Dying in their prime: determinants and space-time risk of adult mortality in rural South Africa

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Abstract. A longitudinal dataset was used to investigate adult mortality in rural South Africa in order to determine location, trends, high impact determinants and policy implications. Adult (15-59 years) mortality data for the period 1993-2010 were extracted from the health and demographic surveillance system in the rural sub-district of Agincourt. A Bayesian geostatistical frailty survival model was used to quantify significant associations between adult mortality and various multilevel (individual, household and community) variables. It was found that adult mortality significantly increased over time with a reduction observed late in the study period. Non-communicable disease mortality appeared to increase and decrease in parallel with communicable mortality, whilst deaths due to external causes remained constant. Male gender, unemployment, circular (labour) migrant status, age and gender of household heads, partner and/or other household death, low education and low household socio-economic status were identified as significant and highly attributable determinants of adult mortality. Health facility remoteness was a risk for adult mortality and households falling outside a critical buffering zone were identified. Spatial foci of higher adult mortality risk were observed, indicating a strong non-random pattern. Communicable diseases differed from non-communicable diseases with respect to spatial distribution of mortality. Areas with significant excess mortality risk (hot spots) were found to be part of a complex interaction of highly attributable factors that continues to drive differential space-time risk patterns of communicable (HIV/AIDS and tuberculosis) mortality in Agincourt. The impact of HIV mortality and its subsequent lowering due to the introduction of antiretroviral therapy was found to be clearly evident in this rural population.

Keywords: adult mortality, spatial risk, survival modelling, Bayesian inference, determinants, attributable fractions, health and demographic surveillance, South Africa.

Introduction

Adult mortality in many developing countries has received scant attention in recent decades in contrast to childhood mortality (Murray and Feachem, 1990). This lack of focus is especially surprising in sub-Saharan Africa (SSA) where the risk of dying before 60 years of age remains excessively high (Murray and Feachem, 1990). Despite a worldwide reduction in communicable disease (Murray and Lopez, 1997), high levels of communicable disease (HIV/AIDS) have drastically reduced life expectancy in SSA and South Africa. This has slowed the expected health transition where communicable disease gives way to non-communicable disease as a result of progress in health care as well as social and economic development (Preston and Nelson, 1974). Simultaneously, many parts of SSA are experiencing an upsurge in non-communicable disease, such as cancer and cardiovascular disease, that is projected to increase until 2020 (Murray and Lopez, 1997), largely due to lifestyle-related factors such as obesity, smoking and alcohol consumption (WHO, 2002). This projected upsurge is particularly important because of its impact on economically productive adults (WHO, 2008), who are responsible for the welfare of younger and older age groups (Feachem et al., 1992). Thus, adult mortality in SSA presents a changing set of dynamics challenging the limited healthcare resources of the region (Murray and Feachem, 1990) because of its impact on the availability and produc-

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tivity of working adults (Schatz and Ogenmefun, 2007; Sartorius et al., 2011b).

Adult mortality is a vital indicator for planning health care interventions, but data are often lacking in SSA (Kaufman et al., 1997). Health and demographic surveillance systems (HDSS), though not representative at the national level, are often the only means to assess and better understand population levels and trends and allow the assessment of cause-specific mortality on a longitudinal basis (Kaufman et al., 1997; Kuh and Shlomo, 2004). Adult mortality can be influenced by a combination of variables at the individual, household and community level. A conceptual framework (Fig. 1) was developed to guide and interpret the analysis of adult mortality determinants. The framework expands previous work to include the effect of historical legacies, as well as account for a spatial temporal aspect (Victora et al., 1997).

Individuals that emerge from households are unique biologically (and differentially frail[1]) but are also a product of their surrounding environment, including their ethnic norms, experience and behaviour. Historical legacies have a pervasive long-term effect on the cultural dimensions of a society, as well as the location and efficiency of its institutions (Hofstede, 1986; Williamson, 2000). In South Africa, household characteristics have been shaped by a 100+ years of colonial and apartheid rule and have had a profound impact on the location of infrastructure and forced

ethnic settlement in geographically defined areas (Bryceson, 2004; Mertz et al., 2005; Sherbinin et al., 2008). This has led to differential education and health care quality (Williamson, 2000) and impacted the socio-economic status (SES) of many households (Machethe, 2004). Household characteristics that have been influenced over the medium term include household size, access to services, ethnicity, physical location, employment, health, access to land and education (Schwarze and Zeller, 2005; Vermeulen et al., 2008; Xiangxing et al., 2008). Individual characteristics that can influence adult behaviour and lifestyle choices include age, gender, nationality, religion, education (intelligence), income and partner outcome (direct and indirect consequences). Moreover, a combination of these individual attributes, determines the likelihood of disease type and the risk it poses with respect to their mortality (Victora et al., 1997; Brown et al., 2004). Finally, exogenous shocks like drought, famine or disease (e.g. HIV/AIDS), have had a major influence on mortality in SSA (Hosegood et al., 2004; Kahn et al., 2007).

Given the projected burden of disease in SSA and associated socio-economic impact, this paper investigates the dynamics, trends, causality and implications of adult mortality in rural South Africa. It builds on previous work in this setting by (i) assessing neglected adult mortality within a detailed conceptual framework; (ii) introducing population attributable fractions to quantify determinant impact for policy makers; (iii) analysing the importance and potential emergence of non-communicable adult mortality as a result of lifestyle and nutritional transitions; (iv) using a more complex analytical framework (continuous time-

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[1]Unobserved susceptibility to death (frailty) is a concern in survival analyses, where individual survival probability variations cannot be ignored.
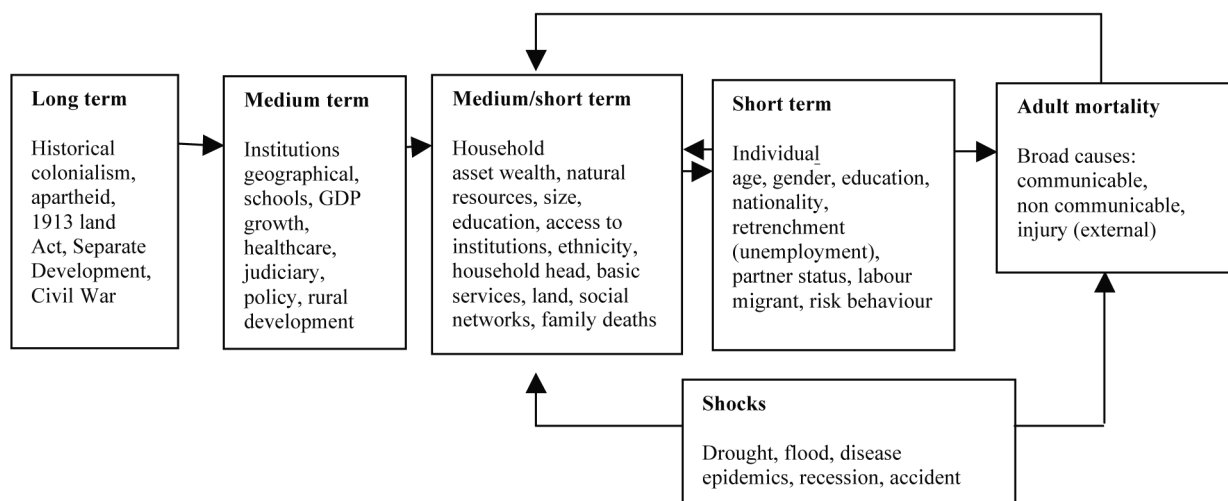

Fig. 1. The dynamics of adult mortality: a conceptual framework.

to-event frailty modelling); and (v) highlighting potential gaps in health service delivery as a function of critical proximal threshold distance of households to nearest facility.

Materials and methods

Study area and population

The Agincourt HDSS, located in northeast South Africa (Fig. 2), was established in 1992 with annual updates of births, deaths, in- and out-migrations (Tollman et al., 1999). It is a poor, rural sub-district that includes former Mozambican refugees, temporary migrant workers and a more stable permanent population (Tollman et al., 1999). The present site covers an area of about 400 km² and contains 25 villages and 13,500 households[2], 84,000 individuals in all. An annually updated geographical information system (GIS), containing locations of all households within the site, has been established. Verbal autopsies (VA)[3] were introduced in 1993. A full VA is conducted on every death recorded during the annual census update (Kahn et al., 2007). The main cause(s) of death is used in these analyses. The study population comprised all adults (15-59 years old) in the original 21 villages during the period 1993-2010. Data from four new villages added to the site since 2007 were not included in the analysis as they contribute minimal data to the study period.

Outcome and explanatory variables

The outcome in this study was defined as time (in years) contributed by an adult (15-59 years old) during the study period until right censoring[4] (0) or death (1). The time to right censoring was set to either the date of permanent out-migration during the study period or as 31 December 2010 if the individual was present and alive at this endpoint. The explanatory variables included factors regarding the individual (age, gender, nationality, education, migrant pattern), the household (size, household age, death numbers, SES, household head demography, distance to nearest health facility) and the village (size, number of deaths, proportion of deaths attributed to HIV/AIDS and tuberculosis, migration patterns). A temporary migrant is defined as a labour migrant who resides in the household for less than six months but whose return is assumed, i.e. a significant link to the base household is retained (Collinson et al., 2006a). Household SES was based on living conditions, assets and services including building materials of the main dwelling, water and energy supply, ownership of modern appliances and livestock, and means of transport.

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[2]A household is defined as a group of people who reside and eat together, plus linked temporary migrants who would eat with the household periodically.

[3]Verbal autopsy (VA) is a method of determining an individual's cause of death in the absence of a complete vital registration system. VAs consist of a trained interviewer using a questionnaire to collect information about the signs and symptoms of a recently deceased person from an individual familiar with the deceased. Physicians then assign the most likely cause(s) of death.

[4]Right censoring occurs for individuals who are still alive when they are lost to follow-up or when the study ends, i.e. a missing data problem. One makes the assumption that censoring is non-informative, i.e. event times are independent of the censoring mechanism, e.g. "missing at random".
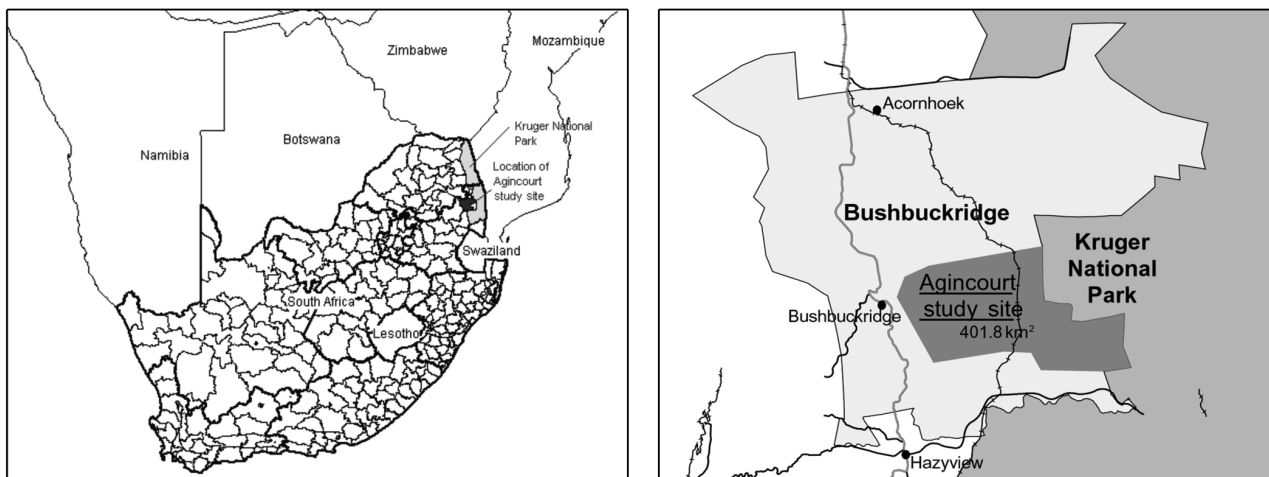

Fig. 2. Maps showing the regional location of the Agincourt HDSS.

These assets were used to construct an SES index using multiple correspondence analysis (MCA) (Sartorius et al., 2011b).

Statistical analysis

Selected explanatory variables (e.g. education years by gender or ethnicity) were compared against one another using the standard *t*-test to better identify any potential significant underlying causal processes as suggested by risk factor analysis. A preliminary, non-parametric Cox survival analysis (Cox, 1972) was initially conducted to assess the bivariate relationship between adult mortality and each covariate. Time contributed by adults was split into discrete yearly segments to incorporate any changes in any time varying parameters such as household location. Covariates significant at the 10% level were then incorporated into the multivariable model. The assumption of proportional hazards was not upheld in the multivariable model and various parametric survival models were tested with the one providing the best fit finally adopted (the Weibull distribution (Weibull, 1951) in this case).

Given the inherent spatial and temporal correlation of longitudinal HDSS data, problems arise when using standard statistical methods as they assume independence of outcome measures, e.g. mortality. Objects in close proximity are often more alike and common exposures may influence adult mortality similarly in households of the same geographical area, introducing spatial correlation in mortality outcomes. Inclusion of the spatial effect of proximity is therefore important for efficient estimation of parameters and prediction (Wikle and Royle, 2002). Ignoring this correlation introduces bias in the risk factor analysis as the standard error of the covariates is underestimated, thereby overestimating significance. Thus, Bayesian geostatistical models are needed to analyse longitudinal spatial data as they relax assumptions of independence and assume that spatial correlation is a function of distance between locations. Bayesian approaches are being applied to the analysis of many social and health problems in addition to disease mapping and modelling or kriging (Langford et al., 1999). Their full estimation has only become possible in the last decade (Diggle et al., 1998) through software such as WinBUGS (Spiegelhalter et al., 1999) using Markov chain Monte Carlo (MCMC) simulation (Gelfand and Smith, 1990).

A Weibull Bayesian geostatistical frailty survival[5] model was used to examine the multivariable association between significant covariates and adult mortali-

ty. A spatial random effect at the village level, included to take account of spatial correlation, was modelled using a multivariate Gaussian distribution with a covariance matrix expressed as a parametric function of the distance between pairs of village centroid points (Diggle et al., 1998). Furthermore, an unstructured individual-level random effect was included to account for differential frailty and repeated individual observations where time episodes were split to incorporate any time varying issues such as change of household location. MCMC simulation was employed to estimate the model parameters using WinBUGS.

Statistical model

We analysed the data assuming a parametric Weibull distribution for the survivor function, where t_{ikj} is the failure time of an adult i (for censored observations the survival distribution is a truncated Weibull with an upper bound corresponding to the censoring time) for year k at location j with covariate vector X_{ik} and β is a vector of unknown regression coefficients and including an unstructured individual random effect or frailty h_i and structured village-level spatial random effect w_j in the exponent of the hazard model as follows:

$$t_{ikj} \sim \text{Weibull}(\rho, \mu_{ikj}) \ i = 1, ..., N$$

with a baseline hazard function of the form:

$$l_0(t_{ikj}) = \rho t_{ikj}^{r-1}$$

and means for the various models as follows:

(i)   multivariate non-spatial model:
      $\log(\mu_{ikj}) = \beta_0 + \beta X_{ik} + h_i$

(ii) mutlivariate spatial model:
      $\log(\mu_{ikj}) = \beta_0 + \beta X_{ik} + h_i + w_j$

(iii) spatial kriging model:
      $\log(\mu_{ikj}) = \beta_0 + h_i + w_j$

where β_0 is $\sim$Normal(0, 0.1) and w_j has a multivariate normal distribution, $w_j \sim \text{MVN}(\underline{0}, \Sigma)$ with variance-

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[5]Parametric survival model (assuming an underlying Weibull distribution for the survival function) incorporating a structured spatial (geostatistical) random effect and an unstructured individual-level random effect (frailty) within a Bayesian framework.

covariance matrix Σ expressed as a parametric function of distance between villages. We also assumed an isotropic stationary spatial process, where $\Sigma mn = \sigma_w^2 \exp(-\varphi d_{mn})$, d_{mn} is the Euclidean distance between villages m and n, σ_w^2 is the geographical variability known as the sill, φ is a smoothing parameter that controls the rate of correlation decay with increasing distance and measures the range of geographical dependency (Diggle et al., 1998). We specified φ as a uniform distribution between φ_{min} and φ_{max} (Gelfand and Vounatsou, 2003). The range was defined as the minimum distance at which spatial correlation between locations is below 5%. This distance can be calculated as $3/\varphi$ meters. The individual-level frailty was assumed to follow an independent normal distribution $h_i \sim N(0, \sigma_h^2)$. Vague Normal distributions were adopted for the β, inverse gamma priors for the variance parameters and a uniform prior for ρ. The shape parameter of the Weibull survival distribution (ρ) was given a non-informative gamma distribution with a mean and variance of 1.

MCMC simulation was applied to fit the models. We ran a single chain sampler with a burn-in of 5,000 iterations. Convergence was assessed by running the simulation until the Monte Carlo error for each parameter of interest was less than 5% of the sample standard deviation. The chains thereafter were sampled every single iteration until a sample size of 10,000 had been attained.

Model assessment

The analysis was carried out in STATA, version 12.0 SE (Stata Corp., 2007) and in WinBUGS (Spiegelhalter et al., 1999). Model comparison in STATA was based on the Akaike information criterion (AIC). We selected the model with smallest value of AIC and then graphically examined the model fit in STATA using Cox-Snell residual plots. The Deviance information criterion (DIC) was used to assess the various multivariate models (Spiegelhalter et al., 2002). Generally, the smaller the AIC/DIC value, a measure of the relative goodness-of-fit of a statistical model, the better the fit.

Population-attributable fractions (PAR)

The PAR approach is needed as measure that an effect does not factor in the prevalence of exposure to selected determinants in a population and thus allows identification of relevant exposures for targeting by policy makers at the population level. The following standard formula for calculating PAR for each determinant is based on the proportion of the total population exposed to the risk factor (p_e) factoring in the multivariable-adjusted model risk coefficient (HR):

$$PAR = \frac{p_e \,(HR - 1)}{1 + p_e \,(HR - 1)}$$

Risk maps

Simulation-based Bayesian kriging (Gelfand et al., 1999) at regular grid points was used to produce smoothed maps of all-cause and cause-specific adult mortality risk within the study area. Apart from a constant, these models included only the random effects. All identifying features, e.g. village centroids and village boundaries, were removed from the maps to ensure confidentiality and avoid potential stigmatisation of high-risk villages. Also, the HIV/AIDS and tuberculosis mortality risk map is not shown for this reason. Model estimates were exponentiated to relative risks. A simple map showing potential high-risk areas as a function of the straight-line distance to nearest health facility was constructed using a circular buffer zone around health facilities based on the significant cut-off found in the bivariate risk factor analysis. The spatial risk maps were constructed in MapInfo Professional version 9.5 (MapInfo, 2008).

Results

Descriptive analysis

Between 1993 and 2010, there were 104,969 adults (15-60 years old) and 5,675 adult deaths within the 21 villages. The mean age at entry was 24.6 years (standard deviation (SD) 11) and the majority were female (59,781 or 57%). Of those whose nationality was known, 33,192 or 32% were of Mozambican origin with the remainder mostly being South African. The average level of education, as expressed by the number of years at school completed, was 6.2 (SD 4.5) with this mean being significantly higher in males compared to females (6.29 *versus* 6.06, P <0.001). Similarly, the mean number of years attained by South Africans in general was significantly higher than that of their Mozambican counterparts (7.14 *versus* 4.30, P <0.001). Males, on average, were significantly more likely to spend fewer resident months within the site each year compared to females (mean of 9.76 *versus* 7.98, P <0.001). This figure for South African adults in general was also lower compared to Mozambicans (8.93 *versus* 9.01, P <0.001).

Main cause of death

Of the 5,675 adult deaths that occurred from 1993 up to the end of 2010, the majority were attributed to communicable causes (2,989 or 53%), largely attributed to HIV/AIDS and tuberculosis, with 2,527 deaths or 45% (95% confidence interval (CI), 43.7-46.3%). Non-communicable diseases were responsible for 1,262 or 22.2% of all adult deaths over the study period. Approximately 11% (643) adult deaths were attributed to external causes. Mozambican adults had a significantly higher proportion of deaths attributed to communicable causes (58% *versus* 51%, P <0.001). Conversely, Mozambicans had a significantly lower proportion of deaths attributed to non-communicable disease (17% *versus* 24 %, P <0.001). There was no significant difference in the proportion of adults deaths attributed to external causes by nationality (P = 0.303). Females had a significantly higher proportion of deaths attributed to communicable causes (56% *versus* 50%, P <0.001) and a significantly higher proportion of deaths attributed to non-communicable causes (25% *versus* 20%, P <0.001). Males did, however, have a much higher proportion of deaths attributed to external causes (17% *versus* 5%, P <0.001).

Temporal trend analysis

During the period 1993-2010, the overall adult mortality rate was 8.2 (95% CI, 8.0-8.4) adult deaths per 1,000 person-years. Mortality significantly (P <0.001) increased over the study period, with the most pronounced increase occurring from 1999 onwards to reach a plateau of ~13 deaths per 1,000 person-years in 2004 with similar levels observed

through to 2007, after which we observed a sharp decline in adult mortality (Fig. 3). Males generally had a higher mortality rate except for a convergence that occurred around 2001, during the upsurge in mortality related communicable disease, largely HIV/AIDS and tuberculosis (Fig. 1). A concurrent (though at a lower level) rise in non-communicable disease mortality occurred over the 1993-2004 period with a decline thereafter. Levels of external mortality remained fairly constant over the study period.

Risk factor analysis and impact

Increasing the time period (1999-2004 and 2005-2010 *versus* 1993-1998) was found to be a significant risk factor for adult mortality and confirms the temporal trend (Table 1) seen in Fig. 3. The most prominent and significant individual level risk factors for adult mortality following multivariable adjustment were younger adult age (15-44 years), male gender, partner having died, low level of education, migrant status and unemployment (Table 1). Conversely partner being alive was found to be significantly protective when compared to the baseline group of never married. No significant difference in adult mortality risk by nationality (former Mozambican *versus* South African) was identified (P = 0.592) and was thus not included in the final multivariable model. Similarly, no significant difference in mortality risk was identified when comparing older (aged ≥45 years) adult Mozambicans to older South Africans.

Following multivariable adjustment, household-level determinants that remained significantly associated with adult mortality were: increasing number of other adult deaths in the household, residing in a
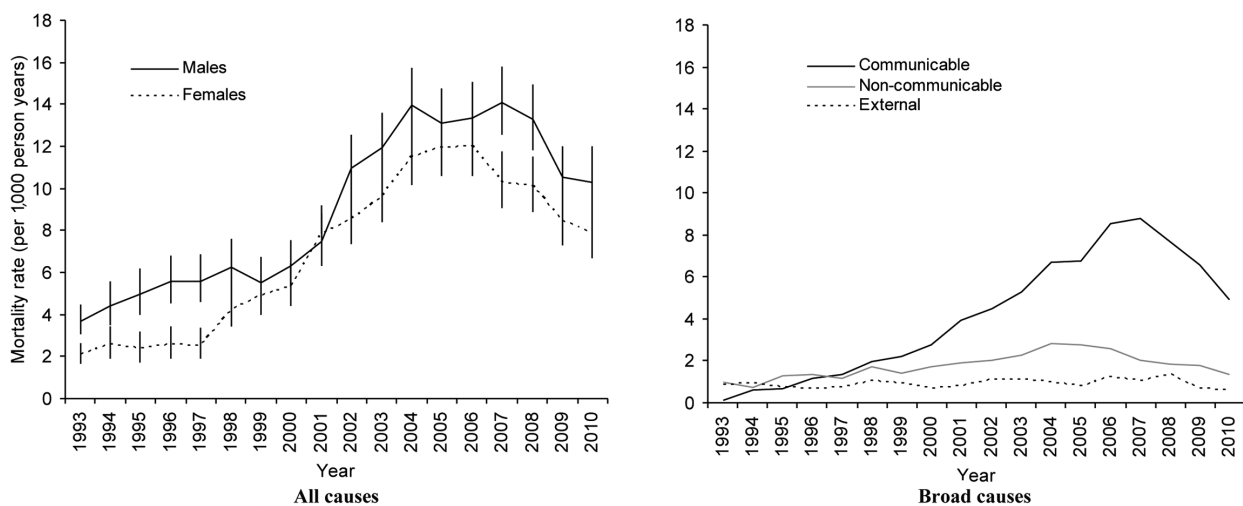

Fig. 3. Annual adult (15-59) mortality rates per 1,000 person-years by cause, Agincourt sub-district, South Africa, 1993-2010.
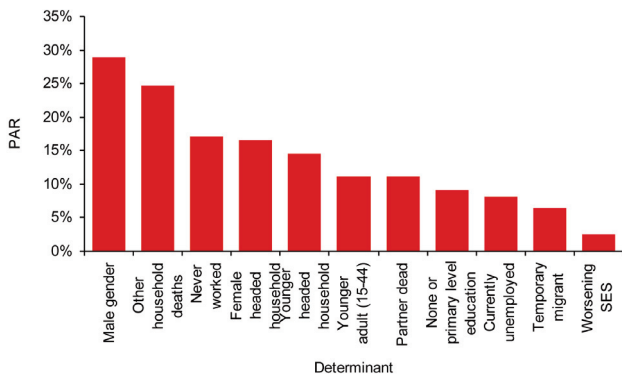
Fig. 4. Descending population attributable fractions (PAR) of high impact determinants found to be significantly associated with adult mortality following multivariable adjustment, Agincourt, 1993-2010.

household either headed by a female, a younger adult (<40 years of age) or where the household head had died (Table 1). Worsening SES status was also found to be a significant risk factor for increased adult mortality risk. Large distance to a health facility was found to be significantly associated with adult mortality risk at a bivariate level. This was, however, not statistically significant following multivariable adjustment. Increased distance from a main road was found to be a significant risk factor for adult mortality and, conversely, significantly protective with regard to injury-related (external) mortality (Table 1).

At the village or community level, villages with a lower proportion of deaths attributed to HIV/AIDS and tuberculosis (proxy for prevalence) were found to have a significantly lower risk of adult mortality based on bivariate association. This was no longer significant following multivariable adjustment. No significant relationship was identified between more mobile (migrant) communities or villages and adult mortality (Table 1). The most attributable determinant was male gender, followed by other household adult deaths, unemployment, female and younger household head followed by partner death (Table 1, Fig. 4). Other relevant exposures can be seen in Table 1 and Fig. 2.

Spatial risk maps of adult mortality

Five distinct foci of higher adult mortality can be seen in Fig. 5. Three are in the central to upper central region of the site and two in the south-east. These mainly correlate to areas with higher risk of communicable disease mortality, largely HIV/AIDS and tuberculosis. Higher, non-communicable disease mortality risk was observed in five distinct foci in the upper-central, south-east and western parts of the site (Fig. 5). The strong clustering of injury-related (external) mortality was evident in the central region of the site and in an area in the western part. Based on the circular buffer zones around health facilities (relating threshold straight-line distance to a health facility seen in risk factor analysis), we see that households in five villages in particular appear to have a higher mortality
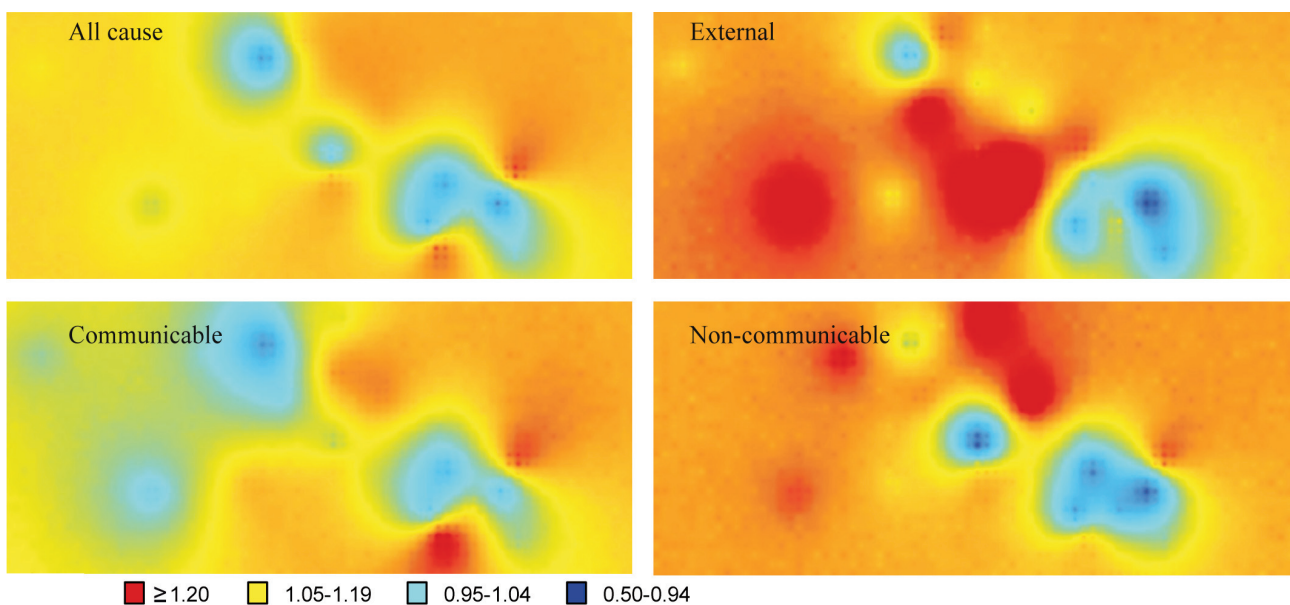

Fig. 5. Spatial relative risk (RR) of broad cause-specific adult mortality based on prediction estimates from Bayesian spatial kriging models, Agincourt sub-district, 1993-2010.

Table 1. Bivariate and multivariable analysis of risk factors for adult mortality (15-59 years), Agincourt sub-district, 1993-2010.

Risk factors	Bivariate n	HR (95% CI)	P-value	Multivariable HR (95% BCI)	P-value	PAR[a]
Temporal						
1993-1998	53,752	1.00		1.00		
1999-2004	62,002	2.19 (2.02, 2.37)	<0.001	4.83 (4.22, 5.53)	<0.001	-
2005-2010	64,835	2.84 (2.63, 3.07)	<0.001	6.35 (5.49, 7.35)	<0.001	-
Individual factors						
Age (45-60 *versus* 15-44 age group)	17,102/97,568	0.61 (0.56, 0.66)	<0.001	0.53 (0.48, 0.58)	<0.001	11.2%
Male gender	44,637	1.36 (1.29, 1.43)	<0.001	1.86 (1.74, 1.99)	<0.001	28.9%
Mozambican nationality	32,910	1.02 (0.96, 1.08)	0.592	-	-	-
Partner status						
Never married	46,848	1.05 (0.98, 1.12)	0.163	1.00		
Partner alive	51,206	0.74 (0.69, 0.79)	<0.001	0.75 (0.70, 0.81)	<0.001	13.3%
Partner dead	5,424	2.12 (1.96, 2.30)	<0.001	2.76 (2.52, 3.02)	<0.001	11.2%
Education status						
Secondary or higher level education	57,314	1.00		1.00		
None or primary level education	31,702	1.24 (1.17, 1.32)	<0.001	1.28 (1.2, 1.38)	<0.001	9.1%
Last employment status						
Employed	24,524	1.00		1.00		
Not employed	9,172	1.60 (1.48, 1.73)	<0.001	1.70 (1.57, 1.84)	<0.001	8.2%
Never worked	36,640	1.40 (1.30, 1.51)	<0.001	1.61 (1.48, 1.75)	<0.001	17.0%
Unknown	33,142	3.94 (3.68, 4.22)	<0.001	7.99 (7.33, 8.71)	<0.001	-
Temporary migrant[b]	97,477	1.10 (1.04, 1.16)	0.001	1.17 (1.10, 1.25)	<0.001	6.4%
Household level factors						
Household size	103,329	1.00 (0.99, 1.01)	0.821	-	-	-
Average education status of adult occupants						
Secondary or higher level education	57,583	1.00		Not included as correlated with individual education status		
None or primary level education	45,895	1.20 (1.13, 1.26)	<0.001			
Any other adult household deaths						
None	100,911	1.00		1.00		
1+	985	59.9 (53.4, 67.2)	<0.001	34.61 (30.6, 39.2)	<0.001	24.7%
Female household head	103,190	1.61 (1.53, 1.70)	<0.001	1.53 (1.44, 1.63)	<0.001	16.6%
Older household head, aged ≥40 years	103,190	1.47 (1.39, 1.57)	<0.001	1.65 (1.55, 1.77)	<0.001	14.5%
Mozambican household head	102,606	1.00 (0.94, 1.06)	0.942	-	-	-
Household head death	103,478	1.46 (1.33, 1.61)	<0.001	1.21 (1.09, 1.34)	<0.001	1.4%
Maximum household SES tertiale						
Least poor	10,940	1.00		1.00		
Poor	11,197	1.27 (1.17, 1.38)	<0.001	1.11 (1.02, 1.21)	0.013	2.0%
Most poor	10,741	1.57 (1.45, 1.69)	<0.001	1.17 (1.07, 1.27)	<0.001	3.0%
Unknown	70,600	0.6 (0.56, 0.65)	<0.001	0.60 (0.53, 0.67)	<0.001	-
Euclidian distance to nearest health care facility						
<5km	97,116	1.00		1.00		
≥5km	3,726	1.14 (1.00, 1.30)	0.056	1.03 (0.89, 1.18)	0.690	0.1%
Increasing distance (km) from road (all-cause)	103,478	1.03 (1.00, 1.07)	0.064	-	-	-
Increasing distance (km) from road (HIV/TB)	103,478	1.07 (1.01, 1.12)	0.017	-	-	-
Increasing distance (km) from road (external)	103,478	0.86 (0.77, 0.97)	0.010	-	-	-
Community (village) level factors						
Average adult migrant months per village and year	97,477	1.02 (0.97, 1.07)	0.530	-	-	-
Proportion of adult deaths due to HIV/TB (<40%)	103,478	0.92 (0.85, 0.99)	0.050	0.97 (0.89, 1.06)	0.529	0.4%

[a]Population attributable fraction; [b]four or more months each year outside the site

risk as a function of increased distance to the nearest local primary health care clinic (Fig. 6). These specific areas are numbered in this figure with many households falling outside the risk catchment zone in location 2, particularly in the upper-central region of the site.

Discussion

Trends and leading causes of death

A substantial and significant increase in adult mortality was observed between 1999 and 2006, which is in line with other estimates for South Africa (Dorrington et al., 2001; Hosegood et al., 2004). HIV/AIDS and tuberculosis was the leading cause-of-death among adults (~45%) and largely drove the observed temporal pattern. This is comparable to other estimates for SSA in 2001 where HIV/AIDS was estimated to account for 40-45% of adult mortality (Mathers et al., 2006). The levelling out of adult mortality could possibly be linked to the antiretroviral therapy (ART) rollout which began in South Africa round 2004. Non-communicable mortality is prevalent despite the larger pronounced impact of communicable disease (HIV/AIDS and tuberculosis) mortality (Tollman et al., 2008). Non-communicable disease mortality accounted for approximately 22% of all adult deaths in our study population over this period, which is in line with estimates of 20% for SSA

(Mathers et al., 2006). Thus, while communicable disease mortality remains high, indicating a relatively early stage of the epidemiological transition, increases in non-communicable disease mortality indicates the need for preparedness to deal with this potential double burden.

Spatial hotpots

The spatial hotspots of increased adult mortality risk, largely driven by communicable diseases, were observed in the upper-central and south-eastern regions of the Agincourt sub-district. This distribution is due to a complex web of interacting factors that include increased communicable disease mortality (HIV/AIDS and tuberculosis) and non-communicable mortality, in particular in high-risk areas. Lifestyle-related mortality among more affluent (South African) households may be driving the observed non-communicable mortality risk in the upper-central and western parts of the sub-district. However, whatever the cause, the risk maps (Fig. 5.) can be used for the evaluation, design and implementation of relevant interventions, e.g. ART rollout. Further research into the underlying reasons for higher risk among older adult South Africans relative to Mozambicans is needed to better inform relevant policy and interventions.

Male gender was found to be a prominent risk factor in this study and this has been demonstrated on numerous occasions (Mathers et al., 2006; WHO,
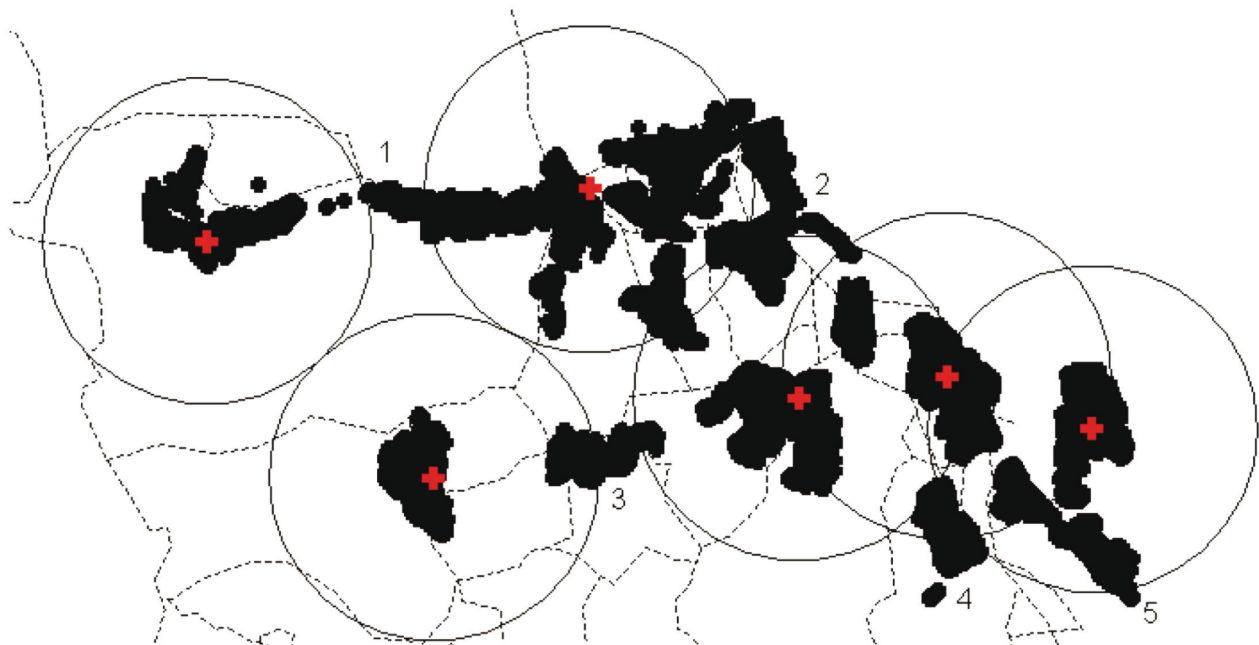

Fig. 6. Household (•), road (----) and health facility (✚) locations with concentric circles showing the 5 km capture zone of these health facilities, Agincourt sub-district. Note: potentially higher risk household areas discussed above are numbered 1-5.

2006) due to, for example, inherent biological differences and a tendency for males to engage in higher risk activities such as alcohol consumption (Ezzati et al., 2002). Males have also been shown to be more likely to be labour migrants than females (Lurie, 2000; Collinson et al., 2006a). We also observed a significantly higher mortality risk in younger to middle-aged adults (15-44 years) compared to older adults (45-59 years), likely due to HIV. This determinant was also found to have a relatively high attributable fraction, thus suggesting a high impact in this population. It is likely that an underlying interplay of higher-risk behaviour, sexual activity (exposure to HIV) and mobility (migration) is driving this observed age-risk differential (Lurie, 2000; Ezzati et al., 2002; Collinson et al., 2006a). Education has been previously associated with improved adult survival in other African settings (Berhane et al., 2002). We have similarly demonstrated that no, or only primary level, education was a significant and high-impact predictor of adult mortality in Agincourt. Worsening SES or poverty seems to be an important determinant of adult mortality in Agincourt as has been demonstrated in other African settings (Fantahun et al., 2008). Poor SES and high unemployment have led to external migration for work, while low education levels may explain false perceptions of HIV exposure risk; over 90% of men perceived little or no personal risk (Collinson et al., 2006b). A previous study in Agincourt has shown that long-distance migrants, who returned once or twice a year, report having many partners, leading to increased risk for their partners in Agincourt (Collinson et al., 2006b). This has all led to an explosive spread of HIV in this and other rural settings. We observed a strong and high impact association between partner status and adult mortality risk. Strategies that enable more frequent contact between migrant men and their rural families are urgently needed, as are HIV prevention and the need to raise awareness of this risk amongst all men in this area (Collinson et al., 2006b).

Mozambican nationality was not a risk factor for adult mortality. Previous studies in this area have shown an increased risk of mortality among Mozambican children in the age group of the 1-5 years old (Hargreaves et al., 2004; Sartorius et al., 2011a), suggesting a normalisation of risk in adulthood. This is likely due to the adjustment for lower education and SES in the model (which was more evident among the Mozambicans) and as a result of these settlements being further away from health facilities. The risk for adult mortality was higher in the poorest villages, sug-

gesting that the benefits of improved health care are not evenly distributed throughout the study area.

Female-headed households, those headed by males or females younger than 40 years, or other adult household arrangements appeared to be the highest impact household-level determinants. Other adult household deaths as a risk factor for adult mortality is in line with previous findings (Sartorius et al., 2010, 2011a). This in turn impacts SES through loss of working-age adults. Cost of funerals and the loss of income (impacting household SES) are also some of the reasons explaining this phenomenon (Collins and Leibbrandt, 2007). Direct transmission of HIV between unreported partnerships may also explain a more direct link to other adult household deaths. A cycle of greater male deaths (see above), leading to more female headed households is likely. The pronounced impact of HIV/AIDS and tuberculosis in this setting is also likely to have reduced the age of household heads as a result of previous mortality of those heading households. Given that a male household head conferred a survival advantage to adults (also shown in previous studies for infants and children (Sartorius et al., 2010, 2011a) and that male migrants are at increased risk, could potentially compound adult mortality over time as household head dynamics change. This cycle coupled with the direct and indirect impacts of adult mortality on children and the elderly is leading to vulnerable households that should be targeted for social support (Feachem et al., 1992). Female-headed households also need to be targeted as they appear to be more vulnerable and at higher risk for child, adult and overall mortality.

Adult populations in mortality hotspots likely experienced differential access to health care as a large distance from the nearest health facility emerged as a significant risk factor in the bivariate analysis. This association has been shown in other studies on adult mortality (Ali et al., 2007) and specifically with regards to ART access in South Africa (Ingle et al., 2010). This study found that with in service access need to be addressed. Critical distance threshold catchment maps for facilities can further highlight areas at increased risk of adult mortality for policy makers.

In this study we also observed an increased risk of adult mortality in households closer to main roads. A recent study in rural Kwazulu-Natal found significant HIV prevalence clustering near a national road and a strong exponential decrease in HIV prevalence with increasing distance from this road (Tanser et al., 2009). Individuals living in communities with better access to transport and transport routes may be at

higher risk of HIV infection (Arroyo et al., 2006; Ferguson and Morris, 2007; Tanser et al., 2009). Our study thus confirms that risks for HIV (mortality) are associated with specific, socio-geographical locations, which would allow targeting of tailored education and behavioural interventions in these areas.

Villages with a high fraction of adult deaths attributed to HIV/AIDS and tuberculosis (a crude proxy for the underlying prevalence) were also found to be a significant risk factor at the bivariate level. However, following multivariable adjustment this was no longer significant, suggesting that more proximal household level determinants may be more important.

Despite major improvements in vital registration in South Africa, cause of death data still suffer from potential underreporting, "ill-defined" over-classification and misclassification, especially with regards to HIV/AIDS and injury-related mortality (Bradshaw et al., 2010; Groenewald et al., 2010). HDSS implementing physician-coded verbal autopsies are thus often the only way to assess cause-specific mortality fractions and trends (Kaufman et al., 1997; Kuh and Shlomo, 2004). However, physician-coded VAs have known limitations, such as relying heavily on household recall of medical records and related information, which affects its applicability in low-resource settings (Murray et al., 2007). Misclassification of data could thus have occurred with respect to our study, especially with regard to underestimating non-specific HIV/AIDS-related and non-communicable disease. However, a previous validation study of VAs in Agincourt has shown that it performs well in this high-HIV prevalence setting (Kahn et al., 2000). Other studies have also confirmed that VA data can be used to reasonably estimate the distribution of AIDS- and non-AIDS-related deaths, even in a rural population with relatively low levels of education (Doctor and Weinreb, 2003).

Conclusions

Despite HDSS not necessarily being representative of national patterns, given the validity of our findings in relation to other studies, identified trends in this setting may reflect the level and changing nature of adult mortality in rural South Africa.

This study demonstrates the use of advanced methods to:

(i) pinpoint high risk areas for adult mortality and that variation is present even in a small geographical area; and

(ii) correctly estimate and identify high impact risk factors.

PAR is extremely important for policy makers as it provides additional information above strength of association in that one can estimate the reduction of an outcome if a given risk factor is removed. This gives the policy maker the sense of were resources might be most effectively allocated or targetted in resource-poor settings. Health programmes need to take this into account when assessing and further planning the comprehensive plan to tackle adult mortality in this and other rural populations.

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