

FACTORS ASSOCIATED WITH THE HEALTH AND WELLBEING OF OLDER PEOPLE IN A RURAL AFRICAN SETTING

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Dedicated to

la mare who would have loved to see my thesis finished.

She had a vocation of looking after those older in the family

and she taught me to open the home to those in need.

and to

l'àvia Pilar who showed me that quality of life

at older ages does not depend on how many

chronic diseases you may have but on

being positive and keeping a good sense of humour

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Original papers

1- Assessing health and well-being among older people in rural South Africa.

Published: 27 September 2010 in Global Health Action, Supplement 2, 2010:23-35.

DOI: 10.3402/gha.v3i0.2126

Applicant coordinated and supervised the preparation and implementation of field work, data collection and data quality. He also led the data analysis and the writing of the first draft of the manuscript.

2- Self-reported health and health care use in an ageing population in the Agincourt sub-district of rural South Africa.

Published: 24 January 2013 in Global Health Action 2013, 6: 19305 –

[http://dx.doi.org/ 10.3402/gha.v6i0.19305](http://dx.doi.org/10.3402/gha.v6i0.19305)

Applicant coordinated and supervised the preparation and implementation of field work, data collection and data quality. He also led the data analysis and the writing of the first draft of the manuscript.

3- Sleep problems and mortality in rural South Africa: novel evidence from a low-resource setting.

Published: January 2014 in Sleep Medicine 15(1): 56-63.

Applicant coordinated and supervised the preparation and implementation of field work, data collection and data quality. He supervised and discussed data analysis with the statistician and did the writing of the first draft of the manuscript.

4- Prevalence of HIV among those 15 and older in rural South Africa.

Published: 11 January 2013 in AIDS Care. DOI: 10.1080/09540121.2012.750710

Applicant coordinated and supervised the preparation and implementation of field work, data collection and data quality. He supervised and discussed data analysis with the statistician and did the writing of the first draft of the manuscript.

5- Social conditions and disability related to the mortality of older people in rural South Africa

Published: May 2014 in International Journal of Epidemiology. DOI: 10.1093/ije/dyu093

Applicant coordinated and supervised the preparation and implementation of field work, data collection and data quality. He also led the data analysis and the writing of the first draft of the manuscript except for the added analysis of the census data which was done by Phillip Bocquier in collaboration with the applicant.

Permission for reprinting published papers has been granted by publishers.

Abstract

1. Background

South Africa is experiencing a massive HIV epidemic that together with the new epidemic of non-communicable diseases is directly affecting the health and wellbeing of older people. For policy makers, there is a crucial need for information on how this dual epidemic is evolving and how this may affect older people's health, mortality and health care needs.

2. Aims

To better understand factors that influence the health, wellbeing and survival of older people, and their need for care in rural South Africa at a time of a growing dual epidemic of chronic diseases (non-communicable and communicable). To provide information which may assist in the planning of health services for older people.

3. Methods

Applying the WHO Study on Global Ageing and Adult Health (SAGE) and a study on HIV and non-communicable diseases (NCD), we investigated the health, wellbeing and mortality of the population 50 years and older in the Agincourt sub-district in north-east South Africa which is underpinned by health and demographic surveillance. A random sample of the population 50 years and older was selected for the SAGE survey. A random sample of the population 15 years and older was selected for the HIV and NCD study. All available adults 50 plus were invited to participate in the SAGE module in the 2006 census round. We assessed self-reported health, anthropometric measures, blood pressure and HIV status using dried blood spots. Statistical analysis included simple frequencies, univariate and multivariate analysis and Cox proportional hazard models.

4. Findings

The usual pattern of mortality, of increasing death rates with age, is not observed in this population, where those in their 50s have higher mortality compared to older age groups. The high prevalence of HIV in this age group (50 to 59) appears to be the main explanation for the observed pattern. Hypertension affects two thirds of this older population and, although there are no differences by gender, women are more aware of their condition. This is reflected in more women attending primary health care services. Reporting lower quality of life and greater disability are associated with higher likelihood of death. We observed gender differences in the process of ageing with women reporting higher prevalence of mortality risk factors but living longer than men, a phenomenon known as the "survival paradox".

5. Conclusion

The older population of this rural South African setting suffers from a double burden of non-communicable diseases and HIV/AIDS which, together with poor quality of life and function, increases the mortality risk even of those in their 50s and 60s. The high HIV prevalence among this older population is striking. This issue has been neglected and needs urgent action. Awareness of suffering from a chronic condition is correlated with health care use. This should be taken into account when planning new interventions which should include prevention, treatment and awareness as part of the programme. Our data highlights the need for new policies to prepare the primary health care system to respond to an expected increase in demand by an ageing population.

6. Key words

Adult health, ageing, Agincourt, health and demographic surveillance system, health care use, HIV, hypertension, mortality, non-communicable disease, self-reported health, sleep problems, South Africa, WHODAS, WHOQOL.

Foreword

In the interview for the job in Agincourt, I was asked "How do you see yourself in the next five years?". I remember saying "I would like to be remembered as someone who has helped African researchers to develop their careers". A pretentious statement given the stage of my research career at that time, but an evolution from my childhood when, inspired by my incipient religious beliefs, I decided to become "A doctor for the poorest". A few years later, as a young teenager, I said to my best friend that I would go to Africa to work as a doctor.

In my third year as a medical student I met the person who was going to be my first mentor, Manel Corachan, a medical doctor who had been working for many years in Tanzania and who was the head of the Tropical Medicine Unit in the Hospital Clinic in Barcelona. With him I saw my first *Plasmodium* and *Schistosoma* in a microscope, I heard my first word in Kiswahili and, most importantly, I learnt to be empathetic with those who come to you seeking for health care, and to treat everybody equally no matter the race, rank or position in life. He motivated me to do an MSc in Tropical Medicine. When I finished he offered me work in his unit as a researcher, something I declined because all I had in mind was to be a clinician in a District Hospital somewhere in Africa.

My first job was in Rwanda in 1995 and was to build a health district with 8 clinics and one referral hospital. By that time I had been married to Montse for 5 years and we had a daughter, Xènia, 1 year old. In Rwanda I lived my dream and I also discovered what would be my real passion. I discovered this passion through the case of a teenager who came in diabetic coma to the health centre where I was working on three different occasions. The third one was too late. Only then I asked myself why he was repeatedly coming in a coma. The problem was he had no fridge at home in which to keep the insulin and he was living too far from the health centre. Nothing a clinician could solve.

We moved to London where I did an MSc in Communicable Disease Epidemiology at the London School of Hygiene and Tropical Medicine and initiated my interest in Public Health. At the time we left London, Marc, our son, was two months old.

With this new passion we moved to Mozambique in 1999 where I worked as an Epidemiologist for six years. During this time I started a PhD, but with my out-migration to Agincourt in 2005 the studies were discontinued. The time we stayed in Mozambique gave us many experiences, friends and two little boys, Oriol and Ferran.

In 2006 I had the opportunity to lead the field work for the Study on Global Ageing and Adult Health in Agincourt which greatly increased my interest in the health and wellbeing of older people. A year later, at the O.R. Tambo airport, I met Gillian Hundt on my way back to Agincourt. She

was also going to Agincourt where she had already done some research in early 2000. This was the first time I had met her and in the first twenty minutes of our first conversation she convinced me to start a new PhD.

These last five years have been very intense. Our family increased with two teenage girls, Eulender and Zinhle, my responsibilities in the Agincourt Research Unit have multiplied, and there were many trips to Oxford to Margaret Thorogood's home where I can say I have drafted and analysed all papers included in this thesis. I will never forget her asking: "A cup of tea?" I would answer "Yes, thank you" starting to move from my computer... "No... you keep writing... I'll bring it to you".

Glossary of abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Treatment
BMI	Body Mass Index
CVD	Cardiovascular diseases
DALY	Disability-Adjusted Life Years
DBS	Dried blood spot
DHS	Demographic and Health Survey
DoH	Department of Health
GBD	Global Burden of Disease
HAART	Highly Active Antiretroviral Treatment
HCT	HIV counselling and testing
HDSS	Health and Demographic Surveillance System
HIV	Human Immunodeficiency Virus
HSDU	Health Services Development Unit
INDEPTH	The International Network for the Demographic Evaluation of Populations and Their Health in Developing Countries
LINC	Learning, Information, Dissemination and Networking with the Community
LMIC	Low and Middle Income Countries
MRC	Medical Research Council
MSM	Men who have sex with men
NCD	Non-communicable diseases
NGO	Non-governmental organisation
PHC	Primary Health Care
PMTCT	Prevention of mother-to-child transmission
SAGE	Study on Global Ageing and Adult Health
SANHANES	South African National Health and Nutrition Examination Survey
SASPI	South African Stroke Prevention Initiative
SES	Socio-economic status
SSA	Sub-Saharan Africa
STEPS	Stepwise approach to surveillance
TB	Tuberculosis
TFR	Total Fertility Rate
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
VCT	Voluntary Counselling and Testing
WHO	World Health Organization
WHODAS	World Health Organization Disability Assessment Scale
WHOQoL	World Health Organization Quality of Life measurement

A. Introduction

The purpose of this thesis is to describe some of the complex issues related to health and wellbeing in a South African rural population of 50 years and older in the context of demographic, epidemiological and social transitions. This work is based in a rural sub-district in north-east South Africa where the Agincourt Health and Demographic Surveillance System (HDSS) site of the University of the Witwatersrand has been functioning since 1992.

This research is informed by a conceptual framework (see Figure 1) which considers the transitions in this population as a starting point for explaining the changes in lifestyle and ageing and which predicts an increasing demand for health services. This increased demand would be due to three main factors: an increase in chronic disease prevalence, an increase in HIV/AIDS prevalence and a higher survival to older ages once antiretroviral treatment (ART) and chronic disease treatments are more comprehensively available in this community. When this occurs, non-communicable diseases (NCDs) and HIV may be grouped and considered as a single entity: chronic diseases.

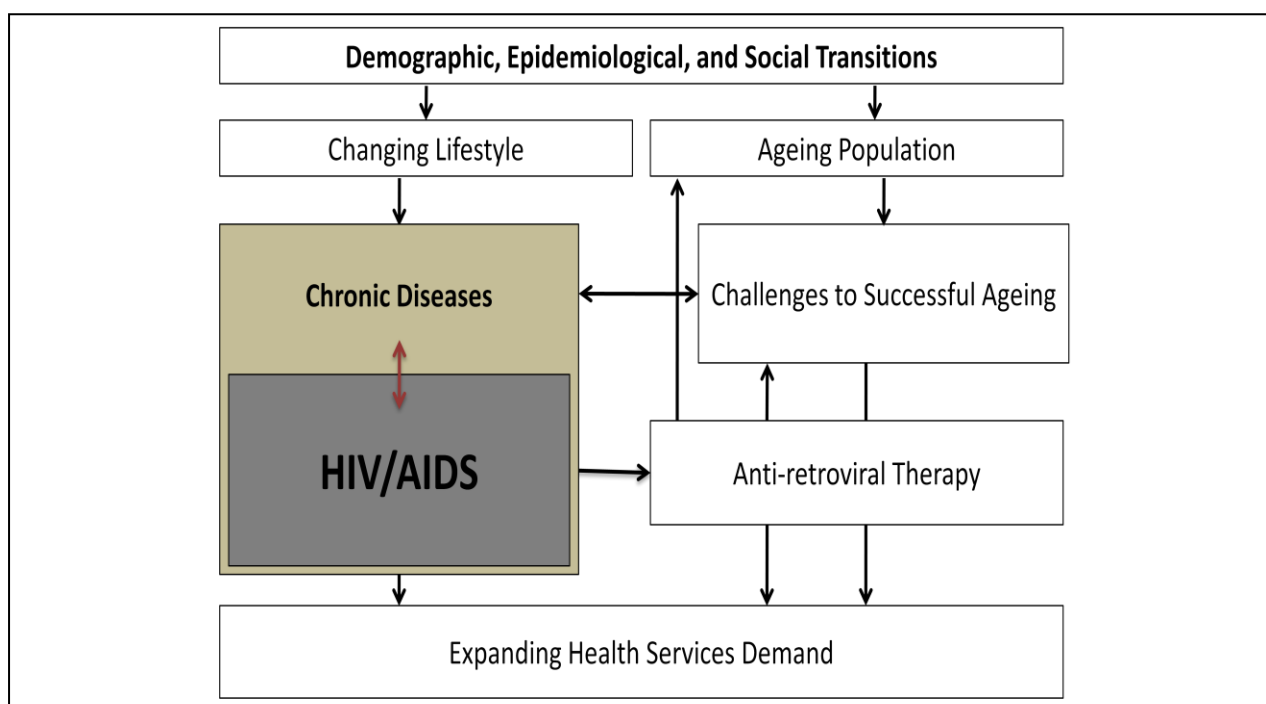


Figure 1. Conceptual framework

The World Health Organization (WHO) uses a classification of diseases based on their broad causes thus grouping diseases in "communicable, maternal, peri-natal and nutritional conditions", "non-communicable diseases" and "injuries" (1). Ackland et al have proposed that the term "non-communicable" diseases be changed for "chronic". They argue that using the term "non-communicable" is confusing as some diseases classified as non-communicable are actually

communicable and describe a number of situations where an NCD is due to an infection. They go on to argue that some health risk behaviours cause NCDs, and that the psycho-social, cultural, ethnic and socio-economic attributes of populations may be the determinants to taking behaviours of risk and they should be considered "vectors for chronic diseases". This situation would be especially important in poorly educated and low income societies (2) where the population would tend to be more exposed to those potentially harmful vectors or social determinants that may be linked to higher levels of NCDs.

Unwin et al argue that any classification of diseases "should serve the needs of those using it" and so different professionals need different ways of classifying diseases. A cause classification would be useful for clinicians while an effect classification would be more useful to health system planners (3). The term "chronic" is useful if it "refers to conditions requiring long term management by health systems", which will then have implications for how health systems should be organised. From a public health perspective it is important to know whether a disease, communicable or non-communicable, requires care for a long time.

In reporting and discussing my results in this thesis I, therefore, decided to use the term "chronic" for all diseases needing chronic care, independent of their cause.

Other important aspects of this thesis are the discussion of the ageing of the World's population, especially in Low and Middle Income Countries (LMIC), and the study of the ageing process by describing the wellbeing and function of older people in a rural South African setting. Successful ageing includes both active (4) and healthy ageing (5) which are related to the potential of older people to enjoy good health, participate in the society as they desire and to receive assistance when necessary. The main goal of active ageing is to extend the expectation of a healthy and good quality life for all people as they age, independent of their level of frailty, disability and need of care (4). WHO describes health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (http://www.who.int/topics/mental_health/en/). However, health research has mainly focussed on studying diseases and not on understanding health, maintaining health and improving quality of life and function (5). This thesis aims to study and discuss health, quality of life and functioning of older people.

The research for this thesis was conducted in South Africa between 2006 and 2011, a time of rapid political transition following the first democratic election on the 27th of April 1994. After a long period under the Apartheid system, the new South African Constitution (promulgated on 4 December 1996) emerged as one of the most modern in the World enshrining human rights and protecting the most vulnerable, opening up the possibility of many social and political changes.

Undoubtedly the new South Africa has experienced many changes with improvements in political rights and freedoms. This likely accelerated the progression of demographic and epidemiological transitions including a rapidly ageing population process and an increase in chronic diseases. However, South Africa is also experiencing a massive HIV epidemic which is affecting the health and wellbeing of older people and slowing down the progress of demographic and epidemiological transition.

In this thesis I will discuss the findings from the Study on Global Ageing and Adult Health (SAGE - a WHO/INDEPTH collaboration) together with a study on HIV and NCDs, work that I have undertaken from 2006 to 2011. I will also use socio-demographic data on older people and their households from the Agincourt HDSS census for which I have been responsible since 2005.

B. Background

In this section I discuss the theory of the Epidemiological Transition and review how the transition in sub-Saharan Africa has been slowed down and complicated by the impact of the HIV epidemic. South Africa, where there is a high prevalence of HIV infection, has been particularly affected. The ageing of the population is discussed, followed by an introduction of the development of the dual epidemic of non-communicable diseases and HIV in the sub-Saharan region and particularly in South Africa. Finally, I summarise the health service response to these new demands.

1. Demographic and Epidemiological transition

I. Theory

In 1971, Omran developed the Epidemiologic Transition Theory and its stages as a better way to explain the complex changes in health and disease patterns that happened from the mid 18th century and the interaction of those changes with their socio-economic and demographic determinants (6). To explain his theory Omran put forward propositions that can be summarised as an attempt to explain demographic changes based, first, on mortality changes followed by fertility changes. The change in mortality and fertility trends, together with a decrease in the number of epidemics given advances in socio-economic status, would, eventually, result in an increase in life expectancy. The speed of the process will vary in different societies depending on how these changes occur .

In all societies, at the beginning of the epidemic transition, mortality is the fundamental factor in population dynamics as fertility persists at a very high level. In Western societies, mortality decline started by mid 17th century and stabilised at low levels by the 20th century. At this time fertility became the pacemaker of population growth. Other societies, Omran predicted, would

experience mortality and fertility changes in a shorter time period, while yet others, mainly low and middle income countries (LMIC), would see a delayed transition with mortality decreasing while fertility is still high, leading to exponential growth. The early stage of the transition is dominated by infectious and nutritional disorders affecting children mainly ("the age of pestilence and famine") with high mortality and low life expectancy; next there is a decrease in the number of epidemics ("the age of receding pandemics") with lower mortality, increased life expectancy and exponential population growth. The final stage will see mortality decline and stabilise at low level ("the age of degenerative and manmade diseases") with life expectancy at birth of over 50 years and fertility becoming the main factor influencing population growth. Deaths occur in an older population due to NCDs and injuries. Omran states that "during the epidemiologic transition the most profound changes in health and disease patterns obtain among children and young women" as they were the groups most at risk of early death. Women's survival will surpass men's and, with the survival of children, fertility will decrease and family units will be smaller.

II. Critiques of the theory

While Omran continued working on the development and application of epidemiologic transition theory (7, 8), Olshansky and Ault (9) and then Rogers and Hackenberg(10) proposed a fourth stage in the transition. This new stage was termed "Age of Delayed Degenerative Diseases". The pattern of causes of death is similar to the latest stage proposed by Omran, but with a shift of mortality to even older people, extending life expectancy for both genders to the mid eighties and bringing a change in the population structure with a higher proportion of elderly and a lower proportion of young people.

In 1998 Omran published a review of the epidemiologic transition theory, accepting the fourth stage and emphasising the importance of the decline of cardiovascular disease (CVD) in developed countries due to lifestyle modifications, early diagnosis and treatment, including the treatment of risk factors such as diabetes, stress and hypertension. Finally he added a Stage Five where he hypothesised that in the 21st century life expectancy may increase further into the nineties and degenerative, stress related and man-made diseases would be the main causes of death. In this stage CVDs will be the primary cause of death worldwide. Developing countries, still in Stage Three and with a high level of CVDs, will become the main worldwide source of cardiovascular disease related deaths(11).

In a crucial paper from 1999, Pearson emphasised the importance of preparing developing countries for the coming epidemic of CVDs. He argued that

“Efforts to control CVD should invest strategically in research to understand the prevalence of, and risks associated with CVD risk factors, as well as in studies of new risk factors, measures to prevent or modify risk, and clinical trials to demonstrate the efficacy of these interventions...”. He emphasised that *“A global epidemic of CVD in developing countries may be inevitable unless there is a better understanding of its origins, a prediction of its magnitude and the organisation of preventive and case-management strategies early enough to control it.”* (p.95)(12).

Although the theory of epidemiological change and the successive amendments and improvements have contributed enormously to the understanding of global population health, they have also been criticised (13-16). Caldwell argued that Omran gave too much emphasis to ecological and socio-economic change as the primary reason for mortality changes and ignored improvements in the medical and public health domains. Caldwell argues that doctors have led many of the changes that happened in the last decades of the 19th century which had a huge role in mortality decline, like the concept of personal hygiene, the importance of midwifery training and child care, pasteurisation, safer sewage disposal, immunisation programs and curative medicine in general(17).

In a later paper, reviewing the Epidemiological Transition Theory, Omran accepted that the implementation of medical advances and public health interventions in developing countries may have accelerated a process that took centuries in Western societies (11).

III. Sub-Saharan African development of the epidemiologic transition in the context of HIV

The positive changes in life expectancy in sub-Saharan African (SSA) countries from the mid 1950's were not homogeneous, placing these countries at different levels of progressing to the second stage of Omran's epidemiologic transition (18, 19). Most countries showed a significant decrease in infant and child mortality, but at a very slow pace. Those countries that managed to control infant and child mortality, however, experienced a faster increase in life expectancy, entering further into the second stage.

However, the progress made up to the 1980's and 90's (20-22) was lost in many SSA countries due to the arrival of the AIDS epidemic which led to not only stagnating but even reversal in infant, child and adult life expectancy (19, 23, 24). In some countries, the AIDS epidemic caused a reduction of close to 20 years in life expectancy at birth (25) jeopardising the chances of a linear transition to Omran's third stage. Timaeus' analysis of adult mortality in 11 countries showed that those 6 countries affected by AIDS suffered a sharp increase in adult mortality, while in the 5 non-

affected countries it decreased. Between 1988-89 and 1994 Zimbabwe experienced a threefold increase in the probability of death between 15-69 years of age for males and a doubling for females, while Senegal had a decline of 25% for males and 40% for females (23). In 1999 life expectancy in the SSA region had decreased to 47 from 64 (26). In 2004 life expectancy was still 47 years, but it was estimated that it would have been 62 years without the deaths from AIDS (27). Caselli (18) describes how the AIDS epidemic has altered the epidemiological transition in SSA countries, giving two reasons why most SSA countries have not yet entered the third stage of the transition: first, the mortality increase due to the AIDS epidemic which has kept mortality rates at a very high level; and second, a shortage of financial support to the health systems due to the economic crisis in the 1980's.

It is expected that the rollout of ART will reverse the situation as people survive longer with HIV (28). In this new situation mortality rates would decrease and reach the low levels that fertility rates have already reached. The survival of people to older ages will bring an increase of chronic diseases, moving SSA countries into the third stage of the epidemiological transition.

IV. The Epidemiologic Transition in South Africa and the effect of HIV in its development

South Africa experienced the same setback as many other SSA countries. In 1990 life expectancy was 62 years, but the impact of the HIV epidemic resulted in a loss of life expectancy of 12 years by 2007 (29).

Indeed South Africa is experiencing a complex epidemiological transition with a quadruple burden of disease (30) involving both deaths related to the first stage of Omran (maternal and infant deaths, and HIV/TB) and to the third stage (NCD and deaths due to injuries and violence) (30).

South Africa's Total Fertility Rate (TFR) fell from 6.1 in the mid 20th century to 2.5 by the beginning of the 21st century. This decline in fertility should result in the ageing of the population as the proportion of older people in the population increases while the total number of children decreases. Without the HIV epidemic the control of infant mortality and survival of older people would have produced a rapid ageing of the population in South Africa. The reality is that the ageing process, although slower than projected, has continued and the mid-year estimates of Statistics South Africa for 2013 showed that 7.8% of the South African population were 60 years or older and 15.7% were over 50 years of age (31). Moreover, it is predicted that the proportion of the South African population aged 60 years and over will increase to around 10% by 2025.

The Agincourt population is experiencing this quadruple burden and slow progress through Omran's second stage with a loss of life expectancy of 16 years in a period of 10 years (32) from

1994 to 2004. The population is suffering from high maternal (33) and infant deaths, malnutrition in children (34) and adults (35), HIV/TB, which has become the first cause of death in young men and women (36) and a high prevalence of stroke (37) and hypertension (38, 39). All this together with a decrease in fertility (40) gives a complex epidemiologic transition with high mortality, low fertility and increase in NCDs.

2. Ageing populations

The world is experiencing huge demographic changes especially in the older age groups. The population 60 years and over has increased from approximately 200 million persons in 1950, to 350 million in 1975 and a total of 590 million in the year 2000. Projections for 2025 are that over 1,100 million people would be alive and over the age of 60 years, that is, an increase of 224 per cent since 1975. In 1982 it was estimated that during the same period of time the World Population would have experienced an increase of 102 per cent (41).

In 1978, the United Nations (UN) recognised the need to launch a programme to secure the economic and social security of older people. In 1982 the United Nations "World Assembly on Ageing" reflected on the fact that the ageing process, although positive and desirable, was going to create a new burden in the poorest and less developed societies of the world; women would need special attention as they would outnumber men (especially in the group 80 plus); and government interventions like pension schemes would be necessary to economically support this older age group (41).

Following the second World Assembly on Ageing in 2002 (42), the UN published estimates for the 21st century stating that the population over 60 in the world had increased from 8% in 1950 to 10% in 2000 and was expected to reach 21% in 2050 (19). This older population will also experience higher survival than that experienced by older people in the mid 20th century, resulting in a higher number of the oldest. Comparing the oldest with the youngest, it has been estimated that by 2015 the population older than 65 will outnumber children under 5 years (43), while by 2050 the proportion of 60 plus will outnumber those under 15 (19, 44). This ageing process is not only happening in high income countries but also in LMICs. Demographers have predicted an increase in the population 60 plus in LMICs of 140% between 2006 and 2030(45) and estimated that by 2025 three quarters of older people in the world will be living in LMICs (41). Although the UN's calculation predicted that the increase in ageing in SSA would be at a slower pace due to the HIV epidemic(42), the rapid increase in access to ART in the public health sector ("ART roll out") may change these predictions (46, 47).

3. Non-communicable diseases

The Global Burden of Disease (GBD) study 2010 shows that, globally, there has been a shift in the leading causes of death from communicable, maternal, neonatal and nutritional deaths towards non-communicable diseases. The enormous increase in mortality due to NCDs is driven by two factors: i) the population growth, responsible for a 23% increase in deaths related to NCDs; and ii) the ageing of the population responsible for 39% increase in deaths related to NCDs (48).

This group of diseases, however, was overlooked in 2000 when the Millennium Development Goals were established to address malaria, HIV, neonatal and concomitant poverty and maternal diseases (<http://www.un.org/millenniumgoals/>) (49, 50). Only in 2011 did the United Nations General Assembly call for a High-level Meeting on the Prevention and Control of NCDs and acknowledge the threat that the global burden of NCDs represents for social and economic development all over the world and call for global measures to prevent and control NCDs (51).

Strong et al estimated that in 2005 there would be 35 million deaths globally due to chronic diseases, 80 % of them in LMICs. Their estimations predicted that in 2005, 72% of the global burden of disease in the population over 30 would be due to chronic disease and that the population under 70 years of age would carry more than 80% of this burden. By 2015 they estimated a total of 41 million deaths due to chronic diseases, with a total lost years of healthy life due to these diseases higher in those 30 to 59 years of age than those 60 and older (52). Using 2008 data, the WHO estimated that 63% of the 57 million deaths worldwide were due to NCDs, affecting men and women equally (53). In addition, 8% of all deaths were related to HIV and/or TB (54). The GBD study 2010 corroborates these estimates. Since 1990, deaths due to NCDs increased by nearly 8 million reaching a total of 34.5 million deaths worldwide in 2010 (65.5% of all deaths). Of these, 37% were due to ischaemic heart disease and stroke. Mortality related to diabetes doubled since 1990 reaching 1.3 million deaths in 2010 (48).

Traditionally NCDs have been considered a problem of developed regions. However, the 2005 report from the WHO estimated that 80% of NCDs worldwide occurred in LMICs. These were cardiovascular diseases, cancers, chronic respiratory diseases and diabetes (54). Abegunde et al estimations for 2005 based on 23 selected LMICs, reported that NCDs were responsible for 50% of the total burden and that the age-standardised death rates for chronic diseases were 50% higher than in developed countries (55). With the increase in size of older population in LMICs, it is estimated that these regions will suffer a further increase in NCDs. In 2008 Alwan et al showed that in 23 LIMCs the 2005 estimations were not only reached but surpassed, approaching levels of age-standardised death rates in men 58% higher than in developed countries and in women 69% higher

(56). In a systematic review in 2007 Addo described a high prevalence of hypertension in sub-Saharan Africa with lack of awareness and low control (57). The multi-country SAGE study showed a very high hypertension prevalence in Ghana (57%) and South Africa (78%), the two African countries that participated in the study (58). A similar situation is presented for type 2 diabetes in Africa where an estimated 5% of the population 20 to 79 years old are diabetic, and less than half of them are aware of their condition (59). The proportion of people with diabetes not on treatment rises to 70% in the poorest countries and to 87% in Mozambique with low treatment coverage even of those aware of their condition (60). By 2035 a 110% increase in diabetic cases in Africa is predicted (59) which, in a context of low awareness, will challenge the adequate care of those in need (60) and potentially increase the cardiovascular complications of diabetes resulting from the lack of treatment (61). With an increase in hypertensive and diabetic cases there is a high likelihood of an increase in multi-morbidity due to NCD as already observed in South Africa (62).

Many studies have pointed out that the increase in NCDs is affecting poor communities in both urban (63) and rural South African settings (36). The first South African burden of disease study calculated that, by the year 2000, NCDs were responsible for 37% of the mortality burden compared to 30% due to HIV and 21% of years of life lost compared to 38% due to HIV (64). The estimations of risk factors in South Africa for the year 2000 indicated that excess body weight was responsible for 7% of all deaths (65) and hypertension for 9% (66). The South African population has a high prevalence of NCDs and their risk factors (21, 65-69). However, as Bradshaw stated in 2007, "establishing such an evidence base is an ongoing process that is still at an early stage in South Africa" and, therefore it is essential to produce research that will help describe the impact and progression of the quadruple burden of diseases in South Africa and the interventions necessary to reduce this burden (70).

4. HIV

More than 70 million people have become infected and around 30 million people have died from AIDS in the 30 years of the epidemic (calculation based on 2006 (71) and 2010 (72) UNAIDS reports). The impact of the epidemic varies around the world with diverse incidence figures and wide variation in the successful control of the epidemic (72). By 2005 it was estimated 38.6 million people were living with HIV globally (7% of them 50 years old or older), while 4.1 million were newly infected and 2.8 million deaths were AIDS related. By 2010 the highest burden of the epidemic was in sub-Saharan Africa with 68% of all people living with HIV/AIDS and 72% of AIDS related deaths worldwide (72). Within SSA the epidemic is unevenly distributed with low HIV prevalence (2%) in West Africa and middle levels in East and Central Africa (7% in Uganda). Southern African countries

experience the highest HIV prevalence in Africa and worldwide. In 2009 this region was hosting most of the world's HIV cases, new infections and HIV-related deaths. Ten countries were host to 34% of all people living with HIV globally, 31% of all new infections and 34% of all AIDS-related deaths. South Africa alone hosts 17% of all HIV cases in the world (72).

In South Africa the epidemic progressed slowly in the 1980s with a tremendous increase in the 1990s and early 2000s. The first HIV cases were diagnosed in 1982 among haemophilic patients and men who have sex with men (MSM) (73). The Apartheid government did not respond other than by providing some economic support to those affected. In the late 1980's, the epidemic slowly extended to the general population with a rapid increase from 1995. During this time South Africa was in a process of transition to a democratic system and did not manage to tackle the epidemic. The first years of democracy saw a huge increase in the prevalence of HIV estimated by antenatal care surveillance sites with levels rising , from 7.6% in 1994 to 20.5% in 2000 (73). By 2010 the estimated prevalence was 30.2%.

Traditionally HIV programs and studies have focused on those under 50 years of age, with little knowledge of the situation in those 50 years and older. Recent studies have highlighted the importance of HIV infection in older populations given the expected increase in HIV prevalence in this age group with the introduction of ART (46, 74); and the need to prepare society and health systems for potential interactions of HIV with chronic non-communicable diseases in this population (47, 75).

Denial of the epidemic by then President Thabo Mbeki and his Minister of Health Tshabalala-Msimang prevented the early implementation of an effective programme of prevention of mother-to-child transmission (PMTCT) leading to some 2.2 million years of life lost (76). This policy response slowed down the roll out of ART resulting in an estimated 3.8 million life years lost from 2000 to 2005 (77). The AIDS denial arguments have since been resoundingly discredited (78). Eventually ART became available in rural areas in 2005, but involved a complicated and costly system for accessing treatment.

In the recent years positive new strategies in the fight against the epidemic have emerged. In April 2010, the President of South Africa, Jacob Zuma, launched the HIV counselling and testing (HCT) campaign (79) which many believe has facilitated access to and uptake of testing and treatment. Monitoring of the epidemic shows that prevalence of HIV among pregnant women at public health clinics has stabilised since 2007 at around 29.5% (80). Rehle et al, comparing data from 2002-2005 to 2008 in National HIV surveys, estimated decrease in incidence of 60% in adolescents and young adults (age group 15-24) and an increase in condom use and HIV testing (81). In the latest

National Antenatal Sentinel Survey report released in January 2013 it is reported that by mid-2011 the number of people on ART had increased from 0.9 million in February 2010 to 1.4 million in May 2011. The progress in access to treatment has been massive and its impact can be seen in both decreasing mortality related to HIV/AIDS (28) and increasing of life expectancy of those who initiated treatment (82).

A systematic review has highlighted the high percentage of people lost to the health system across different stages from a first HIV positive test until ART is initiated (83), emphasising the importance of improving the health information system to enable tracking of patients, in order to reduce loss to follow-up. To effectively address the HIV epidemic in older people it will be necessary to act on several fronts: i) increasing the number who take a test and know their HIV status; ii) increasing the number of HIV positive people, eligible for ART, who receive treatment; iii) achieving high rates of adherence; iv) obtaining reliable data to define and monitor the epidemic ; and v) measuring the impact of all interventions on incidence and mortality related to HIV.

I. Increasing the number of people that know their HIV status

Encouraging everyone at risk to be aware of their HIV status is difficult given lack of resources on one hand and stigma associated with an AIDS diagnosis on the other. At present it is estimated that only around 20% of the population know their HIV status (84). Unfortunately, without this knowledge, programmes to prevent transmission and treat those in need cannot succeed. In 2002, Pronyk et al piloted voluntary counselling and testing (VCT) in rural Mpumalanga and found that HIV testing increased considerably and that VCT was well accepted among medical staff (85). Four years later, Snow et al, working in the same area, found that HIV testing had doubled year on year since 2002 although 73% of those taking the test were women. Men mostly attended at older ages and when referred by medical staff (84). This gendered pattern is reflected in the data on VCT uptake in the Agincourt study site in 2008 (86). This work found that, though VCT users were increasing in number in the Agincourt area, the speed of increase was so slow it would be at least a decade before VCT reached everybody. By contrast, data from the South African HCT campaign launched in 2010 indicated that by June 2011 over 13 million South Africans had been tested for HIV (87). New and imaginative interventions like mobile services may be the response needed to include those who do not attend health facilities, especially men (88).

II. Increasing the number of eligible HIV positive people on ART

In 2011 it was shown that treatment with ART can prevent the transmission of HIV infection in 96% of cases (89) giving a new tool to control the epidemic and greater grounds to promote HCT. This evidence showed that, in the absence of a vaccine, the best way to control the epidemic is to

treat infected people as soon as possible. However, the population of many LMICs experience delays in accessing ART and by 2006 only an estimated 20% of HIV infected people who needed treatment globally were receiving it (90). The high cost of treatment and lack of physical and human resources, especially in rural areas, may be part of the explanation for the delay. Cultural beliefs about the causes of death and misfortune may also have played a role in delaying the response from governments in SSA (91).

It is crucial to retain HIV positive people within the health system from testing to the time of ART eligibility. However, as Rosen and Fox showed there is a long way to go. In their estimation, based on 28 studies, less than a third of those testing positive are followed up until the time they are eligible to initiate ART (83).

Scaling up of ART has been a highly successful public health intervention with the result that, by the end of 2008, more than 4 million HIV infected people had initiated ART in SSA (92). ART rollout has increased survival of those infected with HIV and reduced mortality of those suffering from AIDS (28, 46). Since the launch of the ART rollout program in South Africa, nearly two million people have ever initiated ART. The number of patients on ART doubled from 2010 to 2011, a change that can be attributed to the 2009 treatment guidelines revision; this increased the CD4 count level at which to initiate treatment in pregnant women and patients co-infected with TB and HIV to 350 cells/mm³.

III. Adherence

Once people initiate ART it is important to retain them in the programme. A review of 39 cohorts explored retention rates and found a 70% retention in a period of three years but reported that it remained difficult to maintain patients on treatment after 24 months of follow up with an attrition rate of 5% per year (92). In South Africa Cornell et al expect a deterioration of the ART programme over time, particularly through increasing loss to follow up, which may have a major impact on overall effectiveness of the programme (82). Those who adhere to treatment will have all the benefits of ART and live longer, surviving into old age (46) but it is expected high mortality on those who leave the ART programme (93). Both health system features like access to services, and community level factors such as stigma, fear to disclose and lack of partner support, may affect the success of ART and PMTCT programmes (94, 95). It is, therefore, crucial for the success of the ART programme to develop good health information systems that would allow both follow up of patients and monitoring and evaluation of the programme (82, 93).

5. Health service response

Health systems in most of Africa, including South Africa, developed before the health transition and were designed to be reactive, treating acute infections and once-only visitors without any requirement to follow patients (36, 96). Yet the new epidemic of NCDs will require a pro-active approach with systems to keep individual records and follow-up patients and integrating care for chronic diseases (22).

After the wide spread introduction of ART HIV infected people in all age-sex groups can expect to have a close to normal life expectancy (28, 90, 97). Hontelez et al predict that more than 9 million people over 50 years of age will be HIV infected by 2040 in SSA, a three-fold increase from the present situation (46). With the introduction of ART HIV patients on treatment will become lifelong users of chronic care, with many of the same health service demands as those with hypertension and diabetes such as regular reviews, reliable record keeping and continuous medication (36).

Hypertension and HIV together create a chronic disease burden that, if not managed appropriately, may jeopardise attempts to control the HIV epidemic as health centres will need to put resources into controlling both epidemics. Maher et al have highlighted a need to improve health services to tackle the coming chronic disease epidemic (98, 99). They proposed a global framework to improve the response to chronic diseases and quality of care of primary health care based on political will, case-finding among PHC patients, standard protocols to diagnose and treat these conditions, regular drug supply and proper monitoring and evaluation (100). There have been recent efforts to prepare the primary health care systems in South Africa (101) including the PHC re-engineering plan and Integrated Chronic Disease Management system. This is being piloted in three districts, including Bushbuckridge. These national initiatives aim to serve all chronic patients both infectious and non-communicable chronic disease. Some success has also been shown in Cambodia where an integrated chronic care system managed to increase survival of both HIV and NCD patients after 24 months of follow up (102).

There is little known on health care use by older people in South Africa. However, health service providers need to be aware that more than 80% of known chronic disease patients will seek health care at least once per year (39) and that more than 60% of older people may return for appointments and to receive treatment for chronic conditions (103). The use of health facilities is much higher among women than men, especially with respect to the use of HIV services (84).

The combination of the unfinished agenda of preventable and treatable infectious diseases, a rising incidence of NCDs, and increasing numbers of people with AIDS surviving long-term on ART

will be a gigantic challenge for the already weak health system in LMICs including South Africa (104). To successfully meet this challenge and plan for the new demands on the health system, more and better information is needed on the mortality, morbidity and well-being of older people. The data generated in this thesis is trying to partially fill in this gap.

C. Context

In this section I describe the district and the area where I carried out the work for this thesis and the research platform, including the longitudinal database, in which the work is embedded. This is followed by a summary of the demographics of the Agincourt population together with some of the main socio-demographic changes this population has experienced during the 20 years of longitudinal follow up.

1. History of the district

The work of this thesis was carried out in the MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt) which is affiliated with the School of Public Health of the University of the Witwatersrand in Johannesburg, South Africa. Its rural research site is based in Ehlanzeni District in the Mpumalanga Province. This province is in the north-east of South Africa, bordering Mozambique in the East and the Kingdom of Swaziland in the South. The Province is divided into three districts: Ehlanzeni, Nkangala and Gert Sibande. Ehlanzeni District is further divided into five sub-districts, one of which is Bushbuckridge which includes the Agincourt HDSS.

The Bushbuckridge sub-district was originally the southern part of the Gazankulu Bantustan, the "Homeland" for Shangaan people. In 1994, with the advent of democracy, the district was named Bohlabela and was administratively part of Limpopo Province. In 2005 the 12th amendment of the South African Constitution declared that the Bohlabela district was to be split and Bushbuckridge Municipality would become part of Ehlanzeni district in Mpumalanga Province (see Figure 2) (105).

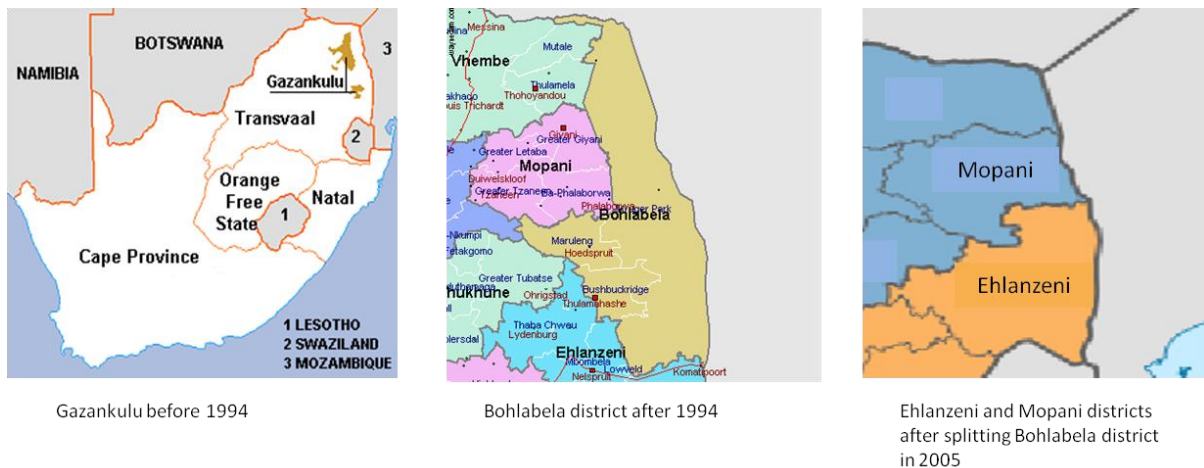


Figure 2. Evolution of the bordering areas of Bushbuckridge from before 1994 to 2005

2. Agincourt Health and Demographic Surveillance System

Soon after the end of the Apartheid regime the new Department of Health (DoH) organised and created the health districts. Data was needed to run these districts effectively but in the early 1990's there was very little, if any, demographic and health information for most rural areas. Agincourt sub-district was no exception. Without knowledge about the size of the population to be served or the main health problems in the area it was very difficult to plan health programmes and establish priorities. Monitoring and evaluation of any intervention implemented in the health system was close to impossible. By the time all these changes were happening, the Health Services Development Unit (HSDU) from the Wits Faculty of Health Sciences had already been working in the area since 1982. Its programme aimed to: " Determine the current health status of local communities and investigate the determinants of this; to pilot district and local level health and development interventions based on this information; and to assess the impact of such interventions (1992)" (106).

The Agincourt sub-district provided everything needed to implement this programme. It was a rural setting with a network of decentralised primary care facilities. In 1992/93, the HSDU ran a baseline census of this area as part of a decentralised, primary health care (PHC) orientated, rural health and development programme. This first census registered a total of 57,600 people in 8,900 households and provided the baseline information on population structure and the socio-administrative situation (107) . Moreover, it served as the basis of a longitudinal surveillance system that has been used and improved over the years. Since then the MRC/Wits- Unit, inheritor of the HSDU, has gone through different stages of development: i) decentralised health systems development (1993-97); ii) university health and population research unit (1998-2000); iii) field-

based research and training programme linked to the University of the Witwatersrand and the South African Medical Research Council (2003-2007); iv) extended portfolio to a balanced programme of observation, intervention research and clinical trials (2008 - now) (108).

To create a longitudinal dataset census updates collecting vital events have been carried out since 1993 and then every two years until 1999. Yearly updates have happened from 2000 up to the present day. The existing population cohort could only be enlarged with births and in-migrations and could only decrease with deaths and out-migrations as described in the Figure 3 below. Other more specific socio-demographic data was collected at household or individual level at regular time intervals.

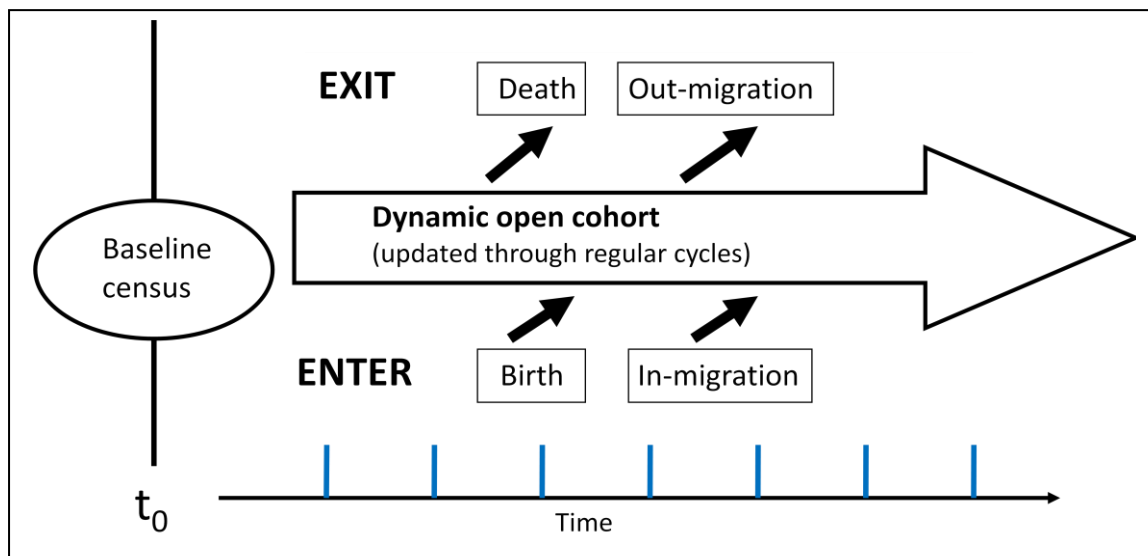


Figure 3. Health and Demographic Surveillance System general outline

Adapted from INDEPTH 2008

Since 1993 the probable causes of death have been established using verbal autopsies by visiting the caregivers of all deaths registered in the study site (109). Since the first census the area has been extended to 31 villages and around 110,000 people and the methodology has evolved with improvement in all aspects of field work and data entry systems (32, 110).

I. Description of census updates

The yearly updates consist of household visits by a team of trained fieldworkers who uses previous year's household roster to check thoroughly for any changes in the population and update the information when necessary. This is recorded using "vital events" registration of births, deaths, in and out-migrations. For each individual relation to the household head, identification of mother,

father, cell phone numbers, national ID number and demographic data, including residence status and pregnancies, is confirmed and updated when required.

Data collected provide basic demographic information at various levels: firstly, at individual level, especially on vital events; secondly, at household level providing information on the household structure; thirdly, at population level providing data on population structure and changes over time.

Further individual and household data are collected to complement this information in order to understand population and health trends and dynamics of this population. These complementary data collection exercises are carried at different times depending on an appropriate time frame to observe change (See table 1)

Table 1. Sequence of socio - demographic information collected during annual census updates in Agincourt.

MODULES (from year 2000)	00	01	02	03	04	05	06	07	08	09	10	11	12
Education (1992, 1997)													
Labour													
Household assets													
Temporary migrations													
Child care grants													
Health care utilisation				All			<5				>50		
Food security													
Father support													
Pensions													
Vital documents													
National ID													
Cell phone numbers													
Other names respondent uses													

II. Migration

On the yearly census update the population cohort is extended with the in-migrations and births and it is shortened with the out-migrations and deaths. In this thesis I follow the definitions for migrants used in the Agincourt unit: 1- Permanent out-migrants are those who leave the area permanently; 2- Temporary migrants are those who leave the area for more than 6 months per year, commonly related to labour or education reasons but return regularly and regard the Agincourt sub-district as "home". Temporary migrants are registered as part of the "de jure" population in the study site.

In order to fully follow the existing cohort it is necessary to track movements within the study site, i.e. people that move from one dwelling to another due to marriage, a job etc... The

registration of these movements of residents within the study site is essential to avoid duplications, to follow the individual's history, to describe social networks and to create research cohorts. For those who move within the study site we have established a system of Migration Reconciliation to reconcile the in and out-migration records from the same individual between the household of origin and the household of destination (see Figure 4).

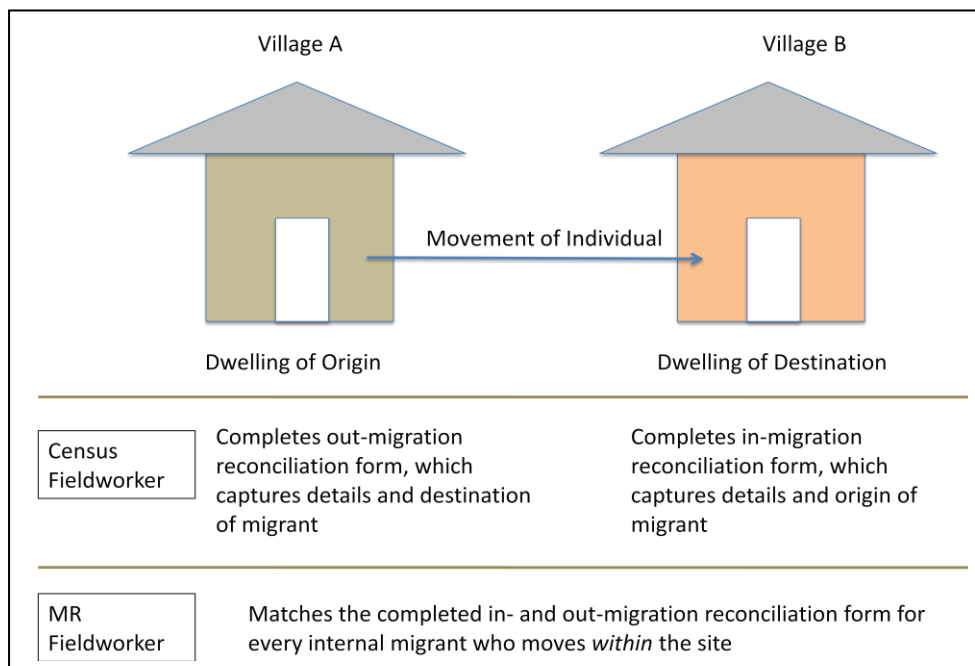


Figure 4. Migration-reconciliation method to reconcile movements within the study site

Source: Agincourt HDSS. Author: Ryan Wagner, Census Coordinator.

III. Death registration and verbal autopsy

Although the South African vital registration system has improved in recent years, at the time the HDSS was established, many people died at home and did not get a death certificate. This situation has improved since 1994, when less than half of deaths had a certificate, to 2004 when 82% of deaths were registered (111). However, death certificates in South Africa, at the time the data was collected for this thesis, were classified as poor quality due to incompleteness and many ill-defined cases (112). South African statistics on cause of death are produced at national level with lack of information at local level (63, 113). To fill this gap in information the Agincourt team visits all households that report a death, between 1 month and 11 months after the reported death, to carry out a verbal autopsy. This verbal autopsy consists of a detailed interview with the deceased person's carer that includes questions on signs and symptoms presented by the deceased in the latest months of his/her life. Many other questions are asked on health care use, medication taken and

situation under which death occurred e.g. accident, pregnancy or delivery, etc. All verbal autopsies are then distributed to two different doctors who read and evaluate the information collected and independently assign a probable cause of death for that person. If both doctors agree on the cause of death this is accepted as the probable cause. Otherwise, they meet and try to arrive at a consensus; failing that, the verbal autopsy is sent to a third doctor who acts as an arbitrator. Around 10% of all verbal autopsies do not lead to the assignment of a final probable cause of death and the cause of death is considered ill defined or unknown(111).

HIV and TB are co-infections in many patients. Respondents of VA questionnaires may describe general symptoms of these two diseases in very similar terms making it difficult for doctors to distinguish between them when resolving the most probable cause of death. In this thesis, as other authors have done previously (36, 63), these conditions are combined into a single cause of death (HIV/TB)

IV. Geographic platform

The demographic platform sits on top of a well defined geographical area. In the first few years of the census maps were hand drawn and produced by members of the field team. In 1997 all village maps were digitised and geo-referenced. In 2003 a full geographical information system was put in place to store the exact geographic position of each dwelling in the study site and each dwelling was represented in geo-referenced aerial photographs as shown in the Figure 5 below.

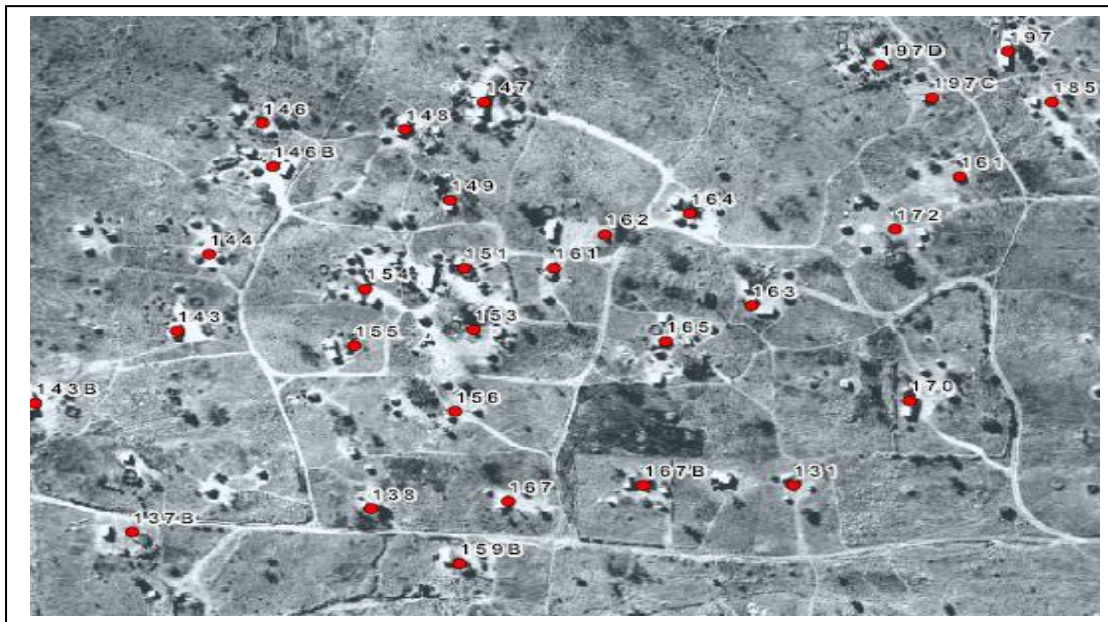


Figure 5. Aerial photograph of a portion of one of the villages of the Agincourt HDSS with dwelling's geo-referenced position represented by red dots

V. Data entry system and quality control

Data collected in the field are stored in a relational database with multiple tables and use the Microsoft SQL Server relational database management platform which is maintained at the site. The "front end" used to enter data was especially built for the Agincourt Unit. Quality of the data is assured by a system of integrity constraints, checks on ranges and compatibility of the new data with existing information. Data management of this longitudinal dataset produces an individual's life history and household structure changes. Data extractions are produced by custom made queries on SQL that allow for links between different census updates, socio-demographic information collected at different time points and surveys run in the study site. Backups of the data are produced weekly and a copy is kept at the server in the main Acornhoek offices 45 km from Agincourt.

An important part of all field operations is the continuous training, monitoring and quality control of field staff. Supervisors undergo a four day training session a month before the census starts so that they become familiar with the scientific and logistic plans for the next round. Supervisors are active in the phases before the implementation of the new update round, especially in the selection and training of field workers. If new field workers are needed a vacancy call is sent to all villages of the study site. A transparent and well documented selection process chooses the best candidates for the census field team. At the beginning of the census round a certain number of dwellings are allocated to each team. Manual and barcode based monitoring systems are in place to follow daily progress. In 2007 a form tracking system, based on barcodes, was introduced for monitoring and quality control purposes. All forms are scanned in order to track their progress through the system. Barcodes are linked to field workers to evaluate performance at individual and field team level. Once a week all supervisors meet with the Project Site Manager and the Census Coordinator to monitor progress and discuss problematic situations.

Quality measures include three different steps. In the initial phase field workers have to check their own forms. Supervisors then check completeness of forms. Quality checkers go through all forms thoroughly. Correct forms are sent for data entry and forms with mistakes are returned to the field for correction. The data entry process also includes quality checks and filters to identify inconsistencies with existing information and/or new data.

3. Study area

The Agincourt HDSS located in Mpumalanga Province, Ehlanzeni District and Bushbuckridge sub-district, covers an area of 402 km² in the North-East of South Africa. At 40km from the border with Mocambique it is delimited by the Kruger National Park to the East (32). The area is a more or less flat terrain with some small prominences that are generally lower than 600 meters above sea

level. The average temperature is around 22°C with mild winters and hot, humid summers. The mean annual rainfall ranges between 500 and 700mm, which is concentrated in the rainy season from October to April. The vegetation is characteristic of semi-arid savannah with a mixture of trees, shrubs and grasses (114). Due to the quality of the soil it is not suitable for extended agriculture and although some families may have small subsistence gardens, this situation forces many families to purchase maize and other food, making them dependent on a cash economy (115).

This rural area has experienced significant infrastructural development since 1994 although it is still short of some basic services. The main infrastructure developments have been in electricity and water supply. At present all villages have access to electricity and most areas use piped water from a dam constructed in the vicinity. Security street lights have also been installed in some villages. There are approximately 40 primary schools, at least one primary school per village; and 26 high schools, so many children have to walk or commute to school. Although these investments have improved the general infrastructure, not everybody benefits equally: electricity is still expensive for most families; water is not accessible in all dwellings; and the rural education system does not give enough opportunities to the new generation of young South Africans due to overcrowded schools and problems with teachers' absenteeism (32, 110).

The PHC system consists of 6 clinics and 2 health centres (one of them in public private partnership with the local health authorities). There are three rural hospitals between 20 and 60 km from Agincourt village(32, 110). In the last few years some health facilities have been refurbished or new buildings have been constructed in the health facility's yard. Most of the health facilities host a Health Committee with clinic staff and community representatives. The map below shows the 31 villages under surveillance placing all health facilities in the study area (See Figure 6).

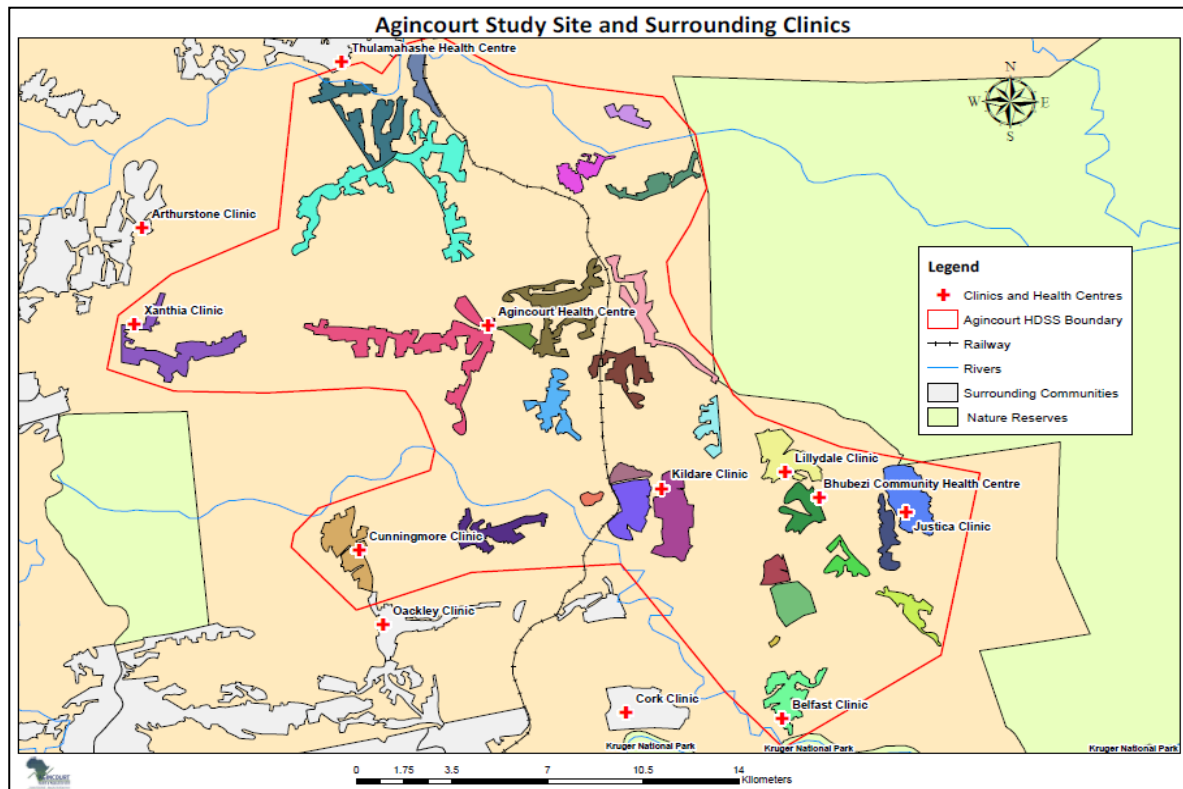


Figure 6. Map of the Agincourt HDSS, including the 1991 original villages and the 2007 and 2013 extensions

4. Study population

In 2006, when most of the work reported in this thesis was done, there were 71,587 people distributed in 11,734 households (32). The majority of the population is Shangaan with Xi-Tsonga being the most common spoken language.

The population structure is continuously changing and this is reflected in the data collected over the past 20 years. In 1992 the nearly 58,000 people living in the site had a population pyramid similar to a traditional low income country's structure, with 44% of the population under 15 years of age and a dependency ratio¹ of 93%. The population 50 years or older accounted for 9.0% and the population 65 plus accounted for 5% of the total population (107). Twenty years later the population structure has changed and the population pyramid is now more comparable to a middle income country with a population under 15 years accounting for 36% (116), mainly as the result of a continuous decrease in fertility rates and an increase in child and infant mortality caused by AIDS. The population aged over 50 in 2011 had increased to 12.7% and the population aged 65 plus has increased to 6% (32), following the ageing process that this population is experiencing (see Figure 7).

Prior to 1993 there were many Mozambicans who found refuge in the border area of Bushbuckridge when fleeing from the RENAMO/FRELIMO war. The Mozambican population settled

in all villages although they were unevenly distributed (107). This population was registered as Mozambican in the Agincourt database and coded as refugees. Although the majority have settled down after 20 years of living in South Africa, there are still socio-economic and development differences between people of Mozambican origin and South African natives. These refugees represent around 30% of the total population in the area.

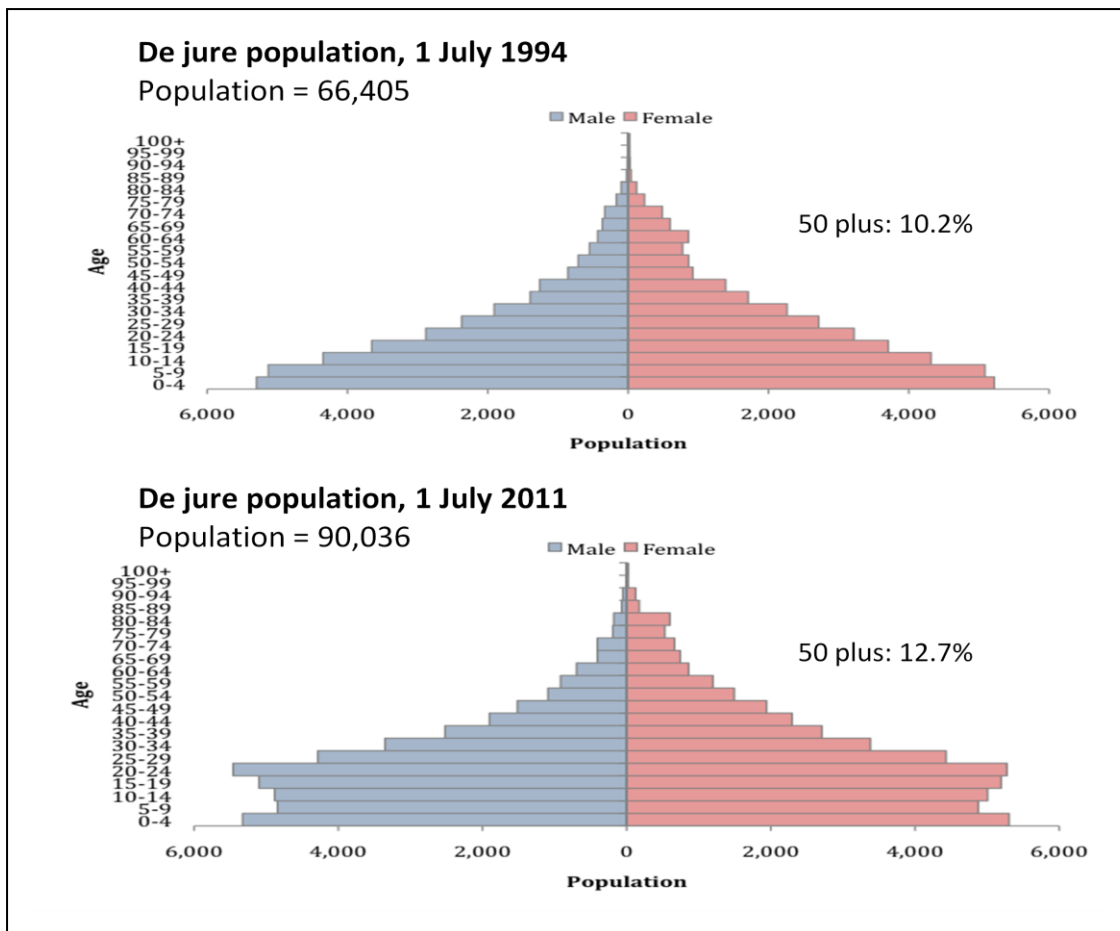


Figure 7. Comparison of population pyramids 1994 and 2011, highlighting the proportional increase in population 50 plus

The population under surveillance is living in very disadvantaged conditions with regard to housing, water and electricity supply, schooling and wealth. Household structures are seriously affected by the labour migration of adult males due to the low job opportunities in the area. Historically Agincourt HDSS has felt the impact of labour migration in the socio-demographic development of this rural community and its potential impact on health. Unemployment has forced around 60% of men and just about 20% of women between 40-59 years of age to out-migrate looking for better job opportunities. Unemployment in the area for those between 20-40 years of age is high. In 2004 29% of men and 46% of women were unemployed(116). The situation has worsened for women with an increase of 6% in the following 5 years while men have relatively improved their situation with a decrease of 3% in unemployment (116).

Most labour migrants consider the Bushbuckridge area as their home. For this reason the Agincourt Health and Demographic Surveillance System (HDSS) has always followed and retained information of all household members , even for those labour migrants who spend more than six months per year living in their working place, outside the study site. Labour migrants have mainly been adult men, so that the demographics of the area are biased towards more women. This raises

the question of what is the most appropriate population to study when trying to describe this rural population. This thesis focuses only on those people who live permanently in the study site, because permanent residents are those exposed to risk factors present in the community and are the main users of the local primary health care services. However, labour migrants may be important sources of changes in lifestyle in these rural communities, influencing risk factors for chronic diseases.

Levels of formal education among older people are very low, with 59% of the population 50 years or older having no formal education, especially among women and the oldest age group(35). This situation is reversing since universal primary education was introduced after the first democratic elections with higher access to formal education in younger age groups.

A fertility transition in the last quarter of the 20th Century in Agincourt has seen a decline in the Total Fertility Rate (TFR) from 6.0 in 1979 to 2.3 in 2004 (40). Since 2004 fertility has stabilised with a TFR of 2.5 in 2009. There is now a convergence of South African and Mozambican TFR, mainly due to a small increase in TFR in the local population and a large decrease in that of the population of Mozambican origin. This change is linked to better socio-economic status and better education in the youngest women of Mozambican origin (117).

Mortality trends show vast change in life expectancy from early 1990 to 2010 (see Figure 8). In 1993, women had a life expectancy at birth of 74 years and men of 67 years. However, life expectancy was drastically reduced in the following years with a clear reversal especially in younger adults (24). By 2004 women had lost 13 years of life expectancy and men 15, but by 2009 there was evidence of an improvement, with an increase of 5 years of life expectancy in women and of 2.5 years in men(32).

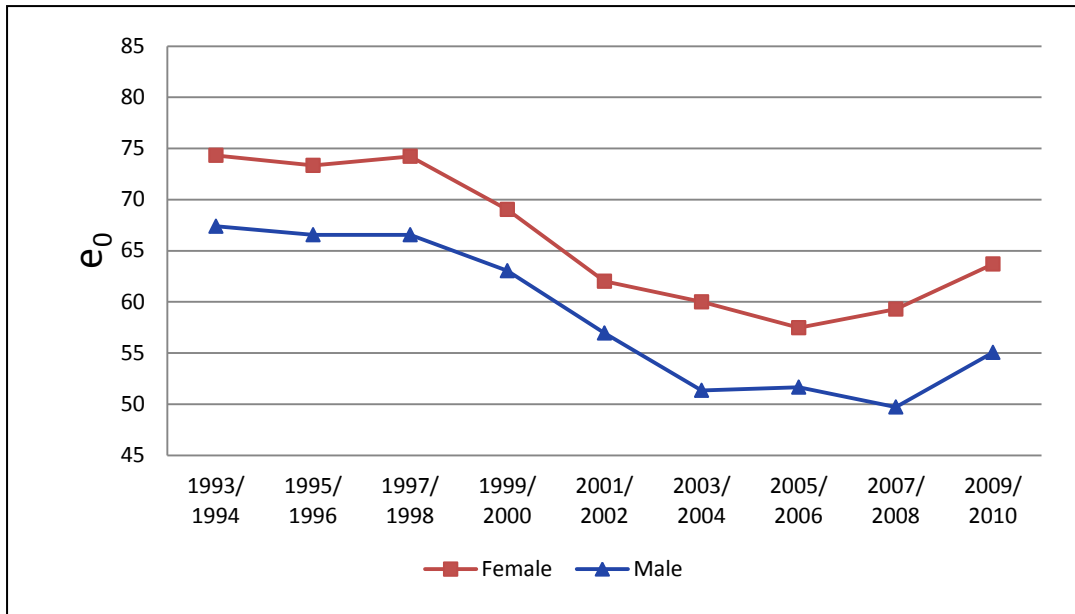


Figure 8. Trends in life expectancy at birth in Agincourt, 1993-2010

Source: Michel Garenne 2011

(unpublished).

5. INDEPTH network

The longitudinal nature of the follow up of this typical rural population is important to understand their health and socio-demographic changes and trends. However, working in isolation would not serve the purpose of understanding health problems of rural African settings more generally and informing policy makers to take evidence based decisions. The International Network of the Demographic Evaluation of Populations and Their Health (INDEPTH Network, www.indepth-network.org), of which Agincourt is a member, provides a network conducting longitudinal demographic and health research of populations in low and middle income countries. Part of the role of INDEPTH is to facilitate the formation of working groups to raise funds for and implement areas of research. In this respect the Agincourt centre leads two working groups, namely "Migration, Urbanisation and Health" and "Adult Health, Ageing and Wellbeing". The research in this thesis is part of the work of the latter.

D. Aims, Objectives and Themes of thesis

1. Overall aim

There is a recognised gap in knowledge of older people's health, survival and health care needs in rural South Africa that this thesis aims to address. The thesis focuses on older people living in the area covered by the Agincourt HDSS, where they are called on to play an active role in society late in their lives. This thesis aims to understand factors that influence the health, wellbeing and survival of these older people and their health needs, providing information which may assist in the planning of health services for older people.

2. Specific objectives

The specific objectives of this thesis are to:

- Determine the consequences of the changing age structure of a rural South African community for the health and the well being of the population 50 years and older, measured by self reported health, disability and quality of life in order to understand their health, welfare and social support needs;
- Quantify the prevalence of self reported health focusing on diseases that require chronic care by using self reported health conditions (NCDs) or measured conditions (hypertension);
- Understand the health care needs and health seeking behaviour of older people especially those making use of Primary Health Care;
- Discuss the epidemiology of HIV and its interaction with the growing epidemic of NCDs affecting older people;
- Describe socio-demographic factors associated with survival in older people and explore how function and quality of life may predict survival.

3. Thesis themes

This thesis focuses entirely on older people and considers the following themes:

1. Wellbeing of older people;
2. their Need for Health Care, and;
3. patterns of Mortality among those 50 plus.

Throughout the thesis I describe the impact of the HIV epidemic and the diseases of ageing.

Table 2. Wellbeing, health care use and mortality of older people in a rural African setting: summary of themes by cover story and papers

	Papers				
Themes	I Assessing health and wellbeing	II Self reported health and health care use	III Sleep and mortality	IV HIV prevalence in older people	V Social conditions, disability and mortality
Wellbeing	Describing quality of life, disability and health status controlled by selected socio-demographic determinants.	Evidence of association between quality of life and disability with existing levels of NCDs.	New description of nocturnal sleep problems and difficulty related to daytime function as public health problem in this rural African setting. Importance of sleep problems as a proxy for depression, anxiety, poor function, reduced quality of life and undiagnosed chronic conditions.		Evidence of increased risk of death associated with different measures of self-reported wellbeing (health today, difficulty with work or household duties, disability, quality of life and health status).
Need for health care	Health services in rural settings need to adapt to the ageing population with impaired functionality and poor health.	Exploring the use of health care among older people and its association with chronic diseases, quality of life and disability.	Importance of depression and anxiety and the need to identify sleep problems to prevent potential adverse health outcomes.	Failure to recognise high levels of HIV which will require attention especially through PHC.	Emerging NCDs in a highly HIV prevalent population which will increase need for PHC. Important to prepare PHC systems for this coming burden.
Mortality			Evidence of sleep problems and increased mortality in population older than 50 years.		Evidence of increased mortality in those aged 50 to 70 due to HIV/TB and NCDs. Women present most socio-demographic determinants associated with higher mortality but have lower mortality risk than men.

E. Methods

This thesis focuses on the health and well-being of older people, using data collected in the HDSS census rounds together with data from three cross-sectional surveys carried out between 2006 and 2011 in the research site.

This section summarises the methods used. These methods are explained in more detail in the five papers included in the annexes. Here I outline the preparation of the census variables used and the three surveys used. The last two sections summarise the statistical methods used and discuss the ethical issues

1. Data collection

The target population of this thesis is people 50 years old or over who were living in the Agincourt HSDSS during the census round of 2006. In this section I describe the collection of data which includes the Study on Global Ageing and Adult Health (SAGE) and the HIV/NCD study and their integration with the HDSS data.

I. Sample selection

In 2006, two SAGE studies were carried out in this population. The first of them, SAGE survey, used an adapted version of the WHO Survey on Global Ageing and Adult Health research instrument. In this survey 575 individuals 50 years and older from the Agincourt HDSS were invited to participate. The survey collected data on socio-demographic characteristics, self reported health, self reported prevalence of chronic diseases and risk factors, health care utilisation and anthropometric measures. The second study, SAGE module, used only two sections of the SAGE survey instrument, namely "Self-reported health" and "Subjective Well-being and Quality of Life". In this study 6,206 men and women permanently living in Agincourt in 2005 were invited to participate during the 2006 Agincourt update census round . These two groups were followed up annually through the annual census update.

The HIV/NCD study was carried out between 2010 and 2011. A random sample of 7,662 people 15 years and older from the HDSS and stratified by age and sex were invited to participate. All those who completed the SAGE survey in 2006 and were still living in the area plus a sample of those who were 46 to 49 years old in 2006, so not eligible for the 2006 SAGE survey then, were included. In total this sample contained 2034 people aged 50 years or older. Figure 9 below presents the selection process for this thesis.

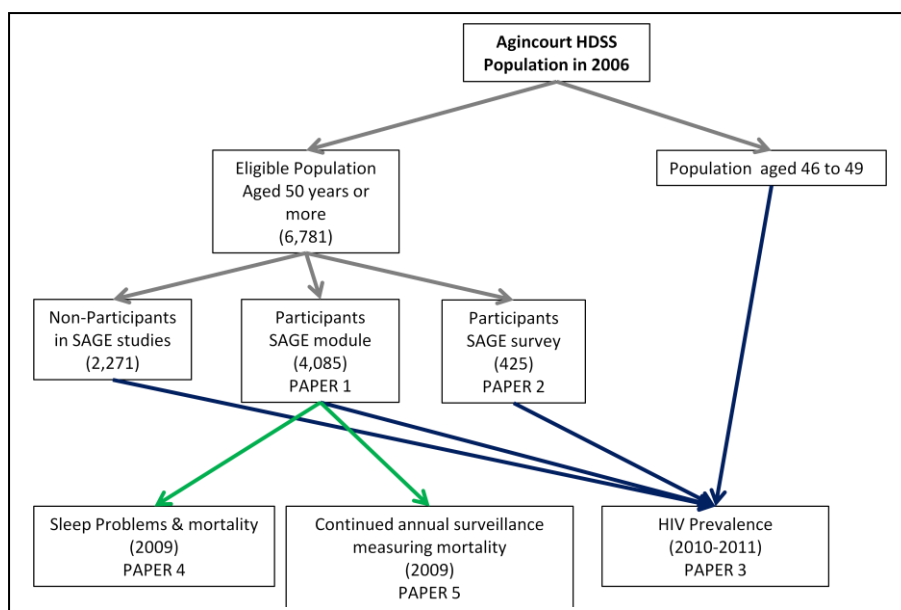


Figure 9. Groups Sampled from the Agincourt population for the studies reported in this thesis

II. Socio-demographic variables constructed for and studies carried out in this thesis

i. Socio-Demographic variables.

Demographic factors such as gender, age, education, union status, household assets, nationality of origin, employment status, household conditions and existence of a public health facility in the village of residence were extracted from the Agincourt database and used to examine their association with levels of quality of life, disability and health status in our population. These outcomes were also used as risk factor variables when measuring influences on survival.

Age was calculated using birth dates and the date of the study, ages were grouped in 5 or 10 year age group for analyses.

Highest level of education was collected at baseline and then for every in-migrant into the study population. Education level was updated every five years until 2006 and then every 3 years. Education was categorised according to WHO recommended categories of: no formal education; less than 6 years of formal education; and 6 years or more of formal education.

Union status (whether an individual has a partner) is updated yearly allowing researchers to describe current union status for all individuals. For analyses union status was grouped into two categories: those in a current union (married or living as married); and those without a current partner (never married, separated, divorced or widowed).

Socio-economic status (SES) was measured using the absolute values of a household asset score, developed using principal component factor analysis and 34 variables derived from the 2005 household asset survey. Each asset variable was coded to ensure that increasing values correspond to greater SES. Each asset was given equal weight by rescaling so that all values of a given asset variable fall within the range [0, 1]. The assets were categorized into five broad groups – ‘modern assets’, ‘power supply’, ‘water and sanitation’, ‘quality of housing’, and ‘livestock assets’. For each household and asset group, the rescaled asset values were added together and then rescaled to get a specific value in the range [0,1] Finally, for each household these five group-specific scaled values were added to get an overall asset score which has a value in the range [0, 5] (118). This score was then divided in quintiles by household.

As explained above (section " History of the Agincourt HDSS"), in the study area South African citizens live together with self-settled former refugees of Mozambican origin. To allow for a comparison between these groups, we created a variable called "nationality of origin" with South African and Mozambican as the only two categories.

The concept "work" was defined as an economic activity that gives cash income to the person doing it. Employment status was based on the combination of either having a job or the willingness to work. Using 2004 data, (the most recently available information on labour), a variable was created with the objective of describing whether a person was working. In this sample, the majority of those not working were not looking for job, but had retired in the sense that they had concluded their working career.

A dichotomous variable was created to define older people's household structure. The variable divided the sample of people 50 years and older between those who were living in households composed only of older people and those who were living with people younger than 50.

ii. SAGE survey

The SAGE studies and HIV/NCD prevalence work included self-reported health conditions and self-reported life-style risk factors for CVD such as tobacco and alcohol use. Finally, we carried out measurements for weight, height, waist and hip circumference, blood pressure and HIV status.

This survey, coordinated by INDEPTH and the WHO, followed the standard field methods used by the MRC/Wits-Agincourt Unit. Detailed information on how these measurements were taken can be found in the self-reported health and health care use paper from this thesis (39). In summary, potential participants were visited at home a maximum of three times for recruitment. Those who were found at home and agreed to participate signed an informed consent and responded to the survey questionnaire. Anthropometric measures included height, weight, hip and

waist circumference. Blood pressure measurements were collected as well as performance tests that included grip strength, vision, measures of function and cognition.

iii. SAGE module

In the 2006 census round all individuals 50 years or older permanently living in the study site and who had not participated in the SAGE survey were invited to respond to a summary SAGE module. The standard procedures described above were used in carrying out visits and in obtaining informed consent. The questionnaire was adapted from the SAGE survey, including only sections on self report of health conditions and subjective wellbeing and quality of life. More detailed information is presented in the first paper of the thesis (35).

Participants were followed through successive annual census updates until 2009 and mortality data was collected with verbal autopsy used to define the probable cause of death. Mortality from the sample was compared with Agincourt census mortality data to corroborate the findings (119). More detailed information can be found in paper 5 of this thesis (119).

iv. HIV and NCD survey

To describe the prevalence of HIV and double burden of HIV and NCDs in the study site, 7,662 men and women 15 years and older and permanently living in Agincourt were selected from the 2009 census and visited at home between August 2010 and June 2011 (120). Strenuous efforts were made to make sure that a reason for not participating was collected for all non-respondents.

A team of 10 field workers and a supervisor were carefully trained to introduce the study to obtain informed consent and to carry out the questionnaires with anthropometric measures and collection of dried blood spots (DBS). Lipid sub-fractions and blood glucose were measured using point of care instruments. A data quality checker was responsible for assuring data completeness and quality. Two data typists double entered the data. Software for this study enabled comparison of the two entries and listed all inconsistencies. A data quality supervisor was responsible for checking inconsistencies and making sure that the correct entry remained in the system. The team was coordinated in the field by a project manager. Weekly meetings with the principal investigators (PIs) were established for continuous supervision, problem solving and feedback to on site researchers. These meetings proved fruitful and were adapted for other studies in Agincourt.

Written informed consent was obtained from respondents and a copy given to them in English or Xi-Tsonga depending on their preference. Participants were asked to respond to two questionnaires, namely, a Chronic Disease and Life Style questionnaire (adapted from the SAGE (<http://www.who.int/healthinfo/sage/en/>), WHO-STEPS questionnaires

(<http://www.who.int/chp/steps/en/>) and the adapted STEPS version used in nine INDEPTH Asian sites (121)); and a Sexual Behaviour questionnaire developed together with the ALPHA Network (<http://www.lshtm.ac.uk/eph/dph/research/alpha/>).

For confidentiality reasons the questionnaires mentioned above did not have participant identifiers which were kept in a study check list. The participant study number was used to link the two questionnaires to each other and with the check list. A laboratory barcode was placed on the check list and the dried blood spot (DBS) paper to link the DBS with the respondent.

Anthropometric measures (weight, height, waist and hip circumference), blood pressure (Boso blood pressure, BOSCH + SOHN GmbH u. Co .KG. Fabrik mediz, Germany – a digital machine recommended by the World Health Organization for the SAGE study and used throughout this thesis work), dried blood spots, lipids (CardioChek PA Analyzer, Polymer Technology, System, inc., Indianapolis) and glucose (CareSens POP Blood Glucose Meter Equipment, i-SENS.inc., Seoul) were collected.

Blood pressure was taken three times and the final blood pressure recorded was calculated by the average of the second and third measurements taken. Hypertension was classified as a diastolic blood pressure equal to or higher than 90mmHg or systolic blood pressure equal to or higher than 140mmHg. The ranges for BMI and blood pressure used for analyses are presented in Table 3 below.

Blood pressure results, glucose and body mass index (BMI) were provided immediately after the interview and participants were referred to the nearest clinic if results were outside the normal range. Participants were given a stamped ID card with a code that included the study number, gender and age in order to anonymously collect their HIV result from a health centre.(At the time of the study, two health centres were available to provide care to HIV positive people).

Table 3. Body mass index and blood pressure levels used to create analysis categories

BMI	Values
Underweight	<18.5
Normal weight	18.5-24.9
Overweight	25.0-29.9
Obese class I	30.0-34.9
Obese class II	35.0 - 39.9
Obese Class III	40.0 plus
Blood Pressure JNC7*	
Normal BP, no treatment	SBP<140 and DBP<90
Normal BP on treatment	
Stage 1 hypertension not on treatment	SBP= 140-159, or DBP>=90-99
Stage 1 hypertension on treatment	
Stage 2 hypertension not on treatment	SBP>=160 or DBP >=100
Stage 2 hypertension on treatment	

*The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (122).

Using a modified version of the South African Hypertension Guidelines 2011 (123) to measure cardiovascular risk of the population in the HIV/NCD study (see Table 4 below for the variables used), we defined two groups of risk namely, "No or low risk" and "Moderate or greater added risk".

Table 4. Modified South African Guidelines: Risk factors and associated clinical conditions used in this thesis

Risk factors	Associated clinical conditions
Age/sex: Men >55 yrs, Women > 65 yrs	Self-reported coronary heart disease
Smoking at least every day	Self-reported heart failure
Dislipidaemia	Self-reported Stroke or Transient Ischaemic Attack
Family history of CVD (M<55yrs, W<65yrs)	
Waist circumference (M>94cms, w>80cms)	

HIV testing was done with bloodspots using the screening assay Vironostika Uniform 11 (Biomerieux, France). Positives were confirmed by the SD Bioline HIV ELISA test (Standard

Diagnostics Inc., Korea). If screening and confirmatory assays did not agree, a third assay was done. Following WHO criteria, this third assay determined the final result.

v. Health and well-being variables

Health Status, Disability and Quality of Life Scores are composite measures that, based on WHO methods, were used to estimate Health Status of participants, the WHO disability assessment schedule (WHODAS) and a person's quality of life (WHOQoL). Details on how these composite measurements were calculated, their domains and scales are provided in the Paper 1 of this thesis (35).

The exposure to alcohol and smoking were measured in the SAGE survey by asking the participant whether the person smoked at present (even if not daily) and whether the person had an alcoholic beverage in the last 30 days.

Due to the lack of morbidity data and technical difficulty of collecting objective clinical information, the WHO/SAGE team used self-reported data on health conditions. Participants responded to the SAGE standard question of "Have you ever been diagnosed with (the condition)?". This was used to obtain self-reported information on diabetes, hypertension, musculoskeletal pain, stroke, angina, respiratory disease and depression. Health and function were also self reported using questions on "Overall health today" and "Difficulty in doing work or household activities".

To study the relation between sleep problems and mortality, feelings of depression and anxiety were assessed using responses to questions on feeling sad, low, depressed, worried or anxious , from the SAGE module. Sleep problems were assessed with two questions, the first reflecting nocturnal sleep problems and the second focusing on day time function difficulty. Categorical variables were created for the four questions: none/mild/moderate and severe/extreme. Mortality was measured using the follow-up from census rounds until end 2009. More detailed information on the procedures is presented in Paper 3 (124).

2. Statistical analysis

The analysis conducted for each manuscript is presented in the data entry and analysis sections of the different papers.

The SAGE data was entered using CSPro 3.1 data entry programme (<http://www.census.gov/ipc/www/cspro/index.html>), which includes validation checks, and then extracted for analysis to Stata10 for the first, third and fifth papers; and to Stata11 for the second and fourth papers (Stata Corp, College Station, Texas, USA).

Demographic variables including vital events were extracted from the Agincourt database, linked to the SAGE or HIV/NCD respondent and included in the final table for analysis. Some new variables were created as explained in Methods above and in the manuscripts.

Each paper includes a descriptive analysis of the sample used and the socio-demographic characteristics of the participants including comparisons between respondents and non respondents.

Logistic regression was used to study the association between the outcome (dependent) variable and various explanatory variables. P-value threshold and methods used to include variables in the final model are explained in detail in each paper.

Cox proportional hazard models were used to determine hazard ratios for mortality risk in Papers 3 and 5. In these cases we performed a test of proportionality for each predictor using the Schoenfeld and scaled Schoenfeld residuals. If the tests were not significant (p-values >0.05), proportionality was not rejected and we assumed that there was no violation of the proportional assumption. Age could not be treated as a continuous variable due to the complex relation between age, gender and risk of dying. To allow independent estimation of risk for each age group, age was entered in the Cox proportional hazard model as a categorical variable in five-year age groups.

Given the unexpected relationship between age and mortality found in Paper 5, we carried out an analysis on the full Agincourt population from 1993 to 2006 to compare sample trends with general population trends. To compute hazard mortality ratios we used number of deaths as the numerator and length of time lived in the study area over the period as the denominator, expressed in person-years. We compared all-cause mortality and HIV/TB mortality in five-year birth cohorts for three time periods prior (1993-1997; 1998-2002; 2003-2006), and for the thesis follow up period of 2006-2009. For all periods we calculated death rates in five-year age groups.

3. Ethics

All census activities have carried an unconditional ethical clearance since 1996 from the University of the Witwatersrand's Committee for Research on Human Subjects (Medical). This ethical clearance (protocol M960720) was renewed in 2011 (protocol M110138).

The University of the Witwatersrand's Committee for Research on Human Subjects (Medical) has also reviewed and approved all other aspects of this research, i.e. thesis protocol (Ref. No. M090832), the SAGE survey (Ref. No. M060214) and the HIV/NCD survey (Ref. No. M10458).

Collection of data for research in Agincourt is based on a long history of good relationship and mutual understanding between the Agincourt research team and the communities living in the research site. As part of the community consent for the first baseline data collected in 1992/93, it was stipulated that the Agincourt Unit would share research results with the community (106). This agreement has been fulfilled by the Unit ever since then by informing the community of planned research before field work is undertaken and by organising regular feedback after work is completed. In these feedback meetings, the Unit, through its Learning, Information, Dissemination and Networking with the Community (LINC) office, invites a wide range of people including community members, political and traditional leaders, nurses, NGO members, health committee members, representatives of the Department of Home Affairs and teachers.

In all studies carried out by the Agincourt Unit individual written informed consent has been collected and a copy of the consent and the information sheet, in Shangaan, has been given to all participants to retain.

As explained above clearance was obtained by the University of the Witwatersrand's Committee for Research on Human Subjects (Medical) to use oral informed consent from the start to collect census data at household level. Field workers are trained to identify a knowledgeable adult member of the household who can give the oral consent and respond, on behalf of all other household members of the general family, to social and demographic questions necessary to update the census roster.

As part of research governance the MRC/Wits Agincourt Unit has put in place rigorous systems to protect the confidentiality of both census and survey data. Field staff is carefully trained and the storage of data and the archiving of forms is done under very strict conditions. Original data is backed up regularly and protected by a password system. Archives are locked with restricted access. When individual data or their household or immediate community data is shared, it is first made anonymous to assure that no identifiers could link back to the individual.

F. Results

This section starts by presenting a full description of all samples used in this thesis. It is followed by a summary of findings in each paper and the association between explanatory variables and outcomes, organised by the three themes presented above, that is wellbeing, health care use and mortality. It ends with a presentation of results in specific areas of work

1. Sample description

A total of 4,085/6206 people responded to the SAGE module, 424/575 to the SAGE survey, both in 2006, and 4,362/7,662 consented to the interview and HIV test in 2010/11. The main reason for non-participation was the difficulty in finding potential participants at home due to individuals being at work or out-migrated at the time of the visit (26% SAGE module, 20.5% SAGE survey, 24% HIV study). Although all efforts were made to find respondents, many people were not available at the time of the home visits. Among those at home the response rate was 98% for the SAGE survey, 93% for the SAGE module and 87% for the HIV/NCD study. The response rate and general demographic characteristics of the different samples are presented in Table 5 below. Those not found at home make the largest proportion of non-respondents.

The SAGE module sample was followed for three years for mortality analysis: August 2006 to end July 2009 for the general mortality paper (paper 5) with a total of 377 deaths recorded; and August 2006 to December 2009 for the mortality paper related to sleep (paper 3) with a total of 394 deaths recorded.

Table 5. Comparison of samples of the studies making up this thesis

	SAGE survey N (%)	SAGE module N (%)	HIV/NCD N (%)
	Sample 2006 follow up to 2009	Sample 2006	Sample 2010 including SAGE survey
Total sample selected	575	6,206	7,662
Response rate from selected sample	425 (73.9)	4,085 (65.8)	4,362 (56.5)
Interviewed but no blood test done	--	--	322 (4.2)
Not found	118 (20.5)	1,616 (26.0)	2,156 (28.1)
Refusals	10 (1.7)	47 (0.75)	353 (4.6)
Deaths	22 (3.8)	218 (3.5)	--
Unable to respond	--	240 (3.9)	--
Ineligible	--	--	469 (6.0)
Selection criteria	Random sample. Age 50 plus Permanently living in the study area. Informed consent	Age 50 plus. Permanently living in the study area. Oral consent.	Random sample stratified by age and sex. Age 15 plus Permanently living in the study area. Informed consent
Age structure #			
50-59	37.0	31.7	30.2
60-69	29.9	29.9	34.7
70-79	23.4	26.4	20.7
80 plus	9.7	12.0	14.4
Gender# (% male)	32.0	24.8	48.0
Education# (% none)	65.9	63.7	60.6
Nationality origin# (% South African)	74.4	71.8	70.0
Union# (% single)	52.9	54.4	59.9

Proportion among those who participated in the study

This older age group has low levels of literacy, while younger people (under 50) in the population have greater levels of education and a higher household SES. Household structure is characterised by men being more likely to be married and living in households with members over 50 years of age only.

The studies presented in this thesis have created an older adult cohort that, in respondents, will allow future follow up and research on this older age group. Figure 10, below, shows the overlap between studies using: SAGE survey (N = 425), SAGE module (N = 4,085) and HIV/NCD study (N = 5,037).

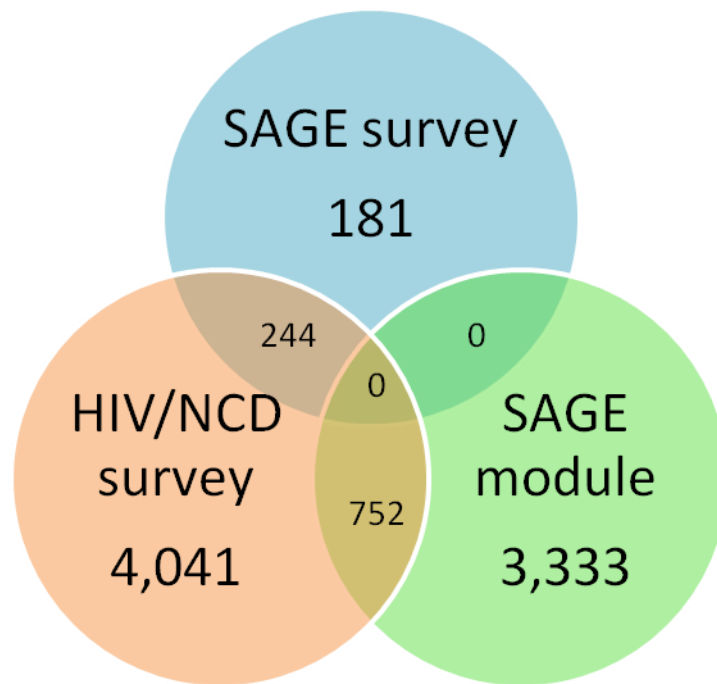


Figure 10. Diagram showing the overlap of participants between studies in this thesis

2. Results overview

Table 6 below provides a summary of factors associated with health and wellbeing presented by the three working themes of this thesis, namely, wellbeing, health care use and mortality. To complement this information Table 7 presents associations and trends between the outcomes studied and potential explanatory variables. Older people report lower general wellbeing and experience higher mortality. There is a double peak in mortality with an excess of deaths among those in their fifties compared to older age groups until the age of 80 or older. There is an important difference in life experience between men and women with women experiencing poorer wellbeing and accessing health care more frequently. However women have higher survival than men. Although there is a low level of formal education in this older age-group, having some education is related to increased wellbeing, higher health care use and lower mortality. Being single and having a low SES are associated with poorer wellbeing, poorer health and higher mortality.

Table 6. Factors associated with health and wellbeing of older people in a rural African setting: summary of significant findings by themes and papers

Themes	Papers				
	I Assessing health and wellbeing	II Self reported health and health care use	III Sleep and mortality	IV HIV prevalence in older people	V Social conditions, disability and mortality
Wellbeing	<p>Female gender, older age, lower levels of formal education, being single and unemployment are associated with poorer health status and greater disability.</p> <p>Extreme old age, lower levels of formal education, being single, lower socio-economic status and unemployment are associated with lower quality of life</p>	<p>High prevalence of NCDs are associated with lower levels of quality of life and higher disability.</p>	<p>Prevalence of Sleep difficulties</p>		<p>High levels of disability and lower quality of life were associated with higher mortality.</p>
Need for health care		<p>Greater use of health care is associated with reported high prevalence of chronic diseases, low levels of quality of life and high disability.</p>			






<p>Mortality</p>			<p>Not feeling rested or refreshed during the day is associated with a two-fold increase of mortality risk in men older than 50 years of age.</p>		<p>Male gender, extreme old age, being single, lower socio-economic status, lower quality of life and higher disability are associated with higher mortality. Women are exposed to most socio-demographic determinants and composite measurements associated with higher mortality but have lower mortality levels. Mortality from NCDs is higher in those 75 years and older while mortality due to HIV is higher in those in ages 50 to 69.</p>
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Table 7. Association between outcomes and socio-demographic variables, self reported health and composite variables (quality of life and function)

Explanatory variables	Outcomes							
	Wellbeing			Need for health care			Mortality	
	Lower Quality of life	Lower Health status	Higher Disability	Hypertension	Higher risk HIV infection	Low Health Care Use	Higher mortality sleep	Higher Mortality
Age	Older	Older	Older		Young women Old men		Older	Double peak
Gender		Women	Women			Men	Men from 60s Women from 70s	Men
Education*	None or <6y	None or <6y	None or <6y	Women with <6 years	None	None or <6y	Lower	
Union**	Single	Single	Single		Single	In union	Men single Women union	Single
Working ^Δ	No	No	No					
Socio Economic Status	Low				Low		Women lower	Low
Any NCD condition ^{ΔΔ}						None		
Waist circumference				Men Increased or substantially increased				
Alcohol consumption				Men				
Waist-hip ratio [‡]				Women with substantially increased				

Nationality origin		South African		South Africans	Mozambicans		
Depression						Sever/extreme	
Anxiety						Sever/extreme	
Nocturnal sleep problems						Sever/extreme	
Daytime function difficulty						Sever/extreme	
Quality of life					High	Lower	Low
Disability					Low	Higher	High

Education**: categorised as No formal education; Less than six years of formal education; Six or more years of formal education. *Union**: categorised as Single (never in a union, widow, divorced or separated); In a union (currently married - including traditional unions- or living as married). [&]**Working**: a person that is employed and receiving a salary. ^{&&}**Any NCD condition**: all conditions are self reported and these include: musculoskeletal pain, stroke, angina, diabetes, respiratory disease, depression, hypertension. [#]**Waist/Hip ratio**: Calculated by dividing waist circumference by hip circumference both in cm. Normal values men under 0.90 and women under 0.85

Paper order	Paper title	Code
Paper 1	Assessing health and wellbeing	
Paper 2	Self reported health and health care use	
Paper 3	Sleep and mortality	
Paper 4	HIV prevalence in older people	
Paper 5	Social conditions, disability and mortality	

3. Ageing and extreme old age

For the first paper, where we describe the health and wellbeing of older people, age was divided into 10 year age groups. However, the results of further analyses for later papers showed that due to rapid changes with increasing age, the 10 year age grouping was obscuring some important changes in survival and that the complex relation between age, gender and risk of death was better explained using 5-year age groups.

The population in the MRC/Wits-Agincourt research site is experiencing an ageing process. Population 80 years and older in the SAGE studies are represented by 41 people in the SAGE survey (66% women) and by 490 in the SAGE module (70% women). The HIV/NCD study had 249 participants 80 years and older (52% women as it was stratified by sex and age).

The government-provided old-age pension is available to all South African citizens and provides some economic support for older people and their families. In 2012, 88% of the population aged 70 plus reported receiving an old age pension, compared to 71% of people aged 60 to 69 years. In the oldest age group (80 plus), 87% of women were receiving a pension compared to 91% of men (p value=0.049).

Among the group of older persons 50+, older age groups have lower levels of education (p<0.001), are more likely to be single (p<0.001) and report worse health status (p<0.001), quality of life (p<0.001) and functionality (p<0.001). Table 8 below presents the self reported health conditions in five different categories as reported by population 80 years and older. The highest percentages are in the poorest or poor categories. Nonetheless, 25.6% reported good or best health status, 23.7% high or highest function and 30.2% good or best quality of life. In multivariate analyses comparing with those in their fifties, these differences were all significant (35).

Table 8. Self reported health conditions of population 80 plus

Composite measure	Poorest (%)	Poor (%)	Moderate (%)	Good (%)	Best (%)
Health status	178 (36.3)	111 (22.7)	76 (15.5)	63 (12.9)	62 (12.7)
WHODAS*	205 (41.8)	96 (19.6)	73 (14.9)	47 (9.6)	69 (14.1)
WHOQOL#	153 (31.2)	106 (21.6)	83 (16.9)	71 (14.5)	77 (15.7)

*WHODAS: World Health Organization Disability Adjusted Score

#WHOQOL: World Health Organization Quality of life

The youngest age group (50-59 years old) is more affected by the HIV epidemic. Men in their fifties have an HIV prevalence over 30% (50-54 years: 30.6% (95%CI 19.9-41.2); 55-59 years: 34.6% (95% CI 24.2-44.9)), while women in this same age group have an HIV prevalence of 27% (50-

54years: 26.9% (95% CI 19.4-34.4); 55-59years: 26.8% (95% CI: 19.5-34.0)). Even among the very old age (80 to 84 years old) there are 1.3% of men (95% CI: 0.0 - 3.8) and 1.8% of women (95% CI: 0.0 - 5.3) with HIV infection.

In the SAGE survey, 58% of men (n=7) and 73% of women (n=19) 80 years or older were found to have raised blood pressure levels indicating hypertension. Women over 80 suffered 5 times greater levels of hypertension than women in their 50s (OR = 5.04; 95% CI: 1.7 - 14.9) while there was no significant difference in men (OR = 0.92; 95% CI: 0.1 - 5.5) despite the large confidence interval is very large. This thesis demonstrates "a double curve of mortality" as explained below. The increase in mortality among those in their fifties and sixties is only surpassed by the oldest age group of 80 plus.

4. Gender

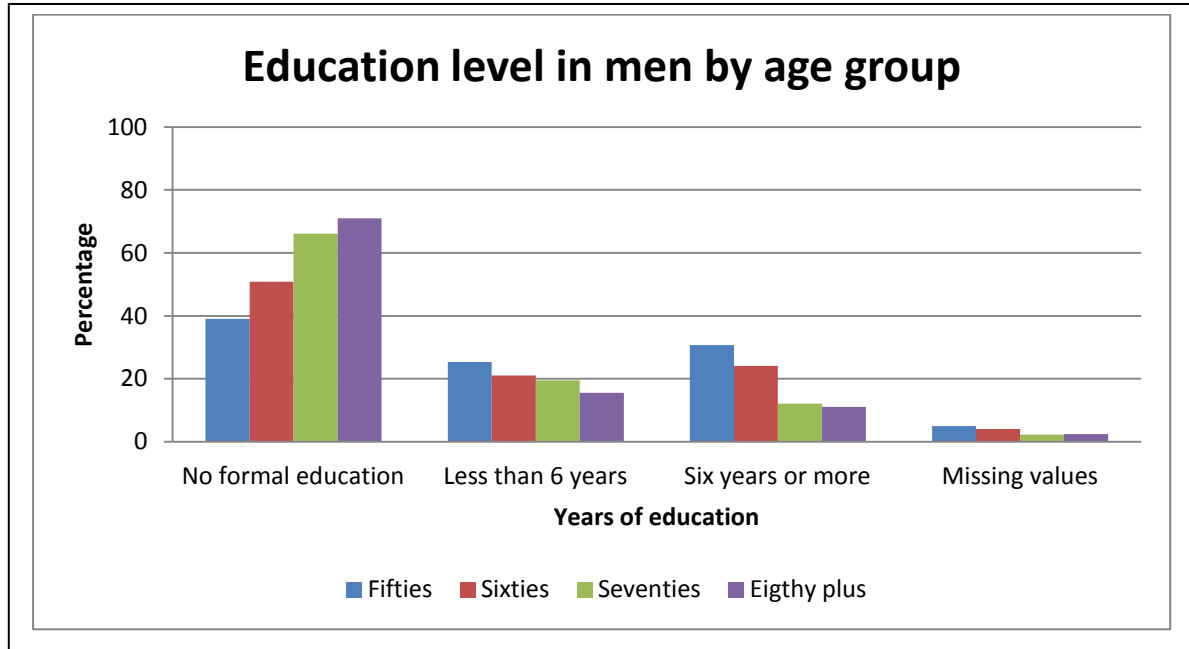
It is apparent that women experience ageing in a markedly different way to men. Older women are more likely to be living with a higher apparent risk of adverse outcomes. Two thirds of women are single, have lower formal education, live in poorer households and have lower levels of employment, all of which are associated with higher mortality. Yet while women suffer higher levels of nearly all risk factors associated with higher mortality, they have a 64% higher survival when compared to men.

Women also report poorer levels of all composite measurements studied. They are more likely to report poor levels of health status (OR = 1.30, 95%CI 1.09, 1.55) and disability (OR = 1.38, 95%CI 1.14,1.66). Women also reported poorer quality of life than men in the univariate analysis, but this effect disappeared when controlling for other variables. By contrast, we did not find significant differences by gender in most of the self-reported health conditions, with the exception of respiratory diseases which are more frequently reported by men ($p = 0.039$), and hypertension for which women report higher levels ($p = 0.001$). When asked about alcohol and tobacco consumption, men reported higher levels of use. Anthropometric measures show that women have a higher BMI ($p < 0.001$) and waist circumference ($p < 0.001$). However, there are no significant differences in levels of measured hypertension by gender ($p = 0.117$). HIV prevalence (though not significant) is higher among men than women from 50 years of age until 69; women surpass men after 70 years of age. Although women do not have a higher prevalence of any objective measure of disease, they report higher levels of health care use ($p = 0.041$).

In studying the association between sleep and mortality, we studied nocturnal sleep problems and diurnal function related to being rested¹. We produced two models: a reduced model with socio-demographic variables only; and a fully adjusted model also including composite measures, depression and anxiety. The reduced model for the association of nocturnal problems with mortality showed that both men and women who reported severe/extreme nocturnal sleep problems have a higher risk of mortality (HR=1.65, 95%CI:1.18-2.31; HR=1.42, 95%CI:1.07-1.88, respectively). However, this relationship was no longer apparent in the fully adjusted model when nocturnal sleep problems are explored. Men reporting severe/extreme difficulty in daytime function experienced a two-fold increase in mortality risk (HR=2.01, 95%CI: 1.32-3.07) in a fully adjusted model but this relationship was not seen in women.

5. Education as predictor of health and mortality and other socio-demographic variables

From all the socio-demographic variables considered in this thesis, education has proved to be the most important predictor of health and mortality. In this sample aged over 50 years, many people have had little or no formal education. This is particularly true of the oldest people in our sample. Moreover, at all ages, women have had less access to education than men (Figure 11).



¹ Sleep problems: refer to the concepts included in the questions used. See Paper 3 page 7. Nocturnal sleep problems: "Overall in the last 30 days, how much of a problem did you have with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning?". Diurnal function: "Overall in the last 30 days, how much of a problem did you have due to not feeling rested and refreshed during the day?"

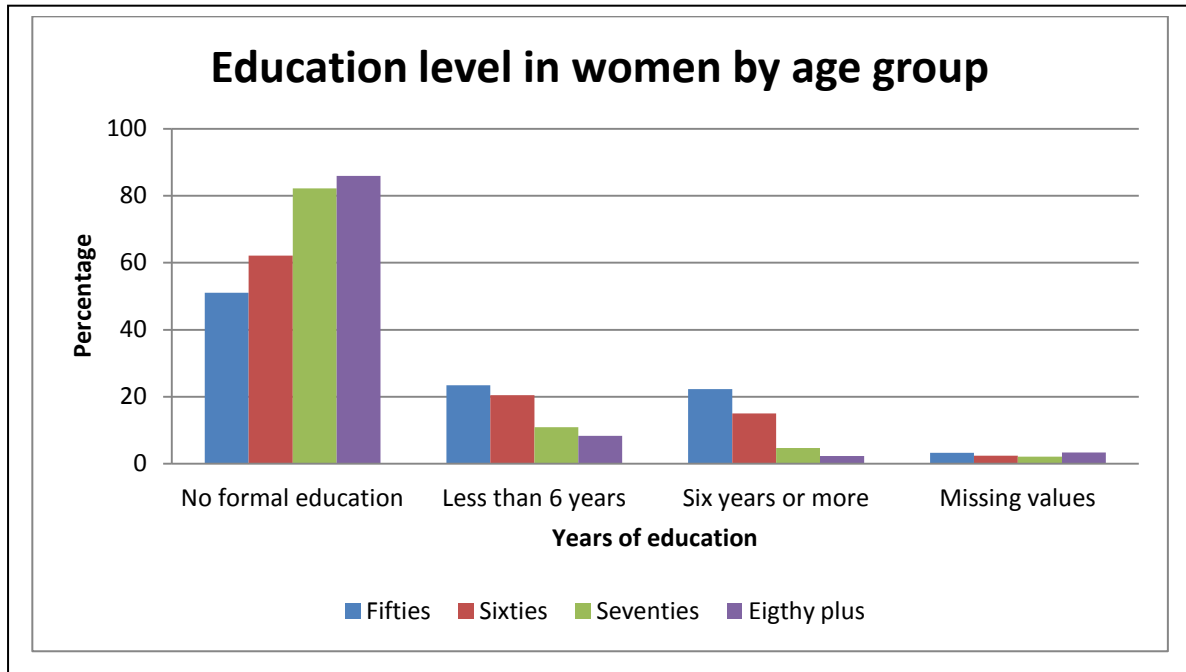


Figure 11. Combined participants' levels of education by age and sex in the Agincourt study site

Those who reported the lowest levels of health status, function or quality of life ($p < 0.001$) reported lower levels of education. In fully controlled multivariate models poorest health status (OR=1.62, 95% CI 1.31 - 2.00), lowest function (OR=1.57, 95% CI 1.26,1.97) and poorest quality of life (OR=1.39, 95% CI 1.11 - 1.73) were all significantly related to educational level.

Women with less than 6 years of formal education had double the risk of hypertension (OR = 2.3; 95% CI 1.1 -4.8) compared with those having higher education. The association with lower levels of education and higher risk of mortality is present in men ($p=0.011$) and women ($p=0.038$) in the unadjusted model, although this relationship was not significant in the Cox proportional hazard analysis. In general, those who have higher education levels have a lower probability of being infected with HIV ($p = 0.028$). Furthermore, those with higher levels of education tend to make more use of health care facilities ($p=0.066$).

Compared to Mozambicans being South African was associated with reporting lower health status and with a greater use of health facilities ($p = 0.005$). Moreover, people of South African origin have a higher risk of being HIV positive ($p = 0.031$).

6. Single questions predicting mortality

Apart from composite measures on quality of life and functionality presented in the papers, there were two simple questions related to "Health status today" and "Difficulty in performing routine work and responsibilities in the previous 30 days" that were not included in the mortality Cox proportional hazard models because the composite measures had a better fit. However, Cox proportional hazard models that exclude composite measures but explore the association of these two simple questions with mortality show a significant association of those single questions with mortality (see Table 9) .

Table 9. Cox proportional hazard model assessing the association of "Health status" and "Difficulty in daily work/activities" with mortality

	Health today Hazard ratio (95% CI)			Difficulty with daily work/activities Hazard ratio (95% CI)		
	General	Men	Women	General	Men	Women
Sex						
Male	Reference			Reference		
Female	0.36 (0.28-0.46)			0.36 (0.28-0.46)		
Age groups						
50-54	Reference	Reference	Reference	Reference	Reference	Reference
55-59	0.88 (0.55-1.40)	1.12 (0.51-2.47)	0.79 (0.45-1.42)	0.92 (0.58-1.46)	1.20 (0.54-2.65)	0.82 (0.46-1.46)
60-64	1.05 (0.67-1.66)	2.02 (0.97-4.20)	0.65 (0.35-1.21)	1.08 (0.68-1.70)	2.04 (0.98-4.26)	0.67 (0.36-1.26)
65-69	1.39 (0.92-2.11)	1.86 (0.93-3.74)	1.20 (0.70-2.05)	1.40 (0.93-2.12)	1.92 (0.96-3.85)	1.18 (0.69-2.02)
70-74	1.08 (0.69-1.70)	1.37 (0.63-2.95)	1.00 (0.57-1.77)	1.10 (0.70-1.72)	1.35 (0.62-2.92)	1.02 (0.58-1.81)
75-79	1.09 (0.70-1.70)	1.18 (0.54-2.61)	1.10 (0.63-1.90)	1.09 (0.70-1.71)	1.15 (0.52-2.53)	1.11 (0.64-1.92)
80-84	1.46 (0.88-2.41)	1.43 (0.57-3.56)	1.52 (0.82-2.82)	1.43 (0.86-2.37)	1.28 (0.51-3.19)	1.57 (0.85-2.90)
85 +	2.78 (1.78-4.35)	3.48 (1.68-7.20)	2.61 (1.45-4.72)	2.69 (1.72-4.21)	3.31 (1.59-6.88)	2.52 (1.40-4.56)
Education status						
More than-6years	Reference	Reference	Reference	Reference	Reference	Reference
Primary or <6years	1.17 (0.77-1.76)	1.21 (0.69-2.12)	1.14 (0.62-2.11)	1.17 (0.78-1.77)	1.22 (0.70-2.13)	1.14 (0.62-2.11)
No formal education	1.20 (0.83-1.74)	1.27 (0.77-2.09)	1.13 (0.65-2.00)	1.22 (0.85-1.76)	1.32 (0.80-2.16)	1.14 (0.66-1.98)
Marital status						
In current partnership	Reference	Reference	Reference	Reference	Reference	Reference
Now single	1.52 (1.18-1.95)	1.46 (1.01-2.10)	1.54 (1.08-2.20)	1.50 (1.17-1.92)	1.45 (1.00-2.09)	1.52 (1.06-2.17)
Socioeconomic quintiles						
Highest (5th)	Reference	Reference	Reference	Reference	Reference	Reference
High	1.20 (0.86-1.69)	1.05 (0.62-1.77)	1.31 (0.83-2.06)	1.23 (0.88-1.73)	1.06 (0.63-1.79)	1.34 (0.85-2.11)
Medium	1.29 (0.91-1.82)	1.29 (0.77-2.14)	1.24 (0.77-2.00)	1.27 (0.90-1.80)	1.28 (0.77-2.13)	1.24 (0.77-1.99)
Low	1.42 (1.00-2.02)	1.79 (1.03-3.00)	1.23 (0.76-1.98)	1.41 (0.99-2.00)	1.68 (1.00-2.82)	1.27 (0.79-2.05)
Lowest (1st)	1.73 (1.22-2.46)	1.61 (0.96-2.70)	1.79 (1.11-2.89)	1.75 (1.23-2.48)	1.64 (0.98-2.76)	1.80 (1.11-2.90)

Health today			
Good	Reference	Reference	Reference
Moderate	1.40 (1.10-1.80)	1.26 (0.85-1.88)	1.54 (1.11-2.14)
Bad	1.86 (1.40-2.46)	2.05 (1.36-3.10)	1.68 (1.14-2.49)
Difficulty with daily work/activities			
None		Reference	Reference
Moderate		1.28 (0.99-1.66)	1.35 (0.91-2.00)
Severe		2.07 (1.58-2.72)	2.02 (1.33-3.05)
			Reference
			1.24 (0.89-1.73)
			2.08 (1.45-2.99)

7. Health care use

Socio-demographic differences in health care use are shown in Paper 2. More than 80% of people who indicated being told that they suffer from diabetes, hypertension, depression or lung disease reported having taken medication at some time during the last 12 months. Note that this is not a measure of complete treatment or compliance with chronic medication but rather a proxy measure of contact with health facilities related to their disease. Public health care (81%) was far more frequently used than private care (19%). Importantly, a minority (13%) of the population was responsible for 48% of all reported visits to health care in the past twelve months, possibly representing those with chronic diseases that use health facilities more frequently. There were 28 (33%) individuals who reported having one of the above mentioned chronic conditions but never needing care.

When exploring health care use of older people we did not find any significant difference trends in use with age despite the fact that those who reported higher disability ($p = 0.001$) and lower quality of life ($p = 0.001$) reported higher use of health facilities. At present I do not have any data to support potential factors that may affect health care use. With respect to gender differences, women reported greater use of health facilities than men ($p = 0.041$).

8. Clinical conditions determining health care need

I. Risk factors and awareness of hypertension

Hypertension has been shown to be the most frequent chronic condition affecting the health of this older population. This together with the HIV impact, explained below, provides evidence of a double burden of chronic diseases in this older population.

When measured in the SAGE survey in 2006, 57% of the population could be classified as hypertensive. Four years later in the HIV/NCD study, the prevalence of hypertension was 61% suggesting an increase in the hypertension prevalence. A third of this older population reported that they had high blood pressure. Women are more aware; 54% with hypertension reporting it, compared to 31% of men ($p = 0.025$)¹. In general, 44% (112/255) of those who reported normal blood pressure were actually hypertensive. Unawareness of a hypertension condition among those who were measured as hypertensive was 52% (112/215). From the 215 participants identified as having hypertension, 63 (29%) reported being on treatment and only 30 of them (47.6%) had blood

¹ These results are different from those presented in paper 2. A corrigendum was published in the journal (Glob Health Action 2014, 7: 24080 - <http://dx.doi.org/10.3402/gha.v7.24080>)

pressure controlled. This means that only 14% (30/215) of hypertensive participants had blood pressure controlled.

Risk factors for hypertension in our sample differ in men and women. In the multivariate analysis risk factors for men are larger waist circumference and current consumption of alcohol (OR 5.2; 95% CI 1.5-18.1). Women presented higher risk of hypertension with higher waist-hip ratio (OR 2.7; 95% CI 1.4-5.2). Other factors like age (with a U-shape relationship) and education were inconsistently associated with hypertension in women. Women have significantly higher BMI ($p < 0.001$) and waist circumference ($p < 0.001$) than men but women do not suffer significantly higher levels of hypertension than men ($p = 0.117$).

Some of these risk factors have changed in the short period of four years as shown in two independent studies: SAGE survey in 2006 and an HIV/NCD study in 2010 - 2011 (see Table 10). Factors that have increased are abdominal obesity (although not significantly) and alcohol consumption (which has increased significantly in men). The proportion of participants with high waist/hip ratio has significantly decreased in men and women, as has the mean BMI. On the other hand, hypertension prevalence has increased for both sexes, significantly in women.

Table 10. Cardiovascular risk factors for Adults 50 years and older*

Indicator	Adults 50+ yrs 2006 N=425		Adults 50+ yrs 2010/11 N=1475	
	Male	Female	Male	Female
	N=136	N=289	N=602	N=873
	% (95% CI)	N (95% CI)	% (95% CI)	N (95% CI)
Mean age (years)	65.4	64.8	66.9	65.7
Abdominal obesity	27.9 (20.3-35.6)	74 (69.0-79.1)	34.4 (30.6-38.2)	84.2 (81.8-86.6)
High waist / hip ratio level	73.5 (66.0-81.0)	81.0 (76.4-85.5)	60.0 (56.0-64.0)	71.9 (68.8-75.0)
Body mass index (mean)	25.5 (24.4-26.6)	29.4 (28.6-30.3)	23.5 (23.1-23.9)	27.4 (26.9-27.8)
Raised blood glucose			5.1 (3.3-6.9)	5.3 (3.8-6.8)
Ever smoked	53.8 (45.2-62.4)	26.9 (21.8-32.1)	43.1 (39.1-47.1)	3.1 (1.9-4.2)
Consumed alcohol in the 30 days previous to interview	37.8 (29.5-46.1)	13.5 (9.6-17.5)	51.4 (46.8-56.0)	11.6 (9.3-14.0)
Hypertension	56.9 (47.7-66.0)	56.7 (50.6-62.7)	63.8 (60.0-67.7)	67.5 (64.4-70.6)
HIV positive			16.3 (13.2-19.3)	14.0 (11.7-16.4)

Abdominal obesity: Men equal or over 102cm. Women equal or over 88cm. **High waist/hip ratio:** Men over 0.90. Women over 0.85. **BMI:** Underweight <18.5; Normal weight 18.5-24.9; Overweight = 25-29.9; Obese ≥ 30. **Alcohol consumption:** Consumed alcohol in the 30 days previous to interview. **Hypertension:** Systolic BP ≥ 140mmHg or diastolic BP ≥ 90mmHg or on hypertensive treatment. **Raised blood glucose:** random blood glucose >11 mmol/l

The study did not have information on target organ damage or associated clinical conditions which are necessary to identify high and very high added risk of CVD. For this reason overall risk may have been underestimated. Even with this underestimation 56% of the population 50 years and older (57% men vs. 55% women) are at moderate or greater risk of cardiovascular disease as result of their hypertension and other risk factors. Table 11 below shows these results by sex and age group.

Table 11. Prevalence of "moderate or greater added risk" by age sex group in the Agincourt population, 2010

Age group	Men			Women		
	N with condition	Total N	%	N with condition	Total N	%

50-59	76	156	48.7	129	248	52.0
60-69	124	197	62.9	139	256	54.3
70-79	73	122	59.8	76	134	56.7
80+	49	89	55.0	60	95	63.2
Total	322	564	57.1	404	733	55.1

II. HIV prevalence

Paper 4 shows the importance of the HIV epidemic in this older population affecting all aspects of their lives. The HIV epidemic has affected their household structure, responsibilities in the family and, by extension, in the community and, of course, their own health. At the time this work was done, ART was not easily available in this rural setting so HIV infection was directly related to higher morbidity and mortality.

The direct measurement of HIV status gave a general prevalence of 16.5% for the population 50 years and older. Prevalence is still over 30% for men and over 25% for women in their 50s and higher than 10% in men and women up to age 70 years. Overall, the population aged 50 plus has an HIV prevalence of 16.5% (17.7% in men and 16.1% in women).

Understanding the sexual behaviour of older people will help us understand the epidemiology of HIV in this age-group. That is, to understand whether older people get infected at early ages and survive longer, or get infected at older ages. Both explanations would fit the surprisingly high rates of HIV infection up to 70 years of age. Findings suggest that older men are more likely to be sexually active than older women and also to have extramarital partners. Those that are HIV positive are more likely to have used condoms during last intercourse. However, only around 60% of women and 66% of men report being tested for HIV in the last 5 years. Discussing HIV with a partner is still uncommon, with less than 5% of older people knowing the status of their last partner, independent of HIV status or sex (125).

Mortality related to HIV peaked in 2006 when most of the data reported in this thesis was collected. Since then mortality has declined slowly with the introduction of ART, although HIV remains the primary cause of death (see Figure 12).

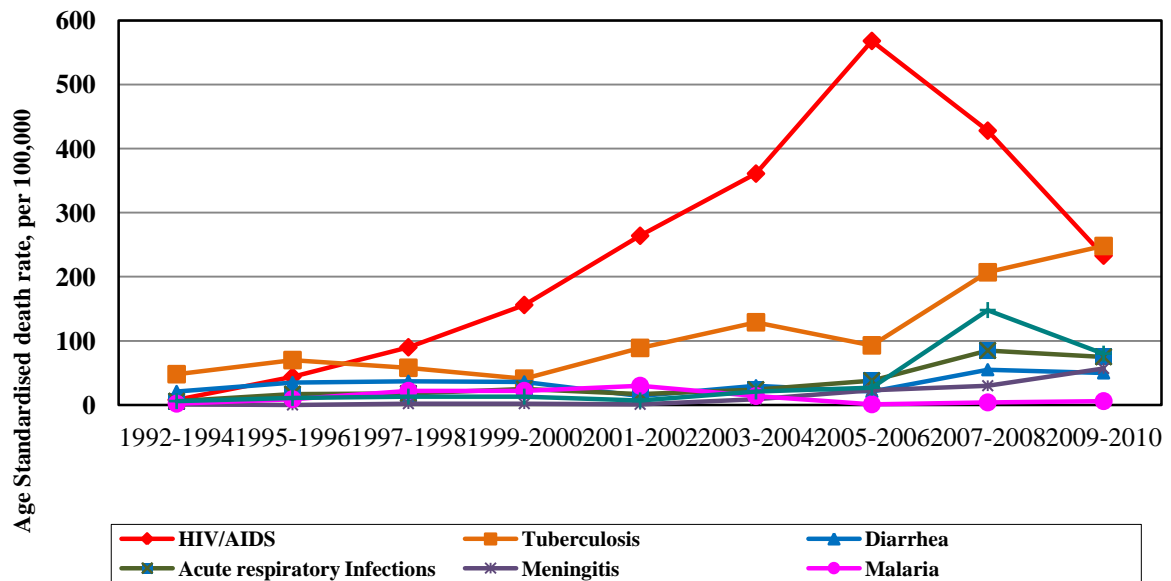


Figure 12. Trends in cause specific mortality in Agincourt, 1992 to 2010. Selected infectious and parasitic causes of death

Figure: Michel Garenne, October 2011 (unpublished)

We investigated the cause of the 377 deaths, determined by verbal autopsy, that occurred in the SAGE survey population during 3 years of follow-up (see paper 5). There were 21 deaths (5.6%) due to diabetes, 21 (5.6%) to hypertension, 45 (11.9%) to stroke, 25 (6.6%) to heart failure, 35 (9.3%) to neoplasm and 78 (20.9%) to HIV. The death rates from HIV decreased with age while NCD increased in older ages(119).

G. Discussion

This thesis focuses on the population aged 50 years and older; a group which has been largely ignored in the past. The data in this thesis fills part of a gap in knowledge about the wellbeing, health problems, survival and use of health care in an older rural African population.

1. Strengths

The great strength of this thesis is that the work is based in a Health and Demographic Surveillance System site with longitudinal follow-up and excellent quality control. The surveillance system gave me access to a long history of longitudinal data, such as socio-demographic variables of each participant, that are difficult or impossible to get otherwise. The longitudinal system ensured little loss to follow-up among the participants followed for three years. Moreover, the existence of population-based information allowed me to estimate prevalence rates at a population level. Trust between the community and research team after so many years of working in the site was rewarded with very high response rates when the person was found at home. Data quality was assured with different levels of quality control at the field level and validation checks at data entry level. Data entry was done by a group of well trained data typists with many years of experience. Double entry system was used for the HIV/NCD study.

This thesis uses data on probable cause of death collected through verbal autopsies. In settings where people do not know the cause of death of their family members, verbal autopsies offer the possibility to establish the relationship between specific diseases and the change in death rates across age-groups.

We report an unusual peak in mortality in the population 50 to 70 years compared to the older population aged 70-79. We do not believe that this double peak in mortality is due to errors in the reported age. Most of the population has a national ID which includes the date of birth. This has allowed us to collect reliable data on date of birth even at older ages.

2. Weaknesses

Three issues should be considered. Firstly, whether the samples used for this thesis are representative; secondly, whether the data, especially the self-reported data, is sufficiently valid; and, thirdly, whether the failure to adjust for health behaviours such as smoking and exercise and BMI has affected our results.

The population from which the samples were drawn for this thesis was the population permanently living in the study site. This meant that labour migrants (who spend 6 months or more each year away from the study site) were excluded. Migrant population are exposed to different risk

factors to the permanent population and their use of the health facilities in the study area is limited to the short periods of time they visit their families. Because the majority of labour migrants are men, women are over-represented in the study sample. Labour migrants return home when they feel sick and need health care. This phenomenon has been phrased as "returning home to die" (120). This could introduce a selection bias, with more sick people easily accessible for an interview at home. However, we excluded from the samples anyone who had not been permanently resident in the site for 12 months before the interview, so this is unlikely to be an important source of bias. In all three samples, it proved difficult to find certain people at home to be interviewed, despite returning three times. Those missing from the study for this reason were more likely to be men, younger, employed and with higher levels of education. Their absence from the studies may have biased our samples towards less healthy people.

Parts of the thesis are based on analysis of self-reported health status which we did not corroborate with objective measures except for hypertension. Although this is not ideal, it was the best way available to collect health information in a population without clinical records. Everything indicates that many of those affected by chronic diseases are unaware of their condition and so our results, if anything, would be an under-report of the actual situation of chronic diseases in this population. In the case of hypertension, where we were able to corroborate self-reports with objective measurement, the comparison of the two sources of data provided new information on the large number of people who were unaware of having the condition. This has implications for the way in which hypertension management should be addressed.

We did not have reliable information on smoking and alcohol consumption because there is no specific question that measures a consumption that is not common in these communities. Cigarette consumption is linked to personal income, that is, people will smoke when they have spare cash to purchase them. Alcohol is often brewed at home which does not give easy, commercially measurable quantities. In papers 1, 3 and 5 we did not take anthropometric measurements.

3. Active ageing

In their ageing policy framework in 2002 the World Health Organization defined "*active ageing*" as "the process of optimising opportunities for health, participation and security in order to enhance quality of life as people age" (4). Social participation is an important aspect of active ageing. Older people in South Africa are facing a new family and social reality due to the HIV/AIDS epidemic. The traditional family organisation that supported older people has shifted so that there is an increasing burden of family responsibilities in the older population. The Mpumalanga Older People's survey (2004) showed that older people were the main breadwinners in three quarters of

multigenerational households, half of older people's households were supporting children or grandchildren and this support was given even by those up to 80 years of age (126). Support is mainly given by older women who have become the main resource for younger generations. As described by Schatz, women are facing the additional family burden of looking after sick children, fostering children and adopting family orphans (127). At the same time they have become the breadwinners in many families as a result of their old age grants (128).

Agincourt population is experiencing an increase in the percentage of older people which is especially true for women. It is, therefore, expected that older people, and mainly women, will take a more active role in the day to day life of this society. However, due to the HIV epidemic which has caused and still causes the death of many young adults, who leave behind many orphans, there has been an abrupt change in their responsibilities in their families and communities. This situation increases the burden of responsibility on older people, particularly women (127). Older women are now responsible for looking after their sick children and their orphan grandchildren. This brings extra costs for health, transport, food, and school fees. Fortunately, South Africa has an old age pension and a child grant system that helps these families to cope with the situation where there is no bread winner at home (128, 129). Even with that support many families have been obliged to depend on wild natural resources as a buffer for their impoverishment and hunger(130).

As people age, it is expected that there will be a decline in health (131) with an increase in non-communicable diseases that may come together with higher frailty and disability (4). This is especially important in the South African context where the population over 80 will nearly double in the first quarter of this century (132) and where, by 2050, it is expected that they will represent as much as 20% of the older population (19). Arthritis, stroke and diabetes, all highly prevalent in Agincourt, are correlated with higher disability and lower mobility especially in those over 80 years of age. In India, self-reported bad or very bad health was associated with higher mortality (133). In Agincourt a relationship between higher mortality and poorer quality of life, lower reported function, lower socio-economic status and poorer education was found. Preventive interventions to diminish the prevalence and impact of chronic diseases at older ages will increase the well-being and quality of life of the older population, improving their ageing experience and increasing the number of years with good quality of life. In addition, the introduction of rehabilitation services, especially for those with stroke, may also improve their quality of life. In this sense there is already an increasing debate among researchers, journal editors, and representatives of non-governmental organisations on the importance of promoting a proper ageing process where older people can continue enjoying an active and healthy life (134, 135).

Older people can be a resource for and can participate in family, social and work life supporting those that have the main responsibilities. Complex co-morbidities, lack of function, deteriorating wellbeing and quality of life can jeopardise this great potential of a longer life and have to be well defined and studied. Brändström has argued that a multidisciplinary effort is necessary for a better understanding of the implication of population ageing. This would involve medical, social, behavioural and humanistic researchers (136).

4. Gender

The higher number of women than men in the settled rural population, which is especially the case in those over 50 years of age, has been explained mainly as a gender difference in the temporary circular migration pattern (116). However, the different mortality experience, discussed below, also impacts on the demographic distribution of the sexes.

The results from this rural setting have demonstrated that men and women have different experiences of old age and the ageing process. Firstly, women considerably outnumber men in these older age groups. Secondly, women carry a much greater responsibility for providing care. Thirdly, the pattern of ill health varies, including lung disease, HIV infection and knowledge of a person's hypertension diagnosis. Finally, although women overall report poorer health and quality of life (both factors related to higher mortality) they enjoy much better survival than men. It is important to understand these differences and study how they affect the ageing process and the society in which the men and women live. Understanding the gender differences will provide information to guide the development of new interventions and policies for the optimum care of older people.

We did not find many differences by gender in self-reported morbidity apart from lung diseases, reported more by men, and hypertension, reported more by women. A possible reason for higher lung disease prevalence in men is the higher prevalence of smoking. However, men in this area cannot afford to smoke every day and buy a few cigarettes when money is available (38). Work related out-migration to mines and agricultural fields is another possible explanation (137) due to the fact that working in mines and on agricultural farms may have increased their exposure to silica (138) or quartz which may affect their respiratory capacity (139, 140). It is also well established that working conditions in these settings may increase the risk of TB transmission(141).

The DHS-1998 (142) and South African National Health and Nutrition Examination Survey (143) show that South African women are generally more aware of their hypertensive condition than men. Our SAGE survey also shows higher awareness in women. Among the black community in the national DHS-1998, 64% of women and 32% of men were aware of their condition, while we found an awareness level of 54% in women and 33% in men which are very similar to the national levels.

The higher awareness in women may be explained by higher use of health care (144). This corroborates other findings that women are more likely to have been diagnosed, be on treatment and have blood pressure under control than men(57).

The distribution of risk factors differs by gender. In this thesis, although women have a much higher BMI than men, this is not reflected in different levels of hypertension by gender. This confirms the results of the South African Stroke Prevention Initiative study (SASPI) done in 2002-3 in the same area (38) and corresponds with findings from the SANHANES-1 study (143). However, contradictory findings come from the South African 1998 Demographic and Health Survey (DHS-1998) which showed that obese black women had nearly double the risk of hypertension than non obese black women, and that women had a lower risk of hypertension than men (68).

In general, women present higher levels of factors significantly associated with mortality (higher levels of disability and poorer health status) than men. Nevertheless, women had 64% higher chances of survival than men. This paradox, where women report worse health and function and have higher need of health care than men, but enjoy lower mortality was already described for Western countries as early as 1975 (145). There have been many attempts to explain what has been called the "gender paradox" or the "male-female health-survival paradox". Nathanson offered three possible explanations: i) women may have more illness than men due to the stress of their social roles; ii) it may be culturally more acceptable for women to be ill; or iii) it may be that the sick role fits with other roles and responsibilities that women have (145). There have been other theories to explain this paradox drawing on biological, psychological and social approaches (146). Ballard compares men to oaks, strong until a breaking point, while women behave like reeds "able to survive despite an accumulation of health deficits" (147). Other authors refer to women accumulating lower levels of risk factors such as smoking during the life course (148). In summary, better survival in women combined with worse reported health has been observed in high income countries but with no definitive explanation. There has only been limited attention to this paradox in LMICS (131, 149, 150).

5. Quality of life and levels of disability as predictors of mortality

As people get older physical and cognitive function and quality of life may decline. However it is not inevitable that a decline in function will be associated with a decline in quality of life. Many very old people in this study reported good quality of life even with considerable limitation of function. Both limitations in function and decline in quality of life were associated with increased mortality.

While there is evidence that quality of life is worse in those aged over 70, participants in their sixties report better quality of life than in the younger group aged 50 to 59. This may have two possible explanations. Schatz et al have argued that older people, especially women, report a better quality of life after reaching pension age(151). They describe this as the old adult pension "honeymoon effect". On the other hand and as described elsewhere in this thesis, the younger age groups are suffering from higher levels of HIV (120) and higher related mortality (119) which may account for their lower quality of life.

In this thesis I have shown that simple questions on difficulty of daily life and on health status are significantly associated with higher mortality. Single questions are easy to use in day to day clinic work and so may be useful to identify those older people in more need of care and attention. This will complement a more academic use of the three composite measurements under study in this thesis (health status, WHOQOL, WHODAS) which are also directly related to lower survival.

Lower levels of formal education have been associated with lower levels of self reported health, quality of life and functionality, together with higher prevalence of HIV infection and higher risk of mortality. These results show the importance that ensuring access to education for all may have in health and mortality for coming generations.

Although the population of Mozambican origin in the study site are poorer, have less employment and are socially more isolated, due to lack of official documentation, than their South African neighbours (107, 152), they report better health status (35). It may be that this is a healthy immigrant selectivity effect (35, 153). However, this better health status can also be related to the lower levels of HIV prevalence found in this population of Mozambican origin(120).

In paper 3 we have shown that men who reported not feeling rested and refreshed during the day experienced a two-fold increased risk in all-cause mortality (124). This relationship was not apparent in women. Although any explanation of sex differences can only be speculative given the scope of existing information, worth considering is that more men than women are infected by HIV (120), there is a higher burden of undiagnosed non-HIV chronic diseases in men, and higher use of alcohol in men all of which could contribute to somnolence during daytime.

6. Health care use

More than 80% of those who reported a chronic health condition had used PHC in the last year and it can be expected that as the older population increases there will be an increased demand for PHC.

Women are more frequent users of health care. Although reasons may depend on different cultures and diseases suffered (154, 155), it may also be explained by the early and continuous contact of women with health services due to pregnancy and seeking care for their children resulting in more familiarity with health services and hence more willingness to use them later in life. Further, men appear more reluctant to accept that they are sick, and also to ask for help (146, 156).

Individuals with Mozambican nationality of origin use health care less frequently than those of South African origin. This could be related to the lack of documentation providing entitlement to health care among Mozambicans. However, two thirds of Mozambican people in the study site now have South African ID cards. A further explanation may be the lower level of HIV prevalence among those of Mozambican origin.

Unexpectedly, we did not find any association between being in the oldest age group and higher health care use. Apart from the difficulty of access, another possible explanation is that the HIV epidemic, one of the main reasons for people feeling sick and accessing care, is affecting mainly people in their 50s and 60s. This demand for care could exceed the need for health care in the older age-groups.

7. Non-communicable diseases

We estimated population level prevalence of chronic conditions by asking people to report whether they had ever been diagnosed with certain conditions. We were not able to confirm the reported diagnosis because at the time there were no records kept in the clinics. The three most frequently reported chronic conditions were musculoskeletal pain, hypertension and diabetes (39). Similar findings come from the Global Burden of Disease where musculoskeletal disorders account for 7% of the disability-adjusted life years (DALY) and are one of the six main causes of DALYs in older people together with CVD, diabetes, chronic respiratory diseases, cancers and digestive diseases (157).

The overall prevalence of hypertension in the Agincourt population 50 plus in 2010 was 67%. It is alarming that, in a situation where two thirds of the older population are suffering from hypertension and more than fifty per cent of older people are at moderate or greater risk of cardiovascular disease, only a third of them report having high blood pressure and over 50% of hypertensive people regard themselves as having normal blood pressure (representing a negative predictive value of 43.9%). Our results are comparable to those reported in the South African national SAGE study, also in population 50 years and older (62). In this study a third of black participants reported having high blood pressure, the same as in our study, with a measured prevalence of hypertension of 75%, higher than in the Agincourt study site population possibly

because the national SAGE included urban, as well as rural areas, where the prevalence of hypertension is known to be higher(57, 158).

The Agincourt population is suffering a double burden of HIV and NCD's. HIV/ TB were responsible for 21% of the 377 deaths that occurred among SAGE survey participants compared with the 112 deaths (30%) from cardiovascular causes and diabetes. In the next section I discuss the contribution of HIV/TB to the burden of disease and new challenges and demands involving older people.

8. The impact of HIV

In paper 4 we have shown how important HIV infection is in the population 50 years and older in this rural setting where nearly a fifth of older people are HIV positive with rates above 10% through to age 70. Moreover, in paper 5 we show that HIV is also impacting the mortality risk, especially for those in their 50s and 60s, creating a double peak of mortality. The high HIV prevalence and potential high HIV mortality rates in this older population may have a negative impact on South African, and other southern African countries progression, into the later stages of the demographic and epidemiological transition, as suggested by Caselli (18).

Different reasons, such as a greater focus on antenatal data and prevention of mother to child transmission and the belief that HIV is mainly an epidemic affecting only young adults have excluded the older population from HIV reports both in the South African (80) and the international arena (159, 160). Our data support those voices that have drawn attention to the fact that older people are neglected in the fight against AIDS (161, 162). The older population has responded to the consequences of the epidemic by increase care for their descendants, at the same time that they lose support from their adult children (163). This situation is changing with increasing concern in this population about their own risk of infection (163). This concern is becoming a reality with a rising prevalence of HIV infection in the older population, possibly due to the increased availability of ART (164). In combination this appears to lead to a decrease in well-being and functionality in African older population (165, 166) as I have also described in paper 5. Moreover, we describe in paper 4 that Agincourt HIV prevalence in older people is higher than reported in Kwa-Zulu Natal, the South African province with the highest HIV prevalence. With this thesis I join the call of many authors to realise the importance of taking into account this older group in all HIV discussions and policy planning due to their increasing contribution to the overall number of people infected by HIV (75, 165).

9. Implications for policy, practice and future research

The findings presented raise the need for new research to address unresolved issues. This work also allows for policy recommendations to tackle current health problems facing the older adult population.

I. Policy

Low levels of awareness about hypertension indicate a need for health education at all levels which include health professionals, patients and the general population. All need to understand the importance of measuring blood pressure regularly in adults and especially in older adults given the high prevalence of hypertension. Special emphasis is needed at PHC level to enhance active screening in all adults in order to identify early both patients with hypertension and the population at hypertensive risk. This requires training and appropriate supervision of health professionals. Moreover, and as shown in a previous study in the Agincourt study site, there is an urgent need for working blood pressure machines at PHC level with adequate cuffs for all body types (167). This speaks to the need for national and provincial health policies that include screening, awareness and proper maintenance of blood pressure machines equipment.

With population ageing and the high prevalence of HIV South Africa will likely see a dramatic increase in the burden of chronic diseases over coming decades (55). Interventions at a local level are necessary to prepare PHC services to cover the increasing demands for chronic care. Older people are suffering not only from NCDs like hypertension, diabetes and musculoskeletal pain but also from HIV/AIDS, an infectious condition which has become chronic following the introduction of ART (168). This means that older people need to be treated taking account of their co-morbidities. Multi-sectoral efforts in this direction could have a high impact on extending healthy life in rural populations at older ages.

II. Practice

In September 2011 the evolving NCD epidemic in South Africa was made a priority after the Minister of Health convened a national Summit on the Prevention and Control of NCDs (169). National leaders highlighted the urgency of dedicating resources “to reduce the incidence and mortality from non-communicable diseases” and proposed interventions to reduce risk factors and improve the control of those already suffering any of the chronic conditions.

It is of enormous interest to society to ensure that people with chronic diseases receive continuous care together with the introduction of primary and secondary prevention programmes. For those on treatment, it will be necessary to enhance counseling on lifestyle change and create

proper follow-up systems, similar to those for patients with HIV in antenatal care services (30, 170). The goal is to increase treatment adherence possibly by including lay health workers in the existing Primary Health Care system who could accompany patients through the assessment and treatment process in the clinics. To accomplish these important objectives and strengthen the PHC system, the Department of Health in South Africa is piloting an integrated chronic care system in three districts (including Agincourt) and has developed the "re-engineering" approach for Primary Health Care systems (171). This very important step in the organisation of PHC, is still in the implementation phase and will need proper collaboration between the different stakeholders, training of sufficient community health workers and an effective monitoring and evaluation system to achieve success.

As described, lower SES and education levels are associated with higher mortality in adults. This finding reinforces the need for policy change and political efforts to strengthen formal education levels and fight poverty.

III. Future research

There are important issues related to the double burden of disease and the still unfolding HIV epidemic in older people that remain unresolved. It will be necessary to investigate whether and how the HIV and NCD epidemics interact. Further, and in order to control the HIV epidemic in older people, it is important to understand whether they are infected at younger ages and survive longer or whether infection occurs at older ages. Early infection would explain high mortality in the fifth decade of life, while late infection would explain why we still find a high percentage of the older population infected in their late 60s and without easy access to ART. It is, therefore, essential to conduct research on sexual behaviour of older people and time of sero-conversion to explain the HIV epidemic in this population. Cohort studies of those known to be HIV negative in their 40s and 50s, with repeated annual HIV tests, together with quantitative and qualitative methods exploring sexual behaviour in older populations would help to disentangle this question.

HIV prevention studies should also include awareness of HIV infection, utilisation of services, treatment uptake and adherence to ART. It is important to investigate how ART rollout will impact on older people's survival and the implications for their family responsibilities (including those under their care) and in society.

Considering the high proportion of older persons that are unaware they suffer from chronic conditions, it is vital to undertake new research on how to raise awareness among this population. With an improvement in awareness and the expected rise in chronic conditions in the older population further research on how to improve access to treatment will be needed.

All of this underlines how important it is to consider older people in policy planning and in research on HIV and NCD prevention and treatment programmes. Equally, it is essential to prepare PHC systems to serve the growing population of older people with chronic diseases.

H. Conclusions

The data presented in this thesis show that in this quite typical rural setting, the total population over 50 years of age has increased in the past decade, hypertension is increasing and the HIV epidemic is far more prevalent than expected.

Hypertension is increasing in the older population and this needs attention at both prevention and treatment levels in order to reduce avoidable deaths and expense treating those with stroke and other CVD. In our study area the increase in hypertension, affecting both men and women, especially the latter, has taken place over a short period of time. However, women are more aware of their condition and consequently seek health care more frequently than men.

HIV infection in older populations has been neglected in the past mainly due to a focus on those between 15 and 49 years of age. Our data show that HIV infects nearly 20% of the older population and consequently every policy on HIV prevention and treatment should include those over 50 years of age even in rural areas.

This double burden of NCD and HIV in an increasingly ageing population may well have a serious impact on the already weak Primary Health Care system. The South African government initiative to re-engineer the PHC system is encouraging but still needs to be fully implemented and evaluated before we can say that PHC is prepared for the coming expansion in demand for care.

We have observed interesting differences in how women and men experience the ageing process. At the same time that women become caregivers of and breadwinners for their children and grandchildren, they report poorer health status, function and quality of life (though to a lesser degree), higher levels of hypertension and present with most risk factors for higher mortality. However, women survive longer than men showing that, as in high-income countries, this rural setting also presents the male-female "survival paradox" which needs further investigation.

The association of WHO quality of life and WHO disability assessment scale with higher mortality and higher health care use raises the question of whether these composite measures could be a good way to assess expected health outcomes in older populations. However, these composite measurements would be impractical to use in daily clinical life, so we have assessed how much single questions on self-reported health and function serve the same purpose. In our analysis, we showed that those single questions are good predictors of mortality and, consequently, may be a good indirect approach to assess health status. Further research would help to fully respond to this question.

The MRC/Wits Agincourt Unit is in an exceptional position to develop and evaluate the potential impact of new interventions on health and wellbeing of the older persons in the future. This is because the Unit is based in a HDSS study site where older people, their health seeking behaviour and interventions at health facility and community level can be monitored through time.

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J. References

1. World Health Organization. The Global Burden of Disease: 2004 Update. 2008.
2. Ackland M, Choi BC, Puska P. Rethinking the terms non-communicable disease and chronic disease. *Journal of epidemiology and community health*. 2003 Nov;57(11):838-9. PubMed PMID: 14600102. Pubmed Central PMCID: 1732319. Epub 2003/11/06. eng.
3. Unwin N, Epping Jordan J, Bonita R. Rethinking the terms non-communicable disease and chronic disease. *Journal of epidemiology and community health*. 2004 Sep;58(9):801; author reply PubMed PMID: 15310808.
4. WHO. Active Ageing: A Policy Framework. Geneva. 2002.
5. Rattan SI. Healthy ageing, but what is health? *Biogerontology*. 2013 Dec;14(6):673-7. PubMed PMID: 23852043.
6. Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. *Milbank Mem Fund Q*. 1971 Oct;49(4):509-38. PubMed PMID: 5155251.
7. Omran AR. Epidemiologic transition in the United States: the health factor in population change. *Popul Bull*. 1977 May;32(2):1-42. PubMed PMID: 12335110.
8. Omran AR. A century of epidemiologic transition in the United States. *Prev Med*. 1977 Mar;6(1):30-51. PubMed PMID: 322119.
9. Olshansky SJ, Ault AB. The fourth stage of the epidemiologic transition: the age of delayed degenerative diseases. *Milbank Q*. 1986;64(3):355-91. PubMed PMID: 3762504.
10. Rogers RG, Hackenberg R. Extending epidemiologic transition theory: a new stage. *Soc Biol*. 1987 Fall-Winter;34(3-4):234-43. PubMed PMID: 3451366.
11. Omran AR. The epidemiologic transition theory revisited thirty years later. *World Health Statistics Quarterly*. 1998;51:99-119.
12. Pearson TA. Cardiovascular disease in developing countries: myths, realities, and opportunities. *Cardiovasc Drugs Ther*. 1999 Apr;13(2):95-104. PubMed PMID: 10372224.
13. Caldwell JC. Demographers and the study of mortality: scope, perspectives, and theory. *Ann N Y Acad Sci*. 2001 Dec;954:19-34. PubMed PMID: 11797858.
14. Gaylin DS, Kates J. Refocusing the lens: epidemiologic transition theory, mortality differentials, and the AIDS pandemic. *Soc Sci Med*. 1997 Mar;44(5):609-21. PubMed PMID: 9032829.
15. Beaglehole R, Bonita R. *Public Health at the Crossroads. Achievements and Prospects*. Second Ed: Cambridge University Press ed2004.
16. Gribble JN, Preston SH, eds. *The epidemiological transition: Policy and planning implications for developing countries*: Washington DC: National Academy Press; 1993.
17. Caldwell JC. Population health in transition. *Bull World Health Organ*. 2001;79(2):159-60. PubMed PMID: 11242823.
18. Caselli G., Meslé F., Vallin J. Epidemiologic transition theory exceptions. *Genus*. 2002;58(1):9-51.
19. United Nations. *World Population Ageing: 1950-2050*. New York 2001. United Nations publication Sales No. E.02.XIII.3 2001.
20. Puoane T, Tsolekile L, Sanders D, Parker W. Chronic non-communicable diseases. In: Barron P, Roma-Reardon J, editors. *South African Health Review 2008*: Durban: Health Systems Trust; 2008. p. 73-87.
21. Steyn K, Levitt NS, Patel M, Fourie J, Gwebushe N, Lombard C, et al. Hypertension and diabetes: poor care for patients at community health centres. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2008 Aug;98(8):618-22. PubMed PMID: 18928041. Epub 2008/10/22. eng.
22. Coovadia H, Bland R. From Alma-Ata to Agincourt: primary health care in AIDS. *Lancet*. 2008 Sep 13;372(9642):866-8. PubMed PMID: 18790293. Epub 2008/09/16. eng.

23. Timaeus IM. Impact of the HIV epidemic on mortality in sub-Saharan Africa: evidence from national surveys and censuses. *AIDS*. 1998;12 Suppl 1:S15-27. PubMed PMID: 9677186. Epub 1998/07/24. eng.
24. Tollman SM, Kahn K, Garenne M, Gear JS. Reversal in mortality trends: evidence from the Agincourt field site, South Africa, 1992-1995. *Aids*. 1999 Jun 18;13(9):1091-7. PubMed PMID: 10397540.
25. UNAIDS. Report on the global HIV/AIDS epidemic 2008. WHO Library Cataloguing-Publication Data. UNAIDS/08.25E / JC1510E.
26. Logie D. AIDS cuts life expectancy insub-saharan Africa by a quarter. *BMJ*. 1999 Sep 25;319(7213):806. PubMed PMID: 10496819. Pubmed Central PMCID: 1116661. Epub 1999/09/25. eng.
27. Ogunbodede EO. HIV/AIDS situation in Africa. *International dental journal*. 2004 Dec;54(6 Suppl 1):352-60. PubMed PMID: 15631096. Epub 2005/01/06. eng.
28. Johnson LF, Mossong J, Dorrington RE, Schomaker M, Hoffmann CJ, Keiser O, et al. Life expectancies of South African adults starting antiretroviral treatment: collaborative analysis of cohort studies. *PLoS medicine*. 2013;10(4):e1001418. PubMed PMID: 23585736. Pubmed Central PMCID: 3621664. Epub 2013/04/16. eng.
29. South Africa Survey 2007/2008. Health and Welfare. South African Institute of Race Relations.
30. Mayosi BM, Flisher AJ, Lalloo UG, Sitas F, Tollman SM, Bradshaw D. The burden of non-communicable diseases in South Africa. *Lancet*. 2009 Sep 12;374(9693):934-47. PubMed PMID: 19709736.
31. Statistics South Africa. Mid year population estimates 2013. <http://www.statssa.gov.za/publications/P0302/P03022013.pdf> 14 May 2013. Available from: <http://www.statssa.gov.za/publications/P0302/P03022013.pdf>.
32. Kahn K, Collinson MA, Gomez-Olive FX, Mokoena O, Twine R, Mee P, et al. Profile: Agincourt health and socio-demographic surveillance system. *International journal of epidemiology*. 2012 Aug;41(4):988-1001. PubMed PMID: 22933647. Pubmed Central PMCID: 3429877. Epub 2012/08/31. eng.
33. Michel Garenne, Kathleen Kahn, Mark Collinson, F. Xavier Gómez-Olivé, Tollman S. Maternal mortality in rural South Africa (Agincourt): The impact of case definition on levels and trends. *International Journal of Women's Health*. 2013;5(1-7).
34. Kimani-Murage EW, Kahn K, Pettifor JM, Tollman SM, Dunger DB, Gomez-Olive XF, et al. The prevalence of stunting, overweight and obesity, and metabolic disease risk in rural South African children. *BMC public health*. 2010;10:158. PubMed PMID: 20338024. Pubmed Central PMCID: 2853509. Epub 2010/03/27. eng.
35. Gomez-Olive FX, Thorogood M, Clark BD, Kahn K, Tollman SM. Assessing health and well-being among older people in rural South Africa. *Glob Health Action*. 2010;3(Supplement 2):23-35. PubMed PMID: 20963188.
36. Tollman SM, Kahn K, Sartorius B, Collinson MA, Clark SJ, Garenne ML. Implications of mortality transition for primary health care in rural South Africa: a population-based surveillance study. *Lancet*. 2008 Sep 13;372(9642):893-901. PubMed PMID: 18790312.
37. Connor MD, Thorogood M, Casserly B, Dobson C, Warlow CP. Prevalence of stroke survivors in rural South Africa: results from the Southern Africa Stroke Prevention Initiative (SASPI) Agincourt field site. *Stroke*. 2004 Mar;35(3):627-32. PubMed PMID: 14963282.
38. Thorogood M, Connor M, Tollman S, Lewando Hundt G, Fowkes G, Marsh J. A cross-sectional study of vascular risk factors in a rural South African population: data from the Southern African Stroke Prevention Initiative (SASPI). *BMC public health*. 2007;7:326. PubMed PMID: 17999764.
39. Gomez-Olive FX, Thorogood M, Clark B, Kahn K, Tollman S. Self-reported health and health care use in an ageing population in the Agincourt sub-district of rural South Africa. *Glob Health*

- Action. 2013;6:19305. PubMed PMID: 23364087. Pubmed Central PMCID: 3556700. Epub 2013/02/01. eng.
40. Garenne ML, Tollman SM, Collinson MA, Kahn K. Fertility trends and net reproduction in Agincourt, rural South Africa, 1992-2004. *Scand J Public Health Suppl.* 2007 Aug;69:68-76. PubMed PMID: 17676506.
 41. United Nations. Report of the World Assembly on Ageing, Vienna, 26 July to 6 August 1982. United Nations publication, Sales No. E.82.I.16, chap. VI, sect. A. 1982.
 42. United Nations. Report of the Second World Assembly on Ageing, Madrid, 8 to 12 April 2002, United Nations publication Sales No. E.02.IV.4, chap I, sect. 1. 2002.
 43. Kinsella Kevin, He W. U.S. Census Bureau, International Population Reports, P95/09-1, An Aging World: 2008, U.S. Government Printing Office, Washington, DC, 2009.
 44. United Nations. World Population Ageing 2009. Department of Economic and Social Affairs. Population Division. Sales No. E.10.XIII.5 2010.
 45. US National Institute on Aging. National Institutes of Health. Why Population Aging Matters. A Global Perspective. 2007;Publication No. 07-6134(March).
 46. Hontelez JA, de Vlas SJ, Baltussen R, Newell ML, Bakker R, Tanser F, et al. The impact of antiretroviral treatment on the age composition of the HIV epidemic in sub-Saharan Africa. *AIDS.* 2012 Jul 31;26 Suppl 1:S19-30. PubMed PMID: 22781175. Epub 2012/09/26. eng.
 47. Negin J, Barnighausen T, Lundgren JD, Mills EJ. Aging with HIV in Africa: the challenges of living longer. *AIDS.* 2012 Jul 31;26 Suppl 1:S1-5. PubMed PMID: 22713477. Epub 2012/06/21. eng.
 48. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012 Dec 15;380(9859):2095-128. PubMed PMID: 23245604. Epub 2012/12/19. eng.
 49. Fuster V, Voute J. MDGs: chronic diseases are not on the agenda. *Lancet.* 2005 Oct 29-Nov 4;366(9496):1512-4. PubMed PMID: 16257330. Epub 2005/11/01. eng.
 50. Horton R. The neglected epidemic of chronic disease. *Lancet.* 2005 Oct 29-Nov 4;366(9496):1514. PubMed PMID: 16257331. Epub 2005/11/01. eng.
 51. United Nations. World Population Prospects. The 2004 Revision. Department of Economic and Social Affairs, Population Division. New York: United Nations ed2005.
 52. Strong K, Mathers C, Leeder S, Beaglehole R. Preventing chronic diseases: how many lives can we save? *Lancet.* 2005 Oct 29-Nov 4;366(9496):1578-82. PubMed PMID: 16257345.
 53. World Health Organization. Cause-specific mortality: regional estimates for 2008. Geneva, 2011 Available at: http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html. Last accessed: 18 April 2012.
 54. World Health Organization. Preventing chronic diseases - a vital investment. 2005.
 55. Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet.* 2007 Dec 8;370(9603):1929-38. PubMed PMID: 18063029.
 56. Alwan A, Maclean DR, Riley LM, d'Espaignet ET, Mathers CD, Stevens GA, et al. Monitoring and surveillance of chronic non-communicable diseases: progress and capacity in high-burden countries. *Lancet.* 2010 Nov 27;376(9755):1861-8. PubMed PMID: 21074258. Epub 2010/11/16. eng.
 57. Addo J, Smeeth L, Leon DA. Hypertension in sub-saharan Africa: a systematic review. *Hypertension.* 2007 Dec;50(6):1012-8. PubMed PMID: 17954720. eng.
 58. Lloyd-Sherlock P, Beard J, Minicuci N, Ebrahim S, Chatterji S. Hypertension among older adults in low- and middle-income countries: prevalence, awareness and control. *International journal of epidemiology.* 2014 Feb;43(1):116-28. PubMed PMID: 24505082. Pubmed Central PMCID: 3937973.
 59. Peer N, Kengne AP, Motala AA, Mbanya JC. Diabetes in the Africa Region: an update. *Diabetes research and clinical practice.* 2014 Feb;103(2):197-205. PubMed PMID: 24315460.

60. Silva-Matos C, Gomes A, Azevedo A, Damasceno A, Prista A, Lunet N. Diabetes in Mozambique: prevalence, management and healthcare challenges. *Diabetes & metabolism*. 2011 Jun;37(3):237-44. PubMed PMID: 21236716. Epub 2011/01/18. eng.
61. Kengne AP, Amoah AG, Mbanja JC. Cardiovascular Complications of Diabetes Mellitus in Sub-Saharan Africa. *Circulation*. 2005; (112):3592-601.
62. Phaswana-Mafuya N, Peltzer K, Chirinda W, Musekiwa A, Kose Z, Hoosain E, et al. Self-reported prevalence of chronic non-communicable diseases and associated factors among older adults in South Africa. *Glob Health Action*. 2013;6:20936 - <http://dx.doi.org/10.3402/gha.vi0>. PubMed PMID: 24054088. Pubmed Central PMCID: 3779355. Epub 2013/09/24. eng.
63. Groenewald P, Bradshaw D, Daniels J, Matzopoulos R, Bourne D, Blease D, et al. Cause of death and premature mortality in Cape Town, 2001-2006. Cape Town: South African Medical Research Council. 2008.
64. Bradshaw D, Groenewald P, Laubscher R, Nannan N, Nojilana B, Norman R, et al. Initial burden of disease estimates for South Africa, 2000. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2003 Sep;93(9):682-8. PubMed PMID: 14635557.
65. Joubert J, Norman R, Bradshaw D, Goedecke JH, Steyn NP, Puoane T. Estimating the burden of disease attributable to excess body weight in South Africa in 2000. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2007 Aug;97(8 Pt 2):683-90. PubMed PMID: 17952225. Epub 2007/10/24. eng.
66. Norman R, Gaziano T, Laubscher R, Steyn K, Bradshaw D. Estimating the burden of disease attributable to high blood pressure in South Africa in 2000. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2007 Aug;97(8 Pt 2):692-8. PubMed PMID: 17952226.
67. Levitt NS, Steyn K, Dave J, Bradshaw D. Chronic noncommunicable diseases and HIV-AIDS on a collision course: relevance for health care delivery, particularly in low-resource settings--insights from South Africa. *The American journal of clinical nutrition*. 2011 Dec;94(6):1690S-6S. PubMed PMID: 22089433. Pubmed Central PMCID: 3226022. Epub 2011/11/18. eng.
68. Steyn K, Bradshaw D, Norman R, Laubscher R. Determinants and treatment of hypertension in South Africans: the first Demographic and Health Survey. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2008 May;98(5):376-80. PubMed PMID: 18637309.
69. Alberts M, Urdal P, Steyn K, Stensvold I, Tverdal A, Nel JH, et al. Prevalence of cardiovascular diseases and associated risk factors in a rural black population of South Africa. *Eur J Cardiovasc Prev Rehabil*. 2005 Aug;12(4):347-54. PubMed PMID: 16079642.
70. Bradshaw D, Norman R, Lewin S, Joubert J, Schneider M, Nannan N, et al. Strengthening public health in South Africa: building a stronger evidence base for improving the health of the nation. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2007 Aug;97(8 Pt 2):643-9. PubMed PMID: 17957837. Epub 2007/10/26. eng.
71. UNAIDS. 2006 Report on the global AIDS epidemic. Geneva. UNAIDS.
72. UNAIDS. Global report: UNAIDS report on the global AIDS epidemic 2010. 2010.
73. Abdool Karim SS, Churchyard GJ, Karim QA, Lawn SD. HIV infection and tuberculosis in South Africa: an urgent need to escalate the public health response. *Lancet*. 2009 Sep 12;374(9693):921-33. PubMed PMID: 19709731. Pubmed Central PMCID: 2803032. Epub 2009/08/28. eng.
74. Wallrauch C, Barnighausen T, Newell ML. HIV prevalence and incidence in people 50 years and older in rural South Africa. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2010 Dec;100(12):812-4. PubMed PMID: 21414272. Epub 2011/03/19. eng.
75. Mills EJ, Barnighausen T, Negin J. HIV and aging--preparing for the challenges ahead. *The New England journal of medicine*. 2012 Apr 5;366(14):1270-3. PubMed PMID: 22475591. Epub 2012/04/06. eng.
76. Chigwedere P, Seage GR, 3rd, Gruskin S, Lee TH, Essex M. Estimating the lost benefits of antiretroviral drug use in South Africa. *J Acquir Immune Defic Syndr*. 2008 Dec 1;49(4):410-5. PubMed PMID: 19186354. Epub 2009/02/03. eng.

77. Gow JA. The adequacy of policy responses to the treatment needs of South Africans living with HIV (1999-2008): a case study. *Journal of the International AIDS Society*. 2009;12:37. PubMed PMID: 20015346. Pubmed Central PMCID: 2804692. Epub 2009/12/18. eng.
78. Chigwedere P, Essex M. AIDS denialism and public health practice. *AIDS and behavior*. 2010 Apr;14(2):237-47. PubMed PMID: 20058063. Epub 2010/01/09. eng.
79. South African National AIDS Council. The national HIV counselling and testing campaign. 2010 Last Accessed 19/02/2012. Available from: <http://www.info.gov.za/speeches/2010/10032611051001.htm>.
80. The National Antenatal Sentinel HIV and Syphilis Prevalence Survey, South Africa, 2011, National Department of Health. 2012.
81. Rehle TM, Hallett TB, Shisana O, Pillay-van Wyk V, Zuma K, Carrara H, et al. A decline in new HIV infections in South Africa: estimating HIV incidence from three national HIV surveys in 2002, 2005 and 2008. *PloS one*. 2010;5(6):e11094. PubMed PMID: 20559425. Pubmed Central PMCID: 2885415. Epub 2010/06/19. eng.
82. Cornell M, Grimsrud A, Fairall L, Fox MP, van Cutsem G, Giddy J, et al. Temporal changes in programme outcomes among adult patients initiating antiretroviral therapy across South Africa, 2002-2007. *AIDS*. 2010 Sep 10;24(14):2263-70. PubMed PMID: 20683318. Pubmed Central PMCID: 2948209. Epub 2010/08/05. eng.
83. Rosen S, MP F. Retention in HIV Care between Testing and Treatment in Sub-Saharan Africa: A Systematic Review. *PLoS medicine*. 2011;8(7):e1001056. doi:10.1371/journal.pmed.
84. Snow RC, Madalane M, Poulsen M. Are men testing? Sex differentials in HIV testing in Mpumalanga Province, South Africa. *AIDS care*. 2010 Sep;22(9):1060-5. PubMed PMID: 20824559. Epub 2010/09/09. eng.
85. Pronyk PM, Kim JC, Makhubele MB, Hargreaves JR, Mohlala R, Hausler HP. Introduction of voluntary counselling and rapid testing for HIV in rural South Africa: from theory to practice. *AIDS care*. 2002 Dec;14(6):859-65. PubMed PMID: 12511218. Epub 2003/01/04. eng.
86. Gómez-Olivé FX, Kabudula C. Bushbuckridge sub-district report on VCT. Data collected at the VCT service of the Primary Health Care units based at the Agincourt Health and Population study site. Report to DoH, Mkhulhu, Bushbuckridge sub-district. February 2011.
87. Global AIDS response progress report 2012. Republic of South Africa. Available at: http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries/ce_ZA_Narrative_Report.pdf Last accessed 03 August 2013.
88. van Schaik N, Kranzer K, Wood R, Bekker LG. Earlier HIV diagnosis--are mobile services the answer? *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2010 Oct;100(10):671-4. PubMed PMID: 21080998. Epub 2010/11/18. eng.
89. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *The New England journal of medicine*. 2011 Aug 11;365(6):493-505. PubMed PMID: 21767103. Pubmed Central PMCID: 3200068. Epub 2011/07/20. eng.
90. Quinn TC. HIV epidemiology and the effects of antiviral therapy on long-term consequences. *AIDS*. 2008 Sep;22 Suppl 3:S7-12. PubMed PMID: 18845925. Pubmed Central PMCID: 2753265. Epub 2008/10/18. eng.
91. Caldwell JC, Orubuloye IO, Caldwell P. Underreaction to AIDS in Sub-Saharan Africa. *Soc Sci Med*. 1992 Jun;34(11):1169-82. PubMed PMID: 1641678.
92. Fox MP, Rosen S. Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007-2009: systematic review. *Tropical medicine & international health : TM & IH*. 2010 Jun;15 Suppl 1:1-15. PubMed PMID: 20586956. Pubmed Central PMCID: 2948795. Epub 2010/07/14. eng.
93. Badri M, Cleary S, Maartens G, Pitt J, Bekker LG, Orrell C, et al. When to initiate highly active antiretroviral therapy in sub-Saharan Africa? A South African cost-effectiveness study. *Antiviral therapy*. 2006;11(1):63-72. PubMed PMID: 16518961.

94. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. *Journal of the International AIDS Society*. 2013;16(1):18588. PubMed PMID: 23870277. Pubmed Central PMCID: 3717402. Epub 2013/07/23. eng.
95. Barnighausen T, Chaityachati K, Chimbindi N, Peoples A, Haberer J, Newell ML. Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies. *The Lancet infectious diseases*. 2011 Dec;11(12):942-51. PubMed PMID: 22030332. Epub 2011/10/28. eng.
96. Coovadia H, Jewkes R, Barron P, Sanders D, McIntyre D. The health and health system of South Africa: historical roots of current public health challenges. *Lancet*. 2009 Sep 5;374(9692):817-34. PubMed PMID: 19709728.
97. Jahn A, Floyd S, Crampin AC, Mwaungulu F, Mvula H, Munthali F, et al. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. *Lancet*. 2008 May 10;371(9624):1603-11. PubMed PMID: 18468544.
98. Maher D, Sekajugo J. Research on health transition in Africa: time for action. *Health research policy and systems / BioMed Central*. 2011;9:5. PubMed PMID: 21272381. Pubmed Central PMCID: 3038153. Epub 2011/01/29. eng.
99. Maher D, Sekajugo J, Harries AD, Grosskurth H. Research needs for an improved primary care response to chronic non-communicable diseases in Africa. *Tropical medicine & international health : TM & IH*. 2010 Feb;15(2):176-81. PubMed PMID: 20002618. Epub 2009/12/17. eng.
100. Maher D, Harries AD, Zachariah R, Enarson D. A global framework for action to improve the primary care response to chronic non-communicable diseases: a solution to a neglected problem. *BMC public health*. 2009;9:355. PubMed PMID: 19772598. Pubmed Central PMCID: 2758871.
101. Global Health Initiative Strategy. South Africa. Available from: <http://www.ghi.gov/whereWeWork/docs/> 2011-2016.
102. Janssens B, Van Damme W, Raleigh B, Gupta J, Khem S, Soy Ty K, et al. Offering integrated care for HIV/AIDS, diabetes and hypertension within chronic disease clinics in Cambodia. *Bull World Health Organ*. 2007 Nov;85(11):880-5. PubMed PMID: 18038079. Pubmed Central PMCID: 2636263. Epub 2007/11/27. eng.
103. Ameh S, Gomez-Olive FX, Kahn K, Tollman SM, Klipstein-Grobusch K. Predictors of health care use by adults 50 years and over in a rural South African setting. *Glob Health Action*. 2014;7:24771. PubMed PMID: 25087686.
104. Beaglehole R, Epping-Jordan J, Patel V, Chopra M, Ebrahim S, Kidd M, et al. Improving the prevention and management of chronic disease in low-income and middle-income countries: a priority for primary health care. *Lancet*. 2008 Sep 13;372(9642):940-9. PubMed PMID: 18790317.
105. Government Gazette 23 December 2005. Volume 486. No. 23 of 2005: Cross-boundary Municipalities Laws Repeal and Related Matters Act, 2005. Republic of South Africa.
106. Tollman S.M. The Agincourt field site - Evolution and current status. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 1999;89:853-8.
107. Tollman SM, Herbst K, Garenne M, Gear JS, Kahn K. The Agincourt demographic and health study--site description, baseline findings and implications. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 1999 Aug;89(8):858-64. PubMed PMID: 10488362. Epub 1999/09/17. eng.
108. Tollman SM. Closing the Gap. Applying health and socio-demographic surveillance to complex health transitions in South and sub-Saharan Africa: Umea University; 2008.
109. Kahn K, Tollman SM, Garenne M, Gear JS. Who dies from what? Determining cause of death in South Africa's rural north-east. *Tropical medicine & international health : TM & IH*. 1999 Jun;4(6):433-41. PubMed PMID: 10444319.
110. Kahn K, Tollman SM, Collinson MA, Clark SJ, Twine R, Clark BD, et al. Research into health, population and social transitions in rural South Africa: data and methods of the Agincourt Health and

- Demographic Surveillance System. *Scand J Public Health Suppl.* 2007 Aug;69:8-20. PubMed PMID: 17676498.
111. Kahn K. Dying to make a fresh start. Mortality and Health Transition in a New South Africa: Umea Universitij; 2006.
 112. Mathers CD, Fat DM, Inoue M, Rao C, Lopez AD. Counting the dead and what they died from: an assessment of the global status of cause of death data. *Bull World Health Organ.* 2005 Mar;83(3):171-7. PubMed PMID: 15798840. Pubmed Central PMCID: 2624200. Epub 2005/03/31. eng.
 113. Groenewald P, Bradshaw D, Daniels J, Zinyakatira N, Matzopoulos R, Bourne D, et al. Local-level mortality surveillance in resource-limited settings: a case study of Cape Town highlights disparities in health. *Bull World Health Organ.* 2010 Jun;88(6):444-51. PubMed PMID: 20539858. Pubmed Central PMCID: 2878147. Epub 2010/06/12. eng.
 114. Madubansi M, Shackleton CM. Changes in fuelwood use and selection following electrification in the Bushbuckridge lowveld, South Africa. *Journal of environmental management.* 2007 Jun;83(4):416-26. PubMed PMID: 16930808. Epub 2006/08/26. eng.
 115. Collinson MA, Mokoena O, Mgiba N, Kahn K, Tollman SM, Garenne M, et al. Agincourt Demographic Surveillance System (Agincourt DSS). In: Sankoh O, Kahn K, Mwageni E et al (eds). *Population and Health in Developing Countries. Volume 1. Population, Health and Survival at INDEPTH sites.* IDRC, Ottawa, Canada, 2002.
 116. Collinson MA. Striving against adversity: the dynamics of migration, health and poverty in rural South Africa. *Glob Health Action.* 2010;3():1-14. PubMed PMID: 20531981.
 117. Williams J, Ibisomi L, Sartorius B, Kahn K, Collinson M, Tollman S, et al. Convergence in fertility of South Africans and Mozambicans in rural South Africa, 1993-2009. *Glob Health Action.* 2013;6:19236. PubMed PMID: 23364078. Pubmed Central PMCID: 3556705. Epub 2013/02/01. eng.
 118. Mark A. Collinson, Samuel J. Clark, Annette A.M. Gerritsen, Peter Byass, Kathleen Kahn, Stephen M. Tollman. *The Dynamics of Poverty and Migration in a Rural South African Community, 2001-2005.* Working Paper no 92 Center for Statistics and the Social Sciences University of Washington. 2009:1-38.
 119. Gómez-Olivé FX, Thorogood M, Bocquier P, Mee P, Kahn K, Berkman L, et al. Social conditions and disability related to the mortality of older people in rural South Africa. *International journal of epidemiology.* 2013;Submitted.
 120. Gomez-Olive FX, Angotti N, Houle B, Klipstein-Grobusch K, Kabudula C, Menken J, et al. Prevalence of HIV among those 15 and older in rural South Africa. *AIDS care.* 2013 Jan 11. PubMed PMID: 23311396. Epub 2013/01/15. Eng.
 121. Nawi Ng, Hoang Van Minh, Sanjay Juvekar, Abdur Razzaque, Tran Huu Bich, Uraiwan Kanungsukkasem, et al. Using the INDEPTH HDSS to build capacity for chronic non-communicable disease risk factor surveillance in low and middle-income countries. *Global Health Action.* 2009;Supplement 1:DOI: 10.3402/gha.v2i0.1984.
 122. Aram V. Chobanian, George L. Bakris, Henry R. Black, William C.ushman, Lee A. Green, Joseph L. Izzo, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report . *JAMA.* 2003;289(19):2560-71.
 123. Y K Seedat, B L Rayner. South African Hypertension Guideline 2011. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde.* 2012 (102):57-84.
 124. Gomez-Olive FX, Thorogood M, Kandala NB, Tigbe W, Kahn K, Tollman S, et al. Sleep problems and mortality in rural South Africa: novel evidence from a low-resource setting. *Sleep medicine.* 2014 Jan;15(1):56-63. PubMed PMID: 24333221. Epub 2013/12/18. eng.
 125. J. Williams, F.X. Gómez-Olivé, N. Angotti, C. Kabudula, J. Menken, S. Clark, et al. HIV risk and recent sexual behaviour of older adults in rural South Africa. *XIX International AIDS Conference; Washington DC, USA2012.*

126. Kimuna SR, Makiwane M. Older people as resources in South Africa: Mpumalanga households. *Journal of aging & social policy*. 2007;19(1):97-114. PubMed PMID: 17347119. Epub 2007/03/10. eng.
127. Schatz EJ. "Taking care of my own blood": older women's relationships to their households in rural South Africa. *Scand J Public Health Suppl*. 2007 Aug;69:147-54. PubMed PMID: 17676516.
128. Schatz E, Ogunmefun C. Caring and Contributing: The Role of Older Women in Rural South African Multi-generational Households in the HIV/AIDS Era. *World Development*. 2007;35(8):1390-403.
129. Case A, Menendez A. Does money empower the elderly? Evidence from the Agincourt demographic surveillance site, South Africa. *Scand J Public Health Suppl*. 2007 Aug;69:157-64. PubMed PMID: 17676518.
130. Hunter LM, Twine W, Patterson L. "Locusts are now our beef": adult mortality and household dietary use of local environmental resources in rural South Africa. *Scand J Public Health Suppl*. 2007 Aug;69:165-74. PubMed PMID: 17676519.
131. Phaswana-Mafuya N, Peltzer K, Chirinda W, Kose Z, Hoosain E, Ramlagan S, et al. Self-rated health and associated factors among older South Africans: evidence from the study on global ageing and adult health. *Global Health Action*. 2013;6:19880 - <http://dx.doi.org/10.3402/gha.v6i0>.
132. Joubert J, Bradshaw D. Chapter 15. Population ageing and health challenges in South Africa. In: Krisela Steyn JF, Norman Temple (eds), editor. *Chronic Diseases of Lifestyle in South Africa: 1995 - 2005 Technical Report*. Cape Town: South African Medical Research Council; 2006. p. 204-19.
133. Hirve S, Juvekar S, Sambhudas S, Lele P, Blomstedt Y, Wall S, et al. Does self-rated health predict death in adults aged 50 years and above in India? Evidence from a rural population under health and demographic surveillance. *International journal of epidemiology*. 2012 Dec;41(6):1719-27. PubMed PMID: 23175517. Epub 2012/11/24. eng.
134. Lloyd-Sherlock P, McKee M, Ebrahim S, Gorman M, Greengross S, Prince M, et al. Population ageing and health. *Lancet*. 2012 Apr 7;379(9823):1295-6. PubMed PMID: 22480756. Epub 2012/04/07. eng.
135. Ageing well: a global priority. *Lancet*. 2012 Apr 7;379(9823):1274. PubMed PMID: 22480755. Epub 2012/04/07. eng.
136. Brandstrom A. Ageing - a cross-cutting research and policy challenge. *Scand J Public Health*. 2007;35(3):225-7. PubMed PMID: 17530542.
137. Collinson M, Wolff B, Tollman S, Kahn K. Trends in internal labour migration from the rural Limpopo Province, male risk behaviour, and implications for spread of HIV/AIDS in rural South Africa. *J Ethn Migr Stud*. 2006 May;32(4):633-48. PubMed PMID: 20396611.
138. Sonnenberg P, Murray J, Glynn JR, Thomas RG, Godfrey-Faussett P, Shearer S. Risk factors for pulmonary disease due to culture-positive *M. tuberculosis* or nontuberculous mycobacteria in South African gold miners. *The European respiratory journal*. 2000 Feb;15(2):291-6. PubMed PMID: 10706494. Epub 2000/03/08. eng.
139. Swanepoel AJ, Kromhout H, Jinnah ZA, Portengen L, Renton K, Gardiner K, et al. Respirable dust and quartz exposure from three South African farms with sandy, sandy loam, and clay soils. *The Annals of occupational hygiene*. 2011 Jul;55(6):634-43. PubMed PMID: 21685408. Epub 2011/06/21. eng.
140. Swanepoel AJ, Rees D, Renton K, Swanepoel C, Kromhout H, Gardiner K. Quartz exposure in agriculture: literature review and South African survey. *The Annals of occupational hygiene*. 2010 Apr;54(3):281-92. PubMed PMID: 20172918. Epub 2010/02/23. eng.
141. Godfrey-Faussett P, Sonnenberg P, Shearer SC, Bruce MC, Mee C, Morris L, et al. Tuberculosis control and molecular epidemiology in a South African gold-mining community. *Lancet*. 2000 Sep 23;356(9235):1066-71. PubMed PMID: 11009142. Epub 2000/09/29. eng.
142. Steyn K, Gaziano TA, Bradshaw D, Laubscher R, Fourie J. Hypertension in South African adults: results from the Demographic and Health Survey, 1998. *Journal of hypertension*. 2001 Oct;19(10):1717-25. PubMed PMID: 11593090. Epub 2001/10/11. eng.

143. Shisana O, Labadarios D, Rehle T, Simbayi L, Zuma K, Dhansay A, et al. South African National Health and Nutrition Examination Survey (SANHANES-1). Cape Town: Human Science Research Council Press. 2013.
144. Dennison CR, Peer N, Steyn K, Levitt NS, Hill MN. Determinants of hypertension care and control among peri-urban Black South Africans: the HiHi study. *Ethnicity & disease*. 2007 Summer;17(3):484-91. PubMed PMID: 17985502. Epub 2007/11/08. eng.
145. Nathanson CA. Illness and the feminine role: a theoretical review. *Soc Sci Med*. 1975 Feb;9(2):57-62. PubMed PMID: 1093257. Epub 1975/02/01. eng.
146. Oksuzyan A, Juel K, Vaupel JW, Christensen K. Men: good health and high mortality. Sex differences in health and aging. *Aging Clin Exp Res*. 2008 Apr;20(2):91-102. PubMed PMID: 18431075.
147. Balard F, Beluche I, Romieu I, Willcox DC, Robine JM. Are men aging as oaks and women as reeds? A behavioral hypothesis to explain the gender paradox of French centenarians. *Journal of aging research*. 2011;2011:371039. PubMed PMID: 22175018. Pubmed Central PMCID: 3233703. Epub 2011/12/17. eng.
148. Case A, Paxson C. Sex differences in morbidity and mortality. *Demography*. 2005 May;42(2):189-214. PubMed PMID: 15986983.
149. Debpuur C, Welaga P, Wak G, Hodgson A. Self-reported health and functional limitations among older people in the Kassena-Nankana District, Ghana. *Glob Health Action*. 2010;3(Supplement 2):54-63. PubMed PMID: 20963186.
150. Ng N, Kowal P, Kahn K, Naidoo N, Abdullah S, Bawah A, et al. Health inequalities among older men and women in Africa and Asia: evidence from eight Health and Demographic Surveillance System sites in the INDEPTH WHO-SAGE Study. *Glob Health Action*. 2010;3. PubMed PMID: 20967141. Pubmed Central PMCID: 2958198. Epub 2010/10/23. eng.
151. Schatz E, Gomez-Olive X, Ralston M, Menken J, Tollman S. The impact of pensions on health and wellbeing in rural South Africa: does gender matter? *Soc Sci Med*. 2012 Nov;75(10):1864-73. PubMed PMID: 22884944. Pubmed Central PMCID: 3475956. Epub 2012/08/14. eng.
152. Schatz EJ. Reframing vulnerability: Mozambican refugees' access to state-funded pensions in rural South Africa. *J Cross Cult Gerontol*. 2009 Sep;24(3):241-58. PubMed PMID: 19142721.
153. Jasso. Guillermina, Douglas S. Massey, Mark R. Rosenzweig, Smith JP. "Immigrant Health – Selectivity and Acculturation." Pages 227-266 in Norman B. Anderson, Randy A. Bulatao, and Barney Cohen (eds.), *Critical Perspectives on Racial and Ethnic Differences in Health in Late Life*. Washington, DC: National Academy Press. 2004.
154. Alberti H, Alberti B. The influence of gender on the primary care management of diabetes in Tunisia. *The Pan African medical journal*. 2009;3:2. PubMed PMID: 21532711. Pubmed Central PMCID: 2984293. Epub 2009/01/01. eng.
155. Gerritsen AA, Deville WL. Gender differences in health and health care utilisation in various ethnic groups in the Netherlands: a cross-sectional study. *BMC public health*. 2009;9:109. PubMed PMID: 19379499. Pubmed Central PMCID: 2678118. Epub 2009/04/22. eng.
156. Siu GE, Seeley J, Wight D. Dividuality, masculine respectability and reputation: how masculinity affects men's uptake of HIV treatment in rural eastern Uganda. *Soc Sci Med*. 2013 Jul;89:45-52. PubMed PMID: 23726215. Epub 2013/06/04. eng.
157. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012 Dec 15;380(9859):2197-223. PubMed PMID: 23245608. Epub 2012/12/19. eng.
158. Ibrahim MM, Damasceno A. Hypertension in developing countries. *Lancet*. 2012 Aug 11;380(9841):611-9. PubMed PMID: 22883510. Epub 2012/08/14. eng.
159. UNAIDS. Together we will end AIDS. UNAIDS / JC2296E2012.

160. UNAIDS. World AIDS Day Report. http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/jc2434_worldaidsday_results_en.pdf2012.
161. Edward J Mills, Anu Rammohan, Niyi Awofeso. Ageing faster with AIDS in Africa. *The Lancet*. 2010 (Published online):DOI:10.1016/S0140-6736(10)62180-0.
162. Negin J, Cumming RG. HIV infection in older adults in sub-Saharan Africa: extrapolating prevalence from existing data. *Bull World Health Organ*. 2010 Nov 1;88(11):847-53. PubMed PMID: 21076566. Pubmed Central PMCID: 2971515. Epub 2010/11/16. eng.
163. Chepngeno-Langat G, Falkingham JC, Madise NJ, Evandrou M. Concern About HIV and AIDS Among Older People in the Slums of Nairobi, Kenya. *Risk Anal*. 2012;32(9):1512-23.
164. Bendavid E, Ford N, Mills EJ. HIV and Africa's elderly: the problems and possibilities. *AIDS*. 2012 Jul 31;26 Suppl 1:S85-91. PubMed PMID: 22781181.
165. Nyirenda M, Chatterji S, Falkingham J, Mutevedzi P, Hosegood V, Evandrou M, et al. An investigation of factors associated with the health and well-being of HIV-infected or HIV-affected older people in rural South Africa. *BMC public health*. 2012;12:259. PubMed PMID: 22471743. Pubmed Central PMCID: 3424116.
166. Nyirenda M, Newell ML, Mugisha J, Mutevedzi PC, Seeley J, Scholten F, et al. Health, wellbeing, and disability among older people infected or affected by HIV in Uganda and South Africa. *Glob Health Action*. 2013;6:19201. PubMed PMID: 23364075. Epub 2013/02/01. eng.
167. Connor MD, Hopkins T, Tollman SM, Thorogood M, Modi G. Blood pressure-measuring devices in rural South Africa: an audit conducted by the SASPI team in the Agincourt field site. *Cardiovasc J S Afr*. 2006 Jul-Aug;17(4):192-6. PubMed PMID: 17001422.
168. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. *Lancet*. 2013 Nov 2;382(9903):1525-33. PubMed PMID: 24152939. Epub 2013/10/25. eng.
169. South African declaration on the Prevention and Control of Non-communicable diseases. 12-13 September 2011. http://www.health.uct.ac.za/usr/health/research/groupings/cdia/downloads/SA_NCD_Declaration.pdf Last accessed 22 April 2012.
170. Mayosi BM, Lawn JE, van Niekerk A, Bradshaw D, Abdool Karim SS, Coovadia HM. Health in South Africa: changes and challenges since 2009. *Lancet*. 2012 Dec 8;380(9858):2029-43. PubMed PMID: 23201214. Epub 2012/12/04. eng.
171. Pillay Y. PHC re-engineering in South Africa: are we making progress? PHASA Newsletter 29 February 2012.

K. Publications