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UNIVERSITY OF WITWATERSRAND

FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

MORTALITY IN WOMEN OF REPRODUCTIVE AGE IN RURAL SOUTH AFRICA

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements of the award of the Masters in Science in Epidemiology in the field of Population-based Field Epidemiology

April 2012

DECLARATION

I, Doreen Nabukalu declare that this research report is my own work. It is being submitted for the degree of Master of Science in Epidemiology in the field of Population Based Field Epidemiology at the University of Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other institution of higher learning.

Signature:  16th/04/2012

Doreen Nabukalu

DEDICATION

To my family and specifically my daughter Faith Gracious Nampiina who has endured 18 months of growing up without a mother.

ABSTRACT

Objective: To determine the causes of death and associated risk factors in women of reproductive age in rural South Africa. .

Methods: The study population comprised all female members aged 15-49 years of 11 000 households of a rural South African Health and Demographic Surveillance Site from 2000-2009. Deaths and person-years of observation (pyo) were determined for individuals between 01 January 2000 and 31 December 2009. Cause of death was ascertained by verbal autopsy interviews, based on ICD-10 coding; cause of death were broadly categorized as AIDS/TB causes, Non-communicable causes, Communicable/maternal/perinatal/nutrition causes, Injuries and another category of undetermined (unknown) causes of death. Overall and cause specific mortality rates (MR) with 95% confidence intervals (CI) were calculated. Cox proportional hazard regression (HR, 95% CI) was used to determine risk factors associated with overall and cause-specific mortality.

Results: 42703 eligible women were included; 3098 deaths were reported for 212607 person-years (pyo) of observation. Overall MR was 14.57 deaths/1000 pyo (CI;14.07-15.09), increasing from 2000-2003 (2003: MR;18.15, CI;16.41-20.08) and subsequently decreasing (2009: MR; 9.59, CI;8.43-10.91) after introduction of antiretroviral treatment (ART) for HIV in public health system facilities in South Africa in 2004. Mortality was highest for AIDS/TB (MR;10.66, CI;10.23-11.11) and the cause of death for 73.1% of all recorded deaths. Maternal mortality was 0.07 (CI; 0.04-0.11). Women aged 30-34 years had the highest MR due to AIDS/TB (MR; 20.34/1000 pyo), women aged 45-49 years due to other causes (MR; 4.29/ 1000 pyo).

In multivariable analyses, external migration status was associated with increased hazards of all cause mortality (HR; 1.87, CI; 1.56-2.26) and other causes of mortality (HR; 1.782, CI; 1.24-2.57). Self reported poor health was significantly associated with increased hazards of all cause mortality (HR; 11.052, CI; 4.24-28.82) but not with mortality due to other causes. Positive HIV status was associated with increased hazards of all cause mortality (HR; 8.53, CI; 6.81-10.67) and other causes of mortality (HR; 2.84, CI; 1.97- 4.09).

Conclusion. AIDS was the main cause of death in the current study, with mortality rates declining since introduction of ART for HIV in public health facilities in the surveillance area in 2004. Further ART roll-out, increased community awareness and sensitisation messages are still needed to reduce the spread of HIV and other sexually transmitted diseases.

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GLOSSARY

Underlying cause of death Underlying cause of death is defined by the World Health Organization (WHO) as the disease or injury that initiated the train of events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury.

Membership episodes A membership episode records the membership of an individual to a particular family. It can only be initiated by a DSS entry, a birth or a membership start event. It can only be terminated by DSS exit, a death or a membership end event.

Migration This refers to movement from one area of residence to settle in another area.

Internal migration This refers to movement within the surveillance area

External migration This refers to movement in and out of the surveillance area.

Long-term returning migrants This term refers to migrants who have been home for five years or more.

Short-term returning migrants This refers to migrants who have been back home on a permanent basis for less than five years.

Demographic surveillance This is defined as the process of monitoring births, deaths, causes of deaths and migration in a population over time.

Verbal autopsy This is an epidemiological tool that is used to assess cause of death in settings where hospital based records are lacking.

ACRONYMS

MMR- Maternal Mortality Ratio

HDSS- Health and Demographic Surveillance System

ACDIS- Africa Centre Demographic and Information System

HR- Hazard Ratio

OR- Odds Ratio

MR- Mortality Rate

DSA- Demographic Surveillance Area

WHO- World Health Organization

AIDS- Acquired Immune Deficiency Syndrome

HIV- Human Immune Virus

TB- Tuberculosis

VA- Verbal Autopsy

QC- Quality Control

CI- Confidence Interval

MS-SQL- Microsoft Structured Query Language

ID- Identifier

ICD-10- International Classification of Diseases, Version 10

ANC- Antenatal Care

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

This chapter reviews the burden of mortality and risk factors for mortality in women of reproductive age in developing countries.

1.1 Background Information

In many societies the passage of women from adolescence to adulthood is traditionally symbolized, and to a certain degree defined, by marriage and childbearing. For many women, the years between puberty and menopause offer multiple opportunities for personal fulfilment and development. However, this can also be a time of health risks specifically associated with sex and reproduction that may result in a significant burden of disability and mortality.

Explanations for mortality in women of reproductive age vary in terms of places and regions. According to a World Health Organization (WHO) report and studies done around the world, the two main causes of death in women of reproductive age globally are HIV/AIDS and complications related to pregnancy and childbearing, which account for 19% and 14% of all deaths in women of reproductive age.[1-2] In low income countries pregnancy and child bearing complications explain up to 19% of all deaths with the remaining percentage (71%) being attributed to other causes like malaria, AIDS, suicides, violence, cancers, respiratory infections, heart diseases among others.[2] A reproductive age mortality survey conducted in Ghana reported that out of 9248 deaths in women of reproductive age recorded from hospital records during the period 1st January 2002 to 31st December 2002, 179 deaths were due to

maternal causes and the remaining 9069 deaths were due to other causes. The analysis in the study was restricted to maternal mortality only and did not describe any other causes of mortality in women of reproductive age. The majority of maternal deaths (79%) were of women aged 15-34 years, with 21% of deaths for women aged 35-49.[3] In South Africa, the HIV pandemic is estimated to have reduced female life expectancy in the country by about 13 years from 64 years in 1990 to 51 years in 2005.[4] For the period 2001 to 2004 HIV prevalence was observed to be highest among pregnant women in KwaZulu-Natal (40.7%), Gauteng (33.1%) and Mpumalanga (30.8%) provinces.[5] Non-communicable diseases were reported by the South African Research Council as the second leading cause of death (after HIV/AIDS) in all women of reproductive age, with the highest burden in older women aged 40-49 years.[6]

In Tanzania, 43% of maternal deaths recorded were of women who had had >5 births, followed by women whose parity was 1 (who contributed 23% of the deaths).[7] In Uganda, distance of more than 10 km from a health unit contributed to the risk of maternal death. As the distance increased from the health unit, the risk of death correspondingly increased.[8] Studies in rural South Africa have found significant associations between migration status, level of education and all cause mortality in women of reproductive age.[9-10]

While Millennium Development Goals (MDG) 5 and 6 have set targets to reduce maternal mortality and combat the spread of HIV/AIDS in women of reproductive age in developing countries by the year 2015,[11] there is a need to clearly understand all causes of death in women of reproductive age in the local context and the risk factors associated with these causes. Data on cause of death is not adequate for most

developing countries due to inefficient systems of vital registration and the complexity of differentiating between maternal deaths and deaths due to other causes. As noted by Chandramohan and Byass, demographic surveillance is one of the cornerstones of public health research, particularly in investigating and tackling health disparities in areas where routine health information is incomplete or absent, particularly in developing countries.[12-13] Therefore using Africa Centre's Surveillance system (which is one of the 33 Demographic Surveillance Systems (DSS) in Africa and Asia) offers a unique opportunity to study causes of death based on an efficient record on vital registration conducted through verbal autopsies (VA) (in depth interviewing of caregivers about the signs and symptoms experienced by the deceased before death occurred).

This study used household and individual level data regularly updated by the Africa Centre for Health and Population Studies and community based verbal autopsy data to investigate the causes of and risk factors for mortality in women of reproductive age in a rural district of South Africa.

1.2 Statement of the problem

Mortality in women of reproductive age in developing countries has been inadequately addressed due to poor registration systems of vital data and limited availability of cause-specific mortality. In addition to that, maternal mortality has been seen as the most important problem, and more recently, HIV/AIDS related deaths which were subsequently assessed in more detail. As a result, studies in most parts of developing countries have focussed on causes of deaths in infants/children and maternal deaths due to pregnancy related issues.

1.3 Justification of the study

Maternal mortality has been seen as the most important problem, until recently when HIV/AIDS related deaths have been subsequently assessed in more detail. As a result, risk factors for non maternal deaths are not adequately addressed. This study looked at mortality in all women of reproductive age (15-49 years) using a methodologically comprehensive analysis based on longitudinal data regularly collected and updated by Africa Centre for Health and Population studies.

Evidence based results obtained in this study will be made available for appropriate policy developments, prioritisation and implementations. In addition results obtained here will provide a foundation for other scientists/researchers interested in understanding different aspects related to mortality in women of reproductive age in Sub-Saharan Africa.

1.4 Hypothesis

- Maternal conditions are not the leading underlying causes of death in women of reproductive age in this area
- Risk factors for all cause mortality do not differ from risk factors for cause specific mortality in women of reproductive age in this area

1.5 Aims and Objectives of the Study

The aim of the study is to investigate the causes and associated risk factors of mortality in women of reproductive age in rural South Africa using Africa Centre (ACDIS) data for the period 2000-2009.

Specific Objectives

- To determine the main underlying causes of death in women of reproductive age.
- To investigate the main risk factors associated with all cause mortality and cause specific mortality in women of reproductive age controlling for woman age, migration status, HIV status, parity, self reported health, history of pregnancy out comes, employment status, marital status, education level and contraception use.

1.6 Literature Review

1.6.1 Mortality in women of reproductive age

More than 30% of all deaths that occur in middle and low income countries are of middle aged (15-59) women as compared to 15% of deaths in high income countries of the same age group.[14-15]

Findings of a community based study in Pakistan show that the mortality rate of women of reproductive age was 171 per 100000 women, of which maternal deaths contributed 28% with a maternal mortality rate of 48 per 100000 women aged 15-49 years and all causes constituted 72% of all deaths in women of this age group with a mortality rate of 123 per 100000 women aged 15-49 years.[16] Implying that the contribution of each cause of death (other than maternal causes) was not investigated further as the focus was on maternal deaths.

A reproductive age mortality survey conducted in Ghana reported a total of 9248 deaths of women of reproductive age occurring in 2002. Only 179 (1%) of these

deaths were due to maternal causes mainly occurring in women aged 15-34 years. Given that this was a reproductive age mortality survey, emphasis was put on maternal deaths and details on other causes of death (99%) was neither surveyed nor reported.[3]

1.6.2 Causes of death in women of reproductive age

Globally, non communicable conditions are reported as the leading causes of death in women of reproductive age. While communicable diseases (including HIV/AIDS and maternal causes) are the leading cause of adult women death in Sub-Saharan Africa, (followed by non-communicable diseases and injuries) [14-15] in developed and high income countries, non-communicable diseases are the leading cause of death in women of reproductive age followed by injuries and communicable diseases.[14-15]

A maternal mortality and morbidity study carried out in Nepal in 2008, found that injuries were the leading causes of death (contributing 25% of all women deaths) in women of reproductive age, followed by undetermined/unclassified causes (12%) and pregnancy/child birth related causes(11%).[17] Cause of death in this study was determined basing on community verbal autopsy forms and similar results were reported for a longitudinal study carried out in the North Eastern part of South Africa where injuries were reported as the leading cause of death in women of reproductive age contributing 16% of all deaths in this age group.[18] The main aim of this study was to determine the cause of death in the entire population and thus the contribution of other causes was not stratified according to gender but rather reported as a whole across both sexes.

An earlier longitudinal study conducted in 2000 to assess the levels and causes of adult mortality in a rural area of South Africa, reported AIDS and / or TB as the

leading cause of death (77.6%) in women of reproductive age followed by other communicable conditions including maternal causes (8.8%), whereas non-communicable chronic diseases and injuries contributed each 5.1% and the remaining percentage (3.4%) of deaths was due to unknown or ill defined causes.[19]

1.6.3 Risk factors associated with deaths in women of reproductive age years

1.6.3.1 All cause mortality

A study to assess major risk factors for global and regional burden of disease found that globally, unsafe sex (92 million DALY, 6·3%), chronic health conditions (e.g. high blood pressure) (64 million DALY, 4·4%), tobacco smoking (59 million DALY, 4·1%), and alcohol use (58 million DALY, 4·0%) were reported as the leading causes of global burden of disease. In the poorest regions of the world, unsafe sex, poor living standards (in the form of unsafe water, sanitation, and hygiene, indoor smoke from solid fuels) and various micronutrient deficiencies were found to be the major contributors to loss of healthy life, while tobacco smoking, alcohol intake and chronic health conditions (in the form of high blood pressure and high cholesterol) remained the major causes of disease burden in both developed and developing countries.[20]

Age

A study carried out in KwaZulu-Natal (South Africa) reported increasing mortality rate in women with increasing age, i.e. MR increased steadily from as low as 2 per 1000 person years (CI:1-4) in women aged 15-19 years to as high as 23 per 1000 person years (CI: 18-29) and 24 per 1000 person years (CI:17-34) in women aged 35-39 and 45-49 years respectively.[19] In the same study, the contribution of AIDS to

mortality was quantified. Mortality was reported to be highest (MR= 17 per 1000 person years (CI: 13-23)) in women aged 35-39 years.

HIV status

In a hospital based cross sectional study in Western Kenya, women who were HIV positive had a 20.03 (CI:2.04-197.00) increased odds of mortality compared to those who were HIV negative and the effect was greatest in women aged 21-34 years.[21] This was however a cross sectional study focusing on women who came to hospital for treatment or had been admitted.

Migration status

A population based study conducted in one of the rural areas of South Africa, showed that long-term returning females migrants aged 20-39 years were 2.0 (OR 2.089, CI:1.151-3.791) times more likely to die compared to female residents in the same age group. In addition to this, short-term returning females aged 40 years and above were 63% (OR 1.633, CI:1.230-2.166) more likely to die compared to long-term returning and resident(combined) females in the same age group.[9]

1.6.3.2 Mortality due to AIDS

Age

Results of a 10 year period study among participants in the Women's Interagency HIV Study in the US, showed that the adjusted hazards of dying from AIDS increased by 2% for every year increase in woman's age.[22]

In a population based study carried out in South Africa, participants aged 26 to 40 years were 3.47 (OR 3.47, CI: 2.36-5.11) times more likely to die from AIDS compared to those aged 18 to 25 years.[10]

Migration status

In a study to investigate the association between migration and mortality in rural South Africa, external in-migrants were most likely to die than residents and particularly they were79% (OR 1.79, CI: 1.162-2.78) more likely to die from AIDS than residents.[10] It is important to note that this study was focussed on all cause mortality but results were stratified according to gender.

1.6.3.3 Mortality due to all other causes

Age

In rural Tanzania women aged 35–49 years had a higher risk of dying from maternal causes (OR 4.0) compared to those in the group of 25–34 years.[23] In another study in Tanzania, however, there was no significant difference reported between injury deaths that occurred in rural and urban Tanzanian districts for women aged 15-49 years. [24]

Findings of an earlier study done in Egypt showed that deaths of younger women (less than 24 years) were found to be more likely due to acute conditions of child births or accidents whereas deaths of older women (more than 35 years) were more likely to be due to chronic conditions of cancers, diabetes and high blood pressure among others.[25] In the same study, there was an association between age and deaths due to injury (attributed to burns and transport accidents-injuries), where younger women (15-34 years) were twice as likely as older women (35 – 49 years) to die of an injury related death (OR 2.0, CI: 1.6, 2.7).[25]

In a population based study conducted at the Africa Centre for Health and Population Studies (South Africa) to investigate the associated risk factors of adult injury

mortality, women aged 40-49 years had a 3.0 (CI: 1.4-6.9) fold increased risk of dying from injury compared to those who were aged 15-19 years. No significant association was found between mortality due to injuries and factors like education, migration, asset index and area of residence.[26]

HIV status

A Zimbabwean HIV maternal and morbidity study reported that the mortality rate for HIV positive mothers was 38.2 per 1000 person years as opposed to that for HIV negative mothers which was only 2.3 per 1000 person years. This was a randomised controlled trial whose main aim was to investigate the effect of Vitamin A supplement on cause specific mortality in HIV positive and HIV negative postpartum women enrolled in the Zimbabwe Vitamin A for Mothers and Babies (ZVITAMBO) project.[27]

CHAPTER 2: METHODOLOGY

2.1 Study Design

This was a secondary data analysis using data from a DSS (Africa Centre for Health and Population Studies) to construct a retrospective cohort for the period 2000 to 2009.

2.2 Study Area and study population

The surveillance area is located near the market town of Mtubatuba in the Umkanyakude district of KwaZulu-Natal. The area is 438Km^2 in size and includes a population of approximately 90000 people who are members of approximately 12000 households. The population is almost exclusively Zulu-speaking. The area is typical of many rural areas of South Africa in that while predominantly rural, it contains an urban township and informal peri-urban settlements. [28-29] Most households are multi-generational with an average size of 7.9 (SD $\pm$ 4.7) members. Despite being a predominantly rural area, the principle source of income for most households is waged employment and state pensions rather than agriculture. The Africa Centre surveillance system (ACDIS) consists of all individuals who are members of households within the Demographic Surveillance Area (DSA) regardless of whether they are residents or non residents and makes a distinction between membership (self-defined on the basis of links to other household members) and residency (residing at a physical structure within the surveillance area at a particular point in time). A resident is a member of a household who normally lives in the same homestead as the other members, whereas a non-resident household member normally lives elsewhere but retain links to the household.[29]

2.3 Study Sample

The study sample constituted all women in the age bracket of 15-49 years who were members of households within the Demographic Study Area (DSA) during the period 2000 to 2009.

Inclusion Criteria

- All membership episodes of female members of households which are resident in the DSA and who were aged 15-49 years at any date during the period 2000-2009 were included.

Exclusion criteria

- Membership episodes prior to residence were ignored.
- Membership episodes of women after turning 50 years of age were excluded from the analysis.
- Exposure of women who were no longer members of a Household which is resident in the DSA at any point during the period 2000 to 2009 were also excluded.

2.4 Data Sources

2.4.1 Data

The Africa Centre has built up since January 2000, an extensive longitudinal database of demographic, social, medical and economic information about the members of its DSA.[28-29] The Centre has two separate cycles of data collection— household and individual. During the household data collection cycle, a set of questionnaires are

routinely administered every 6 months to a key informant in each household, while individual data is collected once every year using a number of different data collection forms (questionnaires). These questionnaires record key attributes and events regarding physical structures, households and individuals and their relationship to each other. Other modules which are administered annually are HIV surveillance, house hold socio-economic data, and individual socio-economic (SES) data and child grants. These provide further descriptive variables for the subjects over time and are intended to extend and enhance the core dataset for specific research purposes.

Table 1 Data collected at each routine household visit, 2000 and ongoing

Subject	Types of Information
Homestead	Latitude, longitude
	Owner
	Number of households
Household	Formation and dissolution
	Household head
Individuals	Individual details: incl. Date of birth, sex, parents
	Household memberships
Household members	Update household list: members who join, leave or die.
	Residency status: incl. patterns of return visits, marital and partnership status relationship to household head
Births	Pregnancy outcomes: abortions, still and live births. Delivery environment: incl. assistance, place, birth weight, APGAR
Deaths	Location and care provision at time of death. Open description

	of circumstances
Migrations	Details of place of origin or destination
	Type of migration, e.g. household or individual migration
Child health	On first birthday: vaccination history

2.4.2 Mortality data

All notified deaths (of both resident and non-resident household members) are followed up by a verbal autopsy interview which is conducted by a trained nurse with the closest caregiver of the deceased. Verbal autopsy is an epidemiological tool that is used to assess cause of death in settings where hospital based records are lacking. The verbal autopsy interview occurs on average 9 months after a death is reported at routine surveillance visits. During these interviews, informants are asked to narrate the course of the illness or events leading to death. A structured interview is then administered. Two experienced clinicians independently assign the cause of death based on the information collected in the verbal autopsy and their clinical judgment. A third physician reviews the death causes assigned by the first two physicians and where there is no agreement on the cause of death, s/he arranges a consensus meeting; if no agreement is reached then the cause is assigned as undetermined or unknown. [10, 18-19, 26] The third physician assigns a cause of death code using the 10th version of the International Classification of Diseases (ICD-10) coding system.

2.4.3 Women data

Women data - on age, education, self reported health condition, marital status, contraception use, pregnancy outcome, parity, migration status and HIV status - is collected and updated once every year using a semi structured questionnaire. This

questionnaire is administered to women aged 15-49 years by the field workers. At the start of each annual round, an eligibility list of women who at that date are recorded in ACDIS as fulfilling the eligibility criteria is drawn. The HIV sero-survey comprises part of the individual data collection cycle and requires an interview with the eligible individual in person because of the sensitivity of the questions.[28]

2.4.4 Household asset data

The Africa Centre uses the Household Socioeconomic Form (HSE) to annually collect information on housing structure, sources of energy, and amenities; government grants for household members; financial assets; livestock and land ownership; and education and employment of household members. Based on this information collected in the HSE, the ACDIS computes a household asset index specifically utilising information on house ownership, water source, energy, toilet type, electricity and ownership of assets which included items that can be used for consumption, production or both, such as beds, bicycles, tables, telephones, television sets, sewing machines, block makers, wheelbarrows, tractors, cattle, and other livestock.[30-31] This is done by use of the method of principal component analysis and as Filmer suggests,[32] the first principal component is obtained from this method. For this study the household assets index was used to measure wealth of the households in the study. According to Morris,[33] household assets indices are valid proxies for wealth in health surveys in rural Africa.

2.5 Measurements

Mortality

The main outcome variable for this study was death of a woman aged 15-49 years and was coded as 1 for dead and 0 for alive. Cause specific mortality data were derived from coded verbal autopsy reports using the ICD-10 coding system. Following the WHO burden of disease classification, these causes were divided into broad categories: communicable causes (AIDS/TB causes, maternal causes, etc) non communicable chronic causes, injuries and unknown causes. [34] Communicable causes were further categorised into AIDS/HIV/TB related causes, maternal causes and other communicable causes including perinatal and nutritional causes.

Risk factors for mortality of women of reproductive age

Risk factors included as independent variables were; age of the woman, migration status, HIV status from the HIV surveillance, area of residence, maximum parity, pregnancy outcome summarized across maternity history, marital status, self reported minimum general health condition, highest education level, contraception use, employment status and wealth index of the household where the woman lives.

Woman's age was included because previous studies established an association between woman's age and the likelihood to die [3, 16, 19, 23, 25-26] Other studies found an association between an individual's migration status (categorized as never moved, internal migration only, external migration only and both internal and external migrations combined) and death as a dependent event. [9-10, 35] We further included HIV status because it is well documented that in this part of the country, mortality

rates have been increasing since the start of the HIV epidemic. [5, 19, 21] HIV status was obtained from the regular HIV surveillance and was categorized as HIV tested and found negative, HIV tested and found positive and never tested. Self reported minimum health condition (good, fair and poor), pregnancy outcomes (summarized across maternity history as never pregnant, all live births, at least 1 pregnancy was a miscarriage/abortion/still birth) was included because studies in different developing countries found significant association between these factors and deaths due to maternal and non communicable causes of death.[25, 36] Highest education level (Never gone to school, less than 8 years of education and 8 or more years of education) has previously been found to be associated with mortality in different studies. [26, 37] Furthermore employment status (employed-yes/no) and household asset index (categorized as either belonging to the poorest 40%, the middle 40% or the wealthiest 20% on the assets index scale) as a measure of wealth, key in determining the ability to pay for health services were included.

2.6 Quality control

At Africa Centre, the quality control (QC) strategy used is a complete system which checks for errors from the time forms are produced to data entry. The QC section does quality control of data collection (through adequate training of field workers); checking for completeness, consistency and accuracy of the collected data from study participants (through supervised visits, QC visits and a unified report). The data entry system has constraints and validation rules placed on the database to help in checking data quality during data entry.[38] To ascertain cause of death, a verbal autopsy interview is conducted by a trained nurse with the caregiver of the deceased. This follows a death notification form filled in by field workers on routine household

visits. This method ensures that no deaths are skipped or missed. Two independent physicians assign a cause of death based on the information collected by the nurse. These physicians only meet if their causes of death disagree, thus they do not bias the cause of death as they do not get to discuss the symptoms presented on the Verbal autopsy questionnaire. In this study, quality of data was assessed in terms of completeness (i.e how many women have data for that variable), some variables collected for certain years and not other years were dropped. Consistency was checked by running consistency checks developed in Stata. Inconsistent records especially in terms of start date, end date and age were dropped.

2.7 Data cleaning

Missing values, inconsistent and incorrect values discovered during the cleaning process were clarified with the help of the data manager. The cleaning process involved for example verifying that the age of the mother is not less than 15 years. Based on this criterion, records that were found with unrealistic age were dropped. Further still, education levels were redefined to use the grade system other than a mixture of both grade and standard systems. Observation start and end dates were verified to make sure they fell within the period 1st January 2000 to 31st December 2009.

2.8 Data processing methods and analysis

2.8.1 Data processing

The data collected at ACDIS is stored in a single Microsoft Structured Query Language (MS-SQL) server database in a longitudinal format. SQL scripts were written by the data manager to extract data from the primary database to STATA

release 11 (StataCorp, College Station, TX, USA),[39] where cleaning (see section 2.7) quality checks (section 2.6) and analysis were done.

2.8.2 Data Analysis

Descriptive and inferential analysis was performed as shown below.

Descriptive analysis

The mean and standard deviation respectively was used to describe the woman's parity measured as the maximum parity at the time a death occurred or at the time the study ended. Significant difference between mean parity of women alive and those dead was tested using the student-t test; p value was reported. Cross tabulation of categorical variables and vital status was performed with chi square tests of significant differences within the different variable groups (as defined in section 2.5 above) and woman vital status; p values were reported.

Available verbal autopsy data was used to determine the underlying causes of death classified according to WHO broad categories of causes of death. This was done by computing the mortality fractions of broad categories for cause of death.

Inferential analysis

Data was set for survival analysis with vital status as the failure variable. The time variable was the difference in years between the entry date (which in the ACDIS is referred to as the start observation date and it is the date on which an individual was first observed/visited) into the study and the exit date (which in the ACDIS is referred to as the end observation date and it is the date that an individual was last observed/visited) out of the study (i.e. for deaths the exit date was the date of death

while for the alive participants it was the end of study date). Participants who left the study before the end point or before 31st December 2009 (due to outmigration or lost to follow up) were censored on the dates last observed and the person years they contributed were computed up to their last observation dates.

Hypothesis 1/Objective 1

Mortality rates for the different causes of death as well as the general mortality rates were computed per 1000 person years of observation. Results from this analysis were used to determine the leading cause of death in women of reproductive age in this rural part of South Africa.

Hypothesis 2/Objective 2

A Cox regression model was fitted with each of the factors to test any association with mortality over time. Selection into the multivariable model was set at 20% level of significance to allow for all confounding factors which may not have been significant at the 5% level of significance. Another criteria used for selection into the multivariable model was biological plausibility even if factors were not found to be significant at the univariable level. Woman age was found to modify the effect of minimum general health on all cause mortality as well as cause specific mortality. Also investigated was a modified effect of woman age and parity. Thus interaction terms between minimum general health versus woman age; woman age versus parity were introduced into the multivariable model. Log likely hood ratio tests (lrtest) were used to compare and select the best model at 5% level of significance (with and without interaction terms).

Scaled Schoenfield residuals were used to test the final model for violation of the assumption of proportionality over the study time (2000 to 2009). HIV status, self reported minimum health, employment status and woman's age violated the assumptions and causing the whole model not to satisfy the model assumptions for a Cox regression. The model was stratified according to these variables but still the assumptions were violated. Thus a parametric model (the Weibull distribution) was used instead.

Factors found to be significant (at 5% level) in the multiple regression model were fitted in the final model and were used to explain the risk factors associated with all cause women mortality as well as cause specific mortality.

It is important to note at this point that due to few deaths reported for majority of causes (see result section), it was not possible to model risk factors for each broad cause of death category as had been planned. Instead causes of death were divided into 2 categories; deaths due to AIDS/TB and deaths due to other causes (without deaths with unknown causes) combined. Varying contribution of person-time is considered in the statistical analysis explained above of survival analysis.

Therefore in the result section risk factors for all cause mortality, risk factors for mortality due to AIDS/TB and risk factors for mortality due to other causes combined are presented.

Loss to follow up

Though the loss to follow up fraction in ACDIS was less than 5%, sensitivity analysis was performed to understand the effect of loss to follow up on all cause mortality. This was performed by assigning the worst possible outcomes (assumed dead) to the

missing women at that time point and the best possible outcomes (assumed alive) to the missing women at the time point, and evaluating whether the new analysis contradicts or supports the results of the initial analysis.

Results for both descriptive and inferential statistics were presented by use of graphs and tables as shown in the results section below.

2.9 Ethical considerations

The current study was approved by the University of Witwatersrand Committee for Research on Human Subjects (Clearance number M10M101159, see appendix A). Permission to use ACDIS data was granted with a letter of approval after filling in and signing a data user agreement form. Ethical approval for the ACDIS research was obtained from the Research Ethics Committee of the Nelson R. Mandela School of Medicine, University of Natal. The title of the approved protocol is: '*A Socio-demographic platform for population-based reproductive health research in a rural district of KwaZulu-Natal'* (Ref E009/00, September 2000*)*. This protocol is recertified annually for any changes to that protocol or development of new modules; separate protocols are submitted to the Research Ethics Committee as an amendment to the approved protocol. Information is collected from people in the DSA following informed consent. Efforts are made to ensure that all individual members of the community understand the research project and the type of information to be collected. Two consent processes are followed in ACDIS; in DSS, consent is verbal rather than written, while in HIV surveillance consent is written. A consent form is read to each potential participant, followed by a discussion which includes responding to participant's questions and clarification of issues. Participation is voluntary.[38] In this study, participant confidentiality was observed by excluding names of the

participants in all datasets and instead using unique indentifying (ID) numbers for linking (merging) member information in different tables at analysis and report writing levels.

CHAPTER 3: RESULTS

3.1 Description of Participants

3.1.1 Baseline characteristics

A total of 42703 women were enrolled in the study. Of this total, 3098 women had died between 2000 and 2009 inclusive and 39605 were alive throughout the entire period with a total of 212607 person years of observation. Most of the deaths occurred in women aged 25-29 years (21.14%) followed by those aged 20-24 years (19.85%) and then 30-34 years (17.24%). The differences in these age groups were statistically significant ($p<0.001$). Overall, most of the participants lived in a rural setting, and though most of the women (42.65%) who were alive had moved both internally and externally, most of those who died (42.41%) during the study period had actually never moved ($p<0.001$). Details are shown in Table 2 below. Although overall, most of the participants had completed more than 8 years in school, a relatively high percentage (31.44%) of those who died had completed less than 8 years of education. There were significant differences between women who had died and those who were alive across the three categories of HIV status – namely; ever tested and found to be HIV positive, tested and found to be HIV negative and those who were never tested for HIV as shown in Table 2 below.

Table 2 Baseline characteristics of women of reproductive age enrolled into the study, ACDIS

Variable	Woman Alive (0) (Mean, SD, n, %)	Woman Dead (1) (Mean, SD, n, %)	P-value (chi-square test of differences or t-test)
Overall (n=42703)	(n=39605) 92.75	(n=3098) 7.25	
Age in years at entry			<0.001
1. 15-19	(18220), 46.0	(491), 15.85	
2. 20-24	(6174), 15.59	(615), 19.85	
3. 25-29	(4722), 11.92	(655), 21.14	
4. 30-34	(3579), 9.04	(534), 17.24	
5. 35-39	(2895), 7.31	(402), 12.98	
6. 40-44	(2346), 5.92	(293), 9.46	
7. 45-49	(1669), 4.21	(108), 3.49	
Area of residence			<0.001
1. Rural	(22737), 57.4	(1802), 58.17	
2. Urban	(4023), 10.16	(142), 4.58	
3. Peri-Urban	(12753), 32.20	(1154), 37.25	
Migration Status			<0.001
1. Never moved	(11495), 29.02	(1314), 42.41	
2. Internal only	(3982), 10.05	(273), 8.81	
3. External only	(7237), 18.27	(606), 19.56	
4. Internal and External	(16891), 42.65	(905), 29.21	
Minimum HSE class index *			<0.001
1. Upper 20%	(4568), 12.73	(225), 7.59	
2. Middle 40%	(12064), 33.61	(1007), 33.96	
3. Lower 40%	(19263), 53.66	(1733), 58.45	
Ever Married			0.015
1. No	(32752), 82.7	(2615), 84.41	
2. Yes	(6853), 17.3	(483), 15.59	
Ever employed			0.353
1. No	(29701), 74.99	(2300), 74.24	
2. Yes	(9904), 25.01	(798), 25.76	
Highest level of education **			<0.001
1. More than 8 years	(24647), 71.88	(1469), 62.25	
2. Less than 8 years	(8083), 23.57	(742), 31.44	
3. No school	(1559), 4.55	(149), 6.31	
Self Reported minimum general health***			<0.001
1. Good	(17095), 79.68	(770), 69.43	
2. Fair	(3808), 17.75	(253), 22.81	
3. Poor	(551), 2.57	(86), 7.75	
Woman HIV Status			<0.001
1. HIV tested and Negative	(9532), 24.07	(117), 3.78	
2. HIV tested and Positive	(4645), 11.73	(532), 17.17	
3. Never tested	(25428) 64.20	(2449), 79.05	
Maximum Parity (M, SD)	1.79, 2.13	2.28, 2.06	<0.001
Pregnancy Outcome summarised from maternity history			<0.001
1. All live births	(22005), 55.56	(1917), 61.88	
2. >=1 pregnancy was a still birth	(2968), 7.49	(317), 10.23	
3. No outcome reported	(14632), 36.94	(864), 27.89	

***9% (n=3843) had missing data. **13% (n=5567) had missing data. ***47% (n=20140) had missing data**

3.2 Causes of death

Table 3 below shows AIDS/TB to be the leading cause of death with a mortality rate of 10.66 per 1000 person years (95% CI: 10.23-11.11) contributing almost 73% of all deaths to women of reproductive age in this study area. Maternal causes of death

contributed 0.45% of all deaths to women of reproductive age in this area with a significant mortality rate of 0.07 per 1000 person years (95 CI: 0.04-0.11) and non communicable diseases (with cancers taking the lead) contributed 8.42% with a mortality rate of 1.23 per 1000 person years (95% CI: 1.09-1.39).

Table 3 Causes of death in women of reproductive age, 2000-2009, ACDIS

Causes of death	Cause specific numbers	Mortality fraction (%)	Mortality rate /1000 person years	95% confidence intervals	
				Lower	Upper
AIDS/TB	2266	73.14	10.66	10.23	11.11
Maternal causes	14	0.45	0.07	0.04	0.11
Other communicable causes	266	8.59	1.25	1.11	1.41
Injuries	109	3.52	0.51	0.42	0.62
Non Communicable Diseases	261	8.42	1.23	1.09	1.39
Unknown	182	5.87	0.86	0.74	0.99

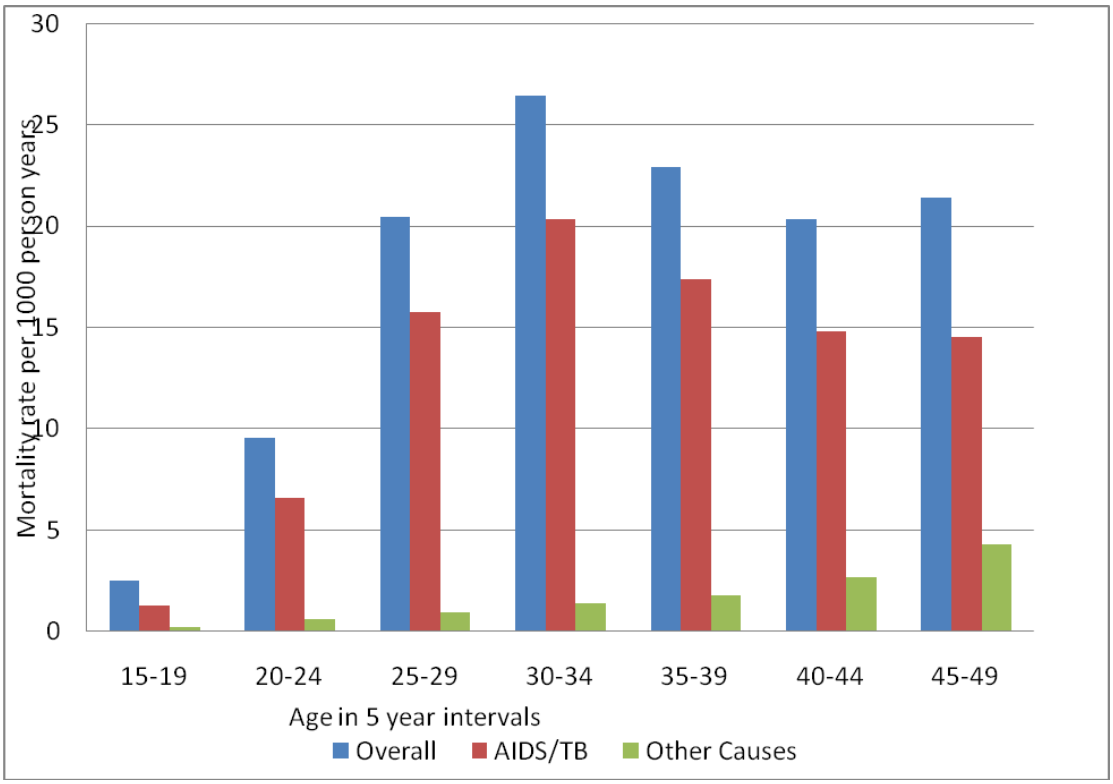


Figure 1 Overall and cause specific mortality rates by age group from 2000 to 2009, ACDIS

Figure 1 above shows, the mortality rate to be highest in women aged 30-34 years (26.43 per 1000 person years, 95% CI: 24.49-28.51) as compared to women in other age groups. Given that most deaths are AIDS/TB related, mortality due to AIDS/TB

follows a similar pattern to all cause mortality, where the rate is highest in women aged 30-34 years (20.34 per 1000 person years) as opposed to mortality due to other causes combined where the rate is highest in women aged 45-49 years (4.29 per 1000 person years).

Mortality levels

The average mortality rate for women of reproductive age was 14.57 per 1000 person years (95% CI: 14.07-15.09). Over time mortality increased from 2000 to 2003, peaking at 18.15 per 1000 person years (95% CI: 16.41-20.08), and then started reducing from 2004 to 2009 with significant differences in mortality rates as shown in figure 2 below. Mortality due to AIDS/TB follows a similar pattern (as all cause mortality) over the years, unlike mortality due to other causes other than AIDS/TB (combined) which keeps on fluctuating at low rates.

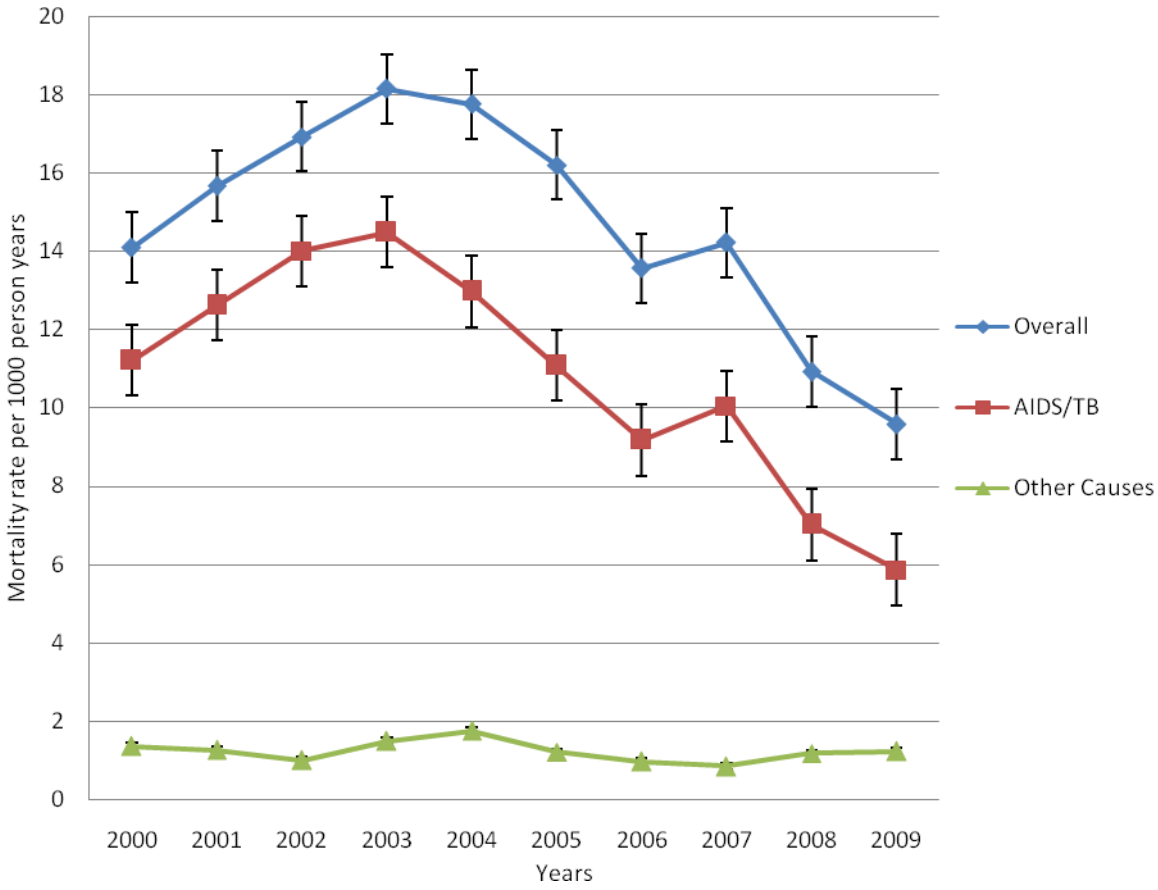


Figure 2 All cause and cause specific mortality rates for women of reproductive age from 2000 to 2009, ACDIS

Further analysis showed that the increasing and decreasing pattern in AIDS/TB mortality rate can be linked to the ART rollout as shown in figure 3 below where AIDS/TB mortality rate decreases with increasing number of people on the public ART program. That is to say, before ART rollout in 2004, the AIDS/TB mortality rate was 14.63 per 1000 person years (95% CI: 13.82-15.49) which is statistically significant from the AIDS/TB mortality rate after ART rollout (MR; 8.203, 95% CI: 7.73-8.71).

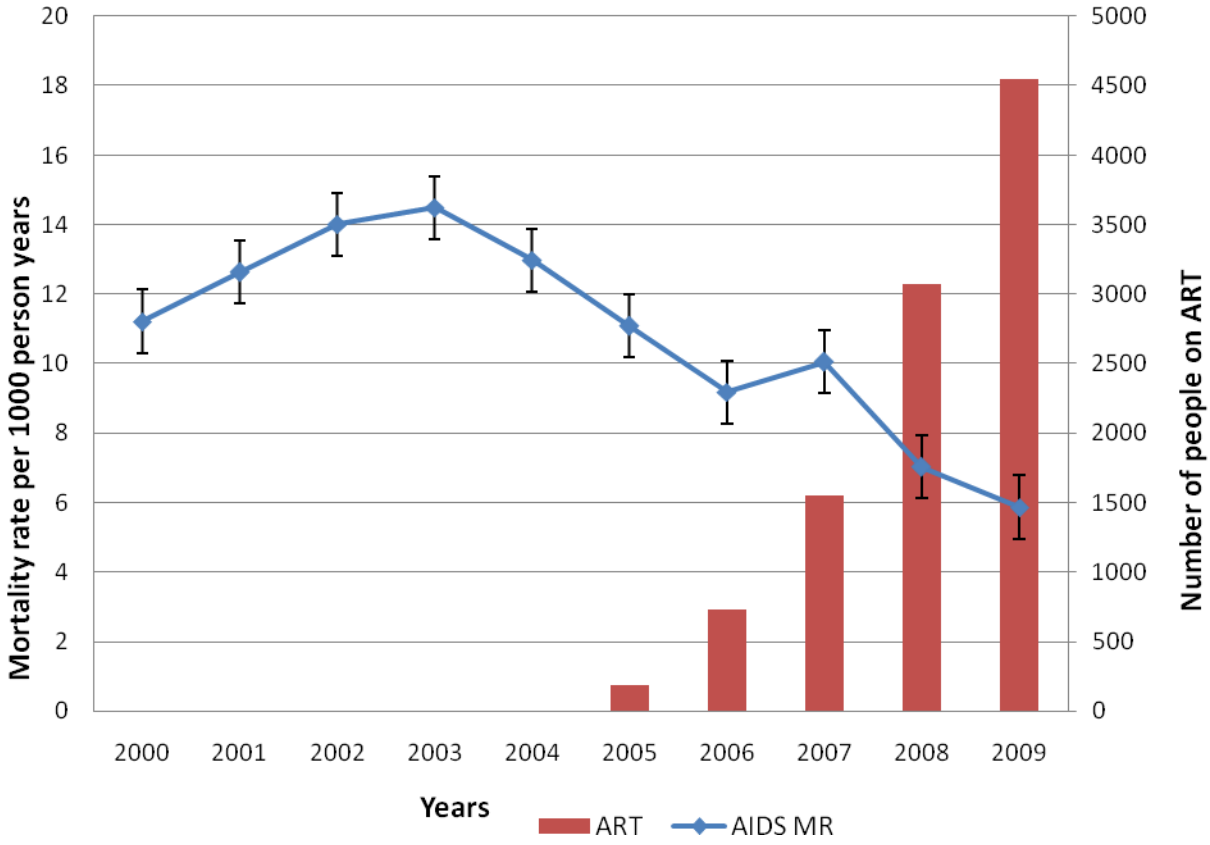


Figure 3 Relationship between mortality due to AIDS/HIV/TB and ART roll out in the study area, ACDIS

3.3 Associated risk factors

3.3.1 All cause mortality

Results in table 4 below show that all factors were significantly associated with all cause mortality at 5% level of significance. These were all included into the multivariable model one by one starting with the most significant ones while at the same time checking for effect modification which led to introduction of two interaction terms of woman age and minimum health as well as parity and woman age. The hazards of dying increased by 4% (Adjusted HR: 1.04, 95% CI: 1.03-1.06, $p<0.001$) for every year increase in the woman's age after adjusting for other factors. Women who reported their minimum general health as poor, had increased hazards of dying compared to those who reported their minimum health as good/very good or excellent (Adjusted HR: 11.05, 95% CI: 4.23-28.81, $p<0.001$) after adjusting for other factors shown in table 4 below. Older women with poor or fair health status were associated with less than 1% decrease in the hazards of dying from all cause mortality compared to older women with a good health status.

Table 4 Risk factors associated with all cause mortality in women of reproductive ages, ACDIS

Explanatory variables	Categories of explanatory variables		Univariable analysis			Multivariable analysis		
			Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Women Age			1.051	1.047, 1.054	<0.001	1.048	1.034, 1.062	<0.001
Self reported minimum	1.	Good	1.000			1.000		
General Health	2.	Fair	1.293	1.122, 1.491	<0.001	2.894	1.592, 5.260	<0.001
	3.	Poor	2.927	2.343, 3.658	<0.001	11.052	4.239, 28.817	<0.001
Ever Employed	1.	No	1.000			1.000		
	2.	Yes	0.622	0.574, 0.675	<0.001	0.799	0.698, 0.916	<0.001
Ever Married	1.	No	1.000			1.000		
	2.	Yes	0.665	0.604, 0.733	<0.001	0.485	0.406, 0.579	<0.001
Migration Status	1.	Never moved	1.000			1.000		
	2.	Internal only	0.451	0.396, 0.514	<0.001	0.659	0.536, 0.809	<0.001
	3.	External only	1.549	1.405, 1.709	<0.001	1.874	1.558, 2.255	<0.001
	4.	Both Internal and External	0.377	0.346, 0.410	<0.001	0.512	0.438, 0.599	<0.001
Minimum Household	1.	Upper 20%	1.000			1.000		
Index class	2.	Middle 40%	1.505	1.302, 1.739	<0.001	1.070	0.804, 1.426	0.642
	3.	Lower 40%	1.527	1.329, 1.754	<0.001	1.142	0.852, 1.531	0.375
Highest Education level	1.	More than 8 years	1.000			1.000		
	2.	Less than 8 years	1.855	1.698, 2.026	<0.001	1.281	1.091, 1.505	0.003
	3.	Never gone to school	1.618	1.367, 1.915	<0.001	1.316	1.009, 1.716	0.042
Ever Used	1.	No	1.000			1.000		
Contraception	2.	Yes	1.211	1.128, 1.301	<0.001	1.334	1.154, 1.542	<0.001

Table 4 Cont'd

Explanatory variables	Categories of explanatory variables	Univariable analysis			Multivariable analysis		
		Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Pregnancy outcome	1. All live births	1.000			1.000		
history	2. >1 pregnancy a Still birth/Abortion	1.202	1.068,1.354	0.002	1.096	0.907, 1.325	0.344
	3. No outcome reported	1.239	1.142,1.344	<0.001	1.367	1.096, 1.704	0.005
Maximum parity		1.021	1.005, 1.037	0.009	0.719	0.603, 0.856	<0.001
Area of residence	1. Rural	1.000			1.000		
	2. Urban	0.635	0.535, 0.753	<0.001	0.803	0.549, 1.172	0.255
	3. Peri-Urban	1.281	1.189, 1.379	<0.001	1.166	1.013, 1.342	0.032
HIV Status	1. HIV tested and negative	1.000			1.000		
	2. HIV tested & positive	11.425	9.348, 13.963	<0.001	8.527	6.813, 10.671	<0.001
	3. Never tested	5.421	4.485, 6.551	<0.001	3.535	2.826, 4.422	<0.001
Minimum General	1. Good & Age				1.000		
health & woman's age	2. Fair & Age				0.965	0.949, 0.981	<0.001
	3. Poor & Age				0.947	0.923, 0.972	<0.001
Parity & Age					1.005	1.001, 1.009	0.009

A similar association was observed with those who reported their health as fair with increased hazards of dying in the adjusted model (Adjusted HR: 2.89, 95% CI: 1.59-5.26, p<0.001). In addition, women who were external migrants had almost a 2 fold increase in the hazards of dying compared to those who had never moved (Adjusted HR: 1.87, 95% CI: 1.55-2.25, p<0.001). In comparison to women who were HIV tested and found negative, women who were HIV tested and found positive had increased hazards of dying in both univariable and adjusted models (Adjusted HR: 8.52, 95% CI: 6.81-10.67, p<0.001). A similar association was observed with women who were never tested (Adjusted HR: 3.53, 95% CI: 2.82-4.42, p<0.001).

On the other hand, ever been employed and ever been married were associated with decreased hazards of dying in the adjusted model with hazards ratios of 0.79 (95% CI: 0.69-0.91, p<0.001) and 0.48 (95% CI: 0.40-0.58, p<0.001) respectively. In addition to the above, for every increase in woman's parity, the hazards of dying from all causes reduced by 28% with 95% statistical significance (Adjusted HR:0.719, 95% CI:0.603-0.856, p<0.001). However, the hazards of all cause mortality almost remained constant with every increase in parity and age (adjusted HR:1.005, 95% CI: 1.001-1.009, p=0.009).

3.3.2 Mortality due to AIDS or TB

Results in table 5 below show that all factors were significantly associated with mortality due to AIDS or TB at 5% level of significance except summarised history of pregnancy history (which was significant at 20% level of significance-set criteria for selection into the multivariable model). These factors were added one by one starting with the most significant ones while at the same time testing for effect modification. In the multivariable analysis, the hazards of dying increased by 5% (Adjusted HR:

1.05, 95% CI: 1.04-1.07, p<0.001) for every yearly increase in the woman's age after adjusting for other factors. In addition, women who were external migrants had a 89% increase in the hazards of dying compared to those who had never moved (Adjusted HR: 1.89, 95% CI: 1.51-2.37, p<0.001).

Table 5 Risk factors associated with AIDS and /or TB mortality, ACDIS

Explanatory variables	Categories of explanatory variables	Univariable analysis			Multivariable analysis		
		Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Women Age		1.053	1.049, 1.058	<0.001	1.053	1.036, 1.071	<0.001
Self reported minimum General Health	1. Good	1.000			1.000		
	2. Fair	1.519	1.285,1.797	<0.001	4.360	2.167, 8.771	0.001
	3. Poor	3.675	2.857,4.729	<0.001	13.724	4.659, 40.419	<0.001
Ever Employed	1. No	1.000			1.000		
	2. Yes	0.553	0.501, 0.610	<0.001	0.728	0.618, 0.858	<0.001
Ever Married	1. No	1.000			1.000		
	2. Yes	0.625	0.556, 0.702	<0.001	0.466	0.375, 0.580	<0.001
Migration Status	1. Never moved	1.000			1.000		
	2. Internal only	0.475	0.409, 0.553	<0.001	0.676	0.526, 0.872	0.002
	3. External only	1.602	1.432, 1.793	<0.001	1.895	1.513, 2.374	<0.001
	4. Both Internal and External	0.377	0.341, 0.417	<0.001	0.585	0.485, 0.706	<0.001
Minimum Household Index class	1. Upper 20%	1.000			1.000		
	2. Middle 40%	1.904	1.579, 2.294	<0.001	1.417	0.960, 2.092	0.175
	3. Lower 40%	1.999	1.669, 2.394	<0.001	1.471	0.989, 2.187	0.131
Highest Education level	1. More than 8 years	1.000			1.000		
	2. Less than 8 years	1.972	1.778, 2.187	<0.001	1.312	1.083, 1.589	0.006
	3. Never gone to school	1.645	1.347, 2.009	<0.001	1.349	0.983, 1.852	0.063
Ever Used Contraception	1. No	1.000			1.000		
	2. Yes	1.316	1.211, 1.431	<0.001	1.481	1.239, 1.769	<0.001

Table 5 Cont'd

Explanatory variables	Categories of explanatory variables	Univariable analysis			Multivariable analysis		
		Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Pregnancy outcome history	1. All live births	1.000			1.000		
	2. >1 pregnancy a Still birth/Abortion	1.124	0.976, 1.295	0.091	1.083	0.860, 1.363	0.498
	3. No outcome reported	1.144	1.039, 1.259	0.008	1.416	1.076,1.863	0.013
Maximum parity		1.036	1.018, 1.055	<0.001	0.875	0.637, 0.967	0.266
Area of residence	1. Rural	1.000			1.000		
	2. Urban	0.517	0.415, 0.643	<0.001	0.730	0.435, 1.226	0.235
	3. Peri-Urban	1.296	1.189, 1.412	<0.001	1.218	1.029, 1.442	0.022
HIV Status	1. HIV tested and Negative	1.000			1.000		
	2. HIV tested and Positive	25.567	18.606,35.134	<0.001	19.489	13.492, 28.151	<0.001
	3. Never tested	10.232	7.509, 13.942	<0.001	7.054	4.869, 10.218	<0.001
Minimum General health & woman's age	1. Good & Age				1.000		
	2. Fair & Age				0.958	0.939, 0.977	<0.001
	3. Poor & Age				0.947	0.919, 0.975	<0.001

The hazards of dying remained high for women whose self reported health was poor compared to those whose self reported was good in both univariable analysis and multivariable analysis (Adjusted HR: 13.72, 95% CI: 4.65-40.41, p<0.001). An interaction term of age and self reported health showed that old women who reported their health as poor or fair were associated with decreased hazards of dying than old women who reported their health as good. In comparison to women who were HIV tested and found negative, women who were HIV tested but found positive had higher hazards of dying in both univariable and adjusted models (Adjusted HR: 19.48, 95% CI: 13.49-28.15, p<0.001). A similar association was observed with women who were never tested (Adjusted HR: 7.05, 95% CI: 4.87-10.21, p<0.001). An interaction term between age and parity was not found to be significant as shown in appendix C.

Ever been employed and ever been married were protective in the univariable model and adjusted model with adjusted hazards ratio of 0.72 (95% CI: 0.62-0.85, p<0.001) and 0.46 (95% CI: 0.37-0.58, p<0.001) respectively. No significant association was found between parity and mortality due to AIDS/TB or with the combined effect of parity and woman age on mortality due to AIDS/TB (as shown in Appendix C below).

3.3.3 Mortality due to other causes (combined) other than AIDS and /or TB

Results in table 6 below show that at 20% level of significance, all factors were associated with mortality due to other causes (other than AIDS/TB) except for contraceptive use and household social economic status. That is to say; increase in a woman's age was associated with higher hazards of dying from other causes other than AIDS in both the univariable and multivariable model with adjusted hazard ratio of 1.02 (95% CI:1.00-1.05, p=0.036). The hazards of dying from other causes for

external migrants also remained relatively high in both univariable and multivariable models with an adjusted hazard ratio of 1.78 (95% CI: 1.23-2.56, p=0.002) compared to those who had not moved at all. The hazards of dying from other causes for women who were HIV tested and found positive remained higher in both the univariable model and adjusted model with adjusted hazard ratio of 2.83 (95% CI: 1.96- 4.09, p<0.001) compared to those who were tested and found HIV negative. Being married was highly protective in both unadjusted and adjusted models with statistical significance (Adjusted HR: 0.54, 95% CI: 0.39-0.76, p<0.001) as well as a combination of internal and external migrants relative to those who had never moved (Adjusted HR: 0.35, 95% CI: 0.26-0.48, p<0.001). Keeping other factors constant, as a woman's parity increased, the hazards of dying from other causes combined (other than AIDS/TB) reduced by 47% with 5% level of statistical significance (Adjusted HR: 0.539, 95% CI: 0.38-0.77, p=0.001).On the other hand, as woman age increased with increase in parity, the hazards of dying from other causes combined slightly increased by 1% and this was statistically significant at 5% level of significance (Adjusted HR: 1.01, 95% CI:1.00-1.02, p=0.004).

From tables 4, 5 and 6, it can be deduced that the most important risk factors associated with all cause mortality and cause specific mortality are woman age, migration status, parity, HIV status, self reported health, marital status and employment.

It is however important to note that significant differences have been observed between these factors and all cause as well as cause-specific mortality. That is to say; while poor self reported health is significantly associated with increased hazards of all cause mortality and mortality due to AIDS/TB compared to good self reported health,

no significant association was found between poor self reported health and mortality due to other causes (other than AIDS/TB) combined.

Another difference was observed with parity. That is to say, while increase in parity was associated with reduced hazards of all cause mortality and mortality due to other causes (other than AIDS/TB) combined, no significant difference was observed between parity and mortality due to AIDS/TB.

Also observed here is that while a positive HIV status was significantly associated with increased hazards of all cause mortality and cause specific mortality, it is important to note that the magnitude of the effect of a positive HIV status on mortality significantly different within the three categories of mortality. That is to say all cause mortality (Adjusted HR: 8.53, 95%CI: 6.81-10.67), mortality due to AIDS/TB (Adjusted HR: 19.49, 95%CI: 13.49-28.15) and mortality due to all other causes other than AIDS/TB (Adjusted HR:2.84, 95% CI:1.97- 4.09).

Thus risk factors for all cause mortality slightly differ from risk factors for cause specific mortality and for those which are similar; the magnitude of the effect significantly varies from one cause of mortality to the other.

Table 6 Risk factors associated with other causes (Combined) other than AIDS and /or TB, ACDIS

Explanatory variables	Categories of explanatory variables	Univariable analysis			Multivariable analysis		
		Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Women Age		1.045	1.037, 1.053	<0.001	1.026	1.002, 1.051	0.036
Self reported minimum General Health	1. Good	1.000			1.000		
	2. Fair	0.836	0.608, 1.149	0.269	0.559	0.395, 0.791	0.001
	3. Poor	1.694	0.986, 2.908	0.056	0.815	0.437, 1.520	0.520
Ever Employed	1. No	1.000			1.000		
	2. Yes	0.814	0.689, 0.961	0.015	1.094	0.833, 1.436	0.519
Ever Married	1. No	1.000			1.000		
	2. Yes	0.794	0.651, 0.969	0.023	0.549	0.391, 0.769	0.001
Migration Status	1. Never moved	1.000			1.000		
	2. Internal only	0.405	0.306, 0.536	<0.001	0.588	0.396, 0.872	0.008
	3. External only	1.255	1.008, 1.568	0.045	1.782	1.237, 2.568	0.002
	4. Both Internal and External	0.312	0.259, 0.375	<0.001	0.356	0.260, 0.489	<0.001
Minimum Household Index class	1. Upper 20%	1.000					
	2. Middle 40%	1.116	0.846, 1.473	0.437			
	3. Lower 40%	1.055	0.809, 1.375	0.690			
Highest Education level	1. More than 8 years	1.000			1.000		
	2. Less than 8 years	1.636	1.351, 1.982	<0.001	1.171	0.845, 1.623	0.344
	3. Never gone to school	1.547	1.082, 2.211	0.017	1.297	0.771, 2.183	0.327
Ever Used Contraception	1. No	1.000					
	2. Yes	0.976	0.833, 1.143	0.762			

Table 6 Cont'd

Explanatory variables	Categories of explanatory variables	Univariable analysis			Multivariable analysis		
		Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Pregnancy outcome history	1. All live births	1.000			1.000		
	2. >1 pregnancy a Still birth/Abortion	1.554	1.219, 1.982	0.002	1.317	0.919, 1.886	0.133
	3. No outcome reported	1.586	1.332, 1.888	<0.001	1.179	0.782,1.778	0.433
Maximum parity		0.985	0.949, 1.021	0.415	0.539	0.379,0.767	0.001
Area of residence	1. Rural	1.000			1.000		
	2. Urban	0.701	0.488, 1.006	0.067	0.615	0.319,1.184	0.146
	3. Peri-Urban	1.287	1.095, 1.513	0.025	1.204	0.929, 1.558	0.160
HIV Status	1. HIV tested and Negative	1.000			1.000		
	2. HIV tested and Positive	3.315	2.387, 4.604	<0.001	2.839	1.967,4.099	<0.001
	3. Never tested	2.399	1.822, 3.159	<0.001	1.857	1.333,2.587	<0.001
Parity and Age					1.012	1.004,1.020	0.004

CHAPTER 4: DISCUSSION

Findings from this study have shown that the leading cause of death in women of reproductive age in this rural part of South Africa is AIDS/TB (which is in line with the hypothesis that maternal mortality is not the leading cause of death in this area) and that the most important risk factors associated with all cause mortality and cause specific mortality are woman age, migration status, parity, HIV status, self reported health, marital status and employment whose effect and /or magnitude of effect significantly differs within the different mortality groups (all cause, AIDS/TB and other causes mortality), significantly disagreeing with the hypothesis that risk factors for all cause mortality do not differ from risk factors for cause specific mortality.

4.1 Description of participants

74.08% of all deaths occurred in women aged 15-34 years while the remaining 25.92% was for women aged 35 years and above. This distribution of deaths is in line with other studies carried out in Ghana, Pakistan and Tanzania [3, 16, 23] respectively. Furthermore, results from this study have shown that a larger percentage of the participants were from peri-urban or rural areas with a relatively high percentage of deaths for external migrants. These results agree with findings from longitudinal studies carried out in Mpumalanga and KwaZulu-Natal provinces of South Africa where the majority of deaths were for individuals who had returned home to die.[9-10]

4.1.2 Mortality levels

Mortality rate in women over the entire period of 2000 to 2009 was 14.57 deaths per 1000 person years. Mortality rates significantly differed across years, from as low as 9.59 per 1000 person years in 2009 to as high as 18 per 1000 person years in 2003.

From the results we see a significant increasing trend from 2000 to 2003 and then a significant decreasing trend from 2004 onwards.

A similar trend was observed with mortality rates due to AIDS/TB given that 72% of all deaths were related to AIDS/TB. This was further verified with the higher mortality rate of AIDS as compared to other causes shown in the result section above. Recent trends of declining AIDS mortality and thus all cause mortality can therefore be attributed to the introduction of ART in public health facilities within the study area from 2004 onwards as shown by other studies.[29, 40-41] As the number of people on the ART program increased, the AIDS/TB mortality rate decreased over the years implying a positive effect of ART on mortality. Availability of ARV's from private health facilities from 1998 onwards contributed to the overall decrease of AIDS mortality.[42] This relationship between ART and mortality should not be a surprise as earlier studies[29] in the same rural area have investigated and proven the association over the years; results reported previously are in line with results obtained in the current study.

4.2 Causes of death

The leading cause of death in women of reproductive age was found to be AIDS/TB combined. This was followed by maternal and non-communicable causes of death. These results agree with the findings of a study previously conducted at the Africa Centre in 2004 (to quantify the contribution that AIDS makes to adult mortality in rural South Africa) where 73% of deaths in women aged 15-44 years were due to AIDS followed by communicable causes and non communicable causes of death.[19] On the other hand, these results differ from findings of other studies conducted in Pakistan[16] and Nepal,[17] where maternal causes and injuries were the leading cause

of death in women of reproductive age group respectively. While the burden of maternal mortality is reported to be highest in sub Saharan Africa,[14, 34] KwaZulu-Natal province is reported to have the highest percentage of pregnant women who are HIV positive,[5] which at the end these deaths (if they occur) are most likely to be due to AIDS unless one died of a pregnancy or birth related complication or within the first 6 weeks after delivery. These findings should also not take us by surprise since the well established PMTCT programme in public health facilities presents with many strengths coupled with trained nurses and councillors to help specifically HIV positive mothers and their children, thus reducing further complications that could result from child birth.[43]

As the mortality rates due to AIDS and all cause mortality rates were decreasing over the years, the mortality rates due to other causes were fluctuating at low rates but then began to rise slightly after 2008. A breakdown according to age groups shows that middle aged women (30-39 years) were more likely to die of AIDS related causes while older women (45-49 years) were more likely to die of other causes. These results differ slightly from findings of another study carried out in the same rural area of South Africa in 2004,[19] where all cause mortality rate was highest in women aged 45-49 years (23 deaths per 1000 person years) and AIDS mortality rate was highest in women aged 35-39 years (17 deaths per 1000 person years).

Further research in this area is required to assess the relationship between AIDS and fertility and the role of ART in such situations. At the same time, while the South African government is making efforts to reduce the spread of HIV, other causes of death like injuries and non-communicable causes shouldn't be ignored especially in older women.

4.3 Associated risk factors

4.3.1 Age

A one year increase in age was statistically associated with high hazards of all cause mortality as well as cause specific mortality. These results can be comparable to findings of a study done at the Africa Centre (to study the association between migration and mortality) were women aged 26 to 40 years were 3 times more likely to die of AIDS than their younger counter parts aged less than 26 years.[10] In addition, two more studies done in Tanzania (cross sectional study) [23] and south Africa (Africa Centre) [26] reported more/or less similar results to the findings of this current study where women aged 35-49 years and 40-49 had higher odds of dying from maternal causes and injury related cause than their younger counterparts respectively.

On the other hand, these results contradict the findings of a study done in Kenya where younger HIV positive women (21-34 years) were at greater risk of dying than the older HIV positive women.[21] This was however a hospital based cross-sectional study focusing on only HIV positive women who came to the hospital for treatment which is not representative of all. Further still these results contradict the findings of an earlier study in Egypt where women aged 15-34 years were two times more likely to die of an injury death than the older women.[25] These variations in age and mortality are occurring in different countries because of the different causes of death in women of reproductive age. Naturally mortality is expected to increase with increase in age in cases where there are no causes of death responsible for mortality at earlier ages.

4.3.2 Self reported minimum general health

Women who reported their health as poor were associated with increased hazards of all cause mortality and AIDS/TB related mortality and decreased hazards of mortality due to other causes combined though not statistically significant. This variable is measured by how one perceives her health status at the time of interview; which may not be the best measure of risk of dying although it can give an estimate to the person's health status.

4.3.3 Migration status

External migration status was associated with increased hazards of all cause mortality and cause specific mortality. This is comparable to findings of an earlier study conducted at the Africa centre which showed that external migrants were likely to return home when they are severely ill and thus at higher odds of dying from AIDS.[10] These results are also in line with findings of a study carried out in Agincourt HDSS[9] in which the annual odds of dying from all causes for returned migrants was between 1.1 and 1.9 times higher than for residents. Thus it is important that in resource poor settings with high HIV/AIDS prevalence, effective interventions to better health conditions should be put in place.

4.3.4 Maximum parity

With statistical significance, higher parities were associated with lower hazards of all cause mortality and mortality due to all other causes combined other than AIDS. These findings are in line with findings of another study done in Africa where high parity was associated with high maternal mortality.[37] This was however an ecological study focused on maternal mortality and was conducted in more than 1 African country where the pattern of mortality in women of reproductive age differs. The lack of significant association with AIDS mortality or lower hazards of all cause

mortality could still be explained by our results where the leading cause of death in this area is AIDS\TB and not maternal causes of death (which contribute 0.45% of all deaths in women of reproductive age).

4.3.5 HIV status

Having positively tested for HIV was associated with higher hazards of all cause mortality and cause specific mortality than ever been negatively tested for HIV, though the magnitude of the effect was significantly higher in all cause mortality and mortality due to AIDS/TB than mortality due to other causes. These results agree with findings from other studies done elsewhere (South Africa, Kenya, Zimbabwe) though much emphasis was put on all adult mortality, maternal deaths and child birth related deaths. [19, 21, 27]

4.3.6 Ever employed

Being ever employed was associated with lower hazards of all cause mortality and cause specific mortality which implies that employment as an economic measure of standard of living empowers women with the ability to pay for adequate health services from the private sector in addition to the free public primary health care services and they are also more likely to be able to afford better standards of living than those unemployed.

4.3.7 Ever married

Ever been married was found to be associated with lower hazards for both all cause mortality and cause specific mortality. These findings are in line with a United States based study to investigate factors associated with pregnancy related deaths, where unmarried women had a higher all cause mortality ratio as compared to the married women.[44]

4.4 Limitations and Strengths

4.4.1 Limitations

The current study is not representative of all rural areas within South Africa but looks at only a small portion in one selected rural district of KwaZulu-Natal, which is dominated by a particular cause of death.

Some causes of death are not clearly classified by verbal autopsy since they present with the same symptoms.

Most of the information is retrospective and is based on a key household informant which may lead to misreporting.

There were a few missing values on particular variables of household socio economic index, highest level of education and self reported minimum general health, though sensitivity analyses showed no significant differences between results with and without missing values.

The study was limited to only variables included in the ACDIS interview questionnaires. For instance, it would be good to add more variables on contraceptive use like method used, and how often the method is used, to adequately measure the effect of contraception. It would also be good to clearly distinguish women who have never given birth from those who don't respond to the pregnancy outcome question.

4.4.2 Strengths

In this report, mortality in women of reproductive age has been looked at over an extended period of time, allowing me to look at trends over a ten year period and at the effects associated with ARV-roll-out in the public sector.

The longitudinal set up of ACDIS gives ground for proper follow up of participants and recording of events as they occur. Thus, no events are missed and also the loss to follow up fraction was <5%.

ACDIS has a well established verbal autopsy system, where all deaths are reported by a key informant in the community at any time they occur before being followed by a verbal autopsy interview where the cause of death is ascertained.

This study calculated and reported mortality rates with 95% level of confidence. This implies that results can be validated with statistical significance and hence be used as a basis for further studies.

CHAPTER 5: CONCLUSION and RECOMMENDATIONS

5.1 Conclusion

In this study in women of reproductive age all cause mortality rate was as high as 14.57 per 1000 person years, being highest in 2003 before the rollout of ART in public health facilities in South Africa. After the rollout of ART, the mortality rate decreased to 9.59 per 1000 person years in 2009.

AIDS/TB was found to be the leading cause of death (73.14%) in this area followed by other communicable causes (8.59%) and non communicable (including cancers and diabetes) causes (8.42%). Maternal causes contributed 0.45% of all deaths in women of reproductive age during this period (2000-2009). Middle aged women (30-39 years) overall had a higher mortality rate and were most likely to die from AIDS/TB (MR:20.34 per 1000 person years), while older women (45-49 years) had a higher mortality rate due to other causes (combined) (MR:4.29 per 1000 person years) than AIDS/TB.

Thus we can conclude that since mortality in women of reproductive age in this area is mainly determined by AIDS/TB (which contributes 73.14% of all deaths in women of reproductive age), intensifying the ART program in the public health facilities will greatly reduce the mortality rate of these women of reproductive age in this area.

The most important risk factors associated with all cause mortality and cause specific mortality are woman age, migration status, parity, HIV status, self reported health, marital status and employment whose effect and /or magnitude of effect significantly differs within the different mortality groups (all cause, AIDS/TB and other causes mortality). These findings disagree with the above hypothesis (risk factors for all cause mortality do not differ from risk factors for cause specific mortality in women

of reproductive age) and thus can be concluded that risk factors for all cause mortality are different from risk factors for cause specific mortality.

5.2 Recommendations

ARV rollouts need to be intensified and continuously monitored in this area where AIDS is the main cause of death in women of reproductive age. More HIV-positive women eligible for treatment need to be initiated on the ART program and continuously monitored for default to reduce the burden of AIDS morbidity and mortality in this age group.

More community awareness and sensitisation messages are still needed to reduce the spread of HIV and other sexually transmitted diseases.

Further research is needed to investigate the impact of AIDS/TB on fertility and the association between ART and fertility in a longitudinal setting, women's sexual behaviour and their use of contraceptives and characteristics of women who frequent ANCs in relation to their health status and HIV status.

Appendix A: Ethics clearance certificate for "Mortality in women of reproductive age in rural South Africa"

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Doreen Nabukalu

CLEARANCE CERTIFICATE	**M10M101159**
PROJECT	Mortality in women of Reproductive Age in Rural South Africa
INVESTIGATORS	Ms Doreen Nabukalu .
DEPARTMENT	School of Public Health
DATE CONSIDERED	26/11/2010
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 26/11/2010 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof K Klipstein-Grobusch

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix B: Overall description of all causes of death in women of reproductive Age, ACDIS 2009

ICD10Description	Freq.
Abdominal and pelvic pain	1
Abscess of liver	1
Abscess of lung and mediastinum	1
Acute myocardial infarction	4
Acute pericarditis	1
Angina pectoris, unspecified	1
Antepartum hemorrhage, not elsewhere cl	1
Assault (homicide) by blunt object	2
Assault (homicide) by handgun discharge	21
Assault (homicide) by hanging, strangul	4
Assault (homicide) by other and unspeci	3
Assault (homicide) by sharp object	12
Assault (homicide) by unspecified means	5
Asthma	6
Bacterial meningitis, unspecified	1
Burn and corrosion, body region unspeci	3
Car occupant injured in collision with	22
Cardiac complications of anesthesia dur	1
Cardiomyopathy	8
Cerebral infarction	1
Cervix uteri, unspecified	1
Cholecystitis	1
Cholera	1
Chronic ischemic heart disease	2
Complete or unspecified, complicated by	1
Congenital malformation of the heart, u	1
Contact with venomous snakes and lizard	1
Degenerative disease of nervous system,	3
Diarrhea and gastroenteritis of presume	11
Discharge from other and unspecified fi	1
Disease of digestive system, unspecifie	1
Disorder of kidney and ureter, unspecif	1
Disseminated intravascular coagulation	1
Don't Know	52
Drowning and submersion following fall	1
Eclampsia	5
Ectopic pregnancy	1
Encephalitis, myelitis, and encephalomy	17
Encephalitis, myelitis, and encephalomy	2
Epilepsy	5
Essential (primary) hypertension	8
Exposure to other specified smoke, fire	1
Exposure to unspecified electric curren	1
Exposure to unspecified factor	1
Fibrosis and cirrhosis of liver	4
Gastric ulcer	2
Gastrointestinal hemorrhage, unspecifie	3
Gestational [pregnancy-induced] hyperte	5
Gestational [pregnancy-induced] hyperte	2
HIV disease resulting in mycobacterial	1
HIV disease resulting in other infectio	1
Heart disease, unspecified	1
Heart failure	29
Hepatic failure, not elsewhere classifi	2
Human immunodeficiency virus [HIV] dise	261
Incomplete, with other and unspecified	1
Intentional self harm (suicide) by hand	1
Intentional self harm (suicide) by hang	8
Intentional self harm (suicide) by shar	2
Intentional self harm (suicide) by smok	1
Intentional self-poisoning (suicide) by	1
Intraspinal abscess and granuloma	1
Liver disease, unspecified	1
Malignant neoplasm of anus and anal can	1
Malignant neoplasm of bladder	1
Malignant neoplasm of bone and articula	1
Malignant neoplasm of bone and articula	1
Malignant neoplasm of brain	3
Malignant neoplasm of breast	8
Malignant neoplasm of cervix uteri	18
Malignant neoplasm of esophagus	2
Malignant neoplasm of liver and intrahe	3
Malignant neoplasm of other and ill-def	3

Malignant neoplasm of other and ill-def	1
Malignant neoplasm of other and unspeci	2
Malignant neoplasm of other and unspeci	1
Malignant neoplasm of uterus, part unsp	2
Malignant neoplasm without specificatio	2
Maternal infectious and parasitic disea	1
Meningitis due to other and unspecified	98
Miliary tuberculosis	2
Multi-drug resistant tuberculosis (MDR	2
Neoplasm of uncertain or unknown behavi	1
Not applicable	6
Other abnormal uterine and vaginal blee	1
Other acute ischemic heart diseases	8
Other and unspecified malignant neoplas	2
Other aplastic anemias	1
Other arthritis	1
Other complications of labor and delive	1
Other complications of obstetric surger	2
Other diseases of the digestive system	1
Other inflammatory liver diseases	4
Other malignant neoplasms of skin	1
Other obstetric trauma	1
Other peripheral vascular diseases	1
Other septicaemia	8
Paralytic ileus and intestinal obstruct	2
Passenger injured in traffic accident	3
Pedestrian injured in collision with ca	8
Peptic ulcer, site unspecified	1
Phlebitis and thrombophlebitis of other	1
Pleural effusion, not elsewhere classif	1
Poisoning by and exposure to other and	1
Portal hypertension	1
Postpartum hemorrhage	9
Premature separation of placenta, unspe	1
Puerperal sepsis	7

Pulmonary embolism	2
Query	7
Refusal	81
Respiratory tuberculosis, bacteriologic	118
Retained placenta and membranes, withou	2
Retained portions of placenta and membr	2
Rheumatic fever with heart involvement	2
Sarcoidosis	1
Sequelae with surgical and medical care	1
Stroke, not specified as hemorrhage or	37
Subarachnoid hemorrhage	1
Toxic effect of other and unspecified s	1
Toxic liver disease	1
Tuberculosis of bones and joints	1
Tuberculosis of intestines, peritoneum,	1
Tuberculosis of nervous system	5
Tuberculosis of other organs	7
Tuberculosis of spine	1
Unable to contact caregiver for VA inte	31
Unspecified abortion	1
Unspecified acute lower respiratory inf	76
Unspecified diabetes mellitus	22
Unspecified human immunodeficiency viru	1,830
Unspecified malaria	7
Unspecified maternal hypertension	1
Unspecified mental retardation	1
Unspecified renal failure	17
Unspecified transport accident	1
Unspecified viral hepatitis	6
Victim of lightning	2
Volume depletion	1
Others not classified	59
Total	3,098

Appendix C; Results of the Weibull distribution for mortality due to AIDS/TB with Interaction term

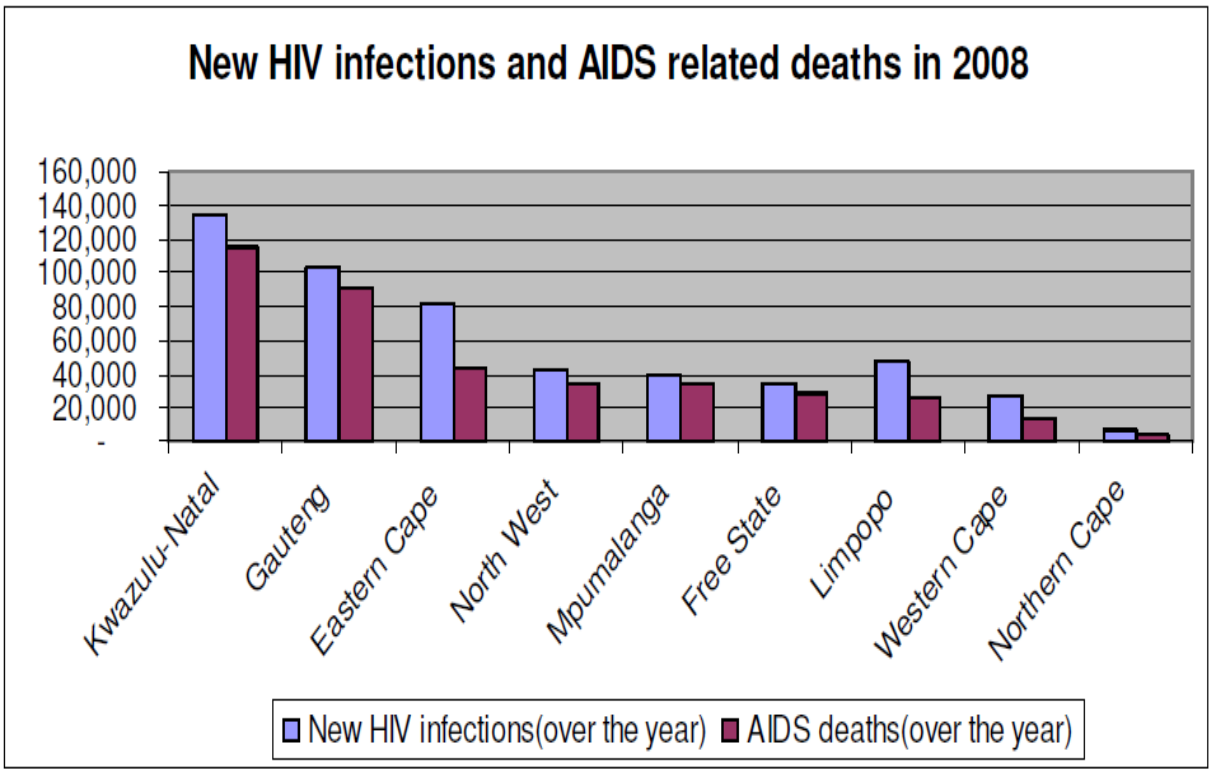
Explanatory variables	Categories of explanatory variables	Univariable analysis			Multivariable analysis		
		Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Women Age		1.053	1.049, 1.058	<0.001	1.053	1.036, 1.071	<0.001
Self reported minimum General Health	4. Good	1.000			1.000		
	5. Fair	1.519	1.285,1.797	<0.001	4.360	2.167, 8.771	0.001
	6. Poor	3.675	2.857,4.729	<0.001	13.724	4.659, 40.419	<0.001
Ever Employed	3. No	1.000			1.000		
	4. Yes	0.553	0.501, 0.610	<0.001	0.728	0.618, 0.858	<0.001
Ever Married	3. No	1.000			1.000		
	4. Yes	0.625	0.556, 0.702	<0.001	0.466	0.375, 0.580	<0.001
Migration Status	5. Never moved	1.000			1.000		
	6. Internal only	0.475	0.409, 0.553	<0.001	0.676	0.526, 0.872	0.002
	7. External only	1.602	1.432, 1.793	<0.001	1.895	1.513, 2.374	<0.001
	8. Both Internal and External	0.377	0.341, 0.417	<0.001	0.585	0.485, 0.706	<0.001
Minimum Household Index class	4. Upper 20%	1.000			1.000		
	5. Middle 40%	1.904	1.579, 2.294	<0.001	1.417	0.960, 2.092	0.175
	6. Lower 40%	1.999	1.669, 2.394	<0.001	1.471	0.989, 2.187	0.131
Highest Education level	4. More than 8 years	1.000			1.000		
	5. Less than 8 years	1.972	1.778, 2.187	<0.001	1.312	1.083, 1.589	0.006
	6. Never gone to school	1.645	1.347, 2.009	<0.001	1.349	0.983, 1.852	0.063
Ever Used Contraception	3. No	1.000			1.000		
	4. Yes	1.316	1.211, 1.431	<0.001	1.481	1.239, 1.769	<0.001

Appendix C Cont'd

Explanatory variables	Categories of explanatory variables	Univariable analysis			Multivariable analysis		
		Crude Hazards ratio	95%CI	P value	Adjusted Hazards ratio	95%CI	P value
Pregnancy outcome history	4. All live births	1.000			1.000		
	5. >1 pregnancy a Still birth/Abortion	1.124	0.976, 1.295	0.091	1.083	0.860, 1.363	0.498
	6. No outcome reported	1.144	1.039, 1.259	0.008	1.416	1.076,1.863	0.013
Maximum parity		1.036	1.018, 1.055	<0.001	0.875	0.637, 0.967	0.266
Area of residence	4. Rural	1.000			1.000		
	5. Urban	0.517	0.415, 0.643	<0.001	0.730	0.435, 1.226	0.235
	6. Peri-Urban	1.296	1.189, 1.412	<0.001	1.218	1.029, 1.442	0.022
HIV Status	4. HIV tested and Negative	1.000			1.000		
	5. HIV tested and Positive	25.567	18.606,35.134	<0.001	19.489	13.492, 28.151	<0.001
	6. Never tested	10.232	7.509, 13.942	<0.001	7.054	4.869, 10.218	<0.001
Minimum General health & woman's age	4. Good & Age				1.000		
	5. Fair & Age				0.958	0.939, 0.977	<0.001
	6. Poor & Age				0.947	0.919, 0.975	<0.001
Parity and Age					1.004	0.999,1.009	0.151

Appendix D: New HIV Infections and AIDS related deaths in 2008

Graph 4: Provincial distribution of new HIV infections and AIDS related deaths for 2008



Source: SUMMARY OF PROVINCIAL HIV AND AIDS STATISTICS FOR SOUTH AFRICA

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