Age Related Patterns of Disease and Mortality in Hospitalised Adults in Malawi

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Abstract

Background
The epidemic of non-communicable diseases (NCDs) in low and middle income countries (LMICs) is widely recognised as the next major challenge to global health. However, in many LMICs, infectious diseases are still prevalent resulting in a “double burden” of disease. With increased life expectancy and longevity with HIV, older adults may particularly be at risk of this double burden. Here we describe the relative contributions of infections and NCDs to hospital admissions and mortality, according to age, in Malawi’s largest hospital.

Methods
Primary diagnosis on discharge/death, mortality rates, and HIV status were recorded prospectively on consecutive adult medical in-patients over 2 years using an electronic medical records system. Diagnoses were classified as infections or NCDs and analysed according to age and gender.

Findings
10,191 records were analysed. Overall, infectious diseases, particularly those associated with HIV, were the leading cause of admission. However, in adults ≥55 years, NCDs were the commonest diagnoses. In adults <55 years 71% of deaths were due to infections whereas in adults ≥55 years 56% of deaths were due to NCDs.

Interpretation
Infectious diseases are still the leading cause of adult admission to a central hospital in Malawi but in adults aged ≥55 years NCDs are the most frequent diagnoses. HIV was an underlying factor in the majority of adults with infections and was also present in 53% of those with NCDs. These findings highlight the need for further health sector shifts to address the double burden of infectious and NCDs, particularly in the ageing population.
Background

Populations around the world are ageing, with the most dramatic increases in the number of older adults occurring in low and middle income countries (LMICs).[1] Although the population structure in sub-Saharan Africa (SSA) remains young in relative terms, this region already has double the number of older adults than northern Europe, and this figure is expected to grow faster than anywhere else in the world, increasing from 46 million in 2015 to 157 million by 2050.[2] Worldwide there is a growing burden of non-communicable diseases (NCDs) including cardiovascular diseases, chronic lung diseases, diabetes and cancer[3] along with a projected rapid shift from communicable diseases to NCDs as the dominant causes of morbidity and mortality in LMICs.[4] As NCDs predominate in middle and later life, older adults are likely to carry the greatest burden of NCDs. In addition, the successful roll out of antiretroviral therapy (ART) in many LMICs is leading to an increasing number of ageing adults living with HIV.[5] During this transition, it is feared that many LMICs will experience a double burden of disease with simultaneously high levels of both communicable diseases and NCDs.[6] The disease burden of older adults in LMICs has not been sufficiently studied.[7]

Though ranked among the youngest countries globally, Malawi’s population is rapidly ageing with an improvement in life expectancy from 37 to 58 years in the past decade[8] and an adjusted life expectancy of 77 years for those who live to age 60.[9] The number of adults aged over 60 years is projected to be >1 million by 2030 and >2 million by 2050.[1] Like many countries in SSA, Malawi is relatively early in the health transition, with rising rates of NCD risk factors such as obesity and hypertension[10] alongside a high burden of infectious diseases,[11] including an adult HIV prevalence of 10-6%.[12] In this context, it is likely that Malawi is experiencing a double burden of disease, which is preferentially affecting older adults, a group who are already experiencing complex health needs related to the co-morbidities of ageing.[7,13] We investigated this hypothesis by conducting an age-based analysis of medical inpatient surveillance data from the largest hospital in Malawi. The analysis may serve as a paradigm to guide healthcare policy aimed at better meeting the complex healthcare needs of the rapidly growing numbers of older people in LMICs.

Methods

Study setting and participants

Queen Elizabeth Central Hospital (QECH), Blantyre, Malawi is the largest government funded teaching and referral hospital in Malawi with over 7000 medical admissions per year. Medical care is provided free at the point of delivery. Diagnostic facilities are rudimentary but include smear microscopy and Gene Xpert MTB/RIF for tuberculosis. Blood and cerebrospinal fluid culture is provided by the Malawi Liverpool Wellcome Trust Clinical Research Programme (MLW). In accordance with Malawian national policy, provider initiated HIV testing and counselling (PITC) is offered to all hospitalised adults with unknown HIV status. However, owing to a lack of HIV test kits or trained counsellors, there have been periods when PITC was not conducted.

Hospital inpatient surveillance

The Surveillance Programme of IN-patients and Epidemiology (SPINE) database is an electronic medical record (EMR) that was established at QECH in 2009 as a collaboration between MLW and Baobab Trust under the auspices of the Malawi Ministry of Health (MOH).[11] In accordance with an MOH initiative to develop a fully digital Health Management Information System (HMIS) in government clinical facilities, this ward-based touch-screen system is used
to record demographic and clinical information, vital status and HIV status on all patients admitted to the adult medical wards. At discharge or death, primary and secondary diagnoses are made on the basis of the available clinical, radiological and laboratory data. Diagnoses are selected from a list based on the HMIS diagnostic tree used in healthcare facilities throughout Malawi; the HMIS diagnostic tree was modified from the International Classification of Diseases (ICD-10). The SPINE data management team routinely undertakes systematic data quality checks to ensure the accuracy and completeness of data recorded in the SPINE system compared with the paper-based hospital HMIS which runs in parallel with SPINE. During the study period SPINE captured at least 100% of admissions/discharges, and 96% of deaths compared to HMIS.

Procedures and statistical analysis

We analysed hospital inpatient episodes recorded in the SPINE system from 1st January 2013 to 31st December 2014 for all adults aged ≥16 years; among patients admitted multiple times during the study period only the first admission was included. In this study, the unit of analysis was hospital episode. Individual primary diagnoses were grouped according to the ‘root parent diagnostic group’ which are similar to the ICD-10 classification (S1 File). Diagnoses that were initially classified as ‘other’ were reviewed manually and when appropriate categorized under one of the other root parent diagnostic groups.

Whilst there is no universally accepted threshold for classifying a patient as elderly, the World Health Organization (WHO) suggests that in SSA an age threshold of 55 years may be used.[14] This further seems appropriate since the life expectancy in Malawi is currently 58 years.[8] Consequently the cohort of patients were divided into younger (<55 years) and older (≥55 years) patients. Hospital episodes were classified by primary diagnosis and tabulated in order of frequency. Primary diagnoses were then grouped into ‘Infections’, ‘NCDs’ and ‘Undefined’ (S1 File). For the 20 most common diagnoses, we examined the proportion of mortality by a binary variable for younger versus older age. A multivariable logistic model was developed to examine the effect of gender, disease type (‘NCD’, ‘Infection’, ‘Undefined’), HIV status and age on probability of death. In the model age was treated using cubic splines, which were selected over other spline formulas based on better model fit assessed through AIC value. Interactions by age and HIV, and age and disease type were examined in the model. Inpatient admission rates per 1000 population were calculated by dividing total recorded admissions (including readmission) by the population size within age/ sex strata; population data were obtained from the Malawi 2008 Census.[15]

Ethical considerations

Since all clinical data used for this analysis were collected as part of the MOH HMIS during routine care, individual patient consent was not obtained. Our research team did not have contact with patients and only had access to fully anonymized data. These data were maintained by MLW’s Data Department using institutional data governance standard operating procedures which conform to international standards. This analysis was approved by the University of Malawi College of Medicine Research Ethics Committee.

Results

Between 1st January 2013 and 31st December 2014, 11,645 patients were admitted to the QECH adult medical wards, of which 1133 (9.7%) were readmissions. In total, 184 and 137 patients were excluded from the analysis due to being <16 years old or having missing age data, respectively (S1 Fig). Our final data set included 10,191 first admission hospitalisations.
The raw data file is available as supporting information (S2 File). Overall, 80.1% of admissions occurred in adults aged <55 years (n = 8161) compared to 19.9% in adults ≥55 years (n = 2030). However, the age specific rate of annual hospital admission per 1000 population in Blantyre District rose steadily with increasing age (Fig 1).

Differences in diagnosis by age

Infectious diseases accounted for 6534/10191 (64.1%) of diagnoses, while NCDs accounted for 3052/10191 (29.9%) of diagnoses. Overall the most common diagnoses were tuberculosis (TB) (n = 2283, 22.4%), sepsis (n = 1265, 12.4%), pneumonia (n = 1162, 11.4%), and meningitis (n = 803, 7.9%) (Fig 2). In adults aged <55 years infections predominated, accounting for 70.9% of diagnoses. The top 4 diagnoses in this age group were TB, sepsis, pneumonia, and meningitis which together accounted for 60.3% of all diagnoses. Conversely, in older adults infections made up only 32.6% of diagnoses, while 55.7% of diagnoses were due to NCDs; stroke and heart disease were the two commonest diagnoses in this age group. The likelihood of an NCD diagnosis increased steadily with age (Fig 3). The major NCDs (heart disease, stroke, diabetes and hypertension) accounted for 37.9% of admissions in older adults and only 7.9% in younger adults.

Mortality

Overall mortality among hospital inpatients was 22.7%. The risk of death varied markedly by diagnosis; candidiasis, gastroenteritis, kidney disease, meningitis and cancer were associated with the highest mortality rates, ranging from 31.4% to 58.3% (Table 1). Patients aged ≥55 years had higher overall mortality than those aged <55 years (26.9% vs. 21.6%, p-value < .0001; Table 1); mortality rose to a peak of 27.6% in the 46–65 year age band, and thereafter plateaued.

![Fig 1. Annual incidence of inpatient admissions per 1000 population, by age and sex, Blantyre District, Malawi 2013–2015. The grey line represents ‘Male’, the light blue line represents ‘Female’. doi:10.1371/journal.pone.0168368.g001](image-url)
When analysed by diagnosis, death rates in older patients were higher for TB (36.8 vs. 29.4%), pneumonia (23.2 vs. 12.8%), sepsis (29.6 vs. 13.9%), and meningitis (44.4 vs. 33.0%).

The proportion of mortality due to NCDs and infectious disease differed by age. In adults aged <55 years, 1270/1743 deaths (70.9%) were due to infection, while only 403 (23.1%) of deaths were due to the NCDs. In adults aged ≥55 years, infections accounted for 246/574 (38.2%) of death and NCDs accounted for 286/574 (55.7%) of deaths.

HIV status, gender and disease type significantly influenced risk of death (Table 2). Mortality in HIV-infected patients was 25.0% compared to 13.7% in HIV-uninfected patients. In multivariable analysis controlling for age, gender and disease type, HIV infected patients had double the risk of death, compared to HIV uninfected patients. Infectious disease diagnoses were associated with slightly higher risk of death compared to NCDs and male inpatients had 40% higher risk of death compared to female inpatients (Table 2).

HIV status

In total, 4317 (42.3%) of patients had a recorded HIV status upon admission; a further 1431 (14.0%) had a new HIV test during their inpatient stay. HIV prevalence peaked at approximately 90% in the 36–45 year age group in both sexes (Fig 5). Among those tested HIV prevalence was significantly higher in adults aged <55 years compared to those aged ≥55 years (82.6% vs. 53.3%; p-value <0.001).
Age, gender and diagnosis influenced likelihood of having a known HIV status upon admission and having a new HIV test during the inpatient stay. In multivariable analysis controlling for age, sex and diagnosis, male patients (aOR = 0.59, 95% CI: 0.55, 0.65) and patients aged ≥55 years (aOR = 0.34, 95% CI: 0.29, 0.38) were less likely to be admitted with a documented HIV status. They were also less likely to be tested during the admission; the likelihood of having a new HIV test during inpatient stay was lower in adults aged ≥55 years (aOR = 0.56, 95% CI: 0.47, 0.66) and in men (aOR = 0.72, 95% CI: 0.63, 0.82) (data not shown). On discharge 31.8% of older adults knew their HIV status compared to 62.9% of younger adults, p-value < 0.0001 (Table 3).

Patients with an infectious disease diagnosis were more likely to have a documented HIV status on admission compared to patients with an NCD diagnosis, (aOR = 1.69, 95% CI: 1.54, 1.86) and were 44% more likely than those with an NCD diagnosis to receive an HIV test during their hospital stay (aOR = 1.44, 95% CI: 1.26, 1.67) (data not shown). Among those who were tested, 83.4% with an infectious diagnosis and 53.3% with an NCD diagnosis were HIV infected.
Discussion

In an inpatient surveillance dataset of over 10,000 consecutive adult admissions from a large urban hospital in SSA, we found a double burden of infections and NCDs contributing to hospital admissions and in-patient mortality. Although infectious diseases were the dominant reason for admission, NCD diagnoses represented nearly one third of all admissions, and predominated in older adults, in whom over half were treated for an NCD. Comorbidity with HIV had a strong influence on our patient cohort, across all age groups and diagnoses. More than half of patients aged ≥55 years with a known HIV status were HIV positive and, across all ages, among those diagnosed with an NCD, the HIV prevalence was over 50%. The pattern of diagnoses for both infectious and non-infectious diseases are consistent with other hospital based surveys from the region [16,17] and with the global burden of disease literature which describe TB and respiratory infections as the main infections in adults, and stroke and heart disease as the main NCDs.[18] Our data adds to a limited but growing body of evidence showing that the rising trend of NCDs is impacting high HIV prevalent SSA countries, such as Malawi, where an ageing population are suffering the double burden of infections, including HIV, and NCD co-morbidity.
Our data highlight that more than a decade following the scale-up of ART, HIV remains an important driver of inpatient admission and mortality in this setting. While WHO recommends routine HIV testing in clinical settings, in our cohort only 43% of inpatients knew their HIV status on admission, and only 24% of patients with an unknown HIV status received an HIV test during their hospital stay. These rates are similar to those reported in other inpatient settings in SSA[19] and underline inadequate access to HIV testing in community and clinical settings.[20] Men, older adults and patients with an NCD diagnosis were less likely to have known HIV status on admission or be tested in-hospital. This variation in testing practice may be due to the misconception by both patients and clinicians that older adults and those with NCDs are at low risk of HIV. Higher rates of HIV testing in women compared to men has been noted previously.[21] Overall, 44% of patients in our cohort were discharged without knowing their HIV status. Although we were unable to assess the occurrence of post-discharge HIV testing, we note that there is currently no mechanism in place to facilitate such testing in this high risk group.
Although essential at all ages, strengthening the HIV spectrum of care from HIV testing to ART, and interventions within HIV clinics to address opportunistic infections[22] may be

Table 2. Demographic and clinical characteristics and risk of death among adult inpatients at QECH 2013–2014.

| HIV status | Total number | Deaths\(^1\) N(%) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|------------|--------------|--------------------|------------------------|----------------------|
| Non-Reactive | 1489 | 204 (13.7) | 1.0 — | 1.0 — |
| Reactive | 4551 | 1132 (25.0) | 2.1 (1.8, 2.5) | 2.1 (1.7, 2.5) |
| Unknown | 4151 | 976 (23.5) | 1.9 (1.6, 2.3) | 1.8 (1.5, 2.1) |

| Gender | Total number | Deaths\(^1\) N(%) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|--------|--------------|--------------------|------------------------|----------------------|
| Female | 5071 | 994 (19.6) | 1.0 — | 1.0 — |
| Male | 5120 | 1378 (26.9) | 1.4 (1.3, 1.6) | 1.4 (1.3, 1.5) |

| Age group | Total number | Deaths\(^1\) N(%) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|-----------|--------------|--------------------|------------------------|----------------------|
| 16–25     | 1741 | 276 (15.8) | 1.0 — | 1.0 — |
| 26–35     | 3007 | 626 (20.8) | 1.4 (1.2, 1.6) | 1.2 (1.1, 1.4) |
| 36–45     | 2237 | 546 (24.4) | 1.7 (1.5, 2.0) | 1.4 (1.2, 1.7) |
| 46–55     | 1176 | 325 (27.6) | 2.0 (1.7, 2.4) | 1.8 (1.5, 2.2) |
| 56–65     | 903 | 250 (27.6) | 2.0 (1.7, 2.5) | 2.0 (1.7, 2.5) |
| > 65      | 1127 | 298 (26.4) | 1.9 (1.6, 2.3) | 2.0 (1.7, 2.5) |

| Disease Class | Total number | Deaths\(^1\) N(%) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|---------------|--------------|--------------------|------------------------|----------------------|
| NCD           | 3052 | 638 (20.9) | 1.0 — | 1.0 — |
| Infectious    | 6534 | 1516 (23.2) | 1.1 1.0, 1.3 | 1.2 1.1, 1.3 |
| Undefined\(^2\) | 605 | 161 (26.6) | 1.3 1.1, 1.7 | 1.4 1.2, 1.8 |

\(^1\) 48 Patients who absconded were classified as alive
\(^2\) Undefined cases were predominately complex cases where both infectious diseases and NCDs were present

doi:10.1371/journal.pone.0168368.t002

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Fig 5. HIV Prevalence by age and sex in medical ward in-patients, Blantyre, Malawi, January 2013- December 2014. The red line represents the percent of admitted patients that are HIV infected. The blue bars represent the number of patients admitted.

doi:10.1371/journal.pone.0168368.g005
### Table 3. HIV testing and status by age and diagnosis in adult inpatients at QECH, 2013–2014, ranked by total proportion HIV positive.

| Diagnosis                  | Total admissions | All Ages | HIV status known | HIV % positive of those tested |
|----------------------------|------------------|----------|------------------|--------------------------------|
|                            | N                | %        | N                | %                              | N                | %      |
|                            |                  | under 55 |                  | over 55                        | under 55         | over 55 |
| Kaposis sarcoma            | 126              | 81.7%    | 100              | 86.2%                          | 3                | 30.0%  |
| Candidiasis                | 68               | 72.1%    | 44               | 78.6%                          | 5                | 41.7%  |
| Gastroenteritis            | 401              | 61.3%    | 230              | 65.2%                          | 16               | 33.3%  |
| Tuberculosis               | 2283             | 78.0%    | 1641             | 80.3%                          | 140              | 58.6%  |
| Meningitis                 | 803              | 63.4%    | 476              | 65.1%                          | 33               | 45.8%  |
| Pneumonia                  | 1162             | 56.5%    | 583              | 61.9%                          | 73               | 33.2%  |
| Sepsis                     | 1265             | 52.8%    | 626              | 54.9%                          | 42               | 33.6%  |
| Alcoholism                 | 32               | 12.5%    | 4                | 13.8%                          | 0                | 0.0%   |
| Liver Disease              | 242              | 53.3%    | 117              | 57.9%                          | 12               | 30.0%  |
| Other                      | 534              | 52.8%    | 244              | 57.8%                          | 38               | 33.9%  |
| Malaria                    | 301              | 41.9%    | 119              | 45.4%                          | 7                | 17.9%  |
| Anaemia                    | 515              | 58.3%    | 264              | 64.5%                          | 36               | 34.0%  |
| Kidney                     | 179              | 51.4%    | 69               | 53.9%                          | 23               | 45.1%  |
| Peptic Ulcer Disease       | 70               | 54.3%    | 32               | 59.3%                          | 6                | 37.5%  |
| No Diagnosis               | 78               | 59.0%    | 37               | 67.3%                          | 9                | 39.1%  |
| Diabetes                   | 259              | 27.8%    | 55               | 32.9%                          | 17               | 18.5%  |
| Hypertension               | 205              | 28.3%    | 38               | 39.6%                          | 20               | 18.3%  |
| Cancer                     | 179              | 43.6%    | 62               | 52.5%                          | 16               | 26.2%  |
| Focal Tissue Infection     | 140              | 50.7%    | 58               | 57.4%                          | 13               | 33.3%  |
| Lung disease               | 168              | 33.9%    | 32               | 38.6%                          | 25               | 29.4%  |
| Epilepsy                   | 111              | 25.2%    | 25               | 25.8%                          | 3                | 21.4%  |
| Stroke                     | 484              | 33.7%    | 90               | 52.3%                          | 73               | 23.4%  |
| Heart                      | 500              | 31.8%    | 94               | 46.1%                          | 65               | 22.0%  |
| Psych                      | 86               | 38.4%    | 31               | 38.8%                          | 2                | 33.3%  |
| Total                      | 10191            | 56.4%    | 5071             | 62.9%                          | 677              | 31.8%  |

doi:10.1371/journal.pone.0168368.t003

particularly important in older adults. HIV disease has been found to progress more rapidly in older people,[23,24,25,26] and, in developed countries people with HIV infection may have up to five times the risk of chronic diseases, geriatric syndromes and multimorbidity, even when the HIV infection is well treated and managed.[27] In our study, older adults had higher disease specific mortality rates than younger adults for the major infections associated with HIV.

Inpatient mortality was over 20%; predictors of death were HIV infection, male gender and older age. Alongside HIV, our data revealed that NCDs play an important primary or contributing role to inpatient mortality in older people in settings such as ours. The leading causes of mortality in over 55s (56% of deaths) were due to NCDs. These data underscore the need for all countries undergoing the health transition to develop NCD strategies including prevention as well as chronic care and acute clinical services orientated towards NCD care. The WHO have defined the minimum standards of care for non-communicable diseases in low resource settings.[28] There is also a need for greater integration of HIV/NCD chronic care, which at a minimum might include routine NCD and HIV screening (HIV screening in NCD clinics and NCD screening in HIV clinics) to reduce late presentation of illness to hospital, as well as combined care clinics.

The challenge of strengthening the HIV spectrum of care, scaling up routine HIV/NCD screening, and achieving greater integration of NCD/HIV clinical services need to be
addressed at many levels. Medical education in SSA needs to be reoriented to prepare clinicians to respond to the changing patterns of disease; investment in public health for prevention and screening is needed, restructuring of chronic care and specialist expertise and appropriate specialist services need to be developed. The Malawi Ministry of Health recognises these challenges and is attempting to address them, for example through the development of dialysis units in the government hospitals in Lilongwe and Blantyre[29], pilot projects of integrated NCD/HIV in community sites [30] and national scale-up of NCD services, especially for diabetes and hypertension. However, in a severely resource constrained setting large-scale implementation of many of these measures may be difficult.

Our study has several limitations. Diagnostic resources were limited so many diagnoses were based on clinicians' judgement using available evidence, although diagnoses of blood stream infection and meningitis where supported by good quality microbiology from the MLW programme. We only considered primary diagnoses but older patients may have multiple comorbidities which were not captured by this approach. The allocation of some diagnoses into infectious disease and NCD categories was also challenging. For example, many cancers in our setting are initiated by infections (e.g. cervical cancer and Kaposi's sarcoma). These were classified as NCDs, which obscures the true complexity of the disease aetiology. With some diagnoses, for example chronic liver disease secondary to hepatitis infection, a decision was made not to classify the condition as infection or NCD which accounts for the "undefined" category (S1 File). Our analysis was restricted to first admissions and thus may have under estimated mortality which may be more common in readmitted patients. We were unable to prevalence of NCD risk factors, including smoking, as these are not captured in the SPINE system. Despite these limitations our results are likely to be unbiased as diagnostic data were collected independently in real time, and disease classifications followed pre-established rules developed prior to data analysis.

In conclusion, we have described primary diagnosis, mortality and prevalence of HIV infection in >10,000 Malawian adults admitted over two years at a Malawian central hospital using systematically collected, prospective data. Our age-based analysis demonstrates the complexity of the health needs of the older population. Infections, particularly HIV-associated infections, remain the dominant reason for admission, however, there is an equal balance of NCDs and infections in adults aged over 55, in whom HIV testing rates were considerably lower than in younger adults despite high HIV prevalence. With increased life expectancy, including in the HIV-infected population, LMICs which are poised for a shift in health policy focus toward NCDs must prepare, in the interim, for the challenges of the double burden of both infections and NCDs, particularly in older adults.

Supporting Information

S1 File. Definitions for diagnostic categories.
(DOCX)

S2 File. Diagnoses list.
(XLS)

S1 Fig. Study consort diagram for analysis of age related patterns of disease and mortality in hospitalised adults in Malawi.
(DOCX)

Acknowledgments

The SPINE system is funded by the Malawi-Liverpool-Wellcome Trust Clinical Research Programme which is supported by a Strategic Award from The Wellcome Trust.
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