Trends and measurement of HIV prevalence in northern Malawi

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Background: Most data on HIV prevalence in Malawi come from antenatal clinic (ANC) surveillance and are, therefore, subject to bias.

Objectives: HIV prevalence and risk factors were measured using population-based data to assess the accuracy of ANC surveillance and changes in prevalence and risk factors for HIV over time.

Methods: HIV prevalence was measured in 1988–1993 and 1998–2001 in community controls from case–control studies of mycobacterial disease in Karonga District, Malawi. ANC surveillance studies in the district began in 1999.

Results: Age and area-standardized HIV prevalence in women aged 15–49 years in the community was 3.9% in 1988–1990, 12.5% in 1991–1993 and 13.9% in 1998–2001. For men, HIV prevalence was 3.7%, 9.2% and 11.4% in the same periods. In 1988–1993, HIV positivity was associated with occupations other than farming, with increased schooling and being born outside Karonga District. In 1998–2001, non-farmers were still at higher risk but the other associations were not seen. The age- and area-adjusted HIV prevalence in the ANC in 1999–2001 was 9.2%. The under-estimate can be explained largely by marriage and mobility. Reduced fertility in HIV-positive individuals was demonstrated in both ANC and community populations. A previously recommended parity-based adjustment gave an estimated female HIV prevalence of 15.0%.

Conclusions: HIV prevalence has increased and continues to be higher in non-farmers. The increase is particularly marked in those with no education. ANC surveillance underestimated HIV prevalence in the female population in all but the youngest age group. Although there were differences in sociodemographic factors, a parity-based adjustment gave a reasonable estimate of female HIV prevalence.

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AIDS 2003, **17**:1817–1825

Keywords: HIV, prevalence, surveillance, fertility, Africa, risk factors

Introduction

HIV prevalence in Malawi rose rapidly in the 1980s and apparently stabilized in the late 1990s, in urban areas at 13–30% and in rural areas at 6–21% [1]. These data come from antenatal clinic (ANC) surveillance. However, HIV is associated with lower fertility, both directly and indirectly, so ANC sources tend to under-estimate HIV prevalence [2]. Furthermore, pregnant women who attend an ANC, particularly the larger

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Received: 7 November 2002; revised: 12 February 2003; accepted: 4 March 2003.

DOI: 10.1097/01.aids.0000076278.54156.7e

ISSN 0269-9370 © 2003 Lippincott Williams & Wilkins

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clinics where surveillance is usually conducted, may differ from others, for example in area of residence or education level; factors which may be associated with HIV status [3,4].

HIV prevalence has been measured in Karonga District, Malawi for over 20 years as part of large-scale epidemiological studies of mycobacterial disease. Population-based data from two rural areas showed that HIV was present by 1982, and that prevalence in adults in 1982–1984 was 0.1% and had risen to 2.0% by 1987–1989 [5]. At that time, HIV infection was associated with recent immigration into the district and travel outside the district and was more common in those with occupations other than subsistence farming, with more schooling and with the best housing.

The current study analyses data from the late 1980s to 2001 for the whole district to assess changes in HIV prevalence and in risk factors for HIV over time. Population-based data are compared with those from ANC surveillance to assess the degree and causes of bias in ANC data, exploring fertility and sociodemographic profiles. The validity of estimating male HIV prevalence using the age of the partners of women seen in the ANC has also been assessed [4].

Methods

As part of the LEPRA Evaluation Project/Karonga Prevention Study, house-to-house total population surveys were conducted in 1981–1984 and 1986–1989 in Karonga District, northern Malawi (population 200 000) [6]. A case–control study of tuberculosis and leprosy began in 1988. Controls were selected from the database of people seen in the second population survey and were matched by age, sex and area to the cases, with up to four controls per case [7,8]. A new case–control study of tuberculosis began in 1998. Since the population database was by then out of date, controls were chosen in the community. The methods have been described in detail elsewhere [9]. Controls were stratum-matched to the cases by age, sex and area. To select a field starting point for each control, an individual was chosen randomly from the 1986–1989 survey. Their household was used as the geographical point from which to choose a control of a prespecified sex and age band, using a method based on spinning a top. The controls at each period were, therefore, randomly selected from the whole district population but with an age, sex and area distribution similar to that of tuberculosis and leprosy cases.

Controls were interviewed and blood was taken for HIV testing, after counselling and if consent was given. Field workers arranged return visits to give post-test counselling to those who wanted to know their HIV results. For the 1988–1993 controls, information on socioeconomic variables was available only from the 1981–1984 survey. From 1998, detailed information was collected at the time of the visit.

ANC sentinel surveillance for HIV started in four clinics representative of the district in 1999, in collaboration with the National AIDS Control Programme. Women attending for their first visit for that pregnancy were interviewed and venous blood was taken for syphilis testing. Treatment for syphilis was provided if indicated. The remaining serum was anonymized, unlinked from personal identifiers and later tested for HIV. Data collection continued in each clinic until 250 women had been seen, and this was repeated each year.

HIV testing was conducted in the project laboratory. In 1988–1993, initial testing used an enzyme-linked immunosorbent assay (ELISA Organon Vironostika, Durham, North Carolina, USA) and particle agglutination test (Edgeware modification of the Serodia; Edgeware, UK). Positives were confirmed using a further Wellcozyme (Wellcome Diagnostics, Dartford, UK) or Behring Enzygnost (Marburg, Germany) and particle agglutination assay (Fujirebio Serodia, Tokyo, Japan). From 1998, the first two tests were conducted as before, and samples giving discrepant results were repeated in duplicate using the same two tests. Syphilis screening used reverse phase passive agglutination (RPR; Becton Dickinson, Sparks, Maryland, USA) with further testing of positive specimens using *Treponema pallidium* agglutination (TPHA; Fujirebio): syphilis was diagnosed if both RPR and TPHA tests were positive.

To estimate HIV prevalence in the whole district and allow direct comparison between the community sample and the ANC, and between different time periods, results were directly standardized by age, sex and area. District data from the 1998 national census were used for the age and sex distribution. The district was divided into six areas and the 1986–1989 survey was used for the percentage of the population in each: area 1 is rural with a trading and truck-stop area; area 2 is rural with farming and fishing; area 3 is peri-urban; area 4 is urban; area 5 is rural with a trading area; and area 6 is rural with an international border. The ANC were in areas 1, 2, 4 and 5 but women came from all six areas: area of residence was used in the analyses and for standardization.

Analyses of risk factors for HIV were conducted for the community sample in each time period, using logistic regression. For 1988–1993, since the sample was chosen from those already on the database, it was not possible to examine recent migration, but place of birth was available. The biases in using ANC data were

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explored by examining differences in sociodemographic and fertility-related factors between women in the ANC and in the community, and by seeing how far the differences in HIV prevalence could be explained by adjusting for these factors using logistic regression [4].

The effect of HIV on fertility was investigated. For women attending an ANC, the birth interval was calculated assuming that the current pregnancy went to term. For women in the community, the time since the last birth was used. The effect of HIV on these intervals was determined using Cox regression.

The studies were approved by the Health Sciences Research Committee, Malawi and the ethics committee of the London School of Hygiene and Tropical Medicine.

Results

Of the community sample sought from the database in the early period, 3.6% had died and 17.0% were not found. Of those who were found, 9.5% refused HIV testing [7]. In 1998–2001, when individuals were sought in the field, refusal for interview was very rare ($< 0.5\%$) but 16.5% refused HIV testing. Refusal was more common in women, those under 30, and those living in the urban centre but was not associated with schooling, occupation or recent moves into the district. Of those who accepted testing, 77% asked for the result.

HIV prevalence in the community increased over the period (Fig. 1). Standardized rates are given in Table 1. In each time period, there was considerable variation by area. In 1988–1993, after adjusting for age, sex,

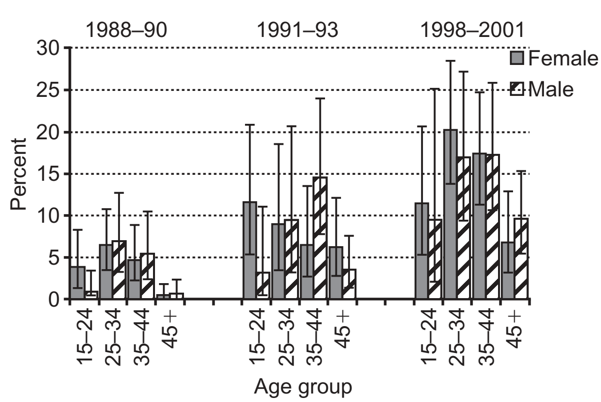

Fig. 1. HIV prevalence among individuals seen in the community as controls. The bars show the 95% confidence intervals on the estimates.

time period and area, HIV positivity was associated with occupations other than subsistence farming [adjusted odds ratio (OR), 2.0; 95% confidence interval (CI), 1.1–3.6], increased schooling ($p = 0.04$ for trend) and being born outside Karonga District [adjusted OR 1.8 (95% CI, 1.1–3.1) for those born elsewhere in Malawi and 2.3 (95% CI, 1.3–4.1) for those born in other countries]. After adjusting each of these factors for each other, only the association with being born outside Malawi was statistically significant.

In 1998–2001, after adjusting for age, sex, area and year, there was no longer any association with schooling or with place of birth, but non-farmers continued to be at higher risk of HIV (adjusted OR 1.9; 95% CI, 1.1–3.1). More detailed data were available for this period. HIV prevalence was much higher in those who were divorced or widowed than those currently married (24.1% compared with 12.4%; adjusted OR 3.3; 95% CI, 1.9–5.8), with lower prevalence in the never-married (10.4%; adjusted OR, 0.85; 95% CI, 0.33–2.2). HIV prevalence was higher in those who had lived elsewhere in the last 5 years compared with 10.4% (56/537) in those who had not moved: the HIV prevalence was 18.4% (26/141; adjusted OR, 1.9; 95% CI, 1.1–3.3) in those who had moved within the district, 22.6% (30/133; adjusted OR, 2.2; 95% CI, 1.3–3.7) in those who had moved from outside the district and 13.6% (3/22, adjusted OR, 1.1; 95% CI, 0.3–4.0) in those who had moved from outside Malawi. Marriage, divorce or widowhood led to about 40% of movements within the district. After adjusting for current marital status, movement within the district was no longer associated with HIV status (OR 1.5; 95% CI, 0.86–2.7) and the association with living outside the district was less strong (OR, 1.8; 95% CI, 1.1–3.1). There were slight increases in HIV prevalence with better housing and increased possession ownership, but these trends were not statistically significant in either crude or adjusted analyses.

The HIV prevalence in the ANC was similar in the 3 years 1999–2001 (Table 2), but varied between clinics: 11.1, 6.0, 14.6 and 9.5%. It is compared with the HIV prevalence in the community in Fig. 2. Directly standardized estimates of HIV prevalence using the ANC data for ages 15–49 years were 9.2% (95% CI, 8.1–10.3) for women and 9.4% (95% CI, 7.2–11.5) for men (using the age reported by women for their partners).

Differences in HIV prevalence in women aged 15–49 years in the ANC and the community in 1998–2001 are shown in Table 2. For both groups, HIV prevalence varied by area, was highest in those who were divorced or widowed, those with secondary or tertiary education, non-farmer households and those who had moved in the last 5 years. Women in the

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Table 1. HIV in the community sample (age 15 years or more) at three different time periods.

	1988–1990			1991–1993			1998–2001		
	HIV+/total No.	%	OR[a] (95% CI)	HIV+/total No.	%	OR[a] (95% CI)	HIV+/total No.	%	OR[a] (95% CI)
HIV prevalence									
Total	50/1720	2.9		53/723	7.3		115/833	13.8	
By area									
1 (rural + truck-stop)	14/354	4.0		11/109	10.1		15/146	10.3	
2 (rural)	8/383	2.1		3/76	4.0		19/149	12.8	
3 (peri-urban)	10/270	3.7		4/87	4.6		23/138	16.7	
4 (urban)	9/188	4.8		13/88	14.8		34/168	20.2	
5 (rural + trading area)	4/147	2.7		10/160	6.3		14/126	11.1	
6 (rural + border)	3/368	0.8		12/202	5.9		10/106	9.4	
By occupation									
Farmers/fisherman	24/995	2.4	ref	25/414	6.0	ref	79/624	12.7	ref
Not farmers/fisherman	20/497	4.0	1.8 (0.76–4.2)	22/224	9.8	2.1 (0.89–4.7)	35/196	17.9	1.9 (1.1–3.1)
By schooling									
None	4/314	1.3	ref	4/131	3.1	ref	12/101	11.9	ref
Primary 1–5	12/650	1.9	1.4 (0.43–4.5)	21/258	8.1	2.6 (0.84–8.0)	23/247	9.3	0.69 (0.31–1.5)
Primary 6–8	26/430	6.1	2.1 (0.66–6.8)	12/155	7.7	2.1 (0.59–7.2)	50/345	14.5	0.96 (0.45–2.0)
Secondary/tertiary	2/39	5.1	1.5 (0.22–9.6)	3/15	20.0	8.0 (1.3–47)	29/138	21.0	1.3 (0.55–3.0)
By birth place									
Karonga	25/1098	2.3	ref	34/462	7.4	ref	75/572	13.1	ref
Other Malawi	12/245	4.9	2.5 (1.2–5.3)	11/123	8.9	1.3 (0.59–2.7)	17/141	12.1	0.93 (0.51–1.7)
Other country	12/199	6.0	3.6 (1.7–7.9)	8/73	11.0	1.6 (0.66–3.7)	23/118	19.5	1.5 (0.86–2.6)
Standardized HIV prevalence[b] [% (95% CI)] at age 15–49									
Men	3.7 (1.9–5.5)			9.2 (6.2–12.1)			11.4 (7.3–15.6)		
Women	3.9 (2.3–5.5)			12.5 (7.3–17.8)			13.9 (10.1–17.7)		

OR, odds ratio; CI, confidence interval; ref, reference for calculation of OR.
[a]Adjusted for age, sex and area.
[b]Directly standardized to the age (5-year age groups), sex and area distribution of the district, see text.

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Table 2. HIV prevalence among women aged 15–49 years in the antenatal clinic and community 1998–2001.

	Antenatal clinics		Community	
	HIV+/total No.	%	HIV+/total No.	%
Total	312/3013	10.4[a]	58/342	17.0
Age (years)				
15–19	44/779	5.7	1/28	3.6
20–24	108/936	11.5	8/51	15.7
25–29	87/663	13.1	11/49	22.5
30–34	46/356	12.9	14/75	18.7
35–39	22/204	10.8	16/84	19.1
40–44	5/60	8.3	8/55	14.6
45–49	0/15	0.0	3/45	6.7
Area				
1 (rural + truck-stop)	81/723	11.2	9/70	12.9
2 (rural)	44/757	5.8	5/65	7.7
3 (peri-urban)	32/331	9.7	13/65	20.0
4 (urban)	79/422	18.7	23/79	29.1
5 (rural + trading area)	51/552	9.2	7/60	11.7
6 (rural + border)	25/224	11.2	4/48	8.3
Marital status				
Never	5/77	6.5	4/37	10.8
Current	280/2835	9.9	37/293	12.6
Past	25/92	27.2	20/57	35.1
School				
None	15/164	9.2	5/39	12.8
Primary 1–5	67/714	9.4	11/133	8.3
Primary 6–8	171/1761	9.7	31/171	18.1
Secondary/tertiary	58/369	15.7	14/43	32.6
Occupation of head of household				
Farmer/fisherman	193/2353	8.2	36/275	13.1
Non farmer/fisherman	113/603	18.7	25/111	22.5
Moved last 5 years				
No move	156/1646	9.5	25/229	10.9
Within district	113/1127	10.0	20/86	23.3
Outside district	36/199	18.1	15/65	23.1
Outside country	7/40	17.5	1/7	14.3
Time period				
1998			4/59	7.7
1999	104/947	11.0	18/93	19.4
2000	103/1038	9.9	23/155	14.8
2001	105/1028	10.2	16/80	20.0
Standardized HIV prevalence[b] [% (95% CI)]	9.2 (8.1–10.3)		13.9 (10.1–17.7)	

CI, confidence interval.
[a]HIV in antenatal clinic overall is 10.3%, including eight women under 15 years and one with unknown age.
[b]Directly standardized to the age (5-year age groups) and area distribution of the district, see text.

ANC were younger than those seen in the community, were more likely to be currently married, had fewer children, were more likely to be farmers and had a higher education level. Compared with women in the community, a lower proportion of ANC women had moved in from outside the district but more had moved within the district, and fewer of the ANC women lived in or near the town.

All of these factors were treated as possible confounders of the association between ANC use and HIV status to see which influenced the relationship. Overall the crude OR for the association of ANC attendance and HIV was 0.62 (95% CI, 0.46–0.83), reflecting the lower HIV prevalence in the ANC. Adjusting for age and area this rose to 0.65 (95% CI, 0.47–0.91), and additionally adjusting for marriage gave 0.76 (95% CI, 0.53–1.1). Neither adjusting for schooling or occupation had much effect on this adjusted estimate, but adjusting for moves within the last 5 years moved the OR value closer to one (0.87; 95% CI, 0.60–1.3). Adjusting for number of previous births, or for time since the last birth (in multiparous women), had no effect on the results. However, the HIV prevalence in the ANC, adjusted for age and area, was similar to that in the population for those with no previous births

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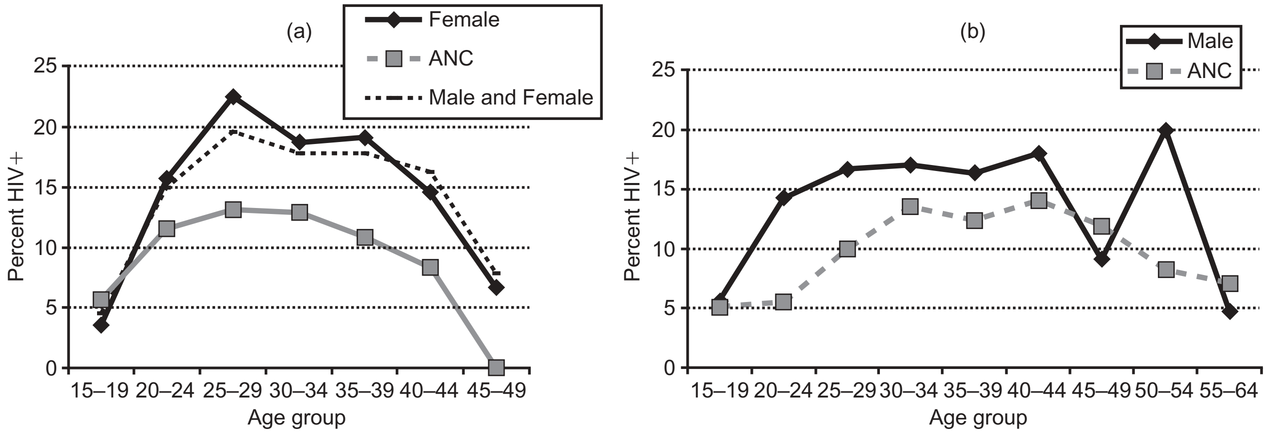

Fig. 2. HIV prevalence in the antenatal clinics and in the community in 1998–2001 for (a) women and estimated combined men and women (b) men. The combined prevalence assumes equal numbers of men and women in each age group. For (b) the HIV prevalence in women in the antenatal clinics is plotted by the age of the father of the unborn child.

(OR 1.0; 95% CI, 0.30–3.4; n = 860) and for those less than 2 years since the last birth (OR, 1.1; 95% CI, 0.55–2.4; n = 425): the underestimate was seen only in those with longer birth intervals (OR 0.45; 95% CI, 0.28–0.70; n = 2091).

Compared with HIV-negative women, HIV-positive women had longer birth intervals, were more likely to have used contraceptives and had an increased chance of still birth and of death of the last child (Table 3). Syphilis was associated with stillbirth, but the association of HIV status and stillbirth persisted after adjusting for syphilis. The lower proportion of nulliparous women among HIV-positive individuals (Table 3) was caused by confounding by age, but there were fewer children among multiparous HIV-positive than HIV-negative community women even after adjusting for age.

In the ANC, HIV-positive women had longer birth intervals than HIV-negative women: hazard ratio (HR) 0.81 (95% CI, 0.71–0.92) or 0.83 (95% CI, 0.72–0.94) after adjusting for age and area. The birth interval was longer in older women, women who were not currently married, non-farmers, those who had not moved in the last 5 years, those seen after 1999, those with more prolonged postpartum abstinence and postpartum amenorrhoea, those with a miscarriage since the last live birth and those using modern contraception. The interval was shorter in those whose last child had died or been a stillbirth, and, after adjusting for age, shorter in those with more previous children. The birth interval was not associated with schooling, syphilis or age at first birth. Additionally adjusting for these confounders gave HR 0.91 (95% CI, 0.79–1.0).

The time since the last birth in women in the community was longer in the HIV-positive than in the HIV-negative group (HR 0.61; 95% CI, 0.44–0.83) even after adjusting for age and area (HR, 0.56; 95% CI, 0.41–0.78). Adjusting for other factors had little influence on the results (adjusted HR, 0.61; 95% CI, 0.43–0.87).

Discussion

In Karonga District, Malawi, we have documented the HIV epidemic since its first introductions in the early 1980s [5,10]. By using data from the national census and survey data on population distribution by area, HIV prevalence for adults in the whole district has been estimated. Although the data were collected for case–control studies, the sample was selected randomly from the community and, after adjusting for age, sex and area, should be representative of the whole district.

Together with our earlier study of the total population in two areas of the district [5], we have shown that immigration into the district and travel are important risk factors for HIV at all stages of the epidemic. Throughout the 1980s and 1990s, HIV risks have been higher in those who were not subsistence farmers, particularly in skilled manual workers, clerical workers and those in professional or managerial posts [5]. A clear trend with increased schooling was lost in the later period: HIV prevalence continued to be highest in those with at least secondary education, but rates in those with no schooling also rose considerably. A change in the association with schooling has been seen in Uganda and Zambia (but not elsewhere in Malawi) [11–14]. However, in Uganda and Zambia, this change reflected a fall in HIV prevalence in the most educated rather than a rise in those with least schooling as seen here.

Throughout the period, there were large variations in HIV prevalence by area, and those areas most affected

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Table 3. Reproductive history by HIV status among women age 15–49 years attending antenatal clinics and in the community in Malawi (1998–2001).

	Antenatal clinics			Community		
	HIV−	HIV+	*P* value	HIV−	HIV+	*P* value
All women						
No.	2701	312		312	61	
Mean age (years)	24.4	25.6	0.004	33.1	32.9	0.9
Nulliparous women (%)	28.3	18.3	< 0.001	11.4	8.5	0.5
Syphilis (%)	2.8	5.8	0.004	2.3	1.7	0.8
Nulliparous women (no previous births)						
Number	762	57		37	5	
Mean age (years)	18.7	19.7	0.005	20.8	29.2	0.009
Previous induced abortions (%)	0	0				
Previous spontaneous miscarriages (%)	2.8	3.5	0.7			
Modern contraceptive use (%)	2.0	7.0	0.02			
Multiparous women (⩾ 1 previous birth)						
Number	1933	255		289	54	
Mean age (years)	26.7	26.9	0.7	34.6	32.7	0.09
Mean age at first birth (years)	18.8	18.9	0.5			
Birth interval (months)[a]	36.0	38.6	0.01	27.5	33.9	0.2
< 24 months	12.9	12.3		44.8	30.8	
24–47 months	68.5	59.7		24.7	30.8	
48+ months	18.6	28.1	0.002	30.6	38.5	0.2
Duration postpartum amenorrhoea (months)[a]	5.9	5.7	0.6			
0–6 months	48.3	48.3				
7–12 months	38.2	35.8				
> 12 months	13.5	16.0	0.5			
Duration postpartum abstinence (months)[a]	4.7	5.1	0.01			
⩽ 3 months	27.3	25.4				
4–6 months	55.7	52.7				
7–11 months	8.7	9.0				
⩾ 12 months	8.4	12.9	0.1			
Spontaneous miscarriages since last pregnancy (%)[b]	4.8	1.4	0.07	5.9	5.7	0.9
Last birth was still birth (%)	3.7	8.8	< 0.001			
Last child died (%)	9.7	17.9	< 0.001			
Number of previous births[a]	2.2	2.1	0.08	4.1	3.1	0.004
1	30.6	33.9		11.1	16.7	
2–3	41.7	41.7		18.3	35.2	
4+	27.7	24.4	0.4	70.6	48.2	0.05
Modern contraceptive use since last birth (%)	10.1	20.3	< 0.001			

[a]Geometric mean given.
[b]Only recorded from mid 2000 in antenatal clinics.

early on continue to have high rates of HIV. The calculations assumed equal population growth rates in all areas. Increased urbanization may have led to overestimation of prevalence in the urban areas in the later period. For analysis, the district was divided into six areas, but the variation in the smaller areas recorded in the data was even greater than that presented: HIV prevalence among ANC women ranged from 0–8% in remote areas to 18–19% in areas closer to roads and truck-stops. Small area variation in HIV prevalence is often seen [15,16], though this level of variation is extreme and is important for interpretation of non-representative samples, such as ANC sentinel surveillance, particularly if different clinics are included in different surveys.

The problems of using ANC data to estimate population HIV prevalence have been much discussed. They depend both on sociodemographic differences and on the association of HIV and fertility [2,3]. Overall, the comparison of HIV prevalence in the ANC with women in the community showed the usual pattern, with overestimation of HIV prevalence in the youngest group (probably due to selection of sexually active women) and underestimation of HIV prevalence at other age groups and overall [2–4,11,17–21]. In this dataset, the overall difference could be explained largely by sociodemographic factors: age, area of residence, marital status and moving household within the last 5 years. This has not been the case in previous studies [4] and highlights the difficulties of standard adjustments for ANC data.

Other studies have emphasized the importance of fertility differences. We found decreased fertility associated with HIV. The effect on the birth interval seen

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in the ANC is very similar to that reported in Côte d'Ivoire, Kenya, Zambia and Cameroon [22,23]. It underestimates the actual effect of HIV on fertility since non-sexually active and non-fertile women are not seen in the ANC and subfertile women are under-represented [24]. This is demonstrated by the greater effect of HIV on fertility in the community women. Although time since the last birth is not the same as the birth interval, the relative effect of HIV should be equivalent. Given these large effects on fertility, it is surprising that adjustment for parity, or for the birth interval among multiparous women, did not explain any of the difference between the HIV prevalence in the ANC and the community.

One adjustment method for ANC data, based on HIV prevalence ratios for fertile and infertile women in previous community surveys [25], applies 80% of the prevalence rate in nullipara to childless women in the population, and 150% of the prevalence rate observed in multipara to mothers. In Malawi, as 21.5% of women aged 15–49 are childless [26], this adjustment gives an estimated female HIV prevalence of 15.0%, compared with 13.9% estimated from the community sample. Of course the community estimates may themselves be biased because of refusal of HIV testing and non-inclusion of more mobile individuals.

The age of the ANC women's partners has been used previously to estimate male HIV prevalence [4]. In the present study, it underestimated HIV prevalence for the age group 15–49 years (9.4% compared with 11.4%).

In this community, we have had the unusual opportunity to document the first 20 years of the HIV epidemic. The recent stabilization of HIV prevalence seen elsewhere in Malawi was also seen here. Despite the changes in prevalence, the risk factors for HIV have been similar in all periods, with HIV being associated with occupations other than farming, with immigration and travel, and being most common in those with most schooling (Table 1) [5]. The trend with increased schooling has become less strong, unfortunately because of a rise in HIV prevalence in those without schooling rather than a fall in prevalence in the more educated [14]. As in other populations, HIV sentinel surveillance data in ANC provide only a partial picture of the epidemic.

Acknowledgements

We thank the Government of the Republic of Malawi for their interest in and support of the Project and the Malawi Health Sciences Research Committee for permission to publish the paper.

Sponsorship: Until 1996, the Karonga Prevention Study was funded primarily by LEPRA (The British Leprosy Relief Association) and ILEP (The International Federation of Anti-Leprosy Organizations) with contributions from the WHO/UNDP/World Bank Special Programme for Research and Training in Tropical Diseases. Since 1996, the Wellcome Trust has been the principal funder. JRG was supported in part by the British Department for International Development and the Department of Health (Public Health Career Scientist award).

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