ASSESSMENT OF THE ASSOCIATION

BETWEEN HIV-INFECTED MOTHERS AND THE

MORTALITY OF CHILDREN LESS THAN TWO YEARS

IN KHAYELITSHA HEALTH DISTRICT OF THE WESTERN CAPE:

A CASE-CONTROL STUDY

Mini-thesis submitted in partial fulfillment of the degree Master of Public Health.

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Prematurity
Causes of death amongst children less than two years

DECLARATION

I, Angela Dunn declare that the contents of this mini-thesis represent my own unaided work, and that the mini-thesis has not previously been submitted before for any degree or examination towards any other qualification. Furthermore it represents my own opinions, and all the sources I have used or quoted have been indicated and acknowledged as complete references.

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Date: 13 August 2007

ABSTRACT

Introduction

Amongst child deaths, most occur in the first year of life and, according to the World Health Organisation, the mortality of children in the second year of life is due mostly to environmental factors and infections. Since 1960 the infant mortality rate and the under-five year mortality rate declined globally. However, the South African National antenatal HIV sero-prevalence increased from less than 1% in 1990 to 30% in 2005. This increase in HIV prevalence coincided with an increase in child deaths. This has been attributed to mother-to-child transmission of HIV/AIDS. There has been insufficient proven association or causation of HIV-positive mothers with child deaths. If there is an association between the HIV-positive status and deaths of children under-two years, the under-two year deaths will be further exacerbated by HIV/AIDS. The significance is that most infant and child deaths are preventable and it is important to identify disease factors associated with mortality in order to take preventative measures.

The study setting

The study setting is in Khayelitsha, a peri-urban district in the Western Cape composed mainly of informal settlements.

Study population

The study population includes all 10 670 infants born alive at Khayelitsha Midwife and Obstetric Units during the study period.

Objectives

The objectives are to determine the under-two year mortality in the Khayelitsha district, the association between the mothers' HIV status at the time of pregnancy and the <2 year mortality as well as the causes of death.

Study method

This is a case-control study of infants born at the Midwife Obstetric Units in Khayelitsha over a 19-month period from 01 September 2000 to 31 March 2002. The cases are the infants born alive and who died before the age of two years. The controls are the infants who were born immediately after the birth of the case, whose names were recorded in the Khayelitsha birth registers and whose names were not in the death records. The delivery register and the mothers' folders as well as the death registers were used to collect data.

Analysis

Analysis was done on the Epi-info 6 programme. The odds ratio was calculated and confounders excluded by means of bivariate as well as by multivariate regression on the SYSTAT 11 programme.

Results

Maternal HIV infection is strongly associated with death of children less than two years. The Odds Ratio is 4.16 (2.04-8.56). The infant mortality rate (IMR) and under-two year mortality rate (U2MR) in Khayelitsha is 41.05 and 46.03 respectively.

HIV/AIDS is the leading cause of death amongst all deaths of children less than two years. When the mother was HIV-positive, more than half of the children died of HIV/AIDS and about a third died due to potentially HIV-related infections. The results of this study highlight the need for preventative and supportive interventions.

Conclusion

The main finding of this study was that there is a strong association between the HIV-positive mothers and the deaths of children less than two years. This finding was statistically significant and none of the potential confounders measured had any confounding effect. It is highly likely that the association is causal, although it could be diluted by a confounding effect of several potential confounders that could not be measured. HIV is the leading cause of death.

Recommendations

The challenge is to use this data to reduce the number of deaths in children <2 years. Mothers need to be kept healthy and alive in order to care for the children. Interventions to prevent the vertical spread of HIV/AIDS to children through effective implementation of MTCT should be strengthened. Recordkeeping needs to be urgently improved and standards stringently maintained with uniformity in the different health institutions.

Ethics

System approval was obtained from the Health Department to collect data of children as well as the HIV status of their mothers. Strict confidentiality was adhered to. The proposal was approved by the ethics committee of the University of the Western Cape.

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LIST OF ABBREVIATIONS AND ACRONYMNS

AIDS	Acquired Immuno-deficiency Syndrome
ARV	Antiretroviral
AZT	Azidothymidine (Zidovudine)
HAART	Highly Active Antiretroviral therapy
HIV	Human Immunodeficiency Virus
IMR	Infant mortality rate
IUGR	Intra-uterine growth retardation
MDG	Millennium Development Goals
MOU	Midwife Obstetric Unit
MTCT	Mother-to-child-transmission
PMTCT	Prevention of mother-to-child transmission
PCP	Pneumocystis carinii pneumonia
RNA	Ribonucleic acid
SAINT	South African Intrapartum Nevirapine Trial
TB	Tuberculosis
U2MR	Under 2 year mortality rate
U5MR	Under 5 year mortality rate
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
VCT	Voluntary HIV counselling and testing

<2 years	Less than two years of age
WC	Western Cape
WHO	World Health Organisation

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1. BACKGROUND TO THE STUDY

1.1 INTRODUCTION

The mortality of infants and children less than five years has always been of public concern as it is regarded as one of the key indicators that reflect the socio-economic status of a community or a country and is therefore a useful index for policy formation and planning purposes (WHO, 1981). Mortality among these age groups steadily declined globally from 1960 until the 1990's (World Bank, 1993; UNICEF, 2002; UNICEF, 2004).

However, since then, the mortality of infants and children under five years in sub-Saharan Africa showed an increase. During the same period, elsewhere, in developed countries such as in Europe, North America and Australasia, there was a consistent downward trend in child deaths (UNICEF, 2004). While these differences could be due to the better socio-economic circumstances and better health care in the developed countries, there should have been the same trend in developing countries, albeit at a much slower rate.

There appears to be a link between the trends in child deaths and the trends in the human-immunodefiency virus (HIV) prevalence. Since the 1990's HIV statistics showed an increase globally. This increase in HIV prevalence coincided with an increase in the infant mortality rate (IMR) and mortality of children less than five years (U5MR) (UNAIDS & WHO, 2005; WHO, 2005). This increase in child mortality has been attributed to the mother-to-child transmission (MTCT) of HIV that results in high morbidity and mortality

of under-five year olds, mainly due to infections. (Bobat, Coovadia, Coutsoudis & Moodley, 1996; Bobat, Coovadia, Moodley & Coutsoudis, 1999; Spira et al., 1999; Taha, et al., 2000; UNAIDS & WHO, 2005). The relationship between MTCT of HIV and child mortality is suspected to be the cause because of increased levels of both in the same period and because the increased deaths in children are mainly due to infections (Lucas et al., 1996; Zwi, Pettifor & Sönderlund, 1999; Graham, Mtitimila, Kamanga, Walsh, Hart & Molyneux, 2000; Ansari et al., 2003; Gisselquist, Potterat & Brody, 2004; Colvin, 2005; Grandin, Westwood, Lagerdien & Shung-King, 2005). HIV in children causes increased susceptibility to infections (Gisselquist et al., 2004). In addition, HIV increases the severity of infections (Colvin, 2005; Scarlatti, 1996) and consequently results in early deaths (Colvin, 2005).

The South African national HIV sero-prevalence amongst pregnant women increased from 0.73 % in 1990 to 30.2% in 2005 (Department of Health, 2005) and the MTCT of HIV during pregnancy, labour, delivery as well as through breastfeeding has been shown to be approximately 30-40% when there are no prevention interventions (Spira et al., 1999; Bobat et al., 1999; Taha et al., 2000). Over 90% of HIV-1 (the HIV type most common in South Africa) infection in childhood occurs by vertical transmission and the increasing number of HIV-infected women will therefore lead to an increasingly large number of HIV-infected children (Bobat et al., 1996; UNAIDS & WHO, 2005).

Differences between the IMR of children of HIV-positive mothers and those of HIV-negative mothers have been confirmed in studies (Spira et al., 1999; Bobat, Moodley,

Coutsoudis & Coovadia, 1997). Therefore, during the 1990's, a programme for the prevention of mother-to-child transmission (PMTCT) of HIV was initiated (Conner et al., 1994). Subsequently, the infant mortality and the under-five mortality decreased due to the implementation of the PMTCT programme in Europe and the United States of America (Moodley & Moodley, 2001; Scarlatti, 2004; Coovadia, 2005).

On the other hand, HIV also increases the probability of morbidity and mortality amongst HIV infected mothers (Pattinson, 2001, UNAIDS & WHO, 2005; UNAIDS, 2006). The PMTCT programme prevents the transmission of the HIV to the child, but does not assist the mother who is HIV infected. Currently no vaccine or cure is available for HIV/AIDS although at present South Africa is taking a leading role in testing an AIDS vaccine (Gray, 2003; Daniels, 2004). Therefore the mother may become ill and be unable to care for the child or she may die (UNAIDS, 2004) decreasing the children's chances of survival (Ryder et al., 1989).

However, there is insufficient proven association or causality between HIV infection of the mother and increased child mortality. There has even been controversy over whether HIV causes AIDS. This prompted the South African Government to constitute a panel of scientists in 2001 to interrogate the evidence underlying the dominant view that HIV causes AIDS (Presidential AIDS Advisory Panel Report, 2001). The dissidents view malnutrition, chemical stressors in the environment, physical stressors affecting the immune system, biological and mental stressors as the risk factors for AIDS, with some even disputing the fact that HIV is an infectious and transmittable disease (Noble, no date). On the other hand,

proponents of the view that HIV causes AIDS argue that the virus could be isolated, and that HIV is present in almost all AIDS cases and that the virus does cause the disease when introduced into a healthy person quoting Koch's postulate linking disease-causing agents to disease (Noble, no date). The arguments of the dissidents had the impact of delaying the implementation of the South African Government policy to provide pregnant mothers with antiretroviral (ARV) treatment.

If this association of HIV/AIDS infection of the mother with child mortality is correct, then the HIV/AIDS epidemic now poses a major challenge to child health in South Africa, therefore more recent data to validate and assess the extent of this challenge is needed (Solarsh & Goga, 2004).

1.2 SETTING

Khayelitsha, the area of study, is an under resourced peri-urban district of Cape Town in the Western Cape and is situated 30 km from the centre of Cape Town (Abdullah, Young, Bitalo, Coetzee & Myers, 2001). Khayelitsha had a growing population of about 364 793 people in 2001 (Groenewald et al., 2001a). Based on the baseline 1996 census 83% of the dwellings are informal, 73% of the dwellings have piped water or water on site. More than half of the households have an income below the poverty line and 40.2% are unemployed (Equity Gauge Project, 1996).

Most of the deliveries, namely the actual birth, of newborns in Khayelitsha take place in the two Midwife Obstetric Units (MOU's) present in the district. A MOU is a type of primary level health facility where deliveries of babies of uncomplicated pregnancies are done by midwives. Any complicated pregnancies or complicated deliveries encountered at the MOUs are referred to the secondary or tertiary hospitals.

Khayelitsha had an HIV sero-prevalence rate of 14.2% in 1996, which had increased to 24.7% by 2002 amongst pregnant women (Abdullah et al., 2001; Department of Health, 2001c). Therefore a PMTCT programme was conducted as a pilot study at Khayelitsha in January 1999 (Abdullah et al., 2001) and is now permanently implemented (Department of Health, 2001b). At their first antenatal visit, pregnant mothers were offered voluntary counseling and given the option of an HIV test and ARV treatment to prevent transmission of HIV to the unborn child if they were HIV-positive. (Abdullah et al., 2001; Department of Health, 2001b). This PMTCT programme provided an opportunity to do this study because of the data available for the study.

1.3 PROBLEM

Infant mortality has been declining over the years due to improved public health strategies. However, with the advent of HIV/AIDS, the IMR has been steadily increasing in South Africa. Research has shown that providing the mother with antiretroviral drugs reduces the risk of MTCT of HIV/AIDS. Therefore, this PMTCT should reduce infant mortality. Infant

mortality remains high in the absence of such programmes. This programme does not cure HIV-positive mothers. There may therefore be an increase in morbidity and mortality amongst HIV-positive mothers which could possibly influence the quality of life of both mother and child and the likelihood of death of the children.

However, there has been some doubt and controversy as to whether HIV causes AIDS and hence whether HIV-positive mothers are associated with increased deaths of infants and children less than two years of age (<2 years). This study sets out to determine if there is an association between HIV-positive mothers and mortality of children <2 years.

Most studies assess the U5MR, however, this study will concentrate on the under-2 year mortality rate (U2MR), as assessing the U5MR will take too long. This is deemed appropriate considering the public health urgency and the lack of time and resources available in which to complete the masters mini-thesis.

1.4 PURPOSE

The purpose of this research is to determine whether there is an association between HIV positive mothers and the mortality rate of children <2 years. This would help to inform policy makers and consequently might contribute to recommendations designed to improve the health of children and the community. It is important to identify factors associated with disease and mortality in order to provide preventative measures at local level. There is also

a need to determine the association between the mortality of children <2 years and their mothers' HIV status because the healthy future of a society depends on the health of the children as well as their mothers who are the guardians of the future (UNICEF, 2004). This study will provide information to the Department of Health on the possible association between HIV-positive mothers and <2 year deaths, as well as the causes of death. The information obtained from this study would also serve to identify further research needs on intervention measures to reduce child mortality.

2. LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter the literature will be reviewed in order to develop an appropriate approach to the methodology for determining whether the deaths of children <2 years are associated with the HIV infection of their mothers before or during pregnancy.

Since there is a paucity of literature on the U2MR, the literature on the IMR and on the U5MR in both the developed and developing countries will be reviewed. Mortality rates are always calculated per 1000 live children and this will be the point of departure for all mortality rates stated in this document.

Thereafter, a discussion will follow on HIV and the global, national and local HIV prevalence among women leading to the MTCT of HIV infection and the resultant increased mortality of children <2 years. The influence of various confounders such as the maternal and infant risk factors for infant deaths, which could be mixed in with the association of HIV-positive mothers and child mortality, will also be reviewed. Lastly literature on the causes of death of children will follow.

2.2 INFANT AND CHILD MORTALITY RATES

Globally more than 10 million children in low-and middle-income countries die before they

reach their fifth birthday and most of these deaths are due to just five preventable and treatable conditions namely diarrhoea, respiratory infections, tuberculosis, pneumonia and infectious diseases. According to literature children die primarily due to poor socio-economic determinants of health (WHO, 1981; Hussey, 2004; World Bank, 1993; WHO, 2005).

Many efforts have been developed to reduce the IMR and the U5MR such as developmental programmes between 1960 and 1990 (Walker, Schwartländer & Bryce, 2002). There are also several international and national structures in place to ensure child survival such as the United Nations Convention on the Rights of the Child, the Millennium Development Goals of the United Nations and the South African Constitution (World Bank, 1993; Republic of South Africa, 1996; UNICEF, 2002).

2.2.1 Infant and child mortality in developed countries

In the developed countries, such as in the Americas, Europe and South East Asia, there have been vast improvements in child health (WHO, 2005). Infant and child mortality started to decline in Europe, North America and Australasia about two centuries ago. The improvement in living conditions in the developed world has influenced the health of infants positively and hence the lower IMR and U5MR. The control of communicable diseases as well as a fertility decline also contributed to the lower IMR and U5MR (World Bank, 1993; WHO, 2005).

2.2.2 Infant and child mortality in developing countries

Between 1960 and 1990, enormous reductions in U5MR occurred in many countries. For example, child mortality in Chile dropped from 155 to 20, in Tunisia from 254 to 45, and in Sri Lanka from 140 to 22 and in India from 242 to 93 (World Bank, 1993; UNICEF, 2002). At the start of the 1960's nearly one in five children died before they were five years old. In 2001, the global U5MR had dropped from to 82 per 1000, a rate still unacceptably high as it represents an estimated 11 million preventable deaths each year (UNICEF, 2002). During the same period, namely 2001, the IMR decreased in Chile from 118 to 10, in Tunisia from 170 to 21, in Sri Lanka from 83 to 17 and in India from 146 to 67 (UNICEF, 2002).

Many countries are striving towards meeting the Millennium Development Goal (MDG) Number 4 which aims for a two-thirds reduction of the U5MR between 1990 and 2015 (UNICEF, 2004). See Annexure 3 for a table on the average annual U5MR and IMR reduction rate of various countries and the progress made towards the Millennium goal. Progress has been uneven as the child's chance of survival differs markedly depending on where they are born (WHO, 2005). Due to poverty and limited resources, the IMR and U5MR of children in developing countries still remain high (World Bank, 1993; WHO, 2005). In 2002, seven of every 1000 children in industrialized countries died before they were five. In contrast, in sub-Saharan Africa, 174 of every 1000 children died and in South Asia, 97 of 1000 children died before five years (UNICEF, 2004).

Recently the decline in the IMR and the U5MR have "stagnated, or even reversed", especially in sub-Saharan Africa (Walker, Schwartländer & Bryce, 2002: 1; WHO, 2005). Sadly, the sub-Saharan Africa mortality rates showed the slowest improvement (WHO, 2005). Studies have shown that this increase in IMR and U5MR is likely to be associated with HIV (Department of Health, 1998; Bradshaw & Nannan, 2004; Bradshaw & Dorrington, 2005).

2.2.3 Infant and child mortality in South Africa

Infant mortality data in South Africa has been unreliable and therefore it was not possible to effectively assess the health needs and plan appropriately (Nannan, Bradshaw, Mazur & Maphumulo, 1998; Bradshaw & Nannan, 2004; Bradshaw, Masiteng & Nannan, 2000). Previous information is based on the best available data from numerous sources. Data should thus be interpreted cautiously, and with recognition of potential inaccuracy (Nannan et al., 1998).

Published estimates of infant mortality from 1990, ranged from 11 to 81, attributed to the incompleteness of birth registration. This was further complicated by the underreporting as well as exclusions of previous areas such as the so called "homelands" identified by the previous apartheid government; namely Transkei, Venda, Bophuthatswana and Ciskei from the surveys (Nannan et al., 1998). See Annexure 4 for estimates of the South African IMR from 1990. Likewise, the number of registered births during 1994 also differed with the health authorities in the nine provinces in 1994, which influences the infant mortality

calculation (Nannan et al., 1998). This problem led to a revised death registration form in 1998 (Nannan et al., 1998). Furthermore, HIV/AIDS causes additional deaths and impacts on the statistics (Bradshaw et al., 2000; Dorrington, Bradshaw & Budlender, 2002).

2.2.4 Infant and child mortality by province

Infant mortality and child mortality also differs across provinces. Poorer provinces with a large rural population experienced higher infant mortality than others. The highest IMR was in rural Eastern Cape (61) and the lowest in the Western Cape (30) (Bradshaw et al., 2000: 99). Annexure 5 reflects the data obtained from 1994 to 1998 (Nannan et al., 1998) giving details about the U5MR and the IMR in the provinces and by population group. According to Dorrington et al. (2002), the projected U5MR for the Western Cape appears to have the lowest figure of 46. This U5MR, however, is still unacceptably high. An increase in IMR and U5MR has been noted in all the provinces and it has now been recommended that a mechanism should be developed to monitor the impact of the AIDS epidemic on the mortality of children (Dorrington et al., 2002).

2.3 HUMAN IMMUNO-DEFICIENCY VIRUS INFECTION IN WOMEN

The human immuno-deficiency virus has now posed a threat to the mortality of children. A discussion will follow on the global HIV prevalence, the HIV prevalence in South Africa, the provinces of South Africa and the Western Cape.

2.3.1 Global prevalence of HIV infection amongst women

HIV/AIDS have now been identified in nearly all countries (Coulter, 1998; Jackson, 2002; UNAIDS, 2004). Women are biologically more susceptible to acquiring HIV through heterosexual means than men, and social factors often add to the risk (World Bank, 1993). During 2005 about 17.5 million women were living with HIV, one million more than in 2003 (UNAIDS & WHO, 2005). The impact of HIV/AIDS is extensive (Abdool Karim, 2005). Since 1981 when AIDS was recognized, 20 million people died by 2001 with HIV/AIDS still spreading relentlessly (UNAIDS, 2004). In 2005 3.1 million adults and children died of HIV/AIDS (UNAIDS & WHO, 2005).

More than 95% of the global HIV infection is concentrated in the developing world (Gayle, 2000), mostly in countries that are least able to afford adequate care. Infection rates are rising rapidly in Asia, Eastern Europe and Southern Africa. Many countries such as those in Latin America, Thailand, Uganda and some West African Countries experience rising HIV infection rates in some parts of the country and falling or stable rates in other parts (UNAIDS, 2004). In the Caribbean, one of the most affected areas in the world, the overall HIV prevalence showed no change from 2003 to 2005 (UNAIDS & WHO, 2005).

Although the national HIV prevalence is low in China (0.1%) and India (between 0.4% and 1.3%), these two countries are the world's most populous countries and therefore the low prevalence still represents a large number of infected people. However, the HIV prevalence is increasing in China, Indonesia, Papua New Guinea and Vietnam and there are signs of HIV outbreaks in Bangladesh and Pakistan (UNAIDS, 2006).

There were 3.5 million adults and children newly infected with HIV at the end of 2002 in sub-Saharan Africa. Of significance is that a high proportion (90%) of the children living with HIV in the world are in sub-Saharan Africa, where there are high fertility rates as well as high HIV-prevalence rates among women (WHO, 2005). This is due to the fact that more women in the childbearing age are infected with HIV in Africa than elsewhere. These women have more children on average than in other countries and therefore pass the virus on to more children (UNAIDS, 2004). Southern Africa remains the "epicenter" of the global AIDS epidemic (UNAIDS & WHO, 2005: 20). Among the notable new trends are the recent declines in national HIV prevalence in Kenya and Zimbabwe. These downward trends have been attributed to behavioural changes, increased condom usage and delayed sexual debut (UNAIDS, 2006).

2.3.2 HIV prevalence in South Africa

South Africa is estimated to have the largest number of HIV-positive people i.e. 5.3 million as at December 2002 (Abdool Karim, 2005). Alarmingly, HIV-infection in South Africa accounts for 10% of the global burden of HIV infection (Gouws & Abdool Karim, 2005).

The antenatal surveys provide reliable estimates of HIV infection among the South African population. These surveys measure the burden of HIV infection among women attending antenatal clinics. Nationally the HIV prevalence amongst pregnant women in South Africa steadily increased from 0.7% in 1990 to 30.2% in 2005 (Department of Health, 2002a; Department of Health, 2005). The results show that the prevalence rate of HIV has reached its highest levels to date (Department of Health, 2005; UNAIDS & WHO, 2005). Although South Africa experienced the fastest growing HIV population previously, the national antenatal HIV and syphilis sero-prevalence surveys found that the slight increase from 2004 to 2005 was not significant and that the prevalence rate might have stabilized (DOH, 2004a; Department of Health, 2005). Nevertheless, the HIV prevalence of 30% in 2005 remains unacceptably high (Gouws & Abdool Karim, 2005). See Annexure 6 for the national HIV prevalence among pregnant women attending antenatal clinics in South Africa.

2.3.3 HIV prevalence in the provinces of South Africa

In 2002 the province that recorded the highest HIV prevalence rate among antenatal clinic attendees was KwaZulu-Natal with a rate of 36.5%. The Western Cape had the lowest HIV prevalence rate of 12.4% (Department of Health, 2002a). There is a considerable geographic variation in the distribution of HIV infection, showing a higher HIV infection rate in the east coast than the west coast (Gouws & Abdool Karim, 2005). See Annexure 7 for HIV prevalence among pregnant women in the difference provinces of South Africa from 1998 to 2005.

2.3.4 HIV prevalence in the Western Cape

Previously the Western Cape had the lowest antenatal HIV-positive rates but this increased steadily from 0.7% in 1990 to 5.2% in 1998, to 12.4% in 2005 (Department of Health, 2001a; Department of Health, 2004a; Department of Health, 2005). In 1999 Khayelitsha HIV sero-prevalence was much higher than the Western Cape average, and increased from 18% to 24.9% in 2002 (Department of Health, 2004a). See Annexure 8 for HIV prevalence in the Western Cape and Khayelitsha. As women increasingly become infected, more infants will become infected (Gayle, 2000). A discussion on MTCT of HIV will now be discussed.

2.4 HIV-POSITIVE MOTHERS AND MTCT OF HIV INFECTION

Infants are infected through vertical transmission. MTCT of HIV is a serious complication in pregnancy (Gayle, 2000; Dabis & Ekpini, 2002). The virus is transmitted to unborn babies (in utero infection), neonates during delivery (intrapartum infection), when they are exposed to maternal birth fluids as well as to infants after birth through breastfeeding (Dunn, Newell, Ades & Peckham, 1992; Bobat et al., 1996; Scarlatti, 1996; Abdullah et al., 2001). The risk of infection is estimated to be 5-10% during pregnancy, 10-20% during labour and delivery, and 10-20% through non-exclusive breastfeeding (mixed feeding) by untreated women who continue to breastfeed beyond the first year in life. Globally an estimated 600,000 children are infected with HIV through MTCT each year (WHO, 2005) with varied rates reported in different regions.

Whereas the impact of the epidemic on adult mortality in Africa is well documented (Dorrington, Bourne, Bradshaw, Loubsher & Timaeus, 2001; Doherty & Colvin, 2004; UNAIDS, 2004; UNAIDS, 2006), the impact on child mortality is harder to measure (Nakiyingi et al., 2003).

2.5 HIV AS A CAUSE OF CHILD DEATHS

This HIV pandemic spread globally and threatens to engulf millions of adults in China, India and Africa increasing the number of deaths among children substantially. HIV/AIDS is a significant contributor to child mortality in Africa (Coovadia, 2005). Globally, about 58 000 children died of HIV/AIDS in 2001 (Jackson, 2002). In 2000 HIV/AIDS accounted for 60% of child deaths in Malawi (WHO, 2005). If no drastic action is taken to prevent this catastrophe, children will die. According to Coovadia: "In all the plagues which have swept the world, it is often women and children who are most effected...children have to carry the promise of new life and the rebirth of nations in any catastrophe that has the potential to wipe out whole civilizations" (2005: 183). See Annexure 9 for summary results from HIV-prevalence studies amongst paediatric users of health services in Southern and East Africa. Annexure 10 provides the IMR with and without AIDS for selected countries in 1998 as well as the projected IMR for selected African countries for 2010.

Currently the burden of HIV is high in South Africa, especially with the on-going MTCT rates (Bobat et al., 1996; Scarlatti, 1996; Abrams et al., 1998, Spira et al., 1999, Abdullah et al., 2001, Coovadia, 2005). HIV could cause the death of children because of a number

of possible reasons which will be explored in the literature. Children could die because their mothers are infected with HIV and become ill with opportunistic infections; or because their mothers died due to HIV/AIDS; or because the children contracted HIV with recurrent infections which could subsequently lower their chance of survival.

2.6 HIV POSITIVE MOTHERS AND DEATH OF CHILDREN

A number of studies have pointed to increased child mortality as a result of the AIDS epidemic (WHO, 2003; UNAIDS & WHO, 2005, WHO, 2005, UNAIDS, 2006). Mothers with HIV often become immune-compromised and may suffer from disease conditions such as pneumonia, tuberculosis, chronic diarrhoea and other AIDS defining illnesses with additional symptoms such as severe tiredness and lethargy (Jackson, 2002). Therefore she will be less able to care for the child. In addition these mothers are often not able to work and therefore have more medical and transport expenses and less money to spend on food or milk for the child. All these aspects contribute to the possible inability of women to nurture their babies which may ultimately result in the death of the children.

A Zaire study found that the difference in IMR between sero-positive and sero-negative women appears to be due to a number of factors. Those with symptomatic infection usually deliver more premature and low birth weight babies which influence the survival of the infants (Ryder et al., 1989). In Tanzania the risk of death associated with having an HIV positive mother was found to be 2.5 (WHO, 2002). In Zimbabwe the U5MR increased from

77 to 102 between 1990-1994 and 1995-1999 respectively due to the increase in HIV-infected mothers (WHO, 2002). In the rural Rakai district of Uganda, the IMR amongst infants born of HIV-infected and uninfected mothers were 209.4 and 97.9 respectively (Sewankambo et al., 2000). A study in Malawi also found that that the mortality rate amongst children of HIV-positive mothers was substantially higher (223 at 12 months, 317 at 24 months) than children of HIV-negative mothers (68 at 12 months, 106 at 24 months).

The HIV prevalence and IMR also differs within areas. The HIV prevalence in Khayelitsha reflects the national prevalence and is much higher than the prevalence in the City of Cape Town. While the HIV prevalence in Khayelitsha increased, the infant mortality rate decreased. This could be partly attributed to the implementation of PMTCT programme in Khayelitsha. Annexure 8 provides comparative data on the HIV prevalence in South Africa, the Western Cape and Khayelitsha and as well as a comparison between infant mortality in South Africa, the city of Cape Town and Khayelitsha. Some data was not available.

2.7 DEATH OF HIV-POSITIVE MOTHERS AND DEATH OF CHILDREN

The survival chances of children may be adversely affected by the death of their mothers as children who are motherless have an increased chance of dying (Ryder et al., 1989; WHO, 2005). HIV-infected persons have a ten-fold higher risk of premature mortality than HIV-negative persons (WHO, 2003). See Annexure 11 for maternal deaths in South Africa, Western Cape as well as causes of death. The years prior to and following a mother's death

are a high risk period for children as a disproportional number of deaths, most likely before one year, occur in this relatively short period (Nakiyingi et al., 2003). Maternal and child mortality were highly correlated. In the year up to and following the mothers' death, the mortality rates of children in Uganda, born to HIV-positive mothers were five times higher than those with "living" mothers (Nakiyingi et al., 2003).

HIV/AIDS has transformed orphanhood into a long term chronic problem that will worsen in coming decades (Frohlich, 2005). Even if HIV infection rates drop, the number of orphans in southern Africa will continue to rise as parents and heads of households continue to die of AIDS-related deaths (Frohlich, 2005). The worse orphan crisis is in sub-Saharan Africa, where 12 million children have lost one or both parents to AIDS and by 2010, this number is expected to reach 18 million (UNAIDS, 2004). Globally, in 2006, children who have lost one or more parents to AIDS comprised about 9% of the children less than 15 years old (UNAIDS, 2006). Children may be physically and socially neglected and when the mother is sick, dying, or dead, the emotional suffering may often be overlooked and not responded to (Jackson, 2002). Often, after the death of their mother, children live with other relatives rather than with their father alone (Jackson, 2002). The extended family in Africa has always taken care of orphaned children, long before the emergence of HIV/AIDS. However, with the gradual breakdown of the extended family in many countries, the escalation of poverty (Victora, Wagstaff, Schellenberg, Gwatkin, Claeson & Habicht, 2003) and the increasing numbers of children being orphaned by AIDS, the care of children are compromised (UNAIDS, 2004). With the additional burden

of another child, the household income and security usually decline and often the households are now headed by a child (Frohlich, 2005).

HIV/AIDS accounts for a significant proportion (9.3%) of deaths in young women in Cape Town (Groenewald et al., 2003b). The high levels of HIV infection among people in their reproductive years in many countries mean that AIDS cases and deaths of mothers will continue to rise for years. HIV prevalence is especially high in Khayelitsha. Deaths due to HIV/AIDS amongst females in Khayelitsha contributed 23% (n=1101) to all female deaths in 2001 (Groenewald et al., 2003b). An HIV test was performed in only 37.6% of all the maternal deaths in South Africa, Therefore the number of deaths due to HIV/AIDS related illness is likely to be understated. Poor infrastructure leading to the underestimation of the contribution of HIV to maternal deaths has been a barrier (Pattinson, 2001).

Life expectancy is the average number of years lived by all those in the population concerned born alive (WHO, 1981; Bradshaw & Dorrington, 2005). In developed countries the life expectancy at birth is 70, whereas in developing countries it is 40 (WHO, 1981). This disparity highlights the difference in socioeconomic development. Since 1999, primarily as a result of AIDS, the average life expectancy has declined in thirty-eight countries. In seven African countries where HIV prevalence exceeds 20%, the average life expectancy of a person born between 1995 and 2000 is now 49 years and in Swaziland, Zambia and in Zimbabwe it has dropped to 35 years (UNAIDS, 2004). HIV will lead to many AIDS widows and orphans being cared for by their ageing grandparents with limited resources and therefore deepening poverty and decreasing the chances of child survival

(Frohlich, 2005).

2.8 HIV-POSITIVE MOTHERS AND MTCT AND HIV INFECTION IN CHILDREN

The infant could become HIV-infected and subsequently die because of MTCT. As mentioned previously MTCT accounts for 90% of all HIV infections in children in the world (Gayle, 2000; Coovadia, 2005). Currently the burden of HIV is high in Africa, especially with the on-going MTCT rates.

As more pregnant women are infected, more infants become infected with HIV-1 through MTCT thereby increasing the IMR (Gayle, 2000; Coovadia, 2005). Annexure 8 provides an estimated IMR with and without HIV/AIDS for 1998 as well as a projected estimate for the IMR with or without AIDS for 2010 (Jackson, 2002). According to these graphs, the infant mortality without AIDS will decrease, while the infant mortality with AIDS will remain the same or increase in selected countries. The accuracy of the data is not certain due to the reliability of the data collection methods and samples. Therefore the data cannot be strictly comparable. Some data may overestimate the HIV infection at a national level if more accessible urban sites are the main or sole source of information (Jackson, 2002). Nevertheless, this data provides an estimate of the problem and children are dying of HIV/AIDS.

An average of 30% of children will acquire HIV from their HIV infected mothers. The overall MTCT rate is higher in developing countries (21-43%) than in developed (14-25%) countries (Gayle, 2000; Department of Health, 2002b). In contrast, according to Gayle: "HIV strikes down people in the prime of their lives, such as young women, whether in the developed, newly developed or developing world" (2000: S8).

In 1995 AIDS in South Africa accounted for 3.2% of deaths of children aged less than five years (Bradshaw et al., 2000). While an antibody test is possible in adults, it is more complicated in children as all infants of HIV-positive mothers are born with antibodies acquired passively from the mothers (Boylan & Stein, 1991). The patterns of disease expressions and progression differ among HIV-1 infected children. At birth a very low proportion of children have signs of infection. The mortality rate for children who develop features of AIDS early in life is substantially higher that for those who become symptomatic later during childhood (Scarlatti, 1996).

During 2002, 29% of outpatient children aged 2 to 59 months seen at the district hospital in Kwa-Zulu Natal were HIV-infected. It is estimated that HIV in paediatric out-patients may range from 0.5 to one or more times the HIV prevalence in women seen for antenatal services in the same community and it was suggested that iatrogenic HIV- infection among children requires further research (Gisselquist et al., 2004). Annexure 9 reflects HIV prevalence studies among paediatric users in southern and East Africa data. This data indicates that mortality is higher if the child is HIV-positive (Colvin, 2005).

2.9 HIV-POSITIVE MOTHERS, MTCT AND INTERVENTIONS

Various trials proved the efficacy of antiretroviral drugs in preventing MTCT. In 1994 the Pediatric AIDS Clinical Trial Group conducted a study, protocol 076, in the USA and demonstrated a 67% reduction in the risk of HIV transmission from 26% to 8% in the absence of breastfeeding (Connor et al., 1994; Moodley & Moodley, 2001). This regimen has become standard practice for HIV positive-women in many industrialized countries and many women are receiving a combination of ARV treatment (UNAIDS & WHO, 2005). This long-course treatment is often not available for women in developing countries due to cost and lack of infrastructure (Moodley & Moodley, 2001; Mofenson, 2003).

The HIVNET 012 randomized trial in Uganda found that a single course of Nevirapine given during labour and to the child 72 hours later, reduced transmission during the first 14-16 weeks of life by 47% in a breastfeeding population (Guay et al., 1999). South Africa was also part of the PETRA trial, a randomized, double-blind, placebo-controlled trial, together with Tanzania and Uganda to assess the efficacy of different short course regimens of ARV therapy in preventing early and late transmission of HIV-1 from mother to child in breastfeeding and formula-fed populations (Coovadia, 2005). A MTCT reduction of 63% was shown in the PETRA trial by using combination antiretrovirals. However, the efficacy was lost after 18 months, which was attributed to breastfeeding transmission (Moodley et al., 2003; Coovadia, 2005). The South African Intrapartum Nevirapine Trial (SAINT) confirmed that ARV treatment reduces MTCT and those short course regimens such as Nevirapine regimen and the more involved and expensive Zidovudine regiment

demonstrated comparable efficacy in reducing MTCT rate in the peri-partum period (Moodley et al., 2003; Coovadia, 2005). A concerted effort is made to give AZT orally from 34-36 weeks of pregnancy through to labour. This treatment does not prolong the life of the mother, but has been found to be effective in reducing transmission of HIV to the infant (Connor et al., 1994; Abdullah et al., 2001; Mofenson, 2003).

In the Western Cape, two treatment protocols have been successfully implemented to reduce MTCT (Department of Health, 2001b). These programmes were initiated in six districts with the highest prevalence of HIV. In January 1999, an MTCT programme was initiated in Khayelitsha. A short regiment of AZT is taken twice daily by the mother during late pregnancy i.e. from 34 weeks gestation. With the onset of labour, AZT was taken three hourly until delivery. Babies were not treated with ARV agents. The mothers were offered replacement feeds for nine months to prevent MTCT (Department of Health, 2001b).

At other institutions a single dose of Nevirapine was offered. Although both regimens reduced transmission rates, ARV treatment for MTCT is more costly than Nevirapine (Coovadia, 2005). However, the main concern with the use of ARV treatment for prevention of MTCT has been that the drug may cause resistance with subsequent viral exposure (Jackson, 2002).

Pilot programmes were initiated in some parts of the country. In 1999 the Minister of Health announced that such interventions should cease due to financial constraints in the country and that money could be spent more wisely on primary preventative measures such

as vaccine development and behavioral strategies. Dissidents are opposed to ARV treatment on the basis of the unreliability of diagnostic tests, the toxicity and drug resistance found (Presidential AIDS Panel Report, 2001). This argument was challenged on the basis that the PMTCT programme will be more beneficial, cost effective, will enhance preventative strategies as well as moral obligations (Hussey et al., 1999; Lurie, Lurie, Ijsselmuiden & Gray, 1999). The delay in implementing the appropriate drug and infrastructure further increased the HIV infections among mothers and subsequent mother-to-child transmission of HIV. Mothers can only access this treatment if tested and found HIV-positive. Of significance is that HIV testing is not universal and needs consent (Jackson, 2002).

In order to reduce mortality amongst infants and to avoid babies contracting HIV, a PMTCT programme has been established in Khayelitsha (Department of Health, 2001b). While the MTCT has decreased due to this programme (Connor et al., 1994; Moodley & Moodley, 2001; Coovadia, 2005) and the IMR has decreased (City of Cape Town, 2005), the prevalence of HIV among women remains high (Department of Health, 2001c) since there is no treatment for mothers. This is in contrast to developing countries where the infant and child deaths due to HIV had decreased as a result of the implementation of highly active antiretroviral therapy (HAART) (Lurie et al., 1999; McIntyre & Gray, 2002).

HIV is therefore linked to IMR indirectly; because as the HIV prevalence rises, the IMR increases. With the initiation of the MTCT programme, and the implementation of ARV therapy for mothers and children in developed countries, the IMR decreased.

2.10 MECHANISMS MEDIATING INCREASED DEATHS OF CHILDREN AMONGST HIV-POSITIVE MOTHERS

The factors associated with the health of mothers that could be possible confounders associated with death of infants and children <2 years will be explored. This includes the mothers' HIV status and the viral load, not booking delivery, age, partner support, parity, education, employment status, method of delivery, complications during antenatal care, delivery, postnatal care and illness of mothers at time of delivery.

2.10.1 HIV-positive mothers, viral load and increased child deaths

Most people infected with HIV do not know that they have become infected. Mothers are encouraged to attend voluntary counselling and testing (VCT) services to find out their HIV status. One of the factors that contribute to the vertical transmission is the HIV viral load which is increased during periods of infection (Puren, 2005). A large perinatal cohort, the Women and Infants Transmission Study showed a strong association between HIV virus load during early infancy and poor clinical outcome. The initiation of aggressive ARV treatment for infants and young children to improve their clinical course and preventing deaths is recommended (Abrams et al., 1998). This study was conducted to assess the prognostic ability of HIV-1 virus load on disease outcome. The HIV-1-infected children unexposed to peripartum zidovudine prophylaxis, and monitored from birth, also retained a high RNA virus load level within the first week in life, sustained throughout life and were highly associated with disease progression. The study suggests that the pattern of disease for HIV-1-infected children may be determined during the first week in life (Abrams et al.,

1998). Twenty-seven (30%) of the 89 children progressed according to the Center for Diseases Control - C classification, which indicates severe signs and symptoms, and 14 children subsequently died (Abrams et al., 1998).

2.10.2 HIV-positive mothers, not booking deliveries and child deaths

Other factors such as booking the delivery at the maternity health facilities in the early stages of pregnancy also impacts on mortality and may prevent child deaths. In high-income and middle-income countries today, the use of antenatal care by pregnant women is almost universal, except among marginalized groups such as unmarried adolescents and the poor (WHO, 2005). While more use is made of these facilities in the Caribbean and Latin American countries, Africa is still falling behind (WHO, 2005). Not booking or booking the delivery late in pregnancy contributes to complications. Pregnant women who are HIV infected have an almost four times greater chance of having a stillbirth and two times greater risk of preterm labour (Pattinson, 2001). Infant deaths have been attributed to avoidable factors which include the fact that some mothers either never initiated antenatal care, or booked deliveries late in pregnancy or delayed seeking medical care during labour (Pattinson, 2001; WHO, 2005).

2.10.3 HIV-positive mothers, age and child deaths

In sub-Saharan Africa, HIV/AIDS is an epidemic of young people, especially women (UNAIDS, 2004). Household surveys in seven countries in sub-Saharan African, found that

15-24 year-old women were 2.7 times more likely to be HIV-infected than males (UNAIDS, 2004). Levels of pregnancy are very high among teenage and young adult women in South Africa (Harrison, 2005). Teenagers who had their first sexual encounter aged between 10 and 14 years are more likely to be at increased risk of sexually transmitted infections and HIV. A study in Uganda found a high mortality of children born to teenage mothers in the univariate analysis. This was attributed to age confounding and most children died in less than one year. The Risk Ratio was 3.12 (95% CI = 2.45-3.99). However, when the child's age was controlled for, on multivariate analysis, independent predictors of mortality in children born to teenage mothers remained with the Risk Ratio of 1.7. (95% CI= 1.33-2.20) (Nakiyingi et al., 2003).

HIV status of pregnant women has been monitored annually in South Africa (Department of Health, 2002b; Department of Health, 2005). Of significance is that the HIV-prevalence is stabilizing among the teenagers. In 2004 there was a forty percent HIV prevalence increase in the 25-29 age groups, with 30 percent HIV prevalence among the 35 – 40 age groups. However, there was an observed rise in the HIV prevalence in the 35 to 39 year age group, which may be due to the shift in the cohort i.e. from one age group (30-34) in the previous survey, to the next (35-39 year) age group (Department of Health, 2004). With the rise in HIV prevalence, many infants may become infected and die.

2.10.4 HIV-positive mothers, partner support and child deaths

Persons infected with HIV have a variety of psychological and social stresses that may

differ in degree of severity, depending on the stage of illness and whether or not symptoms have appeared. The stresses are compounded by the age of the population affected, the high mortality rates, accompanying anxiety and depression, the social stigma, fear, ostracism and discrimination associated with diagnosis, the symptoms of the disease and its contagious nature (Frohlich, 2005).

The largest percentage of needs identified (31.9%) among HIV-positive women in the USA involved psychological needs. Women with HIV often lacked the support of partners, family and friend networks. The psychological needs most reported were the need for support groups followed by the need not to have HIV/AIDS. Other needs included involvement of the fathers with their children (Bunting, Bevier & Baker, 1999). This finding was supported in a Johannesburg study where 25% of the fathers did not support their children (Jones, Sherman & Varga, 2005). Furthermore, mothers may be left without partner support as it was estimated that as many as 40% of the current generation of young men will die of AIDS in adulthood if drastic measures to prevent HIV are not taken (Harrison, 2005).

Women of low socio-economic status experience more stressful life events during their pregnancy. Poverty is associated with chronic stress caused by financial insecurity, poor and crowded housing conditions, living without a partner, unsatisfying marital relationships, domestic violence and stressful working conditions. In addition, they have a more restricted social support network, with less social support during their pregnancy (Frohlich, 2005; UNAIDS, 2004) and the ability to comply with the PMTCT programme

(Jones et al., 2005).

2.10.5 HIV-positive mothers, parity and child deaths

Parity does not seem to be a risk factor for increased child deaths. The European collaborative study (1992) on risk factors for MTCT of HIV-1 found that vertical transmission was not significantly associated with parity of more than three children. HIV-positive primaparous Zimbabwean women were also not significantly associated with infant mortality (Katzenstein et al., 1999). On the other hand a substantial reduction (29%) was observed in fertility among HIV-infected women compared to HIV-negative women (Hunter, Isingo, Boerma, Urassa, Mwaluko & Zaba, 2003). However, a South African study found that the proportion of pregnancies in patients above a parity of three increased (Paruk & Godi, 2002).

2.10.6 HIV-positive mothers, employment status and child deaths

Employment is a means of alleviating poverty and health improves rapidly when people escape from poverty (World Bank, 1993). In Brazil it was found that the income in the hands of the mother has a bigger effect on family health than income controlled by the father, while in Sri Lanka an increase in public spending on health was twenty-two times more effective in reducing infant mortality than was the same increase in average income (World Bank, 1993).

The Mandela/Human Science Research Council study showed that the higher the socio-economic status of the home, the lower the HIV prevalence when all participants were considered. However, the study found no significant difference in HIV prevalence between persons who were employed (14.2%) or unemployed (12.1%). The study concluded that all strata of society are at risk and not only poorer persons (Shisana, 2002). This was supported in Zaire where HIV-1 infected mothers with advanced disease was the precursor of premature or low birth weight babies which strongly influenced the death of babies rather than the socio-economic status of mothers (Ryder et al., 1989). In addition low income is also associated with lower levels of education (Victora et al., 2003), which in turn influences the employment opportunities.

2.10.7 HIV-positive mothers, education and child deaths

Low education is associated with child deaths, as in a poor household, knowledge can make a difference between washing their hands, and not doing so (Victora et al., 2003). Education greatly strengthens women's ability to fulfill their vital role in creating healthy households (World Bank, 1993). The literacy rate of mothers is particularly important as they provide the health care to infants at home especially in the management and control of common diseases (WHO, 1981; Victora, et al., 2003). This is supported in a Nigerian study where maternal education is shown as the most single determinant of mortality in childhood, even after controlling for factors such as paternal education and occupation, area of residence and access and use of medical facilities (Flegg, 1981). It is suggested that the main reasons being that educated mothers are less fatalistic about health and will seek

therapeutic and alternative childcare, demand attention of health professionals and regard health as a right. Educated women also change the traditional balance of relationships, which influence childcare, as she will assume more personal responsibility for care rather than the influences of the mother-in-law (Flegg, 1981). In contrast, a study found that the association with maternal education was weaker in sub-Saharan African countries than elsewhere (Hobercraft, 1993). This weak association was not found to be due to structural differences in the educational systems or the level of autonomy of women (Hobercraft, 1993). Generally, educated mothers are able to reduce diarrhoeal diseases through oral rehydration solution, but their children are equally at risk of fevers and coughs as those of less educated mothers. However, educated mothers use health facilities more often for the treatment of diarrhoea, fevers and coughs. The author concluded that it was not possible to assess the child survival as all the children in the study were still living and that the weaker association with less educated women in sub-Saharan Africa cannot be concluded as causal (Hobercraft, 1993). With regards to HIV, higher educational attainment can also be associated with risky sexual behaviours and therefore an increased risk of HIV-1 (Buvé, Bishikwabo, Nsarhaza & Mutangadura, 2002), which may influence the child's chance of survival. In contrast, analysis in South Africa has suggested that school enrolment lowers the sexual risk for young people (Harrison, 2005). The author, however, remarks that some may leave school due to pregnancy and thus it appears as if those remaining in school are at lower risk (Harrison, 2005).

2.10.8 HIV-positive mothers, method of delivery and infant deaths

The virus is transmitted to unborn babies, neonates during labour and during delivery. During pregnancy, the placenta actually shields the foetus from the HIV infection, as the infection does not cross the placenta from the mother to the foetus. However, if the mother has a viral, bacterial or parasitic infection and becomes HIV-infected during pregnancy, is immune-compromised or malnourished, the protection from the placenta may break down (Jackson, 2002).

Transmission during delivery may be due to the mixing of maternal and fetal blood during contractions, contamination through mucous membranes, via swallowing infected blood or cervical-vaginal secretions when the foetus passes through the birth canal. In addition, premature rupture of membranes could lead to ascending transmission of HIV-1 through invasion of the amniotic cavity (Scarlatti, 1996).

The European Collaborative Study (1992) showed that there were some protective effects of elective caesarian section delivery, the results were not significant. The reason that the association between mode of delivery and transmission rate is more if the surgery was elective, could be largely due to the fact that elective surgery was performed on HIV-positive mothers. The odds of infection in children was 0.65 times that of children delivered vaginally or 0.56 (95%CI= 0.30-1.04) times for combined elective and emergency surgery (European Collaborative Study, 1992). In a subsequent analysis of the study, it was found that the transmission rate was higher in children who were delivered vaginally (17.7%) than

those delivered by caesarian section (11.7%). However, women who had caesarian sections were more advanced in their disease progression, which may cause the protective effect to be underestimated and therefore this study did not provide conclusive evidence (European Collaborative study, 1994). Because of the known route of transmission during the intrapartum period (European Collaborative study, 1992), caesarian sections as well as vaginal douching are performed as methods of reducing MTCT. However, caesarian sections are found to be too expensive in developing countries. Another intervention used to reduce MTCT, was to cleanse the birth canal with chlorhexidine which is found to be ineffective (Scarlatti, 1996).

2.10.9 Antenatal, delivery, postnatal complications and infant deaths

The overall aim in patient management in antenatal care is to ensure a healthy mother and a well nourished baby, who are both prepared for childbirth in order to ensure an uncomplicated delivery and postnatal period (Pattinson, 2001). Over 95% of pregnant women attend antenatal care in South Africa in order to prevent and manage complications of pregnancy early. Women not attending antenatal care are regarded as a high risk group (WHO, 2005). Research shows that there are more pre-term deliveries amongst antenatal women who did not receive antenatal care compared to the group who received antenatal care (Pattinson, 2001b). A perinatal survey of South Africa revealed that the most common primary cause of neonatal death in the City and Town group was spontaneous preterm delivery (7.48/1000 births) followed by antepartum haemorrhage (7.0/1000 births) and intrapartum asphyxia and birth trauma (6.8/1000 births) (Pattinson, 2001). If pregnant

mothers seek early antenatal care, premature deaths are avoidable (Pattinson, 2001).

2.10.10 Illness of mothers at time of delivery and infant deaths

Problems during pregnancy that affect infant death include threatened abortions, illness not specific to pregnancy such as malaria and other infections, pregnancy induced diabetes as well as hypertensive disorders of pregnancy (WHO, 2005). Classic complications of pregnancy include pre-eclampsia, eclampsia, haemorrhage and ectopic pregnancy which can influence the mother as well as the child's lives (Pattinson, 2001; WHO, 2005). Pre-existing medical disease constitutes one of the five major causes of maternal deaths in South Africa (Paruk & Godi, 2002).

Cardiac disease contributed towards 43.3% (n=74) of maternal deaths. While complications of hypertension were the common direct causes of death of mothers (19.1% of all deaths), obstetric haemorrhage and pregnancy-related sepsis accounted for the main direct causes of maternal death, and anaesthetic complications were found to be the third most common causes of death. Regrettably, ways to prevent these deaths are known and could be addressed (Pattinson, 2001).

AIDS is the most common cause of maternal deaths at all levels of health care (Mhlanga, Tiebere and Simelela, 2002; Pattinson, 2001; Bradshaw & Dorrington, 2005). MTCT has been discussed (See 2.4). The impact of the AIDS epidemic has been clearly demonstrated in a report on confidential enquiries into maternal deaths (Department of Health, 2004b).

Furthermore, all children born to mothers with advanced disease or whose mothers died are at considerably increased risk of dying and this association is especially strong for uninfected children (Newell, Coovadia, Cortina-Borja, Rollens, Gaillard & Dabis, 2004).

2.11 ALTERNATIVE EXPLANATIONS FOR ASSOCIATION BETWEEN HIV-POSITIVE MOTHERS AND CHILD DEATHS

There are alternative explanations for some or all of the association of increased child deaths with HIV-positive mothers. More specific determination of the factors influencing the death and causes of death could allow for more specific and effective preventative measures to be taken at local level. Regular monitoring of inequities in health and use of resulting information for education and improvement of services has been advocated. (Bradshaw & Dorrington, 2005). This is often redressed through change in policy and preventable measures. Therefore it is important to determine the factors influencing infant and child deaths <2 years. The factors present at birth such as the Apgar score, prematurity, birth weight, gender, population group and some socio-economic factors will now be discussed.

2.11.1 Apgar score and infant deaths

The first examination done on a newborn is the Apgar score. Apgar scores determine the infant's clinical condition within one to five minutes and 10 minutes of birth. It consists of scoring the infants heart rate (which should be above 100 beats per minute) breathing

(infant should breathe well or cry), colour (the tongue hands and feet should be pink), tone (arms and feet should move actively in the air in the supine position), and response to stimulation if drying with the towel or flicking the feet (the infant should respond with a cry and movement of the limbs (Adhikari & Woods, 2004).

If the above are present a score of 2 is given for each of these five assessment criteria, if any deviation from the normal is identified, a score of 1 is given and if there is no heart rate, breathing, if cyanosis present and no muscle tone or response to stimulation, then a score of 0 is given. The causes for a low Apgar score include foetal distress due to hypoxia before delivery, maternal anaesthesia or recent analgesia, prematurity, difficult or traumatic delivery, excessive suctioning and severe respiratory distress. All infants with a one-minute Apgar score below 7 require resuscitation. The lower the Apgar score, the higher the risk of death among the infants (Adhikari & Woods, 2004).

In Zaire, at Hospital A (serving patients with a low socio-economic status) 9.9% of the children born to HIV sero-positive mothers had a 5 minute Apgar score of less than 8, as compared with 2.2% of infants born to sero-negative mothers, but these differences were not noted in Hospital B, which served patients of a higher socio-economic status (Ryder et al., 1989). This indicates that low socioeconomic conditions and not the HIV status of the mother, increase the risk of a low Apgar score.

2.11.2 Prematurity and infant deaths

Premature infants are those infants born before 37 weeks of gestation. Prematurity is often associated with intra-uterine growth retardation (IUGR) and low birth weight (Ryder et al., 1989).

Newell et al. (European Collaborative study, 1992) attribute prematurity to various possible reasons. HIV infection *in utero* could affect the foetal development, or that women with AIDS may be more likely to deliver prematurely or possibly due to concurrent genital infection of pregnant women. Several authors confirm that the incidence of prematurity was higher amongst infants of sero-positive mothers (12.5%) compared to infants born to sero-negative mothers (3.8%; $p<0.001$) (Halsey, 1990; Ryder et al., 1989; Taha et al., 1995).

2.11.3 Birth weight and infant deaths

Low birth weight is classified as a weight of below 2500grams (Taha et al., 1995). Low birth weight and IUGR are major determinants of child survival (Adhikari & Woods, 2004; Taha et al., 1995).

Several authors concur that infants born to women who test positive for HIV-1 are more likely to be underweight and have higher mortality rates than children born to sero-negative women (Ryder et al., 1989; Halsey, 1990; Taha et al., 1995). Similarly, infants born in Africa, born of HIV-infected mothers compared to those born to uninfected mothers, also have a higher frequency of low birth weight and were more likely to have complications in

the newborn period (Bobat et al., 1999; Taha et al., 1995). A study in Malawi showed that children with low birth weights, born of HIV-positive mothers, had a higher mortality rate of 223 at one year and 317 at two years compared to children born of HIV-negative mothers with mortality rate of 68 and 106 at one year and two years respectively (Taha et al., 1995).

The mean birth weight was not significantly different in the groups. The mean weight of HIV-positive children was 2956g versus 2864g for uninfected children. However, there were significant differences in mortality among normal birth weight, low birth weight and IUGR infants of sero-positive and sero-negative mothers. The overall incidence of low birth weight was 14.1%, but the incidence was 20.1% among sero-positive mothers and 8.3% among sero-negative mothers. There were also significant differences in the incidence of IUGR among infants born to sero-positive mothers (7.5%) compared to infants born to sero-negative mothers (4.4%) (Taha et al., 1995), although this difference was not found in developed countries (European Collaborative Study, 1992).

2.11.4 Gender and infant deaths

Boys are often known to be cared for more than girls due to the economic value that is attached to them. An Italian study found that girls were more frequently infected (42.8%) than boys (36.5%) as shown by multivariate analysis (OR=1.59; 95%CI= 0.51-3.95). However, it is reasoned that the number of cases were mere coincidence i.e. 80/278 versus 57/296. Furthermore, the denominators differed due to missing data (Gabiano et al., 1992).

2.11.5 Infant mortality and population group

Differences in IMR are also found among ethnic and racial groups within countries and the IMR is especially higher in areas of socio-economic disadvantage (UNAIDS, 2004). In South Africa the IMR for the population in 1985 was 64, though it was higher in black males (73) than females (68) (Bradshaw et al., 2000). The 1990 statistics showed a varied IMR for the White, Indian, Coloured and Black population respectively (Bradshaw et al., 2000). The vast majority of the black population lives in poor socio-economic conditions, and poorer areas such as Khayelitsha and Nyanga are hardest hit by infant and child deaths. Furthermore, a South African household survey showed that poor socio-economic conditions contribute to HIV rather than race (Shisana, 2002).

2.11.6 Socio-economic factors and child deaths

There are many socio-economic factors which influence the mortality of infants and children such as poverty, women's status in society, food security, income, urbanisation, housing, safe and adequate supply of water and sanitation and access to electricity. The most common indicator to monitor health is the adequacy of housing, the number of persons per room, the size, insulation against extreme weather, the exclusion from insects and rodents and the availability of water and sanitation (WHO, 1981), which are often lacking amongst poor people. In general, AIDS-affected households are more likely to suffer severe poverty than non-affected households irrespective of the prevalence in different countries (UNAIDS, 2004).

In sub-Saharan Africa, many countries whose child mortality rates have stagnated or even reversed, emerged with the highest incidence of extreme poverty, and the greatest depth of poverty (WHO, 2005). The woman's status in society and especially in the informal settlements is inferior and often exploited, leaving them with no control over their lives (Evian, 1996; Mathews, 2005; UNAIDS, 2004). This has also been confirmed in a Cape Town study that showed a correlation with the distribution of socio-economic status and intra-urban variations of infant mortality (Cooper, Pick, Myers, Hoffman, Sayed & Klopper, 1991). With regards to the relationship between women's health and urbanization new arrivals to informal settlements were mostly young, unemployed women with limited resources (Cooper et al., 1991).

Similar findings by the Mandela / Human Sciences Research Council study showed that living in informal settlements doubles the risk of HIV and contributed this to socio-economic circumstances (Shisana, 2002). Poverty is associated with increased vulnerability to HIV-1 (Buvé et al., 2002). It appears that the association between poverty or wealth and the risk of HIV-1 infection is not straightforward (Buvé et al., 2002) as higher educational attainment can also be associated with risky sexual behaviours and therefore an increased risk of HIV-1. On the other hand, children from wealthier families may have more access to health care than poorer families (Gisselquist et al, 2004). In contrast, the influence of the socio-economic status on HIV-infection has been further challenged as a study shows that the mortality rates among children of sero-positive mothers are high regardless of socio-economic status (Ryder et al., 1989). Nevertheless, and HIV are interlinked (Haywood, 2005).

2.12 CAUSES OF INFANT AND CHILD DEATHS

In order to respond adequately to infant and child deaths, the causes of death need to be known to provide decision-makers and service providers with an indication of the underlying reasons why children are dying in order to recommend more specific and effective preventative measures. Of significance is that after a multi-country evaluation of child survival in 2000, researchers concluded that in the 42 countries with 90% of child deaths, 63% of these deaths could have been prevented through the implementation of a few known and effective interventions (Bryce et al., 2003).

The most common causes of death will be discussed in more detail. These will include deaths due to infectious diseases, HIV/AIDS, diarrhoeal diseases, respiratory infections, tuberculosis, malnutrition and feeding practices and septicaemia. Other causes of death not related to HIV will be mentioned.

2.12.1 Infectious diseases

In developing countries, and in South Africa, infectious diseases are the leading causes of death, especially among black infants (Bradshaw et al, 2000). Of the most common conditions causing deaths among children less than one year was diarrhoea (16%). Among the South African children aged one to five years, deaths in the year 2000 were caused by diarrhoeal diseases (20%), lower respiratory infections (9%), nutritional deficiencies (5%), congenital abnormalities (5%) and external causes (6%) (Bradshaw et al., 2000).

A more recent study at Red Cross Children's Hospital revealed that children less than one year of age were most likely to die of infectious diseases (69.5%) followed by non-communicable diseases (24.4%) and injuries (1.1%) (Grandin et al., 2005).

2.12.2 HIV/AIDS

The HIV/AIDS pandemic is also taking an increased toll on children (WHO, 2005). With few exceptions, children acquire HIV infections from their mothers (Coovadia, 2005). Although most of the infections occur through MTCT, there is a hypothesis that some children may be infected through non-vertical and non-sexual means i.e. in Africa HIV has been acquired through inadequate health care in the paediatric setting, iatrogenic means and not only via vertical transmission from their mothers (Gisselquist et al., 2004).

At a children's hospital in Cape Town, HIV/AIDS constituted over 60% of the deaths within the infectious and parasitic diseases, and was by far the most prevalent specific cause of death in children (Grandin et al., 2005).

Children with HIV/AIDS are more prone to opportunistic infections because they have a lowered resistance to infections. Clinical features of HIV infection differ in some respects between developed and developing countries. Due to poor hygiene, water supplies, sanitation, nutrition and overcrowding, children in developing countries are highly exposed to infections of the skin, gut, and respiratory tract and are also prone to malnutrition (Seager, 1994; Coulter, 1998).

HIV-positive children also suffer from many HIV-related conditions such as diarrhoeal diseases, respiratory infections, pneumonia, tuberculosis, septicaemia, meningitis and malnutrition (Gisselquist et al., 2004). In addition HIV makes the infections in children more severe (Colvin, 2005; Scarlatti, 1996). This leads to substantially higher mortality among HIV-positive children than HIV-negative children (Colvin, 2005). Annexure 12 provides information on the top ten causes of death of South African children aged 1-4 years.

2.12.3 Diarrhoeal diseases

Diarrhoeal diseases are a major cause of morbidity and mortality and have always been associated with poor socio-economic conditions such as lack of safe water, lack of good personal and domestic hygiene, improper weaning practices and inadequate health services (WHO, 1981; Colvin, 2005). In developing countries a child aged less than five years has on average two to four diarrhoeal episodes annually (WHO, 1981). Several studies have shown that more diarrhoea results in worsened nutritional status and children with poor nutritional status have an increased risk of diarrhoea (Coulter, 1998; Aldo & Guerrant, 1992). In Bangladesh the overall mortality in the Clinical Research and Service Centre is 0.5%, but the mean mortality rate among severely malnourished children with diarrhoea is about 15% with most deaths occurring within the first 48 hours of admission (Ahmad, Lopez & Inoue, 2000).

Gastroenteritis commonly occurs in HIV-infected children (Bobat, Moodley, Coutsoudis, Coovadia & Gouws, 1998). A study at a Soweto hospital reports that gastroenteritis occurred 1.4 times as frequently among HIV-positive children (Colvin, 2005). In the former Zaire (now the Democratic Republic of Congo), 83% of HIV-infected children died from an episode of persistent diarrhoea. HIV-positive infants were 11 times more likely than uninfected infants to die from diarrhoea (Thea, St Louis, Atido, Kanjinga & Kembo, 1993; Scarlatti, 1996). At Chris Hani Baragwaneth Hospital gastro-enteritis comprised 21.6% of the total admissions, with more among HIV-positive children (29.4%) than among HIV-negative and untested (20.7%) children. The total deaths due to gastro-enteritis were 9.5% (Zwi et al., 1999), whilst another study at the same hospital in Soweto found that 31 (17.6%) children were classified as HIV-positive. However if they only consider the children admitted to the general paediatric ward and not include the children admitted to the short stay ward, the HIV infection increased to 27.4% (Johnson et al., 2000). The mortality in this study was lower than in a study of diarrhoeal disease in HIV-positive children in Zaire. Only 2 children died in the hospital in the HIV-positive group (6.5%) and two died in the HIV-negative group (1.5%). The researchers conclude that is possible that this study was biased in only recording deaths that occurred in the hospital as opposed to including community deaths as in other studies. Children with AIDS are likely to be discharged and die at home (Johnson et al., 2000).

An earlier study in Khayelitsha found that a significant proportion (70% for IMR and 64% for U5MR) of reported deaths were due to infection, with gastroenteritis being the main cause (Moodley, Pick, Bradshaw & Cooper, 1996). A later study in 2001 found that

diarrhoea was the third highest cause of death and accounted for 12% of deaths among the ages 0-4 years and 13% among the children less than five years of age (Groenewald et al., 2003b).

2.12.4 Respiratory infections

Respiratory infection is a common cause of death (Gie & Jeena, 2004). However, death due to respiratory infections is more common among HIV positive than HIV-negative children in Abidjan, Côte d'Ivoire and Botswana (Lucas et al., 1996; Ansari et al., 2003). Pneumonia was also the most common admission diagnosis in all children and comprised 36.9% of admissions (January 1992 to April 1997) at the Chris Hani Baragwaneth Hospital. Significantly, the proportion of HIV-positive children was greater (57.9%) than HIV-negative (34.3%) children and the most common cause of death was pneumonia (24.6%) (Zwi et al., 1999). This finding was supported in a Malawian study on children less than 5 (<5) years with pneumonia where it was found that HIV-infection was significantly associated with death. The Odds ratio was 2.98 (95%CI= 1.1-7.9) (Graham et al., 2000: 369-373). A significant factor is that all the HIV-positive children in this study received equally high quality care. By contrast, a study in Rwanda found no significant difference between mortality and morbidity among HIV-infected and HIV-uninfected children. However, there was an increased risk of developing conditions such as pneumonia in uninfected children born to HIV-positive mothers (Spira, et al., 1999).

HIV-infected children also suffer more severe forms of pneumonia (Colvin, 2005). Pneumocystis carinii pneumonia (PCP) is a common opportunistic infection in infants with HIV infection. PCP is associated with poor prognosis even when more intensive treatment and greater therapeutic options are available (Graham et al., 2000). Research also shows that PCP was the AIDS-defining event in 20% of hospitalized children and was associated with a significantly higher mortality (Colvin, 2005; Graham et al., 2000; Scarlatti, 1996), especially among children under 6 months of age (Graham et al., 2000).

2.12.5 Tuberculosis

Primary Tuberculosis (TB) in children is usually contracted via an infected adult with a sputum positive pulmonary TB. Therefore, it has been found that the best way to prevent TB in children is to cure infectious adult cases (City of Cape Town, 2004). Prophylaxis is usually provided for children that are <5 years of age that have been in contact with an adult TB sufferer.

The number of children infected with TB gradually increased and was 469, 535 and 508 annually from 2000 to 2002 respectively in Khayelitsha. It was unknown whether the variances in the number of TB cases reported in the Western Cape were due to over- or under-diagnosis of TB in children (City of Cape Town, 2004). Co-infection of TB with HIV has been well recorded, hence the strong possibility of TB infection amongst children of HIV-positive mothers (Coulter, 1998). In contrast TB amongst children in Abidjan, Côte d'Ivoire was rare, with only one HIV positive child (N=78) identified with TB in the study

(Lucas et al., 1996). One of the biggest problems is that TB in children is difficult to diagnose due to the less specific clinical presentation and the inability of children to produce sputum. Therefore TB may be misdiagnosed in some children with HIV infections (Coulter, 1998). In Khayelitsha TB was responsible for 14% deaths among adults, 2 % deaths among children 0-4 years and 1% deaths for children less than one year (Groenewald et al., 2003b).

2.12.6 Malnutrition and feeding practices

Malnutrition has been mostly protected by breastfeeding. Breastfeeding has been widely accepted as the food of choice for young infants due it its nutritional value and physical, social and psychological and economical advantages to both mother and baby (Solarsh, 2004). Breastfeeding has been known to significantly reduce infant illness, malnutrition and deaths amongst children (WHO, 1981; Bobat et al., 1997; Solarsh, 2004).

On the other hand, feeding of infants with breast milk substitutes has been proven to be especially dangerous in poor communities. An important finding in a nested case-control study in Brazil is that infants who were not breastfed were 17 times more likely than those breastfed, without formula milk, to be admitted to hospital for pneumonia (95% CI=7.7-36.0) (César, Victora, Barros & Flores, 1999). Among poorly resourced communities breast milk substitutes are often unavailable, expensive and difficult to prepare hygienically (Coutsoudis, Khun, Pillay & Coovadia, 2002) especially in sub-Saharan Africa where access to clean water is often not available (WHO, 2005).

With the advent of HIV/AIDS and MTCT there has been much debate over whether to breastfeed or not. Infants, who are not breastfed, have a six times greater risk of dying from infectious diseases in the first two months of life, compared to those who are breastfed. Several authors concur that withholding breastfeeding in poor-resource settings, significantly increased infant morbidity and mortality due to infectious diseases and malnutrition (César et al., 1999; Coutsoudis et al., 2002).

According to Colvin (2005), malnutrition is significantly more prevalent among HIV-positive children as almost half of all HIV-infected children in a study were malnourished. This is because HIV-infected children are often sick, leading to lack of appetite, lack of sufficient nutrient causing malnutrition. Of note are the findings of a study regarding growth of children in Durban born to HIV-positive women, where HIV-infected children who had died early, had more severe stunting, wasting and malnutrition, than infected children who survived (Bobat, Coovadia, Moodley, Coutsoudis & Gouws, 2001).

Breastfeeding has now been posed as a potential health hazard in resource-poor areas where mothers are HIV-positive (Guay & Ruff, 2001; Solarsh, 2004). The problem is that providing formula feeding to women in resource-poor settings is not the same as providing safe alternatives to breastfeeding. Evidence showed that HIV is transmitted through breastfeeding at an increased risk of 14% (Dunn et al., 1992). Women in developing countries have the difficult choice of balancing the risk of transmitting HIV to their infants against the benefits of breastfeeding. The dilemma they face is either to proceed with the traditional practice of breastfeeding and risk the transmission of HIV; or to choose artificial feeding with the added risk of morbidity and mortality from diarrhoea and malnutrition

(Bobat et al., 1997; Coutsoudis et al., 1999; Coutsoudis et al., 2002). This uncertainty led to studies on the impact of breastfeeding on the mortality of infants of HIV-infected mothers. Bobat et al., (1997) found that of the infants in the study who were exclusively breastfed for three or more months and those who were formula-fed, had a similar rate of transmission of 19.4%. However, in the group who received mixed breastfeeding, the HIV transmission rate was much higher (26.1%). The researchers concluded that breastfeeding was not protective in infants of HIV-infected mothers and that the differing mortality rates amongst different feeding groups required further study. A concern is that the small sample size (43) in this study among the infants who were exclusively breastfed makes conclusion dubious. However, according to Coutsoudis et al., (2002) avoidance of breastfeeding is not realistic in developing countries.

The WHO initially recommended that breastfeeding should be continued in populations with a high infant mortality due to malnutrition and infectious diseases (WHO, 1997). The duration of breastfeeding has been shown to affect the rate of transmission. The estimated rate of HIV transmission over 24 months of breastfeeding is about 16% (Coovadia, 2005). On the other hand, Coutsoudis et al. (2002) reported that MTCT is substantially less among those HIV-positive mothers, who exclusively breastfeed for at least 3 months, than among other breastfeeding mothers. Eventually WHO advocated that emphasis should be placed on counselling regarding breastfeeding and therefore mothers will be able to make an informed choice on feeding practices (UNAIDS, 2005).

2.12.7 Septicaemia

In 2001 the Khayelitsha statistic showed that 3% of children from 0-4 years died of septicaemia (Groenewald et al., 2003a) while more children (6.2%) died of septicaemia at Red Cross Children's Hospital (Grandin et al., 2005).

2.12.8 Other causes

Children also die of causes not related to HIV such as due to drowning, fires and accidents.

2.13 SUMMARY OF THE LITERATURE

The literature was reviewed to assess the infant mortality and the under-five-year mortality and if there is a possible association between HIV-positive mothers and deaths of children <2 years old. Secondly, the causes of death among children <2 years old were determined.

According to the literature, the IMR and U5MR gradually decreased from 1960 to 1990, but this reduction has since been reversed and this is thought to be due to HIV/AIDS. The HIV-prevalence has also increased, especially in the developing countries.

There are different aspects to consider when determining if there is an association between HIV-positive mothers and the death of children <2 two years. Firstly, this could be due to the MTCT of the HIV infection. As more women become infected, more children contract HIV through MTCT. The virus is transmitted to unborn babies, to neonates during labour and delivery and through breastfeeding. Secondly, HIV could be the cause of child deaths. More children die if they are born of HIV-positive mothers or if they themselves have HIV/AIDS. Thirdly, because the mother is HIV-positive and immune-compromised, she could be too sick to adequately care for the child. Fourthly, the mother could have died due to HIV/AIDS, leaving the child orphaned, influencing the quality of care. Fifthly, there are interventions that prevent the MTCT of HIV/AIDS. The programme for the prevention of MTCT of HIV has reduced the death of infants and children <2 years. However, this programme does not cure the mothers.

There are also other mechanisms mediating increased deaths of children amongst HIV-positive mothers such as their viral load, their age, their parity, their employment status, their partner support, their education, the antenatal care received, antenatal, delivery and postnatal complications as well as illnesses of mothers at the time of delivery. Some factors could be associated with the IMR and U5MR, whether the mother is HIV-positive or not. Children are more likely to die if mothers do not receive antenatal care and do not book the deliveries at the MOU's. Children are more likely to die if they are premature and have a low birth weight.

Other alternative explanations could also be given for some or all of the association of increased child deaths with HIV-positive mothers. These include the Apgar score at birth, premature birth, birth weight, gender, infant mortality in population groups and socio-economic circumstances.

The common causes of death among infants and children <2 years are infectious diseases, diarrhoea, pneumonia, TB, respiratory conditions and malnutrition, which are also common causes of death if the child is HIV-positive. These common causes of death among children are also more HIV/AIDS related and these common conditions are more severe if children are HIV-infected.

OBJECTIVES

The objectives are to determine the:

- Under-two mortality rate in the Khayelitsha district
- Association between HIV-positive mothers at the time of pregnancy and the mortality of children <2 years of age.
- Causes of death among children <2 years of age.

4. METHODOLOGY

4.1 INTRODUCTION

This chapter outlines the study population and research method used. This research was conducted at the Khayelitsha MOU's and their two referral hospitals. The study population comprised infants from Khayelitsha that were born alive at the above institutions.

4.2 RESEARCH DESIGN

This research design is a case-control study to assess the association between the death of children <2 years of age and HIV infection of their mothers. Ideally this should be a prospective cohort study as it has a greater ability to determine an association and the temporal nature of the association. This is because in a prospective cohort study, it is possible to follow an exposed and an unexposed group directly to determine if there is an association and whether a temporal relationship exists between the exposure and the diseases; whereas in the case-control study, the association can only be indirectly inferred.

The case control study is nevertheless a valid option, although it is less convincing in demonstrating association or causation than a cohort study. Case control studies have the added benefit of allowing for the study of various exposures. A case control research design is however preferred in this case because it is a rapid and cheap method of research. Furthermore, strong associations found in case control studies are likely to be causal,

provided there were no biases and the effect of confounders have been ruled out.

4.3 STUDY POPULATION

The study population included all the infants born alive at the two Khayelitsha MOU's and two referral hospitals.

4.4 SAMPLE

The cases included all the children from Khayelitsha that were born alive at the two MOU's and two referral hospitals over a 19-month period from 01 September 2000 to 31 March 2002, and who died before the age of two years.

The controls were a sample of live births collected from the delivery register, and included infants from Khayelitsha born immediately after the case, at the same institution as the case and who had not died before the age of two years.

4.4.1 Sample size

The required sample was calculated to be 310 cases and 310 controls. This was considered to be a large enough sample in order to exclude the role of chance when analyzing the results. The sample size was calculated based on the prevailing HIV prevalence of 18%

amongst pregnant women in Khayelitsha and acceptance of an odds ratio of 3.0, as a clinically significant association between HIV-positive mothers and deaths under two years. A confidence level of 99% was used in the sample size calculation.

4.4.2 Sampling procedure

The cases were obtained from the death registers of the City of Cape Town Health Department by selecting all the children born in Khayelitsha district in the stipulated period and who died before reaching the age of two years.

The controls were obtained by selecting the child that was born immediately after each case. This data was obtained from the birth (delivery) registers at the facility where the case was born, by selecting the child recorded in the birth register immediately after the record of the birth of the case. If the next child born (control) had also died before two years of age then that child was listed as a case and the next child in the birth register became the control of the first case, with the following child born then becoming the control of the second case (who would have been a control had he/she not died). One control was selected for each case.

4.5 DATA COLLECTION

This was done by means of a record review of the death registers, delivery registers, the

mothers' folders, blood books with records of the HIV status of the mother, as well as the antiretroviral books reflecting the HIV status and medication of the mothers of the children.

The cases were extracted from the death register. The data from the death register then had to be linked to the delivery register and the delivery register was then linked to the mothers' folder. Thereafter, the mothers' folders were linked to the ancillary records namely the VCT consent form, the ARV books and the blood books (books in which the HIV test results were recorded) in order to find a record of the HIV status.

Data on the controls were then easier to obtain as they were, as noted before, simply the next birth recorded in the delivery register.

4.5.1 Death register

All children on the death register who met the criteria of "resident in Khayelitsha and born between 01 September 2000 and 31 March 2002 and who died before two years of age" were included as cases. The child's name, date of birth, address, gender, the date of death and the cause of death were obtained from the death register as well.

4.5.2 Delivery register

The demographic data obtained from the death register, namely the name, date of birth, address and gender was used to find the record of birth of the child in the delivery register. Data obtained from the delivery registers included the name of the mother, the folder

number, the date and time of delivery, the address, the age, the parity, and the delivery booking status as well as the method of delivery and the outcome of the delivery. This delivery register also provided information on the infant's Apgar score, the weight at birth and whether the baby was born premature or full term.

Data on the controls were then easy to obtain as they were, as noted before, simply the next birth recorded in the delivery register. All the data above were collected for the controls as well.

4.5.3 Mother's folder

The mothers' folders of both the cases and controls were obtained using the folder number listed in the delivery record of the children. Sections in the folder from which data of the mother was collected included the notes in the folders, the prescription form, the antenatal record, the summary of labour form, the discharge form, the infant record card and the voluntary consent form. There were four places where the HIV status could be found in the mothers' folders namely the notes in the folder, the prescription form, the voluntary consent form and the discharge form.

4.5.3.1 The notes in the folder

The mother's folder provided some demographic data such as the date of birth of the mother, address, occupational and educational status as well as data on the antenatal record, the record of admission, the summary of labour form, the discharge summary and the HIV

status or the administration of ARV treatment by the health professional. These notes were also verified with the entry of the delivery registers.

4.5.3.2 The prescription form

The prescription form provided data on medication prescribed. In some folders the only indication of the HIV status of mothers were found when the prescription record provided information on ARV treatment prescribed or the administration of ARV treatment was recorded by the health professional.

4.5.3.3 The antenatal record

The antenatal record provided information on whether the delivery was booked, the educational status and the health condition of the mother.

4.5.3.4 The summary of labour form

The summary of labour record provided information on the type of delivery and whether there were any complications during the birth of the child.

4.5.3.5 The discharge form

The discharge summary included information on the type of delivery, postnatal complications, feeding practices, outcome of the baby i.e. if the infant was born alive,

stillborn, adopted, had foetal abnormalities, was discharged or if the child was admitted to the nursery as well as comments for follow-up.

4.5.3.6 The infant record card

The infant record card provided information to confirm the method of the delivery, possible resuscitation of the infant, the sex of the child, the birth weight, tests done, feeding practice, illness of the child and the outcome i.e. whether the child was healthy or died.

4.5.3.7 The voluntary consent form

In the mother's folder, the voluntary consent form provided details of the mother's consent and counselling provided. The HIV status of the mother was obtained from this form. This form also provided the mother's reaction to the result i.e. whether negative or positive. Other details on this form included the mother's occupational status, support system and future preventative options.

4.5.4 The blood book

If the mother's HIV status was not found in the folder, then the blood book was consulted i.e. the book where the results of the HIV status were recorded. These books were either kept in the antenatal clinics, HIV/AIDS counselling rooms or the delivery rooms. At one of the MOUs, the mothers' names were not recorded, only the antenatal numbers. The birth

date and not the mothers' names were recorded for privacy purposes. These birthdates then had to be linked to the folder to ensure that it was the same person and infant.

4.5.5 The antiretroviral register

If no record of the HIV status was found in the folder or the blood book, then a further search was done in the ARV register, detailing the drug and dosages given to the mother.

4.6 VALIDITY

The validity of this study was determined by assessing the sample for selection bias, measurement bias, the influence of absent data, the standardization of records and the sample size as well as by assessing the possible effect of confounding variables. These are all explained in detail below.

4.6.1 The role of chance

By using a large enough sample size, the role of chance was minimised, but this was compromised by the effective reduction of the sample due to an absence of key data, as mentioned before. The names of many of the children <2 years that died could not be linked to the birth register.

4.6.2 Assessing selection bias

By using the method of sampling as described, selection bias was reduced. The names of many of the children under two years that died could not be linked to the birth register. Therefore, there is a possibility of selection bias as it is not known if those mothers of the children whose names could not be linked to the birth register, were more or less likely to be HIV-positive. This link between HIV status and the ability to trace the records, is however unlikely.

The choice of cases and controls were not selected on the basis of the HIV status of the mother and therefore there was no selection bias as the cases were taken from the death register where no record of the mothers' HIV status was recorded. The controls were also selected by taking the child born immediately after the case. Hence, the control selection had no link to the mothers' HIV status.

The cases and controls are also a representative sample of the children of Khayelitsha. This is because the majority of the mothers in Khayelitsha use these MOUs. This is because private obstetric care is very expensive and the vast majority of the population belong to the low-income socio-economic group. A few higher income residents will have used the private obstetric facilities but this is likely to be a small percentage as only 4% were on a Medical Aid Scheme at the time (Equity Gauge project, 1996). The MOU's are therefore the logical choice for the vast majority of the population in Khayelitsha that cannot afford the private health services and because of the proximity of the MOUs. Therefore, although

the controls are "facility controls", they could be considered as very similar to "community controls".

Selection bias could have been introduced due to absent data. Since key data such as the HIV status of the mothers, was missing in very similar proportions in both cases and controls this had minimal to no effect on validity, but it did decrease the sample size.

4.6.3 Assessing measurement bias

The data for the cases were collected from the death register where records are kept of the notification of deaths. The validity of the data in the death registers were previously assessed by the Medical Research Council and the data from the death register has been found to be 90% complete (Groenewald et al., 2003a). Some of the controls could therefore potentially have been cases as they might have died but not been recorded in the register. The names of all the controls were checked in the death register. If their names were found in the death register and they died before two years of age, they were then counted as cases. Four of these were found as indicated in the results. Despite this back checking and since the death registers were not 100% complete, a participant listed as a control could theoretically, in fact, be a case. However, the likelihood of this seems low.

The results could be influenced by measurement bias because the child (case) could have been linked to the wrong mother in the birth register. However, this likelihood is very minimal because the name of the child, as found in the death register, was linked to the

delivery register by fulfilling certain criteria namely the surname of the mother, the address, date of birth of the child and the gender of the child in the birth register had to be exactly the same as the records in the death register.

The data collection sheet was standardised in order to ensure validity. The data items on the data collection sheet have been standardised and designed so that the items reflect the data needed for the study.

Both the delivery register and death register are standardised records of all births and deaths respectively. The health professionals are familiar with the delivery register as it has been used for many years and is completed in a standardised way. The recording of death description codes and causes of death were found to be accurate.The Medical Research Council reviewed the quality of the cause of death coding in Cape Town in 2000 and found that it was done in an accurate and standardised manner (Groenewald et al., 2003a). These standardised records and forms thus ensured the minimisation of measurement bias.

4.6.3 Assessing the effect of possible confounders

The findings were assessed for confounders during the analytical phase by using multivariate analysis to assess the strength of association while controlling for a number of confounding variables simultaneously.

4.7 RELIABILITY

The data items on the data collection sheet have been standardised and therefore if someone else had to collect this data, they are very likely to obtain the same results. The fieldworker was trained on how to complete the data capture sheet. After entering five practice records, the data capture of the fieldworker was checked for correctness and accuracy and found to be 100% accurate. The researcher and a fieldworker collected data together. The researcher always accompanied the fieldworker to check the data sheets captured by the fieldworker in order to avoid possible omissions or incorrect entries. A pilot study would have been ideal, but this was not done due to the time constraints involved in completing this research. Formal testing of reliability was not done.

4.8 ANALYSIS

The data was entered on the data collection tool and captured on the Epi-Info 6 statistical programme. The main outcome measure, namely the association of HIV-infected mothers with deaths of their children before the age of two years, was assessed via the Odds Ratio. The Odds Ratio with 95% confidence intervals is the appropriate measure of association in case-control studies (Rothman & Greenland, 1998).

The effect of all the variables that were considered as potential confounders were assessed using 2×2 tables i.e. bivariate analysis was done. The factors which on bivariate analysis showed significant associations with the under two mortality, were included in a backward

multivariate analysis model, to adjust for the effect of these potential confounders. The SYSTAT 11 programme was used for the multivariate analysis.

The causes of death of the children were firstly analysed as a collective and then stratified and analyzed according to the HIV-status of the mothers using descriptive measures of proportional mortality.

4.9 GENERALISABILITY

The results may be generalised to other groups from similar lower socio-economic status.

4.10 ETHICS

This research received ethical approval from the Higher Degrees Committee of the University of the Western Cape. Permission was approved from the City of Cape Town Health Department to access death records of the children. Permission was also obtained from the Department of Health as well as the facility managers at the MOUs to access the information regarding the deliveries. The Medical Superintendents of the referral hospitals also provided permission to access and collect data related to infant births and the HIV status of their mothers at the MOU's and referral hospitals.

Strict confidentiality was adhered to. The field worker signed a declaration of confidentiality and was trained on the sensitivity of the data collected. No names are part of the report. Feedback will be given to the Department of Health and health workers as part of the ethical responsibility of the researcher.

5. RESULTS

5.1 INTRODUCTION

This chapter will report on the key results relevant to the objectives. Firstly, this will include a description of the sample realisation, followed by the findings of the mortality rates. Thereafter the association between the HIV status of mothers and the death of children will follow. This association could of course be influenced by a variety of confounders and these potential confounders will be assessed. They have been grouped according to whether they are statistically significant or statistically non-significant. Lastly the causes of death of children <2 years will follow. This will include a presentation on the causes of death of the total sample, those born to HIV-positive mothers, those born to HIV-negative mothers and those children whose mothers' HIV status was unknown.

5.2 SAMPLE REALISATION

The required sample was 310 cases and 310 controls. The number of deaths in the period and hence the potential number of cases was 494. The sample realised was 122 cases and 122 controls. The HIV status in the sample of 244 mothers was known among 167 (69%) mothers. Amongst these, data on the HIV status of the mother was obtained for 86 (70%) cases and 81 (66%) controls. A detailed description of the sample realisation and the inability to locate HIV status data for a portion of the sample is provided below. According to the data obtained from the City of Cape Town Health Information Department, 494

children out of a total of 10670 births during a 19 month period i.e. 01 September 2000 to 31 March 2002 died before they were two years of age. Although a concerted effort was made to realise the required sample, it was not possible to link the death records of the children to the delivery register of the mothers for 372 (75%) of the 494 who had died. The delivery registers were kept at the Labour wards or in the record rooms. Initially, after searching the relevant delivery registers at the two MOU's, only 102 names of the 494 who had died were found. In order to increase the sample, a further search was undertaken at the referral facilities namely two secondary hospitals and one tertiary hospital.

At one secondary hospital only 13 names could be matched to the death register and no cases could be found at the other secondary hospital, while at the tertiary hospital only 7 names in the birth register could be matched to the death register. Therefore twenty cases and twenty controls were added, totalling 122 cases and 122 controls. There were no other live births whose names, date of birth, gender or address at the time of death could be matched with the records of children who died before the age of two years. Therefore only 122 (39%) of the intended sample of 310 cases were included in this study.

There are some possible reasons for not finding other names that linked the birth register to the death records. The children in the death register could have been registered under different names e.g. the father's name. The children who died might not have been born in Cape Town as they could have arrived in Cape Town after they were born. The infants could have been born at home and hence there would be no delivery records in the health facility. The other possible reason is incomplete record keeping at the health facilities.

One control was selected per case and therefore 122 controls were included in the final sample. On selecting the controls in the birth register (namely the child born immediately after the birth of the case) four of the potential controls were found to be cases. All the names of the controls were double-checked to see if they were in the death register and died before they were two years of age, and besides the four mentioned above, none of them were. The four potential controls that were actually cases were substituted by taking the next child listed in the birth register.

The process of obtaining the HIV status was complicated and lengthy as several documents had to be consulted. See the methodology section for details. Firstly, the HIV status of mothers was not readily available. Secondly there were physical problems in locating the folders. Thirdly, there were problems with the recording of data and hence some missing data or some ambiguity in the interpretation of the data arose.

The HIV status had to be obtained from the mother's folder, either in the notes, the antenatal record, the prescription form or the voluntary consent form. After finding the folders of the mothers, only some folders had a record of the mother's HIV status in the notes while other folders had the voluntary HIV consent forms completed with the record of the mothers' HIV status, or the status was recorded on the antenatal record, the prescription form or the discharge form. Therefore more possibilities to find the HIV status were explored. If there was no record of the HIV status in the folders, the HIV blood books, where the test result of the HIV status was entered, were consulted. In some HIV blood

books the names of the mothers were not recorded, only their antenatal numbers and birthdates. The mother's birthdates were then verified in the mother's folders by checking if the names, numbers and birthdates matched. If the HIV results were not found in the blood books, the ARV books (i.e. the books detailing treatment) were checked for the mother's HIV status. This would only apply if the mother was positive.

The folder numbers were obtained from the birth registers and then used to locate the folders. There were also problems with locating the folders. Many of the folders of the mothers were not readily available. The folders were not always found in the record rooms as discussed in the methodology section on data collection. The folders of mothers at one MOU were kept in the record room on the premises, while the folders of the other MOU were kept in the record rooms at a referral hospital some distance away, as there was no space for storage. At the secondary hospital the delivery registers and folders were kept in the record rooms whereas at the tertiary hospital the delivery registers were kept at the labour ward and the folder data of mothers was obtained electronically from the micro-fiche slides in the record department as they had to condense the folders to minimise space. Some of the folders could also not be traced at all and hence we could not use this mother-child-pair in the sample.

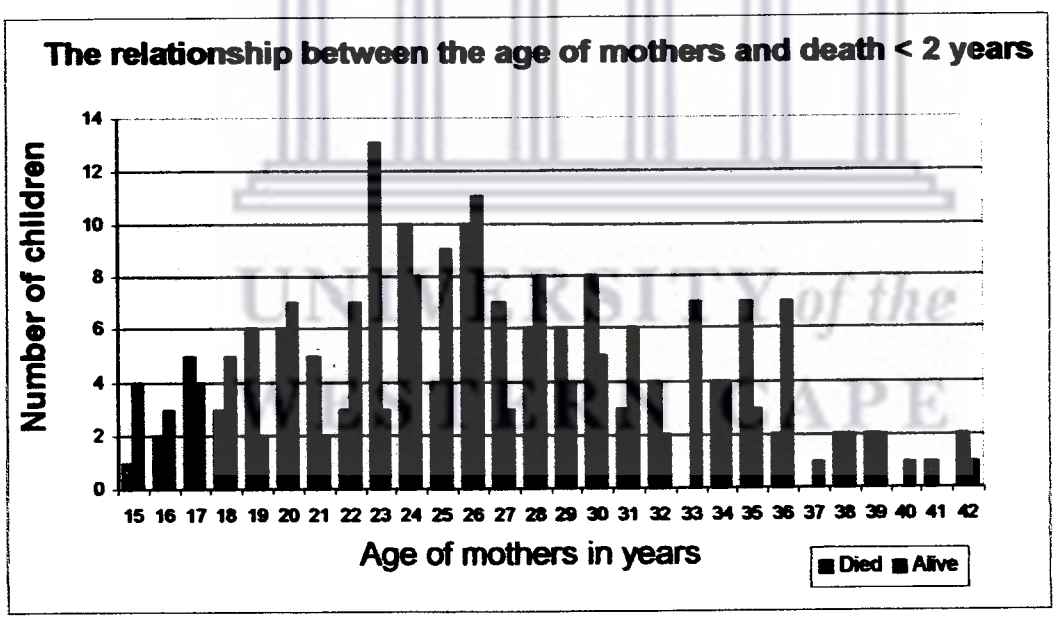
Another problem was that the recording of the data needed for the study was documented only in some of the folders. The place of recording data in the folder was also not uniform. It could be that the staff tried to maintain confidentiality by omitting the HIV status or

because it was just not recorded for reasons such as staff shortages, lack of time or negligence. Other records, such as the educational status of the mothers, lended itself to ambiguity. Some folders required the educational standards and hence the health professional recorded as such, while other health professional recorded the educational grades, currently used in the educational system. Some of the folders did not have a space allocated to record the educational status, hence the recording was omitted. The employment status of mothers was also not always documented. This data was mostly found on the HIV voluntary consent form. Some mothers could have been on maternity leave, receiving a salary and now unemployed due to the pregnancy. This is however, deemed unlikely in this low socio-economic area.

5.3 DEMOGRAPHIC PROFILE

The demographic variables included are the age of the mothers and their parity. The ages of the mothers ranged from 15 to 42 years. The median age amongst mothers in the study is 26 years. There is no difference amongst the cases and controls. The most frequent (mode) age for the mothers of the cases was 23 compared to 26 years for the mothers of the controls. One mother's age was not recorded in the delivery register and the folder could not be traced. See Figure 1 for the age of mothers and death among children less than two years old.

Figure 1: The relationship between the age of mothers and death of children <2 years



Most of the mothers had less than three children. Having less than three children showed no association with the death of children <2 years old. However, the parity of the mothers

should be viewed with caution and cannot be taken as a true reflection. There was ambiguity in the entry of the parity data. Some midwives could have entered the data as para 1 in the delivery register because the mother just delivered the baby, while some of the midwives entered the data as para 0 as it was the first baby. The parity of two mothers was not recorded. See Table 1 for parity of mothers and death of children <2 years.

Table 1: Parity of mothers and death of children <2 years

Number of children	Cases	Controls	Total
0	6	0	6
1	45	55	100
2	34	28	62
3	22	15	37
4	8	14	22
5	3	7	10
6	1	2	3
7	2	0	2
TOTAL	**121**	**121**	**242**

5.3.1 Socio-economic profile

The socio-economic factors assessed in this study included the education of mothers, the employment status and the area of residence at the time of the child's death.

The educational levels of mothers were categorised as those with a primary level education (grade 7 and below) and secondary education (grade 8 to 12) and above. Most mothers amongst the cases and controls had an educational level from grade 8 to 12 and above. Only 13.2% of the mothers had a primary level education amongst the cases and 17.6 %

amongst the mothers of controls.

Most mothers among the cases (76%) and controls (80%) were unemployed. The population in this study was predominantly from a lower socio-economic area (87%). This residential area classification was done based on the suburbs they lived in at the time of the child's death. Because it was not possible to assess the degree of poverty on the basic income of the mother, the suburbs were designated as poor / very poor versus middle class on the basis of the infrastructure and type of housing.

5.3.2 Pregnancy related factors

The factors related to the pregnancy include whether the mothers were ill during pregnancy and or experienced antenatal complications. Only nine mothers had a medical condition. Six mothers of cases suffered from medical conditions compared to three mothers of controls. Amongst the cases, one mother had a history of hypertension, four had epilepsy and one had a history of TB. Among the mothers of controls, two had a history of hypertension and one had asthma.

Four mothers of the cases experienced complications during the antenatal period, while two mothers of the controls experienced complications. See Table 2 for details of antenatal complications.

Table 2: Antenatal complications and death of children <2 years

Complications	Cases	Controls	Total
Anaemia	1	0	1
Pre-eclampsia	2	1	3
Hypertension	1	0	1
Acute Pyelonephritis	0	1	1

Deliveries were mostly uncomplicated with only five caesarean or assisted deliveries amongst the cases and six caesarian or assisted deliveries amongst the controls.

5.4 MORTALITY RATES

In the 19 month study period a total of 10670 infants were born in the Khayelitsha district. A total of 494 children amongst the birth cohort died before they reached 2 years of age and therefore the U2MR equates to 46.3 per 1000 live births.

Amongst this birth cohort 438 infants died before they reached one year of age. Therefore, most deaths (87%) of children actually occurred before they reached one year and the IMR during this study period equates to 41.05 per 1000 live births.

5.5 THE HIV STATUS OF MOTHERS

Amongst the total sample of 244 cases and controls, 72 (30%) mothers were known to be HIV positive and 95 to be HIV-negative. See Table 3 for data regarding known HIV status of mothers grouped by cases and controls.

Table 3: HIV status of mothers and death of children <2 years

	Cases	Controls	TOTAL
HIV-positive	51	21	72
HIV-negative	35	60	95
HIV status unknown	36	41	77
TOTAL	**122**	**122**	**244**

5.6 THE ASSOCIATION BETWEEN THE HIV STATUS OF MOTHERS AND MORTALITY OF CHILDREN <2 YEARS

Limiting the analysis to only those subjects where the HIV status is known, the Odds Ratio comparing mothers' HIV status to the child dying <2 years of age was 4.16 with a 95% confidence interval of 2.04 to 8.56. This means that the children born to HIV-positive mothers are 4.16 times more likely to die before 2 years of age than children born to HIV-negative mothers. The Odds Ratio comparing the mothers' HIV status to the child dying less than one year of age was the same namely 4.16 but with a wider 95% confidence interval of 1.93 to 9.06. See Annexure 13 for details of children that died less that one year of age.

The association between HIV-positive mothers and infant mortality and mortality of children <2 years might be a true association or it might be a mixed association due to confounders, namely there may be other explanations why the children died. Therefore potential confounders have been assessed and the details are shown below.

5.6.1 Description of potential confounders

Although many factors might contribute to the death of children <2 years, this study only addressed selected variables. These include the children's gender, their Apgar score, their birth weight, the area where they were resident during the time of death, their illness at birth, and whether they were born prematurely.

Selected variables of the mothers at the time of delivery that were assessed were the type of delivery, their illnesses during pregnancy, if they were on ARV prophylaxis, their delivery booking status, their age, their employment status, their level of education, their parity, antenatal complications, delivery complications and postnatal complications.

There are other factors that could significantly influence child death, such as income, urbanisation, housing, safe and adequate supply of water and sanitation. However, measuring these variables was beyond the scope of this study.

Table 4 includes the potential confounders assessed and the number of the sample for whom data on those variables could be found. The numbers in brackets are the denominators i.e. the total numbers among the cases, controls and total sample respectively for whom data was obtained for each of the variables.

Table 4: Potential confounders and percentage sample included

Description of variable	% Cases	% Controls	% Total sample
Gender-male	53.3 (122)	46.3 (121)	49.8 (n=243)
Apgar less than 7	2.7 (110)	1.8 (113)	2.2 (n=223)
Weight less than 2500gms	25.0 (120)	13.2 (121)	19.1 (n=241)
Area at death: very poor	88.5 (122)	85.8 (120)	87.2 (n=242)
Premature	17.6 (119)	15.6 (122)	16.6 (n=241)
Illness of infant during and after delivery	5.8 (120)	2.5 (120)	4.2 (n=240)
Mother received AZT	55.1 (69)	84.7 (72)	70.2 (n=141)
Not booking delivery	15.6 (122)	6.6 (122)	11.1 (n-244)
Mothers' age less than 20 years	13.9 (122)	14.9 (121)	14.4 (n=243)
Parity more than 3 children	29.8 (121)	31.4 (121)	30.6 (n=242)
No partner support	79.3 (58)	48.6 (70)	62.5 (n=128)
Unemployment	75.7 (70)	79.5 (73)	77.6 (n=143)
Primary education	13.2 (68)	17.6 (74)	15.5 (n=142)
Assisted delivery	4.1 (122)	4.9 (122)	4.5 (n=244)
Antenatal complications	3.3 (122)	1.6 (122)	2.5 (n=244)
Postnatal complications	2.5 (122)	3.3 (122)	2.9 (n=244)
Illness of mother	5.6 (107)	2.8 (107)	4.2 (n=214)

5.6.2 Determining if variables are possible confounders

In order to determine if variables are possible confounders, three criteria for confounding were explored. The first criterion is that the variable should be associated with the exposure of interest (HIV-positive status of the mother). The second criterion is that the variable

should be a risk factor for the outcome (death before two years of age) among those who are not exposed to the factor of interest. The third criterion is that the variable should not be an intermediate risk factor for the exposure. None of the variables in this study are intermediate variables. Therefore only the first two criteria were explored further.

5.6.3 Odds ratios of potentially statistically significant confounders and exposure

Firstly it was determined if the variables are associated with the exposure i.e. if the variables are associated with the HIV-positive status of the mother. The significant associations by means of the Odds Ratio of potential confounders with exposure to HIV-positive mothers are shown in Table 5. This table includes the list of variables, Odds Ratios and 95% confidence intervals. Prematurity, and having no partner support shows significant associations as indicated by the Odds Ratios. Of interest is that HIV-positive mothers have fewer children and are less likely to have more than three children.

Table 5: Significant association of potential confounders with exposure i.e. HIV-positive mother

Variable	Odds Ratio	95% Confidence interval
Prematurity	3.11	1.08 - 9.23
Parity >3	0.40	0.18 - 0.89
No partner support	2.37	1.00 - 5.72

5.6.4 Odds ratios of potential confounders not associated with exposure

The non-significant association of potential confounders with the exposure of HIV-positive mothers are shown in Table 6.

Table 6: Odds Ratios of potential confounders not associated with exposure i.e HIV-positive mother

Variable	Odds Ratio	95% Confidence interval
Gender	1.13	0.58 - 2.20
Apgar less than 7	1.30	0.00 - 49.36
Weight less than 2500gms	1.13	0.42 - 3.07
Infant ill at delivery	5.55	0.56 - 135.76
Poor/very poor vs middle class	0.47	0.16 - 1.33
Not booking delivery	1.70	0.37 – 7.98
Mothers' age less than 20 years	0.39	0.13 – 1.13
Unemployed	0.46	0.18 – 1.18
Education < less than grade 7	0.81	0.25 – 2.53
Assisted delivery	4.09	0.36 – 106.03
Antenatal complication	Sample too small to determine the Odds ratio (6)	
Postnatal complications	0.00	0.00 – 2.04
Mother ill	2.02	0.26 – 18.10

5.6.5 Odds ratios of potentially statistically significant confounders and outcome

The second criterion is that the variable should be associated with the outcome (death) among those who are not exposed to the factor of interest. Table 7 provides data on the Odds Ratio and 95% confidence intervals of the potentially significant confounders for association with <2-year deaths.

Table 7: Odds Ratios of potential confounders for association with outcome i.e. <2 deaths

VARIABLE	ODDS RATIO	95% Confidence Interval
Not booking delivery	2.63	1.03 - 6.92
On ARV prophylaxis	0.22	0.09 - 0.53
No partner support	4.06	1.71 - 9.76
Birth weight less than 2500gms	2.19	1.6 - 4.54

The ARV prophylactic programme was strongly protective against children dying. Of significance is that the Odds Ratio of 0.22 means that children <2 years are less likely to die if the mothers received ARV prophylaxis. There was a large proportion of mothers whose partner support status was not known, namely 64 (52%) among the cases and 52 (42%) among the controls.

5.6.5 Odds ratios of potential confounders not associated with child mortality <2 years

The Odds Ratios of potential confounders not significantly associated with deaths <2 years are categorized as demographic, socio-economic, pregnancy and delivery related confounders. See Table 8 for the Odds Ratio and 95% confidence intervals found not to be statistically significant confounders for the death of children <2 years in this study.

Table 8: Odds Ratios of potential confounders not associated with outcome i.e <2 deaths

Variable	Odds Ratio	95% Confidence interval
Demographic factors		
Mothers' age less than 20 years	0.93	0.42 - 2.02
Parity	0.93	0.51 - 1.67
Gender	1.32	0.77 - 2.27
Socio-economic factors		
Poor or very poor residential area at time of death	1.27	0.56 - 2.92
Primary education	0.72	0.26 - 1.98
Unemployment	0.81	0.34 - 1.92
Pregnancy related factors		
Illness of mothers	2.42	0.54 - 12.27
Antenatal complications	2.03	0.31 - 16.55
Delivery related factors		
Prematurity	1.16	0.56 - 2.43
Apgar less than 7	1.56	0.20 - 13.79

Generally the children were born healthy and this study found that most children had normal Apgar scores at birth indicating that the infant's heart rate, breathing, colour, tone and response to stimulation was normal after birth. Only five (2.2%) infants had an Apgar score below seven. Most (181) of the infants had an Apgar score of ten.

5.7 BIVARIATE AND MULTIVARIATE REGRESSION ANALYSIS

Firstly the Odds Ratios were calculated by using bivariate analysis to determine the association between the potential confounders and the death of children < 2 years. The 95% Confidence Intervals provided an indication of the significance levels of the association and that the association is not due to chance as indicated in Table 7 and in Table 8.

Thereafter the variables that showed an association with the outcome were further analysed by using a statistical modeling technique SYSTAT 11 to estimate the strength of the relationship while controlling for all of the potential confounders. The model used was the multivariate regression analysis which is commonly used in unmatched case-control studies.

The potential confounders in this study which on bivariate analysis, of at least one aspect of a confounder showed a potential mixing of the association between HIV-positive mothers and death of children <2 years, are the lack of partner support, not booking the delivery at the health facilities, children with low birth weight and if mothers were on the prophylactic ARV programme. However, on multiple regression analysis, no association could be found between any these possible confounders and death of children <2 years old.

5.8 CAUSES OF DEATH

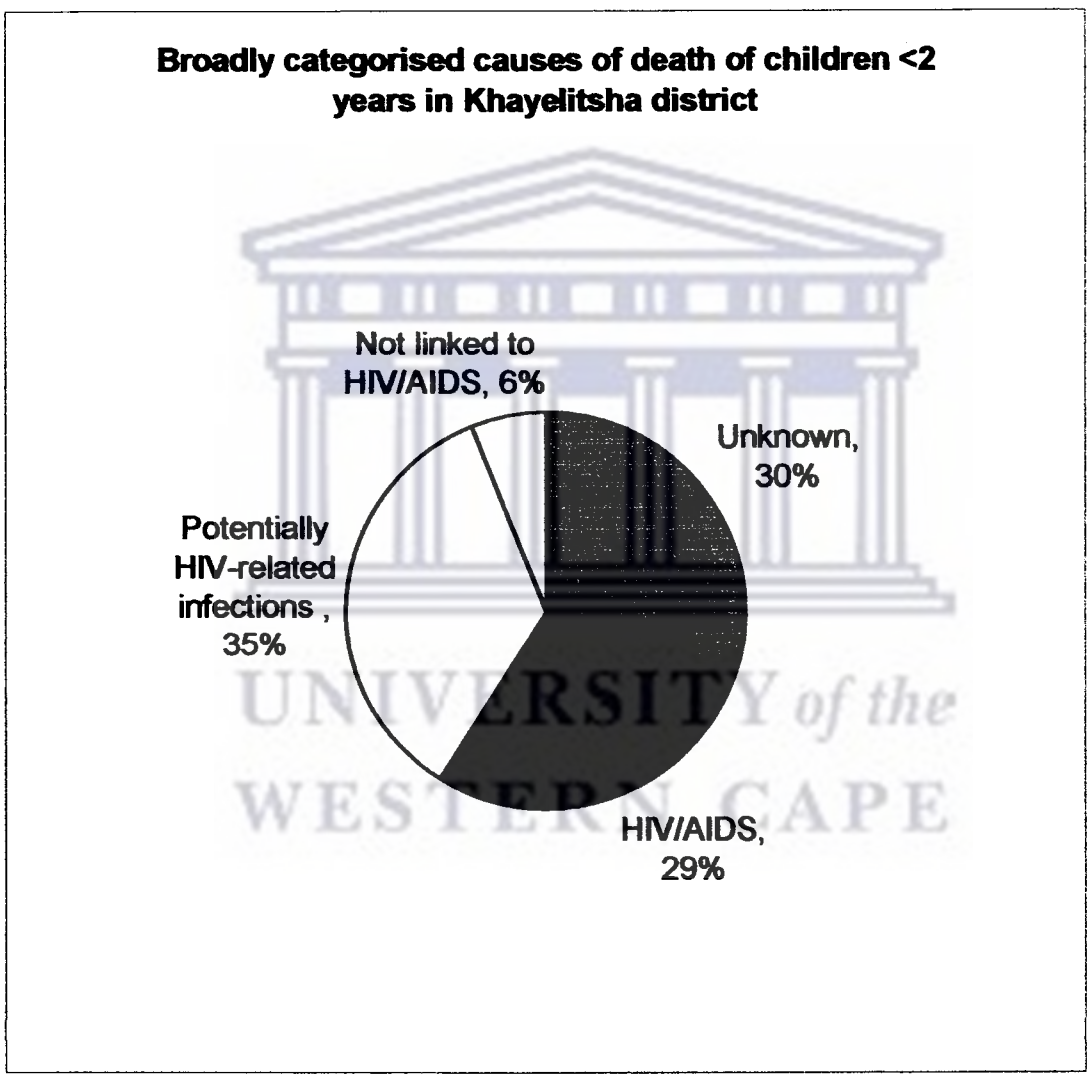
The secondary aim of this study was to determine the causes of death of children <2 years. A brief overview will be given of how the causes of death were classified. Thereafter the results of the causes of death of the children born to HIV-positive mothers will be given, followed by the causes of death of the children born to HIV-negative mothers, as well as the causes of death among the children born to mothers whose HIV status was unknown.

5.8.1 Categorising the causes of death

In the death register, four-digit codes were given for various disease conditions. The causes of death of the 122 children are firstly broadly categorised, then detailed according to the more specific causes of death and thereafter categorised according to the HIV status of the mother. These causes of death are categorized into four broad descriptive categories. These groups are aggregated so that it is easier to address the cause profile.

The four broad groups in this study included the causes of death directly due to HIV/AIDS, causes of death potentially due to HIV infections, unknown causes of death and causes of death not linked to HIV. See Figure 2 for broadly categorised causes of death.

Figure 2: Broadly categorised causes of death among all children



5.8.1.1 Causes directly due to HIV/AIDS

The first category included the cause of death directly due to HIV/AIDS. HIV/AIDS is responsible for more than half of the total deaths in the study. These were grouped as HIV/AIDS even though some children had co-infections with infectious diseases, TB and chronic diseases (Groenewald et al., 2003b). See Figure 2 for broadly categorised causes of death among all children in this study.

5.8.1.2 Causes potentially due to HIV-related infections

The second category was grouped as infections potentially due to HIV. This group was responsible for about one third of the deaths in this study. These infections included diseases such as gastroenteritis, pneumonia, meningococcal meningitis, septicaemia and TB. Also included in the infection category were diseases of the respiratory system, asthma and malnutrition. An explanation of why these three conditions are included in this category will follow. Diseases of the respiratory system may include various conditions such as peripheral airway obstruction, asthma, bronchiolitis and bronchitis (Gie & Jeena. 2004). Asthma is very difficult to diagnose in children <2 years, because it is not possible to perform tests which confirm the diagnosis such as the peak expiratory flow rate and forced expiratory volume in one second (Weinberg, 2004). Asthma is usually characterized by wheezing relieved by bronchodilators. Wheezing in children could also have been due to bronchitis, peripheral airway obstruction or bronchiolitis (Weinberg, 2004). Therefore asthma was included in the infection category as these other associated causes are all due to infections. Malnutrition is not an infection, but has been associated with infections (Hussey,

2004; Wittenberg, 2004) as children often do not receive adequate catch-up feeds after infections leading to the cycle of malnutrition. HIV with malnutrition also causes progressive and irreversible immunodeficiency and is characterized by failure to thrive and recurrent infections (Hussey, 2004; Wittenberg, 2004). See Figure 2 for potentially HIV-related infections and causes of death among all children in this study.

5.8.1.3 Unknown causes of death

Unknown causes included in this study are the ill-defined causes of death such as those with symptoms and signs and abnormal clinical and laboratory findings not elsewhere classified. This included sudden death, natural causes, cot death or sudden infant death syndrome. Respiratory failure was also classified as unknown. Respiratory failure could be due to hyaline membrane disease which is common in premature infants below 33 weeks or due to peripheral airway obstruction (Adhikari & Woods, 2004). See Figure 2 for unknown causes of death among all children in the study.

5.8.1.4 Causes of death not linked to HIV

The fourth category was grouped as causes not linked to HIV. These causes of death included causes due to accidental drowning (1; 0.8%), injury by unspecified means or undetermined causes (1; 0.8%), other external causes (5; 4.1%) and perinatal causes (4%). See Figure 2 for causes of death not linked to HIV among all children in the study.

5.8.2 CLASSIFICATION ACCORDING TO HIV STATUS OF MOTHERS

These broadly categorised causes of death are also presented according to the HIV status of the mothers. This include the causes of death among children <2 years born to HIV-positive mothers, those born to HIV-negative mothers and those born to mothers whose HIV status was unknown, respectively. Infections including HIV/AIDS constitute a large proportion of deaths.

5.8.2.1 HIV-positive mothers and broadly categorised causes of death of children <2 years

Among the children born of HIV-positive mothers, more than 80% died of infections including HIV/AIDS. HIV/AIDS was the cause of death for more than half of the children and those causes potentially due to HIV/AIDS totalled a quarter of the causes.

See figure 3 for broadly categorised causes of death among children <2 years, born to HIV-positive mothers.

Figure 3: Broadly categorised causes of death classified among the children <2 years born to HIV-positive mothers

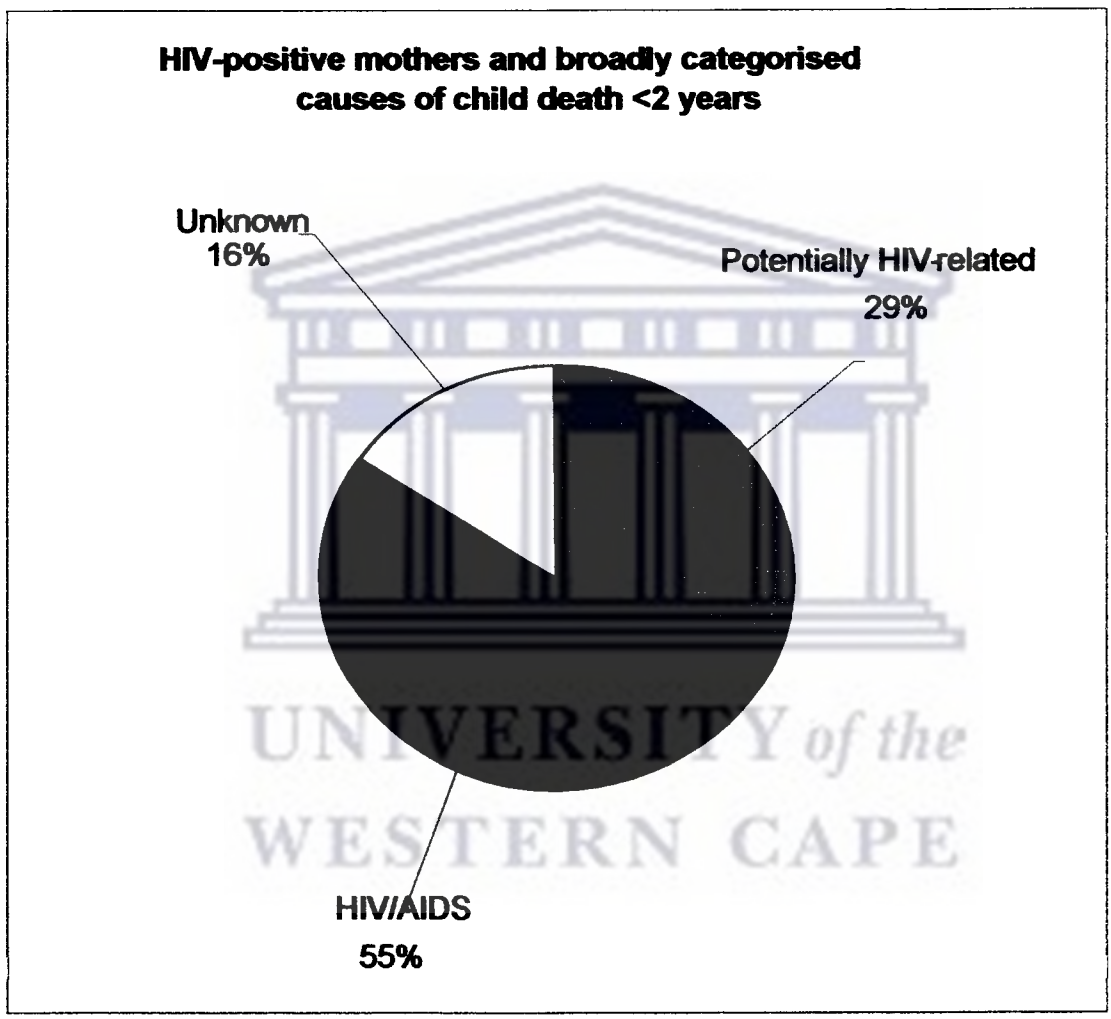
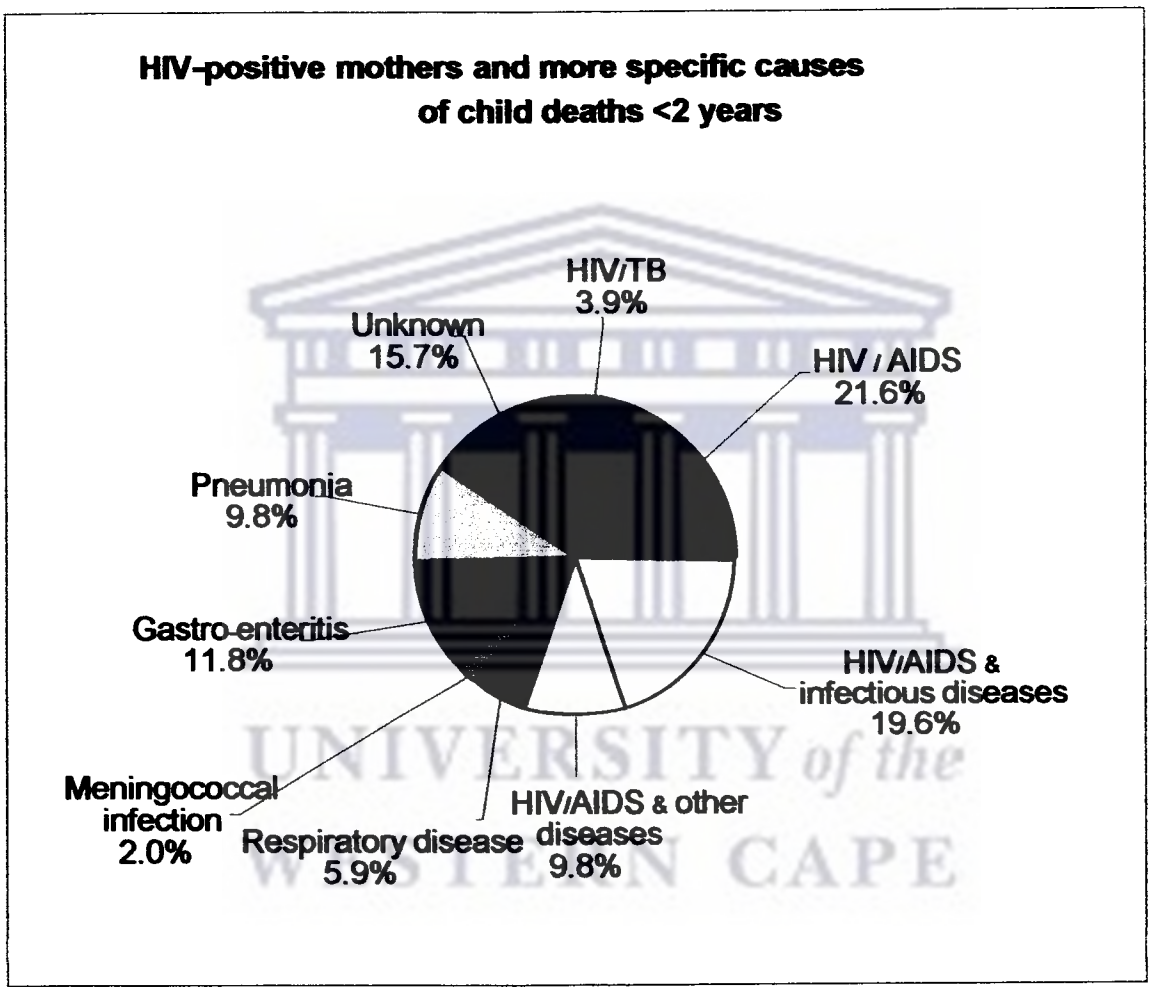


Figure 4 provides more specific causes of death amongst children born to HIV-positive mothers.

Figure 4: Specific categorised causes of death among children <2 years born to HIV-positive mothers



5.8.2.2 HIV- negative mothers and causes of death of children <2 years

See Figure 5 for broadly categorized causes of death among children <2 years born to HIV-negative mothers. It was assumed that no children would die due to HIV/AIDS in this group. However, one child was recorded as dying due to HIV hence there was a misclassification error.

The data regarding the mother's HIV status could be subject to measurement bias. One mother was found to be HIV-negative, but the child died of HIV/AIDS. Therefore, either the mother was incorrectly described as HIV-negative or the child was incorrectly diagnosed as having AIDS. There are a few possibilities for this finding. Firstly, the mother could have been tested early in pregnancy and could have been infected later. Secondly, this mother could have been tested while she was in the window period. Thirdly, the result could have been a false-negative result as she could have been tested once only. Fourthly, there could have been an error with the recording of laboratory results or fifthly, the results could have been incorrectly recorded in the folder.

Figure 5: Broadly categorised causes of death classified among the children <2 years born to HIV-negative mothers

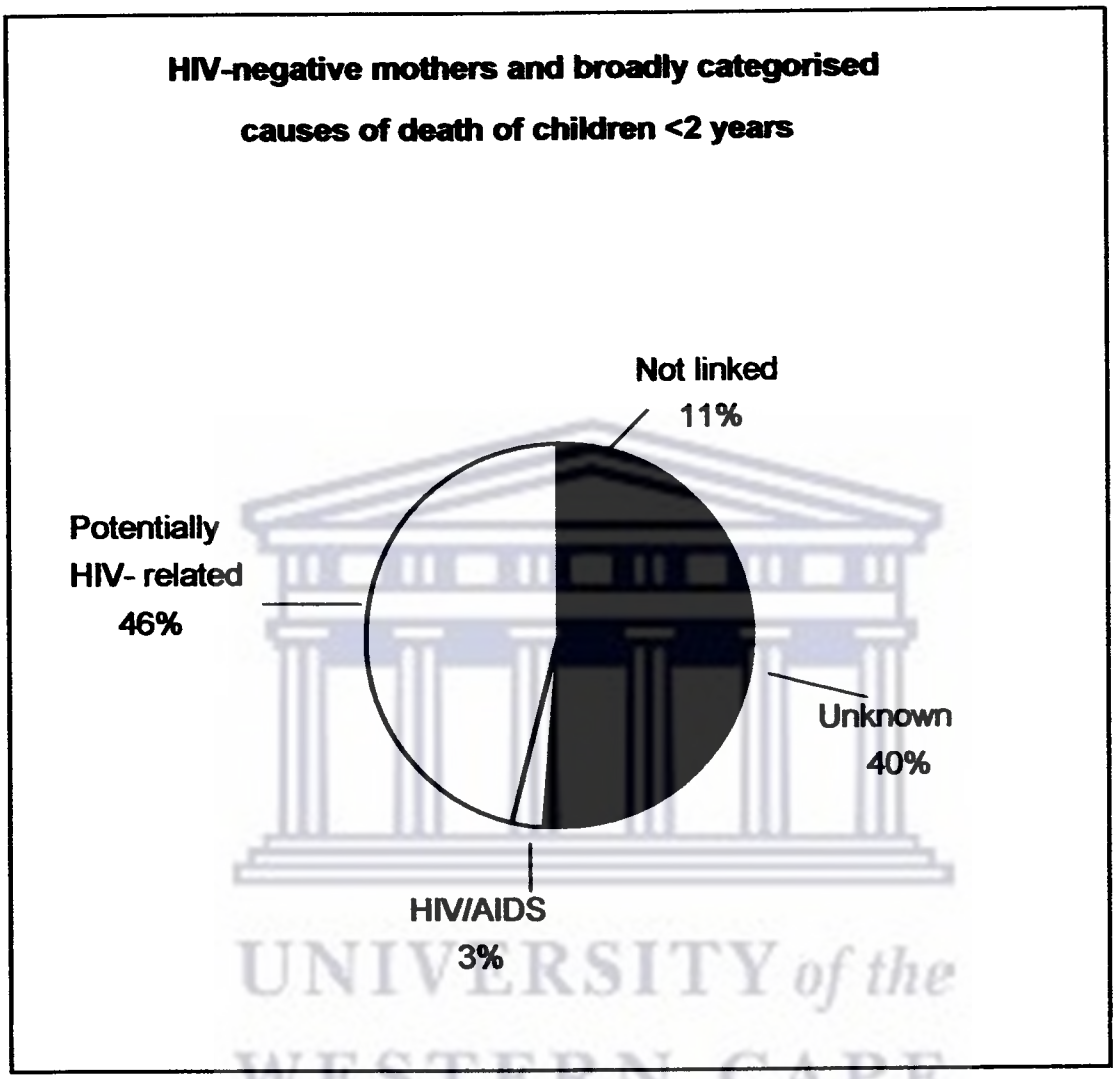
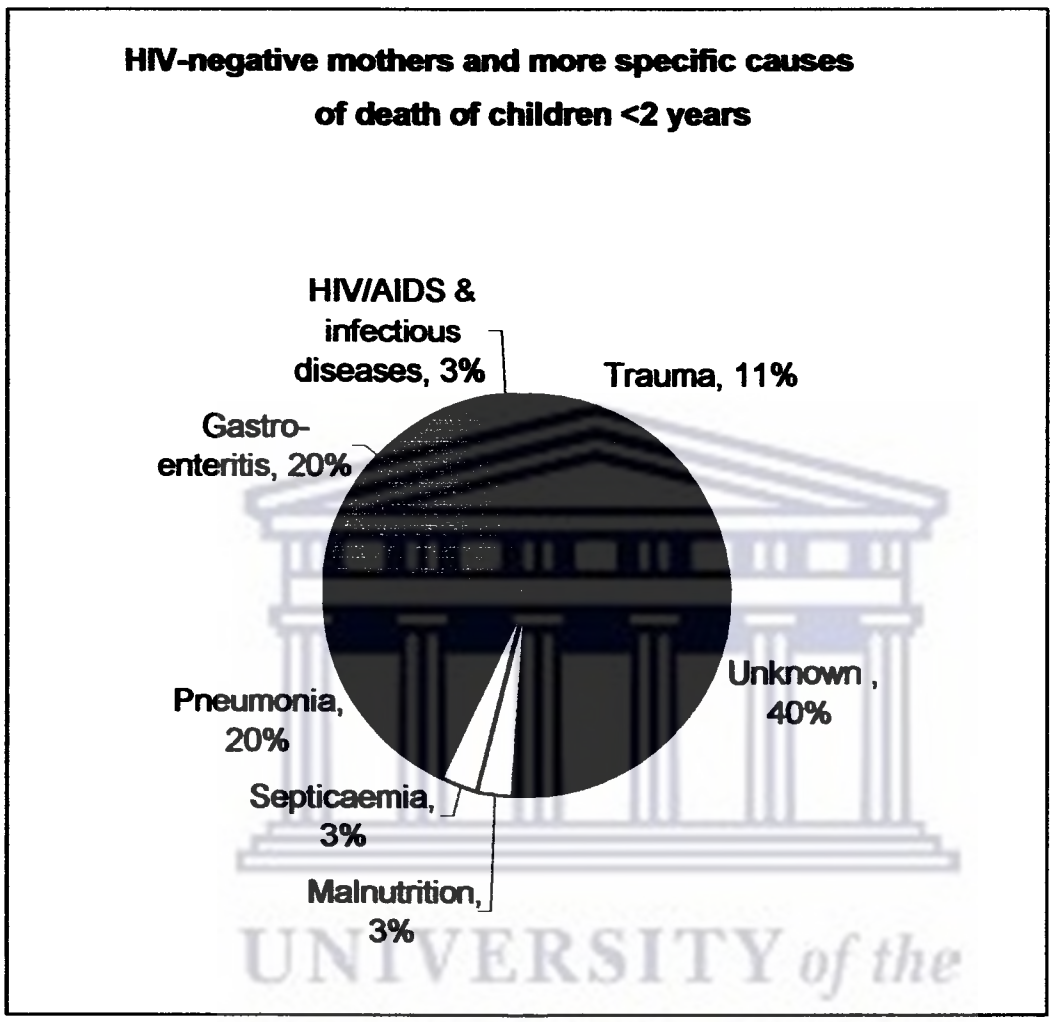


Figure 6 provides information on more specific causes of death of children <2 years born to HIV-negative mothers. One child died of malnutrition. Malnutrition is often associated with repeated infections causing weight loss and insufficient catch-up growth. Of note is that the children of HIV-negative mothers died of infections which are commonly found in informal settlements and areas of low socio-economic status and include gastro-enteritis, septicaemia, pneumonia, respiratory distress as well as malnutrition. These illnesses are also HIV-linked. Amongst the children of HIV-negative mothers, more than a third of children died of unknown causes.

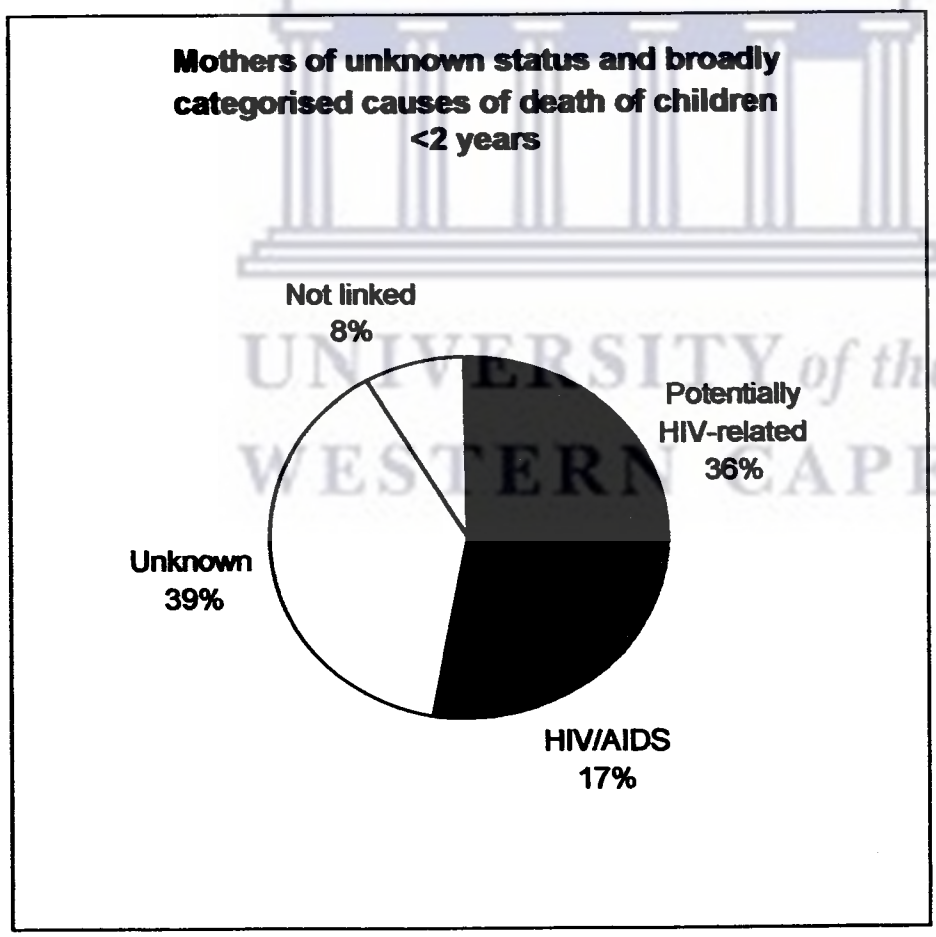
Figure 6: HIV-negative mothers and more specific causes of death of children <2 years



5.8.2.3 Mothers of unknown status and causes of death of children <2 years

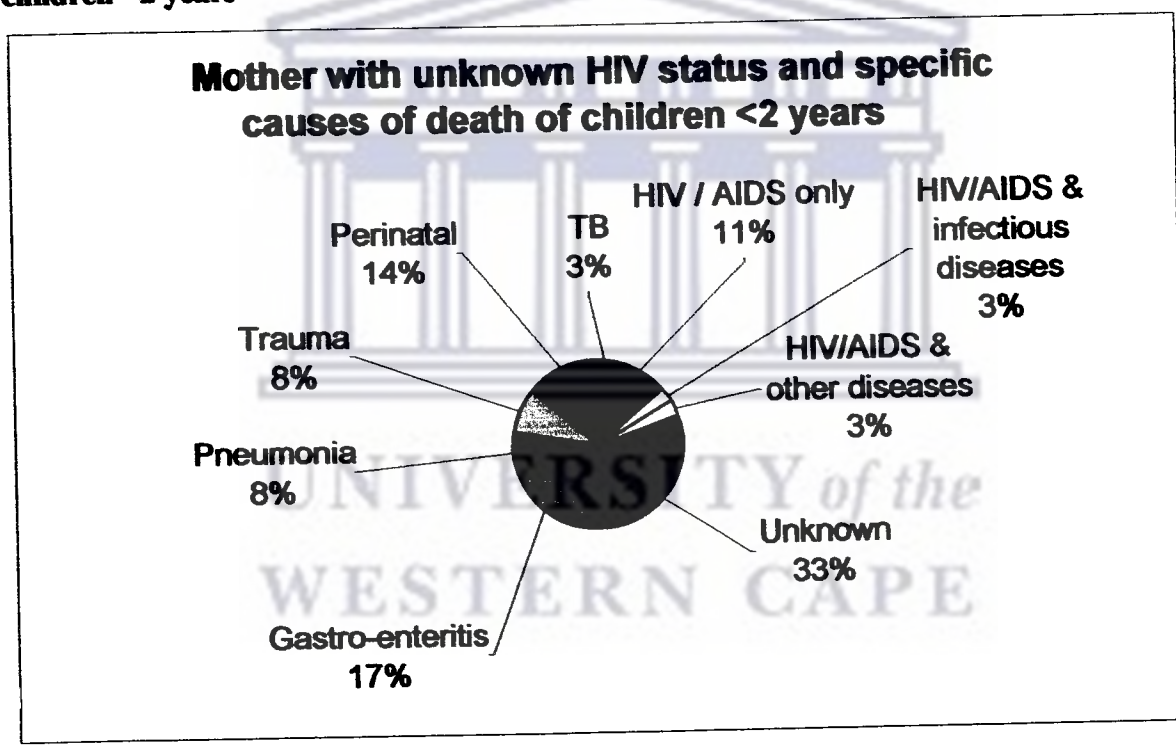
Almost 20% of children whose mothers' HIV status was unknown died of HIV/AIDS. HIV/AIDS related infections such as diarrhoeal diseases and pneumonia were common causes of death. Deaths due to unknown causes, coded as signs and symptoms and laboratory findings not elsewhere classified also comprise a large proportion. See Figure 7 for broadly categorised causes of death among children <2 years born to mothers with unknown HIV status.

Figure 7: Broadly categorised causes of death classified among the children <2 years born to mothers with unknown HIV status.



See Figure 8 for a more detailed inclusion of the causes of death. All the infants who died due to perinatal causes were born of mothers with unknown HIV status. A large proportion of children died due to unknown causes, diarrhoea and pneumonia and other respiratory diseases. These causes are also HIV-related. The implications are that these deaths could have been prevented, had mothers known their HIV status or if these diseases could have been treated effectively.

Figure 8: Mothers with unknown HIV status and more specific causes of death of children <2 years



5.9 SUMMARY OF FINDINGS

The U2MR of 46.3 as well as the IMR of 41.05 in Khayelitsha is very high when compared with statistics from the City of Cape Town which had an IMR of 30 births during that time period. There has been a gradual decrease in the IMR in Khayelitsha District which is concurrent with the implementation of the PMTCT prophylaxis programme. Although the IMR is decreasing, many children in this study died of HIV/AIDS.

This study shows a strong association between HIV-positive mothers and death of children <2 years. The Odds Ratio in this study shows that children born of HIV-positive mothers are 4.16 times more likely to die before 2 years of age than the children born of HIV-negative mothers.

Criteria for confounding were explored. The variables that were found to be significantly associated with the HIV-positive status of the mothers on bivariate analysis were prematurity, parity of less than three children and lack of partner support. Statistically significant confounders for the death of children on bivariate analysis were the lack of partner support, the low birth weight of infants, and if mothers did not book the deliveries as well as if the mothers were not on the ARV programme. The ARV prophylactic programme was found to be a preventative variable for death of children <2 years. However, these confounders were excluded by multivariate regression analysis. None of the variables in this study are intermediate causes of death.

When considering the causes of death, children <2 years died mostly of HIV/AIDS and causes that are potentially HIV-related. Among the children of HIV-positive mothers, the cause of death is predominantly HIV/AIDS and potentially HIV-related infections (55%). Seventeen percent of children born of mothers with an unknown HIV status, died of HIV/AIDS and one child of a HIV-negative mothers died of HIV/AIDS. As HIV in children is mostly due to MTCT of HIV the inference of an association is highly likely.

6. DISCUSSION

6.1. INTRODUCTION

This discussion will cover the main objectives of this case-control study i.e. mortality of children <2 years of age, the association between the deaths of children <2 years and their mothers' HIV status, as well as the actual causes of death amongst these children.

6.2 THE MORTALITY OF CHILDREN <2 YEARS

The results show a high mortality rate for a cohort of children less <2 years old, who were born in Khayelitsha, a peri-urban district in Cape Town, South Africa during a nineteen month period from 01 September 2000 to 31 March 2002. The IMR in this study is 41 per 1000 and the mortality of children <2 years is 46 per 1000 live births.

Most children (87%), amongst those who died before two years of age, actually died before they were one year old. Therefore, in the discussion below, the IMR is used as proxy for both IMR and U2MR as the U2MR is not a universal measurement. This finding that most children who die young (<5 years) die before one year of age is consistent with other studies (Nakiyingi, 2003, Solarsh, 2004). This also means that children less than one year of age are at greater risk of dying and therefore special care is required to ensure protection against death in this age group.

The IMR in Khayelitsha is high compared to elsewhere in Cape Town, with the IMR in other districts in this area ranging from 13 to 40 and an average of 25 for the entire city in 2002 (City of Cape Town, 2005). This is an expected but unacceptably high result for an impoverished peri-urban area with rapid urbanization. This high IMR and U2MR can be attributed to the setting, social circumstances and living conditions in Khayelitsha. Most of the influx of people to Khayelitsha comes from impoverished rural areas with high unemployment levels (Cooper et al., 1991) especially from the Eastern Cape where the child deaths are higher than the national average. While the average IMR for South Africa is 59, the IMR in the Eastern Cape, a more rural province is much higher at 72 (Bradshaw & Nannan, 2004) in 2002. This vast difference between the mortality rates in rural versus urban areas, reflect deficits in the socio-economic conditions and access to health services between the rural and urban areas. The implications are that influx of people from rural areas will continue unless more job creation and poverty alleviation is created in both the rural Western Cape and the Eastern Cape.

Throughout the world the IMR has consistently decreased in recent years and this has been attributed to improved social development (World Bank, 1993; UNICEF, 2004). This is borne out by the evidence showing that as the countries' living conditions improve, then the IMR correspondingly decreases (World Bank, 1993). A reverse trend in the IMR has however been noted in several countries. This reverse trend shows that in areas of high HIV prevalence such as in India, China and many African countries the mortality among children has increased (Katzenstein et al., 1999; Nakiyingi, 2003 et al., 2003; UNAIDS, 2004; Coovadia, 2005; Gouws & Abdool Karim, 2005; Grandin et al., 2005).

One would expect a rising IMR as the IMR and U5MR have been attributed to HIV prevalence, which was rising over the same time period (UNAIDS, 2004; Coovadia, 2005; Gouws & Abdool Karim, 2005). The IMR in Khayelitsha also demonstrated a rising trend from 1997 to 1999 with a subsequent gradual decrease thereafter (City of Cape Town, 2005). Likewise, results of this study also reflect a decline in the IMR when comparing the mortality rates of the previous two years (City of Cape Town, 2005).

This finding was unexpected as it did not correlate with the high HIV prevalence amongst mothers attending the antenatal clinics in Khayelitsha and one would expect a rise in infant mortality, given the rising HIV prevalence in Khayelitsha. The background HIV-sero-prevalence in Khayelitsha increased over the years 1998 to 2002 (Abdullah et al., 2001; Department of Health, 2001; Coetzee et al., 2004). Initial studies showed that the infant and child mortality increases significantly in children who were infected via their mothers (Bobat, 1999; WHO, 2001; Dabis & Ekpini, 2002; Coovadia, 2005). Other studies, however, showed that the IMR and U5MR decreases significantly when a PMTCT programme was introduced (Conner et al., 1994; Guay et al., 1999; Moodley & Moodley, 2001; UNAIDS, 2005). In areas of high HIV prevalence and in the absence of a PMTCT programme, the IMR is a sensitive marker of the prevalence of HIV among pregnant women (Bradshaw and Dorrington, 2005). This study did not assess vertical MTCT of HIV and child death <2 years. The IMR decline in this study may be attributed to the PMTCT programme which is in operation in the Khayelitsha district. A PMTCT programme has been functional since 1999 to prevent children from contracting HIV and no other intervention besides the PMTCT programme was in place to reduce the IMR. The PMTCT

programme does not provide treatment to HIV-infected mothers. Therefore the programme has no effect on the mothers' illness. It was therefore important to establish whether there was an association between HIV-positive mothers and deaths of children <2 years in Khayelitsha, in order to recommend that appropriate care be provided to them.

6.3 THE ASSOCIATION BETWEEN CHILD MORTALITY <2 YEARS AND HIV-POSITIVE MOTHERS

The most important finding of this study is that there is a strong association between the death of children <2 years and the HIV-positive status of the mothers. The Odds Ratio is 4.16 with a 95% Confidence Interval of 2.04 to 8.56 which shows that this association is not due to chance. This result is consistent with studies in Rakai, Uganda where children <2 years of HIV-positive women experienced a 2.8-fold increase in mortality in a smaller study and 3.9 in a larger cohort (Nakiyingi et al., 2003).Other studies have also shown that if the mother is HIV-positive, the IMR and the U5MR increased (Bobat et al., 1996; Bobat et al., 1999; Spira et al., 1999; Taha et el., 1999; Coovadia, 2005; WHO, 2002; UNAIDS & WHO, 2005) Similarly, when children are HIV-positive, the IMR and U5MR increased (Ryder et al., 1989; Thea et al., 1993; Lucas et al., 1996; Scarlatti et al., 1996; Ansari et al., 2003; Colvin, 2005; Grandin et al., 2005).

The validity of the association above could, however, have been influenced by selection bias and measurement bias. Similarly, the association could have been affected by

confounders. These will be discussed and then a judgement on causality will be provided.

6.3.1 Selection bias

Cases and controls were not selected on the basis of the HIV status of the mothers as previously noted in the methodology section. Therefore selection bias was reduced. The controls, although formally facility-based controls, were very similar to community controls and hence selection bias of controls was less likely.

Many folders of the cases could not be found and hence they were not included in the sample. This had the effect of drastically lowering the sample size, but unless the folders of cases with HIV-positive mothers were differently stored from those with HIV-negative mothers, this would not have introduced selection bias. The association could be falsely high if the records of HIV-positive mothers were better kept than the records of HIV-negative mothers. This is because the cases would then have had a falsely high percentage of HIV-positive mothers, as the records of HIV-negative mothers would be harder to locate. There was, however, no evidence that the folders of HIV-positive mothers were better stored than the folders of HIV-negative mothers. Therefore, this did not have an influence on selection bias of the eventual sample used to evaluate the association above.

Incomplete records with an absence of data for key data items could influence selection bias. This is because those participants whose folders had missing data would have to be excluded from the analysis of that data item, and hence this exclusion of some could

introduce selection bias. However, the incomplete records were similar for cases and controls, hence this would have had minimal to no effect on selection bias. For example selection bias could influence the results because of the large proportion of mothers with unknown HIV status. However, because there were no marked differences in the proportion of those with unknown HIV status amongst the cases and controls, selection bias was unlikely.

6.3.2 Measurement bias

Measurement bias may be present if the records were incorrect or the records were not standardized. One HIV-positive child of an HIV-negative mother died and since this finding is incongruous, the results were affected by measurement bias. The possible ways in which this measurement bias could have occurred were detailed in the methodology section. The mother could have been incorrectly diagnosed as HIV-negative or the child could have been incorrectly diagnosed as HIV-positive. The effect of the mother being falsely recorded as HIV-negative would be to decrease the strength of the association. If there were many of these errors the "real" association would have been stronger. The cause of death of the child could have been falsely recorded as HIV-positive and the association would have been falsely high. This is however, unlikely as greater care is taken to record the cause of death if due to HIV/AIDS.

If any of the mothers were falsely positive, the strength of the association would have been falsely high. But this is very unlikely in reality, as greater care is taken with determining

and recording the results when HIV-positive. Usually, the diagnosis needs to be certain before documenting that the mother is HIV-positive. Furthermore, a second test for HIV is taken and these tests have high specificity and sensitivity.

There could have been more children that died amongst those identified as controls as 10% of deaths are not recorded (Groenewald et al, 2003a). This could be because people in a peri-urban community such as Khayelitsha are quite mobile and therefore these controls could have died elsewhere. Another possibility is that the mother did not register the deaths. Therefore if these cases are misclassified as controls then it would falsely lower the strength of the association.

As detailed in the methodology section, the delivery (birth) register, death register and the mothers' folders are highly standardized. This means that the possibility of measurement bias due to non-standardised recording is minimal.

6.3.3 Confounders

Children could die of multifactoral causes and not only because their mothers are HIV-positive. Most of these possible risk factors were excluded systematically as possible confounders by firstly determining their association with the HIV infection of the mothers and secondly determining their association with mortality of children <2 years of age. On determining the association with the HIV infection of mothers, a few factors namely prematurity, parity of more than three children and lack of partner support showed some

association with the HIV status of mothers. (See Table 5). A few factors, namely; not booking the delivery, low birth weight, being on the PMTCT of HIV programme and not having partner support showed an association with the death of children <2 years, independently of the HIV status of mothers. These potential confounders are discussed in more detail below.

The finding of this study shows that maternal HIV infection is associated with prematurity and the death of children <2 years. Prematurity may be the direct result of maternal HIV or lack of antenatal care or both (European Collaborative Study, 1992; Pattinson, 2001). This study concurs with other cohorts in Zaire and Malawi where prematurity, illness of children at time of delivery and death of children <2 years was also found to be significantly associated with the HIV-status of mothers (Ryder et al., 1989; Taha et al., 1995). Adequate antenatal care may have prevented some of the premature deliveries and they could have developed into full-term infants. Ill mothers often deliver premature infants and this could be also have been due to the mothers' rising viral load during illness and this high viral load could have been reduced if ARV treatment was available for mothers (Abrams, et al., 1998; Puren, 2005).

Although this study found an association between the HIV-positive status of mothers and having more than three children, this should be viewed with caution as very few HIV-positive mothers had more than three children. In Zimbabwe HIV-positive nulliparous women were also not significantly associated with infant mortality (Katzenstein et al., 1999). Other studies have attributed low parity to the decline in fertility among HIV-

positive mothers (Hunter et al., 2003; Gray, 2000). Another possible reason is that mothers who are HIV-positive prefer not to have more children.

A significant finding of this study is that more children died if the HIV-positive mothers had no partner support. A plausible reason for no support is that the father could have died or absconded leaving the family with no income. If the mothers had some support, some deaths of children could have been avoided. With the lack of partner support, being sick due to the lowered immunity, mothers may not be able to adequately care for the infants or take them to a health facility, leaving them vulnerable to infections, malnutrition and neglect.

No association was found between HIV-positive mothers and gender of the child, apgar score, low birth weight, resident area at time of death, not booking the delivery, unemployment of mothers and education less than grade 7. Neither was an association found with the type of delivery such as caesarian section or assisted delivery, antenatal, postnatal complications or if the mother was ill, possibly as assisted deliveries and complications are minimal and those with complications are usually not managed at the MOUs, but attended to in the secondary health facilities. See Table 6 for non-significant association with HIV-positive mothers.

Cognizance needed to be taken of the fact that this study cannot comment on the effect of poverty on the death of the children <2 years. The absence of an association is probably due to the broad categorization of living in poor, very poor versus middle class areas at the time

of death.

In this study a significant association was found between the death of children <2 years and not "booking" the delivery at the health facility. If mothers do not book the delivery at the MOU, which usually occurs on the first visit, they may not be tested for HIV and would not get the appropriate antenatal care which could influence the outcome (Pattinson, 2001). Most mothers in this study booked the deliveries and therefore received antenatal care. However, attention should be given to those who did not book deliveries as the chance of delivering a stillborn infant is almost four times greater, and delivering a preterm infant is two times greater if the mother is HIV-infected (Pattinson, 2001).

This study found that children <2 years are less likely to die if their mothers received PMTCT treatment. This is consistent with results of many trials (Conner et al., 1994; Guay, 1999; Moodley et al., 2003). This study, however, did not assess ARV prophylaxis given to children. Several mothers were HIV-positive, but no data was available as to whether they were given ARV prophylaxis. Therefore, sample of mothers on ARV treatment was small and this could skew the results. It is also not certain whether the mothers took the prescribed doses at regular intervals prior to delivery. If the mothers did not take the ARV treatment properly, the effect would be that the infants would not be protected against MTCT of HIV. A further study is needed to determine the support given to mothers to promote compliance with ARV prophylactic therapy.

Having no partner support showed a significant association with the death of children <2

years in this study. As indicated above, lack of partner support was also associated with HIV-positive mothers. The association with the death of children <2 years was even stronger with an Odds ratio of 4.06. Women need the involvement of fathers with their children (Bunting et al., 1999) or other support systems, yet as many as 25% of fathers in South Africa do not support their children (Jones et al., 2005). If mothers have no support from their partner, the health of the child could be affected via several other mechanisms namely socially, mentally and financially (Bunting et al., 1999), with the consequent risk of death increasing.

This study found a strong association between low birth weight and death of infants. Low birth weight infants are more likely than normal weight infants to have health problems, develop complications and die in the first year of life (Bobat et al., 1999). Although not found in this study, several other studies found that infants born to women who test positive for HIV are more likely to be underweight and have higher mortality rates than children born to sero-negative women (Ryder et al., 1989; Halsey, 1990; Taha et al., 1995; Bobat et al., 1999). Similarly, infants born in developing countries in Africa born to HIV-infected mothers compared to those born to uninfected mothers, also have a higher frequency of low birth weight and were more likely to have complications in the newborn period and die (Bobat et al., 1999; Taha et al., 1995). Furthermore, the number of children with low birth weight that died (30) constituted a quarter of the sample of the cases in this study and this is deemed high, whereas other studies found that low birth weight was an association in 11% of all deaths of children less than five years in South Africa during the year 2000 (Solarsh & Goga, 2004).

This study showed no association with the death of children <2 years and having teenage mothers, mothers having more than three children, living in a poor or very poor residential area at the time of death, mothers having only primary education or unemployed mothers. Neither was there an association between antenatal complications or illness of the mother and the death of children <2 years.

Although each of these potential confounders above showed some association with either mothers being HIV-infected or children dying before two years of age, only "lack of partner support" showed an association with both of them. Despite this, all of them were assessed in a multivariate regression analysis and none were found to have any significant confounding effect.

6.3.4 Assessing causality

Given the strength of the association, the consistency with other studies, the biological plausibility, the certainty that exposure preceded effect, and given the absence of chance and confounding as explanations, and despite the small possibility of bias, as discussed above, it is highly likely that the association is causal.

6.4 MECHANISMS VIA WHICH MORTALITY OCCURRED

The association between the death of the children and their HIV-positive mothers could have been mediated via three mechanisms. Firstly, the children could have died because their mothers were sick and/or died. Secondly, the children could have died because their mothers died due to HIV/AIDS. Thirdly, the children could have died because they could have become HIV-positive and died of HIV/AIDS. These three possible reasons were not explained in this study and therefore only brief comments on them are provided below.

6.4.1 HIV-positive ill mothers and child death <2 years

Mortality of children has been closely linked to the morbidity and mortality of mothers (Day & Gray, 2001). The high child mortality associated with the HIV-positive status of mothers may be due to the illness of the mother. Compared with healthy mothers, those who are immuno-deficient or clinically unwell might be less able to provide appropriate child care. Children could therefore, have died because the mother is too weak to sufficiently care for the child due to her own illness (Jackson, 2002) and this effect would be worsened if there was a lack of partner support (Bunting et al., 1999).

The high child mortality could also arise because the household resources are channeled into the care of the mother. Ill mothers may have no longer been employed with a consequent decrease or absolute lack of income. Mothers may not have the resources to seek health services or to increase her immunity. Furthermore, the elevated IMR and U2MR could be a result of forced weaning, malnutrition or diarrhoeal diseases associated

with cessation of breastfeeding (WHO, 1981; Dunn et al., 1992; Bobat et al., 1997; Solarsh, 2004).

Mothers that are HIV-positive may be too ill to breastfeed exclusively and are likely to resort to mixed feeding. Contributory to this is that there is an increased likelihood of HIV-transmission during weaning, especially during periods of mixed feeding (Bobat et al., 1997; César et al., 1999; Coutsoudis et al., 1999; Coutsoudis et al., 2002; Colvin, 2005).

6.4.2 Death of HIV-positive mothers and child death <2 years

The association between HIV-positive mothers and death in children <2 years could be due to the increased number of deaths among women infected with HIV (Scott et al., 2003; Bradshaw & Dorrington, 2005). Maternal death has been significantly associated with child survival (Taha et al., 1996; Nakiyingi et al., 2003; Newell et al., 2004). When mothers die, the children are orphaned leading to a loss in the nurturing and socialization of the child. Other consequences of the mothers' death may be the loss of financial income, nutritional neglect, emotional deprivation and abandonment (Frohlich, 2005).

Mothers should therefore be prevented from dying. In the first instance, HIV prevention strategies should be strengthened. Secondly those that are already infected with HIV should be provided with ARV drugs and given support to take the medication. Thirdly, programmes should be set in place, monitored and evaluated improve their quality of living. In this study it was not possible to assess the mortality status of the mothers due to a

lack of accessible data on adult deaths.

6.4.3 HIV-positive mothers and death of their HIV-positive children <2 years

The children, on the other hand, could have died because the mothers passed on the HIV to them. Amongst women who were HIV-positive, 55% of their children who died, died as a direct result of HIV infection. This study therefore concurs with others that many children die due to HIV transmission from their mothers (Bobat et al., 1996; Scarlatti, 1996; Zijenah et al., 1998; Taha et al., 2000; Colvin, 2005). MTCT was not assessed in this study due to a lack of accessible data. As mentioned, the mothers of children who died had access to the prevention of MTCT of HIV programme at the time of study. This study highlights that the support to monitor and evaluate the effectiveness of the PMTCT programme is essential.

6.5 CAUSES OF DEATHS OF CHILDREN

One of the most important aspects of child deaths is the underlying causes which provide information on the reasons for the deaths. The causes of death of all the children in this study will be discussed and thereafter grouped into four categories. Firstly the deaths are categorised as deaths due to HIV/AIDS only, secondly deaths due to potentially HIV-related causes, thirdly deaths due to unknown causes and lastly, causes not related to HIV/AIDS. Thereafter a discussion will follow on the causes of death of the children if the mothers are HIV-positive, causes if the mothers are HIV-negative as well as the causes

where the HIV status of mothers was not known.

6.5.1 Causes of death of the children due to HIV/AIDS only

An important finding of this study is that almost a third of the broadly categorised causes of death were due to HIV/AIDS among all the children. See Figure 2. Furthermore the result concurs with studies in Southern and East Africa data confirming that mortality is higher if the child is HIV-positive (Groenewald et al., 2003b; Taha et al., 2000; Colvin, 2005; Grandin et al., 2005). This is demoralising because HIV amongst mothers as well as babies are both preventable and treatable.

Studies show that mortality in the first year of life of vertically infected children in Europe was 15% before the introduction of ARV treatment. However, with the introduction of ARV treatment, disease progression and death is extremely rare amongst children (Newell et al., 2004). However, in developing countries ARV treatment should be given in conjunction with improving social conditions.

Some reasons for the deaths of children <2 years old could be because the HIV prevention and treatment campaigns are not reaching the target population, or there is a reluctance of people who would like to know their HIV status, or it could be due to the slow roll-out of the PMTCT programme, or the reluctance to enroll on the PMTCT programme. Other causes could be the lack of access to health care, financial, physical and emotional support.

It has been documented that HIV/AIDS is commonly not diagnosed or not documented as the underlying cause of death (Coovadia & Bobat, 2004; Bradshaw & Dorrington, 2005). and therefore more children could have died of HIV/AIDS. This is probably due to not identifying symptoms as HIV/AIDS-related as these symptoms are very common to most childhood diseases. Another reason could be the incorrect documentation of the correct diagnosis due to the social stigma and broadening confidentiality (Bradshaw & Dorrington, 2005). Therefore, more attention is needed to train health professionals to recognise the early signs and symptoms of HIV/AIDS in children as well as to train them to identify and treat these diseases appropriately as well as to appreciate the importance of correct coding of causes of death. This study thus highlights the need for early diagnosis of HIV infection in infants, and provision of appropriate and effective therapy.

Of the mothers that did not know their status, some children died of HIV/ AIDS. Mothers could therefore have been HIV-positive and not tested. Mothers are often reluctant to be tested due to the stigma attached to HIV/AIDS or fear of the unknown (Bradshaw & Dorrington, 2005; Colvin 2005; Wilson & Fairall, 2005). Therefore, it is essential to promote testing so that mothers know their HIV status in order to apply preventative measures.

6.5.2 Child deaths due to potentially HIV-related causes

This study found that the causes of death due to HIV/AIDS included concurrent infections such as diarrhoea, pneumonia, septicaemia as also found in other studies (Aldo & Guerrant,

1992; Moodley et al., 1996; Bobat et al., 1998; Zwi et al., 1999; Bobat et al., 1999; Ahmed et al., 2000; Groenewald et al., 2003b; Coovadia & Bobat, 2004; Colvin, 2005). See Figure 4 for HIV-positive mothers and more specific causes of child deaths.

Infections such as diarrhoea and respiratory conditions are common causes of death especially in developing countries (Boylan & Stein, 1991; Bobat et al., 1997; Bobat et al., 1999; Solarsh, 2004) irrespective of the HIV status of the child (Gie & Jeena, 2004). Diarrhoeal diseases and respiratory infections do not identify the child as HIV-positive. However, some of these infections could be due to underlying HIV (Thea et al., 1993; Bobat et al., 1999; Spira, 1999; Zwi et al., 1999; Taha et al., 2000; Hussey, 2004).

On the other hand the child could have died because the infections were not properly treated or properly followed up. This result highlights the need for health professionals to be trained to inform the mother or carers how to identify the early need for treatment (Bobat et al., 1999).

There was only one death due to malnutrition among the cases. This small number may be due to improved management of malnutrition or it could be that malnutrition was not identified or not regarded as an important underlying cause of death and hence not recorded on the death certificate.

6.5.3 Child deaths due to unknown causes

Of significance is the large number of deaths where no specific cause is listed. See Figure 2. This highlights the need to properly record the cause of death on the death certificate.

6.5.4 Causes of deaths of children not related to HIV/AIDS

This study shows that only 6% of children died of causes that could not be linked to HIV. A small proportion of deaths were due to trauma. None of the children who died of causes not linked to HIV were born of mothers who were HIV-positive.

6.5.5 Causes of death amongst children born to HIV-positive mothers

More than half of the children (55%) amongst those born to HIV-positive mothers in Khayelitsha died due to HIV/AIDS. See Figure 3. This indicates that the HIV-positive status of the mothers is threatening young children's chance of survival. Other infections causing death among the children born to HIV-positive mothers are strongly HIV/AIDS related such as gastro-enteritis, pneumonia, other respiratory diseases and meningococcal meningitis. Hence the actual proportion of children who died of HIV could be even higher than 55% and this highlights the need for an effective PMTCT programme. Further research is also needed to determine the most effective health management of children with HIV/AIDS.

6.5.6 Causes of death amongst children born to HIV-negative mothers

Of note is that the children of HIV-negative mothers died of infections which are commonly found in informal settlements and areas of low socio-economic status and include gastro-enteritis, septicaemia, pneumonia, respiratory distress as well as malnutrition. These illnesses are also HIV-linked (Lucas et al, 1996; Scarlatti, 1996; Moodley, 1998; Graham et al., 2000; Johnson et al., 2000; Ansari et al., 2003; Colvin, 2005). The study highlights the need for better socio-economic conditions such as housing, clean water and proper sanitation as well as the provision of better physical, and social care of children.

6.5.7 Causes of death amongst children whose mothers' HIV status is unknown

Almost one fifth (17%) of children whose mothers' HIV status was unknown died of HIV/AIDS. Although there are other ways in which the child could have contracted HIV/AIDS, the MTCT is by far the most common cause (Dunn et al., 1992; Bobat et al., 1996; Scarlatti, 1996, Abdullah et al., 2001; WHO, 2005). If the status of these mothers were known, the PMTCT treatment could have been provided. Therefore more support and encouragement is needed for mothers to accept VCT.

6.6 LIMITATIONS

Several limitations are worth mentioning such as the sample realized, selection bias, measurement bias, the absence of key data, the standardization of records, the sample size and the possible effect of confounding variables.

- It was not possible to link all the names of children in the death register to the names of mothers in the birth register or to find the HIV status of all the mothers of the infants born during the study period. Regrettably this resulted in the proposed sample not being realized with only 122 of the 494 children that died being included in the study as cases. Therefore the records of only 25% of all the cases could be obtained. If more cases could be linked to the delivery register then the precision of the study as measured by the confidence interval, would be greatly increased (Rothman & Greenland, 2004).
- HIV measurement error at the laboratory is a possibility but it is beyond the scope of this research.
- Some misclassification could have occurred as some could have been incorrectly recorded as HIV-positive.
- Misclassification could also have occurred as some of the controls could have been cases and hence this could have decreased the strength of the association found.
- Although socio-economic status impacts very strongly on mortality of infants and children <2 years, and therefore could have acted as a confounder, it was not possible to measure key socio-economic factors such as water supply, type of toilets used, electricity availability, income and type of housing, due to the time and resource

constraints of this study.

- The method of assessing the socio-economic status in this study was very crude and therefore the ability to measure the potential confounding effect of socio-economic status was limited. However, most of the children included in the sample are from the same socio-economic group.
- The data in the death registers was taken from the data given by the Department of Health and some information error could have occurred with the recordkeeping.
- In some instances many records, as previously indicated, had to be consulted to determine the HIV status of the mothers hence some error could possibly have occurred, despite meticulously checking all data together with the fieldworker and the researcher.

7. CONCLUSIONS

The main finding of this study is that there is a strong association between the HIV-positive mothers and the deaths of children <2 years. This finding was statistically significant and none of the potential confounders considered had any confounding effect.

It is highly likely that the association is causal, although it could be diluted by a confounding effect of several potential confounders that could not be measured.

The IMR and the U2MR among the children in Khayelitsha is high compared to the province and city, which is expected for an area with a high HIV sero-prevalence rate amongst pregnant women.

Most children died under one year of age and therefore, more attention should be given to determine, apply and support interventions to reduce death among children less than one year.

HIV/AIDS is the leading cause of death of children <2 years. When the mother was HIV-positive, more than half of the children died of HIV/AIDS and about a third died due to potentially HIV-related infections. The results of this study highlight the need for preventative and supportive interventions.

8. RECOMMENDATIONS

The challenge is to use this data to reduce the number of deaths in children <2 years. There are two issues that need to be addressed. Firstly, the mothers need to be kept healthy and alive in order to care for the children. Secondly, interventions to prevent the vertical transmission of HIV/AIDS to children and to prevent avoidable deaths amongst HIV-infected children should be strengthened. Thirdly, recordkeeping needs improvement.

7.2.1 Recommendation to keep mothers healthy and alive.

Preventative measures as well as effective management of HIV infection are needed. As mothers' HIV-positive status is the main determinant of children contracting HIV-infection, measures to prevent HIV amongst mothers should be in strengthened. HIV-positive mothers should receive holistic care including effective antenatal care and ARV treatment as required.

7.2.2 Recommendation to keep children healthy and alive.

Children should be prevented from contracting HIV by the effective implementation of the PMTCT programme.

7.2.3 Recommendations to improve record keeping

Record keeping needs to be urgently improved and standards stringently maintained.

Uniformity in the different health institutions, with regards to records, should be reached. This could be done through internal and external auditing of records as well as through participatory workshops to discuss and formulate solutions and interventions. Health professionals should be given training on the importance of recordkeeping of health data.

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Wittenberg, D.F. (2004). Ch 10 - Nutritional disorders. In H. Coovadia & D. Wittenberg. *Paediatrics & child health. A manual for health professionals in developing countries*. 5th edition. Cape Town: Oxford University Press: 194-218.

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WHO. (1981). *Development of Indicators for Monitoring progress towards Health for All by the year 2000*. Geneva: World Health Organization.

WHO. (1991). *Programme for control of diarrhoeal diseases: 8th programme report 1990-1991*. WHO/CDC/92.38.

WHO. (1997). *Fact sheet* no. 180. September 1997. Reducing mortality from major childhood killer diseases. http://www.who.int/child-adolescent-health/New_Publications/IMCI/fs_180.htm. [Downloaded: 15/05/01].

WHO. (2003). *HIV/AIDS Epidemiological Surveillance Update for the WHO African Region*. Geneva: WHO.

WHO. (2005). The World Health Report 2005: Make every mother and child count. Geneva: World Health Organisation.
http://www.deathreference.co./Me-Nu-mortality-infants.html. [Downloaded: 26/09/06].

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http://www.ncbi.nlm.nih.gov.sites.entrez?cmd=retrieve&db=pubmed&dopt=Abstract
[Downloaded: 01/02/07].

Zijenah, L., Mbizvo, M., Kasule, J., Nathoo, K., Munjoma, M., Mahomed, K., Maldonado, Y., Maszima, S. & Katzenstein, D. (1998). Mortality in the first 2 years among infants born to Human Immuno-deficiency virus- infected women in Harare, Zimbabwe. *The Journal of Infectious diseases*. 178: 409-113.

Zwi, K., Pettifor, J. & Söderlund, N. (1999). Paediatric hospital admissions at a South African urban regional hospital: The impact of HIV, 1992 – 1997. *Annals of Tropical Pediatrics*. 19: 135-142.

ANNEXURE 1

DATA COLLECTION TOOL

Record of Child:

Case		Control		Questionnaire number			

Name:.....
Surname:.....

Folder Number:

Mother:.....
Surname:.....

Folder Number:

1. Date of birth: Time: Date of death:

Under 1		Under-2	

2. Gender:

Male	
Female	

3. Address:

Suburb	
1	Very poor
2	Poor
3	Middle class

4. Apgar score after 5 minutes

1	2	3	4	5	6	7	8	9	10

5. Birth weight

1	<2500gm
2	≥2500gm

6. Prematurity

1	No
2	Yes

7. Illness at birth

1	No
2	Yes

Describe illness:.....

.....

8. Cause of death

.....

.....

9. Underlying cause of death

.....

.....

Record of mother

Delivery date: | | **Time:** | |

10.

1	HIV positive	
2	HIV negative	
3	Indeterminate	
4	Unknown	

11. **Antiretroviral prophylaxis**

1.	Yes	
2.	No	
3.	Unknown	

12. **Booking**

1	Booked	
2	Unbooked	

13. **Age of mother**

Years

14. **Parity (Actual number)**

15. **Partner support**

1	Yes
2	No
3	Unknown

16. Employment status

1	Yes	
2	No	
3	Unsure	

17. Type of employment

18. Education. Grade passed

19. Type of delivery

1	Normal vaginal	
2	Caesarian	
3	Assisted	

20. Complications: Antenatal

Describe .....

.....

21. Complications During delivery

Describe: .....

.....

Complications

Postnatal

Describe:.....

.....

22. Transferred another hospital

1	No
2	Yes

Name of hospital:.....

Reason:.....

23. Illnesses:

1	Hypertension	
2	Diabetes	
3	Syphilis	
4	Cardiac condition	
5	Other	

Describe.....

.....

ANNEXURE 2

LETTERS OF PERMISSION TO CONDUCT RESEARCH

1. City Health Directorate: City of Cape Town
2. Mowbray Maternity Hospital for Khayelitsha MOU
3. Mowbray Maternity Hospital for mothers' folders
4. Metro District Health Services for Michael Mapongwana MOU
5. Tygerberg Hospital as referral hospital
6. Somerset Hospital as referral hospital

1. City Health Directorate: City of Cape Town

Civic Centre
12 Hertzog Boulevard
P O Box 2815, Cape Town 8000
Ask for: H Mahomed
Tel: 400B2883
Fax: 421-1980
E-Mail:
Ref:
Filename:

Iziko loLuntu
12 Hertzog Boulevard
P O Box 2815, Cape Town 8000
Cela: H Mahomed
Umnxeba: 400B2883
Ifeksi: 421-1980
hmahomed@capetown.gov.za
Iref:
N:\WPDOCS\RESEARCL.WPD

burgersentrum
Hertzog-boulevard 12
Posbus 2815, Kaapstad 8000
Vra vir: H Mahomed
Tel: 400B2883
Faks: 421-1980

Verw:

CITY OF CAPE TOWN
ISIXEKO SASEKAPA
STAD KAAPSTAD

City Health Directorate

To
Angela Dunn

2003-02-27

Dear Ms Dunn

RE: Assessment of the association between HIV positivity of mothers and mortality rates among infants and children under two years of age in Khayelitsha in the Western cape.

Thank you for your request to conduct research using our organisation's services and facilities. Permission is hereby granted for you to conduct the research as set out in your letter and proposal. (the MOUs and CHCs fall under the CHSO and separate approval will be needed for access to their records). We would value any research recommendations which would help to improve our organisation's services. However, we do expect the following from you:

1. **All individual patient or death information obtained must be kept strictly confidential.**
2. **Ethics approval for your research should have been obtained from your institution's Ethics Committee.**
3. **A copy of your final report should be sent to the Health Directorate within three months of its completion and a feedback session to the services and staff should be held.**
4. **Access to the Site B clinic and its patients should be arranged with the relevant managers (e.g. Pat Collis Ph 360 1153) such that normal activities are not disrupted. Access to death records can be arranged through Johan Daniels at 938 8278.**

In general, all research conducted in our services should be done in an ethical and sensitive manner. Please let me know if you need any assistance.

We thank you for your co-operation.

_____
For the Director: City Health Services

2. Mowbray Maternity Hospital for Khayelitsha MOU

MOWBRAY MATERNITY HOSPITAL

Telephone:
(021) 685-3026
Fax: (021) 685-2991

Private Bag
MOWBRAY
7705

5th January 2004.

Ms Angela Dunn
47 Visser Crescent,
Tuscany Glen 7100

UWC Research project – access to information

Permission is hereby granted conduct Masters Research at Khayelitsha Midwife Obstetric Unit.

Arrangements should be made with the Sister in Charge at the unit, and the research explained to the staff:
Khayelitsha Sr Qwaqwa

Please put in your project schedule to feedback to us, preferably through Dr Kroon! The MOU should please be acknowledged in your papers.

Dr Nils Bergman
MEDICAL SUPERINTENDENT.

Copy Dr Kroon.
Dr Fawcus
Mr Nkwana
Sr Qwaqwa

3. Metro District Health Services for Michael Mapongwana MOU

ENQUIRIES Dr GM Perez
TELEPHONE (021) 460918
FAX (021) 4476728

REFERENCE

DATE 14 JANUARY 2004

PROVINCIAL ADMINISTRATION: WESTERN CAPE
DEPARTMENT OF HEALTH

PROVINSIALE ADMINISTRASIE: WES-KAAP
DEPARTEMENT GESONDHEID

ULAWULO LWEPHONDO: INTSHONA KOLONI
ISEBE LEZEMPILO

RE: UWC Research Project

Dear Ms Dunn

You are hereby granted permission to conduct your Masters research at Michael Mapongwana MOU. Logistical and other arrangements can be made with the Sr Matinisi, the unit manager at Michael Mapongwana MOU.

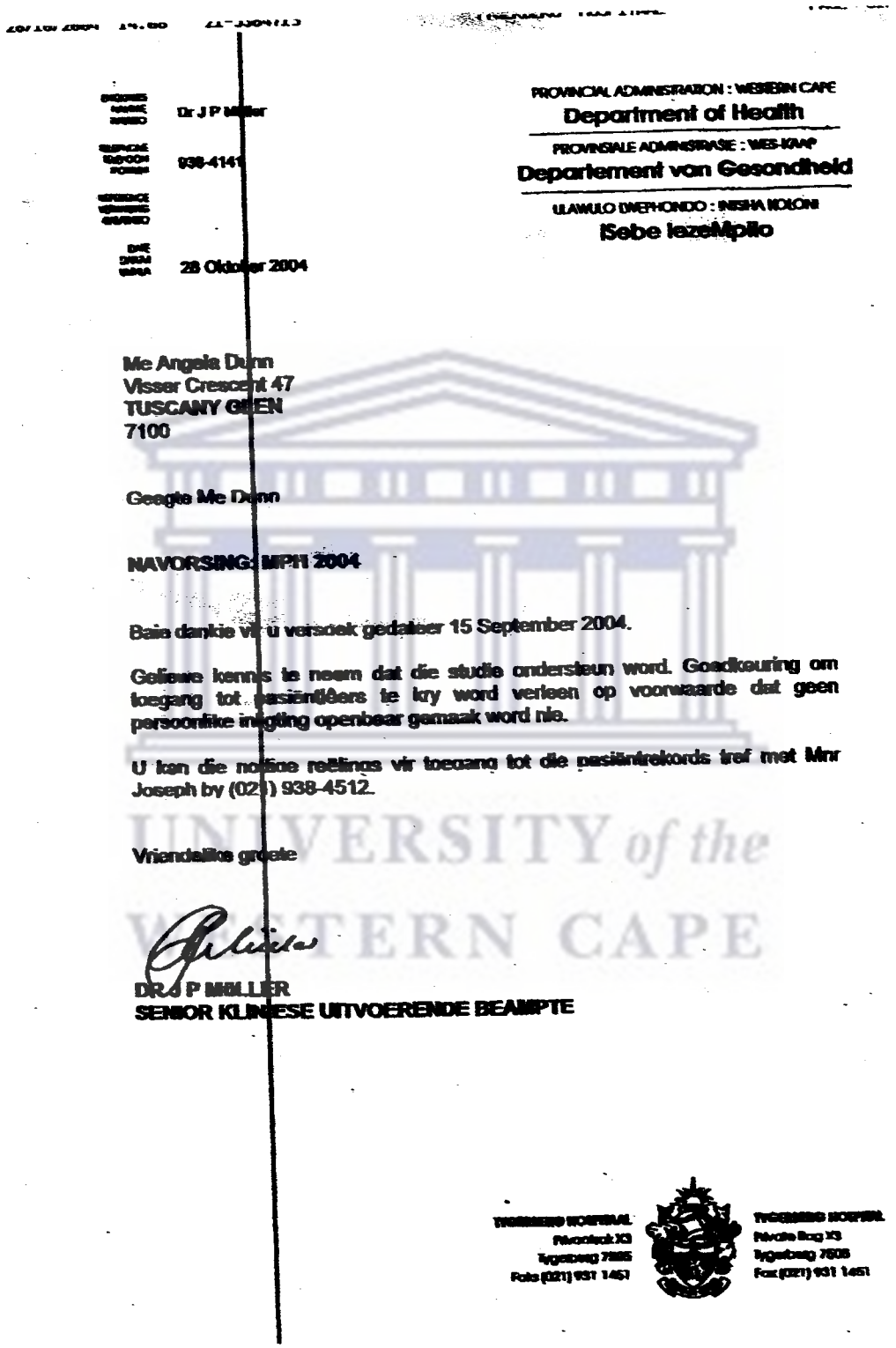
A copy of your final report would prove most helpful in our planning cycle.

Sincerely

Dr Gio Perez
METRO DHS

METRO DISTRICT HEALTH SERVICES
STEDELIKE DISTRIK GESONDHEIDSDIENSTE
PRIVATE BAG 7 PRIVAAT SAK 7 WOODSTOCK CAPE TOWN 7915
TELEPHONE 021-4609100 TELEFOON 021-4609100 FAX 021-447-6728

4. Tygerberg Hospital as referral hospital



PROVINCIAL ADMINISTRATION : WESTERN CAPE
Department of Health
PROVINSIALE ADMINISTRASIE : WES-KAAP
Departement van Gesondheid
ULAWULO LWEPHONDO : INTSHA KOLONI
ISebe lezeMpilo

Dr J P Miller

938-4141

28 Oktober 2004

Me Angela Dunn
Visser Crescent 47
TUSCANY GREEN
7100

Geagte Me Dunn

NAVORSING: MPH 2004

Baie dankie vir u versoek gedateer 15 September 2004.

Geliewe kennis te neem dat die studie ondersteun word. Goedkeuring om toegang tot pasiëntlêers te kry word verleen op voorwaarde dat geen persoonlike inligting openbaar gemaak word nie.

U kan die nodige reëlings vir toegang tot die pasiëntrekords tref met Mnr Joseph by (021) 938-4512.

Vriendelike groete

DR J P MILLER
SENIOR KLINIESE UITVOERENDE BEAMPTE

Tygerberg Hospital
Private Bag X3
Tygerberg 7505
Tel (021) 931 1451

Tygerberg Hospital
Private Bag X3
Tygerberg 7505
Fax (021) 931 1451

5. Somerset Hospital as referral hospital

11/10/2004 11:28 27012[illegible] NS

A603193

Enquiries / Imibuzo / Navrae: Dr K [illegible]

Reference / Isalathiso / Verwysing: Medical Superintendent

Date / Usuku / Datum: [illegible] September 2004.

Telephone / Ifowuni / Telefoon: [illegible]

SOMERSET HOSPITAL

Serving the Community

PROVINCIAL ADMINISTRATION
WESTERN CAPE
DEPARTMENT OF HEALTH

ULAWULO LWEPHONDO
INTSHONA KOLONI
ISEBE LEZEMPILO

PROVINSIALE ADMINISTRASIE
WES KAAP
DEPARTEMENT GESONDHEID

Ms. Angela Dunn
47 Visser Crescent
Tuscany Glen
7100

Dear Madam

RE: RESEARCH : MPH 2004 : REQUEST TO ACCESS MORE DATA

Permission is hereby granted for you to do research at the Somerset Hospital. You are to have access to the delivery register of Somerset Hospital and the mothers' folders which are kept at this hospital.

Please make arrangements with Mr K. Smith or Mr R. Solomons in our Records Department - they can be contacted on 4026524 or 4026380 between the hours of 7.30am and 4pm every week day.

Yours faithfully

pp

DR K. [illegible]
SENIOR MEDICAL SUPERINTENDENT
/[illegible]

c.c. Mr K. Smith/Mr R. Solomons - Medical Records, Somerset Hospital

SOMERSET HOSPITAL
PRIVATE BAG
GREEN POINT
8051
TEL. (021) [illegible]
FAX (021) [illegible]

ANNEXURE 3

U5MR and progress towards Millennium Development Goal 4

Country	U5MR 1990	U5MR 2002	MDG target 2015	Progress 1990 -2000	Requirement 2002-2015
Sub-Saharan Africa					
Botswana	58	110	19	-5.3	13.4
Zimbabwe	80	123	27	-3.6	11.8
Swaziland	110	149	37	-2.5	10.8
South Africa	60	65	20	-0.7	9.1
Uganda	160	141	53	1.1	7.5
Malawi	241	183	80	2.3	6.3
Lesotho	120	87	40	2.7	6.0
Eritrea	147	89	49	4.2	4.6
South Asia					
Sri Lanka	23	19	8	1.6	6.9
India	123	93	41	2.3	6.3
Nepal	145	91	48	3.9	4.9
Latin America and Caribbean					
Jamaica	20	20	7	0.0	8.4
Costa Rica	17	11	6	3.6	5.1
Chile	19	12	6	3.8	5
Brazil	60	36	20	4.3	4.5
Industrialised countries					
Japan	6	5	2	1.5	7.0
United States	10	8	3	1.9	6.8
United Kingdom	10	7	3	3.0	5.8
Australia	10	6	3	4.3	4.6
Germany	9	5	3	4.9	3.9
Denmark	9	4	3	6.8	2.2

Unicef. (2004). Progress for children. A child survival report card. Volume 1. 2004.

ANNEXURE 4

Estimates of the South African IMR from 1990

Source	Year	IMR/1000
Development Bank of Southern Africa	1990	40.2
Department of Welfare*	1991	46.0
UNICEF*	1992	71.0
SALDRU Poverty Survey	1993	81.0
October Household Survey	1993	14.6
Development Bank of Southern Africa	1994	41.8
UNICEF*	1994	52.0
Ministry for Welfare and Population Development	1994	41.0
October Household Survey	1994	11.0
Institute for Futures Research	1991-96	56.1
Development Bank of Southern Africa	1990-95	46.0

The Development Bank of Southern Africa estimates of the IMR for the period 1990 – 1995 are published by population group while the national IMR from the same analysis of 46/1000 was obtained through personal communication with JMCalitz. Cited by Nannan et al., 1998:1583-1587

ANNEXURE 5

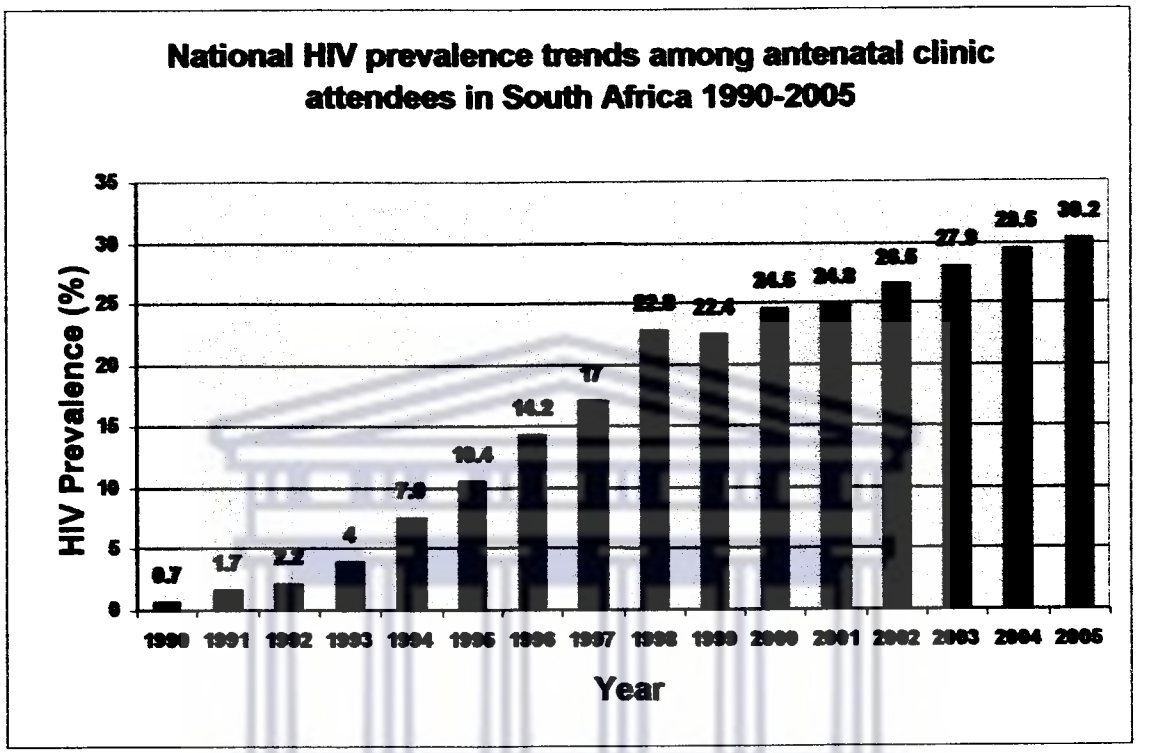
Infant and child mortality by province and population group, 1994-1998.

Province	**Infant mortality rate (per 1000 live births)**	**Under-5 Mortality rate (per 1000 live births)**
Eastern Cape	61.2	80.5
Free State	53.0	72.0
Gauteng	36.3	45.3
KwaZulu-Natal	52.1	74.5
Mpumalanga	47.3	63.7
Northern Cape	41.8	55. 5
Northern Province	37.22	52.3
North West	42.0	56.0
Western Cape	30.0	39.0
Population group		
African	47.063.6	
Coloured	18.828.2	
Indian	*	*
White	11.4	15.3
South Africa	45.061.0	

Denotes a figure based on fewer than 250 cases that have been suppressed.
Nannan, Bradshaw, Mazur & Maphumulo. (1998). Ch 4. Health Status and Determinants. In *South African Health Review*. Medical Research Council.: 9

ANNEXURE 6

The national HIV sero-prevalence among antenatal clinic attendees in South Africa



Department of Health. (2005). *Report. National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2005.*

ANNEXURE 7

HIV prevalence of antenatal attendees by province, 1998-2005

Province	1998	1999	2000	2001	2002	2003	2004	2005
WC	5.2	7.1	8.7	8.06	12.4	13.1	15.4	15.7
NC	9.9	10.1	11.2	15.9	15.6	16.7	17.6	18.5
Limpopo	11.5	11.4	13.2	14.5	15.6	17.5	19.3	21.5
EC	15.9	18	20.2	21.7	23.6	27.1	28.0	29.5
NW	21.3	23	22.9	25.2	26.2	29.9	26.7	31.8
FS	22.8	27.9	27.9	30.1	28.8	30.1	29.5	30.3
GP	22.5	23.9	29.4	29.8	31.6	29.6	33.1	32.4
MP	30	27.3	29.7	29.2	28.6	32.6	30.8	34.8
KZN	32.5	32.5	36.2	33.5	36.5	37.5	40.7	39.1
National	22.8	22.4	24.5	24.8	26.5	20.08	20.04	30.2

Department of Health. (2001a). *National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2002.*

Department of Health. (2005). *Report. National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2005.*

ANNEXURE 8

HIV prevalence amongst pregnant mothers in South Africa, the Western Cape and Khayelitsha and IMR in South Africa, Cape Town and Khayelitsha.

Year	HIV-prevalence among antenatal attendees in South Africa **	HIV-prevalence among antenatal attendees in the Western Cape#	HIV prevalence in Khayelitsha	IMR in South Africa ***	IMR in Cape Town *	IMR in Khayelitsha *
1996	14.2**		14.2	46.00***		
1997	17.0**		17.0	25.94***		
1998	22.8**	5.2#	22.6	47.80***		
1999	22.4**	7.1#	22.4	55.40***		PMTCT started
2000	24.5**	8.7#	19.3**	45.75***		
2001	24.8**	8.6#	22#	42.91***		
2002	26.5**	12.4	24.7**	42.70***	25*	44.0*
2003	20.08**	13.1		42.12***	25.16*	42.62*
2004	20.04**	15.4		36.62***	23.74*	36.62*
2005	30.2**	15.7			22.29*	34.72*

*City of Cape Town. (2005). www.capetown.gov.za

**Department of Health. (2001a). National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2002. Summary report, 2001.

**Department of Health. (2004a). National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2004.

**Department of Health. 2005. National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2005.

***Development Bank of Southern Africa, 1990-1995.Source: Nannan et al., 1998, 1583-1387.

Empty spaces reflect no data available.

The provincial; & District HIV Antentatal Survey. Department of Health Western Cape 2001.

ANNEXURE 9

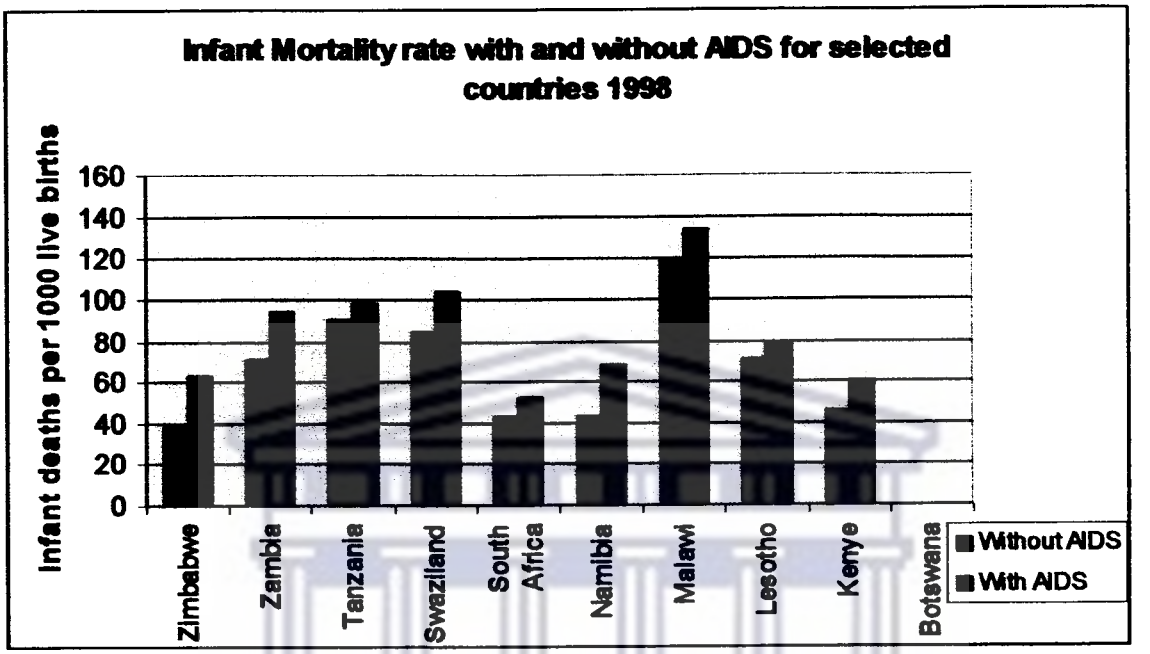
Summary results from HIV-prevalence studies among paediatric users of health services in Southern and East Africa

Reference	Study setting	Year	No. tested	HIV+ve %	Mortality % HIV+ve	Mortality % HIV-ve
Pillay 2001	Paediatric wards Tertiary Hospital, KZN	1997	160	63	20	12
Meyers 2000	Paediatric wards Tertiary Hospital, GAU	1996	507	29	17	5
Johnson 2000	Paediatric wards Tertiary Hospital, GAU	1998	176	18	NA	NA
Young 2000	Paediatric wards Rural Hospital, KZN	1996/7	281	26	21	7
Roux 2000	Paediatric wards 18 Hospitals, Cape Town	1999	1264	8.3	NA	NA
Kawo 2000	Paediatric wards Dar es Salaam	1995/6	2015	19.2	21.4	8.4

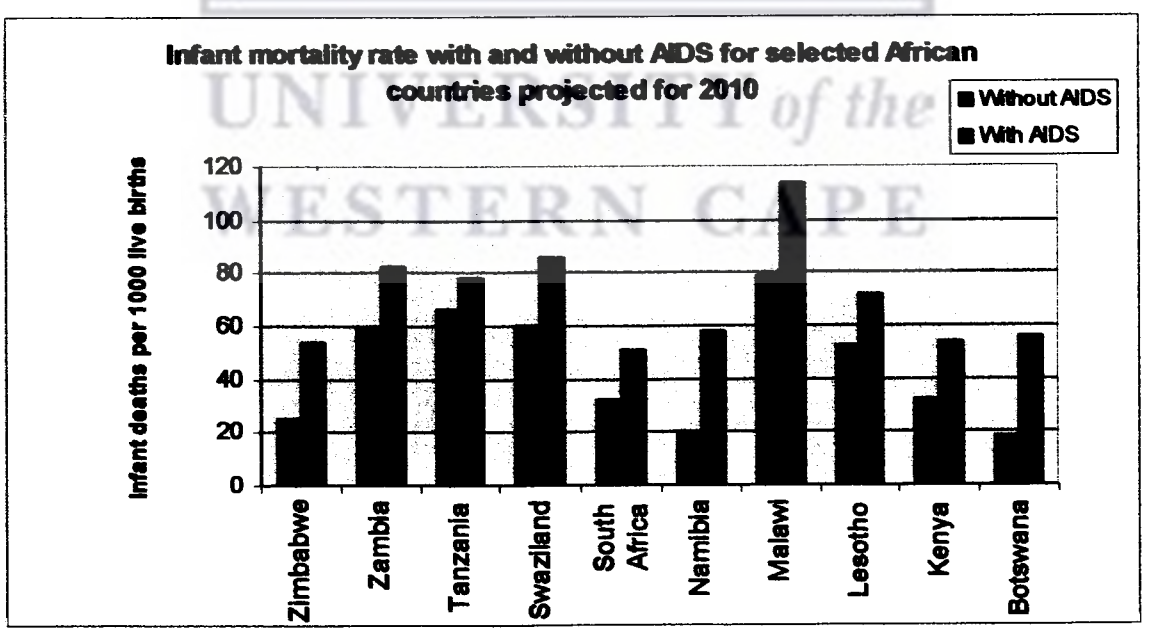
Colvin, M. (2005) Table taken from: *HIV/AIDS in South Africa* in S.S.Abdool Kariem, & Q. Abdool Kariem. (eds). 2005: 341.

ANNEXURE 10

Infant mortality rate with and without AIDS for selected African countries



Projected infant mortality rate with and without AIDS for selected African countries: 2010



Cited by Jackson, H. 2002. *AIDS in Africa*. Continent in crisis. 2002: 13-14.

ANNEXURE 11

Maternal deaths in South Africa and the Western Cape and primary causes of maternal deaths

Year	Maternal deaths in South Africa Deaths per 10000 live births (Stats SA)	No. of Maternal deaths in South Africa Dept of Health	% of Direct causes of death **	% of Non-pregnancy related sepsis mainly due to AIDS**	AIDS** [%]	Maternal deaths in the Western Cape	Maternal deaths in Khayelitsha
1997	NA	NA				25.94	NA
1998	73.8	656	63.4	33.6	14.5	47.80	NA
1999	88.4	790	59.2	36.5	15.6	55.40	NA
2000	116.8	940	58.5	38.6	19.2	45.75	NA
2001	114.5	NA	NA	NA	NA	42.91	22.9
2002	135.6					42.70	
2003	165.5						
2004	147.0	2002-2004 3406***		2002-2004 37.8***	2002-2004 20.1***	2002-2004 6.1***	

** Department of Health. 2000: Third interim report on confidential enquiries into maternal deaths in South Africa. National committee on confidential enquiries into maternal deaths.

**Department of Health. 2002. National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2002. Summary report, 2002

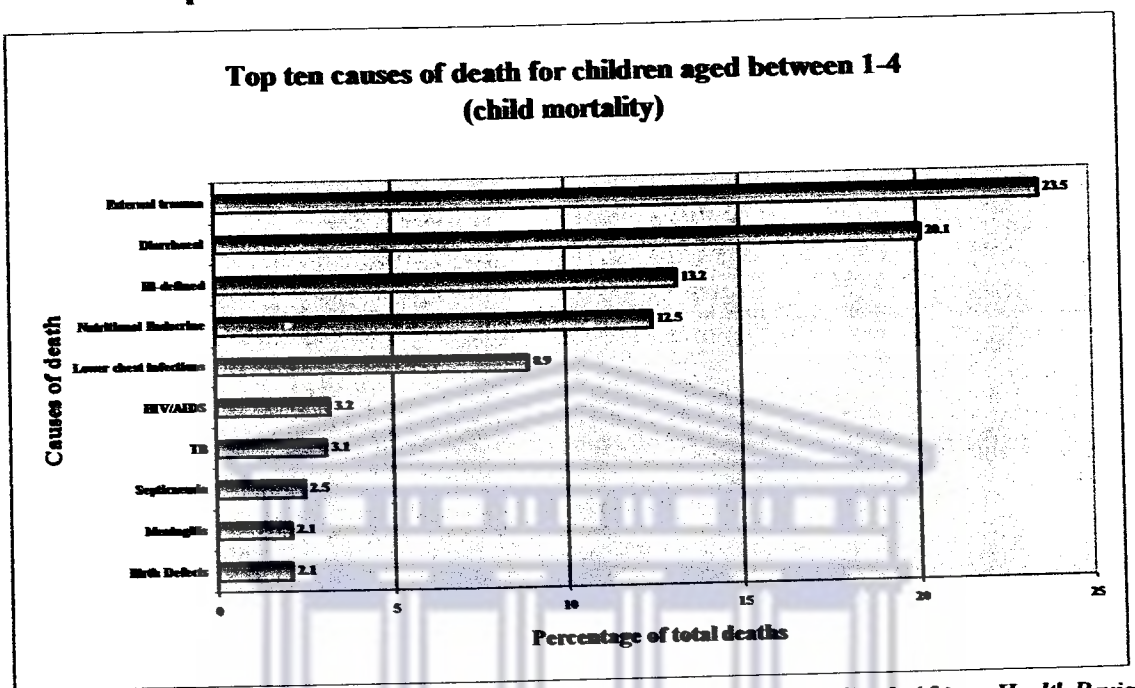
*** Department of Health. 2000: Third report on confidential enquiries into maternal deaths in South Africa. 2002-2004. Executive summary.

Department of Health. 2004. National HIV and Syphilis antenatal sero-prevalence survey in South Africa 2004.

NA=Not available

ANNEXURE 12

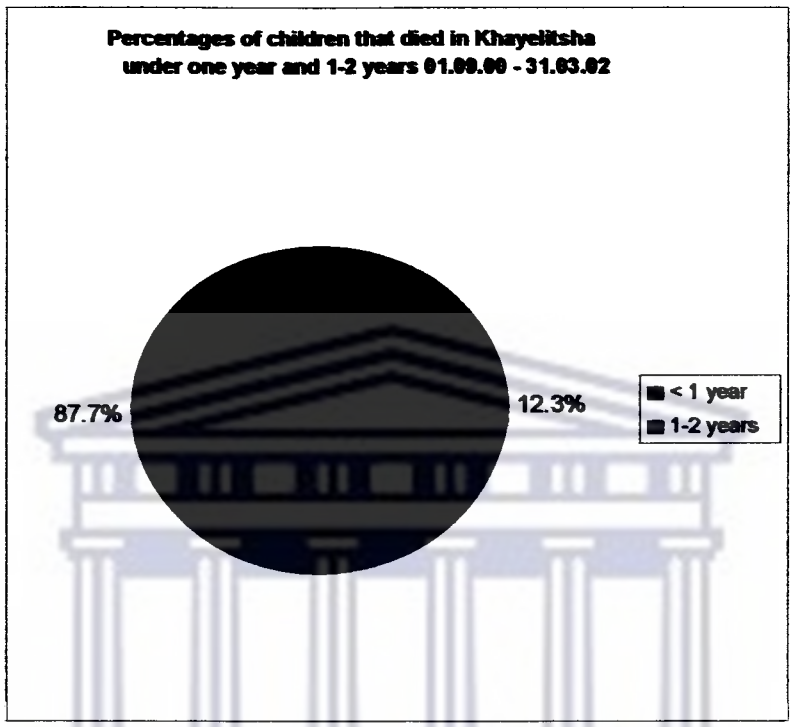
Top ten causes of death for children aged between 1-4 years



Bradshaw, Masiteng & Nannan. Health status and determinants. Ch 4 – *In South African Health Review 2000*. Durban: Health Systems Trust.
Some data missing. Data was used as a baseline reference for future use.

ANNEXURE 13

Percentages of children that died in Khayelitsha under one year and 1-2 years



Results of current study

ANNEXURE 14

Odds Ratios for child deaths less than one year of age born to mothers with known HIV status

Variable	Case	Control	Odds Ratio	95% Confidence Interval
Mother HIV-positive	43	18	4.16	1.93 – 9.06
On MTCT programme	33	55	1.19	0.07 – 0.52
Delivery not booked	8	1	8.61	1.03 – 191.61
Mother <20 years	13	10	1.32	0.49 – 3.58
Parity >= 3 children	16	25	0.53	0.23 – 1.18
Partner support	39	31	4.47	1.71 – 11.98
Employment	43	50	0.79	0.29 – 2.17
Primary education	6	9	0.71	0.20 – 2.45

Results of current study