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Research Article

Relative Risks of Women Dying from Maternal, Infectious or Non-Communicable Causes in Kintampo, Ghana: A Study Protocol, Using Competing Risks Analysis

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Abstract

Introduction: Maternal, infectious and non-communicable causes of death combine to be simultaneously a major health problem for women of reproductive age (WRA) in low and middle-income countries (LMICs), particularly sub-Saharan Africa (SSA). Yet, little is known about the relative risk of each of them when considered together and their demographic impact. Consequently, the focus of research and funding has been on maternal health. However, the evolving demographic and health transitions in LMICs suggest a need for a comprehensive methodology to addressing women's health challenges beyond maternal causes.

Objective: To examine the relative risks of women of reproductive age dying from maternal, infectious or non-communicable causes, using a competing risks analysis.

Methods: This is a fifteen-year study of the Kintampo North Municipality and the Kintampo South District, of the Bono East Region of Ghana which are the study sites of the Kintampo Health and Demographic Surveillance System (KHDSS), administered by the Kintampo Health Research Centre (KHRC). Deaths and person-years of exposure were calculated by age for WRA (15 - 49) of the KHDSS area from January 2005 to December 2019. Causes of death were diagnosed by means of the physician coding and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), using the verbal autopsy questionnaire. Identified causes of death were categorised into three broad groups: maternal, infectious and non-communicable diseases. The gains in life expectancy as well as the decomposition of the total gains by age were estimated, using multiple decrements together with the associated single decrement life table methods.

Discussion: The study uses competing risks analysis technique to examine the relative risk of women of reproductive age dying from maternal, infectious or non-communicable causes in the Kintampo North Municipality and Kintampo South District of Ghana. The study will provide valuable information on the relative risk of women dying from the three causes of death among the women. Both research and policy on mortality among women focus on maternal death. Meanwhile, cause of death by NCDs has been rising globally and among women in low and middle-income countries. This study aimed at examining death among WRA more comprehensively, using data on the three causes of death. The research evidence from the study will be useful for adopting policies and developing and implementing programmes where life expectancy returns will be highest. In addition, reliable data on causes of death is not readily available in most low-income countries, including Ghana. The verbal autopsy method used in this study provides valuable information on causes of death that are essential for monitoring and evaluating the targets of the health indicators of the Sustainable Development Goals.

Keywords: *Verbal Autopsy; Women of Reproductive Age; Health and Demographic Surveillance System; Low and Middle-Income Countries*

Introduction

Traditionally, infectious diseases have been the main causes of death in low and middle-income countries (LMICs) [1]. Infectious causes of death affect all segments of the population including women of reproductive age (WRA) [2-4]. However, as a result of the epidemiological transition taking place in LMICs, deaths from non-communicable diseases (NCDs) are rising in LMICs [5,6]. NCD causes of death also affect all segments of the population including WRA. Meanwhile, maternal mortality that affect only WRA has been declining since the introduction of the millennium development goals (MDGs) in 2000 [5,7].

It is reported that approximately 800 women die every day globally due to maternal-related complications and 99 percent of them occur in LMICs, especially in sub-Saharan Africa (SSA) [8]. On the other hand, some scholars have estimated the proportion of infectious diseases among adult deaths to be 40 percent [9] and even as high as 74 percent in earlier studies [10].

In addition, studies in recent times have argued for the need to expand maternal health to cover women's health in general and to address the rising causes of death from non-communicable diseases (NCDs) among women. Labrique., *et al.* (2013) reported that 48 percent of deaths among WRA in Bangladesh were due to NCDs [11]. Another study in Ethiopia reported that NCDs were the top causes of death [12]. Increasing prevalence rates of NCDs have been observed in the developing world more than a decade and the levels are still high [13,14]. It was indicated less than a decade ago that the situation is expected to exacerbate with more than 80% rise in NCDs in developing countries by 2030, compared to less than 8% rise in the same conditions in developed countries [14].

The 2021 WHO Key Facts on Noncommunicable diseases indicate that each year, more than 15 million people aged between 30 and 69 years die from NCDs; and 85% of these deaths (termed "premature" deaths) occur in low- and middle-income countries [15]. Again, 77 percent of all NCD deaths are recorded in low- and middle-income countries [15]. Meanwhile, deaths from infectious diseases are also still high in low- and middle-income countries [12]. Generally, women in the reproductive ages in LMICs, especially those in SSA, suffer from the triple burden of dying from maternal, infectious and non-communicable diseases [16].

There is, therefore, evidence that maternal, infectious and non-communicable causes of death combine to be simultaneously a major health problem for women of reproductive age (WRA) in low and middle-income countries especially in SSA countries. In view of this, the present study used health and demographic surveillance (HDSS) data to examine the major causes of death among the WRA and the relative risks of these causes of death in the Kintampo North Municipality and Kintampo South District of Ghana.

The study was guided by the following research questions:

- Are WRA in Kintampo more likely to die from maternal than infectious or NCD causes of death?
- Are the socio-demographic, economic, physical, behavioural and health determinants of maternal deaths different from infectious or NCD causes of death among the WRA in Kintampo?
- What is the effect of eliminating maternal, infectious or NCD causes of death on life expectancy among the WRA?
- Which age group will contribute most to the overall change in life expectancy among the WRA in Kintampo, following elimination of any of the causes?

Methods and Results

Study design

This study was based on a fifteen-year quantitative research. The study sample consists of a prospective open cohort of women aged between 15 and 49 years of age living in the Kintampo HDSS area during the period from 1st January 2005 to December 31st, 2019.

Data source

Data for this study was from the Kintampo Health and Demographic Surveillance System (KHDSS) of the Kintampo Health Research Centre (KHRC). KHDSS is made up of field and computing operations to manage the longitudinal follow-up of persons and their households as well as their residential units and all their demographic and health characteristics within the Kintampo North Municipality and the Kintampo South District of the Brong Ahafo Region of Ghana [17,18].

The Kintampo HDSS area has been mapped by geo-referencing of residential units, using geographic information system (GIS) technology; global positioning system (GPS) coordinates are assigned as location attributes of the residential units within the database [17,18]. It is one of the three Ministry of Health/Ghana Health Service health research centres in the country. The KHDSS is strategically located in the middle belt of Ghana, with the other two located in the northern belt (Navrongo) and southern belt (Dodowa) of the country. It is also one of the 49 HDSS sites across 19 countries in Africa, Asia and Oceania and they typically engage in monitoring the population dynamics of their respective areas of operation [19].

Pregnancies and their outcomes are recorded for all registered women in the KHDSS during routine update visits. Every live birth is then recorded as a member of the KHDSS, independent of subsequent survival. In KHDSS, field workers take note of live births to visitors to the KHDSS area to notify the field worker in the following round to register the eligible mother and her child or children. This practice is very useful, as it improves the precision of dates of birth for new-borns. In addition, it improves the reporting of births for mothers with repeated in- and out-migration. Furthermore, observation of pregnancy is used to improve the reporting of the outcomes of pregnancies. This is achieved by following up on a notification of pregnancy outcome for each registered pregnancy in the subsequent visit.

Deaths of all registered and eligible members of the KHDSS are recorded, irrespective of where the death occurred. Within the KHDSS, deaths are normally widely known compared to births so deaths are not commonly underreported. However, the deaths of under-five-year children, particularly neonates (eligible and not yet registered) are hardly known, especially, if cultural beliefs do not encourage reporting them. The KHDSS conducts verbal autopsies (VA) on all deaths that occur in the study area to ascertain the causes of deaths among the population.

Under the Kintampo HDSS operations, two types of migration events occur: out-migration-where individuals change residence from or to an area outside the HDSS area of operation. The other type of movement is mobility within the municipality and district-where individuals change residence within the HDSS area of operation. Such mobility does not influence the data in any way since the movement is within the HDSS area. On the other hand, out-migration affects the data to some extent.

A 90-day period is used as inclusion or exclusion criterion for migrants. An individual who moves outside the Kintampo HDSS Area for 90 days or more is considered to have out-migrated. On the other hand, an individual who enters the Kintampo HDSS Area and stays for 90 days or more is considered to have in-migrated.

The Kintampo HDSS is a net exporter of people in the working age group (15 - 60) through out-migration. However, women of reproductive age group (15 - 49) rarely migrate mainly because of marriage and child-bearing. Moreover, WRA who migrate out are likely to be compensated by those who migrate into the HDSS, and are expected to have similar characteristics as those who have moved out. In view of this, migration among WRA is not expected to have significantly influenced the results of the present study.

Community key informants (CKI)

An innovative component of the KHDSS is the Community Key Informants (CKI) system whereby well-known individuals in the various communities are trained to record any pregnancy, birth and death that occurs in their respective communities for a little fee. Their activities are important because some respondents do not report some of these events during the fieldworkers' visits, particularly pregnancy loss through miscarriage or abortion and neonatal deaths. However, with the presence of the CKIs in the communities who record such events and in turn report them to the fieldworker, this challenge is largely reduced or overcome completely.

Verbal autopsy data collection tool

Women in the reproductive ages in LMICs, especially SSA, suffer from the triple burden of dying from maternal, infectious and non-communicable diseases [16]. However, precise and reliable estimates of causes of death for the population or sub-population in many SSA countries are difficult because of the limited access and utilization of health services and most of the deaths occur outside a health facility [20,21]. This situation is further compounded by the lack of comprehensive population-based studies and incomplete or non-existent civil and vital registration systems in many LMICs [22]. In view of these challenges, studies in SSA use estimates by the WHO that are mostly created from very scanty data [23]. Lack of or inadequate data makes the understanding of the causes of death that may reveal the sickness load more complex [16].

Verbal autopsy (VA) has been shown by several studies to be the best available tool for data collection on cause of death in LMICs [9,22,24-26]. In view of this, the VA approach has been used in recent times to ascertain the probable cause of death at the community level in many LMICs [22,25]. Currently, interest in VA for monitoring causes of death is increasing [27]. Several LMICs, including China, India, Brazil, Mozambique, Zambia and Tanzania have used different types of VA in collecting health data in their various jurisdictions [27]. The WHO is advocating the extensive use of VA particularly to monitor the NCD epidemic in many LMICs with inadequate death registration and medical certification [28].

Wider usage of VA for mundane national health information systems could potentially enhance the availability of essential and reliable data on causes of death for disease control programmes. However, there are debates on the reliability of symptom-based data obtained from families and the practicality of depending on clinicians to evaluate unidentified symptom-based forms. Physician Coded Verbal Autopsy (PCVA) is the commonest method of determining the probable cause of death. PCVA is the only available method in the Kintampo HDSS Setup. Two physicians independently review VA questionnaire and assign a single cause using the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). A third clinician examines the case if a consensual cause of death is not reached between the first two. No final cause of death is entered when consensus cannot be reached [22,25]. The PCVA is associated with some challenges. It is costly and it takes a lot of time [27]. In the recent past, computerised algorithms have been created for establishing cause of death, to minimise the difficulties with the PCVA method [27,29]. However, this study used the physician coding verbal autopsy certification to identify maternal, infectious and non-communicable causes of deaths (Appendix I: A sample of the form used by physicians for coding causes of death).

Data management

When completed registers and accompanying forms are brought from the field, the field supervisors checked them for blanks, inconsistencies, and any other type of errors, content or coverage prior to submission to the data management centre. The Household Record Books (HRBs) and their event forms are sent to the data management centre where they are received by filing clerks who log and keep the records. There is strict recording system to ensure that HRBs and their event forms are tracked and accounted for at every stage of the data collection, processing and storage. The HRBs and their event forms are passed on to the data entry clerks for data processing.

During data processing, each of the events recorded in the HRBs and their forms is captured on separate tables in the database. These different tables are linked to each other during data analysis by using each individual's unique identification that was assigned at the point of the initial registration. Similarly, prior to data processing, the main data collection tool for this study, the VA questionnaires were checked for completeness and consistency by research officers with a minimum of first-degree university education. The VA questionnaires were double entered on computers, using Microsoft Visual FoxPro (version 9.0) data management software. Automated range and consistency checks were also performed. Discrepancies were resolved by referring to the original questionnaire and the field manual that was used for training the field workers. In addition, five percent of all scheduled interviews are randomly selected and repeated by a more experienced data collector as quality control to ensure that data quality standards are maintained.

Key variables and measures

The selection of both outcome and explanatory variables for this study were guided by the reviewed literature.

Outcome variables

The outcome variables for this study were deaths due to maternal, infectious or non-communicable causes of death among WRA in the two Kintampo districts from 2005 to 2019. Maternal causes of death were operationally defined to include only direct (obstetric) deaths as the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy. Infectious causes of death were defined to include deaths from all infections and parasitic diseases whilst non-communicable causes of death were operationally defined as non-maternal and non-infectious and non-external or injury causes of death. These outcome variables are broad categories of causes of deaths. They were arrived at after physicians have diagnosed and assigned a probable cause of death to each death that occurred in the Kintampo HDSS area during the death coding process.

Explanatory variables

The age at death for each adult female was determined by linking the death dataset to the individual dataset that contains the basic demographic data, including the date of birth and sex of the person. The age at death is computed by finding the difference between the date of birth and the date of death. All adult females who died and were resident in the study area between 1st January 2005 and 31st December 2014 were included in this analysis. Age was categorized into seven five-year groups namely: 15 - 19, 20 - 24, 25 - 29, 30 - 34, 35 - 39, 40 - 44, and 45 - 49 years. This division made it possible to explore age-related differences associated with maternal, infectious or non-communicable causes of death, including comparing adolescents and their older counterpart in the analysis.

Similarly, other demographic variables were selected and categorised according to the literature and also to ensure that there are enough cases in each cell for analysis. As per the reviewed literature, primigravidae and higher order parity are associated with higher mortality. Therefore, children ever born were categorised into three (3) groups: 0, 1 - 3 and 4 and above to further examine the discussions in the literature. Some aspects of the literature posit that marriage confers some protection on the individual as far as the risk of dying is concerned. However, this assertion is disputed by others. In view of this contention, marital status was grouped into two (2) never-married and ever-married to explore the differences. This dichotomy also allowed for enough cases in the cells especially at the multivariate level of analyses.

Some socio-economic and cultural factors were considered in this study. Education is a key variable discussed in the literature on socio-economic determinants of causes of death. Therefore, the influence of education on causes of death was examined. The level of education, especially among women, is quite low in the study area. In view of this, highest educational level attained by the deceased adult females were re-categorized into three groups to ensure that there are enough cases in all the cells. The three categorizations were: never had any formal education as (none), those who attained up to primary school level (primary) and those who got up to middle or junior high school or senior secondary school or tertiary level (JHS and above). Regarding access to health services which is a factor that is associated with health status, some studies on migration suggest that migrants tend to be disadvantaged compared to the indigenes of a place. Accordingly, the women were categorized as 'migrants' and 'non-migrants' to measure the effects of migration status on the outcome variables on those who came from elsewhere to settle in the study area and those who were indigens.

In addition, ethnicity was measured conventionally by categorizing the ethnic groups in the study area into four: Northern ethnic groups, Akan, Mo and Other ethnic groups. Religion was also re-categorised into Catholic, Pentecostal, Muslim and Other religions but at the multivariate level, it was re-categorised again into three: Christians, Muslims and Other to ensure that there are enough cases in the cells, especially in the case of maternal causes of death that are relatively rare events. For the same reasons, employment status was classified into two (2) categories: unemployed and employed at the multivariate level, but occupation was grouped into six at the bivariate level as follows: no occupation, trader/food seller, labourer/domestic worker, seamstress/hairdresser, professional (teacher, nurse, accountant) and other.

In order to explore the cultural dimension of mortality further, this study considered a measure of female level of independence in the community. The reviewed literature discusses autonomy as very important as far as adult female mortality is concerned. This is because several studies have linked autonomous women with low mortality and vice versa. In view of this observation in the reviewed literature, farmland ownership was used as a proxy to measure the level of female independence in the community. This is quite appropriate because culturally, the head of the family who is a male owns the land in trust for all. Therefore, a woman owning a farmland was an indication of how independent she was in the community. Land ownership was categorised into two in terms of whether the deceased woman owned land or not (yes or no).

The physical and climatic factors, including the household level factors were also considered in this study. The place of residence variable is a household characteristic and it was determined by the location of the compound in which the household was found. The household is in either rural or urban area. The study area is predominantly rural. There are only three communities namely Kintampo, Jema and Babato each with a population of over 5,000 that were classified as urban. The Kintampo HDSS covers two administrative districts. Based on this, the district will also be categorised into 2 namely Kintampo North and Kintampo South. Another physical and climatic factor that was considered in this analysis was the season of death. Malaria is the most dominant cause of death in the study area and it has been documented that its prevalence is highest in the rainy season as per the reviewed literature for this study. Season of death were classified into two: wet and dry whilst the year of death were categorised into ten, from 2005 to 2019.

Factors related to the health system were also considered to reflect the conceptual framework adapted for this study. Distance is one key factor identified in the literature as affecting health service utilisation. Several studies have established a positive correlation between health facility use and a 5-km radius. In contrast, some studies have shown that health facilities beyond 5-km radius tend to reduce health service utilisation. This has the tendency to affect the health status and incidence of death eventually. Therefore, distance to the health facility was dichotomized into 5 km or less and more than 5 km by using the GIS data of the Kintampo HDSS. Another health-related factor considered is the place where the deceased died. This variable was categorised into two: hospital and other to represent WRA who died in and outside hospital respectively. The hospitals have the clinicians and skill birth attendants as well as the equipment needed during emergency situations, but these facilities are not available outside the hospital. Therefore, the 'place of death' is used in this study as a proxy measure for health service utilisation.

Intermediate level factors in this analysis were living standards and lifestyles. These factors were conceptualised to include both individual and household level variables. At the household level, the Principal Component Analysis (PCA) method was used to categorise households into three socio-economic statuses (SES) of most-poor, poor and least-poor. Household assets such as television, radio, refrigerator, telephone, lighting type, type of roofing material, type of floor material, vehicles, motorbikes and livestock will be used in the PCA. Other household level variables considered in this study to reflect the importance of sanitation were source of drinking water and type of toilet facility, which was categorised separately as improved or unimproved. At the individual level, tobacco, alcohol and drug use were measured as in whether it was used or not. They were also put together in a composite as 'substance use' at the multivariate level and classified into two groups in terms of whether the deceased woman used any of the substance or not to allow for enough cases in all the cells for analysis.

Finally, proximate level variables were considered in this study. These variables sought to measure the health status of the deceased WRA. The proximate level variables are the most immediate factors that influence the outcome of interest, which are the risk of dying from maternal, infectious or non-communicable causes of death. The health status in this current study included admission in the last twelve months before dying, whether or not the deceased woman had some surgical operation 24 months before dying and whether or not the deceased woman died suddenly. Responses to each of these variables were categorised into two (2): yes or no.

Analytical methods

Several analyses were conducted to answer the research questions to achieve the objectives of the study after some preliminary investigations including checking for multicollinearity were done. The first part of the analysis involved the generation of frequencies by way of univariate statistics to describe the number and distribution of the distal, intermediate and proximate variables. The second part of the analysis was a series of cross-tabulations between the outcome variables and each of the explanatory variables. The chi-square statistical test was used to examine the statistically significant association between the outcome variables and each of the explanatory variables. P-values of less than 0.05 was considered as statistically significant.

The third phase of the analysis examined the relative risk of dying from maternal, infectious, non-communicable causes of death. To calculate the relative risk, the risk of dying for each of the three-broad causes of death (maternal, infectious and non-communicable) was calculated by dividing the number of deaths for each cause by the person-years of observation for WRA (15 - 49). This was done by year for the respective causes of death. After calculating the risk of dying for each cause, the relative risk for infectious and non-communicable causes of death was calculated separately by using the risk of dying from maternal causes to divide each of them. By using this approach, a relative risk, which is more than 1.0 indicates that there is an increased risk of infectious or non-communicable causes of death, conversely, a relative risk, which is lower than 1.0 shows that there is a lesser risk of infectious or non-communicable causes of death.

A reverse approach was also used where the risk of dying from maternal cause was divided with that for infectious and non-communicable causes separately to arrive at the relative risks of dying from maternal causes with respect to infectious and non-communicable causes of death. With the latter approach, a relative risk of less than 1.0 illustrates that there is an increased risk of infectious or non-communicable causes of death, on the contrary, a relative risk, which is more than 1.0 shows that there is a decreased risk of infectious or non-communicable causes of death.

At the fourth stage of the analysis, four multinomial logistic regression models were used with the maternal causes of death as the reference group or base outcome. The choice of this method was due to the several competing outcomes. The first model was a regression of each variable on the outcome variables. This was done to examine the separate effect of each of the variables on the outcome variables. From the second to the fourth models, hierarchical analysis was done where each of the components of the conceptual framework (Appendix II: a copy of the conceptual framework) namely: distal, intermediate and proximate variables was entered cumulatively one after the other to account for their separate effects. This was done to deepen the understanding of the maternal, infectious and non-communicable causes of death in the study area.

With the hierarchical model, the distal variables were the first to be regressed on the outcome variables to examine its separate effect on the outcome variables. The intermediate variables were then entered cumulatively to study the separate effect of the intermediate variables on the outcome variables. During the third or final model, the proximate variables were also entered cumulatively to investigate their effects on the outcome variables when the distal and intermediate variables were controlled for. The R^2 was determined after each addition. P-values of less than 0.05 was considered as statistically significant. The results of this analysis are reported in Abubakari., *et al*. 2022 [30].

A series of further analysis were conducted to achieve other objectives of the study. Life-table techniques were employed to examine a situation of competing risks that involves the risk of dying from multiple causes of death. This is based on a hypothetical situation that uses life table methods to estimate by how much life expectancy would increase if any of the causes of death (maternal, infectious or non-communicable) were eliminated. This is done by estimating separately for each of the causes of death the expected reduced mortality and the consequent increases in life expectancy that could result in the hypothetical elimination of a specified cause of death (maternal, infectious or non-communicable) (Appendix III: a detailed explanation of the procedure). In addition, the total change in life expectancy was decomposed to determine which age group is likely to contribute most to the overall change in life expectancy because of the eradication of any of the causes of death (maternal, infectious, or non-communicable) (Appendix IV a detailed explanation of the decomposition procedure). Findings of these analyses are also published in Abubakari., *et al*. 2020 and 2021 [31,32].

Data Limitations

The influence of mortality from the various causes may not be estimated accurately since not all deaths recorded by the Kintampo HDSS had successful verbal autopsy interviews but this is expected to be random and therefore, should not have major effects on the study. Also, a proportion of the cases with successful interviews were coded as "cause of death not determined". This is also expected to be random. In addition, ethnicity was used as a proxy for migration status but this is not the usual convention. Furthermore, health system variables (Distance to health facility and Place of death) do not fully consider availability and quality of health services. Moreover, it is well established in the literature that NCDs affect older persons more. Therefore, by restricting this study to WRA, the effect of NCD causes of death may not be well accounted for. However, the analyses in this study were done based on the observation that the three categories of causes of death were recorded among the WRA. Finally, this study used secondary data and other key factors such as pre-conceptional,

conceptional, geo-political contextual variables that may affect maternal, infectious and non-communicable causes of death were not included in the analyses.

Ethical Approval

The Institutional Ethics Committee (IEC) of the Kintampo Health Research Centre reviewed the protocol and all instruments associated with this study and approved it as part of the activities of the Kintampo Health and Demographic Surveillance System with the follow details: Ref: KHRC/IEC/ICF/2010-1; FWA: 00011103; and IOR0004854 on the approval certificate.

Discussion

The study used a multifaceted approach to examine the relative risk of women of reproductive age dying from maternal, infectious or non-communicable causes as well as the determinants of these causes of death in the Kintampo districts. This study may be the first attempt at investigating the relative risks of WRA dying from maternal, infectious or non-communicable causes of death as well as the demographic impact of these causes of death together. The study used multiple-decrement and associated single-decrement life-table techniques to assess separately the overall number of person-years that will be discounted had maternal, infectious or NCD causes of death been hypothetically eliminated from the population given the mortality conditions of the period. This approach allowed the gains in life expectancy as well as the decomposition of the total gains by age to be estimated.

A decomposition of the total difference in life expectancy into specific age groups to establish the ages that a decrease in mortality from the respective causes of death would make the greatest impact on survival. This is essential because changes in life expectancy do not mean that mortality rates or the directions are the same across all age groups. Generally, most age groups will record a decline in mortality and, therefore, contribute to increase in life expectancy. However, mortality may increase for some age groups that would offset the improvement in life expectancy. Hence, decomposition is used to account for the contribution of the various age groups to the total difference in life expectancy. This approach makes it possible for policy intervention to target the age group that yields the highest returns in the mix of scarce resources.

In addition, the study used relative risk ratio to compare the likelihood of dying from infectious and non-communicable causes relative to the maternal cause of death and vice versa. This approach is also important because the maternal cause of death has been the focus of research, policy and funding, especially over the past three decades. Currently, there is a debate on the need for equal attention on other causes of death among WRA, especially as the maternal causes of death are declining and NCD causes are rising whilst infectious causes of death are persistently high.

After providing evidence of the comparative influence of maternal, infectious and non-communicable causes of death in the Kintampo HDSS area, among women of reproductive age between the period 2005 to 2019, the study investigated the determinants of these causes of death to be able to recommend appropriate intervention to contain the problem. Multinomial logistics regression was used to establish the determinants of the causes of deaths. The choice of this method is also due to the several competing outcomes. The reviewed literature on causes of death shows correlations between maternal causes of death and some distal, intermediate and proximate level factors. These factors include socio-demographic (age, parity, marital status); socio-economic and cultural (educational level attained, occupation, religious affiliation, ethnicity), as well as lifestyle and behavioural (dietary practices/nutrition, alcohol and tobacco use) factors among others.

It has recently been observed that NCDs are no more diseases of the affluent and elderly only; they are a major cause of death among WRA in LMICs [20,33]. In 2011, the World Economic Forum (WEF) ranked NCDs among the greatest threats to global economic development [34]. This assertion took cognisance of the significant social and economic impacts of NCDs on society. Moreover, over 9 million NCD deaths equivalent to one fourth of NCD deaths, happen in persons less than 60 years old. These are "premature" deaths and 90 percent of them occur in LMICs. It is increasingly affecting women in LMICs in their most productive years [35]. Women are especially susceptible to NCDs because of biology, gender, and other social determinants [36]. It is therefore imperative for this study to examine demographic and other effects of maternal, infectious and NCD causes of death on women.

Furthermore, information on causes of death is not readily available in most LMICs due to lack of vital and civil registration system [37]. As a result, studies on causes of death are based on demographic and health survey (DHS) and census data. However, studies using data from censuses are limited because of long inter-censal periods [22,37]. Therefore, interventions and policies based on such findings usually fail to achieve the desired results because the vulnerable groups supposed to be the targets are missed or hidden behind large population averages [22]. Longitudinal data can best provide the information needed to understand consequences of women's health outcomes.

Moreover, it is important to indicate that studies such as the demographic and health survey (DHS) are mainly limited to cross-country, regional or rural-urban classification. Currently, there is an emphasis on the need for local data to set priorities for reducing maternal mortality [38]. Efforts to reduce adult female mortality, continue to be elusive because of the lack of appreciation of the effects of the underlying socio-demographic, economic, physical, behavioural and health-related conditions that women are exposed to within their various communities. This study uses data with the needed socio-demographic and economic information that can ensure that these important variables are also considered in mortality analysis among the WRA.

It is important to emphasise that reliable data for monitoring morbidity and mortality and in particular, maternal mortality was a major challenge in tracking the MDG 5A. Reliable data is still crucial for achieving the targets of the health indicators of the Sustainable Development Goals (SDGs). This study is therefore timely and justified because the Kintampo Health Research Centre has over two decades of data. The cause of death data collected using the Kintampo HDSS platform provides the opportunity to understand who, where, when and how adult female deaths occurred. Therefore, this study will make it possible to fashion out feasible and cost-effective interventions to achieve the health-related SDG targets by 2030 [39].

Finally, this study is justified because the settings for most of the reviewed studies so far were mainly health facility-based studies. However, health facility data may not represent the general population since in low-income settings, most deaths occur in homes, thereby making it difficult to obtain medically certified cause of death [22,40]. Fortunately, the verbal autopsy method used by the HDSSs provide valuable information on patterns of causes of death [26,27]; and this is utilised by the present study. In addition, institutional data is fraught with several challenges such as ineffective record system and inability to know the denominator of the study population. The present study used population-based data that is devoid of such data challenges. Therefore, the current study uses health and demographic surveillance (HDSS) data, to provide empirical evidence to examine the major causes of death and their relative risks among the WRA in Kintampo districts of Ghana. It fills the gap created due to the paucity of data and lack of understanding of maternal, infectious and non-communicable causes of death.

Conclusion

Over the last three decades or more, research, policy and funding have been focused on reducing maternal mortality, and these efforts have resulted in significant decline in maternal deaths especially since 2000, but findings from this protocol have shown clearly that NCD deaths are rising whilst deaths from infectious causes are persistently high, and it is essential to pay equal attention to all of them.

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Competing Interests

The authors declare that they have no competing interests.

Appendices

Appendix I

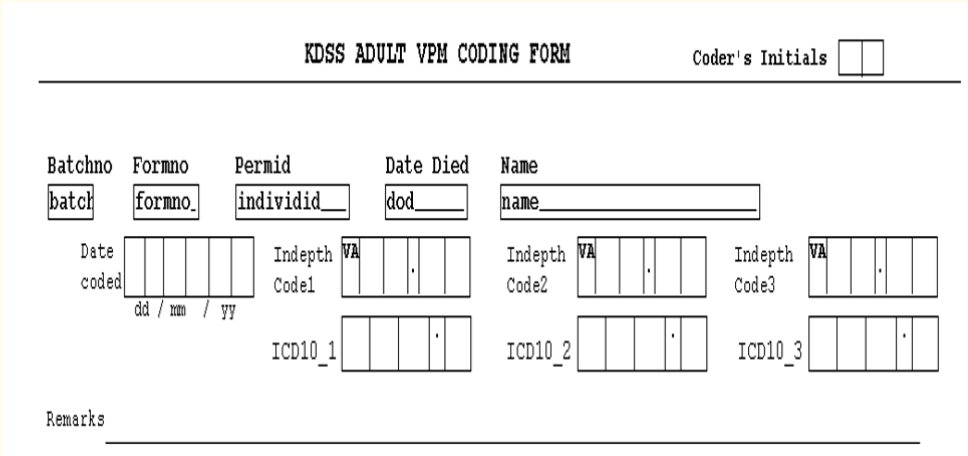

Figure A

Appendix II

Conceptual framework of factors associated with dying from maternal, infectious or non-communicable causes of death

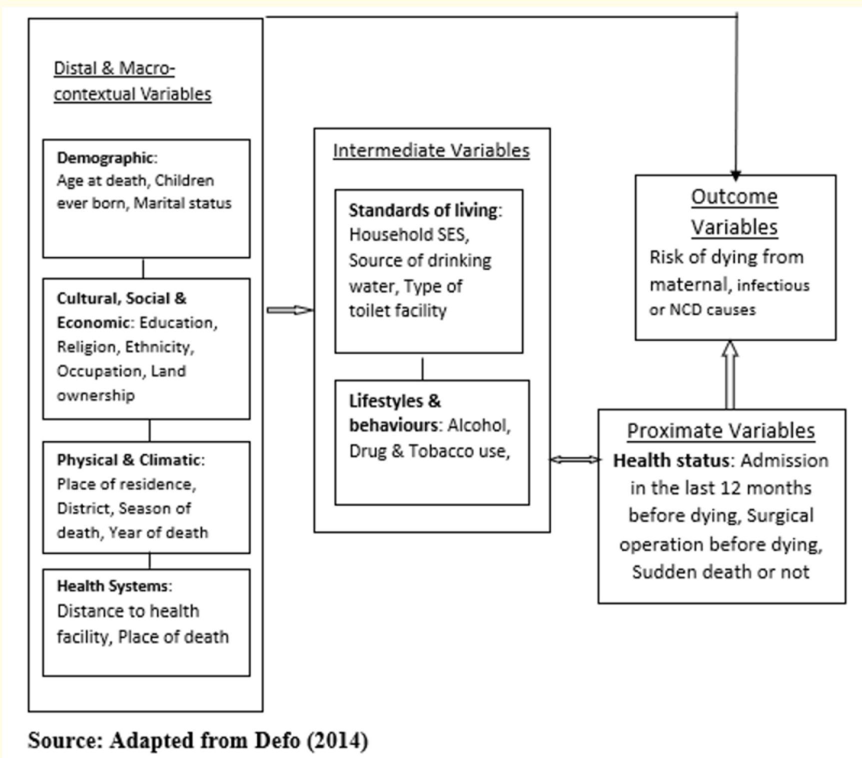

Figure B

Appendix III

Estimation procedure for multiple decrement and associated single decrement

Life tables

In the analysis of causes of death, the force of the mortality function from different causes is additive because disentangling precisely the effects of other causes of death is difficult, especially in settings where precise measurement is not possible. Thus, the sum of the different causes is equal to all causes combined as represented in equation (1) thus:

$$\mu(x) = \sum_{i=1}^{I} \mu_i(x), \quad (1)$$

Where $\mu(x)$ is the force of mortality from all causes combined and parameters $\mu_i(x)$ refer to the death rate for the ith cause of death. This implies that the rates of decrements are also additive:

$$_nm_x = \sum_{i=1}^{i} {_nm_{xi}}, \quad (2)$$

Where $_nm_x$ is the rate of decrement from all causes and $_nm_{xi}$ in this case is the rate of decrement from maternal or infectious or non-communicable causes of death.

Considering the basic relationship between mortality rates ($_nm_x$) and the probability of dying ($_nq_x$) as shown in the conventional life table, the transformation of the rates to probabilities of dying is shown in the following equation as:

$$_nq_x = \frac{n_nm_x}{1 + (n - {_na_x})_nm_x}, \quad (3)$$

Where $_na_x$ is defined as the average number of person-years lived in the interval x to $x + n$ by those who died in the interval. This relationship extends to multiple-decrement processes as follows:

$$_nq_{xi} = \frac{n_nm_{xi}}{1 + (n - {_na_x})({_nm_{xi}} + {_nm_{x,-1}})}, \quad (4)$$

Where $_nm_{xi}$ and $_nm_{x,-i}$ represent decrement rates from maternal or infectious or non-communicable and all other causes other than maternal or infectious or non-communicable combined, respectively. Data concerning the causes of death by age and the corresponding number of person-years by the same sub-categories define the probabilities of dying at each age ($_nq_x$), by cause of death. However, obtaining the $_na_x$ values is often difficult. Therefore, different techniques are employed to estimate the $_na_x$ values. First, it is assumed that those who died in the interval on average lived halfway through the interval. Based on this assumption, an initial value of 2.5 is adopted for all age groups with an interval of 5 years. For the younger than 1-year and 1 - 4-year age groups, a procedure suggested by Coale and Demeny is adopted (Bawah and Binka, 2007).

Using the $_na_x$ values of 2.5 in the $_nm_x \rightarrow {_nq_x}$ conversion formula, $_nq_x$ values are estimated first and the values are used to obtain *ndx* (the number of deaths between age x and $x + n$) in a life table. These $_nd_x$ estimates are plugged into the iteration formula below to obtain new sets of $_na_x$ values. These values are subsequently re-introduced into the $_nm_x \rightarrow {_nq_x}$ conversion formula to re-estimate new $_nd_x$ values, which are re-introduced in the iteration formula to obtain a new set of $_na_x$ values. This process is repeated until stable estimates of $_na_x$ are achieved (Bawah and Binka, 2007). The iteration equation used is specified as follows:

$$_na_x = \frac{-\frac{n}{24}{_nd_{x-n}} + \frac{n}{2}{_nd_x} + \frac{n}{24}{_nd_{x+n}}}{_nd_x}. \quad (5)$$

The stable $_na_x$ values then are used to generate a life table for females in the Kintampo HDSS area through the basic $_nm^x \rightarrow {_nq_x}$ conversion formula. With the overall life table generated, the probability of dying from maternal, infectious or non-communicable causes of death ($_nq_{xi}$) is estimated, by applying the proportion of deaths that are due to maternal, infectious or non-communicable causes of death to the overall probabilities of dying for each age, $_nq_x$, as follows:

$$_nq_{xi} = {_nq_x} \cdot \frac{_nD_{xi}}{_nD_x}, \quad (6)$$

Where $_nq_{xi}$ and $_nD_{xi}$ represent the probability of dying from maternal, infectious or non-communicable causes of death and the observed number of deaths from maternal, infectious or non-communicable causes of death, respectively. The above relationship assumes that the observed death rates for maternal, infectious or non-communicable causes of death ($_nM_{xi}$) are equal to the life-table death rates for maternal, infectious or non-communicable causes of death ($_nm_{xi}$), that is, $_nM_{xi} = {_nm_{xi}}$.

Estimating the contribution of mortality from maternal, infectious or non-communicable causes of death to overall mortality also allow to estimate the effect of eliminating maternal, infectious or non-communicable causes of death through "cause-deleted" lifetable analysis (Bawah and Binka, 2007). If maternal, infectious or non-communicable causes-related morrtality were eliminated as a cause of death, survival at age interval x to $x + n$, will be represented as:

$$_nP_{x,-i} = {_np_x}^{\left(\frac{_nD_{xi}}{_nD_x}\right)}. \quad (7)$$

The approach described above assumes that the force of mortality function from each cause is proportional to all causes combined in the interval x to $x + n$ and constant throughout the interval (Arriaga, 1984). The $_na_x$ values for the associated single decrement life table were obtained using the following formula for all age groups except the first two and the last:

$$_na_{x,-i} = n + R^i \frac{_nq_x}{_nq_{x,-i}} ({_na_x} - n), \quad (8)$$

Where $_na_{x,-i}$ refers to the average number of person-years lived by those dying in the interval from all causes other than maternal, infectious or non-communicable-related death, and Ri represents the proportion of deaths due to maternal, infectious or non-communicable-related mortality. For the other age groups, the iteration procedure used for estimating the $_na_x$ values in the parent life table is used.

Appendix IV

Estimation procedure for decomposition by age

To ascertain the age groups likely to contribute most to the total difference in life expectancy at birth because of the elimination of malaria, the total difference in life expectancy is decomposed into specific age groups, using the procedure proposed by Arriaga. This approach permits estimation of specific reductions in mortality due to the cause of death by age group and consequent increases in life expectancy in the population.

$$
{}_n\Delta_x = \frac{l_x^{all}}{l_0^{all}} \cdot \left(\frac{{}_nL_x^{-COD}}{l_x^{-COD}} - \frac{{}_nL_x^{all}}{l_x^{all}} \right) + \frac{T_{x+n}^{-COD}}{l_0^{all}} \cdot \left(\frac{l_x^{all}}{l_x^{-COD}} - \frac{l_{x+n}^{all}}{l_{x+n}^{-COD}} \right),
$$

Where the superscripts *all* and *–COD* (maternal or infectious or non-communicable) indicate, respectively, with and without maternal or infectious or non-communicable causes of death. The first term at the right side of the equation refers to the direct effect of a change in mortality rates between ages *x* and *x + n*, whereas the second term refers to the sum of both the indirect and interaction effects of contributions resulting from the number of person-years to be added because of additional survivors at age *x + n* exposed to the new mortality conditions. The equation used for the open-ended interval is as follows:

$$
{}_\infty\Delta_x = \frac{l_x^{all}}{l_0^{all}} \cdot \left(\frac{T_x^{-COD}}{l_x^{-COD}} - \frac{T_x^{all}}{l_x^{all}} \right).
$$

Thus, the change in life expectancy ($l_0^{o(-COD)} - l_0^{o(all)} \sum_x {}_n\Delta_x$) can be decomposed according to the contribution of the different age groups.

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