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Medical causes of admissions to hospital among adults in Africa: a systematic review

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Background: Despite the publication of several studies on the subject, there is significant uncertainty regarding the burden of disease among adults in sub-Saharan Africa (sSA).

Objectives: To describe the breadth of available data regarding causes of admission to hospital, to systematically analyze the methodological quality of these studies, and to provide recommendations for future research.

Design: We performed a systematic online and hand-based search for articles describing patterns of medical illnesses in patients admitted to hospitals in sSA between 1950 and 2010. Diseases were grouped into bodily systems using International Classification of Disease (ICD) guidelines. We compared the proportions of admissions and deaths by diagnostic category using $\chi^2$.

Results: Thirty articles, describing 86,307 admissions and 9,695 deaths, met the inclusion criteria. The leading causes of admission were infectious and parasitic diseases (19.8%, 95% confidence interval [CI] 19.6–20.1), respiratory (16.2%, 95% CI 16.0–16.5) and circulatory (11.3%, 95% CI 11.1–11.5) illnesses. The leading causes of death were infectious and parasitic (17.1%, 95% CI 16.4–17.9), circulatory (16%, 95% CI 15.3–16.8) and digestive (16.2%, 95% CI 15.4–16.9). Circulatory diseases increased from 3.9% of all admissions in 1950–59 to 19.9% in 2000–2010 (RR 5.1, 95% CI 4.5–5.8, test for trend p <0.00005). The most prevalent methodological deficiencies, present in two-thirds of studies, were failures to use standardized case definitions and ICD guidelines for classifying illnesses.

Conclusions: Cardiovascular and infectious diseases are currently the leading causes of admissions and inhospital deaths in sSA. Methodological deficiencies have limited the usefulness of previous studies in defining national patterns of disease in adults. As African countries pass through demographic and health transition, they need to significantly invest in clinical research capacity to provide an accurate description of the disease burden among adults for public health policy.

Keywords: adults; Africa; medical admissions; health; transition; ICD; cause of death

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rely on research evidence for guiding policy interventions (17). As this transition occurs, accurate data on the burden of illnesses will be needed as there will be a double burden of endemic non-communicable and residual communicable diseases (2, 15, 18).

Community-based studies provide an accurate picture of the profile of the diseases of adults because they minimize the bias, inherent in hospital-based studies, of variable access to health care (19, 20). However, these surveys are expensive undertakings, and useful information could be gained from analysis of well-conducted routine population and clinical surveillance activities. There are currently substantial efforts to improve vital event registration including the introduction of verbal autopsy methods to better describe causes of death. However, the shortcomings of health facility-based studies have not been systematically analyzed in order to improve future work. Here we report a systematic review of descriptive studies of medical illnesses in adults admitted to hospitals in sSA between 1950 and 2010 to determine the causes of admission and death and to characterize the methodological features of such studies that are likely to yield useful data in the future.

Methods

Literature search

We searched PubMed, African Index Medicus, African Journals OnLine (AJOL) and EMBASE for articles describing the pattern of disease among adults admitted to hospital in Africa. The Internet search was performed on 3 July 2011 using the search filter ‘(medical OR hospital) AND admissions AND adults AND Africa’. We screened titles and abstracts of articles that met specific inclusion criteria and read those that were available online or from academic libraries that we had access to. We reviewed reference lists of selected articles to identify additional secondary articles not found during the online search. Our review was limited to articles either written in or translated into English.

Studies were eligible for inclusion in the review if they were conducted among adult patients admitted to hospitals in sSA between 1950 and 2010. We excluded studies if data on adult admissions could not be extracted from them, if the study was conducted during a period of war, if the articles focused on specific age sub-groups (e.g. adolescents, geriatrics), or if the focus of the study was on a single factor as a cause of admissions to hospital, for example, HIV, injuries or obstetric admissions.

Data extraction

We designed a data extraction form and entered the data from each paper into the form, which was later cross-checked for accuracy. The following data were collected from each study: country where the study was performed, study period, type of hospital, and number and causes of admissions and deaths. The diseases reported were grouped into body systems according to International Classification of Diseases (ICD) guidelines (21). We used the χ² test to compare proportions of observations in each diagnostic category. We calculated risk ratios for disease changes over time by dividing the proportion of admissions and deaths in each category per decade by the corresponding value in the baseline period (1950–9) and we tested the trend in the sub-category with greatest changes by using the χ² test for linear trend. p Values reported are two-sided and proportions reported with 95% confidence intervals (CIs). Data were analyzed using STATA® v11.

Review of methodological quality

We evaluated each paper using a uniform set of questions designed to gauge the quality of the studies. The criteria were adapted by the authors from the principles of descriptive epidemiology (22, 23) and the STROBE statement (24). The criteria and their justification are outlined in Table 1. Each criterion was assigned relative weights based on the authors’ assessment of their influence on study quality. We calculated the sum of all criteria scores to provide an overall methodological score for each study. We performed a methodological sensitivity analysis for the cause of death analysis by comparing the causes derived from studies ranked above the 75th percentile in their methodological score with the causes in the baseline analysis.

Results

The online and hand-based search identified 56 relevant and obtainable full-text articles; 26 of these met the exclusion criteria leaving 30 full-text articles for inclusion in the review (Fig. 1). The geographic distribution of these studies by country and the number of studies published per year are shown in Fig. 2. The methodological characteristics of the studies included in the review are summarized in Table 2. The supplementary appendix (Table S1) lists the studies that were excluded, with reasons.

Methodological quality

The median score for all the studies after applying weighted points to each aspect of the studies (Table 1) was 55% (IQR 47.2–63.9). Only one study (25) satisfied all criteria on methodological quality.

Study design

Only 8 (27%) studies were prospective in nature, the most recent one having been completed in 1995 (25–32). Five of these prospective studies were conducted in university teaching hospitals that had high-level staff and relatively advanced diagnostic facilities. However, given their urban
<table>
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<th>Criterion</th>
<th>Justification</th>
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| **What was the study design?**  
Weight: 4 points | Case ascertainment and record keeping is likely to be superior in prospective studies. |
| **Were case definitions used to define diseases reported?**  
Weight: 6 points | Comparisons can only be made between different studies if they adhered to standard case definitions, preferably those derived from the World Health Organization. For example, failure to use standard definitions has led to over-estimation of the burden of malaria as many patients with febrile illness in Africa are incorrectly classified as having malaria (72). |
| **Were the diseases coded using the International Classification of Diseases (ICD)?**  
Weight: 4 points | Established in 1948, the ICD is the international standard diagnostic classification for all general epidemiological, many health management purposes and clinical use (73). Due to the paucity of diagnostic facilities available in most settings in sub-Saharan Africa, we checked for the broad diagnostic categories of illnesses within the ICD, limiting classification to three character subcategories. Malaria for example would be classified as B50. |
| **Did the hospital have a defined set of criteria for admitting patients?**  
Weight: 6 points | The pattern of illness in any study is a function of (a) the pattern of disease in the local community and (b) the probability of admission with a particular condition once acquired. Patterns and policies of admission can therefore bias hospital data, more or less, as an indicator of the community burden of disease. Some hospitals only accept referrals, while others may have special units with certain diseases such as tuberculosis. |
| **What was the cadre of staff leading care provision at the hospital?**  
Weight: 4 points | It is recognized that there is a significant shortage of medical staff in Africa (50, 74) and that the accuracy of diagnoses made are dependent on the level of training of the personnel available (75). We categorized hospital staff into 3 groups of increasing training and competency and weighted studies on this basis:  
1 point: Non-physician health workers – composed of clinical officers and physician assistants who on average have had 3-4 years of medical training (76).  
2 points: Medical Officers – staff who had a basic medical degree (5-6 years of training at university) with no specialization or who are in the process of specializing, variously referred to as Medical Officers, House Officers, or Residents.  
4 points: Consultants – staff who had an advanced medical training beyond the basic medical degree and were providing specialist care.  
For each study, the highest level of staff available at the hospital during the study period was recorded. |
| **What diagnostic facilities were available?**  
Weight 6 points | The availability of diagnostic facilities is critical for diagnosing some illnesses and facilities lacking basic diagnostic equipment would not be able to accurately describe disease patterns apart from making syndromic diagnoses. Studies could fall into one of 3 categories, weighted as shown:  
2 points: health facilities that had the most basic diagnostic facilities, limited to microscopy, urinalysis and no imaging capability.  
4 points: Health facilities in this category had as a minimum access to basic imaging equipment such as X-ray, laboratory tests including full blood count and chemistry panels.  
6 points: These facilities had access to more advanced imaging and laboratory tests relative to other hospitals in the region. Tertiary referral and teaching hospitals were expected to fall under this category. |
| **Were case fatality/mortality rates reported?**  
Weight: 6 points | Mortality rates give an indication of the severity of the illnesses seen although this is subject to confounding by factors such as availability of medications and quality of care given. In addition, if mortality data are given by diagnostic category this allows us to estimate the ranking of disease burden both at the level of hospital admission and total (in-patient) mortality. We examined articles for reporting on case fatality or overall in-hospital mortality. |

*aCriteria and weights were developed by the authors, see text.*
location the results of these studies may not have been representative of the disease pattern in the majority of the population in the countries studied, a fact acknowledged by all the authors.

Use of standard case definitions
Four studies (13%) provided case definitions for the illnesses that were studied (25–26, 33, 34). One study conducted in Uganda (30) provided a case definition for only one condition (anemia) but this differed from the standard WHO definition (35).

Use of international classification of diseases coding
All of the studies categorized illnesses into various bodily systems as a result of the multiplicity of diagnoses. However, only one third of the studies (25, 32, 34, 36–41) used the WHO recommended ICD system that enables comparisons between studies and aggregation of data across different sites. In one study the coding of illnesses into ICD categories was done retrospectively (32).

Admission criteria
Thirteen studies mentioned the presence of admission criteria for patients to the hospitals where the studies were conducted but only five specified what these criteria were. Two of these studies were conducted in the same hospital at different time points, thus reducing the number of hospitals in which admission criteria were reported to four. In the five reports where admission criteria were described (25, 30, 32, 42, 43), they consisted of seriousness of the illness, referral from lower level facilities, and suitability for teaching and research with patients not meeting any of these criteria being referred to other facilities. The remaining reports did not specify what the admission criteria were.

Cadre of hospital staff
Most of the studies were conducted in hospitals that had consultants as the highest level of staff, and these were responsible for determining the final diagnosis given to patients. In four studies, all of which were conducted in rural areas, Medical Officers served as the highest cadre of medical staff (29, 34, 40, 44). In two studies, the level of training of the staff at the hospitals involved was not reported (45, 46).

Reporting on diagnostic facilities
We postulated that hospitals located in urban areas such as university teaching hospitals would have more advanced diagnostic facilities. Of the 14 studies carried out in university/teaching hospitals nine reported having class III diagnostic facilities (26–28, 30, 42, 43, 47–49). These included more advanced imaging, pathology, and biochemical tests. In three studies, autopsies were performed on more than 50% of deaths (30, 43, 49). Only one study carried out in a rural hospital had advanced diagnostic facilities thus limiting the range and accuracy of diagnoses for rural studies (40).

Reporting on case fatality rates
We found 18 (60%) studies that either reported case fatality rates for individual illnesses or overall in-hospital mortality for patients observed during the study periods. Three quarters of the studies giving mortality rates were conducted in hospitals located in urban areas.

Leading causes of hospital admission
We found 27 studies reporting data on 86,307 medical admissions for the period from 1950–2010 (Table S2). The proportions of admissions and deaths by ICD diagnostic category over the period are shown in Fig. 3. Infectious and parasitic diseases, including malaria, bacterial diseases, and HIV disease, were the leading cause of admission over the period accounting for 19.8% (95% CI 19.6–20.1) of all admissions. Respiratory illnesses were second accounting for 16.2% (95% CI 16.0–16.5) of
admissions while diseases of the circulatory system were third at 11.3% (95% CI 11.0–11.5). When we restricted the analysis to admissions from studies that ranked above the 75th percentile in the methodological score, infectious and parasitic diseases, and respiratory illnesses remained the leading causes of admission, accounting for 27.4% (95% CI 26.9–27.9) and 18.4% (95% CI 18.0–18.9) of all admissions. The remaining leading causes of admission were in descending order: digestive system 13.9% (95% CI 13.6–14.3), genitourinary system 10.6% (95% CI 10.3–11.0) and circulatory system disorders 7.4% (95% CI 7.1–7.7). The class of disease among all admissions varied with time in decades ($\chi^2 = 14,000$, df 30; p < 0.0005). The proportion of admissions due to circulatory system disorders increased five-fold over the period from 3.9% of admissions in 1950–59 to 19.9% of admissions in 2000–2010 (RR 5.1, $\chi^2$ test for trend p < 0.00005). Infectious and parasitic diseases decreased from 18.2% to 13.9% of all admissions over the period, a 24% decrease (RR 0.76, 95% CI 0.71–0.82). Respiratory illnesses decreased from 16.2% of all admissions to 7.7% (RR 0.47, 95% CI 0.44–0.51). Endocrine and nervous system disorders increased significantly over the period, although each accounted for less than 5% of all admissions (Table S2).

**Leading causes of in-hospital mortality**

We obtained in-hospital cause of death data for 9,695 patients from 15 studies for the period 1950–2010 (Table S2, Fig. 3). Infectious and parasitic diseases, disorders of the circulatory system, and digestive system disorders were the leading causes of death accounting for 17.1% (95% CI 16.4–17.9), 16.0% (95% CI 15.3–16.8), and 16.2% (95% CI 15.4–16.9) of all deaths, respectively. The class of disease among all deaths varied with time in decades ($\chi^2 = 1100$, df 30; p < 0.0005). The proportion of deaths caused by disorders of the circulatory system rose from 9.7% in 1950–59 to 19.4% in 2000–2010 (RR 2.0, 95% CI 1.5–2.7). Infectious and parasitic diseases increased significantly over the period, although each accounted for less than 5% of all deaths (Table S2).
### Table 2. Characteristics of studies included in review

| 1st Author  | Country | Year   | No. of patients | Proportion female (%) | Case definitions provided? (6) | Study design (4) | ICD Coding? (4) | Cadre of staff (4) | Diagnostic facilities (6) | Admission criteria specified? (6) | Mortality rates reported? (6) | Score (x/36) | Methodology score % |
|-------------|---------|--------|-----------------|-----------------------|-------------------------------|-----------------|-----------------|---------------------|-----------------------------|--------------------------------|-----------------|--------------------|
| Adekunle (36) | Nigeria | 2004   | 104             | 50                    | –                             | R               | +               | C                   | III                         | –                              | +                            | 23              | 64                 |
| Adetuyibi (42) | Nigeria | 1960-73 | 4,568           | 45                    | –                             | R               | –               | C                   | III                         | +                              | +                            | 25              | 69                 |
| Amsel (26)   | Ethiopia| 1994   | 1,139           | 49                    | +                             | P               | –               | C                   | III                         | –                              | +                            | 17              | 47                 |
| Bardget (78) | Zimbabwe| 1992, 2000 | 2,674       | 52                    | –                             | P               | –               | C                   | III                         | ?                              | +                            | 28              | 78                 |
| Barr (27)    | Kenya   | 1970-72| 784             | 43                    | –                             | P               | –               | C                   | III                         | –                              | +                            | 25              | 64                 |
| Dean (37)    | S. Africa| 1984   | 1,571           | 40                    | –                             | R               | –               | C                   | III                         | –                              | +                            | 23              | 56                 |
| Edginton (29) | S. Africa| 1968-70| 485             | 100                   | –                             | P               | –               | M                   | II                          | –                              | –                            | 20              | 36                 |
| Gill (76)    | S. Africa| 1981, 1990 | 1,052       | N/A                    | –                             | R               | –               | C                   | III                         | –                              | –                            | 13              | 42                 |
| Griffiths (44) | S. Africa| 1959, 1977 | 1,118       | 46                    | –                             | R               | –               | M                   | II                          | –                              | –                            | 15              | 28                 |
| Harries (80) | Malawi  | 1986   | 4,700           | 43                    | –                             | R               | –               | C                   | III                         | –                              | +                            | 10              | 56                 |
| Huerga (33)  | Liberia | 2005   | 1,034           | N/A                    | +                             | R               | –               | C                   | III                         | –                              | +                            | 20              | 69                 |
| Kakembo (34) | S. Africa| 1994   | 2,142           | 45                    | +                             | R               | +               | M                   |                           | –                              | –                            | 18              | 50                 |
| Lester (25)  | Ethiopia| 1971-75| 4,640           | 33                    | +                             | P               | +               | C                   | III                         | +                              | +                            | 36              | 100                |
| Marszalek (38) | S. Africa| 2001-2003 | 462        | 48                    | –                             | R               | +               | C                   | III                         | –                              | –                            | 18              | 50                 |
| Mudiayi (39) | Zimbabwe| 1987-94 | 12,280         | 46                    | –                             | R               | +               | C                   | III                         | –                              | –                            | 18              | 50                 |
| Osuafor (82) | S. Africa| 1990-92| 530             | 47                    | –                             | R               | –               | C                   | III                         | –                              | –                            | 15              | 42                 |
| Pobee (49)   | Ghana   | 1971-72| 462             | 30                    | –                             | R               | –               | C                   | III                         | –                              | +                            | 20              | 56                 |
| Shaper (43)  | Uganda  | 1957   | 2,466           | 33                    | –                             | R               | –               | C                   | III                         | +                              | +                            | 25              | 69                 |
| Tambwe (83)  | DRC     | 1988-89| 1,624           | N/A                    | –                             | R               | –               | C                   | II                          | –                              | +                            | 17              | 47                 |
Comparison of the proportion of deaths caused by digestive system disorders at the beginning of the study period and at the end showed a decrease from 14.9% to 8.1% (RR 0.54, 95% CI 0.40–0.73). Deaths due to disorders of the endocrine, nervous, and genitourinary systems all showed significant decreases (Table S2), but the combined contribution of these diagnostic categories to overall mortality was less than 20%. When we restricted the analysis of causes of death to studies that ranked above the 75th percentile on the methodological score, we observed no meaningful changes in the result.

Case fatality rates for the entire period for different disease categories could not be calculated because of inconsistent reporting on the number of patients admitted with each medical condition. Two recent retrospective studies reported case fatality rates and the diagnostic categories with the highest case fatality rates were infectious and parasitic diseases (25%) and circulatory illnesses (21%) (25, 33).

Discussion
We found 30 eligible studies conducted in 10 sub-Saharan countries and covering a 61-year time period. In most African countries in there are no published data on hospital deaths (Fig. 2) and our illustration of research activity trends (Fig. 3) provides no evidence that this situation is improving over time. All of this is in spite of the fact that Africa bears nearly a quarter of the world’s burden of disease (50).

Despite the limitations identified in the few studies obtained, as indicated by the low methodology scores, some trends were discernible; for example, the proportion of admissions due to cardiovascular illnesses, composed mainly of stroke and heart failure, were found to have increased significantly over the study period. The proportion of admissions due to infectious and parasitic diseases decreased over the study period. However, the proportion of deaths caused by infectious and parasitic diseases increased during the period, which roughly coincides with the emergence of the HIV epidemic. HIV-related illnesses contributed the most to the burden of infectious disease over the past 10 years with a very high case fatality, suggesting that late presentation, due to limited access to HIV testing facilities, continues to be a significant problem on the continent (51). HIV may also increase the risk of heart diseases such as cardiomyopathy (52) and cancers (53) providing one illustration of the links between communicable and non-communicable diseases. Due to the limitations of the data, it is difficult to determine whether or not the observed trends were a result of the ongoing epidemiological transition with an increased burden of non-communicable illnesses in the continued presence of HIV and other infectious diseases. The observed changes could be due to changing hospital admission policies, improved hospital access for certain
Examining burden of non-communicable disease in sSA, including demographic changes resulting in an increase in the number of children surviving to adulthood (4) and an age or disease groups or new treatment availability, factors that we were unable to examine. These would be acting in concert with other explanations for the increasing burden of non-communicable disease in sSA, including demographic changes resulting in an increase in the number of children surviving to adulthood (4) and an
increase in the prevalence of cardiovascular risk factors such as hypertension and diabetes (54, 55). Consistent with these observations as well as our results, community-based data from South Africa showed an increase in non-communicable diseases as a cause of death between 1992 and 2005 (56). This was also accompanied by a large increase in HIV-related deaths (56). However, when compared to estimates based on the global burden of disease model (2), which is itself imperfect (57), our results suggest a bigger contribution from non-communicable diseases. These contrasting results emphasize the importance of defining patterns of disease accurately as the transition proceeds in order to allocate scarce health resources. Research activities and funding also need to be guided by the burden of disease but evidence from the developing world suggests that this does not always happen (58, 59).

This review also exposes the methodological deficiencies of the few studies that have contributed data, an issue that has received little attention (11). The most common shortcoming was the failure to use standard case definitions for the illnesses described. This is attributable to the fact that most of the studies were retrospective in design and it would have been difficult to access records for purposes of verifying diagnoses listed in the discharge records. Without a clear, measurable, and specific definition of an illness, consumers of reports are unable to interpret, compare, and aggregate data from various studies (22). An example of the distortion that can arise from the use of different case definitions was the ‘surge’ in AIDS cases that arose after the Centers for Disease Control and Prevention (CDC) expanded their case definition for AIDS in 1993 (60). The WHO has established case definitions for the most common illnesses such as anemia (35), pneumonia (61), stroke (62), and diabetes mellitus (63). While it might be argued that some of the case definitions did not exist at the time when the earlier studies were conducted, only one of the more recent studies reviewed reported the use of case definitions (33). Obviously, improving the diagnostic capabilities of facilities would permit the use of more sophisticated and differentiating case definitions that rely upon test results.

The failure of two-thirds of the studies reviewed to use standard ICD coding systems also limits our capacity to compare studies or aggregate data. Stroke, for example, was classified as a neurological disorder in some studies while other studies classified it as a cardiovascular disorder in concordance with the ICD coding system. Diarrhea was listed as a digestive system illness in some studies while in others it was classified as an infectious and parasitic disease.

In many countries in sSA diagnostic facilities can only be found in large referral hospitals located in urban areas (64). Our analysis found that most of the studies describing medical illnesses in adults had been conducted in university teaching hospitals and referral facilities located in urban areas. These were also the facilities most likely to be operated by consultants (65) who, by virtue of their more advanced training, are more likely to publish research findings, potentially biasing the sample of reports available for this review. At the time that they were published, most of the population of SSA was living in rural areas with limited access to tertiary referral hospitals thus limiting the generalizability of the findings (20). As the pace of urbanization on the continent increases (66), studies conducted in urban hospitals are likely to be more representative than in the past.

The demographic transition that is driving this urbanization, with its associated increase in endemic non-communicable diseases, argues for substantial improvements in the diagnostic and curative services in adult health in sSA to enable the correct classification of disease and early initiation of control measures, especially for cardiovascular and other non-communicable chronic illnesses (67). Initiatives such as the WHO-supported Health Metrics Network (68) that aim to improve the collection of health-related data in developing countries by providing guidelines and templates need to appreciate that the quality of clinical data from hospitals in sSA will compromise the utility of these systems unless there is substantial investment in instruments and training. Adult demographic surveillance networks, such as the INDEPTH (69) network, could also provide adult morbidity data by linking the data from dedicated hospital surveillance teams to their population registers. Ultimately, well-conducted cohort studies will be needed, where the outcomes (and exposure variables) are compliant with international standards of disease detection and classification, in order to identify risk factors for important illnesses in sSA (70).

Our review had two principal limitations. Many articles publishing findings on research in Africa are not available through the Internet (71). Organizations such as AJOL (www.ajol.info) and HINARI (http://www.who.int/hinari/en/) have succeeded in providing substantial access to publications from Africa online. However, many publications are not available online and we were obliged to access print copies of 20 papers from the British Library and could not find a suitable source for a further six papers. Despite good electronic database we found 20% of the relevant papers through hand rather than online searching. Our exclusion of papers written in languages other than English, which were even more difficult to obtain, also potentially biased our results in favor of English-speaking countries. Despite these shortcomings we believe that the studies reviewed here are a fair representation of the research articles that have been published on the subject in the past six decades.

For some disease categories, such as neoplasms, we found extremely sparse data, which we attribute to the...
lack of appropriate diagnostic facilities rather than to insignificant numbers of patients with these diseases. We also observed an uneven contribution from different regions of the continent to the data through the different time periods studied, most likely due to variations in the availability of health-reporting infrastructure as a result of political or economic instability.

Conclusions and recommendations for the conduct of future studies

We found that there were very limited data on the causes of hospital admissions and death among adults in sSA, and these data had significant limitations. However, the review provides evidence to suggest that cardiovascular diseases account for a significant and increasing fraction of the causes of hospitalization among adults in sSA. As the epidemiology of adult disease in sSA transitions from infectious to non-communicable diseases, health researchers and policy makers will need to establish reliable and consistent systems for diagnosing and recording disease in adults in order to optimize treatments and preventive interventions.

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Conflict of interest and funding

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**Table S1. Studies excluded from review**

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Table S1 (Continued)

Reason for exclusion Study


Table S2. Numbers of admissions and deaths for each decade*

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<tbody>
<tr>
<td>Infectious and parasitic diseases</td>
<td>68 (12%)</td>
<td>453 (13%)</td>
<td>527 (14%)</td>
<td>237 (28%)</td>
<td>218 (63%)</td>
<td>157 (19%)</td>
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<tr>
<td>Respiratory</td>
<td>80 (14%)</td>
<td>424 (13%)</td>
<td>375 (11%)</td>
<td>116 (14%)</td>
<td>21 (6%)</td>
<td>69 (8%)</td>
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<tr>
<td>Circulatory</td>
<td>56 (10%)</td>
<td>593 (18%)</td>
<td>561 (17%)</td>
<td>150 (18%)</td>
<td>36 (10%)</td>
<td>159 (19%)</td>
<td></td>
</tr>
<tr>
<td>Nervous system</td>
<td>62 (11%)</td>
<td>283 (8%)</td>
<td>458 (14%)</td>
<td>1 (0%)</td>
<td>29 (8%)</td>
<td>55 (7%)</td>
<td></td>
</tr>
<tr>
<td>Digestive</td>
<td>86 (15%)</td>
<td>588 (17%)</td>
<td>755 (22%)</td>
<td>63 (7%)</td>
<td>9 (3%)</td>
<td>66 (8%)</td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td>5 (1%)</td>
<td>30 (1%)</td>
<td>23 (1%)</td>
<td>32 (4%)</td>
<td>22 (6%)</td>
<td>79 (10%)</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>37 (6%)</td>
<td>374 (11%)</td>
<td>339 (10%)</td>
<td>0 (0%)</td>
<td>3 (1%)</td>
<td>9 (1%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>183 (3%)</td>
<td>636 (19%)</td>
<td>68 (20%)</td>
<td>248 (29%)</td>
<td>10 (3%)</td>
<td>225 (28%)</td>
<td></td>
</tr>
<tr>
<td>Total deaths</td>
<td>577 (100%)</td>
<td>3,381 (100%)</td>
<td>3,724 (100%)</td>
<td>847 (100%)</td>
<td>348 (100%)</td>
<td>818 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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<th></th>
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</thead>
<tbody>
<tr>
<td>Infectious and parasitic diseases</td>
<td>1,147 (18%)</td>
<td>3,153 (19%)</td>
<td>4,125 (24%)</td>
<td>1,905 (20%)</td>
<td>4,696 (21%)</td>
<td>2,090 (14%)</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>1,018 (16%)</td>
<td>2,422 (15%)</td>
<td>3,172 (19%)</td>
<td>2,074 (22%)</td>
<td>4,151 (19%)</td>
<td>1,151 (8%)</td>
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<tr>
<td>Circulatory</td>
<td>247 (4%)</td>
<td>974 (6%)</td>
<td>768 (5%)</td>
<td>1,253 (13%)</td>
<td>3,495 (16%)</td>
<td>3,001 (20%)</td>
<td></td>
</tr>
<tr>
<td>Nervous system</td>
<td>417 (7%)</td>
<td>619 (4%)</td>
<td>438 (3%)</td>
<td>192 (2%)</td>
<td>499 (2%)</td>
<td>1,595 (11%)</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>817 (13%)</td>
<td>1,839 (11%)</td>
<td>932 (6%)</td>
<td>0 (0%)</td>
<td>347 (2%)</td>
<td>1,412 (9%)</td>
<td></td>
</tr>
<tr>
<td>Digestive</td>
<td>718 (11%)</td>
<td>1,829 (11%)</td>
<td>2,644 (16%)</td>
<td>618 (7%)</td>
<td>1,042 (5%)</td>
<td>1,631 (11%)</td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td>70 (1%)</td>
<td>0 (0%)</td>
<td>54 (0%)</td>
<td>298 (3%)</td>
<td>1,578 (7%)</td>
<td>1,402 (9%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1,933 (31%)</td>
<td>5,795 (35%)</td>
<td>4,802 (28%)</td>
<td>3,450 (36%)</td>
<td>6,165 (28%)</td>
<td>2,751 (18%)</td>
<td></td>
</tr>
<tr>
<td>Total admissions</td>
<td>6,297 (100%)</td>
<td>16,632 (100%)</td>
<td>16,881 (100%)</td>
<td>9,492 (100%)</td>
<td>21,972 (100%)</td>
<td>15,033 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

*Column totals may not add up to exactly 100% due to rounding.
Data for deaths was extracted from references: (25-28, 30, 32, 33, 36, 37, 43, 49, 78, 80, 82).
Data on admissions was extracted from references: (25-31, 33, 34, 37-46, 48, 77-83).