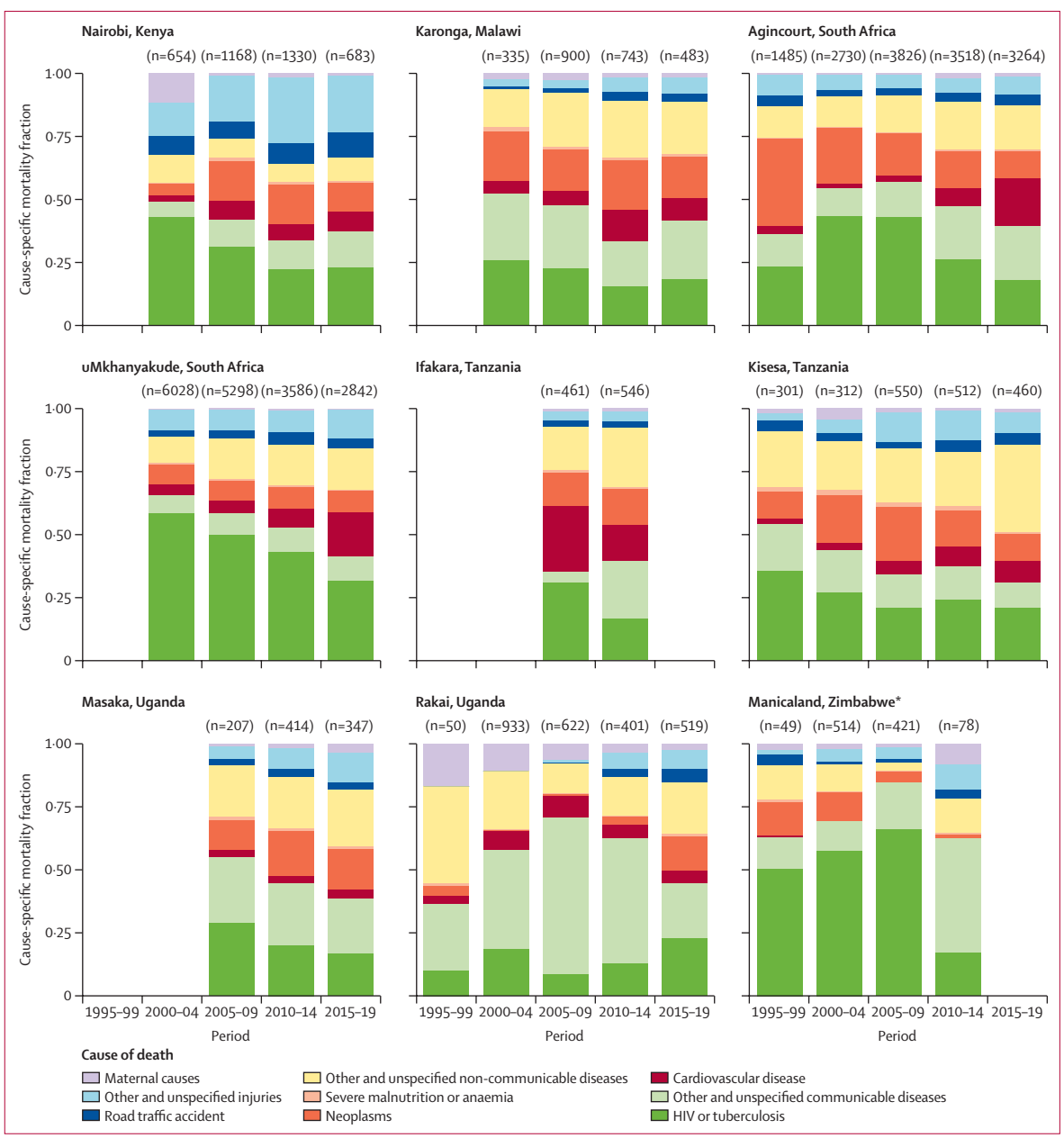

Figure 2: **Cause-specific mortality fractions in people older than 12 years, by HDSS site and calendar periods**
HDSS=health and demographic surveillance system. *Manicaland data was only in adults aged 20–54 years.

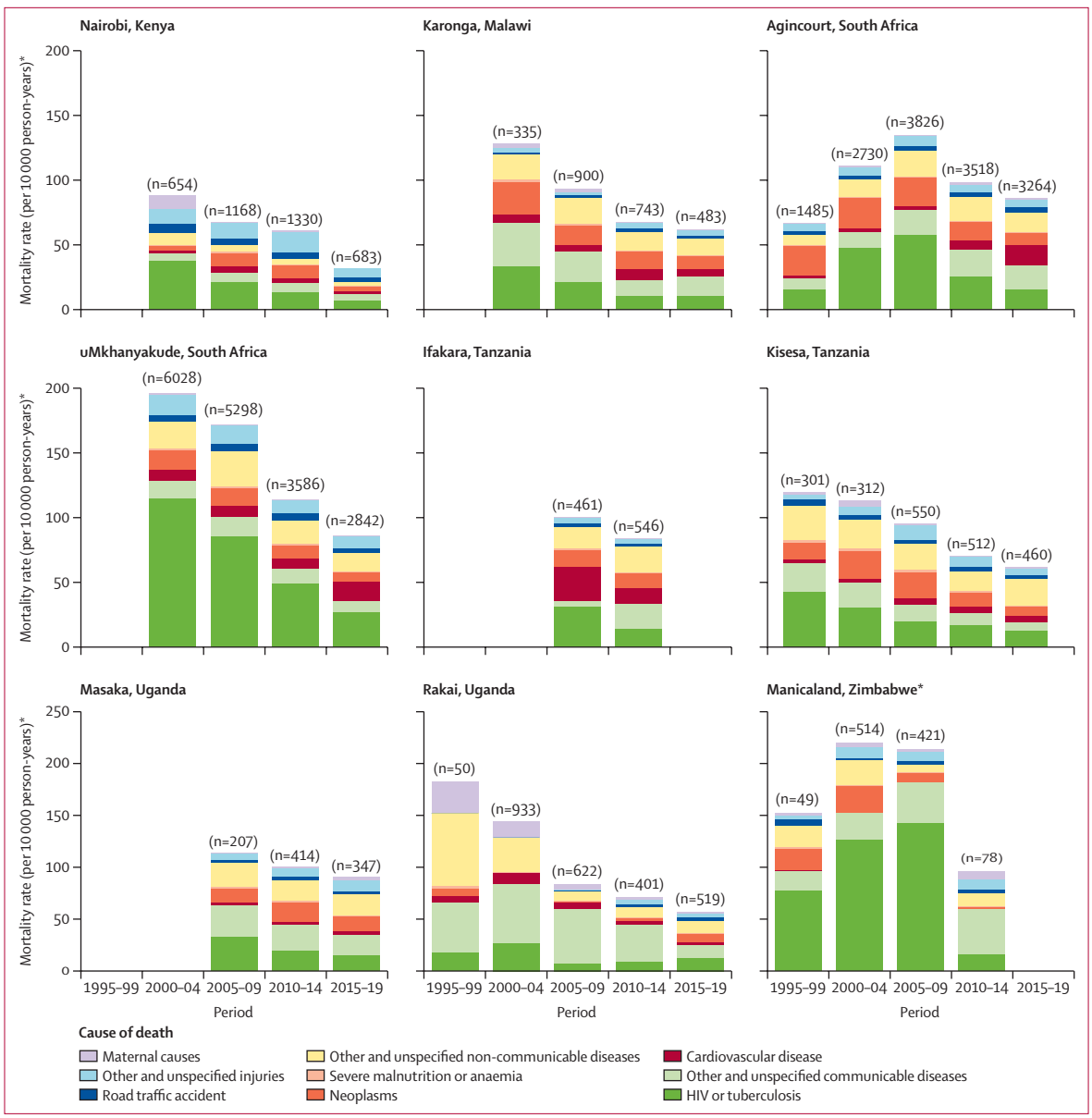

Figure 3: **Cause-specific mortality rates in people older than 12 years, by HDSS site and calendar periods**
HDSS=health and demographic surveillance system. *Manicaland data was only in adults aged 20–54 years.

10 000 person-years in 2005–09. For the other HDSS sites, we found declines in the HIV and tuberculosis mortality rates over the study years, although generally these declines started from an earlier period in Agincourt compared with all other HDSS sites (figure 3; appendix 1 p 23).

Except for a few specific subgroups (eg, women aged 12 years and older in Ifakara and women aged 60 years and older in Masaka), the percentage of deaths attributed to non-communicable diseases generally stayed stable over time. The relative contribution of neoplasms, cardiovascular disease, and other non-communicable diseases did change in some groups. In Kisesa, the percentage of deaths in women aged 60 years and older attributed to cardiovascular disease increased from 10·3% (95% CrI 4·7–17·2) in 2005–09 to 20·4% (13·1–28·6) in 2015–19.

There was variation between the HDSS sites in trends in injury-related mortality. The injury-related mortality rates were stable over time for all HDSS sites, except among Kisesa adolescent boys (although there were a small number of deaths) and Nairobi. In Nairobi, for both women and men, we found declines in injury-related mortality rates among adolescents and adults from 2010–14 to 2015–19, while at the same time increases in injury-related mortality rates among adults aged 60 years and older.

Discussion

This study provides an important overview of the main causes of death in adolescents and adults and documents changing patterns in causes of death from 1995 to 2019 using data from the deaths of more than 52 000 individuals and 5 million person-years from six countries in eastern and southern Africa. We found some consistent patterns over time across the different HDSS sites including mortality rates decreasing, particularly among adults aged 20–59 years. There were also clear age patterns in the cause of death distributions with HIV and tuberculosis being the leading cause for adults and non-communicable diseases the leading cause for adults aged 60 years and older for the 2010–14 period in most of the HDSS sites.

We observed some similar and some divergent patterns in changes in cause of death over time. For most HDSS sites, we saw decreases in HIV and tuberculosis mortality rates among adults, which appeared to explain most of the declines in all-cause mortality rates. This trend has been reported in other studies[11,24] and probably reflects the introduction and roll-out of antiretroviral therapy and broader social and environmental changes during the study period (appendix 1 pp 5–8).[25] These declines appear to have stalled in the most recent study periods in some HDSS sites, such as Karonga and Kisesa. Elsewhere, despite recent declines, HIV and tuberculosis mortality rates remained high (eg, Agincourt and uMkhanyakude). Further commitment will be required to ensure widespread access to testing and treatment and to ensure treatment retention by those with HIV and tuberculosis, to further improve survival of adults in these areas. Non-communicable disease-related mortality rates were stable in most of the HDSS sites, which is consistent with Global Burden of Disease findings for sub-Saharan Africa[26] and is probably explained by the rural location of most of our HDSS sites, where the prevalence of non-communicable diseases is generally lower than in urban areas.[27]

There were different patterns across the HDSS sites for other causes of deaths. The leading causes of death among adolescents were non-communicable diseases in Kisesa, injuries in Nairobi, and communicable diseases (including HIV and tuberculosis) in all other HDSS sites. The fraction of deaths due to communicable diseases were high among adults aged 60 years and older in Rakai compared with adults aged 15–59 years, but not in the other HDSS sites. Trends in maternal mortality rates also varied with some HDSS sites showing little change and others showing declines over time (notably, in Kisesa, Nairobi, Rakai, and uMkhanyakude). Such declines are likely to be associated with (1) decreases in HIV prevalence, because HIV has been linked to increased risk of maternal mortality,[28] and (2) initiatives to reduce the risk of direct obstetric complications, such as increasing institutional deliveries assisted by skilled attendants[29] and removing financial barriers to accessing maternity care.[30]

Given this variation, improving adolescent and adult survival requires local-level data, disaggregated by important individual-level characteristics of the population (eg, sex and age), and extrapolating from one country to another is inappropriate. For example, in Nairobi, we see particularly high proportions and rates of injury-related deaths among adolescent boys, most of which were attributable to assault. Interventions that could be considered to target this burden include programmes addressing high-risk behaviours, such as improving school transition to secondary school, reducing the pronounced school dropout rates,[31] preventing substance abuse,[32] improving employment opportunities, and enhancement of social and legal infrastructure in the informal settlements where the Nairobi study participants live.

Although direct comparison with previous publications is challenging due to differences in age groups and calendar periods, our results generally align with existing estimates in terms of levels and trends in CSMFs from the same study areas. For example, in Nairobi, the share of non-communicable diseases is about 29·9% (95% CrI 27·8–32·2) for adolescents and adults aged 12 and older for 2010–14 in our study, which is close to the 23% for adults aged 18 and older reported in a previous publication using the same data source and algorithm.[24] Compared with a study by Mberu and colleagues,[11] also using the Nairobi HDSS data for the period 2005–09 but only for adults aged 15 years and older, we found a similar ranking of broad causes of death (with communicable diseases accounting for the highest percentage of deaths, followed by non-communicable diseases, and then injuries) despite differences in the algorithm used. The leading causes of death in Agincourt were the same as previous findings using the InterVA algorithm on the same HDSS data, specifically, HIV and tuberculosis, pneumonia, and digestive neoplasms were the top three causes in the early 2010s.[25,33]

Verbal autopsy is an inherently imprecise tool: it assigns cause of death on the basis of signs and symptoms reported from proxy respondents recalling details weeks, months, or sometimes even years after the death occurred. For causes of death that have distinctive symptoms or circumstances (eg, deaths due to assault or maternal causes) misclassification is less likely, but some communicable and non-communicable diseases have common symptoms and assigning cause of death is challenging. For example, some HIV and tuberculosis deaths could have been classified as unspecified infections, particularly if there were atypical verbal autopsy symptom patterns or missing data for key symptoms linked with HIV or tuberculosis. In Rakai, we observed low rates of HIV and tuberculosis deaths and much higher rates of other and unspecified infections (appendix 1 pp 24–25); some HIV and tuberculosis deaths were probably classified as unspecified infections.

Strengths of this study include the large sample size, the long study period, and the standardised analytical

approach that facilitated comparison over time and between different HDSS settings. Our study included comprehensive data for adolescents, which is important as this group is often omitted from mortality analyses due to small numbers. Finally, this study used the InSilicoVA algorithm, which is an easy-to-use, validated algorithm widely used for verbal autopsy cause assignment.[22] Although different methods producing substantially different cause of death trends and patterns at the population level is unlikely, future studies should investigate the robustness of our findings compared with alternative methods of cause of death assignment.[21,34]

There are several limitations that need to be considered. First, although the overall number of deaths included is high, there were small numbers of deaths in some subgroups (eg, sex and age groups for a given HDSS). If these were fewer than ten, we did not calculate CSMFs. Second, local development and adaptation of the verbal autopsy questionnaire and different practices in data collection and management might affect comparability between the HDSS sites. We have put extensive effort into data harmonisation to minimise the impact of changing questionnaires over time, but we urge caution in comparing estimates between the HDSS sites before 2010 when most questionnaires were developed locally, making cross-study comparison challenging. Third, the HDSS sites were set up as censuses within subnational areas rather than nationally representative samples, and so caution needs to be exercised in extrapolating these findings to other areas within a given country. Additionally, for a small number of the HDSS sites there were moderate rates of verbal autopsy coverage in some calendar periods (eg, Ifakara 2010–14, Kisesa 2000–04, and Rakai 2010–2014). Although generally these estimates showed good continuity with surrounding estimates, we urge caution in the interpretation of these results. Fourth, we have focused on quantifying cause-specific mortality and have not attempted to quantify disability arising from different diseases because we did not have sufficient data to do so.

This study shows the value of health and demographic surveillance—specifically where there is comprehensive coverage of verbal autopsy—in providing essential information on cause of death. Historically, assigning cause of death using verbal autopsy was a laborious, time-intensive, and expensive process, requiring physicians to review the verbal autopsy. This study provides some of the most extensive cause of death comparisons by sex, age, setting, and time across eastern and southern Africa and highlights the need for a strategic focus at the local level to continue to improve survival among adolescents and adults in the region.

Contributors

SJC, CC, MM, and YC conceptualised the study. MM, CC, KK, CK, KH, EG, AD, MU, SG, CN, LM, RN, AZ, and TL managed and prepared raw data and reviewed and interpreted the results. YC conducted data analysis and produced the figures and tables. YC, CC, and MM prepared and revised the first draft. All authors critically reviewed the manuscript and approved the final version. YC, MM, and CC accessed and verified the data, and YC, SJC, CC, and MM were responsible for the decision to submit the manuscript for publication.

Equitable partnership declaration

The authors of this paper have submitted an equitable partnership declaration (appendix 2). This statement allows researchers to describe how their work engages with researchers, communities, and environments in the countries of study. This statement is part of *The Lancet Global Health*'s broader goal to decolonise global health.

See **Online** for appendix 2

Declaration of interests

LM reports research grants from Wellcome Trust, the US National Institutes of Health (NIH), and Medical Research Council Centre for Global Infectious Disease Analysis funding from the UK Medical Research Council (MRC) and the UK Department for International Development. SG reports research grants from Wellcome Trust, NIH, Bill & Melinda Gates Foundation, and WHO; financial support for attending meetings and travel from Imperial College London; and participation on a Data Safety Monitoring Board at Kings College London and as a board member at Biomedical Research Training Institute, Harare, Zimbabwe. CC reports research grants from NIH. SJC reports research grants from NIH; and acting as a paid consultant on verbal autopsy implementation methods and software for two non-governmental organisations (Vital Strategies and CDC Foundation). All other authors declare no competing interests. LM, CN, and SG have received funding from the MRC Centre for Global Infectious Disease Analysis (reference MR/R015600/1), jointly funded by the UK MRC and the UK Foreign, Commonwealth & Development Office (FCDO), under the MRC and FCDO Concordat agreement and this centre is also part of the European and Developing Countries Clinical Trials Partnership programme supported by the EU; and LM, CN, and SG have received funding by Community Jameel.

Data sharing

The codes for data processing and analysis are publicly available on GitHub (https://github.com/sinafala/alpha-network-va). Processes for requesting access to data or to data collection tools (eg, verbal autopsy questionnaires) will be provided upon request.

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