Epidemiology and Public Health Sciences
Department of Public Health and Clinical Medicine
Umeå University, SE-901 87 Umeå, Sweden

Dying to make a fresh start: Mortality and health transition in a new South Africa

Kathleen Kahn
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MRC/Wits Rural Public Health
and Health Transitions Research Unit,
South Africa

School of Public Health,
University of the Witwatersrand,
Johannesburg, South Africa

Medical
Research Council,
South Africa

Epidemiology & Public Health Sciences,
Department of Public Health and Clinical Medicine
Umeå University, Sweden.

"We all count"

*"To make people count, we first need
to be able to count people"*

*"It is not because countries are poor that
they cannot afford good health information:
it is because they are poor that they cannot
afford to be without it"*

Abstract

Rationale Vital registration is lacking in developing settings where health and development problems are most pressing. Policy-makers confront an "information paradox": the critical need for information on which to base priorities and monitor progress, and the profound shortage of such information.

Aims To better understand the dynamics of mortality transition in rural South Africa over a decade of profound socio-political change coupled with emerging HIV/AIDS. Thereby to inform health and development programming, policy formulation, and the research agenda; and contribute to debate on the nature of the "health transition".

Methods The Agincourt health and demographic surveillance system is based on continuous monitoring of the Agincourt sub-district population in rural north-east South Africa. This involves annual recording of all vital events, specifically deaths, births and migrations in 11,700 households comprising some 70,000 persons. A "verbal autopsy" is conducted on every death, and special modules provide additional data.

Key findings A major health transition has occurred over the past decade, with marked changes in population structure and rapidly escalating mortality particularly among children and younger adults. A quadruple burden of disease is evident with persisting infectious disease and malnutrition in children, emerging non-communicable disease in the middle-aged and older, high levels of violence in an apparently peaceful community, and rapidly escalating HIV/AIDS and tuberculosis. There is evidence of sex differences and socio-economic differentials in mortality; vulnerable sub-groups include the children of Mozambican immigrants and recently returned labour migrants.

Implications With respect to health transition, empirical data demonstrate a marked "counter transition" with mortality increasing in children and young adults; "epidemiologic polarization" is evident with the most vulnerable experiencing a higher mortality burden; and a "protracted transition" is reflected in the co-existence of persisting infectious disease and malnutrition, emerging HIV/AIDS, and increasing chronic non-communicable disease. With respect to health policy and practice there is urgent need to: strengthen HIV/AIDS prevention, treatment and care; offer effective long-term care to control the rising burden of chronic illness and related risk; maintain and improve maternal and child health services; and address differential access to care. This poses a substantial challenge to a severely stretched health system.

Keywords: Age-specific mortality, Agincourt, demographic surveillance system, epidemiologic transition, health transition, mortality trends, rural, South Africa, verbal autopsy, vital registration.

Original papers

The thesis is based on the following papers:

I   Kahn K, Tollman SM, Collinson MA, Clark SJ, Twine R, Clark B, Shabangu M, Gómez-Olivé X, Mokoena O, Garenne M. Building a programme in health, population and social transitions research in rural South Africa: Data and methods of the Agincourt Health and Demographic Surveillance System. Submitted for publication

II   Kahn K, Tollman SM, Garenne M, Gear JSS. Validation and application of verbal autopsies in a rural area of South Africa *Tropical Medicine and International Health* 2000; 5(11): 824-831

III Kahn K, Garenne M, Collinson MA, Tollman S. Mortality trends in a new South Africa: Hard to make a fresh start. *Scandinavian Journal of Public Health.* Accepted for publication

IV   Kahn K, Tollman SM, Garenne M, Gear JSS. Who dies from what? Determining cause of death in South Africa's rural north-east. *Tropical Medicine and International Health* 1999;4(6): 433-441

V   Kahn K, Tollman SM. Stroke in rural South Africa: Contributing to the little known about a big problem. *South African Medical Journal* 1999;89(1):63-65

VI   Pronyk PM, Kahn K, Hargreaves JR, Tollman SM, Collinson M, Hausler HP, Porter JDH. Undiagnosed pulmonary tuberculosis deaths in rural South Africa. *International Journal of Tuberculosis and Lung Disease* 2004;8(6):796-799.

The publishers have given permission for reprinting of published papers.

Contents

Prologue

My younger sister died of leukaemia when I was nine years old, at which point I gave up my aspiration to be an actress (or was it a ballet dancer?) and decided to become a doctor who would find a cure for cancer. I never deviated from my desire to study medicine, but my interest in oncology was displaced in 1979 by my first encounter with the lives of rural South Africans. As a second year medical student, I participated in an evaluation of "care groups" – voluntary rural women's groups established to promote health in general and prevent trachoma in particular. This was a profoundly formative experience that set my future professional direction towards public health.

I was fortunate in finding a life partner with congruent interests and aspirations, great vision and outstanding leadership. Together we moved to the rural north-east of South Africa – Bushbuckridge – where the Agincourt health and demographic surveillance system, the basis for this thesis, grew from our early work in health systems development. Through careful monitoring of mortality and burden of disease, we have documented a tragic irony: dramatic worsening of mortality concurrent with peaceful democratic change; hope for a better future displaced by the ravages of HIV/AIDS.

The photograph on the front cover was taken in 2004 in the research site by Paul Weinberg, a well-known South African photographer. I find it a powerful image: the fence represents the high levels of mortality that are preventing people and communities from realising the "dream" of a better future following the demise of apartheid. Three people are looking back towards the past which, despite racial oppression, was in some ways better as death rates were lower; one woman is looking ahead with arm outstretched – she represents the persisting hope of those that strive for a better future for themselves and their children.

I thought often, during the writing of my cover story, of Claire, Yonni and Aimée – people who died too young and whose deaths deeply touched my life and those of my loved ones. But it is to the unknown and unnamed families in Agincourt, courageous survivors of the many untimely deaths represented in this thesis, that I dedicate my work.

"Don't pity the dead, pity the living who are forced to go on"
Dona Dalina, a water-carrier who experienced the death of her siblings, children, grandchildren and great-grand-children due to poverty and public neglect. Timbaúba, Brazil, 1987.[1]

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Background

International Initiatives to Promote Health in Developing Countries

In the endeavour to combat poverty and promote evidence-based equitable health and development in the poorest nations of the world, a plethora of global initiatives has arisen during the past decade. Though all of these initiatives are directed at this broad goal, their particular foci differ in various ways. There are initiatives to promote a sound scientific base, such as the *Global Forum for Health Research*, which has the relatively broad aim of promoting health research to combat neglected conditions responsible for ill health in developing countries,[2] and its *Alliance for Health Policy and Systems Research*, with the somewhat more focused aim of promoting the generation, dissemination and use of knowledge for enhancing the performance of health systems.[3] There are initiatives concentrating on disease, such as the *Global Fund to Fight AIDS, TB and Malaria*, which directs resources to programmes targeting three of the world's most devastating infectious diseases,[4] and the *Disease Control Priorities Project*, which assesses a broader range of disease-control priorities, including non-communicable diseases, injuries and mental health, to inform health policymaking in developing countries.[5,6] There are initiatives concentrating on child health, such as the *Global Alliance for Vaccines and Immunization (GAVI)*, a public-private partnership promoting access to a particular technological intervention in the pursuit of child health in impoverished countries.[7] And there are initiatives concentrating on poverty, such as the *United Nations Millennium Project*, established to support achievement of the Millennium Development Goals (MDGs) to address extreme poverty that were adopted by 147 heads of state during the 2000 United Nations Millennium Summit. (The eight goals are commendable in encompassing a broad definition of poverty, including low income, hunger, inadequate education, gender inequality and inadequate empowerment of women, high child mortality, high rates of disease, and poor environmental sustainability.[8] Some critics argue, however, that the approach suffers from a lack of scientifically valid data to evaluate the quantitative targets that have been set.[9])

These examples are in no way comprehensive; they have been chosen to highlight differences in the focus of international initiatives to improve health and development of the poorest nations. Despite these differences, the organisations all share two fundamental and opposing challenges: the need for information on which to base priorities and monitor progress; and the profound shortage of such information in developing countries.

Data for Monitoring and Evaluation

Status of available global information systems

Given the lack of vital registration systems in the developing world, together with weaknesses in existing data, there is an obvious need for alternative information approaches. Currently information comes from censuses, household surveys, facility-based information systems, and various methods of estimation and modeling.[9] Though not without some value, these data sources suffer from serious limitations, and are inadequate as a basis for policies and programmes. Censuses are often too poor in quality and too infrequent to yield up-to-date information. Household surveys usually involve samples too small for reliable estimates of mortality by age, sex and cause, and repeatedly yield under-reporting of perinatal deaths. Facility-based information systems yield data that cannot be translated into population-level estimates of disease burden, because such data are biased towards those able to access health facilities – usually the better-off. And the various methods of estimation and modeling are hindered by the nature of the empirical data they rely on – typically limited in availability and poor in quality.[10,11] Measurement of adult mortality is particularly hampered by limitations in existing methods.[12,13]

South African information sources are no exception. In apartheid South Africa, the so-called "independent" states of Transkei, Bophutatswana, Venda, and Ciskei were systematically excluded from national data systems, resulting in a bias towards the white, urban and better-off minorities. Nevertheless, the Coale and Demeny Model Life Tables,[14] for instance, had no African data to draw on except those derived from registration data of the white South African population. All in all, global health monitoring and reporting needs several improvements, including new measurement techniques, capacity strengthening at national level, development of global norms and standards on key indicators for health interventions and health system functioning, and neutral global reporting systems.[12]

Various initiatives are addressing this need. The *African Census Analysis Project (ACAP)* is an effort to increase the use of African census micro-data for academic and policy-oriented research through archiving of African census data, collaboration with African researchers, and strengthening of demographic capacity.[15] The Demographic and Health Surveys (DHS) – nationally representative household surveys with large sample sizes conducted every five years – provide data for monitoring and impact evaluation in the areas of population, health and nutrition.[16] The *Multiple Indicator Cluster Survey (MICS)*, started by UNICEF in 1995, similarly coordinates five-year household surveys, in this case to monitor the health of women and children; the surveys are beginning to yield trend data.[17] In addition to the DHS and MICS, probably the best known in the public health field, there are many other household-survey initiatives: hence the need for the *International Household Survey Network* to foster better collecting and use of data for policy making and monitoring by national and international agencies.[18] (It is true that household surveys do generally yield valid measures of child mortality, but there is as yet no adequate method to measure adult mortality.)

The 1990 *Global Burden of Disease (GBD)* study measured the health impacts of over 100 diseases and injuries and ten risk factors for eight regions and the world as a whole. It produced estimates of mortality and morbidity by age, sex and region, and developed a new measure to quantify the burden of diseases, injuries and risk factors – disability-adjusted life years (DALYs).[a] This was followed by the 2001 *Global Burden of Disease* study, which used available death registration data, sample registration systems, and data on child and adult mortality

from censuses and surveys to calculate age- and sex-specific death rates. In addition, the 2001 study estimated changes in cause-specific mortality and burden of disease since 1990, examined methodological uncertainty surrounding these estimates, and analysed the cost-effectiveness of interventions for the Disease Control Priorities Project.[19]

The *Health Metrics Network*, established by the World Health Organization in 2005, is a global partnership bringing together international agencies, foundations, and other organisations to develop health information systems in developing countries. The partnership sets standards, provides technical and financial support, and ensures access to and use of the information collected.[20] Now in 2006 the *Health Metrics Network* has committed itself to promoting a step-wise approach to establishing comprehensive health information systems in poor countries. The first step would be a sentinel registration system based on health and demographic surveillance (urban and rural), followed in time by a more representative sample registration system, and aiming finally for near-complete civil registration (Don de Savigny – personal communication, February 2006).

A sample vital registration system is a community-based system implemented in a nationally representative cluster sample.[10] The only two existing nationally representative sample registration systems are the *India Sample Registration System* – a large-scale demographic survey established in 1964 to provide reliable estimates of birth and death rates, and other fertility and mortality indicators at the state and national levels[21] – and the *China Disease Surveillance Point System*, inaugurated by the Chinese Ministry of Health in 1980 to generate cause-specific mortality statistics from a nationally representative sample of sites.[22] Tanzania has partial coverage through a sentinel vital registration system.[10] In any such system, there are possibilities of expansion. *Sample Vital Registration with Verbal Autopsy (SAVVY)[b]* adds verbal autopsy, to help ascertain causes of death. SAVVY consists of a number of demographic surveillance sites across a country, selected using multi-stage probability sampling with the district as the primary sampling unit. An initial census to enumerate resident populations is followed up annually or semi-annually by "census" updates in which all births, deaths and migrations are recorded. Running alongside the census system is mortality surveillance, in which a verbal autopsy interview is conducted on every death.[11]

One recommendation for making the Millennium Development Goals measurable is to establish a large number of new demographic surveillance sites in various countries.[9] Consider the example of the *Tanzanian Essential Health Interventions Project (TEHIP)* of Tanzania's Ministry of Health. In collaboration with Canada's International Development Research Centre (IDRC), the project used local demographic surveillance systems to establish health-intervention priorities in two districts, Rufiji and Morogoro. By applying user-friendly computer-based tools, district health planners were then able to re-orient their budgets to suit local disease-burden priorities. There was also a boost to capacity-development in integrated management of childhood illnesses and to health systems communication and supervision. All these enhancements jointly have led to a dramatic decrease in mortality rates for adults and particularly children. So much so, in fact, that Rufiji and Morogoro might actually achieve the Millennium Development Goal of a two-thirds reduction in

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[a] Disability-adjusted life years (DALYs) quantify the burden of diseases, injuries and risk factors with a single measure based on two factors: years of life lost due to premature mortality (YLL) and years of life lived in suboptimal health.

[b] An initiative of MEASURE Evaluation, University of North Carolina, and the US Census Bureau.

child mortality by 2015. The demographic surveillance systems ongoing in the two districts provide crucial information both for setting priorities and for monitoring progress towards the goal.[23]

Addressing the information gap: health and demographic surveillance systems

A health and demographic surveillance system (HDSS) is an example of a longitudinal community study. It is "a set of field and computing operations to handle the longitudinal follow-up of well-defined entities or primary subjects (individuals, households and residential units) and all related demographic and health outcomes within a clearly circumscribed geographic area".[24] Follow-up is at regular intervals – every three or four months in most HDSSs, annually in others. An initial household census registers all individuals in the study site; subsequent rounds register new households and individuals, record all vital events (births, deaths and in- and out-migrations), and update information on existing members.

Longitudinal studies include all studies in which a defined population is followed over extended periods of time. The HDSS is distinguished from other types of longitudinal study in several respects: its focus on *all* individuals within a geographically defined area, the greater frequency with which data are collected, the smaller range of topics, and particularly its focus on *community*. (While data are collected from individuals and households, the actual unit of observation is the community – hence in-migrants enter the sample as they move into the community but out-migrants are not followed when they leave the community). In contrast, panel studies usually use a broader sample, take the household as sampling unit, and cover a greater range of topics; and cohort studies follow a sample of individuals selected for a common characteristic such as birth date or age.[25]

Despite being resource- and time-intensive, the longitudinal study enjoys advantages over other types of study in better elucidating causal relationships (through detailed information on timing and sequence of events) and monitoring change (such as trends over time, and before-and-after differences). As for the HDSS specifically, as a particular form of longitudinal study, it has its own distinctive set of advantages and disadvantages.[25]

Advantages and disadvantages of the HDSS

What the HDSS does or can do is:
- Measure events (albeit a limited range) in great detail
- Have large sample sizes, thereby enabling observation of rare events
- Follow all members of a community, and hence capably evaluate the impact of intervention programmes
- Promote experimental study design, due to the relatively homogeneous community
- Determine the sequence of events and hence study causality
- Enhance community participation and strengthen local capacity
- Benefit from an established research infrastructure that
  o attracts other scientists to locate independent research in the HDSS site
  o enables the addition of variables to existing protocols at relatively low cost
  o promotes effective capacity-building with respect to research skills and scientific leadership in developing settings
- Enables increasing scientific and policy value the longer the follow-up period continues.

The HDSS is limited in that it:

- Cannot easily generalise findings to a broader area and make inferences, given the restricted geographic focus
- Cannot really elucidate sophisticated statistical analysis of sub-group differences, owing to the relatively homogeneous community with limited community variation and range of characteristics
- Tends to be resource-intensive with respect to funding requirements, design and planning, participation of study subjects, and investigators' time
- Struggles to track and follow up mobile study participants
- Becomes increasingly susceptible to the Hawthorne effect[c] the longer the follow-up period continues.

For a successful HDSS, there are a few requirements. First, the study site is crucially reliant on strong leadership and assertive management, with continuity over time, since directing such long and complex studies takes considerable institutional memory. Then, the HDSS's original study objectives must remain firm: if new studies are added – particularly those investigating sensitive issues or collecting biomarkers – or if several concurrent interventions occur, these could detract from primary goals. Finally, the HDSS needs to comply with two possibly competing demands: on the one hand, resolving the ethical concerns regarding participant anonymity in small-area research and preserving the scientific rights of involved Southern researchers, and on the other hand, increasing public accessibility to the HDSS data.[25]

Verbal autopsy

Health and demographic surveillance systems are usually established in settings where access to health services is limited, and where a substantial proportion of people die at home or elsewhere out of public view. Many deaths are thus overlooked by whatever limited form of vital registration is in operation. To remedy this shortcoming, considerable effort has gone into developing the verbal autopsy (VA) tool – a method of determining probable cause of death using information obtained from a close caregiver. In general, lay fieldworkers administer a questionnaire on the signs, symptoms and circumstances during the terminal illness. The information obtained is then assessed by medical officers, to arrive at diagnoses that contribute to cause-specific mortality data.

Use of VA goes back to the 1950s and 1960s in Khanna and Narangwal areas, India, and in The Gambia.[26] Focus was initially on child mortality and more recently on adult deaths.[27,28] Currently, VA-determined causes of death are available in 36 sentinel sites and two large sample registration systems in India and China.[29] While such information opens up the possibility of estimating and comparing cause-specific mortality across areas lacking death registration, it also highlights the need to address issues of standardisation and validation of different VA instruments and VA assessment procedures. To this end, a number of international workshops have been organised, most recently by the World Health Organization in 2005.

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[c] Hawthorne effect refers to the effect of the research (often positive) on the behaviour of study participants.

INDEPTH: International Network for the Demographic Evaluation of Populations and their Health

In April 1997 in London, leaders of the Agincourt health and demographic surveillance site held a scientific roundtable. Participants from some seven other HDSS sites were invited, together with international academic leaders in the field, and a representative from the Rockefeller Foundation. The roundtable was designed to review Agincourt's contribution to knowledge and policy to-date, decide on its future direction and plan the next phase of work, but it also achieved an unanticipated outcome – a surge of interest in identifying and linking all HDSS sites in the developing world.[30-32] The roundtable was followed by an international symposium in July 1997 on "The role of longitudinal community-based health research for disease control and beyond", convened by the Department of Tropical Hygiene and Public Health at Heidelberg University. Two expert meetings followed in 1998, one convened by the Rockefeller Foundation in Bellagio, and the other by the Ghana Ministry of Health in Navrongo. The upshot was the formation of the INDEPTH Network, established formally at a further meeting in Dar es Salaam in November 1998, and the adoption of its formal constitution in Addis Ababa in January 2002.

The vision of the Network is that "INDEPTH will be an international platform of sentinel demographic sites that provides health and demographic data and research to enable developing countries to set health priorities and policies based on longitudinal evidence. INDEPTH's data and research will guide the cost effective use of tools, interventions and systems to ensure and monitor progress towards national goals." INDEPTH's mission is to "harness the collective potential of the world's community-based longitudinal demographic surveillance initiatives in resource constrained countries to provide a better, empirical understanding of health and social issues and to apply this understanding to alleviate the most severe health and social challenges".[33]

Some 17 HDSS sites participated in the founding meeting in 1998. Since then, 40 active sites have been identified in 20 countries (26 of the sites are in sub-Saharan Africa) with 70% of these established since 1990 (Figure 1). Activities of INDEPTH concentrate on both multi-site research and capacity-building. Key research areas include malaria, HIV/AIDS, health inequities, migration and urbanisation, adult health and aging, appropriate interventions and delivery mechanisms, and monitoring progress towards the Millennium Development Goals. Emphasis is placed on disseminating scientific findings and using these to influence health policy and practice. Three relevant book-length volumes have been published, on mortality patterns in Africa and Asia,[24] INDEPTH model life tables for sub-Saharan Africa,[14] and health equity in small areas.[34] The Network contributed a chapter to *Disease and Mortality in sub-Sarahan Africa*, published in June 2006, and is getting its findings into the peer-review journal literature.[35,36]
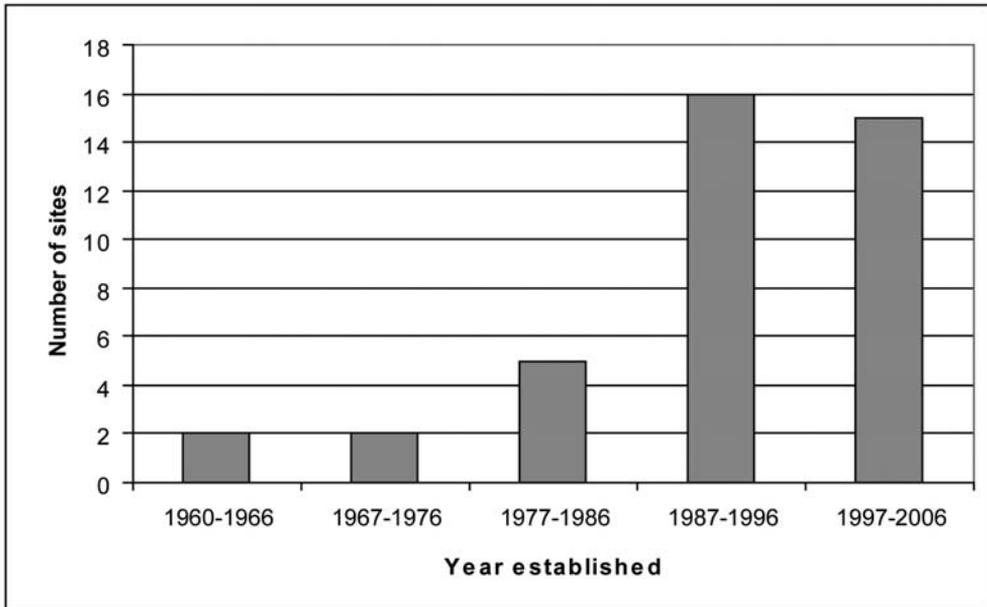
Figure 1. *Establishment of INDEPTH field sites by time period*

Demographic, Epidemiologic and Health Transitions

Thomas Malthus, more than 200 years ago, reflected and wrote extensively on changing population patterns and their impact.[37,38] He argued that population growth would exceed food supply, and that the only solution was to limit reproduction.[39,40] Since then, conceptual developments have taken place, helping to explain the dramatic changes in the patterns and causes of death that have taken place in most countries,[41] and thereby to predict the trajectory of future change. Initially, the concept of *demographic transition* was used to describe fertility and mortality change. This was followed by the *epidemiologic transition* framework, which supplemented mortality change with changes in patterns of disease and disability; and subsequently the concept of *health transition* emerged, which includes the social and behavioural changes that drive the epidemiologic transition.[42]

Demographic transition

Demographic transition theory describes the change from high fertility and high mortality in "traditional" societies to low fertility and low mortality in "modern" societies consequent on economic development. The transition involves four main stages:

Stage 1 – pre-industrial societies: mortality and fertility are both high and fluctuate rapidly in response to natural events such as drought or disease epidemics; the population is relatively young

Stage 2 – developing countries: mortality rates decrease due to better food security and sanitation, and life expectancy increases; there is no corresponding decline in fertility, hence the population increases; the population age structure becomes younger as child survival improves

Stage 3 – middle-income countries: fertility decreases; population growth stabilises; there is gradual population aging

Stage 4 – industrialised countries: low mortality and low fertility; if birth rates fall below replacement level the population decreases in size.[43]

Epidemiologic transition

In 1971 Abdel Omran, recognising the limitations of focusing only on mortality and fertility change in demographic transition theory, developed a theory of epidemiologic transition which broadened the scope of mortality transition to include changing morbidity patterns and the interaction of these with their socio-economic determinants and consequences.[44] He proposed three stages through which societies move sequentially: the "era of pestilence and famine", the "era of receding pandemics", and the "era of degenerative and man-made diseases". These were distinguished by differences in mortality levels, life expectancy, and patterns of underlying morbidity (Table 1).

Table 1. *Key features distinguishing Omran's stages (eras) of epidemiologic transition*[44]

	Era of pestilence and famine	Era of receding pandemics	Era of degenerative and man-made diseases
Mortality	Extremely high mortality, especially in children. No sustained population growth	Mortality declines; sustained population growth	Lower overall mortality with peak at older ages; population growth
Life expectancy	e° is low; varies between 20 and 40 years; male life expectancy often higher	e° increases from about 30 to 50 years	e° increases to exceed 50 years; higher female life expectancy
Morbidity	Epidemic infectious diseases, nutritional disorders, complications of pregnancy and childbirth	Infectious diseases and malnutrition	Non-communicable disease (cardiovascular disease and cancer) and injuries

e°: life expectancy at birth

Three basic models of the epidemiologic transition, typified by Omran, were differentiated by variations in the pattern, pace, determinants and consequences of population change: [44,45]
- the *classical or western model* seen in most western European societies: characterised by progressive declines in mortality and fertility, and largely determined by ecobiologic factors and socio-economic improvements
- the *accelerated model* experienced in Japan and Eastern Europe: started later, more rapid progression, and also determined by socio-economic advances but enhanced by developments in medical technology
- the *contemporary or delayed model* in most developing countries: involves an unfinished transition driven largely by the spread of medical and public health interventions.

Omran's theory of epidemiologic transition has undoubtedly contributed to global public health thinking through focusing on the mortality side of the demographic transition, locating health change within social change, acknowledging the value of public health activities, and stimulating much debate among both population and public health scientists.[37,38] His theory is not beyond criticism, however. Caldwell points out that while epidemiological transition theory emphasises the role of social, economic, ecobiological, and environmental change, it understates the contributions of scientific discovery, medical technology, and public health interventions such as water purification, sewage disposal and immunisation.[37] The sequential progression – moving through one stage and then the next – has been challenged too.[42,46] "The ephemeral nature of health trends in developed countries seriously undermines widely held notions of epidemiologic transition as a stable march of progress."[45] And reducing complex patterns of population change, diseases and their determinants to just the three stages or "eras" is conceptually limited and inconsistent with emerging patterns.

Accordingly, subsequent stages or eras have been added by Omran and others.[42,47-50] There is now a fourth stage or era of "delayed degenerative disease", characterised by older-age mortality due to non-communicable diseases, consequent on sharply declining death rates and a change in population structure (lower proportion of young, higher proportion of elderly).[47,48] The patterns of mortality and morbidity in this stage are widely explained by reference to lifestyle behaviours – an interpretation criticised for emphasising individual-level responsibility rather than social and economic determinants of disease.[42] Then there is a fifth stage or era, proposed by Yusuf and colleagues – the stage of "health regression and social upheaval", in which social disruption and conflict cause worsening mortality and a resurgence of "old" infectious diseases and malnutrition together with cardiovascular disease and violence.[49] This stage is illustrated by transitional patterns in Russia, with declining life expectancy consequent on escalating deaths from cardiovascular diseases, accidents and violence, fuelled by increasing alcohol consumption.[51]

The original epidemiologic transition theory has been disputed as too linear and unidirectional by Frenk and colleagues, using Mexican data to demonstrate the complexity of middle-income countries. They describe a "counter transition" in which patterns of morbidity and mortality are reversed, a "protracted or prolonged transition" in which change does not fully occur and infectious and non-communicable diseases co-exist, and "epidemiologic polarization" where the poorest experience highest death rates due to more pre-transitional diseases including infections and nutritional disorders.[52,53] A further critique comes from Gaylin and Kates: noting that inequalities give rise to different rates of change among diverse social strata within a country, they assert that the formulation of epidemiologic transition is too generalised and fails to differentiate between population subgroups. They further criticise the notion that infectious-disease mortality continues to decline: the emergence of HIV/AIDS as a new infectious disease, they argue, undercuts the plausibility of such a notion, and also clearly shows the exacerbation of mortality differentials between particular subgroups.[45]

Health transition

The "health transition" concept moves beyond demography and epidemiology to include the social and behavioural changes that parallel and drive the changing patterns of fertility, illness, disability, and death. Socio-economic development, in both industrialised and developing settings, has been accompanied by an escalation of socio-behavioural problems – problems that contribute directly and indirectly to morbidity and mortality profiles, and need urgent redress.

Social disruption

One such problem – and the trigger for many others – is that of substance-abuse. Sugar, Kleinman and Heggenhougen discuss the complex interactions between "modernisation" and substance-use disorders, and how these reflect the vulnerability of transitional populations.[54] The take-up of cigarettes, alcohol and drugs increases with exposure to modern lifestyles and western influences, and the greater personal autonomy and freedom of choice resulting from it. Unfortunately, faced with persistent poverty and destructive social changes, people in these transitional populations are often driven to abuse these substances as a way of escaping from chronic stress and sense of alienation. The inevitable cascade of adverse consequences follows. With increasing cigarette smoking, cardiac disease, respiratory illness and malignant conditions are bound to escalate. (Tobacco production and consumption are increasing rapidly in developing countries, without as yet much of the prevention, control and cessation legislation and behavioural interventions evident in industrialised nations.) Alcohol contributes directly to alcoholic liver disease, malnutrition and dementia, and indirectly to violence, suicide and road traffic incidents. Illicit drug-use by parents results in abandoned children and child employment, while drug-use by children results in poor school performance.

Labour migration clearly contributes to social disruption and family breakup, which in turn are strongly associated with negative health consequences. In the mid-1940s, in rural areas of what is now KwaZulu Natal Province, Kark and colleagues documented the transmission of syphilis to rural wives by men who had contracted the disease when working as migrant labourers in the towns.[55] A study in early 2000, in rural Limpopo Province, painted a more nuanced picture of sexual risk behaviours associated with migration, with the risk being dependent upon frequency of return to the rural home: male labour migrants who made frequent return trips were actually *less* likely to have multiple partners than locally employed men, while infrequently returning migrants were more likely.[56]

Non-communicable disease and risk factors

In general, as total mortality declines, so do cause-specific mortality rates for most causes of death. Preston analysed 165 cause-of-death life tables for 43 countries over a century (only 8% of these life tables represented developing-country populations), and found the major causes accounting for the decline in all-cause mortality to be the drop in pulmonary tuberculosis, other infectious and parasitic diseases including diarrhoeal diseases, and pneumonia/bronchitis/influenza. Neoplasms in both sexes, and cardiovascular disease mortality in males, were exceptions; similar observations were made by McKeown in England and Wales.[57]

According to Murray and colleagues, many causes of death in industrialised and developing countries are independent of overall mortality levels. This finding challenges any simple assumption that causes of death are a straightforward function of overall mortality level, and highlights the importance of assessing risk factors when predicting the cause-of-death transition.[57]

Almost all regions of the world are experiencing population aging, with the poorest regions expected to show the greatest proportional increase in older age-groups. And because advancing age is a primary predictor of mortality due to cardiovascular disease and other non-communicable disease including malignancies, these conditions are bound to increase in industrialised and developing countries alike.[40,58-60]

The balance between different conditions, such as stroke and ischaemic heart disease, depends on the prevalence of risk factors. These vary across cultural and socio-economic settings, and are independent of the effect of aging populations. Synthesising existing literature, Connor has linked the predominant cardiovascular diseases and stroke-type with Omran's stages of epidemiologic transition (Table 2).[61] Stroke increases during health transition as risk factors change, and is more common than cardiac disease initially. The type of stroke and its cause also change: hypertension is the major vascular risk factor in the early stages of transition, resulting in haemorrhagic stroke; however, once cholesterol levels increase, ischaemic stroke due to atherothrombosis emerges as the more common type.

Table 2. *Cardiovascular disease and stages of the health transition (adapted from Connor, 2006)[61]*

Stage of transition	Predominant cardiac and vascular disease	Predominant nature of stroke
Era of pestilence and famine	• Rheumatic heart disease (RHD) • Infections • Nutritional cardiomyopathies	• Cardioembolic stroke
Era of receding pandemics	As above plus: • Hypertension • Hypertensive heart disease • More stroke than ischaemic heart disease (IHD) • More RHD than atherosclerotic heart disease	As above plus: • Haemorrhagic stroke due to hypertension • Stroke occurring at relatively young age • Emergence of atherosclerotic stroke
Era of degenerative and man-made diseases	• IHD at relatively young ages • More heart disease than stroke • Far less RHD than atherosclerotic heart disease	• Proportion of haemorrhagic strokes decrease • Atherothrombotic stroke increases
Era of delayed degenerative diseases	• Stroke and IHD at older ages	• Atherothrombotic stroke

Given their patterns of cardiovascular disease, one would classify sub-Saharan Africa, rural India and South America as being in the era of pestilence and famine, with some 5-10% of all deaths caused by these conditions. China by contrast would be classified as being in the era of receding pandemics, and urban India has moved into the era of degenerative and man-made diseases. As for the industrialised nations, they can be assigned to the era of delayed degenerative diseases.[61]

Gillum, in studying patterns of cardiovascular disease among populations of sub-Saharan African descent, has characterised six stages of epidemiologic change. Stage 1 represents the pre-colonial African situation and traditional African societies today; stages 2 and 3 characterise modern urban Africans and West Indians respectively; stage 4 represents rural African-American

populations in southern United States; stage 5 poor inner-city African-Americans; and stage 6 affluent urban African-Americans. Gillum postulates that evolution from one stage to the next is driven by progressive acculturation, urbanisation and affluence, and their associated risk factors, including dietary change (increasing salt and saturated-fat intake) and smoking. In stage 1, cardiovascular disease and stroke are virtually non-existent; hypertension and associated stroke appear in stages 2-4, and atherosclerosis and ischaemic heart disease predominate in stages 4 and 5. Morbidity and mortality due to cardiovascular disease then decline in stage 6, consequent on the impact of prevention programmes and better clinical management.[50]

Since developing countries account for some two-thirds of the world's population and have higher mortality, they are contributing proportionally more to the global burden of cardiovascular disease than developed countries are. Of particular concern is the relatively early age of these deaths in developing countries as compared with developed countries, and the anticipated rise in both proportional and absolute cardiovascular mortality in developing countries over the coming two decades.[58] These patterns are attributable to the increasing incidence of atherosclerotic diseases, their relatively early age of onset, and large populations with a high proportion of young and middle-aged adults. Increasing risk-factor levels – obesity, diabetes, hypertension, cholesterol – accompany urbanisation and higher income levels.[49] It is thought that the prevalence of known risk factors, other than hypertension, is lower among black Africans than other groups within Africa and the world,[62] but detailed data on risk-factor levels for sub-Saharan Africa are limited, and data on trends effectively absent.

The 2001 Global Burden of Disease Study confirms the increasing role of non-communicable diseases in low- and middle-income countries, and highlights the need for more information on risk factors, particularly trends over time. Smoking, though not specifically measured in the study, is thought to be the risk factor that increased most from 1990 to 2001. Hypertension is an important risk factor for stroke in sub-Saharan Africa, and one that can be controlled through effective screening and treatment programmes.[63] For a more complete understanding of disease-burden determinants, though, the range of risk factors studied needs to be widened to include, for example, salt and fat intake.[19,60] In many ways, the developing world looks ill-equipped to cope with the coming disease burden: it has insufficient appreciation of the extent of the burden; there is a lack of resources, health service management is poor, and preventive and treatment programmes are inadequate.

* * * * *

The transition frameworks just outlined, although they usefully describe changing mortality patterns within regions and differences in death rates between countries, do not adequately explain these differences, and do not predict future patterns of disease.[42] If we are to anticipate changes and not simply react to them after they have occurred, empirical data are needed to better understand the diverse characteristics of the health transitions.[53] The body of work contained in this thesis makes a modest contribution to such understanding: it documents the adverse mortality transition in rural South Africa over a decade of major socio-political change and emergence of the HIV/AIDS pandemic; it draws out the implications for health-system planning and health-service provision; and it elucidates the complex patterns of health transition in middle-income countries.

Aims

Overall Aim

To better understand the dynamics of mortality transition in rural South Africa over the past decade, and in so doing, to identify priority issues for health intervention; to inform health and development programming, policy formulation, and the research agenda; and contribute to international debate on the nature of the "health transition".

Specific Aims

In the Agincourt subdistrict of rural northeast South Africa:

- To describe the health and demographic surveillance methodology, and validate the verbal autopsy tool (Papers I and II).
- To describe and interpret overall mortality rates by age and sex from 1992 to 2003[d] thereby assessing the impact of HIV/AIDS (Paper III).
- To establish a profile of probable cause of death by age and sex (Papers IV, V and VI).

Thesis themes

Methodology and findings will be discussed according to three main themes:

1. Population surveillance in developing countries
2. Health policy and practice: implications of changing mortality
3. Health transition

Table 3 presents a matrix that highlights key points from the cover story and from each paper, and indicates the theme under which they fall.

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[d] Papers included in this thesis cover the period 1992-1995 or the period 1992-2003. In parts of the cover story, results are updated to include 2004.

Table 3. *Mortality and health transition in a new South Africa: Summary of themes by cover story and papers*

Themes	Cover story	Papers					
		I Agincourt health and demographic surveillance	II Verbal autopsy validation	III Mortality trends	IV Who dies from what	V Stroke mortality	VI Undiagnosed PTB deaths
Population surveillance in developing countries	Global initiatives to address lack of population-based information. Contribution of HDSS sites. Comparison of HDSS and national data.	Health and demographic surveillance systems: methodological issues, strengths, limitations, links to other study designs.	Validating the VA instrument and process: method and findings. VA addresses hospital bias of official statistics.		Limiting bias: determining causes of death in the community through verbal autopsy.		Undiagnosed PTB deaths identified through verbal autopsy.
Health policy and practice: implications of changing mortality	Implications of changing mortality patterns, morbidity and NCD risk factors, for public health sector services.	Absence of population-based data for health and other public sector planning: health and demographic surveillance sites address this.	Validation study indicates that cause of death data can be used for local health sector planning.	Mortality patterns indicate increasing demand on health services. Effective chronic-care systems needed for HIV and NCDs.	Multiple challenges to public sector: HIV/AIDS prevention, treatment & care; NCD control; maintain & improve MCH services.	Emerging NCDs in rural communty: need for effective programmes to limit risk factors and manage chronic disease.	Missed diagnoses at health facilities result in longer transmission in community; improvements in case detection needed.
Health transition	Critical examination of transition theory in high HIV setting. Vulnerable population sub-groups: the poorest, women, socially marginalised.	Empirical data collected longitudinally – unusual opportunity to monitor transitions. Asset survey permits equity analyses.		Evidence of a counter transition, a protracted transition, and epidemiologic polarization. Mortality worse in most poor / socially marginalised.	Evidence of a protracted transition: co-existing infectious and non-communicable diseases.	Importance of NCDs in remote rural areas not previously recognised.	Infectious diseases remain a priority: new (HIV) and old (PTB and acute diarrhoea).

HDSS: health and demographic surveillance system; VA: verbal autopsy; NCD: non-communicable diseases; MCH: mother and child health; PTB: pulmonary tuberculosis

Data and methods

Study Area

Historical context

South Africa

Segregation, part of South African history since the mid-1600s, culminated in the apartheid policy introduced by the National Party government in 1948. Segregationist legislation was enacted and single-mindedly applied in the social, residential, cultural, economic and political spheres. Key aspects of 20th-century South African history affecting rural populations included: forced resettlement, restriction of movement of black Africans, and separate development with the establishment of "homelands" or "Bantustans".

Restrictions on access to land, together with forced resettlement, resulted in denser population settlements of black Africans in economically and agriculturally inhospitable areas. Under so-called "betterment" policies, people were forced to leave their agricultural homesteads and move to demarcated residential stands where their access to arable land was vastly reduced. One result was the increasing reliance on wage labour to sustain household livelihoods. With the imposition of taxes, these settlement areas were turned into cash economies – a strategy to provide labour for South Africa's mining and industrial sectors. Social effects were severe, including entrenched migration, spousal separation, spatially divided or "stretched" households, and shifts in power relations, with the dependency burden falling heavily onto women and younger wage-earners. These patterns remain common today.

During the 1950s various laws were passed to control the movement of black South Africans, closing the towns and cities to all but those required for the country's economy. The *Group Areas Act* strictly enforced the demarcation of separate living areas for different racial groups. The pass system required all black Africans over the age of 16 years to carry a reference book specifying home areas and showing evidence of permission to work anywhere else. This system limited the influx of people into urban and "white" areas, as transgressions were brutally dealt with. And by effectively restricting free movement to those with employment, the system entrenched the separation of families, as women and children were typically compelled to remain in the rural sending areas. The severe psycho-social impact, including high rates of alcoholism and violence, was inevitable; other health outcomes included the proliferation of sexually transmitted infections, contracted from new sexual networks at the workplace that developed as a result of spousal separation; and tuberculosis and pneumoconiosis contracted by underground mine workers, and aggravated by their crowded living conditions in single-sex mining hostels.[55,64]

Also during the 1950s, as Black representation in the South African political system was denied, so the basis for Black political rights in separate homelands was laid. In 1972, the "homelands" or "Bantustans" acquired self-governing status, legitimised by the doctrine of separate development and ethnic homogenisation. This strategy led to the creation of borders that had not previously existed, and enforced separation of people into ethnic or tribal clusters, thereby further entrenching geographic, social and cultural divides among the country's black majority. Among the other

consequences was the proliferation of costly and often inefficient administrative structures, including the duplication of public-sector offices and services. This wastefulness was all the more regrettable, in that the homelands were established in areas of little industrial and agricultural activity and potential, and suffered from weak health and education systems.

Agincourt sub-district

Two adjacent homelands were situated in the northeast of South Africa – Lebowa and, to its east, Gazankulu. The inhabitants of Lebowa were Sotho-speaking; the inhabitants of Gazankulu belonged to the Shangaan-speaking Tsonga ethnic group. The Agincourt sub-district, forming our study site, is situated in what was the Mhala District of Gazankulu. For the study site's primary health-care clinics, the management and drug distribution were provided by the Tintswalo hospital of Gazankulu, located some 45 km from the closest of the study site villages, Agincourt village. Patients were referred from these clinics to Tintswalo Hospital when necessary, even though Lebowa's Mapulaneng Hospital was much closer, just 25 km from Agincourt village.

The population of the study site is more diverse than this simple picture suggests, with about one-third being of Mozambican origin. During the mid- and late 19th century, Mozambican immigrants arrived in the area, fleeing war in Gaza province. This was repeated in the mid-1980s, when the RENAMO-FRELIMO conflict in Mozambique produced a further influx of refugees. Despite voluntary repatriation programmes organised by UNHCR[e] and non-governmental organisations, many Mozambican nationals elected to remain along the northeast border of South Africa as "self-settled" former refugees. They have strong language, cultural and kinship ties with the South African residents of Gazankulu, and so have assimilated far more easily there than in the adjacent Lebowa homeland. In 1993 they were granted group refugee status, but nevertheless remain a vulnerable group, with persistently poor access to water, sanitation, labour markets and legal rights.[65]

In 1990 Nelson Mandela was released from prison, and in 1994 the first democratic elections were held in South Africa, with Mandela elected president. For the first decade after liberation, the Agincourt sub-district was registered as being in Limpopo Province, but in 2006 was officially reassigned to the adjacent Mpumalanga Province.

Concurrent with and offsetting the great hopes associated with peaceful democratic change has been the emergence of the HIV/AIDS pandemic. Estimates of HIV sero-prevalence among antenatal-clinic attendees in the area indicate an increase from 2% in 1992 (old Transvaal Province) to 33% in 2003, and 35% in 2005 (new Mpumalanga Province); while the figure in 2005 for the general population aged 2 years and older in the same province is 15%, second highest in the country.[66-69] HIV/AIDS has become a scourge now decimating the country's prime-age adults, with devastating consequences for household livelihoods and psycho-social well-being, and major implications for older adults' roles in child-care and income-generation.

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[e] UNHCR: United Nations High Commissioner for Refugees

Agincourt study site

Why the Agincourt sub-district?

In 1982, the Department of Community Health at the University of the Witwatersrand established a Health Systems Development Unit in rural Bushbuckridge to develop models for local health services based on primary health care. Such work at that time was greatly constrained by the influence of apartheid, which was promoting a hierarchical and authoritarian health system dominated by a hospital-centred administration. A decade later, in 1992, the Agincourt field site was established with two key aims: to develop an experimental area for introducing and evaluating district and sub-district health programmes (undertaken in close partnership with the Gazankulu health services); and to provide reliable population-based information for use in health-system planning and practice.[70]

The appeal of the Agincourt sub-district as the study site lay in its promising combination of three particular features: its remote rural location; its possession of an existing health centre and several clinics; and the presence of Mozambican immigrants. The choice was finalised jointly by the University and the Gazankulu health service, which recognised that the impending socio-political change would provide the opportunity to develop rational referral patterns de-linked from homeland boundaries.[71,72]

Work was conducted largely within the resource constraints of the rural public-health sector, to ensure that the findings would be relevant to emerging national health policy.[70,71] Pilot programmes included: the establishment of a district health authority with community representation; the development of a network of clinics and health centre, with "step-ups" of care, effective referral systems, appropriate human-resource capacity, and decentralised laboratory services; and the setting up of community-based health programmes focused on vulnerable sub-groups. Lessons learned were scaled up and introduced into the two Provincial Departments of Health that bordered on the demonstration site.[73] These initiatives were informed by the health and demographic surveillance system (HDSS) established at the same time. This HDSS provided reliable data on population size, structure and geographic distribution for delineating and defining clinic catchment areas, and its cause-of-death findings assisted in targeting district interventions to high-priority conditions affecting vulnerable sub-groups.[70]

Study setting

The Agincourt study site constitutes a sub-district of Bushbuckridge district, Mpumalanga Province,[f] and is situated 500 km from Johannesburg in the rural northeast of South Africa, close to the border with Mozambique (Figures 2 and 3). It covers 402 km² of semi-arid scrubland, ill-suited to agriculture though adequate for game farming and low-density cattle-rearing. Summers are hot (12-40º C) and winters mild (5-27º C). Drought occurs on average every 3.5 years, and even in standard years rainfall is low – 550-700 mm a year, falling mostly during the summer months of November to March – and insufficient for irrigation and domestic needs.[72,74]

Figure 2. *Location of Agincourt field site within South Africa*
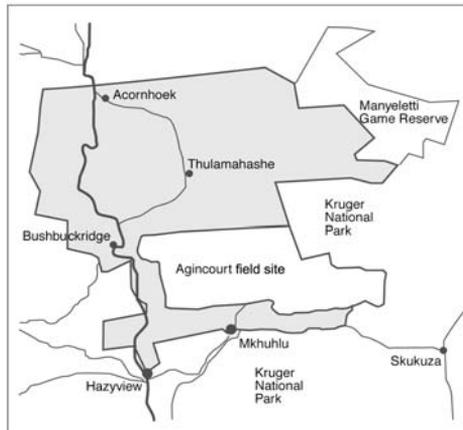
Figure 3. *Location of Agincourt field site within Bushbuckridge district, Mpumalanga Province*

[f] Since the democratic political changes of 1994, administrative areas and borders have changed name and position several times. Hence scientific papers published at different times may refer to the Agincourt sub-district as being located in Northern Province, then in Bushbuckridge region, Limpopo Province, then Bohlabelo district, Limpopo Province, and, most recently, in Bushbuckridge district, Mpumalanga Province.

Within the study site lie 21 villages (Figure 4) and 11,700 households with a population of about 70,000 people, mainly Shangaan-speaking. Almost a third of this population is of Mozambican origin, many of them arriving as refugees in the early to mid-1980s during the civil war, and possibly the largest population of self-settled refugees under health and demographic surveillance. Each village typically has both traditional and civic leaders: the *induna* or chief is hereditary, whereas the representatives of the 17 Community Development Forums (CDFs) are elected. Church affiliation is widespread, whether to mainstream or independent African churches, and many inhabitants adhere to indigenous beliefs alongside their Christianity.
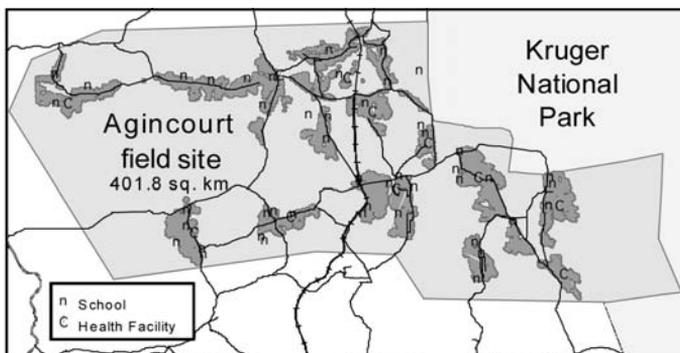
Figure 4. *Agincourt field site villages*

There have been substantial development initiatives recently, including electrification and completion of the Inyaka dam, but the infrastructure is still best described as limited. Pit-latrines remain the norm. Piped water flows erratically, and mainly to communal standpipes, where villagers typically collect it in 25-litre plastic drums. Electricity is too expensive for all but a minority of inhabitants. The roads are seldom tarred, and transport usually takes the form of privately-run minibus taxis. The area has 28 primary schools and 19 high schools, generally of relatively low standards.

The economy is extremely modest. Villagers commonly grow crops which supplement the diet: the household plots of land are generally too small to support subsistence agriculture. Unemployment is high, so many men and women migrate temporarily to find work – whether on nearby farms and timber plantations, or in the mines, or in the manufacturing and service industries of larger towns. Villagers often engage in roadside fruit-vending and suchlike informal-sector activities. For many families, a crucial source of income is that of pensions, particularly the "old-age" pension, and increasingly the "child support grant".[74,75]

The site hosts one health centre and five satellite clinics, all staffed by nurses, and there are three district hospitals situated 25-60 km outside of the site. Most inhabitants access plural health care – from public and private health professionals on the one hand, and from traditional healers or faith healers on the other.[76]

Methods

Overview of study design with timelines

Health and demographic surveillance consists of a multi-round, prospective community study involving continuous demographic monitoring of the entire geographically defined population, in this case that of the Agincourt sub-district. Table 4 provides an overview of the project timeline. The baseline household census was conducted in 1992, with systematic recording of all birth, death and migration events in the population since then. This census was updated at approximately 15-18-month intervals between 1993 and 1999, and on a strictly annual basis since 1999. Verbal autopsies (VAs) to determine likely cause of death are conducted on every death within one year of the event. Data on person-years at risk, death events, and cause of death from baseline to 2003 are included in this thesis.

Table 4. *Timeline: Health and demographic surveillance in Agincourt, 1992-2004*

1992	1993	1994	1995	1996	1997	1998	1999*	2000	2001	2002	2003	2004
Baseline census	CU		CU		CU		CU	CU	CU	CU	CU	CU
	VA		VA		VA		VA	VA	VA	VA	VA	VA
				VAA 1992-1995				VAA 1996-1999				VAA 2000-2003
					VAV 1992-1995							

CU: census and vital events update; VA: verbal autopsy interviews; VAA: verbal autopsy assessment, i.e. medical assessment of completed verbal autopsy questionnaires; VAV: verbal autopsy validation

*Study to determine burden of tuberculosis occured during 1999/2000

Health and demographic surveillance

Maps

Hand-drawn maps of study villages were produced by fieldworkers in advance of the baseline census in 1992 (Figure 5). These maps included every existing dwelling, as well as village-level resources such as schools, shops and water standpipes. Each dwelling was allocated a unique identifying number so as to link individual and household data to a village structure, and enable follow-up visits to specific households. Prior to each census-update round, the maps were updated to incorporate new dwellings, eliminate dissolved households, and record other infrastructural changes. All fieldwork for this thesis relied on hand-drawn maps; however, a full geographic information system with geo-referencing of households has since been introduced, and digital maps have been in use since 2004.
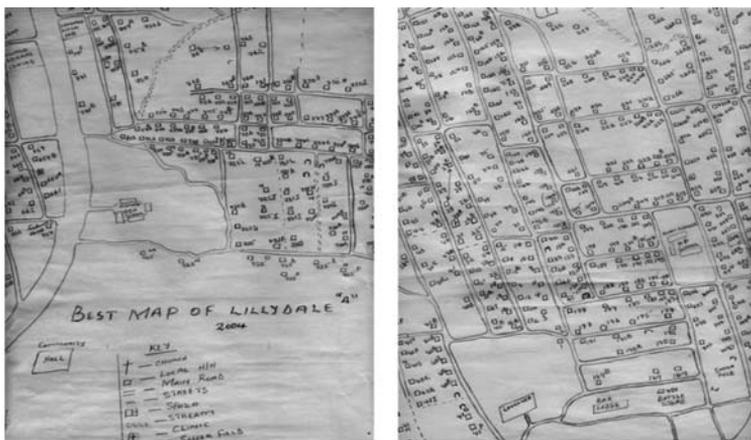
Figure 5. Hand drawn map of Lillydale "A" village, Agincourt study site

Baseline census and update rounds

During the 1992 baseline census, fieldworkers visited each dwelling in the study site and recorded information on household membership and individual status variables. These variables include: relation to household head, nationality, marital status, residence status, and education level. All vital events – death, pregnancy outcome, in- and out- migration – were recorded, and full maternity histories were taken in women of 15-55 years. Key variables related to each event were recorded: in the case of a death, these included: place of death, name of hospital if applicable, maternal death, and whether or not death was registered.

Special modules and status observations, nested within the update rounds, provide basic information relevant to particular research lines. Status observations involve one to three additional questions on individuals or households; for example, screening for conditions of public-health importance such as chronic cough in 1999 – the basis for active tuberculosis case-finding. Special census modules, introduced from 2000, provide explanatory variables for understanding transitions, and may be repeated as necessary to assess changes over time. Household socio-economic status is determined through an asset survey conducted every two years (2001, 2003, and 2005).

Fieldworker conducting household interviews.

In the early years of the project, there was a single data-collection team of ten fieldworkers, some of whom were specially trained to conduct verbal autopsies, and a field supervisor. With increasing numbers of households and the addition of special modules, there are now four data-collection teams, each comprising five fieldworkers and a supervisor, and a separate VA team. Fieldworkers have a census form for each household, completed with information from the previous update round, and structured vital-event forms including the death form. They interview the most senior responsible adult, if necesssary visiting the dwelling a second time to find this person.

Verbal autopsy

Each recorded death is subject to a VA carried out by a specially trained fieldworker who interviews the closest caregiver of the deceased in his or her primary language. The VA team comprises four fieldworkers and a team supervisor. All VAs are conducted between one month and one year of the death. (In keeping with traditional mourning practices, no VA is conducted for at least a month following bereavement.) The interview schedule is a modification of that previously used in Niakhar, Senegal.[77] It covers all ages, was translated into Shangaan, and was modified to include only culturally appropriate terminology. An open section or narrative elicits, in the respondent's own words, the symptoms and signs preceding death. Fieldworkers probe for completeness of information, the sequence of signs and symptoms, and response to treatment. Several filtering questions follow, such as "Did the deceased cough?" A positive answer leads to a detailed module on that symptom. If the answer is negative, the interview proceeds to the next filtering question. Table 5 indicates how signs and symptoms elicited during VA interview are used to distinguish PTB and HIV/AIDS.

VA review entails assessment by three medical practitioners (Figure 6). Two doctors independently review the information and assign a probable cause for each death. Where these correspond, the diagnosis is accepted. Where they differ, the two clinicians discuss the case in an effort to reach consensus. Where this is not achieved, a third practitioner assesses the VA, blind to earlier

findings. If the third assessment is congruent with one other, it is accepted as the "probable cause of death"; if not, the cause is coded as "ill-defined". Where possible, a main (or underlying) cause, immediate cause and contributory factors are identified; classification is consistent with the International Classification of Diseases (ICD-10). The VA review process is similar to that in other studies. [78-81]

Table 5. *Using the verbal autopsy to distinguish between pulmonary TB and HIV/AIDS*

Signs and Symptoms		Diagnosis		ICD-10 code
Productive cough Night sweats Loss of weight during illness; not thin before No respiratory distress in adults No chronic diarrhoea No neurological signs No oral thrush / no rashes	⇒	Pulmonary tuberculosis	⇒	A16
Chronic respiratory symptoms Clinical deterioration and death despite full course of TB treatment	⇒	HIV/AIDS underlying cause with associated pulmonary tuberculosis	⇒	B20
Chronic gastroenteritis Oesophageal thrush Respiratory distress Chronic respiratory symptoms In children, parents that are chronically ill	⇒	HIV/AIDS underlying cause with associated pulmonary tuberculosis	⇒	B20
No history of cough Cough that responded to antibiotic treatment Chronic respiratory symptoms Chronic gastroenteritis Oesophageal thrush Respiratory distress In children, parents that are chronically ill	⇒	HIV/AIDS	⇒	B24
Loss of weight Lymphadenopathy	⇒	Non-specific and unhelpful alone in distinguishing HIV/AIDS and PTB	⇒	N/A
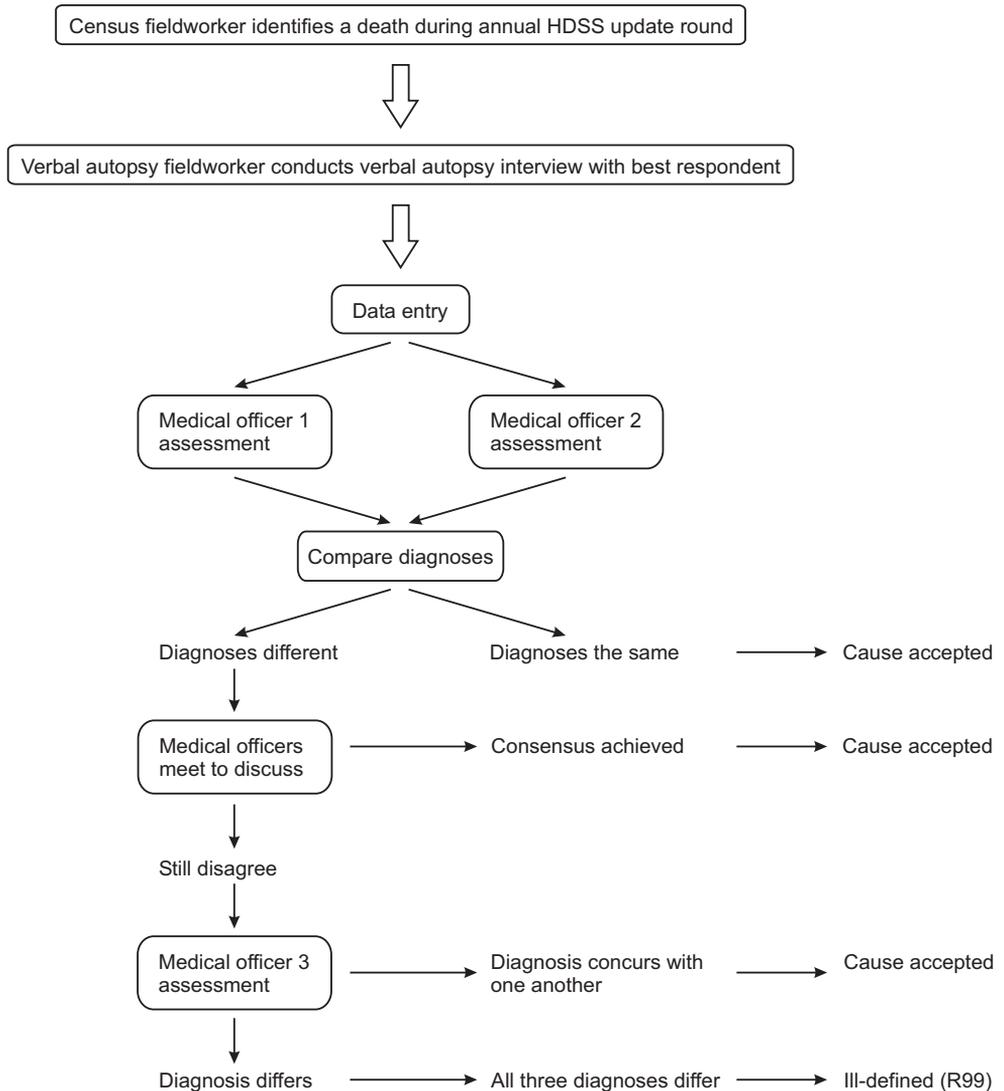
Figure 6. *Process of verbal autopsy data collection and medical assessment, Agincourt HDSS*

In the mid-1990s, the Agincourt VA tool and assessment process was validated. Final diagnoses were compared with hospital reference diagnoses (which satisfied strict inclusion criteria) and sensitivity, specificity and predictive values were calculated for categories and individual causes of death.[82] Validation of VA diagnoses between 2001 and 2005 provides further information on the reliability of HIV/AIDS diagnoses specifically.

Database and data entry

The Agincourt database management system was first held in FoxPro, later re-written into Microsoft Access, and converted in 2001 into SQL Server, enabling a higher standard of database technology, including data protection, and improved means of querying the database. A custom-made data-entry program sits on top of the SQL Server database and, by mirroring the format of the data forms, provides an easy-to-use interface between users and the database. Data is captured via simultaneous data entry, with five networked computers writing to the HDSS database on a server. Despite infrastructural limitations, data is entered within the field site to facilitate working relationships between data and field teams and so enhance quality. The system incorporates built-in validation checks to flag and filter out implausible or unusual data. Raw data are archived in fire-proof filing cabinets; ready access to forms of the preceding five years is retained in case they should be needed in database cleaning.

Data are stored in related tables: the main table, the "Individual" table, stores key information on all individuals encountered; the "Residence" table provides information on individual residence episodes; a "Memberships" table records information on entry and exit from a particular household, and there is a separate table for each death and other vital events. Special module tables, such as the asset survey, are updated with varying frequency.

Data from the VA questionnaire are entered at the same time as the death and other HDSS forms. A new application allows the cause-of-death data to be entered at a later stage, after the VA has been assessed by the reviewing doctors. This ensures that all physician reviews have been made before a final cause of death is assigned. The application simultaneously enters data into the HDSS and the VA databases, while checking consistency between the two data systems.

Quality control

Quality control of HDSS data occurs at five levels from field to data room. Data collection forms are checked at three field levels – by fieldworkers themselves on a daily basis, by fellow team members cross-checking on a weekly basis, and by supervisors making random checks. Errors are corrected in the field office where possible; otherwise a household revisit is conducted. At the main Agincourt field office a specialised "quality checker" carries out a final review in which errors are recorded and forms returned to the field for correction. Checkers also conduct in-service training to address common problems. Once a form passes the quality checkers it is transferred to the data room for data entry. As data are entered, there are programmed computer checks for invalid codes, missing values, inconsistency of records and duplicate entries; any data items that do not pass the pre-determined validation rules are blocked and an error message is produced, resulting in the form being manually re-checked and sent back to the field for resolution if necessary.

Census supervisors observe fieldworker interviews and conduct random duplicate visits on a 2% sample of households; these visits allow constructive feedback as well as the computation of error rates. Information on quality is fed back to the site manager and team supervisors at weekly meetings.

Similarly, completed VA questionnaires are checked first by the fieldworker him/herself, cross-checked by another VA fieldworker, with a final check by the VA team supervisor. During the course of the fieldwork each year, Kahn reads a random selection of completed questionnaires, and gives group and individual feedback on quality.

Ethical issues

Ethical clearance for the Agincourt health and demographic surveillance system has been granted by the University of the Witwatersrand's Committee for Research on Human Subjects (Medical) (No. M960720). Community consent was obtained from both civic and traditional leadership when the study was initiated, and verbal informed consent continues to be obtained at individual and household level. As for the VA, a letter to the Chair of the human subjects committee was required in order to secure clearance as part of the HDSS.

Surveillance work over a prolonged period rests on stable long-term relationships which need to be nurtured and regularly renewed. The relevant primary relationships here are those formed between the Unit's LINC[g] office and the 17 elected village Community Development Forums in the study site. Routine interactions include: informing village leaders and communities of forthcoming census updates and research projects; well-prepared feedback at village meetings, and discussion of research findings; and regular production of village "fact sheets" to support local development initiatives. Information on cause of death is aggregated for the field site as a whole and not presented at village level, so as to avoid the risk of people linking specific causes with particular individuals or households. Health workers from local clinics are included in the village feedback meetings to answer any health-related questions posed by the community.

Since 2002, the LINC office has been compiling and updating information directories on development, education, and home-based care resources for the use of community leaders and local organisations. There is a strong commitment to working with service providers – including those of health and welfare, and education – initially bringing policy-relevant research findings to their attention, and later supporting programme development.

Great importance is attached to ensuring confidentiality in small-area research. Data are captured in a secure computer room onto an isolated local area network. The database is secured using two levels of user-access control: a password to log onto the operating system, and a second password to log onto the database. A hierarchy of database access exists, with the field research manager and data manager having full access, the data supervisor having restricted access, and data typists having data-entry access only.

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[g] LINC: Learning, Information dissemination and Networking with Community. The LINC office is responsible for promoting the use of research findings by public-sector stakeholders and community; community involvement in research governance; general community liaison; and ensuring research of the highest ethical standard.

Results

General Population Characteristics

Population size and structure

The Agincourt study site covers 402 km^2 and has a population density of 174 persons per km^2. This compares to 19 per km^2 in the neighbouring, formerly "white" farming area, 22 per km^2 in Sweden,[83] 103 per km^2 in France and 235 per km^2 in the United Kingdom.[84] Population density as a measure of rural/urban settlement patterns is not useful alone, and should be considered together with other features including levels of infrastructure (such as water supply and sanitation) and distance from larger centres (with their range of civil, municipal and retail services).

In 1992/93 the total population of the Agincourt study site was 56,583 individuals, living in 9,284 households – this included the permanent population as well as temporary migrants who were resident for less than six months of the year but remained closely linked to the rural household. Over the next ten years, the population increased to 69,749 in 11,737 households, with a mean household size of 6 remaining constant.

Age and sex profile

The population pyramid in 1992/93 conformed to a developing-country profile, with a broad base reflecting a relatively young population (Paper 1, Figure 3). By 2003/04 the base had narrowed substantially. There were fewer children aged 0-4 than aged 5-9, suggesting both fertility decline and increasing under-5 mortality. The proportion aged 0-4 decreased from 16% to 11%, while the proportion aged 65 or older increased from 4% to 5%. The dependency ratio (ratio of youth and elderly to the potentially economically active population) dropped from 94% to 70% due to the disproportionate decline in the number of children. This is fairly consistent with the average for middle- and low-income countries as a whole (67%).[85] The ratio of males to females was 0.9; this remained constant over the period.

Population dynamics

Fertility

The crude birth rate declined from 32 to 23 per 1000 person years over the ten-year period. Over the same period, the total fertility rate dropped markedly, from 4.0 children per woman to 2.3. Earlier work in Agincourt had demonstrated a relatively high adolescent pregnancy rate, with a peak of pre-marital fertility observed at approximately age 19, followed by some ten years of fertility control with a second peak at about the age of 29.[86,87]

Migration

Between 1992 and 2003 there was a decline in permanent moves both in and out of the area. In contrast, temporary migration increased from the mid-1990s, following the onset of democracy and a relaxing of the traditional authority structures that had previously controlled people's movements. Temporary migrants spend six months or more each year working away from home, but return regularly and contribute socially and economically to the rural home.

The proportion of temporary migrants increased differentially by age and sex over the period. Overall, the percentage of female temporary migrants increased more than threefold from 5% to 17% of the total female population, and of male temporary migrants from 21% to 31%. Between 1995 and 2003 temporary labour migration remained constant at a high 60% for males aged 35-54 years; for younger men aged 15-34 years, the levels increased from 20% to 36%. Female temporary migration rose particularly steeply over this period, increasing fourfold from 5% to 20% among women aged 15-34 years, and from 15% to 25% among those aged 35-54 years. Reasons for male temporary migration are largely related to work or job-seeking in the formal or informal sector, while female temporary migration is related to work and education.[56]

Civil registration

Extensive effort has over the years gone into improving death registration in South Africa through strengthening of the civil registration system. With the help of strong political will a legal framework was developed, and the structural limitations of the system were jointly addressed by the data producers (Ministries of Home Affairs and Health) and data consumers (Statistics South Africa). The first vital registration laws were introduced in 1959, the "Births and Deaths Registration Act" was enacted in 1992, and a new mortality notification form was introduced through legislation in 1998. The form was modified to allow registration, certification, burial and health information in a single document, and to align the cause-of-death section with international standards. In rural settings without a medical certifier, a different form for completion by a village headman was re-introduced. In 1996, South Africa bridged the ICD-9 coding to ICD-10 at three-character level, but reported statistics according to ICD-9 coding only. Among the strategies to improve

coverage of death registration and the quality of cause-of-death information were: disseminating information to all registered doctors, and distributing death-certification manuals and ICD-10 code manuals to hospitals, academic bodies and organisations training health professionals.[88]

These efforts succeeded in increasing national registration of adult deaths from 54% in 1990 to 89% in 2000[89] – a trend reflected in rural Agincourt, where the percentage of registered deaths at all ages rose from 48% in 1994 to 78% in 2002 and 82% in 2004.[h] There are age differentials, however, with far higher registration in adult age groups than in children under 5 years (Figure 7). The difference partly reflects cultural practice whereby an adult funeral is a community event presided over by the village head or *induna*, whereas a child is generally buried by the grandmother close to the household, and not by the community. Under-reporting of infant deaths, associated also with varying socially constructed definitions of when life begins, has been documented elsewhere in Africa[90,91] and in Latin America.[92]
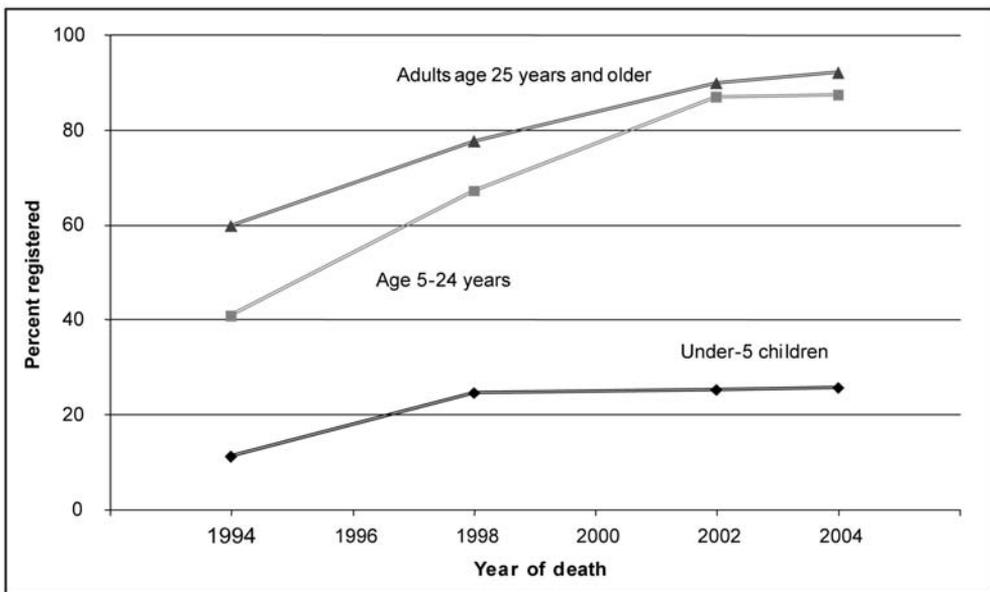
Figure 7. *Trends in completeness of death registration by age group, Agincourt 1994-2004*

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[h] Death registration was assessed for each death by asking the household respondent whether or not it had been officially registered.

Mortality Patterns

Mortality trends

During the surveillance period 1992-2003, the number of deaths recorded in the Agincourt study site was 5,161. For the early part of this period, up to 1996/97, mortality rates were relatively stable, but during the following seven-year sub-period they worsened steadily in almost all age and sex groups.

Life expectancy

More specifically, life expectancy during the earlier sub-period was 66 years for males and 72 years for females; during the later sub-period, male life expectancy dropped to 52 years and female life expectancy to 60 years, a loss of 14 and 12 years of life respectively (Paper III, Figure 1).

Age- and sex-specific mortality

Figure 8 shows mortality trends by age and sex. The surveillance period – beginning two years before the democratic political change and extending a decade beyond – was characterised by the escalation of the HIV/AIDS pandemic. With two exceptions, all age groups duly experienced a significant increase in their mortality rates. The group most affected, for both males and females, was the 20-34 year age group, the group most at risk of AIDS (Figure 8c). The two exceptions were the youth 5-19 (Figure 8b) and the elderly over 65 years (Figure 8f), the age groups at lowest risk of AIDS.

Child and adolescent mortality. For the under-5 age group, mortality declined in the sub-period up to the mid-1990s and then increased sharply in the later sub-period, from 39/1000 to 77/1000. The increase was even more marked for boys than for girls – from 37/1000 to 84/1000 in boys, as against 41/1000 to 71/1000 in girls (Figure 8a). In contrast, for children and adolescents in the 5-19-year age group, mortality stood at the comparatively low level of 18/1000 for the period as a whole, remaining constant in males and increasing only slightly in females (Figure 8b again).

Adult mortality. The two younger adult age groups – 20-34 and 35-49 years – both experienced a steady increase in mortality. For the first group (Figure 8c), the rate rose from 28/1000 to 138/1000 for females, and 35/1000 to 141/1000 for males. For the second group (Figure 8d), the increases were 48/1000 to 174/1000 and 100/1000 to 268/1000 respectively. In the next age group, adults 50-64 years (Figure 8e), the mortality increase, though affecting both sex groups, was more complex. In the oldest age group, 65 years and over, mortality remained at a steady level (Figure 8f).
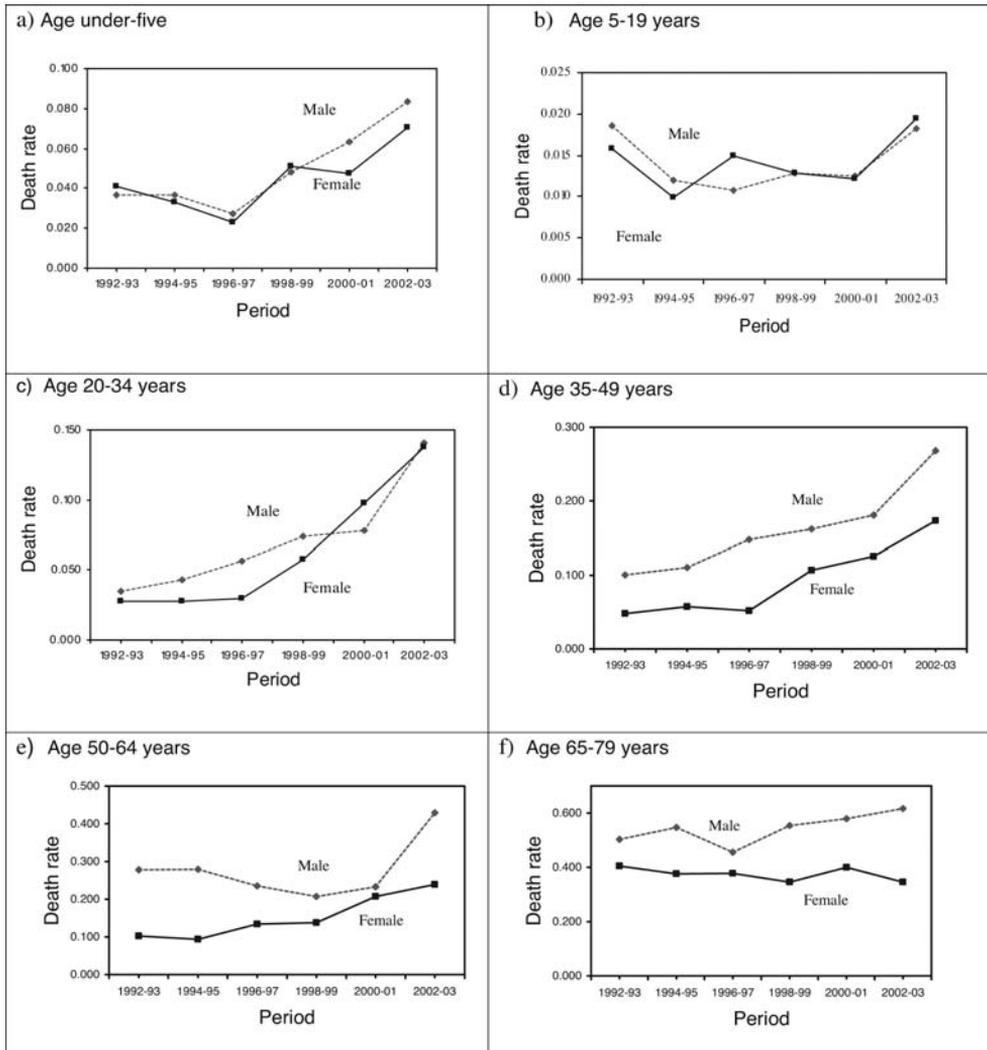
Figure 8. *Mortality trends by age and sex, Agincourt 1992-2003*

Adapted from Paper III, Figure 3.

Sex differentials

Over the full surveillance period, female mortality increased more rapidly than male mortality. For instance, in the 20-34-year age group, female mortality increased fivefold, and male mortality fourfold. And in the 35-49-year age group, despite a higher overall *level* of male mortality, the greater *increase* in mortality again occurred among females – a 3.6-fold increase compared to a 2.7-fold increase.

As just suggested, the trends in the 50-64-year age group are curiously complex (Figure 8e). In 1992, at the start of the surveillance period, male mortality markedly exceeded female mortality. But from then until 2000, male mortality decreased and female mortality increased until they

almost converged. At that point, however, they began diverging, owing to a sudden and far steeper increase in male mortality, which soon overtook the 1992 level. Nevertheless, taking the period as a whole, the mortality increase was once again greater for females than for males – a 2.3-fold increase compared to a 1.5-fold increase.

Maternal mortality

The maternal mortality ratio (MMR) is computed directly by dividing maternal deaths by live births from 1992 to 2004. Over this period, 44 maternal deaths were identified among 20,534 live births, giving an average MMR of 214 per 100,000 (95% CI 159-288). However, MMR is increasing over time, due largely to HIV/AIDS: in 1992-1997 it was 167 per 100,000 (95% CI 102-172), rising to 263 per 100,000 (95% CI 158-436) in 2001-2004. While this trend is not statistically significant (P=0.445), it is sobering to observe that maternal mortality is not declining. Of note is a marked increase in MMR with age (Figure 9). Older women tend to deliver at home, which may explain their high maternal risk. However, the low maternal mortality in adolescents is unusual: while most young girls do deliver in hospital, the low rates could be due in part to concealing of maternal deaths of young, unmarried girls. Although relatively high for a country like South Africa, maternal deaths account for only a small proportion of all deaths of women 15-49 years in Agincourt (4%) because of the very high mortality from other causes, in particular HIV/AIDS.
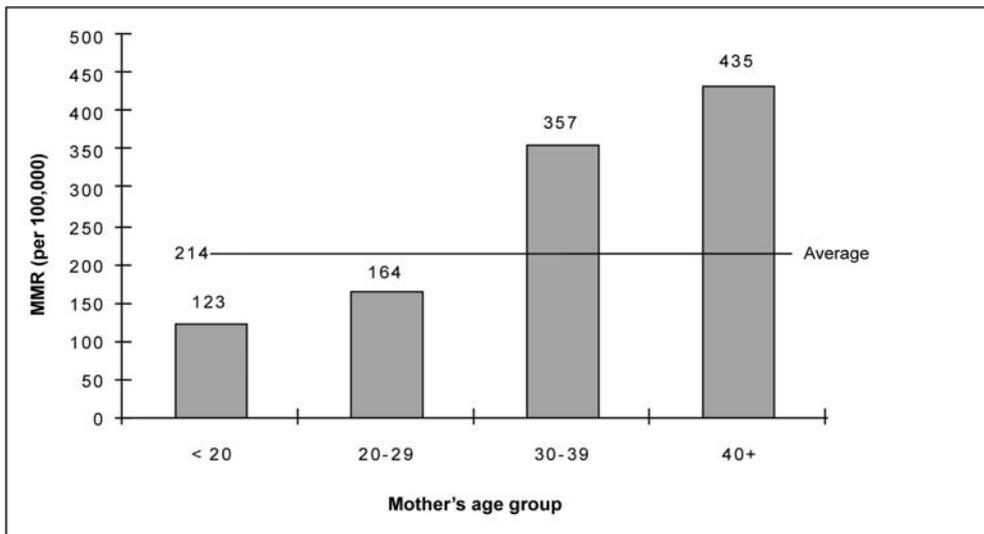
Figure 9. *Maternal mortality ratios (MMR) by age of mother, Agincourt 1992-2004*

Mortality, socio-economic status and migration

Asset-based wealth ranking

In 2001, an asset survey was conducted in all households of the surveillance site. The questionnaire contained ordinal variables on living conditions and assets, including building materials of main dwelling, water and energy supply, ownership of modern appliances and livestock, and means of transport available. Of the variables included, 22 were recoded as dummy variables, each item being assigned "one" if the value reflected higher socio-economic status and "zero" if it reflected lower status. The sum of these scores provided for each household an overall score which could theoretically range from 0 (those with nothing) to 22 (those with everything). Actual household asset scores ranged from 0 to 17 in the sample, and averaged 6. These scores were used to define five socio-economic strata, ranked by increasing value of the score and corresponding closely to five wealth quintiles[i]: most poor (score 0-3), very poor (score 4-5), poor (score 6-7), less poor (score 8-9) and least poor (score 10-17). For each of the strata, a life table was constructed to permit the study of age-specific mortality differentials over the 1992-2000 period. Because mortality surveillance preceded the wealth measure in Agincourt, it is difficult to establish a clear causal direction: on the one hand, poverty can increase mortality risk; on the other hand, death can drive a household further into poverty. Nevertheless, the findings provide some insight into mortality differentials by socio-economic status; further analyses with deaths after 2001 are planned.

[i] The Agincourt population is at the poorer end of the socio-economic spectrum in South Africa; hence wealth quintiles are described from "most poor" to "least poor". This is consistent with the approach adopted by the INDEPTH Health Equity Project.[34]

Economic disparities in mortality

There is an apparent relationship between mortality and wealth, with the poorest experiencing the highest mortality burden. Table 6 provides age- and sex-standardised death rates by the five social strata. Death rates are lowest in the least poor quintile and highest in the very poor; in fact, mortality rates among the poorest 60% of the population are similar. The rate ratio (mortality rate in the poorer economic quintile divided by the rate in the least poor quintile) is significant for all wealth strata. The rate ratio is highest in the bottom three quintiles, with no real differences in rate ratios of the poor, very poor and most poor economic strata. Hence the poorest 60% of the population suffer a similar excess burden of mortality relative to the 40% occupying the less poor economic strata.

Table 6. *Economic disparities in age and sex standardised mortality, Agincourt 1992-2000*

Social stratum	Age and sex standardised death rates	Rate ratio†	95% Confidence Interval	P-value	Significant
Least poor	0.0039	1.0			
Less poor	0.0049	1.3	1.1-1.4	0.000	*
Poor	0.0053	1.4	1.2-1.6	0.000	*
Very poor	0.0055	1.4	1.2-1.6	0.000	*
Most poor	0.0054	1.4	1.2-1.6	0.000	*

† Rate in poorer economic quintile divided by rate in least poor economic quintile
* Significant change, P<0.05

Differentials in mortality by socio-economic status are apparent for all age groups other than the elderly (Figure 10). The relationship is strongest in children and weakens with increasing age. A gradient in infant and child mortality by social stratum is apparent, with a 1.8 times greater risk of dying in the poorest stratum than in the least poor. Or to look at it in a different way, a child in the poorest 60% of households has a 50% or greater risk of dying than a child in least poor households.
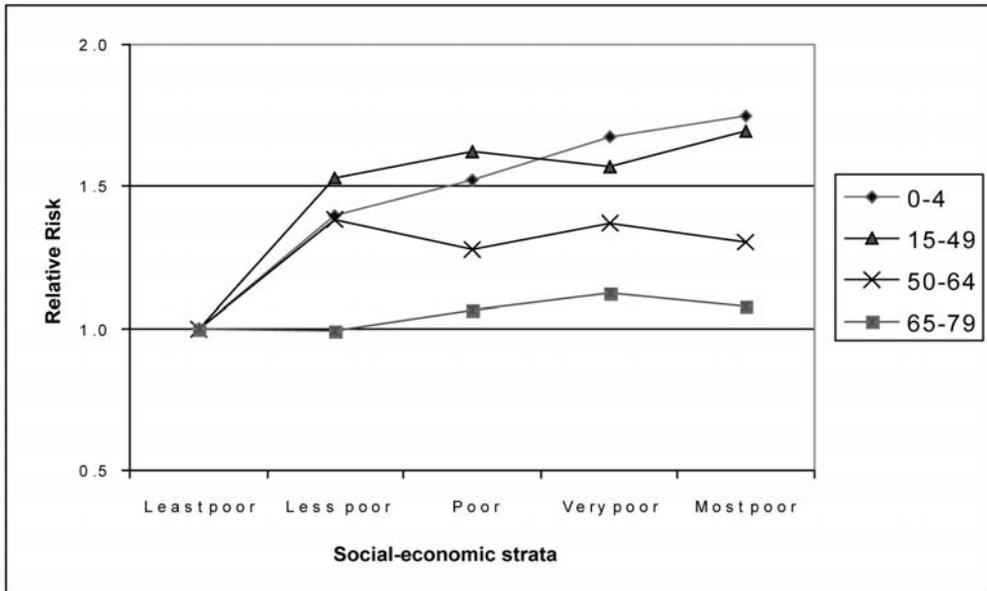
Reference is the least poor socio-economic stratum

Figure 10. *Relative risk of death by age group and socio-economic strata (both sexes), Agincourt 1992-2000*

Child-mortality, socio-economic status and migration

In 2001, almost a third of households were headed by Mozambicans, forcibly displaced into South Africa during the civil war. These households experience social discrimination, uncertain legal status, and barriers to accessing housing, water and sanitation, social grants, education and health services.[65] As the work of Kahn, Hargreaves and colleagues shows, there is considerable correlation between nationality of household head on the one hand, and socio-economic status and mortality on the other.[93,94] Mozambican refugee households were three times more likely than host South African households to be in the poorest quintile of the sample. Children of Mozambican parents living in recognised "refugee villages" (more isolated with less infrastructure) had higher mortality rates than those living in more established villages with a mix of Mozambican and South African residents.

   Although the main influx of Mozambican refugees into the country had occurred more than a decade earlier, differentials in child mortality remained evident between South African and Mozambican residents. The position in 2001 was this: children of former Mozambican refugees had almost a 90% greater risk of dying between age 1 and 5 than indigenous South African children did (IRR 1.9; 95% CI 1.5-2.4). This cannot be adequately explained by differences in health-service utilisation (antenatal clinic attendance and childbirth in a health facility), maternal factors (age at birth of child and level of education), or household factors (sex of household head, number of female adults and other children in household, and maternal presence in household after birth). A striking finding was that in infants 0 to 1 years, the disparity faded, and mortality rates were comparable (IRR 1.0; 95% CI 0.8-1.3). Ironically, uncertain legal status and fewer

job opportunities may be the beneficial factors here: they keep more Mozambican mothers at home and hence prolong the protective effects of breastfeeding and maternal care, in contrast to South African mothers, who were increasingly migrating for work as job opportunities opened up after the 1994 elections.

That said, the impact of female migration on overall child survival does not appear to be detrimental. (Temporary female migrants are typically away from their rural home for at least six months per year, and usually migrate for employment reasons.) Collinson reports that their children do not experience higher mortality than children of non-migrant mothers; instead, he actually observes a small protective effect, albeit non-significant (OR 0.8; 95% CI 0.7-1.0). This is probably due to the higher educational status of migrant women: children of women with post-secondary education have a lower risk of mortality.[95]

Adult mortality and migration

On the relationship between temporary migration and adult mortality, the work of Clark with Kahn and others[96] – noting that social networks and support systems may be stronger in the rural area – investigates whether terminally ill migrants return to their rural homes for care and to die. The analyses compare mortality rates by migrant status, age, sex and time period (1992-1997 with lower HIV/AIDS, and 1998-2002 with higher HIV/AIDS levels). "Short-term" returning migrants are those who returned home permanently less than five years before, while "long-term" returnees returned five years before or more. Both male and female short-term returnees showed a significantly greater risk of dying than long-term returnees or permanent residents in all age groups; this risk increases substantially with time. The suggested explanation is this: with the increase in HIV sero-prevalence, more temporary migrants became ill with AIDS at their workplace; they tended to return to their rural homes for care; and many died fairly soon afterwards. This view is reinforced by VA findings, showing that HIV/AIDS and PTB are increasing rapidly over time in all age, sex and migrant-status groups, and that the greatest increase is in recently returning migrants aged 40-59 years (an increase in HIV/AIDS and PTB deaths in females from zero in 1992-97 to 45% in 1998-2002, and in males from 20% to 42%).

These findings highlight the burden experienced by households in settings with high levels of temporary migration and high levels of HIV – a severe multiple burden: psycho-social impact of death of a prime-age adult; direct loss of household income (the temporary migrant would probably have been a breadwinner); greater household health-care expenditure; and high opportunity cost of caring for a terminally ill relative.

Cause of Death Patterns

Validity of verbal autopsy

Cause-of-death patterns in Agincourt are based on verbal autopsy (VA). The VA tool and process rely on a number of factors that may influence the outcome, including the accuracy of reporting of signs and symptoms by lay respondents, the prevalence of diseases in the community, and the questionnaire, field procedures and medical assessment process employed. It was therefore crucial to validate the VA tool and process within the Agincourt context itself. The method of doing this was to compare main causes of death determined by VA with hospital reference diagnoses; the hospital diagnoses were accepted as a gold-standard once they met a series of inclusion criteria based on quality. The frequency distribution of causes of death from VA and hospital records was compared, and sensitivity, specificity and positive predictive values (PPV) calculated.

The frequency distribution of VA diagnoses in the *overall* population compared with the hospital sample demonstrated an under-representation of accidents and violence and an over-representation of infectious and parasitic disease and non-communicable diseases. However, the cause-of-death distribution based on VAs in the *validated* sample and the hospital sample were similar (no statistical differences), suggesting that performance of the VA in the overall population is likely to be sufficiently valid for the purpose of district health planning and resource allocation.

Table 7 provides the sensitivity, specificity and PPV for broad cause groups for children and adults separately. For *infectious and parasitic diseases*, sensitivity of the VA diagnoses for all ages combined was 82%, specificity 93% and PPV 79%. For *accidental and violent deaths*, these were 88%, 98%, and 70% respectively. While lower for *non-communicable diseases*, most misclassification occurred within the broad disease category itself, owing to the sharing of common signs and symptoms by different chronic conditions.

Table 7. *Validation of deaths by broad cause categories, Agincourt 1992-1995*

	Verbal autopsy compared to hospital diagnosis					
	Children under 5 years			Adults 15 years and older		
Hospital Dx	Sensitivity	Specificity	PPV	Sensitivity	Specificity	PPV
I&P (%)	69	96	90	89	93	76
95% CI	44-94	88-99	71-99	74-99	87-99	58-94
NCD (%)	75	91	86	64	50	80
95% CI	54-96	79-99	67-99	53-76	29-71	69-90
A&V (%)	100	97	80	75	98	60
95% CI		91-99	45-99	33-99	94-99	17-99

Dx: diagosis; I&P: infectious and parasitic; NCD: non-communicable diseases; A&V: accidents and violence
Adapted from Paper II, Table 3.

The focus of papers V and VI of this thesis is on stroke and pulmonary tuberculosis respectively. There were sufficient cases to enable validation of these two diagnoses specifically. High sensitivity was achieved for adults with both conditions: 92% for pulmonary tuberculosis and 87% for stoke. Other conditions with high sensitivity were diarrhoeal diseases (86%) and kwashiorkor (100%)

in children, and AIDS (although numbers for AIDS were small). Specificity for these conditions reached 99%. The Agincourt VA instrument has been re-validated for deaths from 2001-2005. With respect to HIV/AIDS diagnoses, the tool appears to perform satisfactorily on preliminary analysis. However, over half of false negative and over a third of false positive diagnoses were PTB, highlighting the difficulty in differentiating these conditions on VA.

Cause of death profile

Paper IV presents the cause-of-death profile from 1992 to 1995, and reveals a "triple burden": the unfinished agenda of diseases of poverty in children, particularly acute diarrhoea and malnutrition; emerging non-communicable disease in adults; and high levels of accidents and violence. Since then, this picture has progressed to a "quadruple burden" as HIV-related diseases have escalated to become the leading cause of death in children and young adults.

In the mid-1990s, acute diarrhoea was responsible for more than half of infectious-disease deaths (54%) and 20% of deaths overall in children under 5 years. In contrast, the vaccine-preventable diseases, AIDS, and acute respiratory infections were relatively rare (3%, 3% and 5% respectively). Malnutrition deaths, almost all kwashiorkor, contributed to 15% of deaths. And 16% of infant deaths were from birth-related causes, excluding stillbirths.

In adults of 15-49 years, almost a third of deaths overall were due to accidental and violent injuries (similarly in youths of 5-14 years), with a greater burden in males than females. AIDS was the cause of 6% of overall deaths in this age group. There were eight maternal deaths in females over this period (8% of all female deaths 15-49 years). There has been no decline since then: rather, an increase is observed, albeit not significant. This increase is likely due to non-pregnancy HIV-related diseases. Obstetric-related causes of death included postpartum and antepartum haemorrhage, abortion, eclampsia, puerperal sepsis and ectopic pregnancy.

In older adults, aged 50 years or more, death rates were highest for cardiovascular diseases (stroke and cardiac failure). Malignancies, mainly genito-urinary and gastrointestinal, and chronic liver disease were other prominent non-communicable diseases, while in the over-75 age group pulmonary tuberculosis and diarrhoea stood out among the infectious diseases.

Findings in Paper IV highlight the most notable specific causes of death in the mid-1990s. These were persisting child malnutrition, stroke in middle-aged adults as well as the elderly, high levels of violence in a supposedly peaceful area, PTB and emerging HIV/AIDS. In the sections below, these conditions are discussed in turn, drawing on Papers V and VI that focus on stroke and PTB respectively, together with other work contributed to by Kahn.

Persisting child malnutrition

As Paper II showed, kwashiorkor can be reliably diagnosed by VA (sensitivity and specificity both 100%).[82] Paper IV reports a mortality rate from malnutrition in children under 5 years of 110 per 100,000 (95% CI 72-149) in 1992-1995 when HIV rates were relatively low.[26] How has mortality from child malnutrition changed as HIV/AIDS has increased? Between 1992 and 2003, we find a relative risk of 4.6 for the probability of dying of any type of malnutrition between 1 month and 5 years of age. A large part of this increase is associated with HIV/AIDS. Kwashiorkor unrelated to HIV/AIDS, prominent in the early 1990s, did not increase over the study period, but did not decline either. Hence, while other forms of

HIV-related malnutrition have increased dramatically, kwashiorkor remains a public-health problem.

To better understand the underlying risk factors for severe childhood malnutrition, Saloojee with Kahn and others undertook a case-control study in 2003-2004, comparing hospitalised severely malnourished children with better-nourished peers from a similarly disadvantaged environment.[97] Multivariate analysis showed that the risk factors for severe malnutrition included: evidence of HIV in the family (parents or children) (OR 217.6, p<0.001), poor weaning practices (OR 3.0, p<0.001), parental death (OR 38.0, p=0.002), male sex (OR 2.7, p=0.01) and later position in the birth order (third child or higher) (OR 2.3, p=0.05). Protective factors included: a diverse food intake (OR 0.5, p<0.001) and receipt of a state child support grant (OR 0.4, p=0.04). A borderline association was found for: family wealth (OR 0.9 per unit, p=0.08), father smoking marijuana (OR 3.9, p=0.04) and history of a PTB contact (OR 3.2, p=0.06). The contribution of HIV to the development of severe malnutrition certainly showed a marked increase (HIV status was known for only 39% of cases, but of these 87% were positive), but the traditional risk factors clearly remained important – notably, poor nutrition, parental disadvantage and illness, poverty and social inequity.

Stroke

As Paper II demonstrated, stroke in those over the age of 15 years can be reliably diagnosed by VA (sensitivity 87%; specificity 96%; PPV 81%).[82] Paper IV revealed the unexpected prominence of stroke mortality in a relatively under-developed rural African population aged 50 years and older.[26] Paper V examined the pattern of stroke mortality in more detail. Of the 55 stroke deaths between 1992 and 1995, 53% occurred in women; 53% overall occurred at home rather than in hospital; and 29% occurred without help being sought from Western health care. Notable was the relatively young age distribution: almost a quarter of the stroke deaths occurred in those below age 55 years, and 51% in those below age 65 years. Age-specific stroke mortality rates increased with age, and were higher in men than women over 35 years (135 per 100,000 compared to 120 per 100,000). As for the overall proportionate mortality rate, stroke accounted for 5.5% of all deaths, and 10.3% in the 35-64 age group.[98]

These findings highlighted the extent of cerebrovascular disease in rural South Africa (lower than in France and higher than in Senegal[99]), and the need for research on morbidity, disability and risk factors to inform district-level interventions. Research on stroke prevalence, led by Thorogood and Connor with Kahn contributing,[100] estimated a stroke prevalence of 300 per 100,000 in Agincourt – higher than that found in Tanzania but lower than that in high-income countries. Of stroke survivors in Agincourt, 66% required help with at least one activity of daily living, a proportion similar to that in Tanzania (60%) but greater than that in New Zealand (22%). The main risk factor found in stroke survivors was shown to be hypertension (71% had high blood pressure and 84% showed some evidence of hypertension). Only 12% were diabetic and only 9% were cigarette smokers; and HIV did not emerge as a significant cause.

Violence and accidents

External causes of death are reliably diagnosed by VA, as shown in Paper II (sensitivity 88%; specificity 98%; PPV 70%).[82] Paper IV shows the prominence of violent death in a relatively

peaceful rural area.[26] Of all deaths in Agincourt between 1992 and 1995, 15% were due to external causes. Of these, 39% were homicides, 10% suicides, 30% road traffic injuries (RTIs), and 22% accidental injuries including household accidents. Only a quarter of those who died from violence or accident reached a hospital before dying, compared with three quarters of all deaths. Over the period 1992-1995, the death rate from external causes was 74 per 100,000. Mortality was highest among those aged 50 years and over (191 per 100,000), and lowest among those aged 5-14 years (23 per 100,000). However, the injury burden was particularly high in the 15-49 age group, primarily owing to high rates of violence. (More than half of external deaths for both sexes were due to assault. Among males, assault accounted for a quarter of all deaths, and for 60% of deaths from external causes.) In this age group, the percentage of all deaths attributable to injuries was more than double that for all ages combined: 32% compared with 14% overall; for males, the figures were 43% and 20%, for females 16% and 7%. (Table 8.)

Table 8. *All-cause injury mortality by age and sex, Agincourt 1992-1995*

Age	Male				Female				Both			
	No.	% all deaths	Rate*	95%CI	No.	% all deaths	Rate	95%CI	No.	% all deaths	Rate	95%CI
0-4	11	10	75	31-120	4	4	28	1-55	15	7	52	26-78
5-14	9	35	32	11-53	4	22	14	0-29	13	30	23	11-36
15-49	62	43	145	109-181	16	16	33	17-49	78	32	86	67-105
50+	30	11	364	234-495	8	4	69	21-116	38	8	191	130-252
Total	112	20	120	98-142	32	7	31	21-42	144	14	74	62-86

*Rate/100,000

Sex differences are clearly apparent, with the major injury burden falling on males: the injury mortality rate for males of all ages (120 per 100,000) exceeded that of females (31 per 100,000) fourfold, a finding at least as strong in all adult age strata (Table 8). Male death rates exceeded those for females for all four injury types in all age groups, except for RTIs in the 5-14 age group. The male:female rate ratio for assault, for example, was 6.8 and 4.2 (p<0.05 for both) among those 15-49 and 50 years and over respectively. In general, the male:female rate ratio rose with age (Table 9).

Table 9. *Sex differences in intentional and unintentional injury death rates, Agincourt 1992-1995*

Cause	Male:female rate ratio				
	0-4	5-14	15-49	50+	Total
Assault	-	-	6.8*	4.2*	5.6*
Suicide	-	-	4.0	-	6.5*
Road traffic injuries	-	1.0	3.0*	7.8*	3.3*
Other unintentional	2.0	4.0	1.7	2.8	2.3*
All injuries	2.7	2.2	4.4*	5.3*	3.8*

*p<0.05

Pulmonary tuberculosis

Pulmonary tuberculosis (PTB) in adults has been reliably diagnosed by VA in Agincourt, as shown in Paper II (sensitivity of 92%, specificity of 99%, and PPV of 92%).[82] Paper IV documents the very low PTB death rates in children and young adults over the 1992-1995 period, increasing to rates of 138 and 284 per 100,000 in adults 50-74 and 75+ respectively. PTB contributed 7% of all deaths in the 50-74 age group.[26] The age-standardised death rate for PTB over the 1992-2003 period has increased significantly from 231 per million person-years in 1992-1994 to 738 per million in 2001-2003 (RR 3.2; P=0.000) (Kahn et al., unpublished data). While the increase is largely HIV/AIDS-related, PTB death rates in older adults who are unlikely to be affected by HIV have not declined.

Paper VI shows the use of VA to better estimate the burden of undiagnosed PTB in rural South Africa in 1999. PTB deaths were regarded as "diagnosed" if there was VA evidence that the illness had been previously detected by the health service, and "undiagnosed" if evidence indicated that the death occurred before case detection. The PTB deaths represent a mortality rate of 73 per 100,000 among the permanent (non-migrant) Agincourt population over the age of 10 years. There were 28 PTB deaths in 1999; in 27 cases (96%), treatment had been sought before death, though only 15 cases in all (54%) reportedly had a specific diagnosis of PTB. Deaths from PTB cases never detected by the health services therefore seem to be occurring at a rate of 34 per 100,000 per year. This represents a substantial burden of undiagnosed PTB, one that contributes heavily to greater infectiousness and ongoing transmission in the community.[101]

Emerging HIV/AIDS

While sensitivity and specificity of VA diagnoses for HIV/AIDS deaths appeared high in Paper II, the number of cases available in 1992-1995 was small.[82] Preliminary analysis comparing VA diagnoses with hospital diagnoses from 2001 to 2005 indicates that the tool appears to perform satisfactorily, with a relatively high specificity for HIV/AIDS, though a lower sensitivity.

The first cases of HIV/AIDS mortality in Agincourt were assigned by VA in 1993.[102] Over the 1992-1995 period, AIDS constituted 3% of all deaths in children under-5 and 6% in adults 15 to 49 years.[26] By 1999, HIV was thought to have contributed to 61% of PTB deaths (86% of cases diagnosed by the health service and 31% of undiagnosed cases).[101] Preliminary work has begun on cause-of-death patterns underlying the increasing mortality documented in Paper III. VA data over the decade 1992-2003 shows HIV/AIDS to be the major driver of escalating mortality in children and young adults. Infectious and parasitic diseases have increased almost fivefold over the period (RR 4.9; P=0.000) (Table 10).

Table 10. *Age standardised death rates, by broad cause categories, per million person-years, Agincourt 1992-2003 (N= 4922 deaths)*

Broad cause categories	Period				Relative change		
	1992-94	1995-97	1998-00	2001-03	RR	P-value	Signif
All causes	4 969	5 051	6 428	9 612	1.9	0.000	*
Infectious & parasitic	766	1 362	2 280	3 730	4.9	0.000	*
Non-communicable	1 588	1 258	1 662	1 922	1.2	0.020	*
External causes	772	506	624	795	1.0	0.802	
Ill defined or unknown	1 844	1 925	1 862	3 164	1.7	0.000	*

Change is computed from last period (2001-2003) to first period (1992-1994)

* P< 0.05

Most of the increase in infectious and parasitic causes is due to HIV/AIDS and tuberculosis; acute respiratory illness has increased significantly, probably linked to HIV/AIDS; and acute diarrhoeal illness has remained stable. The increase in malaria appears marked because of the very low level in the baseline period, though malaria contributed only 4% to the total causes in this category (Kahn et al. unpublished data). (Table 11).

Table 11. *Age standardised death rates for selected infectious and parasitic causes, per million person-years, Agincourt 1992-2003 (N=1,543 deaths)*

Broad cause categories	Period				Relative change		
	1992-94	1995-97	1998-00	2001-03	RR	P-value	Signif
Diarrhoeal diseases	254	304	309	208	0.8	0.391	
Acute respiratory infection	73	107	241	233	3.2	0.000	*
HIV/AIDS	71	392	1196	2304	32.3	0.000	*
Tuberculosis	231	320	229	738	3.2	0.000	*
Malaria	31	114	157	152	4.9	0.001	*
Other infectious and parasitic	105	125	148	95	0.9	0.767	

Change is computed from last period (2001-2003) to first period (1992-1994)

* P< 0.05

Emerging non-communicable diseases

Non-communicable diseases have increased by 21% (P=0.020) overall (Table 10), and are contributing significantly, along with HIV/AIDS, to the mortality pattern in adults 50-64 years. All-cause mortality in women of this age group has increased steadily over the decade. Figure 11 clearly shows a parallel increase in infectious and parasitic diseases, and non-communicable causes. Analysis of the overall increase in female mortality 50-64 years indicates that HIV/AIDS is now a comparable factor to non-communicable diseases. HIV/AIDS and related conditions, specifically PTB, are responsible for 27% of the increase in deaths, and non-communicable diseases, including stroke, cardiac failure, hypertension, diabetes and neoplasms (other than female genital), constitute a further 23% of the increase.
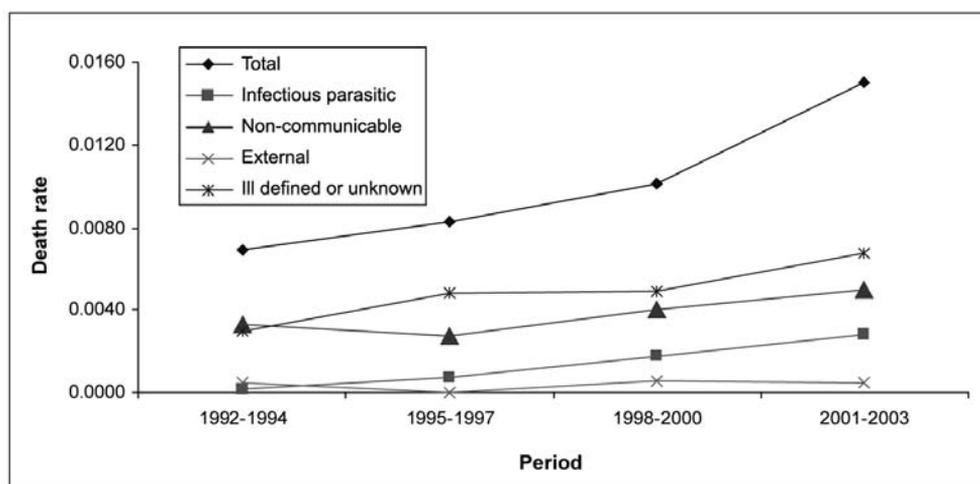
Figure 11. *Change in death rates of women aged 50-64, Agincourt, 1992-2003*

Burden of disease transition

Table 12 lists the top five causes of death by age, sex and period between 1992 and 2003. In so doing, the table usefully summarises the cause-of-death transition in Agincourt. The strongest trend by far is escalating HIV/AIDS, particularly in children under 5 and in adults 15-49 years. By the mid-1990s, HIV/AIDS had become the top cause of death in males and females in both these age groups; and, together with PTB, in males 50-64 years as well. By 2000-2003, HIV/AIDS constituted 27% of all child deaths; and 34% of male and a staggering 47% of female deaths in the 15-49 age group.

In children, malnutrition and acute diarrhoea – unrelated to HIV/AIDS – persist. In adults 50 years and older, non-communicable diseases, particularly cardiovascular disease, were already established in the top five causes of death by the mid-1990s. This was most marked in females. Cancer of the female urogenital tract, largely cancer of the cervix, is the most prominent malignant disease category, appearing amongst the top five causes in every adult age group. In youths 5-14 years accidental injuries are the leading cause of death. Both accidental and intentional injuries remain important causes of death in adults 50-64, particularly amongst males.

Table 12 (a). Top five causes of death in children under-5 (%), Agincourt 1992-2003

1992-1995	1996-1999	2000-2003
Both sexes n=243	**Both sexes** n=270	**Both sexes** n=426
Acute diarrhoea (20)	HIV/AIDS (17)	HIV/AIDS (27)
Malnutrition (13)	Acute diarrhoea (16)	Malnutrition (10)
Perinatal (7)	Acute respiratory infection (9)	Acute diarrhoea (10)
Accidents (7)	Perinatal (7)	Acute respiratory infection (9)
Other infectious (6)	Malnutrition (5)	Perinatal (6)

Table 12 (b). Top five causes of death 5-14 years (%), Agincourt 1992-2003

1992-2003	
Males n=90	**Females** n=76
Accidental injury (13)	Accidental injury (18)
RTI (9)	Malaria (12)
HIV/AIDS (8)	RTI (8)
Violence (8)	Acute diarrhoea (7)
Malaria (6)	Epilepsy (5)

RTI: Road traffic injury

Table 12 (c). Top five causes of adult death (%) by age group, sex and period, Agincourt 1992-2003

Age	Male			Female		
	1992-1995	1996-1999	2000-2003	1992-1995	1996-1999	2000-2003
15-49	n=164	n=307	n=489	n=115	n=219	n=469
	Violence (27)	HIV/AIDS (24)	HIV/AIDS (34)	Maternal (9)	HIV/AIDS (29)	HIV/AIDS (47)
	Accidents (14)	Accidents (15)	Violence (13)	Violence (8)	Violence (5)	PTB (7)
	HIV/AIDS (7)	Violence (14)	PTB (10)	Other malig (8)	Ca UGT (5)	Ca UGT (3)
	PTB (6)	PTB (5)	Accidents (8)	Accidents (7)	Malaria (5)	Malaria (2)
	Other malig (4)	Malaria (4)	Other (3)	Ca UGT (6)	Other infec (4)	Accidents (2)
50-64	n=119	n=115	n=192	n=54	n=84	n=145
	Stroke (13)	PTB (17)	HIV/AIDS (13)	Stroke (15)	Stroke (13)	Ca UGT (7)
	PTB (12)	Violence (10)	PTB (12)	Cardiac (11)	Ca UGT (7)	Cardiac (6)
	Violence (10)	HIV/AIDS (8)	Violence (7)	Liver (7)	Cardiac (5)	HIV/AIDS (6)
	Accidents (8)	Other malig (6)	Other malig (7)	Accidents (6)	PTB (5)	PTB (6)
	Cardiac (6)	Cardiac (4)	Cardiac (6)	Ca UGT (4)	Diabetes (4)	Other (6)
65+	n=181	n=209	n=258	n=190	n=237	n=275
	Cardiac (11)	Stroke (11)	Other malig (11)	Cardiac (11)	Stroke (11)	Cardiac (12)
	PTB (10)	PTB (11)	PTB (9)	Stroke (11)	Cardiac (11)	Stroke (11)
	Stroke (6)	Other malig (11)	Stroke (8)	Ca UGT (6)	Other malig (9)	Ca UGT (6)
	Accidents (5)	Cardiac (7)	Cardiac (7)	PTB (4)	Ca UGT (6)	Other malig (4)
	Other malig (4)	Diarrhoea (6)	Other (4)	Other malig (4)	Diarrhoea (6)	Diabetes (3)

PTB: Pulmonary tuberculosis; Other malig: Other malignancies; Ca UGT: Cancer of the female uro-genital tract; Other infec: Other infectious diseases

Agincourt and South African Mortality: A Comparison

Table 13 compares key mortality indices for Agincourt, national and provincial estimates in two periods. Two different estimates are used: those based on the South African census, and those based on ASSA2003, the demographic model of the Actuarial Society of South Africa (ASSA). The two periods are 1992/93 and 2000/2001, based respectively on the 1996 census and the 2001 census. Maternal mortality is estimated from the South African Demographic and Health Survey (SADHS) 1998.

Despite improved death registration, utility of South African vital registration and census data remains limited as a result of under-registration of deaths – particularly in rural areas and of children – leading to lower estimates of numbers of death, and misreporting of causes.[103] Furthermore, problems with the 2001 national census data on child deaths were so marked that Dorrington and colleagues regard it as too unreliable to generate any meaningful estimates of child mortality. Problems include: coverage errors (duplication or omissions), lack of completeness (missing information on specific questions) and content errors (incorrect recording of individual or household characteristics during data collection or data processing) due to poor capability and diligence of certifying officials.[104]

The ASSA2003 demographic model was developed to provide estimates of the numbers of South Africans directly affected by the HIV/AIDS epidemic, and to estimate its demographic impact. It uses empirical data from different sources and is updated as the course of the epidemic progresses and more information becomes available. ASSA2003 is the latest version of the model, and is calibrated to data including the adjusted census 2001, SADHS 1998 and adjusted vital registration of deaths (for estimates of population size, mortality, fertility and migration rates), antenatal-clinic HIV-prevalence data and household prevalence surveys (for the extent of the HIV/AIDS epidemic and sexual behaviour).[105,106] Mortality rates based on ASSA2003 are not, therefore, rates estimated directly from the census or from vital registration data but are rather a result of a reconciliation of these data sources with the estimates derived by combining mortality from both AIDS (epidemiological data) and non-AIDS causes (historical trends) (Dorrington, personal communication).

Comparison of key mortality indices in 1992/93 indicates a mortality profile in Agincourt that, on either set of estimates, appeared more favourable than that of Limpopo Province or the nation as a whole (Table 13). The only exception was the maternal mortality ratio that was higher in Agincourt. (At national level, the census data and the ASSA2003 model produced similar estimates for life expectancy, IMR, under-5 mortality and young-adult mortality. At provincial level, census data yielded an IMR and under-5 mortality higher than that produced by the ASSA2003 model.)

By 2000/2001, the mortality picture had worsened – at national, provincial and Agincourt levels – for all indices irrespective of the data sources. Life expectancy remained lower at national level than at either provincial or Agincourt level, where estimates were similar. (The census produced a lower IMR and under-5 mortality at both national and provincial level than that produced by the ASSA2003 model. The IMR in Agincourt is comparable to provincial estimates produced from the census, while under-5 mortality in Agincourt is comparable to provincial estimates produced by the ASSA2003 model. Young adult mortality is similar to both sources of provincial estimates; but national figures are higher than both provincial and Agincourt figures.)

Table 13. Comparison of selected Agincourt mortality indices with national and provincial indices, 1992/1993 and 2000/2001

Both sexes combined	1992/1993						2000/2001					
	National		Limpopo Province		Agincourt		National		Limpopo Province		Agincourt	
	Census	ASSA2003	Census	ASSA2003			Census	ASSA2003	Census	ASSA2003		
	(1)	(2)	(1)	(2)			(3)	(2)	(4)	(2)		
Life expectancy	60.9	60.9	63.2	65.1	70.7		54.1	53.6	61.8	60.3	63.0	
Crude death rate (per 1000)		9.0		7.0	5.4			12.0		9.0	7.7	
Infant mortality rate (per 1000 live births)	51.0	52.5	43.0	36.5	21.6		56.2	67.5	34.5	46.0	36.9	
Under-5 mortality rate (per 1000 live births)	70.0	72.5	58.0	51.0	39.6		80.5	99.0	49.5	67.0	61.1	
Young adult $_{45}q_{15}$*	0.310	0.320	0.284	0.260	0.200		0.470	0.460	0.370	0.355	0.334	
Maternal mortality ratio (per 100 000 live births)	150				189		650		300		243	

(1) Derived from the 1996 census and the 1998 SADHS. All races combined. Represents 12-month period prior to 1996 census. Maternal mortality is estimated from the
 SADHS.[107] (SADHS=South African Demographic and Health Survey)

(2) Estimates are for African population; 1992/1993 and 2000/2001

(3) Figures derived from the 2001 census for the African population. Child mortality indices are regarded as unreliable.[104]

(4) Figures derived from the 2001 census for all races combined. Child mortality indices are regarded as unreliable.[104]

* $_{45}q_{15}$: probability of dying between age 15 and 60

Discussion

The body of work covered in this thesis describes trends in mortality and burden of disease in rural South Africa from 1992 to 2003, a period of major socio-political change coincident with emerging diseases. Society's need for information on mortality in poor settings where health and development needs are greatest is hampered by the lack of reliable, population-based information systems. One way of addressing this limitation is by introducing health and demographic surveillance – a means of obtaining high-quality information in a geographically defined rural area that corresponds with an administrative health sub-district. With respect to cause-of-death determination, the verbal autopsy (VA) has been validated, thereby demonstrating the veracity of findings to the scientific and policy-making communities.

This section will demonstrate the plausibility of results by discussing the methods used; highlight key mortality and burden-of-disease findings and discuss these in relation to national and international data; draw out implications for health policy and practice; and examine the application of our findings to health transition theory. The discussion will be organised into three thematic areas outlined in Table 3: Population surveillance in developing countries; Health policy and practice – implications of increasing mortality; and Health transition.

Population Surveillance in Developing Countries

A health and demographic surveillance system (HDSS) provides high-quality data through both its scientific study design and field implementation of data-collection procedures. HDSS is characterised by *regular* collection and *updating* of information on *all* members of the study population rather than on a sample. Hence, population size and structure by age and sex is a primary output, providing accurate denominator data for the calculation of rates. Numerator data on deaths, obtained by capturing all deaths in the study population since the previous update round, is virtually complete in child and adult age groups. Reporting of perinatal deaths may be less complete owing to culturally determined versions of when a life begins (and hence when a death occurs). Recording of pregnancies is useful in addressing this problem. In the Agincourt HDSS, annual census update rounds limit our ability to collect full pregnancy data; we have therefore introduced alternative questions to probe for pregnancies since the last recorded birth (Paper I).

The Agincourt HDSS provides an established research infrastructure critical to high-quality work in an area of otherwise poor resources. This infrastructure ranges from management systems and administrative procedures to IT and telecommunications equipment and maintenance. Local fieldworkers are highly trained in survey and qualitative data-collection methods, are tightly supervised, and are embedded within a multilevel quality-control system. Another quality measure is the locating of data-entry close to the field; this permits the checking of errors at household level where necessary. Fundamental to the ethics of long-term research, and to the completeness and integrity of data collected, is a relationship of trust with study communities; this was established at the outset and is nurtured continuously.

HDSS provides a source of high-quality data in settings where this is lacking, and where the need for cost-effective health and development programmes is arguably greatest. Cause-specific mortality rates derived from such systems can fill gaps in national and global mortality patterns; can be used to assess the impact of particular health interventions; and should feed directly into

evidence-based priority-setting and programme-planning, thereby providing a rationale for decisions on the spending of scarce public resources. So it is crucial to establish the validity of VA for determining cause-specific mortality.

Reliability of verbal autopsy

VA performance is affected at all stages of the process from development of the instrument, through field procedures, to medical assessment. Questionnaire design must take into account culturally acceptable terminology and concepts; at the same time, standardised tools are needed for reliable comparisons between different settings. Training of fieldworkers partly depends on whether health workers or lay fieldworkers are selected; criteria for selection should include knowledge of local language and culture, ability to relate sensitively to bereaved respondents, and coping strategies to deal with the daily stress of conducting detailed interviews on recent deaths. Choice of respondent should hinge on who knows most about the signs and symptoms of the terminal illness, but the quality of information will still depend on the respondent's ability to observe, recall and report relevant information; in addition, quality of data will differ between respondents who have had contact with the health service and those who have not. Medical assessors must be well-versed in the ways of ascertaining cause of death and in the coding procedures.[26,27,108]

VAs perform best for diseases that have distinct signs and symptoms – such as neonatal tetanus, for example. Where signs and symptoms cannot be easily differentiated, as with malaria and pneumonia or meningitis, it becomes more difficult to distinguish between specific diseases, and misclassification is more likely to occur, resulting in an over- or underestimate of cause-specific mortality. Misclassification is usually within the broad-cause category; hence, combining specific causes into sub-group-level mortality rates will produce more reliable mortality estimates, as false positives and false negatives will largely cancel each other out. Assigning causes to the "undetermined" category produces underestimates of both cause-specific and sub-group-specific mortality rates.[109-112]

Validation of VA is clearly necessary, and since performance of the tool is affected by disease prevalence, validation is really needed in all settings in which VA is used.[109] Most validation studies have relied on hospital records, with physician assessment as the gold standard; while the only feasible approach, it is limited by the poor quality of hospital information, which casts doubt on the "gold standard" status; by the difference in knowledge between respondents who had contact with the health service and those who did not; and by the inability to validate VA in populations without access to health services. Clinician assessment has been shown to have higher validity than algorithms, in part because physicians make use of all sections of the questionnaire including the open narrative;[28] yet physician-time is costly, and problems of inter- and intra-observer reliability mean that repeatability becomes doubtful. Alternatives to physician-derived VA interpretation are expert algorithms, data-derived algorithms (based on logistic regression, neural networks, decision trees and probability density), and a method based on Bayes's theorem that defines the probability of a cause given the presence of a particular indicator. Among the advantages of these approaches are: standardisation across different settings and over time, and quick, easy, inexpensive application. While further testing is needed, these approaches look promising, at least for estimating the cause-specific mortality fractions for some diseases of major public health impact.[113-116]

The Agincourt verbal autopsy

Validation of the Agincourt VA tool and assessment process (Paper II) demonstrates that, with rigorous fieldworker training and careful medical assessment, VA can be reliably used in an area lacking vital registration. The tool provides sufficiently valid cause-specific mortality data, including HIV/AIDS mortality, for local-level public health planning; it permits monitoring of trends over time (some of which may be secular and others in response to particular interventions); and it can contribute to our understanding of national and global patterns of disease.

Overall, almost one third of VAs in 1992-1995 were assigned an unknown cause of death. This proportion increased with age and increased over time. The higher proportion of unknown causes since 2000 is due, in part, to increasing HIV/AIDS. There is a trade-off between sensitivity and specificity. VAs can accurately diagnose cases with characteristic signs and symptoms – these will have higher specificity and lower sensitivity – but are far less reliable in diagnosing cases that do not conform to a typical picture. To include these cases would produce many false positives resulting in higher sensitivity but lower specificity. The Agincourt approach is to aim for high specificity. While arguably a more rigorous approach, it results in a relatively high level of unknown causes; and the cost is an underestimate of cause-specific mortality rates.

Contribution of the Agincourt Health and Demographic Surveillance System

The Agincourt HDSS adds to the portfolio of data sources available in South Africa, each of which has its own strengths and limitations. The limitations may be inherent in the study design or may result from sub-optimal implementation of data-collection procedures (including design and piloting of questionnaires, training and supervision of fieldworkers, and quality-control procedures). Table 14 provides a summary of the key South African data sources that generate mortality information, including a brief assessment of the quality of data in each of them. An appreciation of the strengths and limitations of these sources is needed, in order to assess the added-value of the HDSS.
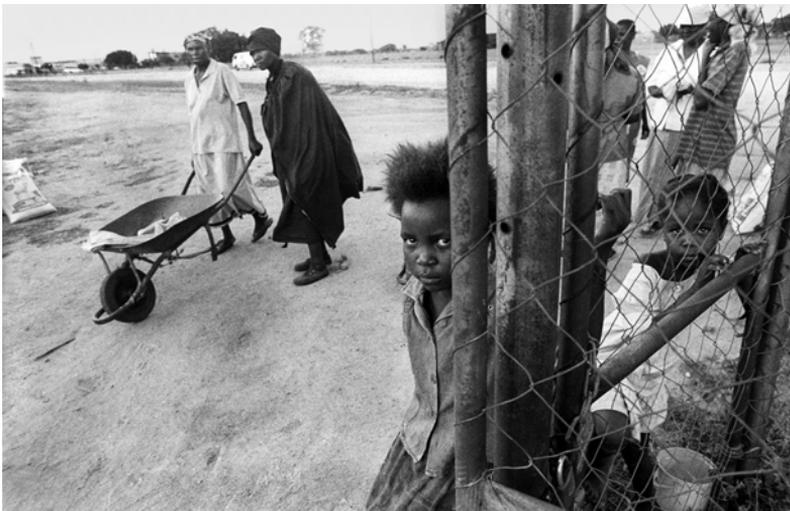
Table 14. Key South African data sources on mortality, 2006

Data source	Mortality data available	Year started	Year last survey	Frequency of survey	Sampling methods	Analytic methods	Quality of data
National census	Children ever born and children died	Questions introduced in 1996 (following democracy)	2001	Every 10 years (after 5 years following democratic change)	All households. Country divided into 80,000 enumeration areas with an enumerator assigned to visit all households within each one	Indirect Brass technique	Appears to overstate child mortality rates as a result of including stillbirths in the reported number of children died.[117] Quality problems in 2001 make data difficult to interpret[104]
	Deaths in past 12 months Broad causes: maternal, injuries, other	Questions introduced in 2001				Direct rates but should be adjusted for underreporting	Plausible adult mortality rates have been calculated, once adjusted for underreporting[104]
Vital statistics	Cause of death coded to ICD	1989 for all South Africans (began 1910 for whites, and ~ 1978 for blacks in selected urban areas only)	Ongoing	Ongoing – but reports have only recently become regular	All deaths should be included	Direct rates but should be adjusted for under-registration and mis-classification	In 1990 only 50% of adult deaths were registered.[118] By 2000, approx 90% of adult deaths were registered.[89] Misclassification of cause of death required further analysis.[119,120] Extent of under-registration of child deaths is not known and unusual coding practice make child mortality data unreliable[121]
Demo-graphic and Health Survey (SADHS)	Levels of child and adult mortality. No cause data	1998	2003	Every 5 years	Nationally representative sample of about 10,000 households drawn from census enumeration areas. Women 15-49 years in sampled house-holds provide birth history and sibling history	Direct child mortality from birth history. Direct adult mortality rates from sibling history	Child mortality rates in 1998 were good quality[117] but results from 2003 survey are not plausible and suggest poor quality data. Adult mortality rates appear to suffer from extensive recall bias with rates for the earlier period being too low. Not included in the 2003 report

Data source	Mortality data available	Year started	Year last survey	Frequency of survey	Sampling methods	Analytic methods	Quality of data
Confidential enquiry into maternal mortality	Maternal deaths that occur in health facilities	1998	2003 (most recent available report)	Ongoing	All provinces collect from all facilities	Proportional mortality for causes of maternal deaths – but difficult to estimate the maternal mortality ratio, as deaths that occur outside a facility are missed	Results extremely valuable in guiding facilities regarding avoidable deaths and for monitoring trends in the cause of death profile – but unable to monitor trends in maternal mortality ratio[122]
PIP: Perinatal Problem Identification Programme. CHiP: Child Problem Identification Programme	Cause of deaths of young babies in participating health facilities; Cause of deaths under 15 years that occur in participating health facilities	1998	2004 (most recent available report)	Ongoing	Self-selected facilities	Proportional mortality for causes of child death; case fatality rates for children	Results extremely valuable in guiding facilities regarding avoidable deaths and for monitoring trends in the cause of death profile – but unable to monitor trends in child mortality rates because it includes deaths in health facilities only, and excludes home deaths or deaths that occur on arrival at a health facility
National injury mortality surveillance (NIMSS)	Manner of death for injury-related deaths; basic demographic characteristics and blood alcohol level provided by participating mortuaries	1997	2004 (most recent available report)	Ongoing	Self-selected mortuaries	Proportional mortality for causes of injury deaths; injury death rates for three cities	Provides valuable information on trends in causes of injuries. Can provide injury death rates for areas that have complete coverage[123]

Agincourt data on age-, sex- and cause-specific mortality are likely to be analogous to those of similar rural populations along the north-eastern crescent of South Africa. Cause-of-death findings have been shown to be valid and can therefore be reliably used for *local* health and development planning.[82] If findings are to contribute to the *national* mortality profile, however, it is important to know how generalisable these data are to other rural parts of the country. And here there are some limitations: Agincourt data derive from a single ecologic area that is relatively ethnically homogeneous; that has yet to meet basic needs with respect to water, sanitation and food security; and that is generally socio-economically depressed. So its mortality picture cannot easily be extrapolated to represent other areas.

There could, however, be considerable value in comparing Agincourt's data with that from other small-area HDSS sites in the region. Two other HDSS sites are operational in South Africa: the Dikgale site in Limpopo Province, some 250 kms from Agincourt but close to an urban centre; and the Africa Centre in northern KwaZulu-Natal. An additional site, Manhiça, is located in southern Mozambique. There is an opportunity, long-planned, for the four sites to jointly characterise the health and population dynamics of rural Southern Africa, and draw out their policy implications. Such "added-value" would fit with the model of sentinel sites established in Tanzania,[10] China[22] and India.[21]

There is value too, in triangulating small-area data with national data: HDSS data provide a more "fine-grained" picture relative to national sources, which yield less detail but have wider coverage. Collaboration with Statistics South Africa has such a comparison effectively under way with respect to migration patterns,[124,125] and joint work to triangulate Agincourt mortality findings with national patterns is now planned. By interrogating any differences, a more sophisticated and nuanced interpretation of findings is possible.

Mortality and burden of disease findings

The period covered by this thesis, 1992-2003, was one of major socio-political change in South Africa and also one marked by the onset of the HIV/AIDS pandemic. The momentous health and social processes had a profound impact on the population, reflected in greatly changing mortality patterns and in a quadruple burden of disease. The shift in mortality patterns includes rapidly increasing mortality in children and young adults (twofold and fivefold increases respectively), and steadily increasing mortality in middle-aged adults. As for the disease burden, the population remains subject to an intractable agenda of infectious disease and malnutrition in children (acute diarrhoea and kwashiorkor unrelated to HIV/AIDS); an emerging agenda of non-communicable disease (particularly stroke and cardiovascular disease) in the middle-aged and elderly; and rapidly escalating levels of HIV/AIDS and tuberculosis. In addition, the levels of violence – both accidental and intentional – remain disconcertingly high in what is outwardly a peaceful community.

The HDSS provided the data to examine mortality differentials to identify population subgroups at greatest risk. The findings showed that the increase in female mortality began at younger adult ages, and progressed more rapidly in middle age, than male mortality did. Higher mortality rates were also experienced by lower socio-economic sub-groups relative to those with greater asset-wealth; by children of Mozambican immigrants relative to South African-born residents; and by recently returning temporary migrants relative to non-migrants or long-standing returnees.

The three sources of data – empirical census data, empirical Agincourt data, and the ASSA2003 demographic model – did show some differences in the apparent *levels* of mortality, but are generally consistent in their accounts of the *trends and patterns* of mortality. Estimates of adult mortality are more robust than those of child mortality. Over the 1992-2003 period there was a rapid increase in adult mortality that was more marked in younger adults and that increased faster in females than in males. In fact, young females lost their survival advantage, with mortality rates surpassing those of males in the 20-44 age group. HIV-related deaths were by far the leading cause in young adults, reaching a peak at younger ages in females than in males; accidents and violence were the main cause of death in male youth 15-24 years; and non-communicable diseases were the main cause in females from age 45 and in males from age 50 years.[26,104,121,126,127]

An undercount of infant deaths has been documented in a number of low- and middle-income settings.[90-92] Recent South African data on child mortality are generally regarded as unreliable by a number of key South African scientists: the 1998 SADHS is out of date, the 2003 SADHS produced implausible results, and the 2001 census failed to provide useful estimates.[104,117,121] In Agincourt, despite intensive fieldworker training and careful probing, an undercount of infant deaths remains possible owing to under-reporting of very young deaths. One explanation relates to cultural interpretations of the age at which life begins and hence whether a death has actually occurred. Another possible factor is incomplete capturing of birth events, when both the birth and death occur during the inter-censal period: the database system will not permit the recording of a death unless there is a prior recording of a birth or an in-migration. Work to assess the extent of this is planned.

Despite inadequate information for reliable monitoring of trends in certain of the data sources, all the different data sources have documented increasing infant and child mortality, mostly due to HIV/AIDS. Disparities in child survival based on race and socio-economic status are evident, and are likely to be exacerbated, as the black African population is worst affected by HIV/AIDS.[93,117]

Child mortality rates in Agincourt and in South Africa as a whole are consistent with the mortality estimates for South Africa produced by the United Nations Department of Economic and Social Affairs, Population Division[j] – the rates are lower than for other sub-Saharan African countries,[24] but, while starting from a lower base,[14,128] are increasing rapidly in both adults and children, much like other African countries affected by HIV/AIDS.[129,130] The impact of HIV/AIDS can be seen from a comparison between South Africa and Russia: the two countries have similar gross national income per capita (although South Africa has a more unequal income distribution); both experienced major socio-political change in the early 1990s; both have a high all-cause mortality and high external-cause mortality (that is, mortality due to accidents and violence). But external-cause mortality is higher in Russia and is increasing at a faster rate, whereas all-cause mortality is higher in South Africa, especially in the 25-55 age group.[127] This almost certainly relates to the lower HIV prevalence in Russia (1.1% in adults at end-2003).[131]

This HIV/AIDS impact on mortality has occurred at the very time in South Africa's socio-political history when improvements may rightly have been expected. So the question arises: what

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[j] United Nations. 2005. World Population Prospects: The 2004 Revision Population Database. http://esa.un.org/unpp/index.asp?panel=7. Accessed 13 July 2006.

might mortality levels have been without HIV/AIDS? In the Agincourt HDSS, the impact of HIV/AIDS was examined by producing cause-deleted life tables. For this purpose a combined HIV/TB cause category was created to eliminate potential misclassification between HIV/AIDS and TB diagnoses. Standard male and female life tables based on the total number of deaths and person-years lived in the Agincourt population were constructed, then the number of HIV-related and TB-related deaths by sex and age tallied. By subtracting HIV/TB deaths from the total deaths a life table excluding HIV/TB was created, and a new life expectancy calculated. Figure 12 illustrates the impact of HIV/AIDS on life expectancy, based on calculating the difference between life expectancy without HIV/TB and current life expectancy with HIV/TB. From zero difference in 1992/93, the divergence increases steadily: without HIV/AIDS, life expectancy in the Agincourt population would likely be some eight years higher in males and ten years higher in females.
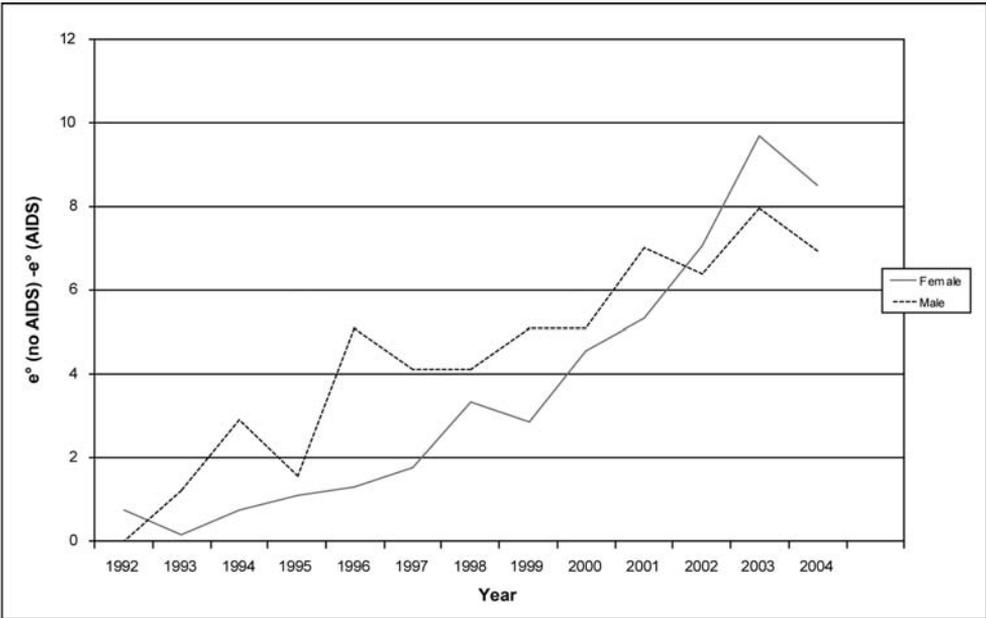

Figure 12. *Impact of HIV/AIDS on life expectancy, Agincourt 1992 to 2004*
(e° (no AIDS) -e° (AIDS): difference between life expectancy without AIDS and life expectancy with AIDS in years)

Health Policy and Practice: Implications of Changing Mortality

Implications of key mortality patterns for the public health sector are illustrated schematically in Table 15, and described in greater detail below.

Table 15. *Implications of changing mortality for rural South African public health services*

Key findings		Implications for health services
Extent of mortality		
• Increasing mortality in children and young adults	⇒	• Increased demand
• Higher mortality among the poorer	⇒	• Address barriers to access
• Higher mortality among recently returned migrants	⇒	• Increased demand
Burden of disease		
• Escalating HIV/AIDS in children under-5, young and middle-aged adults	⇒	• Improve voluntary counselling and testing • Accelerate roll-out of antiretroviral therapy • Build synergy with other chronic care programmmes
• Increasing pulmonary tuberculosis	⇒	• Improve case detection at primary health care level
• Emerging non-communicable disease in adults	⇒	• Develop effective chronic care systems • Focus on prevention and control of risk factors, particularly hypertension
• Persisting infectious disease and malnutrition in children	⇒	• Maintain and improve acute care services, and services for women and children
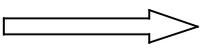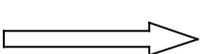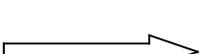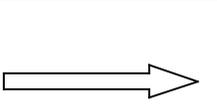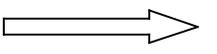
Paper III presents a picture of steadily increasing mortality in children under-5, young adults and middle-aged adults, with the increase commencing at younger ages in females and increasing more rapidly in females aged 50 to 64 years. In other work, Kahn and colleagues describe the "returning home to die" phenomenon, in which recently returning temporary migrants of both sexes show a significantly higher mortality risk than either migrants who returned more than five years earlier or the permanent population.[96] In both papers, HIV/AIDS is identified as the main driver of these mortality patterns; in addition, non-communicable diseases are emerging in middle-aged and older adults. Owing to the chronic nature of these illnesses, a substantial increase can be expected in demand on rural health services at both primary-care level and hospital level. This increase in utilisation starts from a relatively high base, as people already use allopathic services for both chronic non-communicable and infectious diseases,[76,101,132] and has to be absorbed by already-

strained services that are largely understaffed and poorly managed by inadequately trained and demotivated staff. Also documented are mortality differentials by socio-economic status: higher mortality among the poorer; and higher child mortality among the more socially-marginalised Mozambican households.[93,94] These findings pose a further challenge for South African health services: to address inequity in access to care.

The anticipated increase in burden on rural health services is paralleled by an increase in burden on rural households. Death of prime-age adults, following a period of chronic illness, is associated with increased household health expenditure (due to health care and funeral costs), decreased household income (due to illness and death of a breadwinner), and the opportunity costs associated with caring for an ill household member.[96] (Households that have experienced an adult death make greater use of natural resources – collecting fuel wood and consuming wild foods more extensively, for example – to compensate for the loss of an adult household member.[133,134])

Health care organisation

Historically, the focus of rural South African health services has largely been on women and children. This has produced health gains: antenatal services are widely used albeit late in pregnancy and less by adolescents; maternal mortality is low relative to much of the African continent; and death from vaccine-preventable diseases is uncommon.[26] However, the demographic and epidemiologic transitions have progressed so rapidly that health services have lagged behind in their response to an aging population with chronic care needs.[135]

Given the evidence from Agincourt of emerging non-communicable disease, there is a clear need for a shift in health-service organisation towards services for effective chronic, long-term care. However, the persistence of infectious disease and malnutrition argues for caution: any re-orientation of services to chronic care must not jeopardise services for women and children and existing infectious disease-control programmes.[136,137] Rather, these areas need to be maintained and improved in step with the building and financing of chronic-care delivery – an extreme challenge for services that are under-resourced as well as under-skilled and poorly organised and managed.

Rural South Africans make wide use of "plural healing" – consultations with public and private allopathic health providers (for illnesses regarded as having a physiological cause) and with traditional healers, *inyangas*, and prophets (for illnesses with a spiritual or social basis). For both stroke and PTB in Agincourt, allopathic care was generally sought first, followed by visits to traditional or faith healers.[132,138] Since adults are using clinic and hospital services, and not just as a last resort, the onus is on the health service itself to provide quality care. Unfortunately, it is lacking: Paper VI describes the substantial burden of PTB that remains undiagnosed in the community until death, despite presentation to the health service; this is corroborated by other work in the area that found a delay before hospitalisation for PTB, owing to inappropriate treatment being given at clinic level.[138] For stroke and hypertension too there is evidence of poor clinical management in the Agincourt sub-district. While hypertension was found in 43% of the general population, only 24% were on antihypertensive treatment, with just over half of these (51%) having a controlled blood pressure (<140/90 mm Hg). There was evidence of hypertension in 84% of stroke survivors: of these, fewer than a third (29%) reported being prescribed antihypertensive

medication after their stroke; only 8% were taking the drugs; and only 1% had a blood pressure within the normal range. Only one stroke survivor was on aspirin.[139]

These and other insights into PTB and stroke management – examples of infectious and non-communicable disease respectively – point to key elements in the health system that require improvement: health-service organisation and access; clinical management by health-care providers; and supply and maintenance of drugs and equipment.

Health service organisation and access

Knowledge of prevailing diseases and their risk factors is critical for priority-setting, efficient use of resources and effective service delivery. Anyone understanding properly the health transition in rural South Africa will recognise the need to strengthen chronic-care programmes alongside existing services for acute care, maternal health and child health.

Prevention and control of non-communicable diseases and their risk factors can only be achieved through wide-reaching health promotion, primary prevention and screening programmes, coupled with effective clinical management including secondary prevention. But alongside the increase in non-communicable diseases is the escalation in HIV/AIDS and PTB, and what's needed here is a strengthening of voluntary counselling and testing (VCT) and PMTC[k] programmes, an accelerating of the roll-out of antiretroviral therapy, and improvements in early detection of PTB, particularly at clinic level – the first line of care sought by the majority of patients. Given the scale of the HIV pandemic, health-service managers run the risk of letting HIV-related services overwhelm all others; what would be far preferable is to design organisational improvements in this area in such a way that they can actually benefit other areas rather than detract from them.

Referral systems require attention: transport from clinic to hospital needs to be more readily available, and informative two-way communication needs improving between clinic nurses and hospital doctors.

Also requiring remedial action is the current state of differential access to care – a probable contributor to mortality differentials. Despite free primary health care, the costs associated with health-facility visits remain a serious problem,[76] notably transport and opportunity costs. These costs could be reduced, and access thereby increased, by decentralising services appropriately to clinic level.

Such decentralisation could also serve to increase the buy-in and commitment of clinic staff, who are more likely to invest in services if directly involved. The current community-based DOTS[l] system, while fairly well organised, is largely hospital-based, and there is little role for clinics to care for patients after discharge. As a result, clinic nurses may give low priority to the TB programme, and that could contribute to poor detection of symptomatic PTB.[138]

Finally, for both PTB and stroke, patients use plural healing. Although the majority of patients for both conditions tended to seek care first at a clinic or hospital, 15% of PTB patients and 20% of stroke survivors first sought alternative treatment. It would be very helpful to establish cooperative links between traditional healer organisations, churches and clinics: such links could enhance appropriate and timely referrals, as well as patient compliance with medication.[132,138]

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[k] PMTC: Prevention of mother-to-child transmission
[l] DOTS: Directly observed treatment – short course (for tuberculosis)

Clinical management: building and maintaining capacity and morale

Crucial to well-functioning district and sub-district health systems are their human resources: an appropriate mix of skills is needed at all levels of the system, from clinic to health centre to hospital. For the training of health-care providers and on-going professional development, the best basis is knowledge of prevailing health conditions and their determinants. A combination of community education, enhanced patient literacy and health-worker training will contribute most to preventing and controlling non-communicable diseases and their risk factors, as well as promoting early detection and treatment of infectious diseases. Consider how the PTB burden could be alleviated if there were less delay in presentation on the part of patients, and better diagnostic abilities on the part of clinic nurses. For want of prompt diagnosis, there is a poorer clinical prognosis for the individual patient, while from a population perspective there is prolonged infectivity in the community.[138]

The knowledge, attitudes and practices of clinic staff have been identified as problematic in public-sector facilities providing primary care for chronic conditions in South Africa.[140,141] What's needed is continuing professional education, aimed at all levels of clinic staff, to ensure continuity despite high staff turnover and periods of leave, and to avoid senior staff feeling threatened if junior colleagues acquire new skills. Ongoing supervision and support is required, to maintain motivation, focus skills, and sustain high-quality services in remote areas, and also to reduce stress and burnout as VCT and antiretroviral treatment scale up.[142]

There are three other strategies that can improve clinical management at primary-care level by promoting standardised, cost-effective, high-quality treatment of particular conditions: clinical protocols or structured treatment guidelines; an essential-drugs list; and patient-retained records.[76,143] These have particular potential for chronic care in settings of high temporary migration: they ensure a consistent treatment approach, availability of the same drug regimen, and a record of the patient's medical history and progress, irrespective of the location of a follow-up consultation.

Drugs and equipment: improving supply and maintenance

There are persistent problems with drug supply and availability of appropriate and fully functioning equipment in primary-care clinics, and this impairs delivery of clinical care, affects patient compliance, and decreases staff morale. The long-term effects are most significant in the management of chronic conditions requiring on-going care, repeat follow-up visits, monitoring for complications, and life-long medication. Appropriate equipment, including blood-pressure cuffs of various sizes, needs to be supplied and maintained, and health-care providers must be fully trained in its use. Also essential is a reliable distribution system that ensures an uninterrupted drug supply, as well as provision of supplies for VCT and sputum collection. Shortcomings here can cause demotivation and fatigue in health workers; dissatisfaction and non-compliance in patients; poorly controlled disease; and, in the case of PTB and AIDS, an increased risk of drug-resistant strains.

Social implications of changing mortality and burden of disease

While not a major focus of this thesis, social implications of the health transition must get a mention, albeit a brief one. At individual and household level, increasing mortality of prime-age adults is changing the roles required of older adults, particularly older women, within families and the community. Child-care and income-generating roles are being extended to ages at which women would traditionally be relieved of many household responsibilities, and would enjoy the care provided by daughters or daughters-in-law. In fact, a reversal of roles is evident as older women have to care for chronically ill and dying adult children.

At national level, government provides a safety-net of social support that includes monthly payments in the form of a number of non-contributory grants: the old-age pension, disability grant, child support grant, foster child grant, and the child dependency grant for severely disabled children. The demand on several of these grants is linked both directly and indirectly to HIV/AIDS morbidity and mortality. The *child dependency grant* is paid out to children, and the *disability grant* to adults, with AIDS and a CD4 count below 200: payments are likely to increase as AIDS prevalence increases, and as wellness clinics become more accessible and more utilised. On the other hand, as people gain access to antiretroviral therapy and their CD4 count increases, they lose eligibility for these grants. Households that move into poverty, following increased health care-costs and decreased household income consequent on HIV/AIDS, become eligible for the *child support grant*; this is available for all children under the age of 14 years whose primary caregiver plus spouse, if any, fall below the threshold of a means test. The *foster child grant* is to support the care of orphans and children at risk, and is awarded to foster parents by the Children's Court. A complicated judicial process is associated with this grant: it needs to be renewed every two years, and if the primary caregiver changes, the grant needs to be re-awarded to the new caregiver. While these grants are unique in Africa in providing relief to poor families and households, particularly those bearing the burden of HIV/AIDS, the question of sustainability is likely to arise as government expenditure on these grants escalates in parallel with the HIV/AIDS pandemic.

Health Transitions

While calling for further theoretical development of health-transition models, Frenk and colleagues acknowledge the importance of building an understanding of actual transition experience through empirical research[53] – which this thesis attempts to do. How then, has empirical data from the Agincourt HDSS in rural South Africa contributed to our understanding of health transitions in middle-income countries?

Despite socio-political change, economic development, and relatively accessible health services in the country at large, mortality in rural South Africa is increasing in most child and adult age groups. The epidemiological profile underlying these trends is made up of a new infectious disease, emerging non-communicable diseases, persisting child diarrhoea and kwashiorkor, and high levels of violence and accidents. In health-transition terminology, we have a quadruple burden of disease, with co-existence of infectious diseases/nutritional deficiencies and chronic, degenerative and man-made diseases. To properly evaluate, modify and formulate South Africa's health policies, it is essential to gain a full appreciation of the country's position on the health-transition continuum, together with an understanding of the health, social, and environmental

determinants and risk factors of particular disease categories.

Omran's epidemiologic transition theory has contributed substantially by focusing on the mortality side of the demographic transition; locating health change within social change; acknowledging the value of public-health activities; and stimulating debate among both population and public-health scientists.[37] Out of this debate, however, has come criticism of his view of uni-directional change and the sequential progress of change, and his limited focus on sub-group differences. Frenk and colleagues have modified epidemiologic transition theory and put forward a model, based on Mexican data, of a "counter transition", "prolonged or protracted transition" and "epidemiologic polarization".[52]

Empirical data from Agincourt tend to bolster the critiques of Omran's theory, and provide evidence in support of a modified model more appropriate to the experience of middle-income countries. The original stages of epidemiologic transition theory were too narrowly defined, though further stages were subsequently added by Omran himself and others[47-49] – the stages do not necessarily occur in a single direction nor progress sequentially, but may overlap. Data from Agincourt demonstrate a "counter transition" in which earlier mortality gains have been reversed, and mortality is increasing despite socio-economic development and access to health interventions. Similar patterns are seen in other African countries,[129,130,144] and in Russia and parts of Eastern Europe,[51] owing to economic downturns, new emerging diseases, and failure of public-health systems. The Agincourt data also demonstrate a "prolonged or protracted transition" representing partial change in mortality and morbidity patterns, in which the stages of transition overlap. This is evident in the co-existence of "old" infectious diseases (acute diarrhoea and PTB) with "new" infectious diseases (HIV/AIDS) and emerging non-communicable diseases. In addition, mortality differentials in Agincourt illustrate "epidemiologic polarization", with the poorest and most disenfranchised experiencing the highest mortality burden.

HDSS data provide robust, empirical evidence with which to interrogate models of epidemiologic and health transition theory. The Agincourt findings from rural South Africa argue that there is a middle-income country in Africa that supports and reinforces the health transition experience in Mexico, a middle-income country in Latin America.[52] While the two countries differ markedly in the extent of HIV/AIDS (adult HIV prevalence in Mexico at end-2003 was 0.3%),[145] they have high levels of inequality in common.

Conclusion

This thesis commenced with a discussion of the "information paradox": on the one hand, the critical need for reliable population-based information – at national and sub-national levels – on which to base health and development priorities and monitor progress; on the other, the profound lack of such information in settings where problems are greatest. This formed the basis for the primary conclusion of the Commission on Health Research for Development. Its recommendation that every country, no matter how poor, develop the means to conduct "essential national health research" is as timely today as it was when presented to a Nobel conference in Stockholm in 1990.[146]

One means of engaging this paradox is through health and demographic surveillance systems or HDSS – a powerful mechanism for monitoring mortality and burden of disease in settings that lack effective vital registration. The potential of health and demographic surveillance is receiving belated recognition, reflected in the rapid growth and achievement of the INDEPTH Network,[m] and in the goals and approach of WHO's newly established Health Metrics Network which seeks to realise comprehensive health information in poor countries. The step-wise approach envisaged starts with HDSS-based sentinel registration before expanding to a more representative sample registration system and, over the longer term, to near-complete civil registration. HDSS sites should – but seldom do – play a key role in monitoring the impact of national and international efforts to achieve the Millennium Development Goals. Witness the success of the Tanzanian Essential Health Interventions Project (TEHIP) which, through sentinel surveillance, was able to establish the "intervention-addressable" disease burden, support responsive district-level planning, and demonstrate significant improvement in child health indicators.[23] There is similar potential in rural South and Southern Africa, given the presence of several HDSS sites – but realising this potential will require government recognition and investment.

As for the Agincourt HDSS, where the research for this thesis was conducted, it has demonstrated its utility in finely mapping the complex unfolding of a particular health transition. Such intense monitoring should continue: the longer the follow-up period, the more "mature" a site becomes; and it is the mature sites – with depth of longitudinal information and established relationships with community and public sector stakeholders – that can best inform and influence health and development policy. In little over ten years, the Agincourt HDSS has documented the devastating demographic, health and social impacts of the HIV/AIDS pandemic. Now that antiretroviral therapy is finally becoming available to South African communities, the HDSS is ideally placed to evaluate issues of roll-out, uptake, access, adherence, behaviour change and social impact. Similarly, the HDSS has documented a growing burden of non-communicable disease and is well placed to measure major risk factors and monitor their trends as the social, cultural and economic fluxes evolve. The HDSS has also documented the persistence of severe malnutrition in children and is providing invaluable support to investigations into its determinants within the context of HIV/AIDS. Now the Agincourt site is poised to host intervention-research in child growth, nutrition and psycho-social resilience, as well as address risk factors for chronic disease in adults.

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[m] INDEPTH: International Network for the Demographic Evaluation of Populations and their Health

How might such work translate into support for public sector efforts? It can – through communication and collaboration with relevant government departments – make contributions in three areas: guiding public policy and interventions; enhancing official statistics and planning; and influencing the research agenda. First, regarding policy: if findings are conveyed tactfully but clearly to health-service planners and managers, they can help to set service and system priorities and targets. The HDSS can monitor, at local and district level, the impact of the resulting inter-ventions – and, through structured feedback, could help to modify programmes and services in pursuit of a more equitable population benefit. Second, regarding official statistics: empirically-derived HDSS data could, and should, be integrated into national information systems, in order to evaluate and calibrate the assumptions made to their adjusted data, and to assist in modelling and projections. Finally, regarding the research agenda: HDSS findings can help to establish an optimal ranking of national priorities. The South African Medical Research Council's Research Strategy 2005-2010 identifies burden of disease analysis as a "major input (to) research prioritisation" and "key driver for health research priorities in South Africa and the region".[147] Health and demographic surveillance, in South Africa as elsewhere, can make a vital contribution to framing research objectives, posing hypotheses, and guiding efficient use of a nation's limited research resources.

Acknowledgments

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