Who infects whom? HIV-1 concordance and discordance among migrant and non-migrant couples in South Africa

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Objectives: To measure HIV-1 discordance among migrant and non-migrant men and their rural partners, and to estimate the relative risk of infection from inside versus outside primary relationships.

Design: A cross-sectional behavioural and HIV-1 seroprevalence survey among 168 couples in which the male partner either a migrant, or not.

Methods: A detailed questionnaire was administered and blood was collected for laboratory analysis. A mathematical model was developed to estimate the relative risk of infection from inside versus from outside regular relationships.

Results: A total of 70% (117 of 168) of couples were negatively concordant for HIV, 9% (16 of 168) were positively concordant and 21% (35 of 168) were discordant. Migrant couples were more likely than non-migrant couples to have one or both partners infected [35 versus 19%; $P = 0.026$; odds ratio (OR) = 2.28] and to be HIV-1 discordant (27 versus 15%; $P = 0.066$; OR = 2.06). In 71.4% of discordant couples, the male was the infected partner; this did not differ by migration status. In the mathematical model, migrant men were 26 times more likely to be infected from outside their regular relationships than from inside [relative risk (RR) = 26.3; $P = 0.000$]; non-migrant men were 10 times more likely to be infected from outside their regular relationships than inside (RR = 10.5; $P = 0.00003$).

Conclusions: Migration continues to play an important role in the spread of HIV-1 in South Africa. The direction of spread of the epidemic is not only from returning migrant men to their rural partners, but also from women to their migrant partners. Prevention efforts will need to target both migrant men and women who remain at home.

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Introduction

Over the past decade, South Africa has experienced a dramatic and rapid growth in the prevalence of HIV-1 [1]. In 1990 national antenatal HIV prevalence was 0.76%; by 2001 it had reached 24.8% [2]. Prevalence has consistently been highest in KwaZulu/Natal where 33.5% of pregnant women are HIV-infected. Five million South Africans, more then 10% of the country's population, are now infected [3].

Southern Africa has extraordinarily high rates of population movement both within and between countries, and HIV, like other infectious diseases, follows the movement of people [4]. It is estimated that approximately 2.5 million legal migrants have come to South Africa from neighbouring countries, along with an unknown number of illegal migrants. In addition, millions of men migrate within South Africa between rural and urban areas [5]. In Hlabisa, a rural district of KwaZulu/Natal, which was the site for this study, 62% of adult men spend most nights away [6]. Throughout southern Africa, the dominant pattern of migration is men moving on their own to urban centres in search of work, leaving partners and families in rural areas and returning home periodically depending on the distances involved. This 'circular migration' is one of the sequelae of apartheid, the system designed to prevent black men from remaining in 'whites only' areas at the end of their working lives.

The central assumption about the directionality of spread of HIV in the presence of migration has been that men become infected while away from home, and infect their rural partners when they return [7–9]. We are not aware of any studies that have specifically investigated the partners of migrants, or that have considered both partners in migrant and non-migrant couples. We therefore set out to understand the extent to which the HIV-1 epidemic in rural South Africa has been driven by urban migrants returning to their rural homes – as opposed to the spread of infection within rural communities. We also sought to understand the social and behavioural factors that shape and determine the spread of infection between partners. In order to explore the relationship between migrancy and the spread of HIV, this study investigated patterns of HIV infection among migrant and non-migrant couples.

Most studies on HIV discordance among couples in Africa have focused on the effects of couples counselling on the subsequent rates of HIV-1 acquisition [10,11], on the effects of serodiscordance on coping strategies within relationships [12,13], or on the effect of HIV therapies on sexual behaviour among serodiscordant couples [14]. Two African studies have investigated the relative risk of infection among men and their regular female partners. One study [15] compared risk factors for HIV-infection among HIV-negative concordant couples and HIV discordant couples, concluding that, in most cases, husbands acquired HIV infection first and then transmitted it to their wives. A study in Uganda [16] examined HIV-1 infection among couples who were either HIV-discordant or HIV-negatively concordant, and measured the incidence of HIV-1 over 1 year in these couples. Among discordant couples, the male was HIV-positive in 57% of the cases, the female in the remaining 43% of cases. The sample was stratified according to place of residence; in trading and intermediate centres, women were as likely as men to be the source of new infections in a couple. However, in the rural villages, men were the predominant source of new infections [16].

In this study we investigated the rates of HIV-1 infection in migrant and non-migrant couples in order to understand the risk factors and transmission dynamics of the epidemic in South Africa.

Methods

Detailed methodology of the study has been presented elsewhere [17]. Migrant men from Hlabisa and Nongoma, two adjacent health districts in northern KwaZulu/Natal, South Africa were recruited at two frequent migration destinations, Richards Bay and Carletonville. Migrant men were eligible to participate in the study if they were from Hlabisa or Nongoma districts, if they had at least one regular partner living in those districts, and if they had been a migrant for at least the last 6 months.

In Richards Bay, migrant men from the rural districts were recruited at three large factories. A brief census was conducted at each factory to identify men from the rural districts. In Carletonville, a list indicating the origin of all men working on the goldmines was obtained from the agency responsible for recruiting workers. Men from Hlabisa and Nongoma were randomly selected from these lists and invited to participate in the study.

Following recruitment, a detailed questionnaire was administered in Zulu and each participant was asked to undergo a physical examination and to provide a blood sample for HIV testing. All testing was voluntary and included pre- and post-test counselling. Two millilitres of venous blood were collected from each consenting participant. Participants had the option of receiving their HIV results [18]. Enrolment also included a 'tracking sheet' in which participants gave information to locate their rural partners who were then invited to participate in the study. To recruit non-migrant men and their partners, eligible people living within a 1-kilometre radius from a migrant couple's home were asked to participate in the study.

Non-migrant couples were eligible to participate if the man spent most nights at home, if he had not been a migrant for more than a total of 6 months in the last 5 years, and if his regular partner was not a migrant. A 'migrant couple' is one in which the man is a migrant and the woman is not, whereas a non-migrant couple is one in which neither partner is a migrant. The refusal rate was 3.0%; half of those were migrant men and the half were partners of migrant men.

Blood was screened for HIV-1 using the Determine Test (Abbott Diagnostics, North Chicago, Illinois, USA). Samples that tested positive were re-tested using two additional ELISA tests (HIV 1.2.0 - Abbott/Murieux and Vironosticka HIV uniform 2 + 0 - Omnimed, Illinois, USA). A random sample of 10 % of the Determine Test negative specimens were re-tested using an enzyme-linked immunosorbant assay; there were no false negatives.

All participants were offered pre- and post-test counselling, condoms at each visit, and free treatment for symptomatic and laboratory-diagnosed sexually transmitted diseases (STDs). Symptomatic ulcers and discharge were treated on enrolment using the KwaZulu/Natal syndromic management guidelines [19], and laboratory-diagnosed STDs were treated at 10-day follow-up visits. The study was approved by the ethics committees of the University of Natal Durban, and the Johns Hopkins University School of Hygiene and Public Health.

Statistical methods and mathematical model

All data were double-entered entered into a computer using Microsoft Access 1997 (Microsoft, Seattle, Washington, USA). The primary endpoint was the presence of at least one HIV-1 infected individual in a couple. Univariate analysis was used to determine demographic and biomedical factors associated with HIV-1 infection in a couple. Risk factors such as age and age at first sexual intercourse refer to the average characteristics within a couple. The number of lifetime partners and number of current regular partners refer to the combined total within a couple. Migration status and STD symptoms in the last 4 months indicate the status of at least one member of the couple. A logistic regression model was developed to investigate the relationship between HIV and possible risk factors. Variables that had a *P*-value less that 0.20 in the univariate analysis were considered in the logistic regression model. A forward stepwise regression approach was used to identify the final model. The importance of these factors in the logistic model was determined by their significance on a likelihood ratio test. The odds ratio (OR) was used to interpret the relationship of HIV-1 infection in a couple to the risk factors. Confidence intervals (CI) are reported as 95%. The study had 80% power to detect a 14% difference in the risk of HIV-1 between migrants and non-migrants. Data analysis was performed using the statistical package SAS version 6.12 (SAS Institute, Cary, North Carolina, USA).

In order to estimate the relative risk (RR) of infection for migrant and non-migrant men and women from their spouse and from partners outside the relationship, we constructed the model shown in Figure 1.

If the probabilities of infection are known, then the probabilities of each of the four concordance possibilities can be calculated. Combining probabilities in a straightforward fashion gives:

$$P_{nn} = (1 - \alpha)(1 - \beta)$$

$$P_{pn} = \alpha(1 - \beta)(1 - \delta)$$

$$P_{np} = \beta(1 - \alpha)(1 - \gamma)$$

$$P_{pp} = \alpha\beta + \alpha\delta + \beta\gamma - \alpha\beta(\gamma + \delta)$$

where the first subscript indicates the HIV status of the man (positive or negative) and the second that of the woman. We then vary the parameters in order to maximise the likelihood of the fit of the estimated probabilities to the observed probabilities assuming binomial errors. Since there are four parameters and only three independent observations, we assume an appropriate value for the ratio of the likelihood that an infected man infects his wife to the likelihood that an infected woman infects her husband, δ/γ. Various estimates have been made of the relative transmissibility of infection from men to women compared to from women to men [21–24] and most studies in the range of 2 : 1. We therefore used this ratio for the model, but for comparison, we also modelled the effect of transmission probabilities of 3 : 1 and 1 : 1.

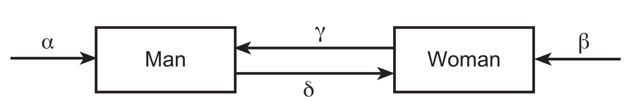

Fig. 1. Mathematical model. For a man and a woman in a partnership the man may be infected from outside the relationship with probability α, the woman from outside the relationship with probability β. The man may also be infected by his wife with probability γ (if she is already infected) and the women may be infected by her husband with probability δ (if he is already infected).

Results

A total of 168 couples were recruited into the study, of whom 98 (58.3%) were couples in which the male partner was a migrant, and 70 (41.7%) in which the male partner was not a migrant. Table 1 shows the demographic and sexual behaviour data for migrant and non-migrant men, and their partners. The overall prevalence of HIV-1 was 19.9% with 24.4% of men and 15.5% of women infected ($P = 0.04$; OR = 1.8; 95% CI = 1.03–3.06).

Table 2 presents the patterns of infection among couples. Among 69.6% of couples, neither partner was infected with HIV-1; migrant couples were as likely as non-migrant couples to have neither partner HIV-1 infected (65.3 versus 75.7%; $P = 0.148$). In 9.5% of the couples, both partners were infected with HIV-1, and this did not differ significantly by the migration status of the male partner. In 20.8% of the couples one of the partners was infected with HIV-1 (HIV-1 discordant), and migrant couples were 2.5 times more likely than non-migrant couples to be discordant for HIV (26.5 versus 12.8%; OR = 2.5; 95% CI = 1.1–5.6; $P = 0.031$;). Of the 35 discordant couples the man was HIV-positive in 25 (71%) of the cases and the woman in the remaining 10 (29%) cases. The proportion of men who were infected in the migrant discordant couples was essentially the same as in non-migrant discordant couples ($P = 0.95$).

Table 3 presents social and behavioural factors associated with migration status among infected and uninfected couples. Migrant and non-migrant couples in infected and in uninfected partnerships are similar in their demographic and behavioural characteristics. There were no significant differences in the age difference between partners, the proportion who were formally married, the duration of the relationship or the number of regular or casual partners. However, among infected couples non-migrant men were more likely to have had more than ten partners and non-migrant women were more likely to have had more than two partners. In those partnerships in which men reported having more than one casual partner, there was more likely to be an infection in either or both of the partners than in those partnerships for which men reported having one or no casual partners (OR = 7.06; $P = 0.032$; 95% CI = 1.18–42.13). Women who reported having two or more lifetime partners were more likely to be in relationships in which one or both members were HIV-1 infected. Neither the number of regular partners nor the number of lifetime partners that men had were significantly associated with the chances of one or both members of a couple being HIV-1 infected.

Table 4 presents the results of the univariate and multivariate logistic models for the risk of one or both partners in a couple being HIV-1 infected. In the univariate analysis all of the variables were associated

Table 1. Socio-demographic and sexual behaviour data among migrant and non-migrant men, and their rural partners.

	Men			Women		
Variable	Migrant men n = 98	Non-migrant men n = 70	Level of significance	Partners of migrant men n = 98	Partners of non-migrant men n = 70	Level of significance
Age						
Mean	39.6	43.9	0.0125	34.3	39.0	0.004
Standard deviation	10.3	11.9		8.6	11.4	
Level of education						
None	21.7%	42.0%		16.5%	26.1%	
Grade 1–5	46.4%	37.7%	0.016	47.4%	52.2%	0.093
Grade 6+	31.9%	20.3%		36.1%	21.7%	
Marital status						
Married (civil + traditional)	25.3%	68.6%	< 0.0001	25.3%	68.6%	< 0.0001
Unmarried but committed or living as married	74.7%	31.4%		74.7%	31.4%	
Number of regular partners						
1	64.3%	64.3%	1.0	100%	100%	1.0
⩾ 2	35.7%	35.7%		–	–	
Number of casual partners						
0	90.8%	97.1%	0.102	100%	100%	
⩾ 1	9.2%	2.9%		–	–	1.0
Number of lifetime partners						
Mean	7.6	16.6	0.0022	1.6	2.1	0.0834
Standard deviation	10.6	22.2		1.2	1.9	
Duration of relationship (years)						
Mean	14.0	15.7	0.2301	14.0	15.7	0.2301
Standard deviation	8.6	9.5		8.6	9.5	
HIV-1 prevalence	27.6%	20%	0.261	15.3%	15.7%	0.943

Table 2. Patterns of infection among couples, overall, and by migration status of male partner

Male	Female	Overall n = 168 (%)	Migrant couples n = 98 (%)	Non-migrant couples n = 70 (%)	*P*[a]
HIV−	HIV−	117 (69.6%)	64 (65.3%)	53 (75.7%)	0.15
HIV+	HIV−	25 (14.9%)	19 (19.4%)	6 (8.6%)	0.05
HIV−	HIV+	10 (6.0%)	7 (7.1%)	3 (4.3%)	0.66
HIV+	HIV+	16 (9.5%)	8 (8.2%)	8 (11.4%)	0.48

[a] *P*-value comparing migrant to non-migrant couples.

Table 3. Demographic and social factors for migrant and non-migrant couples in which one or both partners are infected and in which neither partner is infected. The *P* values are for comparisons between migrants and non-migrants in infected and uninfected couples and for comparisons of infected and uninfected couples.

	One or both partners HIV-1 infected			Neither partner HIV-1 infected			
Variable	Migrant n = 34	Non-migrant n = 17	*P*	Migrant n = 64	Non-migrant n = 53	*P*	*P*
Age (men)							
Mean	35.0	32.6	0.013	35.1	40.3	0.02	0.028
SD	11.3	9.1		8.3	11.2		
Age difference							
Mean	5.1	8.9	0.09	5.4	3.6	0.228	0.411
SD	6.8	8.6		7.9	8.3		
Marital status							
Married	22	8	0.138	49	40	0.770	0.146
Unmarried but committed or living as married	10	9		14	13		
Duration of relationship (years)							
Mean	12.7	14.0	0.64	14.6	16.2	0.34	0.207
SD	9.5	8.6		8.1	9.7		
Number of regular partners							
1	22	9	0.417	41	36	0.661	0.150
⩾ 2	12	8		23	17		
Number of casual partners							
⩽ 1	29	10	0.774	60	53	0.064	0.246
⩾ 2	5	2		4	0		
Number of lifetime partners (men)							
⩽ 10	32	10	0.002	51	33	0.037	0.270
> 10	2	7		13	20		
Number of lifetime partners (women)							
⩽ 1 (n = 96)	20	4	0.017	41	31	0.537	0.094
⩾ 2 (n = 72)	14	13		23	22		

with increased risk of HIV-1 infection in a couple but the association with the total number of lifetime partners and current sexual partners were not significant.

The factors that remained significant in the multivariate model of HIV-1 infection in at least one member of a couple were age, age at first sexual intercourse and whether at least one member of a couple had experienced STD symptoms in the last 4-months (Model II). Migrant couples were more likely than non-migrant couples (OR = 1.64) to have one or both partners infected with HIV-1 and this was retained in the model even though it was not statistically significant. The OR of being in a couple with HIV-1 infection was 5.42 times higher among couples with average age between 18 and 24 years compared to those with average age 35 years or above. The risk of HIV-1 infection in a couple was 2.39 times higher if the average age of the couple at first sexual intercourse was 16 years old or younger, compared to those whose average sexual debut age was over 16 years. Couples with STD symptoms in the last 4 months were 2.07 times more likely to have one or both partners infected with HIV-1 compared to those couples who did not have STD symptoms in the last 4 months.

Mathematical model

Fitting the model to the data as discussed in the methods section gives the results shown in Table 5. Men and women are both more likely to be infected from outside the relationship than to be infected by their spouse, whether or not the man is a migrant. Migrant men are 26 times more likely to be infected

Table 4. Logistic regression models of risk factors for HIV infection in a couple.

		Multivariate models	
	Univariate models	Model I	Model II
Variable	OR [95% CI]	OR [95% CI]	OR [95% CI]
Migration status			
(1 = migrant and 0 = non-migrant)	1.66† [0.93–3.29]	1.75 [0.81–3.79]	1.64 [0.77 – 0.88]
Age (in years)[a]			
18 to 24	6.69* [1.23–36.31]	3.94 [0.58–26.87]	5.421† [0.88–33.23]
25 to 34	1.30 [0.62–2.72]	0.89 [0.35–2.05]	0.96 [0.42–2.22]
35+	1	1	1
Marital status			
(1 = unmarried and 0 = married)	1.98† [0.97–4.03]	1.53 [0.64–3.68]	
Age at first sexual debut (in years)[a]			
(1 = 16 or less and 0 = over 16)	2.79** [1.30–5.98]	2.45* [1.08–5.55]	2.39* [1.06–5.39]
Lifetime partners[b]			
(1 = more than one and 0 = one)	1.78 [0.63–5.08]		
Current sexual partner[b]			
(1 = more than one and 0 = one)	1.14 [0.58–2.27]		
STD symptoms last 4 months			
(1 = yes and 0 = no)	2.23* [1.14–4.36]	1.91† [0.90–4.07]	2.07* [1.01–4.31]

[a]The average within a couple. [B]The total within a couple. OR, odds ratio; CI, confidence interval; STD, sexually transmitted diseases. †$P < 0.1$; *$P < 0.05$; **$P < 0.01$.

Table 5. The probability (expressed as a percentage) that the men and women in the study were infected by someone from outside the relationship or by their spouse. The relative risks (RR) (and associated *P* values) are for the comparisons of risk from outside and from inside the relationship. The data are given separately for migrants and for non-migrants. The model assumes that within a spousal relationship male-to-female transmission is twice as likely as female to male. *P* values are χ^2 tests for significance.

	Outside	Spouse	RR	*P*
Migrants				
Man	26.8 ± 3.7	1.0 ± 0.6	26.3	0.0000
Woman	10.8 ± 3.4	5.1 ± 2.5	2.1	0.1685
Non-migrants				
Man	18.6 ± 3.9	1.8 ± 1.1	10.5	0.00003
Woman	7.0 ± 3.8	9.3 ± 3.6	0.8	0.6573

from outside the relationship than from inside the relationship; women whose partners are migrants are 2.1 times more likely to be infected from outside the relationship than from inside. The same is true for non-migrant couples but with smaller odds ratios: 10.5 for non-migrant men and 0.8 for their partners.

In Table 6 for men and women we compare the relative risk of infection for migrants as against non-migrants from outside versus inside their primary relationships. Both men and women are more likely to be infected from outside the relationship and less likely to be infected by their spouse if they are part of a migrant couple but none of these risk ratios is statistically significant.

The model assumes that within a spousal relationship, male-to-female HIV transmission is twice as likely as female-to-male transmission. For comparison, we also modelled the likelihood of infection from inside versus outside a relationship using transmission probabilities of 3 : 1 and 1 : 1 (data not shown) and found that these changes had very little impact on the outcome of interest. Changing the relative transmissibility from men to women in either direction changes the relative risk estimates by less than 1.5% in all cases.

Table 6. The risk ratio for infection comparing migrants and non-migrants for men and women to be infected by their spouses or from outside the relationship. The significance levels are given in brackets.

	Outside	Spouse
Man	1.44 (0.125)	0.58 (0.548)
Woman	1.53 (0.460)	0.54 (0.327)

Discussion

The patterns of HIV discordance in this study were unexpected and shed light on the role of migration in the spread of HIV-1 to rural areas. It has long been assumed that the primary direction of spread has been from returning migrant men, who become infected while away at work, to their rural partners when they return home. If this were the case, the male would be the HIV-1 infected partner in most of the discordant couples; however, in nearly one-third of the discordant couples the female was the infected partner. Although this confirms the importance of migration as a risk factor for infection in both men and women, it changes our understanding of the way in which migration enhances risk. We found that migration is a risk factor not simply because men return home to infect their rural partners, but also because rural women - both partners of migrants partners of non-migrants - are likely to become infected from outside their primary relationships.

Women with absent partners are more likely to have additional sexual partners, and as a result to increase their risk of becoming HIV infected. The fact that the patterns of HIV-1 discordance are similar in migrant and non-migrant couples indicates that even some partners of non-migrant men become infected prior to their husbands. Serwadda *et al.* [16] found a similar proportion of women in HIV-1 discordant couples to be the infected partner in rural Uganda.

The specific circumstances in which rural women take on additional relationships needs further investigation, as well as the ways in which these relationships increase risk for HIV infection. We have found in key informant interviews [25] that women talk about the need for social, sexual, financial and emotional support, all of which are frequently lacking in long-term 'stable' relationships, particularly when the partner is absent. Research is needed to better understand the complex social and sexual lives of rural women, especially in relation to the migration status of their partners. Understanding these dynamics could help to promote the development of new approaches for HIV-1 prevention among rural women.

The mathematical model presented here makes it possible to estimate the probability that a person is infected either by his or her spouse or by someone outside of the relationship. We found that for everyone the risk of becoming infected from outside is greater than the risk of becoming infected from inside the primary relationship. While we expected that migrant men would be more likely to be infected from outside their spousal relationships, we did not expect that to be true for the other groups, including women whose partners were and were not migrants. The model shows that migration reduces the risk of infection from inside the relationship and increases the risk from outside the relationship, both for men and for women. Since men who migrate to Carletonville, for example, spend relatively little time at home each year, the likelihood of them infecting their rural partners is correspondingly low, presumably as a result of the infrequent exposure.

This study had a relatively small sample size which limits the power of the statistical tests and the cross-sectional design limits the possibilities for making causal inferences. Nevertheless, these findings have important implications for the control of the HIV-1 epidemic in sub-Saharan Africa. While migrant men are clearly at high risk of infection and require their own targeted interventions, programmes are also needed in rural areas.

Interventions that target couples, rather than individuals may well have the most direct benefit. Where possible, interventions should deal with migrant couples as a social unit and not just with one or the other partner. HIV prevention interventions have often been aimed at individuals, encouraging people to use condoms and reduce the number of partners [26]. Interventions designed specifically to address the situation in which one partner is already infected are needed to protect the uninfected partner who is at high risk of infection. These interventions could include couple counselling, more aggressive treatment of STDs, antiretroviral therapy for HIV-infected partners, and education messages aimed at couples. Van Der Straten and colleagues [14] found that including seronegative partners in counselling interventions may decrease sexual risk-taking among serodiscordant couples, and Padian and colleagues [27] found that social support resulting from couples counselling is an effective way of promoting behaviour change. More generally, interventions aimed at couples could help improve communication within relationships, focusing on protecting those who are at high risk [28].

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