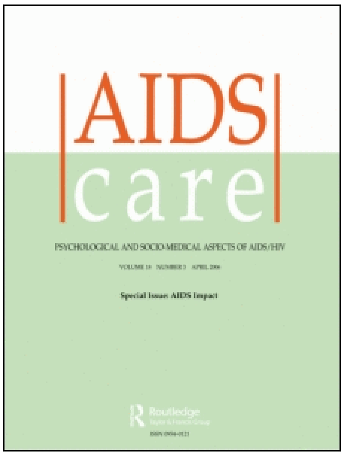

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The epidemiology of HIV infection in Zambia

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Population surveys of health and fertility are an important source of information about demographic trends and their likely impact on the HIV/AIDS epidemic. In contrast to groups sampled at health facilities they can provide nationally and regionally representative estimates of a range of variables. Data on HIV-sero-status were collected in the 2001 Zambia Demographic and Health Survey (ZDHS) and made available in a separate data file in which HIV status was linked to a very limited set of demographic variables. We utilized this data set to examine associations between HIV prevalence, gender, age and geographical location. We applied the generalized geo-additive semi-parametric model as an alternative to the common linear model, in the context of analyzing the prevalence of HIV infection. This model enabled us to account for spatial auto-correlation, non-linear, location effects on the prevalence of HIV infection at the disaggregated provincial level (nine provinces) and assess temporal and geographical variation in the prevalence of HIV infection, while simultaneously controlling for important risk factors. Of the overall sample of 3950, 54% was female. The overall HIV-positivity rate was 565 (14.3%). The mean age at HIV diagnosis for male was 30.3 (SD = 11.2) and 27.7 (SD = 9.3) for female respectively. Lusaka and Copperbelt have the first and second highest prevalence of AIDS/HIV (marginal odds ratios of 3.24 and 2.88, respectively) but when the younger age of the urban population and the spatial auto-correlation was taken into account, Lusaka and Copperbelt were no longer among the areas with the highest prevalence. Non-linear effects of age at HIV diagnosis are also discussed and the importance of spatial residual effects and control of confounders on the prevalence of HIV infection. The study was conducted to assess the spatial pattern and the effect of confounding risk factors on AIDS/HIV prevalence and to develop a means of adjusting estimates of AIDS/HIV prevalence on the important risk factors. Controlling for important risk factors, such as geographical location (spatial auto-correlation), age structure of the population and gender, gave estimates of prevalence that are statistically robust. Researchers should be encouraged to use all available information in the data to account for important risk factors when reporting AIDS/HIV prevalence. Where this is not possible, correction factors should be applied, particularly where estimates of AIDS/HIV prevalence are pooled in systematic reviews. Our maps can be used for policy planning and management of AIDS/HIV in Zambia.

Keywords: HIV/AIDS; Demographic Health Survey; maps; Zambia; non-linear effects

Introduction

Population surveys of health and fertility are an important source of information about demographic trends and their likely impact on the HIV/AIDS epidemic. In contrast to groups sampled at health facilities, they can provide nationally and regionally representative estimates of a range of variables. The Demographic and Health Surveys (www.measur-edhs.com) are a well-established source of reliable population level data with a substantial focus on knowledge of HIV/AIDS and sexual behaviour. However, linking individual survey records with the results of HIV testing has been considered undesirable owing to the absolute need to maintain confidentiality on this most sensitive of health topics. Data on HIV-serostatus were collected in the 2001–2002 Zambia Demographic and Health Survey (ZDHS) and made available in a separate data file in which HIV status was linked to a very limited set of demographic variables.

Background: characteristics of the study area

Zambia is located in the heart of sub-equatorial Africa with a population of about twelve million and a population growth rate of about 1.66% per year (Global Health Facts, 2007). With a gross national product of US$380 per person per year, around two-thirds of the population lives on less than a dollar a day and Zambia is among the 20 least economically developed countries in the world (Rural Poverty Portal, 2006).

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However, Zambia is very rich in mineral deposits. This was the backbone of its economy until the 1970s, when its economy was severely affected by a fall in global copper prices.

More than a quarter (40%) of its population live in two urban areas: Lusaka (the capital city, where 10% of the population lives) and in the industrial towns of the Copperbelt. The rest of population of Zambia is very sparse – particularly in the west and the northeast – and farming is the main activity for the majority of people. HIV prevalence is considerably higher in these urban areas (54% of all adults living with HIV or AIDS) and the highest HIV prevalence has been recorded among pregnant women in Lusaka, Kabwe, Ndola, Mongu and the cross-border tourist and trading centres, Chipata and Livingstone (UNAIDS/WHO, 2004).

Zambia has the fourth highest adult prevalence in the world and the social and economic impact of the pandemic is overwhelming. According to UNAIDS/WHO estimates (2006), in 2005, 17% of people aged 15–49 years old were living with HIV or AIDS and 57% of them were women. The rate of infection among young women aged 15–19 years was six times greater than for males of the same age (WHO/UNAIDS, 2004). In 2005, an estimated 100,000 people died of AIDS and 710,000 children were left orphans by AIDS. As a result of this high mortality, life expectancy has fallen below 37 years (UNAIDS/WHO, 2006). HIV/AIDS has also set back the rates of economic growth in Zambia, although, more recently the country's economic prospects have been transformed by debt relief and rising copper prices but it remains to be seen whether these gains will be converted into human development.

Mobility of population in Zambia is commonplace and the risk of infection is higher among mobile people and those whom they contact. People often work as seasonal labourers, migrant fishermen/women or truck drivers and they spend long periods away from their regular partners, thus spreading the virus from one area to another.

Despite economic difficulties, Zambia has invested in health. Responses to HIV and AIDS in Zambia have aimed to prevent HIV transmission; to care for people who are infected and affected; and to reduce the personal, social and economic impact of AIDS. Since 2002, the government of Zambia has been engaged in a challeging antiretroviral treatment programme and progress on the reduction of HIV prevalence is encouraging, although HIV prevalence remains at a very high level (Central Statistical Office, Republic of Zambia, 2003). Scaling-up the provision of treatment and reducing the number of new infections to so many millions of people is a challenge for the government of Zambia to alleviate the burden of this pandemic.

Data source

The objectives, organisation, sample design and questionnaires used in the 2001–2002 DHS survey have been described in detail elsewhere (Central Statistical Office, 2004). It was a nationally representative household survey of adult men and women (aged 15–49 years). All samples were stratified, the 18 strata formed by the urban and rural areas of each province. The questionnaire included information on socio-economic indicators, fertility patterns, health and care practices, health knowledge, anthropometric status and information about sexual behaviour and knowledge of HIV/AIDS prevention. The survey was carried out by the Central Statistical Office with technical assistance from ORC Macro International, funded by US Agency for International Development (USAID).

Methods

The methods of the ZDHS survey are described, together with an overview report (Central Statistical Office & ORC Macro, 2003). Briefly, this was a random probability sample of women aged 15–49 years and men aged 15–59 years. Approximately 2500 men and a similar number of women were asked to give blood for syphilis and HIV testing. Samples for HIV testing were dried blood spots on a filter paper card taken from a venous blood specimen. A three-stage testing procedure was used with 10% of the negative samples re-tested and discordant results tested by Western Blot. Tests for HIV were performed on 2073 women and 1877 men, representing 79% and 73% of those identified as eligible for testing in the survey. The sample was weighted to account for the unbalance population size of 68.2% from rural areas and 31.8% from urban areas.

We utilized this data set to examine associations between HIV status, gender, age and area of residence so as to improve the precision of the estimates for better public health policy.

Figure 1 shows the geographic distribution of marginal odds ratios from the data and Figure 2 shows marginal probabilities of HIV as a function of age for both males and females. Preliminary results indicated an age by gender interaction ($p < 0.001$). Noting the non-linear association of age and odds of HIV infection we examined the non-linear association of the effect of age on the posterior odds ratio (OR) of HIV infection for men and women separately (Figure 3). Figure 4 shows the total residual spatial

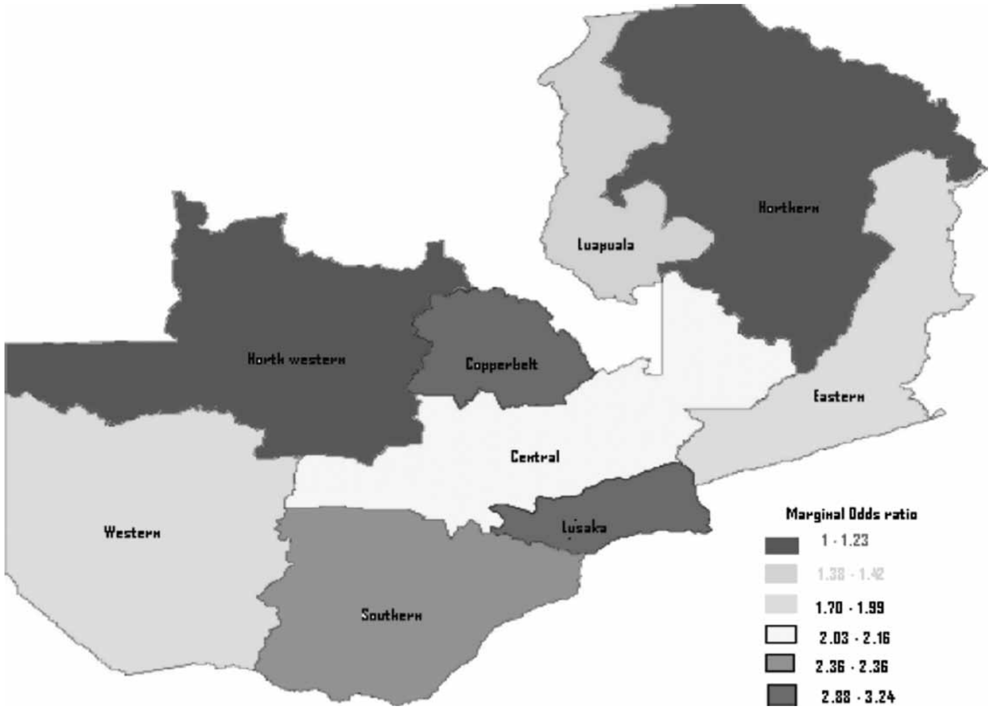

Figure 1. Map of marginal odds ratios of HIV prevalence in Zambia (DHS 2001).

effects after accounting for spatial auto-correlation in the data arising from the population mobility (migration) and other important risk factors in Zambia.

Model description

Instead of using region-specific dummy variables to capture the geographical dimension and account for spatial auto-correlation on HIV infection in Zambia, we applied a novel approach by exploring spatial patterns of the prevalence of HIV infection and possible non-linear effects within a simultaneous, coherent regression framework using a geo-additive semi-parametric mixed model. The model employed a fully Bayesian approach developed in Fahrmeir and Lang (2001) using Markov Chain Monte Carlo techniques for inference and model checking.

The model used for this investigation has been described elsewhere[1] (Fahrmeir and Lang, 2001; Kandala, 2006; Kandala et al., 2007). The response variable in this application is defined as $y_i = 1$ *if HIV sero-positive and* $y_i = 0$ *otherwise*. The standard measure of effects is the posterior OR.

The traditional methods of the study of HIV/AIDS prevalence astonishingly neglect the geographical location, spatial auto-correlation and non-linear effects of covariates, which is likely to result

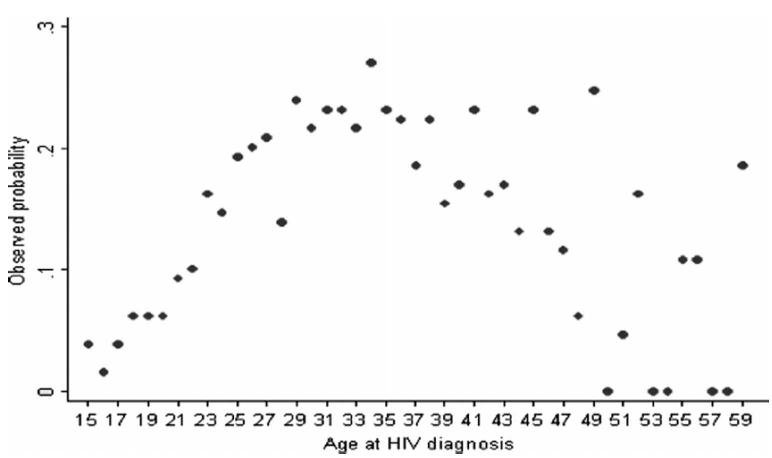

Figure 2. Marginal probability of HIV-positive status as a function of age (ZDHS, 2001–2002).

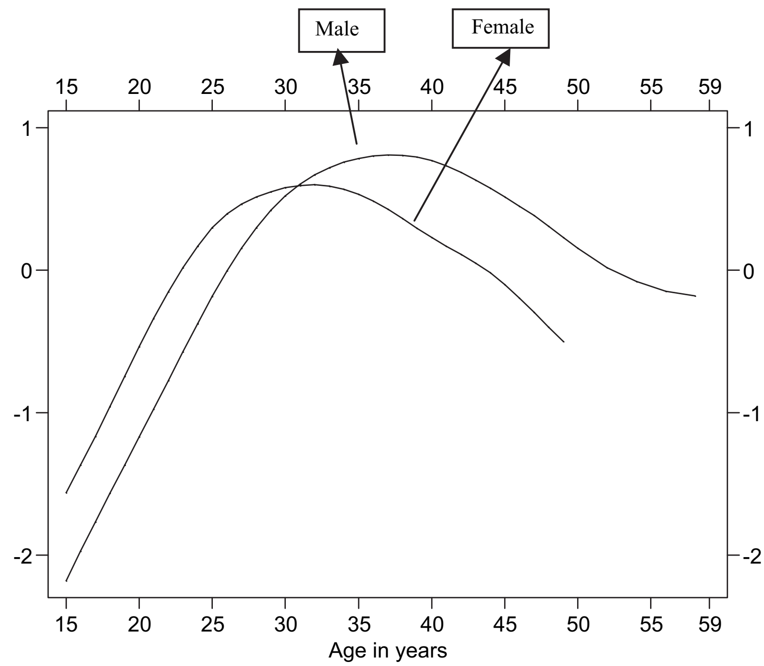

Figure 3. Gender specific estimated non-linear effects of age at HIV/AIDS diagnosis.

in misleading conclusions in prevalence of diseases. Additionally, the more important impact of this neglect would be an underestimation of standard errors of the fixed effects that inflates the apparent significance of the estimates (Kandala, 2006; Kandala, in press). Our analysis included this correlation structure and accounts for the dependence of neighbouring community (mobile population, i.e. truck drivers, seasonal labourers or migrant fishermen/women, spending long periods away from their regular partners) in the model. The ZDHS data are based on a random sample within provinces, that is, the structured component introduced here allows us to 'borrow strength' from neighbours in order to cope with the sample variation of the province effect and obtain estimates for areas that may have inadequate sample sizes or be un-sampled. This gives more reliable estimates of the fixed effect standard error.

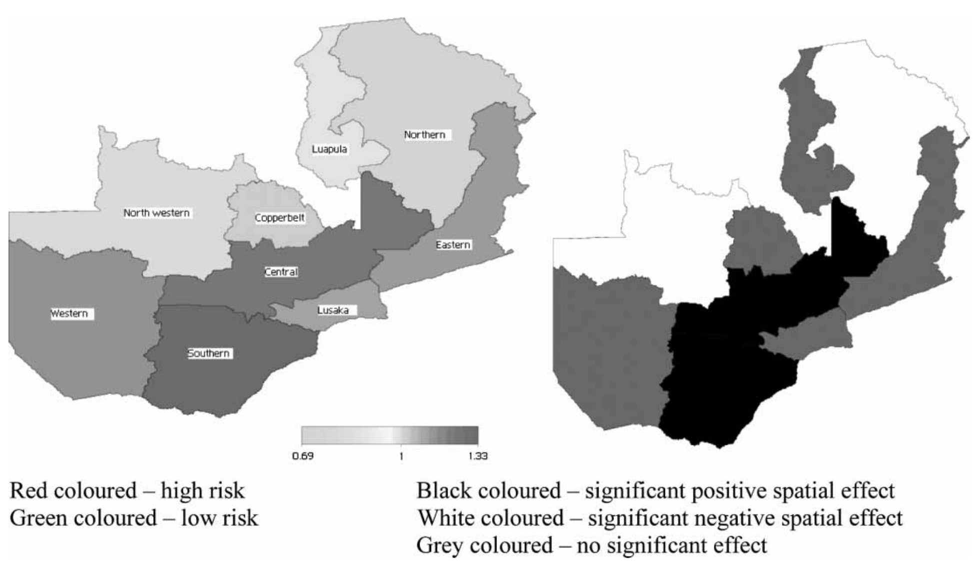

Figure 4. Total residual spatial provincial effects (left) and 80% posterior probability map (right) of the risk of HIV infection in Zambia.

Table 1. Prevalence of HIV/AIDS infection by baseline characteristics: ZDHS 2001–2002).

Variables	Negative: *n*(%)	Positive: *n*(%)	*p*-value
Number	3384(85.7)	565(14.3)	
Gender			
Male	1605(88.3)	212(11.7)	
Female	1779(83.4)	353(16.6)	<0.001
Place of residence			
Urban	966(76.9)	290(23.0)	
Rural	2,418(89.8)	275(10.2)	<0.001
Age at diagnosis			
Age-1 (<24 years)	1,503(92.5)	122(7.5)	
Age-2 (25–35 years)	1,014(78.8)	273(21.2)	
Age-3 (36–49 years)	740(82.3)	159(17.7)	
Age-4 (50–59 years)	127(92.0)	11(8.0)	<0.001
Region of residence			
Central	478(84.9)	85(15.1)	
Copperbelt	400(80.2)	99(19.8)	
Eastern	336(86.4)	53(13.6)	
Luapula	296(88.9)	37(11.1)	
Lusaka	335(77.9)	95(22.1)	
Northern	568(92.1)	49(7.9)	
North-Western	402(90.7)	41(9.3)	
Southern	329(82.7)	69(17.3)	
Western	240(86.6)	37(13.4)	<0.001

Failure to take into account the posterior uncertainty in the spatial location (province) would overestimate the precision of the prediction of the prevalence of HIV infection in regions with inadequate sample size.

In the descriptive analysis, Table 1 was generated to show the prevalence of HIV infection by age, gender and region. Chi-square tests and Mann-Whitney tests were used to investigate the association between factors and disease. Multivariate analysis shows the significance of the posterior OR estimates of fixed effects (Table 2), non-linear effects (Figure 3) and residual spatial effects (Figure 4).

Results

Of the overall sample of 3950, 54% was female. The overall HIV sero-prevalence was 565 (14.3%). The mean age at survey diagnosis of HIV-seropositivity for men was 30.3 (SD: 11.2) and 27.7 (SD: 9.3) for women respectively. It should be noted that, as part of the sample age selection strategy, men were sampled from age 15 up to older ages of 59 and women were sampled from age 15 to 49. As expected from the sampling strategy, the mean age of men at the time of sero-diagnosis of HIV was older (30.3; SD: 11.2) than that of women.

Table 1 compares the prevalence of HIV infection, demographic and geographical characteristics at baseline in the 565 cases with HIV and in the 3384 HIV-seronegative subjects at the time of the survey. The prevalence of HIV infection was higher among women compared with men (16.6% versus 11.7%; $p < 0.001$), higher in urban areas compared with rural areas (23.0% versus 10.2%; $p < 0.001$), higher in the age groups ranging from 25–35 years and 36–49 years but lower in the younger (< 25 years) and older (50–59 years) age groups (21.2%, 17.7% versus 7.5%, 8.0%; $p < 0.001$), very high in Lusaka (22.1%) and Copperbelt (19.8%) provinces, followed by Southern (17.3%) and Central (15.1%) provinces, but lower in the Northern (7.9%) and North-Western (9.3%) provinces compared with Eastern (13.6%), Luapula (11.1%) and Western (13.4%) provinces.

The spatial variation of the observed HIV prevalence in Zambia is drawn in Figure 1 by plotting the marginal OR of HIV at regional level. Northern region is set as reference. All the regions are classified into six marginal OR bands in which North-Western region shares the same band and colour with Northern region. The map also shows that the highest three bands of marginal OR are in the Central and Southern part of Zambia. Further, Lusaka and Copperbelt, as the most developed areas, have the highest marginal ORs (3.24 and 2.88 respectively).

Table 2. Posterior odds ratio of the fixed effect parameters for the risk of HIV infection (Model 2).

Variables	Odds ratio	Std. Error	95%CI	*p*-value
Gender				
Female	1.59	0.09	1.32, 1.89	<0.001
Male	1	reference		
Place of residence				
Urban	2.73	0.10	2.13, 3.28	<0.001
Rural	1	Reference		

We calculated observed probability of HIV infection in the survey and plotted it against age of all respondents. Figure 2 shows that there is a bell shaped, non-linear relationship between age and probability of HIV infection. A watershed is present between 30–34 years at which both men and women have the highest observed probability in the survey. Before 30, the probability of HIV infection rises quickly as age increases. This implies that age has an almost linear relationship with the probability of HIV infection. People who are over 34 years old are likely to have a declining risk of HIV infection, although the variation of the probability increases rapidly at the same time as age continues to increase. The figure also shows that there are no HIV-positive cases detected in the survey for men who are 50, 52, 53, 57 and 58 years old, but this is likely to represent an artefact of the small numbers sampled at the older ages.

Table 2 shows the results of the posterior OR of the fixed effects covariates included in Model 2. Gender and place of residence are the factors considered in the model. The non-linear effects of age and the total residual spatial effects of the region are shown in Figure 3 and Figure 4, respectively. Male respondents and rural area were set as reference groups in the respective factors. Women and men have significantly different risks of getting infected with HIV. Compared to men, women were much more likely to be HIV-seropositive (OR: 1.59; 95%CI = 1.32, 1.89). A higher risk of HIV infection was found among people from urban areas (OR: 2.73; 95%CI = 2.13, 3.28) compared to those in rural areas. These results are consistent with the univariate results in Table 1.

In the observed marginal data we saw Lusaka and Copperbelt showing a high OR (Figure 1). After controlling for the spatial auto-correlation, age-gender profile and its urban status, we found that the prevalence of HIV infection in Lusaka and Copperbelt are no longer as high as might be expected. Similarly, Southern region showed a much higher risk of HIV infection once we controlled for the spatial auto-correlation, age, and gender and residence status (Figure 4).

Figure 4 (left) indicates that people living in Southern province had the highest risk of HIV infection than those in Northern province. Red represents a higher risk of HIV infection while green denotes a lower risk. The risk of HIV infection in the two most developed regions, Lusaka and Copperbelt, appear to be much less than observed. The risk of HIV infection in Luapuala and North-Western provinces are the lowest in the country. The panel on the right of Figure 4 shows the posterior probability maps of the risk of HIV infection at an 80% credible interval. The provinces in black indicated a significant positive spatial effect, while the provinces in white implied a significant negative spatial effect. The rest of the provinces (in grey) had no significant effect on HIV infection. Their corresponding probability maps (Figure 4 – right) suggested that there is no significant difference of the risk HIV infection in these provinces compared to Northern province.

The non-linear effects of age at HIV diagnosis (shown in Figure 3) revealed that both genders have rapidly increasing risk of HIV infection before age 30 and almost linearly declining risk afterwards. Women appeared to have higher risk of being infected with HIV than men in all age groups. The 20–24 years age groups showed the largest gap of the risk of HIV infection between male and female.

In sum, the flexible modelling of the region-specific effects paints a much more nuanced picture than was presented by the observed marginal OR and thus gives a better impression of the spatial variation of HIV infection. Moreover, the geo-additive, semi-parametric Bayesian approach used is able to identify subtle influences of the age at HIV diagnosis on the risk of HIV infection.

Discussion

HIV/AIDS is one of the greatest health, social and economic problems in Zambia and nearly one million people are HIV-positive or have AIDS. An estimated 100,000 died of the epidemic in 2004 (UNAIDS/WHO, 2006). UNAIDS/WHO estimated at the end of 2005 that 17% of people aged 15–49 years were living with HIV or AIDS. According to the same source, 57% of those with HIV or AIDS were women (WHO/UNAIDS, 2006).

In this study we identified the spatial pattern of the risk of HIV infection in Zambia. We found that the risk of HIV infection remains high in the Central and Southern parts of the country in both estimated and observed maps of HIV prevalence.

Many socio-economic factors may account for the above finding. The development of this landlocked country relies much on the train service, which is offered mainly in the central area covering Lusaka, Copperbelt and Central regions. Among these regions, Lusaka and Copperbelt are the most developed and urbanised. However, the economy of Zambia as a whole has been deteriorating since the drop of copper prices in the 1970s. Furthermore, although rural poverty apparently negatively affects local public health and makes people face economic hardship (Rural Poverty Portal, 2006) an urbanised area with high population density faces a more severe burden of HIV infection. In the 2001–2002 ZDHS, the prevalence of HIV infection was 23.0% in urban areas compared to 10.2% in rural area (Table 1). As shown in Table 2, people in urban areas have almost three-fold increase (OR: 2.73; 95%CI: 2.13, 3.28) risk of HIV infection compared to those in rural areas.

In addition, the migration of people from countries sharing a border with Zambia may affect the current HIV/AIDS prevalence in the country. Prior to the 1990s, there was a high prevalence of HIV in the Democratic Republic of Congo and Uganda, which lie to the north of Zambia. Later, the high prevalence moved to the eastern and southern part of Africa. UNAIDS/WHO (2002) reports that Botswana and Zimbabwe are among the countries in which HIV prevalence exceeds 30%. The high ORs of the risk of HIV infection in regions like Southern and Lusaka can be explained partially by this perspective.

The migration of specific groups of people, such as seasonal labourers and commercial sex workers, to urban areas is considered to play an important role in the spread of HIV/AIDS (Mayer, 2005). Seasonal labourers who work away from home are likely to have short-term relationships with women or sometimes have sex with sex workers, which contributes to the pattern of spread of HIV/AIDS across the country. Furthermore, Agyei-Mensah's study (2001) discovered from the case of Ghana that commercial sex workers were likely to migrate from less developed areas to those with much improved economic conditions. Another study (AVERT, 2006) showed that two thirds of sex workers in Zambia were HIV-positive and they may risk loss of income if they request condom use with clients to avoid the spread of HIV inside the country.

Our most important finding is illustrated in the contrast between Figures 1 and 4. A pronounced change of the ORs in Lusaka and Copperbelt is observed following application of the model described here. The spatial distributions of the risk of HIV infection we show are, of course, influenced by the variable selection in the model. Place of residence and spatial distribution are both chosen as the factors in geo-additive regression model. However, it is possible that the place of residence shared the effect of geographic distribution of the regions, especially in Lusaka and Copperbelt as the country is highly urbanised and almost one-half of the country's twelve million people are concentrated in a few urban zones.

Figure 3 shows rapid increase in sero-prevalence in both genders before the age of 30. People in Zambia generally report sexual debut at an early age; some studies (Central Statistical Office, 2004; Garcia-Calleja, Gouws, & Ghys, 2006; Zaba, Pisani, Slaymaker, & Ties Boerma, 2004) revealed that the average age of debut is around 17 years in females and 17.5 years in males. For men, the rapid age-related increase of the risk of HIV infection is probably fuelled by their greater tendency to move from rural to urban areas to look for employment. As young people, they are more sexually active and might have more opportunities to be exposed to unprotected sex than others. For women, many of them have their first sex with men who are, on average, five years older than them. This may explain why, at the same age, young women have a higher risk of HIV infection than young men.

Another factor contributing to the age-related discrepancy between male and female risk of HIV infection is gender inequity. Women have much less access to education and generally are economically dependent on men. Even marriage does not bring many sexual health benefits to women because of a higher frequency of sex, low rates of condom use and their husbands' risky sexual behaviour (Wellings, K et al. 2006). While an effective way to prevent STIs and HIV infection, condom use is mainly dominated by men and it is difficult for women to insist on the use of a condom. Thus the current HIV programme focuses on other interventions such as the female condom and vaginal microbicides for HIV prevention. The latter may have great potential as a 'woman initiated' method, should current clinical trials provide proof of efficacy. Other negative gender pressures on Zambian women include poverty in widowhood, because they do not have the right to inherit the property of the family (UNAIDS/WHO, 2002). Another problem is that other household members may also have sex with these women, following a tradition termed 'sexual cleansing' to dispel evil. This tradition substantially increases women's risk of HIV infection.

Conclusion

We identified the spatial pattern of the risk of HIV/AIDS infection in Zambia at the regional level. A higher-than-expected prevalence is revealed in the Central and Southern parts of the country after controlling for spatial auto-correlation and other important risk factors. Various socio-economic factors have impacts on the current situation of HIV/AIDS epidemic in Zambia. Although sharing the same pattern of age-effect on the risk of HIV/AIDS infection, men and women have a different probability of infection mainly due to gender inequality and lifestyle. Poverty still largely hampers the development of healthcare interventions. However, more efforts are being made by the government and many international organisations and recent achievements have been reported in many studies and by the mass media. Geographic understanding of the pattern of this epidemic using models as presented here can be helpful for the government to target healthcare-intervention plans more effectively.

Note

1. Briefly, we replace the strictly linear predictor $\eta_i = x'\beta + w_i'\gamma$, (1) with a logic link function with dynamic and spatial effects $\Pr(y_i = 1|\eta_\iota) = e^{\eta\iota} / (1 + e^{\eta\iota})$ with a geo-additive semi-parametric predictor $\mu_i = h(\eta_\iota)$: $\eta_\iota = f_1(x_{i1}) + \ldots + f_p(x_{ip}) + f_{spat}(s_i) + w'_{i\gamma}$ (2) where h is a known response function with a logit link function and, $f_1, \ldots, f_p$ are non-linear smooth effects of the metrical covariates (age at HIV diagnosis) and $f_{spat}(s_i)$ is the effect of the spatial covariate $s_i \in \{1, \ldots, S\}$ labelling the region in Zambia. Covariates in w'_i are usual categorical variables such as gender and urban-rural residence. Regression models with predictors as in (2) are sometimes referred to as geo-additive models. P-spline priors are assigned to the functions $f_1, \ldots, f_p$ and for $f_{spat}(s_i)$ we used Markov random field prior (Fahrmeir and Lang, 2001; Kandala, 2006 & 2007). The analysis was carried out using BayesX version 0.9, software for Bayesian inference based on Markov Chain Monte Carlo simulation techniques.

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