The Role of Mobility in HIV Transmission and Control

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De rol van mobiliteit in hiv transmissie en bestrijding

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'Succes is not final, failure is not fatal:
it is the courage to continue that counts'
(Winston Churchill)

Contents

1 General introduction

The studies in this thesis contribute to the knowledge about the influence of mobility on HIV transmission. Most studies thus far have focused on the mobile persons, but we have also looked into the sexual behavior and HIV risk of partners staying behind. We also modeled the impact of mobility (migration and travel) on the effectiveness of HIV interventions. The results inform the choice of intervention strategies and the optimization of resource allocation.

This chapter provides a background to the studies presented in Chapters 2–7. First, information on the global transmission of HIV is summarized, together with information on risk factors (Section 1.1). Thereafter, the different aspects of mobility and the relation between mobility, sexual behavior and HIV infection is described (Section 1.2). Section 1.3 summarizes HIV intervention strategies and the possible impact of mobility on their effectiveness. Section 1.4 provides background information about the microsimulation model STDSIM, in which we have explicitly modeled mobility groups and their risk behaviors. Section 1.5 gives an overview of the studies in Zimbabwe and Tanzania that provided field data for our analyses. The research questions and an outline of the remaining chapters are given in Section 1.6.

1.1 The HIV / AIDS burden: global transmission and risk factors

Acquired immune deficiency syndrome (AIDS) is a major public health problem. In 2007, worldwide over 33 million people were infected with human immunodefiency virus (HIV), the cause of AIDS [1]. In the same year, an estimated 2.7 million new infections occurred. UNAIDS estimated that 2 million people died from AIDS-related illnesses in 2007 [1].

Sub-Saharan Africa (SSA) is the worst affected area (Figure 1.1), with some countries still experiencing an expansion of the epidemic. The prevalence of HIV varies enormously within SSA: it is much higher in east and southern Africa than in west and central countries. The prevalence in several countries in southern Africa is as high as 15% [2-4].

HIV-positive people will develop AIDS within 8 to 10 years after infection and die one to two years later, unless they take antiretroviral treatment (ART). They die from opportunistic infections such as tuberculosis, from cancer (e.g. Kaposi's sarcoma), or from general weakening and wasting [5,6].

HIV is transmitted by unprotected sexual contact (both heterosexual and homosexual), by needle exchange in intravenous drug use, and through vertical transmission from mother-to-child. If infected blood comes into contact with an open wound (e.g. through

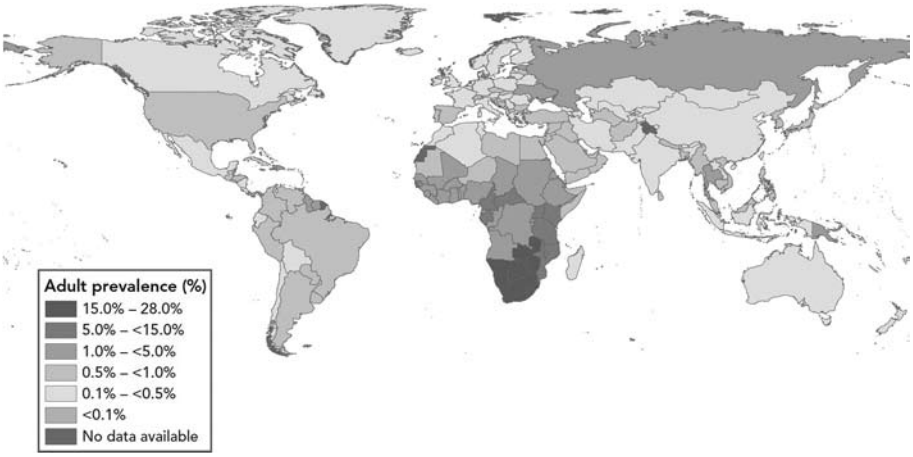

Figure 1.1 HIV prevalence in adults (15-49 years) in 2007 [1].

intravenous drug use or blood transfusions), HIV can be transmitted. The transmission of HIV from mother-to-child can occur during pregnancy, at childbirth or during breastfeeding. Without preventive treatment, the transmission rate from mother-to-child before or during birth is around 25 percent. This can be reduced to one percent if antiretroviral drug treatment and caesarean section are available [7].

Most HIV infections in Africa are due to heterosexual transmission. The estimated risk of HIV infection from unprotected heterosexual intercourse is about 10 per 10,000 exposures for women, and 5 per 10,000 for men [8,9]. Risk factors for HIV transmission include having multiple partners [10], having extramarital sex partners [11], and engaging in paid sex [12,13]. Concurrent sexual relationships, i.e. having more than one partner at the same time, further increase the risk for HIV infection [14,15]. These risks are thought to be substantially higher in the presence of other sexually transmitted diseases (STDs) [16,17], especially herpes simplex virus type 2 (HSV-2) [18,19]. Longitudinal epidemiological studies show that STDs in HIV-negative persons increase susceptibility to HIV [17,20]. Moreover, studies in which shedding of HIV in genital secretions was compared before and after treatment of a concurrent STD have provided evidence for increased infectiousness of people infected with STDs [21-23]. However, estimating the magnitude of these STD cofactor effects from observational studies is confounded by the multiple common risk factors for HIV and STD, including the common mode of acquisition (i.e. sexual intercourse) [24].

1.2 Mobility: migration and travel

Mobility has many aspects, such as reason, distance, duration, and frequency. In the literature, different definitions are used. We divide mobility into two main categories: *migration* and *travel*. *Migration* is defined as moving to a new community and includes both immigration and out-migration (also called emigration). Migrants can cross borders but they also move between different areas within the same country, for example from a rural area to a city. Always, migrants should move to a new home in another town/village or in a different community in the same city. *Travel* as we define it includes all travel with one or more nights away from home. Travel can be related to visiting family, attending ceremonies such as marriages and funerals, spending time with the partner for couples living apart, and work (e.g. market traders, truck drivers). In the different chapters of this thesis, definitions of mobile groups are not always the same. An overview of the definitions used in this thesis is provided in Table 1.1.

Table 1.1 Definitions of mobile groups used in the different chapters of this thesis.

Chapter	Mobility	
1 and 8	**Migration:** moving to another community	**Travel:** one or more nights away from home
2	**Immigrants:** persons in urban areas who moved into the city or town in the last year.	N/A
3	**Out-migrants:** persons who moved out of the 12 studied communities.	N/A
4	**Long-term mobiles:** persons who lived elsewhere once or more during 5 demographic rounds.	**Short-term mobiles:** persons who slept outside the household at least one of the nights before the five demographic rounds.
5	**Couples living apart:** couples in which the man moved to a new household and the woman stayed behind.	**Mobile cohabiting persons:** co-residents who slept outside the household more than ten times per year.
6 (model)	**Immigrants:** simulated persons who moved into the rural study population.	**Family visitors:** simulated persons traveling one week followed by half a year at home. **Market traders / visitors of ceremonies:** simulated persons traveling one week followed by three weeks at home. **Highly mobile persons:** simulated persons traveling three weeks followed by one week at home.

N/A: non applicable.

Mobility and HIV are linked through increased sexual risk behavior. Mobile people are (temporarily or permanently) away from home, and also often from their cultural and social environments. This may lead to unfulfilled sexual needs when being without their regular partner, often together with a sense of anonymity and perceived sexual freedom.

They may meet other people and relatively easily start extramarital relationships or visit commercial sex workers [25].

The impact of migration on the risk of HIV infection has been recognized [26,27]. In Uganda, the highest HIV prevalence was found in people who had moved into the area during the previous three years [26]. A South African study showed that migration was an independent risk factor for HIV infection in men [27]. However, its impact on the total population level has not been assessed. Furthermore, the characteristics of migrants have not been studied in detail. More information on migrants may help to develop and implement HIV interventions for this specific group.

There is evidence that travel also leads to more risk behavior and HIV infection. In a study in Cameroon, traveling men reported more partners and more one-off contacts [28]. The prevalence of HIV in those men increased with time away from home. In a study in rural areas in West Africa, travelers more often reported to engage in casual sex [29]. Usually, it is assumed that men leaving their homes for a longer period of time may become infected and infect their wives when returning home [30-32]. However, it is also relevant to consider risk behavior of those staying behind. Due to loneliness, peer pressure, and lack of financial support, partners staying behind may engage in risky sexual behavior. A South African study investigated both men leaving their homes and their wives staying behind [32]. They found that in one-third of the couples with only one HIV-positive partner, the wife who stayed at home was the one infected. Clearly, understanding the risk behavior in both partners is essential for the successful implementation of HIV interventions.

Most studies looking at separation of married partners focus on work-related long-term absence of the male partner. In South Africa, HIV infection occurred twice as often in couples in which the male partner was absent compared to couples in which both partners were at home [32]. In Bangladesh, people living apart due to the husband's work reported more extramarital sex partners than those not living apart [33]. Not work-related reasons have not been studied. Understanding the sexual behavior in couples in which one of the partners is absent for other reasons, such as polygamy, may help improve the effectiveness of HIV intervention strategies.

HIV and AIDS may also lead to more mobility. This is called reverse causality. For HIV-positive people, avoiding stigmatization and travel to health clinics in another town for testing and antiretroviral treatment could be reasons to move. People with advanced stages of disease may travel for care or return home to die. Furthermore, after a death due to AIDS, the composition of a household changes: widows or widowers may leave the house, and other members may have to move due to loss of income. Reverse causality is not studied in this thesis.

1.3 HIV intervention strategies

Prevention through reducing risk behavior is the key in reducing HIV infection, since ART treatment coverage in the developing world remains low and after more than 20 years of research an effective vaccine is not yet available [34]. Moreover, ART does not cure the patient and the viral load may return to high levels after treatment is stopped. The different behavioral interventions to prevent HIV transmission are described below.

Health education can impact the HIV prevalence by changing risk behavior [35,36]. 'ABC campaigns' are an example of health education in which people are advised to delay sexual debut or abstain from sex (A from Abstinence), to reduce the number of partners and stick to one partner (B from Be faithful), and to use condoms (C from Condom use). Unfortunately, the ABC approach has only occasionally achieved significant behavior change and it continues to be debated among experts in HIV prevention [37].

Correct use of latex condoms reduces the risk of sexual transmission of HIV by about 85% [38,39]. If condoms are used consistently, the effectiveness can be as high as 95% [40]. Disadvantages of condoms are that they are not always accepted, and that they need a continuous supply [41]. Condoms are also not used if pregnancy is wanted. The use of condoms depends on the type of partner: it is often higher during commercial sex contacts than with regular partners [42,43]. The uptake of other physical barriers, such as female condoms [44-46] and diaphragms [47,48], has been modest [41]. Diaphragms may in the future play an important role as a mechanism to deliver antimicrobial or antiretroviral products [49].

The effect of the treatment of STDs on HIV incidence was studied in four community randomized trials. Three trials used improved case detection and treatment of symptomatic STDs: the Mwanza trial in Tanzania [50], the Masaka trial in Uganda [51] and the Manicaland trial in Zimbabwe [52]. The Rakai trial in Uganda [53] used periodic mass treatment of STDs. Only the trial in Mwanza showed a decreasing effect on the HIV incidence. Differences between the outcomes of the Mwanza trial and the trials in Uganda have been explained by the more established HIV epidemic in Uganda with lower risk behavior and less curable STD [54]. Obviously, treatment of STDs has value on its own, but the additional effect of reducing HIV infection may be limited.

Recent trials in Africa showed that male circumcision can halve the risk of HIV infection [55-57]. Consequently, experts from WHO and UNAIDS recommended that "male circumcision should now be recognized as an important additional intervention to reduce the risk of heterosexually acquired HIV infection in men" [58].

Pre-exposure prophylaxis (PrEP) seems promising [59-61]. PrEP means that HIV-negative people take antiretroviral drugs to prevent infection [59,60,62]. Using antiretroviral drugs as a preventive method has proven successful in prevention of mother-to-child transmission [63] and needle accidents (i.e. post-exposure prophylaxis [64]). Animal studies showed that PrEP may be partially effective in preventing HIV infection [65-67]. Clinical trials are currently ongoing to investigate safety and efficacy of PrEP use in humans. Preliminary results of the trial among sex workers in Ghana confirmed safety [68], but efficacy could not be determined due to low numbers of HIV infections. The first PrEP effectiveness data are anticipated in 2010 [69], and if favorable will most likely lead to implementation of PrEP services in AIDS control programs [70]. PrEP will have a direct individual effect in PrEP users, and may affect others indirectly by reduced HIV transmission. Accurate projections of the impact of PrEP on a population level may help policy makers in planning PrEP services.

It is important that new methods are developed for women to protect themselves, since it may be difficult for them to negotiate condom use. PrEP pills and microbicides are good options, since they can be used before sexual intercourse, and women themselves can be in control. Unfortunately, safe and effective microbicides have not been found yet. A recent review of microbicides trials showed that four trials were stopped prematurely due to poor safety and efficacy [71]. One completed trial showed no reduction in HIV acquisition and in an ongoing study a low dose trial arm was discontinued [71].

Some fear that the use of new HIV interventions may lead to risk compensation [72], i.e. the increase in risk behavior when people feel themselves protected by the new intervention [72]. This is especially important if new interventions are only partially effective, which most often is the case. Risk compensation due to a false sense of security has been reported in vaccine safety trials [73] and could also occur in male circumcision [56] and PrEP [74,75]. Additional information and education should be provided to people who visit health care centers to obtain their pills or to undergo circumcision. A recent study showed that participating in a PrEP trial in Ghana decreased risk behavior, probably as a consequence of counseling and associated condom provision [76].

The influence of mobility on HIV interventions

As explained in Section 1.2, mobility increases vulnerability and risk regarding HIV [26-29]. Sexual risk behavior can be influenced by health campaigns and other interventions. However, mobile persons may reduce the impact of these interventions because of non-participation (Figure 1.2). For example, persons who recently moved into an area may

not yet know where to buy condoms or may have limited access to health facilities for STD treatment. Also, prevention programs may not reach people who are absent.

Mobile people may be a small group in the population, but due to their risky behavior they can be disproportionally important in the transmission of HIV and other STDs. This means that targeting of mobile people may be effective in reducing HIV infection (Figure 1.2). Until now, the relation of mobile groups and HIV interventions has not been studied and it is unclear to what extent mobility reduces the impact of interventions and whether targeting is worthwhile.

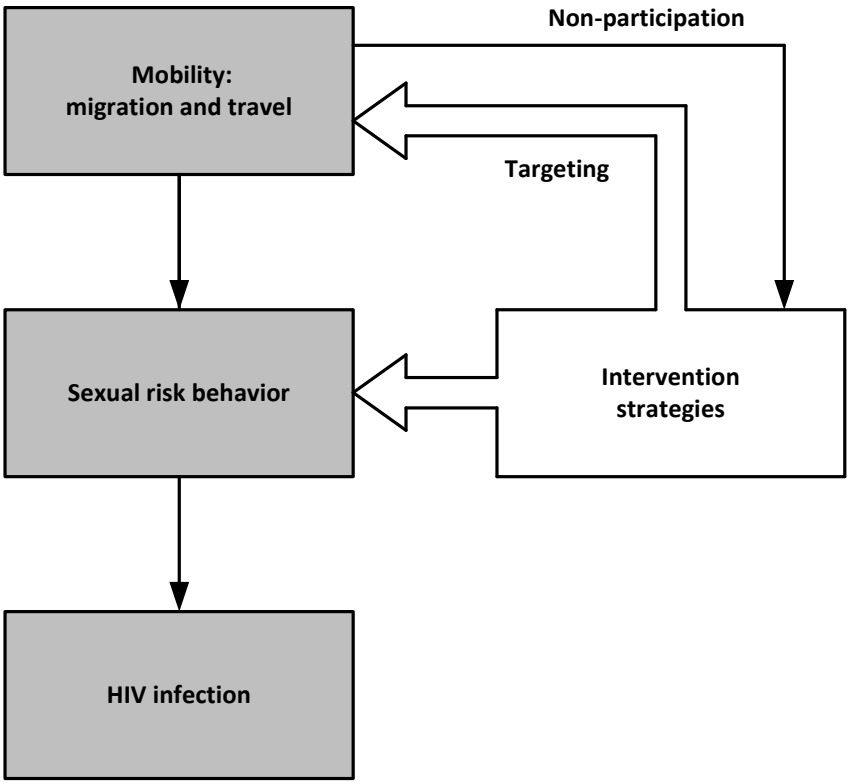

Figure 1.2 Relations between mobility, sexual behavior, HIV infection and interventions. Mobility leads to more risky behavior, leading to higher chances of getting HIV infection. Sexual behavior may be affected by intervention strategies (e.g. condom promotion or health education campaigns to reduce the number of partners). Mobility may reduce the effect of interventions. Targeting of mobile groups may reduce the risk behavior of this high-risk group, resulting in less HIV spread in the whole population.

1.4 Modeling HIV and mobility

Mathematical modeling can help in testing different hypotheses without using expensive and time-consuming empirical studies, although models require data input for parameter quantification and validation. Modeling the dynamics of transmission and control of HIV infection varies from simple deterministic models to complex individual-based microsimulation models. Patterns in sexual partnerships, including heterogeneity in sexual behavior within the population and age-mixing, can be fully captured in microsimulation models [77,78]. Furthermore, such models can realistically represent concurrent partnerships [79]. The disadvantages are that additional data input is required and that substantial computational capacity is needed [79].

Until now, the relation between mobility and HIV infection has not been studied in great detail with the use of mathematical models [79]. A deterministic model included the relation between migration, sexual risk behavior and HIV infection using data of migrant and non-migrant men and their rural partners in South Africa [80]. The results of this study showed that in a more mature epidemic mobility primarily increases HIV prevalence by increasing high-risk behavior. In starting epidemics, migrants may play a role by linking geographically separated areas [80]. An other deterministic model was used to study the impact of migration on declining HIV epidemics [81]. HIV prevalence showed a more marked decline if migration rates were greater.

The STDSIM model

The microsimulation model STDSIM describes the heterosexual transmission of HIV and other STDs, and the effect of various intervention methods [82]. STDSIM mimics the transmission of infection in a population at the level of individuals, who are represented by a number of characteristics, such as sex, date of birth, risk behavior, and status of infection and disease. Events such as acquisition of infection and progression of disease are determined by probability distributions. Consequently, model results are subject to random variation, so that STDSIM also represents the stochastic variation in the dynamics of epidemics. However, usually the combined result of repeated runs is used.

STDSIM consists of different modules (Figure 1.3) [82]. The demography module includes birth, death and migration, and determines the size and sex/age composition of the model population. The sexual behavior module describes how sexual relationships between individuals are established and dissolved, including commercial sex contacts between female sex workers and their clients. In the transmission module, transmission probabilities per type of contact and per gender for the different STDs are specified.

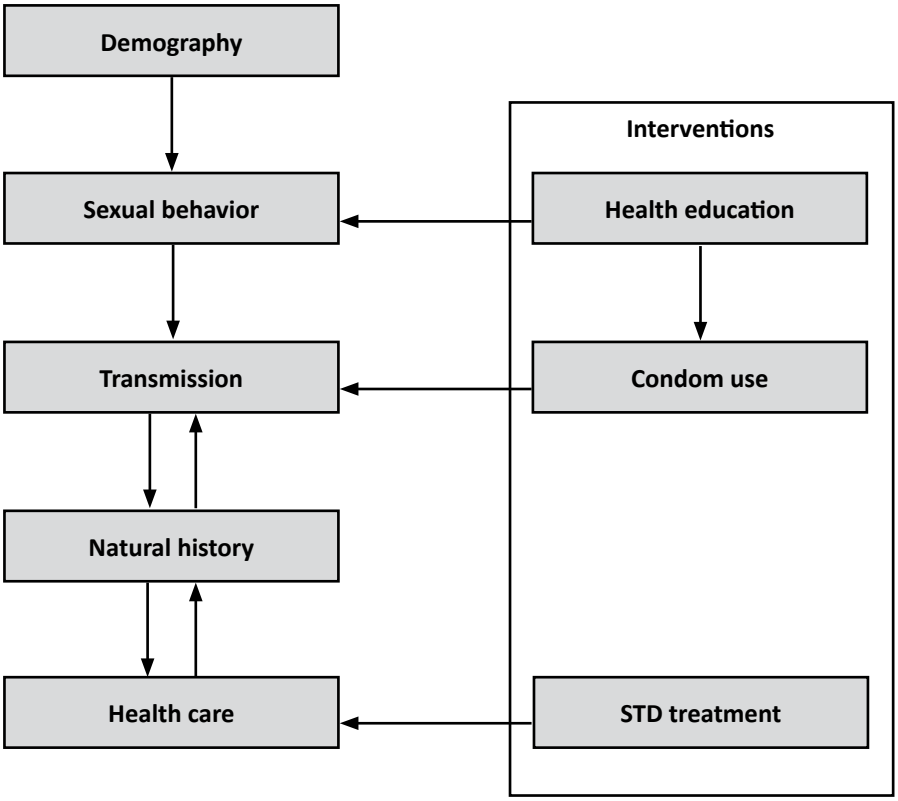

Figure 1.3 The modular structure of STDSIM.

For the transmission of HIV, the presence of cofactor STDs is taken into account. The natural history modules for each of the STDs describe the period of infectiousness and the time course to develop symptoms, in the absence of treatment. The health care module describes the tendency to seek health care, details of diagnostic tests used, and the effect of medical treatment. Finally, in the interventions module timing and effectiveness of control measures can be specified.

For the study in Chapter 6, we have extended STDSIM with detailed mobility options. Below, we first present a short history of STDSIM, followed by a brief description of the new mobility module.

Previous use of STDSIM

STDSIM has been used to study HIV epidemics under four hypothetical sexual behavior scenarios [83-85]. The simulated intervention strategies were condom use, STD treatment [83,84], and changes in risk behavior (e.g. reductions in partner change rate) [85]. These studies showed that concentrated risk behavior leads to a faster initial transmission of HIV, whereas the final HIV prevalence depends more on the level of dispersion of risk behavior into the general population [83-85]. Also, early interventions appeared to prevent more HIV infections [83,84].

STDSIM has also been used extensively to study the hypotheses explaining the contrasting outcomes of the trials on improved STD treatment described in Section 1.3 [86-90]. The impact of single-round mass treatment, sustained syndromic treatment and their combination on HIV incidence was tested in a scenario resembling the Mwanza-trial setting [86]. It turned out that mass treatment, in the short run, might have a comparable impact as sustained syndromic treatment. The transmission of STDs and HIV was also simulated using data from Rakai [87,88]. This revealed that behavior change could have contributed to a decreasing role of curable STDs in HIV transmission. STDSIM was also used to test whether population differences could explain the contrasting results of the Mwanza, Rakai and Masaka trials, suggesting that most of the contrasting results could be explained by differences in sexual behavior, rates of curable STDs and stage of the HIV epidemic in the different areas [54,90].

STDSIM has further been used to understand the differences between the contrasting HIV epidemics in East and West African cities [91,92]. It appeared that differences in male circumcision and in HSV-2 infection were the only factors that could explain why East African cities had a much higher HIV prevalence. The quantification parameterized for the African cities was also used to demonstrate that treating curable STDs and male circumcision may be cost-saving in populations with generalized HIV epidemics [93,94]. Modeling showed that HSV-2 therapy could potentially reduce HIV incidence [95]. The impact of an HSV-2 prophylactic vaccine was also studied with STDSIM [96], which suggested that it could become a potentially important HIV prevention strategy.

STDSIM and mobility

To model the impact of mobility on the transmission and control of HIV, the demography module of STDSIM was extended to mimic migration and travel in a more detailed way. A schematic overview of the mobility options is given in Figure 1.4. Various mobility parameters have to be quantified, including frequency and duration of travel, migration

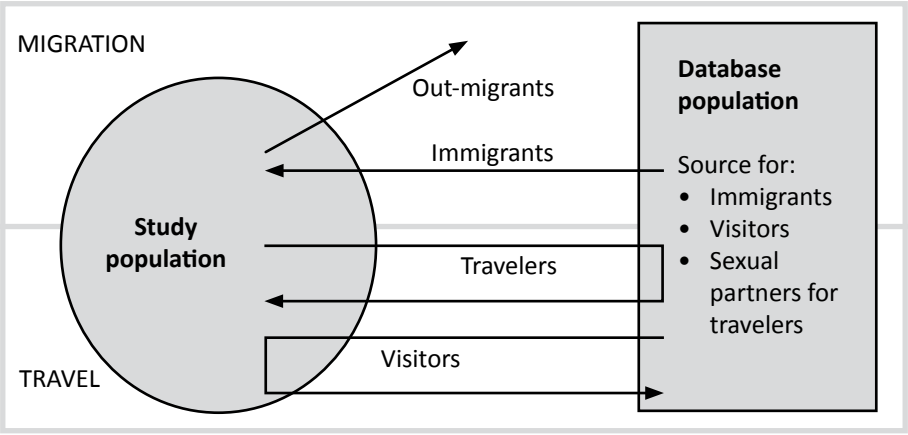

Figure 1.4 Schematic overview of modeling mobility in STDSIM, using a study population and a pre-stored database population. A specific run was done to fill the database population with simulated individuals. Immigrants to the study population are randomly selected from the database population. Out-migrants are removed from the study population. Travelers in the study population can have one-off (or commercial) sexual contacts with random persons (or sex workers) in the database population, during their travel. Furthermore, persons in the study population can have random one-off sexual contacts with visitors from the database population.

rate, and risk behavior of mobile people (e.g. frequency of visiting sex workers by travelers and immigrants). Furthermore, some degree of non-participation of mobile groups in different HIV intervention strategies can be assumed. The mobility options in STDSIM are described in more detail in Chapter 6.

1.5 Study locations in Africa

Three chapters of this thesis used data from cohort studies in Manicaland in Zimbabwe (Chapter 3) and in Kisesa in Tanzania (Chapters 4 and 5).

The Manicaland HIV/STD Prevention Project is a population-based cluster-randomized trial [97]. The study sites in the rural province of Manicaland in Eastern Zimbabwe are six pairs of communities matched by socio-economic type: two small towns, four commercial estates, two roadside trading settlements, and four subsistence farming areas (Figure 1.5) [98]. The total population size in the communities was about 36,000 in 1998, of which almost 12,000 were eligible for the study [52]. The intervention consisted of targeted and population level strategies to promote safer sexual behavior and to improve treatment of STDs that facilitate HIV transmission [52]. The study sites were randomly assigned to receive the intervention or to be a control site.

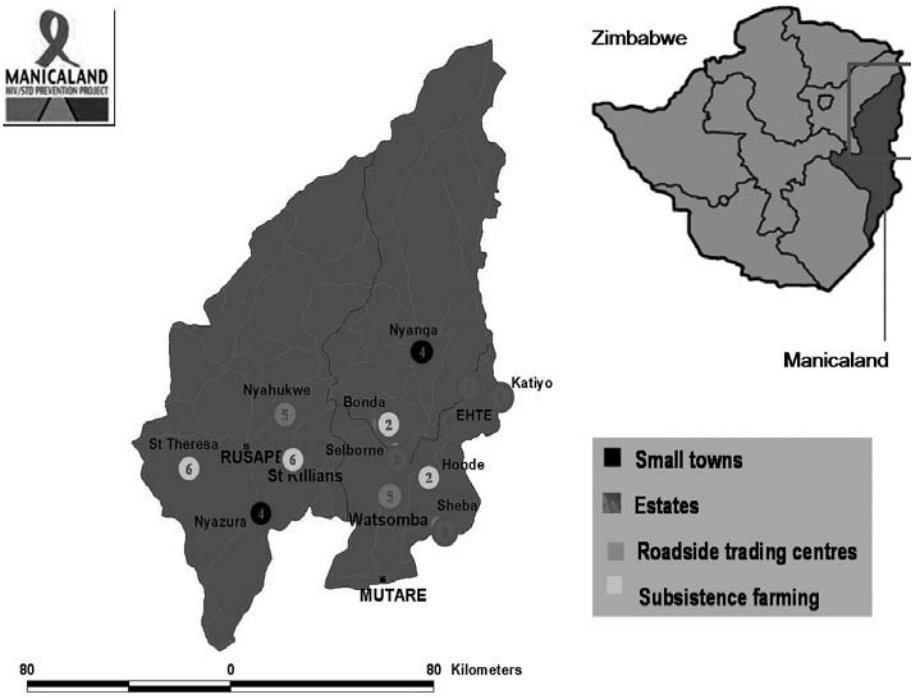

Figure 1.5 Manicaland, Eastern Zimbabwe.

All local residents were enumerated in a household survey in the first round (1998 to 2000, i.e. baseline survey). The second round was 3 years later (2001 to 2003, i.e. follow up survey) [98,99]. Per marital couple one member was randomly selected for enrolment in the study [98]. People were interviewed using a structured questionnaire for demographic, socio-economic and sexual behavior data, and were asked to provide dried blood spots for HIV testing.

The second cohort study is taking place in Kisesa ward in Mwanza region, situated in the northwest of Tanzania close to lake Victoria (Figure 1.6). A ward is an administrative entity that falls under a division of a district, and can be divided into smaller units, such as villages. Kisesa ward consists of a trading center, also called Kisesa, and six surrounding villages [100]. The trading center is located on the main transport route from Mwanza to Kenya. In 2000, the ward had a population of about 26,000 persons [101]. From 1994 onwards, demographic data of all inhabitants of Kisesa ward has been collected every year. In 1996/1997, 1999/2000 and 2003/2004, all adults were asked to attend an HIV survey [101]. Each participant provided information about sexual risk behavior, and their knowledge about STD and HIV, and a blood sample was taken for HIV testing. In 2003, there was additional data collection in a sub-sample of the cohort targeting couples.

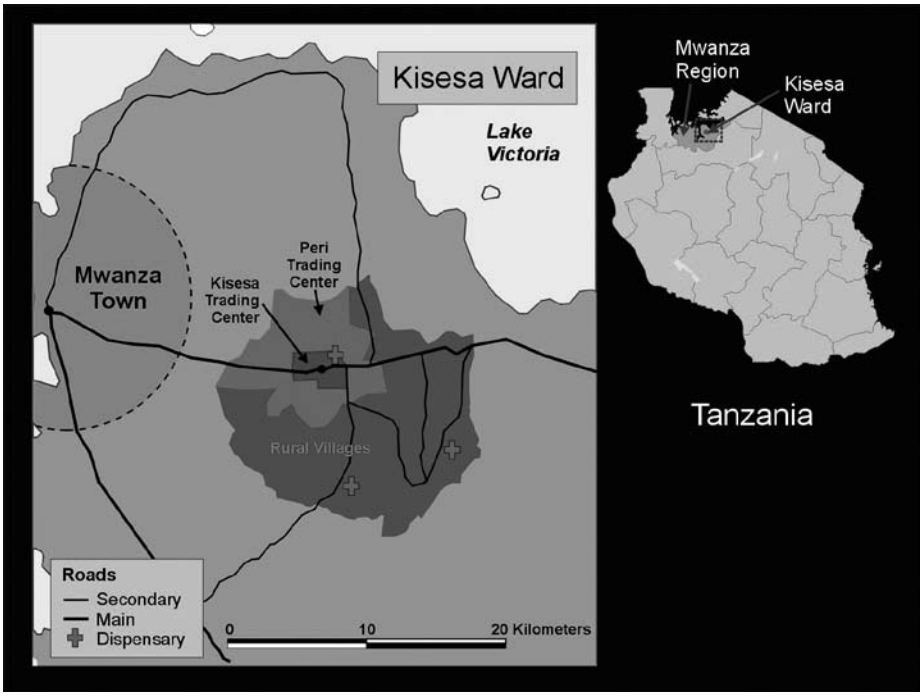

Figure 1.6 Kisesa ward in Mwanza region, Tanzania.

1.6 Aim, research questions and outline of the thesis

The overall aim of this thesis is to investigate the role of mobility on HIV transmission and control. We define the following specific research questions:

1. Can migration explain differences in spread of HIV in Africa?
2. Are migrants a selection of high-risk individuals?
3. Is mobility associated with sexual risk behavior?
4. How much do mobile groups reduce the effect of HIV interventions?

To answer the research questions, we perform an ecological analysis, analyze data from epidemiological cohort studies in Zimbabwe and Tanzania, and perform microsimulation modeling.

Chapter 2 of this thesis addresses research question 1. We compare the HIV prevalence in men and women in urban areas and the percentage of recent immigrants in such areas, comparing data of 28 countries in sub-Saharan Africa (ecological analysis).

Chapter 3 addresses research question 2 and describes characteristics of out-migrants and their influence on a mature HIV epidemic. We analyze two rounds of data from a

longitudinal cohort study in Eastern Zimbabwe. We compare the sexual risk behavior and HIV prevalence of persons who migrated before the second round and were followed up, and of those who stayed behind.

Chapters 4 and **5** address research question 3 and describe studies on the impact of mobility on the HIV prevalence in rural Tanzania. **Chapter 4** focuses on couples in which partners were resident, slept outside their household (travelers) or lived elsewhere (migrants). There is an emphasis on partners staying behind. We study the sexual risk behavior by own mobility status and by the mobility status of the partner. For **Chapter 5**, a specific sub-sample of the longitudinal cohort study in Kisesa is interviewed. This sub-sample consists of married couples living apart or still co-residing. We focus on the sexual risk behavior of these groups further subdivided by mobility behavior and visiting frequency.

Chapter 6 of this thesis addresses research question 4. We study different mobility aspects in the mature HIV epidemic of rural Tanzania using the STDSIM model. Besides the impact of migration, we also look at other mobility aspects, such as intensity of travel. This chapter focuses on three HIV interventions: condom promotion campaigns, health education programs to reduce the number of sexual partners, and STD treatment. We predict to which extent non-participation of mobile groups can reduce the effectiveness of these interventions.

As an additional topic involving modeling of HIV, **Chapter 7** describes the long-term impact of PrEP on HIV transmission in different epidemics in Africa and India. We also formulated different scenarios on condom use during PrEP (e.g. more or less condom use). This study was performed with an existing deterministic HIV transmission model.

In the General Discussion, the different research questions of this thesis are answered and commented on (**Section 8.1**). In addition, we explore the potential effect of targeting preventive interventions in travelers (**Section 8.2**). **Section 8.3** lists the general conclusions and recommendations of this thesis.

References

1. UNAIDS. Report on the global AIDS epidemic 2008; 2008. Available at: http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp.
2. UNAIDS. Zambia epidemiological fact sheet on HIV and AIDS: Core data on epidemiology and response (update). 2008. Available at: http://apps.who.int/globalatlas/predefinedReports/EFS2008/full/EFS2008_ZM.pdf.
3. UNAIDS. Zimbabwe epidemiological fact sheet on HIV and AIDS: Core data on epidemiology

and response (update). 2008. Available at: http://apps.who.int/globalatlas/predefinedReports/EFS2008/full/EFS2008_ZW.pdf.
4. UNAIDS. Namibia epidemiological fact sheet on HIV and AIDS: Core data on epidemiology and response (update). 2008. Available at: http://apps.who.int/globalatlas/predefinedReports/EFS2008/full/EFS2008_NA.pdf.
5. Colebunders RL, Latif AS. Natural history and clinical presentation of HIV-1 infection in adults. *AIDS* 1991; 5:S103-112.
6. Ambroziak J, Levy JA. Epidemiology, natural history, and pathogenesis of HIV infection (Ch.18). In: *Sexually Transmitted Diseases*. Edited by Holmes KK, Mardh P-A, Sparling PF*, et al.* 3rd ed. New York: McGraw-Hill Companies, Inc.; 1999.
7. Coovadia H. Antiretroviral agents – how best to protect infants from HIV and save their mothers from AIDS. *N Engl J Med* 2004; 351:289-292.
8. European study group on heterosexual transmission of HIV. Comparison of female to male and male to female transmission of HIV in 563 stable couples. *BMJ* 1992; 304:809-813.
9. Varghese B, Maher JE, Peterman TA, Branson BM, Steketee RW. Reducing the risk of sexual HIV transmission: quantifying the per-act risk for HIV on the basis of choice of partner, sex act, and condom use. *Sex Transm Dis* 2002; 29:38-43.
10. Malamba SS, Wagner HU, Maude G, Okongo M, Nunn AJ, Kengeya-Kayondo JF*, et al.* Risk factors for HIV-1 infection in adults in a rural Ugandan community: a case-control study. *AIDS* 1994; 8:253-257.
11. Cleland JG, Ali MM, Capo-Chichi V. Post-partum sexual abstinence in West Africa: implications for AIDS-control and family planning programmes. *AIDS* 1999; 13:125-131.
12. Cote AM, Sobela F, Dzokoto A, Nzambi K, Asamoah-Adu C, Labbe AC*, et al.* Transactional sex is the driving force in the dynamics of HIV in Accra, Ghana. *AIDS* 2004; 18:917-925.
13. Leclerc PM, Garenne M. Commercial sex and HIV transmission in mature epidemics: a study of five African countries. *Int J STD AIDS* 2008; 19:660-664.
14. Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. *AIDS* 1997; 11:641-648.
15. Halperin DT, Epstein H. Concurrent sexual partnerships help to explain Africa's high HIV prevalence: implications for prevention. *Lancet* 2004; 364:4-6.
16. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Infect* 1999; 75:3-17.
17. Rottingen JA, William Cameron D, Garnett GP. A systematic review of the epidemiologic interactions between classic sexually transmitted diseases and HIV: How much really is known? *Sex Transm Dis* 2001; 28:579-597.
18. Wasserheit JN. Epidemiological synergy. Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. *Sex Transm Dis* 1992; 19:61-77.
19. Freeman EE, Glynn JR. Factors affecting HIV concordancy in married couples in four African cities. *AIDS* 2004; 18:1715-1721.
20. McClelland RS, Sangare L, Hassan WM, Lavreys L, Mandaliya K, Kiarie J*, et al.* Infection with Trichomonas vaginalis increases the risk of HIV-1 acquisition. *J Infect Dis* 2007; 195:698-702.
21. Eron JJ, Gilliam B, Fiscus S, Dyer J, Cohen MS. HIV-1 shedding and chlamydial urethritis. *JAMA* 1996; 275:36.

22. Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC*, et al.* Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. *Lancet* 1997; 349:1868-1873.
23. Ghys PD, Fransen K, Diallo MP, Ettiegne-Traore V, Coulibaly I-M, Yeboue KM*, et al.* The associations between cervicovaginal HIV shedding, sexually transmitted diseases and immunosuppression in female sex workers in Abidjan, Cote d'Ivoire. *AIDS* 1997; 11:F85-F93.
24. Korenromp EL, De Vlas NJ, Nagelkerke NJD, Habbema JDF. Estimating the magnitude of STD cofactor effects on HIV transmission - how well can it be done? *Sex Transm Dis* 2001; 28:613-21.
25. Mbizvo MT, Machekano R, McFarland W, Ray S, Bassett M, Latif A*, et al.* HIV seroincidence and correlates of seroconversion in a cohort of male factory workers in Harare, Zimbabwe. *AIDS* 1996; 10:895-901.
26. Nunn AJ, Wagner HU, Kamali A, Kengeya-Kayondo JF, Mulder DW. Migration and HIV-1 seroprevalence in a rural Ugandan population. *AIDS* 1995; 9:503-506.
27. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sturm AW*, et al.* The impact of migration on HIV-1 transmission in South-Africa: a study of migrant men and non-migrant men and their partners. *Sex Transm Dis* 2003; 30:149-156.
28. Lydie N, Robinson NJ, Ferry B, Akam E, De Loenzien M, Abega S. Mobility, sexual behavior, and HIV infection in an urban population in Cameroon. *J Acquir Immune Defic Syndr* 2004; 35:67-74.
29. Lagarde E, Schim Van Der Loeff M, Enel C, Holmgren B, Dray-Spira R, Pison G*, et al.* Mobility and the spread of human immunodeficiency virus into rural areas of West Africa. *Int J Epidemiol* 2003; 32:744-752.
30. Pison G, Le Guenno B, Lagarde E, Enel C, Seck C. Seasonal migration: a risk factor for HIV infection in rural Senegal. *J Acquir Immune Defic Syndr* 1993; 6:196-200.
31. Decosas J, Adrien A. Migration and HIV. *AIDS* 1997; 11 (Suppl. A):S77-84.
32. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sweat MD*, et al.* Who infects whom? HIV-1 concordance and discordance among migrant and non-mirant couples in South Africa. *AIDS* 2003; 17:2245-2252.
33. Mercer A, Khanam R, Gurley E, Azim T. Sexual risk behavior of married men and women in Bangladesh associated with husbands' work migration and living apart. *Sex Transm Dis* 2007; 34:265-273.
34. Ferrantelli F, Cafaro A, Ensoli B. Nonstructural HIV proteins as targets for prophylactic or therapeutic vaccines. *Curr Opin Biotechnol* 2004; 15:543-556.
35. Shelton JD, Halperin DT, Nantulya V, Potts M, Gayle HD, Holmes KK. Partner reduction is crucial for balanced "ABC" approach to HIV prevention. *BMJ* 2004; 328:891-893.
36. Stoneburner RL, Low-Beer D. Population-level HIV declines and behavioral risk avoidance in Uganda. *Science* 2004; 304:714-718.
37. Collins C, Coates TJ, Curran J. Moving beyond the alphabet soup of HIV prevention. *AIDS* 2008; 22 (Suppl 2):S5-8.
38. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* 2002:CD003255.

39. NIAID. Scientific evidence on condom effectiveness for sexually transmitted disease (STD) prevention. 2001. Available at: http://www3.niaid.nih.gov/about/organization/dmid/PDF/condomReport.pdf.
40. Pinkerton SD, Abramson PR. Effectiveness of condoms in preventing HIV transmission. *Soc Sci Med* 1997; 44:1303-1312.
41. Padian NS, Buve A, Balkus J, Serwadda D, Cates W. Biomedical interventions to prevent HIV infection: evidence, challenges, and way forward. *Lancet* 2008; 372:585-599.
42. Lagarde E, Auvert B, Chege J, Sukwa T, Glynn JR, Weiss HA*, et al.* Condom use and its association with HIV/sexually transmitted diseases in four urban communities of sub-Saharan Africa. *AIDS* 2001; 15 (Suppl 4):S71-78.
43. Foss AM, Hossain M, Vickerman PT, Watts CH. A systematic review of published evidence on intervention impact on condom use in sub-Saharan Africa and Asia. *Sex Transm Infect* 2007; 83:510-516.
44. Fontanet AL, Saba J, Chandelying V, Sakondhavat C, Bhiraleus P, Rugpao S*, et al.* Protection against STD by granting sex workers in Thailand the choice of using the male or female condom: results from a randomized controlled trial. *AIDS* 1998; 12:1851-1859.
45. Feldblum PJ, Kuyoh MA, Bwayo JJ, Omari M, Wong EL, Tweedy KG*, et al.* Female condom introduction and sexually transmitted infection prevalence: results of a community intervention trial in Kenya. *AIDS* 2001; 15:1037-1044.
46. French PP, Latka M, Gollub EL, Rogers C, Hoover DR, Stein ZA. Use-effectiveness of the female versus male condom in preventing sexually transmitted disease in women. *Sex Transm Dis* 2003; 30:433-439.
47. Howell AL, Edkins RD, Rier SE, Yeaman GR, Stern JE, Fanger MW*, et al.* Human immunodeficiency virus type 1 infection of cells and tissues from the upper and lower human female reproductive tract. *J Virol* 1997; 71:3498-3506.
48. Pudney J, Quayle AJ, Anderson DJ. Immunological microenvironments in the human vagina and cervix: mediators of cellular immunity are concentrated in the cervical transformation zone. *Biol Reprod* 2005; 73:1253-1263.
49. Padian NS, van der Straten A, Ramjee G, Chipato T, de Bruyn G, Blanchard K*, et al.* Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. *Lancet* 2007; 370:251-261.
50. Grosskurth H, Mosha F, Todd J, Mwijarubi E, Klokke A, Senkoro K*, et al.* Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet* 1995; 346:530-536.
51. Kamali A, Quigley M, Nakiyingi J, Kinsman J, Kengeya-Kayondo J, Gopal R*, et al.* Syndromic management of sexually-transmitted infections and behaviour change interventions on transmission of HIV-1 in rural Uganda: a community randomised trial. *Lancet* 2003; 361:645-652.
52. Gregson S, Adamson S, Papaya S, Mundondo J, Nyamukapa CA, Mason PR*, et al.* Impact and process evaluation of integrated community and clinic-based HIV-1 control: a cluster-randomised trial in eastern Zimbabwe. *PLoS Med* 2007; 4:e102.
53. Wawer MJ, Sewankambo NK, Serwadda D, Quinn TC, Paxton LA, Kiwanuka N*, et al.* Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. *Lancet* 1999; 353:525-535.

54. Korenromp EL, White RG, Orroth KK, Bakker R, Kamali A, Serwadda D*, et al.* Determinants of the impact of sexually transmitted infection treatment on prevention of HIV infection: a synthesis of evidence from the Mwanza, Rakai, and Masaka intervention trials. *J Infect Dis* 2005; 191 (Suppl 1):S168-178.
55. Williams BG, Lloyd-Smith JO, Gouws E, Hankins C, Getz WM, Hargrove J*, et al.* The potential impact of male circumcision on HIV in sub-Saharan Africa. *PLoS Med* 2006; 3:e262.
56. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN*, et al.* Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet* 2007; 369:643-656.
57. Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F*, et al.* Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet* 2007; 369:657-666.
58. WHO. Male circumcision: an intervention for HIV prevention in the WHO African region. 2007. Available at: http://www.afro.who.int/aids/publications/male_circumcision_en.pdf.
59. Youle M, Wainberg MA. Pre-exposure chemoprophylaxis (PREP) as an HIV prevention strategy. *J Int Assoc Physicians AIDS Care* 2003; 2:102-105.
60. Smith SM. Pre-exposure chemoprophylaxis for HIV: it is time. *Retrovirology* 2004; 1:16.
61. Stephenson J. New HIV prevention strategies urged: averting new infections key to controlling pandemic. *JAMA* 2004; 292:1163-1164.
62. Grant RM, Buchbinder S, Cates W, Jr., Clarke E, Coates T, Cohen MS*, et al.* AIDS: Promote HIV chemoprophylaxis research, don't prevent it. *Science* 2005; 309:2170-2171.
63. Lallemant M, Jourdain G, Le Coeur S, Mary JY, Ngo-Giang-Huong N, Koetsawang S*, et al.* Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *N Engl J Med* 2004; 351:217-228.
64. Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D*, et al.* A case-control study of HIV seroconversion in health care workers after percutaneous exposure. Centers for Disease Control and Prevention Needlestick Surveillance Group. *N Engl J Med* 1997; 337:1485-1490.
65. Tsai CC, Follis KE, Sabo A, Beck TW, Grant RF, Bischofberger N*, et al.* Prevention of SIV infection in macaques by (R)-9-(2-phosphonylmethoxypropyl)adenine. *Science* 1995; 270:1197-1199.
66. Subbarao S, Otten RA, Ramos A, Kim C, Jackson E, Monsour M*, et al.* Chemoprophylaxis with tenofovir disoproxil fumarate provided partial protection against infection with simian human immunodeficiency virus in macaques given multiple virus challenges. *J Infect Dis* 2006; 194:904-911.
67. Denton PW, Estes JD, Sun Z, Othieno FA, Wei BL, Wege AK*, et al.* Antiretroviral pre-exposure prophylaxis prevents vaginal transmission of HIV-1 in humanized BLT mice. *PLoS Med* 2008; 5:e16.
68. Peterson L, Taylor D, Roddy R, Belai G, Phillips P, Nanda K*, et al.* Tenofovir disoproxil fumarate for prevention of HIV infection in women: A phase 2, double-blind, randomized, placebo-controlled trial. *PLoS Clin Trials* 2007; 2:e27.
69. Clearinghouse AV. PrEP Watch. 2007. Available at: http://www.prepwatch.org.
70. Paxton LA, Hope T, Jaffe HW. Pre-exposure prophylaxis for HIV infection: what if it works? *Lancet* 2007; 370:89-93.

71. Poynten M, Brown JM, Sovero M, Millwood IY, Kaldor JM. Microbicide safety and effectiveness: an overview of recent clinical trials. *Curr Opin HIV AIDS* 2008; 3:574-580.
72. Cassell MM, Halperin DT, Shelton JD, Stanton D. Risk compensation: the Achilles' heel of innovations in HIV prevention? *BMJ* 2006; 332:605-607.
73. Chesney MA, Chambers DB, Kahn JO. Risk behavior for HIV infection in participants in preventive HIV vaccine trials: a cautionary note. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997; 16:266-271.
74. Grant RM, Wainberg MA. Chemoprophylaxis of HIV infection: moving forward with caution. *J Infect Dis* 2006; 194:874-876.
75. Liu AY, Grant RM, Buchbinder SP. Pre-exposure prophylaxis for HIV: unproven promise and potential pitfalls. *JAMA* 2006; 296:863-865.
76. Guest G, Shattuck D, Johnson L, Akumatey B, Clarke EE, Chen PL*, et al.* Changes in sexual risk behavior among participants in a PrEP HIV prevention trial. *Sex Transm Dis* 2008; 35:1002-1008.
77. Morris M, Kretzschmar M. A microsimulation study of the effect of concurrent partnerships on the spread of HIV in Uganda. *IUSSP seminar on Measurement and modelling the spread of AIDS, Kopenhagen* 1998.
78. Ghani AC, Donnelly CA, Garnett P. Sampling biases and missing data in explorations of sexual partner networks for the spread of sexually transmitted diseases. *Stat Med* 1998; 17:2079-2097.
79. Cassels S, Clark SJ, Morris M. Mathematical models for HIV transmission dynamics: tools for social and behavioral science research. *J Acquir Immune Defic Syndr* 2008; 47 (Suppl 1):S34-39.
80. Coffee M, Lurie MN, Garnett GP. Modelling the impact of migration on the HIV epidemic in South Africa. *AIDS* 2007; 21:343-350.
81. Walker PT, Hallett TB, White PJ, Garnett GP. Interpreting declines in HIV prevalence: impact of spatial aggregation and migration on expected declines in prevalence. *Sex Transm Infect* 2008; 84 (Suppl 2):ii42-48.
82. Van der Ploeg CPB, Van Vliet C, De Vlas SJ, Ndinya-Achola JO, Fransen L, Van Oortmarssen GJ*, et al.* STDSIM: a microsimulation model for decision support on STD control. *Interfaces* 1998; 28:84-100.
83. Van Vliet C, Holmes K, Singer B, Habbema J. Effectiveness of HIV prevention strategies under alternative epidemiological scenarios: evaluation with the model STDSIM. In: *Confronting AIDS; public priorities in a global epidemic: background studies*. Edited by European Commission. Brussels: European Commission; 1998.
84. Van Vliet C, Meester EI, Korenromp EL, Singer B, Bakker R, Habbema JDF. Focusing strategies of condom use against HIV in different behavioural settings: an evaluation based on a simulation model. *Bull WHO* 2001; 79:442-454.
85. Korenromp EL, Van Vliet C, Bakker R, De Vlas SJ, Habbema JDF. HIV spread and partnership reduction for different patterns of sexual behaviour - a study with the microsimulation model STDSIM. *Math Popul Studies* 2000; 8:135-173.
86. Korenromp EL, Van Vliet C, Grosskurth H, Gavyole A, Van der Ploeg CPB, Fransen L*, et al.* Model-based evaluation of single-round mass treatment of sexually transmitted diseases for HIV control in a rural African population. *AIDS* 2000; 14:573-593.

87. Korenromp EL, Bakker R, Gray R, Wawer MJ, Serwadda D, Habbema JD. The effect of HIV, behavioural change, and STD syndromic management on STD epidemiology in sub-Saharan Africa: simulations of Uganda. *Sex Transm Infect* 2002; 78 (Suppl 1):i55-63.
88. Korenromp EL, Bakker R, de Vlas SJ, Gray RH, Wawer MJ, Serwadda D*, et al.* HIV dynamics and behaviour change as determinants of the impact of sexually transmitted disease treatment on HIV transmission in the context of the Rakai trial. *AIDS* 2002; 16:2209-2218.
89. Korenromp EL, Bakker R, De Vlas SJ, Robinson NJ, Hayes R, Habbema JDF. Can behaviour change explain increases in the proportion of genital ulcers attributable to herpes in sub-Saharan Africa? A simulation modelling study. *Sex Transm Dis* 2002; 29:228-238.
90. White RG, Orroth KK, Korenromp EL, Bakker R, Wambura M, Sewankambo NK*, et al.* Can population differences explain the contrasting results of the Mwanza, Rakai, and Masaka HIV/sexually transmitted disease intervention trials? A modeling study. *J Acquir Immune Defic Syndr* 2004; 37:1500-1513.
91. Freeman EE, Orroth KK, White RG, Glynn JR, Bakker R, Boily MC*, et al.* Proportion of new HIV infections attributable to herpes simplex 2 increases over time: simulations of the changing role of sexually transmitted infections in sub-Saharan African HIV epidemics. *Sex Transm Infect* 2007; 83 (Suppl 1):i17-24.
92. Orroth KK, Freeman EE, Bakker R, Buve A, Glynn JR, Boily MC*, et al.* Understanding differences between contrasting HIV epidemics in East and West Africa: results from a simulation model of the Four Cities Study. *Sex Transm Infect* 2007; 83 (Suppl 1):i5-16.
93. White RG, Orroth KK, Glynn JR, Freeman EE, Bakker R, Habbema JD*, et al.* Treating curable sexually transmitted infections to prevent HIV in Africa: Still an effective control strategy? *J Acquir Immune Defic Syndr* 2008; 47:346-353.
94. White RG, Glynn JR, Orroth KK, Freeman EE, Bakker R, Weiss HA*, et al.* Male circumcision for HIV prevention in sub-Saharan Africa: who, what and when? *AIDS* 2008; 22:1841-1850.
95. White RG, Freeman EE, Orroth KK, Bakker R, Weiss HA, O'Farrell N*, et al.* Population-level effect of HSV-2 therapy on the incidence of HIV in sub-Saharan Africa. *Sex Transm Infect* 2008; 84 (Suppl 2):ii12-18.
96. Freeman EE, White RG, Bakker R, Orroth KK, Weiss HA, Buve A*, et al.* Population-level effect of potential HSV-2 prophylactic vaccines on HIV incidence in sub-Saharan Africa. *Vaccine* 2009; 27(6):940-946.
97. Lopman B, Nyamukapa C, Mushati P, Mupambireyi Z, Mason P, Garnett GP*, et al.* HIV incidence in 3 years of follow-up of a Zimbabwe cohort – 1998-2000 to 2001-03: contributions of proximate and underlying determinants to transmission. *Int J Epidemiol* 2008; 37:88-105.
98. Gregson S, Garnett GP, Nyamukapa CA, Hallett TB, Lewis JJ, Mason PR*, et al.* HIV decline associated with behavior change in eastern Zimbabwe. *Science* 2006; 311:664-666.
99. Sherr L, Lopman B, Kakowa M, Dube S, Chawira G, Nyamukapa C*, et al.* Voluntary counselling and testing: uptake, impact on sexual behaviour, and HIV incidence in a rural Zimbabwean cohort. *AIDS* 2007; 21:851-860.
100. Boerma JT, Urassa M, Senkoro K, Klokke A, Ng'weshemi JZL. Spread of HIV infection in a rural area of Tanzania. *AIDS* 1999; 13:1233-1240.
101. Mwaluko G, Urassa M, Isingo R, Zaba B, Boerma JT. Trends in HIV and sexual behaviour in a longitudinal study in a rural population in Tanzania, 1994-2000. *AIDS* 2003; 17:2645-2651.

2 Strong association between immigration and HIV prevalence in urban sub-Saharan Africa

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Abstract

Background Enormous variation exists in HIV prevalence between countries in sub-Saharan Africa. The contribution of migration to the spread of HIV has long been recognized, but its effect at the population level has never been assessed. In this ecological analysis, we explore how much variation in HIV prevalence in urban sub-Saharan Africa is explained by immigration.

Methods We performed a linear regression to analyse the association between the proportion of recent immigrants and HIV prevalence for men and women in urban areas, using 60 data points from 28 sub-Saharan African countries between 1987 and 2005.

Results We found a strong association between recent immigration and HIV prevalence for women (Pearson R^2=57%, p<0.001) and men (R^2=24%, p=0.016), taking the earliest data point for each country. For women, the association was also strong within east/southern Africa (R^2=50%, p=0.003). For both genders, the association was strongest between 1985 and 1994, slightly weaker between 1995 and 1999, and non-existent as from 2000. The overall association for both men and women was not confounded by the developmental indicators GNI per capita, income inequalities, or adult literacy.

Conclusions Migration explains much of the variation in HIV spread in urban areas of sub-Saharan Africa, especially before the year 2000, after which HIV prevalences started to level off in many countries. Our findings suggest that migration is an important factor in the spread of HIV, especially in rapidly increasing epidemics. This may be of relevance to the current HIV epidemics in China and India.

Introduction

Enormous variation exists in HIV prevalence between countries in sub-Saharan Africa [1]. Furthermore, HIV prevalence is typically much higher in east and southern Africa than in the west and central regions of the subcontinent. This variation remains poorly understood, which is unfortunate since a clear understanding may aid identification of effective interventions. Cross-country comparison suggests that development is associated with more rapid and extensive spread of HIV in Africa [2,3]. Other studies suggest that biological factors, notably male circumcision [4-6] and HSV-2 infection [7,8] may be more important at the population level than differences in individual behavior [9,10].

The contribution of migration to the spread of HIV has long been recognised [11-15] but its effect at the population level has never been assessed. There have been various attempts to identify factors that explain the variation in HIV prevalence at the population level [10,16], but these did not look at migration. We present measurements of the association between immigration and HIV prevalence in urban areas for 28 countries in sub-Saharan Africa, based on data from Demographic and Health Surveys (DHS) [17] and HIV sentinel surveillance of pregnant women [18]. Separate analyses are presented for men and women, because immigration behavior may be different for men and women.

Methods

Data were analyzed for all publicly available DHS performed within sub-Saharan African countries before 2006 (i.e. between 1987 and 2005). The immigration level was derived from each DHS by calculating the proportions of male and female residents aged 15 to 49 years in urban areas (cities and towns) who had moved into their current place of residence in the last 12 months [17]. Thus, people moving *within* a town or city were not considered as recent migrants. HIV prevalence was derived from sentinel surveillance data by taking the median value reported for "major urban areas" (the capital city and other metropolitan areas) for the year(s) of the DHS survey(s), or by linear interpolation from adjacent years if no data were reported for the year of the DHS survey [18]. In total 12 of the 77 DHS were excluded because HIV data were lacking for the year of the DHS survey and could not be calculated by linear interpolation since a more recent or an older adjacent year was also lacking. Of the remaining 65 DHS, 5 were excluded because the question on immigration was not asked in the DHS. The remaining 60 data points, covering 28 countries, were included in the analysis for women. Following the same procedures, for men 42 data points covering 24 countries could be analyzed (the DHS initially covered women only).

For men and women in urban areas, we related immigration to HIV prevalence through linear regression, whereby Pearson R^2 reflects the proportion explained variance. If more than one DHS was performed in a country, we only included the earliest measure point in our overall analyses. To explore whether any found association could be due to differences between east/southern versus west/central Africa, we also analyzed the association within these regions, whereby countries were allocated to regions based on geographical proximity and existing UN regional groupings [19]. We also analyzed the association between HIV prevalence and immigration for each 5-year period (i.e. '85-'89, '90-'94, '95-'99, '00-'05). To avoid that some countries would have 2 data points within a 5-year period, some data points had to be allocated to an adjacent period (i.e. Ethiopia / Rwanda / Malawi '00 were allocated to '95-'99; Tanzania '99 was allocated to '00-'05).

Because migration is associated with socio-economic development, we adjusted our overall linear regression analyses for socio-economic factors, for both men and women. To this end, we included for each country Gross National Income (GNI) per capita [20,21], the Gini index (representing household inequalities) [22,23], and male or female literacy rate [22,24] as confounders in the linear regression analyses. In case data for the correct year (i.e. corresponding to the DHS measurement) were lacking for any of these three indicators, we included data of the nearest available year; for 80% of the data points, the figures differed less than 5 years. We also looked at interaction between the significant factors in the multivariate models for men and women, but there was no interaction.

We did not control our analyses for other possible population level determinants such as male circumcision, HSV-2 infection, or religion, because our focus was on migration and there was no a priori justification for expecting these determinants to confound the relationship between migration and HIV prevalence. Moreover, we did not include population age composition as a confounder in our multivariate model, because there was no univariate association between female urban HIV prevalence and the proportion of women in urban areas aged 15 to 24 year old, as derived from the DHS datasets (R^2=3%, p=0.4).

Results

We found a strong association between recent immigration and HIV prevalence for women (R^2=57%, p<0.001, n=28) and men (R^2=24%, p=0.016, n=24), taking the earliest data point for each country. Figure 2.1 shows the scatter-plot and the fitted regression line of HIV prevalence versus proportion recent immigrants for women, by country and by region. For women, the association remained strong when the analysis was restricted

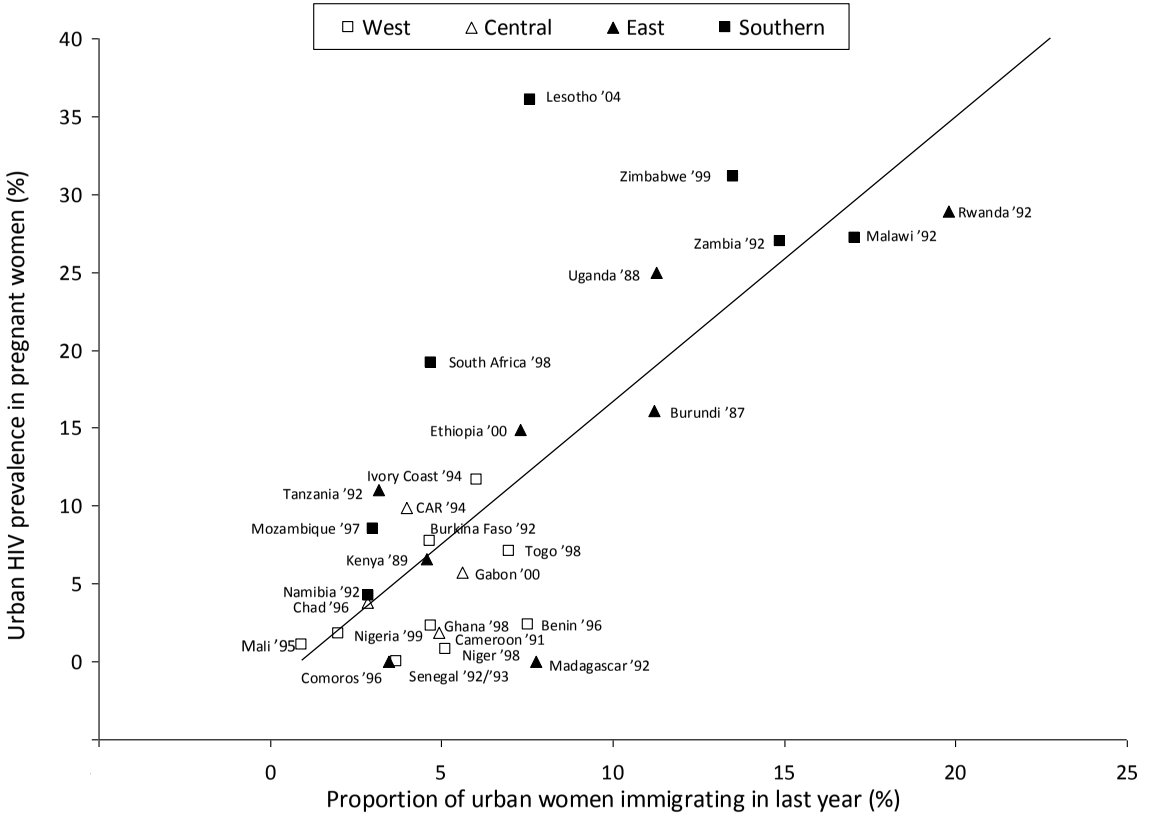

Figure 2.1 Association between urban HIV prevalence in pregnant women (derived from sentinel surveillance data) and proportion of urban women who immigrated in the last year (derived from Demographic and Health Surveys), for 28 sub-Saharan African countries (R^2=57%, p<0.001). The association remains strong when the analysis is restricted to countries in east / southern Africa (R^2=50%, p=0.003).

to countries in east/southern Africa (R^2=50%, p=0.003, n=15); for west/central Africa, where the variation in HIV prevalence is small, there was no association (R^2=13%, p=0.2, n=13). For men, there was no association in either region.

We analyzed the 60 and 42 data points for women and men respectively by 5-year period. The association between immigration and HIV prevalence was strongest in the late eighties (R^2=88%, p=0.061, n=4 for women; no data available for men in this period) and early nineties (R^2=75%, p<0.001, n=15 for women; and R^2=74%, p=0.06, n=5 for men). The association slightly declined in the late nineties (R^2=43%, p=0.001, n=22 for women; and R^2=32%, p=0.01, n=19 for men). After the year 2000, there was no association between immigration and HIV prevalence, for women (R^2=1%, p=0.7, n=19) or men (R^2=4%, p=0.4, n=18).

We included GNI per capita, the Gini index, and female literacy rate as possible confounders in the overall regression models for men and women. In the multivariate model for women, recent immigration remained very strongly associated with HIV prevalence (p<0.001); none of the confounders was significantly associated with HIV prevalence, although R^2 increased from 57% to 67%. In univariate analyses, female literacy explained 20% of the variance in HIV prevalence (p=0.02) whereas GNI per capita and the Gini index were not significant. In the multivariate model for men, immigration remained very strongly associated with HIV prevalence (p=0.006), whereas male literacy (p=0.010) and the Gini index (p=0.04) were also significant and R^2 increased from 24% to 53%. In univariate analyses, male literacy explained 20% of the variance in HIV prevalence (p=0.03), whereas GNI per capita or the Gini index were not significant. Of the variables that we considered, recent immigration had the strongest association with HIV prevalence for women as well as men, and potential socio-economic confounders could not account for this effect.

Discussion

In this exploratory ecological analysis of data from 28 countries in sub-Saharan Africa, we found an unexpectedly strong association (R^2=57%, p<0.001) between the proportion of recent female immigrants and HIV prevalence for urban areas. Differences in urban HIV prevalence within the east/southern region were also highly associated with the proportion of female recent immigrants. The association between immigration and HIV prevalence was strongest in the late eighties and early nineties, when the HIV epidemic rapidly increased in many countries. The association disappeared after the year 2000, probably because the HIV epidemic leveled off in many countries due to sexual behavior

change and selective AIDS-induced mortality. The difference between women and men in the overall analyses (R^2=57% versus R^2=24%), proved to be largely due to the fact that most data points for men were more recent than for women; when stratifying data by 5-year period the R^2 for men and women was comparable.

Our study is the first that demonstrates a strong association between immigration and the spread of HIV at the population level. The observed association could not be explained by confounding with socio-economic development. Economic development often results in higher mobility due to labour migration and improvement in transport infrastructure [3,11, 14]. However, large-scale migration also occurs independently of development (e.g. in times of war and famine) and some aspects of development may constrain the spread of HIV (e.g. greater access to secondary education could facilitate the spread of HIV awareness [25,26]).

In our study we only took confounding by socio-economic development into account, because this is a priori associated with migration. Confounding by other factors such as male circumcision, HSV-2 infection or religion were not taken into account, because this was beyond the scope of our study. Nevertheless, it would be interesting to see if the association between migration and HIV prevalence is confounded by the mentioned factors.

A well-known limitation of ecological analyses is the inability to indicate the direction of causality. The association could also result if larger HIV epidemics induce or intensify migration. Although few studies indicate such a reverse-causal mechanism [27,28], possible results from large HIV epidemics – such as job loss, widowhood and returning home to be cared for or to die – would mean that most people move from urban to rural areas rather than vice versa [29]. On the other hand, a strong causal link between migration into cities and the spread of HIV at the population level is highly plausible. Migration enhances casual and commercial contacts, because of spousal separation and the weaker social control in towns [30-33]. Armed conflicts can increase the risk of HIV infection due to rape, disruption of sexual norms, collapse of health systems, and lack of access to condoms [1]. Moreover, migration increases the size of sexual networks by linking networks from different locations [34].

Our study has more limitations. Sentinel surveillance data are biased towards high-prevalent sites and they reflect HIV prevalence in (pregnant) women rather than men [35]. National data on male HIV prevalence have been lacking till recently, when DHS+ started to collect HIV prevalence data in national representative samples [36]. Because these data have been collected for only a dozen of countries in sub-Saharan Africa, and all but one after the year 2000, we could not use them for our analyses. Furthermore, we

linked migration in "urban areas" as defined in DHS to HIV prevalence in "major urban areas" as defined in sentinel surveillance, which may not completely overlap. Another limitation is that the figures for the socio-economic confounders could often not be found for the correct year (i.e. the year of the DHS), nor adjacent years. Lastly, since one would expect a delay between migration and HIV infection if assuming a causal link through high-risk sexual behavior, we alternatively could have included people who moved longer than a year ago. We performed these analyses, including people who immigrated in the last 5 years, and found similar results as for immigration in the past year.

Although our analyses are exploratory, the results are striking. They suggest that immigration has been an important factor in the spread of HIV in sub-Saharan Africa, especially in the rapidly increasing epidemics of eastern and southern Africa. This finding may be of relevance to other rapidly increasing HIV epidemics such as currently in China and India. Because of its potential importance, further study of the mechanisms underlying the association between immigration and HIV prevalence is recommended.

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References

1. UNAIDS. *2006 report on the global AIDS epidemic*. Gevena: 2006.
2. Gregson S, Waddell H, Chandiwana, SK. School education and HIV control in sub-Saharan Africa: from discord to harmony? *J Int Development* 2001; 13:467-485.
3. Whiteside A. How the transport sector drives HIV/AIDS and how HIV/AIDS drives transport. *AIDS Anal Afr* 1998; 8:5-6,15.
4. Auvert B, Buve A, Lagarde E, *et al*. Male circumcision and HIV infection in four cities in sub-Saharan Africa. *AIDS* 2001; 15 (Suppl 4):S31-40.
5. Moses S, Bradley JE, Nagelkerke JCD, *et al*. Geographical patterns of male circumcision practices in Africa: association with HIV seroprevalence. *Int J Epidemiol* 1990; 19:693-697.
6. Orroth KK, Freeman EE, Bakker R, *et al*. Understanding differences between contrasting HIV epidemics in East and West Africa: results from a simulation model of the Four Cities Study. *Sex Transm Inf* 2007; 83 (Suppl 1):i5-16.
7. Abu-Raddad LJ, Magaret AS, Celum C, *et al*. Genital herpes has played a more important role than any other STI in driving HIV prevalence in Africa. *PLoS ONE* 2008; 3:e2230.
8. Weiss HA, Buvé A, Robinson NJ, *et al*. The epidemiology of HSV-2 infection and its association with HIV infection in four urban African populations. *AIDS* 2001; 15 (Suppl 4):S97-108.

9. Buvé A, Carael M, Hayes RJ, *et al*. The multicentre study on factors determining the differential spread of HIV in four African cities: summary and conclusions. *AIDS* 2001; 15 (Suppl 4):S127-31.
10. Drain PK, Smith JS, Hughes JP, *et al*. Correlates of National HIV Seroprevalence: An Ecologic Analysis of 122 Developing Countries . *J Acquir Immune Syndr* 2004; 35:407-420.
11. Hunt CW. Migrant labor and STD: AIDS in Africa. *J Health Soc Behav* 1989; 30:353-373.
12. Lurie M, Williams BG, Zuma K, *et al*. The impact of migration on HIV-1 transmission in South-Africa: a study of migrant men and non-migrant men and their partners. *Sex Transm Dis* 2003; 30: 149-56.
13. Nunn AJ, Wagner HU, Kamali A, *et al*. Migration and HIV-1 seroprevalence in a rural Ugandan population. *AIDS* 1995; 9:503-6.
14. Pison G, Le Guenno B, Lagarde E, *et al*. Seasonal migration: a risk factor for HIV infection in rural Senegal. *J Acquir Immune Defic Syndr* 1993; 6:196-200.
15. Quinn TC. Population migration and the spread of types 1 and 2 human immunodeficiency viruses. *Proc Natl Acad Sci U S A* 1994; 91:2407-14.
16. Over M. The effect of societal variables on urban rates of HIV infection in developing countries: an exploratory analysis. In: *Confronting AIDS: Evidence from the developing world; Selected background papers for the World Bank Policy Research Report, Confronting AIDS: Public priorities in a global epidemic*. Ainsworth M, Fransen L, Over M (editors). Luxemburg: Office for the official publications of the European Communities; 1998. pp.39-51.
17. Measure DHS. *Demographic and Health Surveys.* Available at: http://www.measuredhs.com/.
18. UNAIDS. *Epidemiological fact sheets on HIV/AIDS and Sexually TransmittedInfections*. 2008 update (and 2006 update; 2004 update; 2002 update; 2000 update). Available at: http://www.who.int/GlobalAtlas/predefinedReports/EFS2008/index.asp.
19. United Nations Statistics Division *Standard Country and Area Codes Classification (M49)*. Available at: http://millenniumindicators.un.org/unsd/methods/m49/m49regin.htm.
20. The Worldbank. *World Development Indicators.* Available at: http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20398986~isCURL:Y~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html.
21. UC Atlas of Global Inequality. *Atlas of Global Inequality Database*. Available at: http://ucatlas.ucsc.edu/gnp/gnp.html.
22. United Nations Development Programme. *Human Development Reports.* Available at: http://hdr.undp.org/en/reports/global/hdr2007-2008/.
23. United Nations University World Institute for Development Economics Research *World Income Inequality Database*. Available at: http://www.wider.unu.edu/research/Database/en_GB/wiid/.
24. United Nations Statistics Division *Common Database.* Available at: http://unstats.un.org/unsd/cdb/cdb_series_xrxx.asp?series_code=25600.
25. JR Glynn, M Carael, A Buve, *et al*. Does increased general schooling protect against HIV infection? A study in four African cities. *Trop Med Int Health* 2004; 9:4-14.
26. Michelo C, Sandoy I, Fylkesnes K. Marked HIV prevalence declines in higher educated young people: evidence from population-based surveys (1995-2003) in Zambia. *AIDS* 2006; 20:1031-1038.
27. Knodel J, VanLandingham M. Return migration in the context of parental assistance in the AIDS epidemic: the Thai experience. *Soc Sci Med* 2003; 57:327-42.

28. London AS, Wilmoth JM, Fleishman JA. Moving for care: findings from the US HIV cost and services utilization Study. *AIDS Care* 2004; 16:858-75.
29. Clark SJ, Collinson MA, Kahn K, *et al*. Returning home to die: circular labour migration and mortality in South Africa. *Scand J Public Health Suppl* 2007; 69:35-44.
30. Chirwa WC. Migrant labour, sexual networking and multi-partnered sex in Malawi. *Health Transit Rev* 1997; 7 (Suppl 3):5-15.
31. Kishamawe C, Vissers DC, Urassa M, *et al*. Mobility and HIV in Tanzanian couples: both mobile persons and their partners show increased risk. *AIDS* 2006; 20:601-8.
32. Coffee MP, Garnett GP, Mlilo M, *et al*. Patterns of movement and risk of HIV infection in rural Zimbabwe. *J Infect Dis* 2005; 191 (Suppl 1):S159-67.
33. Bassett MT, Mhloyi M. Women and AIDS in Zimbabwe: the making of an epidemic. *Int J Health Serv* 1991; 21:143-56.
34. Ghani AC, Swinton J, Garnett GP. The role of sexual partnership networks in the epidemiology of gonorrhea. *Sex Trans Dis* 1997; 24:45-56.
35. Zaba B, Boerma T, White R. Monitoring the AIDS epidemic using HIV prevalence data among young women attending antenatal clinics: prospects and problems. *AIDS* 2000; 14:1633-45.
36. Mishra V, Vaessen M, Boerma JT, *et al*. HIV testing in national population-based surveys: experience from the Demographic and Health Surveys. *Bull World Health Organ* 2006; 84:537-45.

3 No difference in HIV incidence and sexual behavior between out-migrants and residents in rural Manicaland, Zimbabwe

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Abstract

Background Migration is associated with HIV infection, but the relationship is mostly assessed in cross-sectional studies. In this prospective study, we investigated whether out-migrants are a selection of high-risk individuals and whether rural-to-urban migration results in risky sexual behavior for HIV incidence.

Methods A population cohort was enrolled in a stratified household census in four different community types in Manicaland, east Zimbabwe, between July 1998 and February 2000, and followed-up after three years. Out-migrants to the national capital (Harare), the provincial capital (Mutare) and other study areas were followed-up. A structured questionnaire was administered and an HIV test conducted at each interview. HIV prevalence and sexual risk behavior at baseline, and HIV incidence and sexual behavior during follow-up were compared for out-migrants and residents.

Results At baseline, future migrants were significantly younger, better educated and more likely to be single than residents. For men, migration was highest from subsistence farming areas and roadside trading centres and lowest from estates. After adjusting for age, education, marital status, and location, there were no differences in HIV prevalence and sexual risk behavior between future migrants and residents at baseline, for either sex. No significant differences in HIV incidence or sexual behavior during follow-up were detected between rural-to-urban out-migrants and residents.

Conclusions Out-migrants from rural Zimbabwe did not have higher levels of HIV infection or sexual risk behavior than residents either before or after they moved. These findings may be related to the mature stage of the HIV epidemic and the social and living conditions of migrants in Zimbabwean cities.

Introduction

Migration plays a significant role in the spread of HIV/AIDS [1,2]. It has been shown that migration and mobility can increase vulnerability to HIV infection [3-6] – both for those who are mobile [1,7,8,9] and for their partners back home [10,11]. However, patterns of vulnerability to HIV associated with migration may alter over time in large-scale widely disseminated epidemics, so data are needed on this relationship in a range of epidemiological settings.

Most of the studies done to date have been cross-sectional in design, and therefore, it has not been possible to distinguish the effects of selective migration amongst high-risk groups and increased risk behavior following migration [12]. However, the link between mobility and HIV/AIDS is believed to be related to the conditions and structure of the migration process, including poverty, exploitation, separation from families and partners, and separation from the socio-cultural norms that guide behaviors in stable communities [13,14]. Isolation, discrimination, differences in languages and culture, lack of support and friendship, a sense of anonymity and lack of access to sexually transmitted diseases (STD) and other health services are some of the factors that make mobile populations more vulnerable to HIV infection [15].

The current study was conducted using data from two successive rounds (baseline and follow-up) of a stratified population-based cohort study in rural Manicaland, Zimbabwe. Data at follow-up included information on a sample of individuals seen at baseline who migrated to Harare (the national capital), to Mutare (the provincial capital of Manicaland close to the border with Mozambique), or within the study areas. The aims of the study were twofold.

The first aim was to investigate whether migrants were a selection of high-risk individuals before they moved or a random sample of the population. We assessed this by comparing baseline HIV prevalence and sexual risk behavior between future migrants and residents. Future migrants may be people who have more partners – either because they are risk-takers or because they are poor and driven disproportionately into survival sex – which could explain the higher odds ratios for HIV among migrants observed in cross-sectional studies. The second aim was to investigate whether, in a mature epidemic, such as that in Zimbabwe at the turn of the new millennium, the migration process still has an impact on the spread of HIV infection. We assessed this by comparing HIV incidence and associated risk behaviors in residents and a sample of out-migrants.

Methods

A cohort of 9,843 adults in 12 communities was studied in eastern Zimbabwe. The communities (four rural subsistence farming areas, n=3,310; four commercial farming estates, n=3,217; two roadside trading centres, n=1,677; and two small towns, n=1,639) were selected to represent different types of communities in rural Zimbabwe. Data were collected in two successive rounds, baseline (July 1998 to February 2000) and follow-up (July 2001 to February 2003).

During both rounds, data were collected on socio-demographic characteristics and sexual behavior of men aged 17–54 years and women aged 15–44 years old, using a structured questionnaire, after informed and signed consent. Data collected included information on location, socio-economic status, education, recent movement / mobility patterns, marital status, and information on sexual partnerships and frequency of unprotected sex. In the study, 'sexual intercourse' was defined as penetrative vaginal sex and 'casual sex' was defined as sexual intercourse with a cohabiting or non-cohabiting partner with whom the respondent had been having sex for <1 year.

A voting box system was used to improve the reliability of sensitive information on sexual behavior by reducing embarrassment and increasing confidentiality [16]. Participants were also asked to give a dried blood spot (DBS) sample, which was tested for HIV infection using a dipstick-dot immunoassay [17]. To ensure confidentiality of HIV results, participants were assigned unique numbers that were attached to the DBS sample. Free voluntary counseling and testing for HIV and free STD treatment were offered to all study participants.

At baseline, 9,843 (4,419 men and 5,424 women) individuals (80% of those eligible) were interviewed and provided a blood sample. At follow-up, 5,552 (56%) individuals (2,292 men and 3,260 women) were still resident and were interviewed, 374 had died, 41 refused, 23 were in hospital, and 2,344 were said to have out-migrated. In addition, 297 were not found and for 1,212 individuals, their baseline households could no longer be found.

We were able to find out where 1,816 (77%) of the 2,344 migrants had gone: 581 (32%) were said to have moved to Harare; 207 (11%) to Mutare; 249 (14%) within, between or close to the study sites; and 779 (43%) to other areas. Due to financial and logistical constraints, only migrants who moved to either Harare or Mutare or within, between or close to the 12 study communities were followed-up. Of those with known destinations, 321 (36%) were interviewed – 107 (19%) in Harare, 95 (47%) in Mutare, and 119 (48%) in and close to study areas. The main reasons for the low follow-up rates were that

most migrants who moved to Harare and Mutare did not have known fixed addresses and that some of those who did, had subsequently moved again to either new or unknown locations.

Data processing in both rounds was done in SPSS/PC+ for DOS and data analysis was done using Stata Version 8 (Stata Corporation, College Station, Texas, USA). The chi-squared test and the negative binomial test were used to assess the statistical significance of differences in socio-demographic and sexual behavior variables, respectively, at baseline, between future migrants and residents, and between future migrants followed-up and not followed-up. Because migrants were younger, marital status and sexual behavior were adjusted for age.

Multivariate logistic regression was used to explore the relationships between subsequent out-migration and HIV prevalence at baseline, and differences in baseline characteristics between (future) migrants and residents as well as between future migrants followed-up and not followed-up, controlling for location, age, marital status, and education. A Cox regression model was used to compare HIV incidence at follow-up assuming sero-conversion occurred halfway through the follow-up period. Due to the small numbers of sero-conversions observed, dichotomized sexual behavior variables were investigated as secondary outcomes in separate logistic regression models.

Results

At baseline, future migrants were significantly younger and had higher education levels than residents (Table 3.1). For men, migration was highest from subsistence farming areas and roadside trading centres and lowest from estates, relative to the distribution of the residents over the different locations. For women, there were no differences in migration rates between locations. Future migrants were also more likely to be single and to have fewer lifetime partners, but, after controlling for age, these differences disappeared.

No differences were found between future migrants followed-up and not followed-up in the study, except for source location for women (Table 3.1). Women who migrated from towns had low follow-up rates, whereas women who migrated from subsistence farming areas had high follow-up rates.

Male and female future migrants had lower HIV prevalence at baseline than residents. However, after adjusting for location, age, education, and marital status, this difference disappeared, and no differences were found in past or current sexual behavior between future migrants and residents (Table 3.2). Male migrants followed-up had significantly

Table 3.1 Socio-demographic characteristics and sexual behavior at baseline, by sex, of future migrants (by follow-up status) and residents.

	Men						Women					
				Future migrants						Future migrants		
	Future migrants	Residents		FU	NFU		Future migrants	Residents		FU	NFU	
	n=1110	n=2292	p-value[a]	n=140	n=970	p-value[a]	n=1234	n=3260	p-value[a]	n=181	n=1053	p-value[a]
Age (years)												
15–19	36	19	<0.001	34	37	0.6	46	17	<0.001	43	47	0.6
20–24	33	21		33	32		25	17		24	25	
25–29	14	19		13	14		14	17		15	13	
30+	17	41		21	17		15	49		18	15	
Location												
Rural/subsistence	41	27	<0.001	43	40	0.2	43	40	0.3	53	41	0.01
RTC	18	12		16	18		21	21		19	21	
Estates	28	45		33	27		23	27		22	23	
Town	14	16		9	14		13	12		5	14	
Employment status												
Unemployed	79	72	0.06	80	79	0.05	90	90	0.6	85	92	0.05
Manual	15	19		19	14		4	4		10	3	
Skilled	1	9		1	8		5	6		6	5	
Education level												
None	1	2	<0.01	0	1	0.2	2	4	<0.01	3	2	0.5
Primary	22	33		18	22		27	48		24	28	
Secondary/higher	77	65		82	76		71	48		73	70	
Marital status												
Single	73	45	0.1	70	73	0.1	49	16	0.01	44	50	0.6
Married	24	50		29	23		36	64		39	35	
Divorced/separated	4	5		1	4		15	19		17	15	

Table 3.1 (continued).

	Men						Women					
				Future migrants						Future migrants		
	Future migrants	Residents		FU	NFU		Future migrants	Residents		FU	NFU	
	n=1110	n=2292	p-value[a]	n=140	n=970	p-value[a]	n=1234	n=3260	p-value[a]	n=181	n=1053	p-value[a]
Lifetime partners												
0–1	38	25	0.2	38	39	0.4	76	71	0.1	81	75	0.1
2–4	27	30		28	26		21	24		15	22	
5–9	19	25		21	18		2	3		4	2	
10+	16	20		13	16		1	2		1	1	
Partners in last year												
0–1	68	68	0.03	70	68	0.5	96	96	0.4	97	96	0.3
2–4	25	27		24	25		4	3		3	4	
5–9	45	4		4	4		0	1		0	0	
10+	3	1		2	3		0	0		0	0	
Partners in last month												
0–1	92	91	0.5	92	92	0.7	99	98	0.2	99	99	0.7
2–4	7	9		8	7		1	1		0	1	
5–9	1	0		0	1		0	0		1	0	
10+	0	0		0	0		0	0		0	0	
Current sex partners												
0–1	92	91	0.5	92	92	0.8	99	98	0.2	99	99	0.8
2–4	7	9		8	7		1	1		0	1	
5–9	1	0		0	1		0	0		1	0	
10+	0	0		0	0		0	0		0	0	

Values represent percentages.
NFU, not followed-up; FU, followed-up; RTC, roadside trading centre.
[a] Chi-squared test for socio-demographic characteristics and negative binomial test for sexual behavior, both adjusted for age.

Table 3.2 HIV prevalence and sexual risk behavior at baseline in future migrants (by follow-up status) and residents in (a) men and (b) women.

	Future migrants versus residents				Future migrants followed-up versus not followed-up			
Characteristic	FM, % (n)	RES, % (n)	aOR (95% CI)	p-value	MFU, % (n)	MNFU, % (n)	aOR (95% CI)	p-value
(a) Men								
HIV prevalence	11 (1105)	20 (2287)	0.9 (0.7–1.1)	0.2	5 (138)	12 (967)	0.3 (0.1–0.7)	<0.01
Sex before age 18	15 (818)	23 (1948)	1.0 (0.8–1.3)	0.8	16 (108)	15 (710)	0.8 (0.4–1.5)	0.5
At least 3 lifetime partners	71 (812)	77 (1943)	1.0 (0.8–1.2)	0.8	67 (106)	71 (706)	0.8 (0.5–1.2)	0.1
More than 1 partner in last year	44 (811)	38 (1937)	1.1 (0.9–1.3)	0.3	40 (106)	44 (705)	0.9 (0.6–1.3)	0.5
At least 1 new partner in last year	72 (796)	78 (1914)	1.0 (0.8–1.2)	0.8	68 (105)	73 (691)	0.7 (0.5–1.2)	0.2
Casual sex in last year	71 (812)	77 (1943)	1.0 (0.8–1.3)	0.9	67 (106)	71 (706)	0.8 (0.4–1.5)	0.4
More than 1 partner in last month	11 (807)	11 (1938)	1.1 (0.9–1.5)	0.3	11 (105)	11 (702)	1.0 (0.5–1.9)	0.9
More than 1 current partner	21 (809)	18 (1942)	1.2 (1.0–1.5)	0.1	22 (106)	23 (703)	0.9 (0.5–1.5)	0.8
Inconsistent condom use[a]	52 (91)	63 (177)	0.8 (0.5–1.4)	0.5	36 (11)	55 (80)	0.4 (0.1–1.3)	0.1
(b) Women								
HIV prevalence	20 (1228)	24 (3256)	1.2 (1.0–1.4)	0.1	17 (181)	21 (1047)	0.7 (0.4–1.1)	0.1
Sex before age 18	15 (760)	17 (2850)	1.1 (0.9–1.4)	0.3	17 (118)	15 (642)	1.0 (0.6–1.8)	0.9
At least 3 lifetime partners	18 (752)	15 (2825)	1.1 (0.8–1.4)	0.5	13 (118)	20 (634)	0.6 (0.3–1.1)	0.1
More than 1 partner in last year	7 (751)	5 (2824)	0.8 (0.5–1.2)	0.4	5 (118)	7 (633)	0.7 (0.3–1.7)	0.4
At least 1 new partner in last year	18 (746)	15 (2802)	1.1 (0.8–1.4)	0.5	13 (118)	19 (628)	0.6 (0.3–1.1)	0.1
Casual sex in last year	16 (745)	14 (2825)	1.1 (0.7–1.7)	0.7	10 (117)	13 (628)	1.0 (0.3–3.0)	0.9
More than 1 partner in last month	1 (750)	2 (2817)	0.6 (0.3–1.2)	0.3	1 (118)	2 (632)	0.8 (0.1–6.6)	0.8
More than 1 current partner	39 (752)	2 (2821)	0.9 (0.5–1.6)	0.7	1 (118)	3 (634)	0.3 (0.04–2.3)	0.2
Inconsistent condom use[a]	55 (31)	83 (88)	0.3 (0.1–1.1)	0.1	0 (5)	46 (26)	[b]	–

aOR, adjusted odds ratio for age, location, marital status and education; 95% CI, 95% confidence interval; RES, residents; FM; future migrants; MFU, migrants followed-up; MNFU, migrants not followed-up.

[a] Not always having used a condom with casual partners in last year.

[b] No observations in out-migrants followed-up.

Table 3.3 Sexual behavior during follow-up in out-migrants and residents.

	Men				Women			
Characteristic	RES, % (n)	MIG, % (n)	aOR (95% CI)	p-value	RES, % (n)	MIG, % (n)	aOR (95% CI)	p-value
Casual sex in last 3 years	26 (2171)	35 (140)	0.9 (0.6–1.3)	0.5	4 (3205)	4 (192)	0.9 (0.5–1.4)	0.5
More than 1 partner in last 3 years	55 (1806)	54 (120)	0.6 (0.4–1.0)	0.1	12 (2608)	16 (156)	0.8 (0.5–1.4)	0.4
More than 1 new partner in last year	24 (2171)	24 (140)	0.8 (0.5–1.2)	0.2	3 (3205)	4 (180)	0.7 (0.3–1.5)	0.3
More than 1 partner in last month	9 (2166)	6 (140)	0.7 (0.3–1.4)	0.3	1 (3205)	1 (180)	0.7 (0.1–3.2)	0.6
More than 1 current partner	11 (2171)	11 (140)	0.9 (0.5–1.6)	0.7	1 (3205)	2 (180)	0.6 (0.2–2.3)	0.5
Last or previous partner a casual partner	14 (1377)	17 (64)	1.0 (0.4–2.2)	0.9	5 (1946)	6 (106)	0.8 (0.3–2.1)	0.7

aOR, adjusted odds ratio for age, location, marital status and education; 95% CI, 95% confidence interval; RES, residents; MIG, out-migrants.

lower HIV prevalence compared with migrants not followed-up (5 versus 12%; p=0.001), even after adjusting for age, education, marital status and location. However, future out-migrants who were followed-up reported similar sexual behavior at baseline to those who were not re-interviewed.

HIV incidence was not significantly different in migrants and residents, for either men (2.06 versus 2.39 per 100 person-years; adjusted odds ratio [aOR]=0.9; 95% confidence interval [CI] 0.5-2.4) or women (2.23 versus 2.76 per 100 person-years (aOR=0.9; 95% CI 0.4-1.8). Reported sexual behavior in men and women over the 3-year period of follow-up was similar in out-migrants and residents (Table 3.3).

Discussion

In rural Manicaland, Eastern Zimbabwe, future out-migrants did not differ from residents with regard to HIV prevalence or sexual behavior prior to migration, after taking age and other socio-demographic differences into account. They can therefore be considered a random sample of the population. This implies that differences in HIV incidence and sexual behavior seen between migrants and non-migrants are related to the migration process and social and living conditions rather than to migrants being intrinsically risk-seeking individuals.

Several studies have shown that migration can be a risk factor for HIV infection [10]. In the current study, we found no relationship between out-migration and HIV incidence. This may have been due to the small sample size and consequently small numbers of sero-conversions in our study. However, we also found no differences in common sexual risk behaviors.

We were able to trace only small proportions of out-migrants who moved to Harare, to Mutare, or within, between and close to study areas. The true proportion may be smaller even than we recorded because some of those whose baseline households could not be found may also have migrated. This low follow-up rate resulted largely from difficulties in obtaining details of current addresses from respondents at their original households. In some cases, the individuals concerned had left these households 2-3 years before and the addresses given proved to be out of date. In other cases – especially in estates – migrants had been living in single-person households so there was no longer a household respondent to provide forwarding information. Seasonal workers, in particular, rarely left details with their former employers of where they were going after the expiry of their contracts. This could have led to under-estimation of the association between migration and HIV risk, especially because those migrants without known addresses or jobs could

be particularly vulnerable to social circumstances related to sexual risk behavior. Such a bias would be consistent with the higher level of HIV infection at baseline found amongst subsequent out-migrants who could not be traced at follow-up.

We excluded all individuals who died during follow-up, from both baseline and follow-up analyses. HIV infection is the dominant cause of adult mortality in the study areas [18]. Thus, our results may tend to under-estimate baseline HIV prevalence and sexual risk behaviors. However, as these people were sick, it is most likely that their subsequent behavior was safer than that of healthy people, which would make our finding that out-migrants do not have more risky behaviour more conservative.

The relationship between migration and HIV could differ according to reasons for moving or destinations of migration. We therefore grouped out-migrants according to their reasons for moving; with those who moved for marriage and to establish rural homes being taken to be a low-risk group, and those who migrated for work, job loss, partner's work, to stay with relatives, poor health, and other reasons being taken as a high-risk group. However, we still found no differences between migrants and residents in either HIV incidence or behavior (results not shown). Migrants were also grouped according to their type of destination, with those who moved to Harare or Mutare constituting one group and those who moved within the predominantly rural study areas constituting the second group. Once again, no differences were found in multivariate analyses in either group (results not shown).

Our finding that migration did not lead to higher HIV incidence or greater sexual risk behavior could be related to the mature stage and widely-disseminated nature of the HIV epidemic in Zimbabwe [19]. Zimbabwe is one of the more developed countries in sub-Saharan Africa. Rural-to-urban labour migration is high, but a strong cultural attachment to the rural homelands results in extensive spousal separation and circular and return migration [20]. This pattern of movement is facilitated by a good transport infrastructure and seems likely to have contributed to the high levels of HIV infection now seen in rural areas [21,22]. At the same time, risk behavior can also be common within rural communities [10] and this appears to have been the case in Manicaland [20-22]. As a consequence, differences in HIV prevalence between cities and rural areas are now quite modest [19]. Thus, unless rural-to-urban migrants alter their behavior after moving, their exposure to HIV infection is not likely to increase.

We studied primarily migrants who moved to cities. Many of these migrants stay with relatives at first where they may be given social, emotional and financial support. Therefore, urban migrants in Zimbabwe may be less lonely, have less need to search to belong with others, and be less likely to be forced to have survival sex than, for example, mineworkers

and other labour migrants living in single-sex quarters in South Africa [23]. At the same time, the cost of living is high in the cities and it can take time to secure an independent income. Some migrants who stay with relatives may continue to be subject to social controls. Thus, both the pressures and opportunities to engage in casual or commercial sex relationships are probably less pronounced than for migrants to other locations. Finally, in a large and more advanced epidemic, people typically have better knowledge on HIV/AIDS and migrants may be less likely to engage in risky sexual behavior even when they find themselves in situations that could make them vulnerable to HIV/AIDS.

Our study focused mainly on out-migrants and their behavior and HIV risk relative to those of non-migrants in the sending populations. The consequences for receiving populations depend on how HIV prevalence and behavior of immigrants compare with those of the host populations.

Our results suggest that out-migration from rural areas plays little part in HIV transmission at this stage of the epidemic in Zimbabwe. However, we were able to follow only a small sample of out-migrants from our study sites in rural Manicaland. More prospective studies in other countries at different stages of HIV epidemics are needed to assess the generalizability of our findings.

References

1. Nunn AJ, Wagner HU, Kamali A, Kengeya-Kayondo JF, Mulder DW. Migration and HIV-1 seroprevalence in a rural Ugandan population. *AIDS* 1995; 9:503-506.
2. Duckett M. Migrants and HIV / AIDS. *Dev Bull* 2000; 52:18-20.
3. Quinn TC. Population migration and the spread of types 1 and 2 human immunodeficiency viruses. *Proc Natl Acad Sci U S A* 1994; 91:2407-2414.
4. Decosas J, Adrien A. Migration and HIV. *AIDS* 1997; 11 (Suppl. A):S77-84.
5. Soskolne V, Shtarkshall RA. Migration and HIV prevention programmes: linking structural factors, culture, and individual behaviour--an Israeli experience. *Soc Sci Med* 2002; 55:1297-1307.
6. Zuma K, Gouws E, Williams B, Lurie M. Risk factors for HIV infection among women in Carletonville, South Africa: migration, demography and sexually transmitted diseases. *Int J STD AIDS* 2003; 14:814-817.
7. Pison G, Le Guenno B, Lagarde E, Enel C, Seck C. Seasonal migration: a risk factor for HIV infection in rural Senegal. *J Acquir Immune Defic Syndr* 1993; 6:196-200.
8. Chirwa WC. Migrant labour, sexual networking and multi-partnered sex in Malawi. *Health Transit Rev* 1997; 7 (Suppl 3):5-15.
9. Lydie N, Robinson NJ, Ferry B, Akam E, De Loenzien M, Abega S. Mobility, sexual behavior, and HIV infection in an urban population in Cameroon. *J Acquir Immune Defic Syndr* 2004; 35:67-74.

10. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sturm AW, *et al.* The impact of migration on HIV-1 transmission in South-Africa: a study of migrant men and non-migrant men and their partners. *Sex Transm Dis* 2003; 30:149-156.
11. Kishamawe C, Vissers D, Urassa M, Isingo R, Mwaluko G, Borsboom GJJM, *et al.* Mobility and HIV in Tanzanian couples: both mobile persons and their partners behind show increased risk. *AIDS* 2006; 20:601-608.
12. Decosas J, Kane F, Anarfi JK, Sodji KDR, Wagner HU. Migration and AIDS. *Lancet* 1995; 346:826-828.
13. UNAIDS. Population Mobility and AIDS. *UNAIDS Best Practice Digest* 2001.
14. IOM. Population mobility and HIV/AIDS. Geneva; 2004. Available at: http://www.iom.int/documents/publication/en/iom%5Fhiv%5Fbrochure%5Fjuly%5F2004.pdf.
15. IOM Regional Office for Southern Africa. Labour Migration and HIV/AIDS in Southern Africa. Geneva; 2002. Available at: http://www.iom.int/en/pdf%5Ffiles/hivaids/labour%5Fmigration%5Fhiv.pdf.
16. Gregson S, Mushati P, White PJ, Mlilo M, Mundandi C, Nyamukapa C. Informal confidential voting interview methods and temporal changes in reported sexual risk behaviour for HIV transmission in sub-Saharan Africa. *Sex Transm Infect* 2004; 80 (Suppl 2):ii36-42.
17. Ray CS, Mason PR, Smith H, Rogers L, Tobaiwa O, Katzenstein DA. An evaluation of dipstick-dot immunoassay in the detection of antibodies to HIV-1 and 2 in Zimbabwe. *Trop Med Int Health* 1997; 2:83-88.
18. Gregson S, Zhuwau T, Anderson RM, Chandiwana S. The early socio-demographic impact of the HIV-1 epidemic in rural Zimbabwe. *SAfAIDS News* 1997; 5:2-5.
19. Zimbabwe Ministry of Health and Child Welfare. Zimbabwe National HIV and AIDS Estimates 2003. Harare: Zimbabwe Ministery of Health and Child Welfare; 2003.
20. Coffee MP, Garnett GP, Mlilo M, Voeten HA, Chandiwana S, Gregson S. Patterns of Movement and Risk of HIV Infection in Rural Zimbabwe. *J Infect Dis* 2005; 191:S159-167.
21. Gregson S, Mason PR, Garnett GP, Zhuwau T, Nyamukapa CA, Anderson RM, *et al.* A rural HIV epidemic in Zimbabwe? Findings from a population-based survey. *Int J STD AIDS* 2001; 12:189-196.
22. Gregson S, Waddell H, Chandiwana SK. School education and HIV control in sub-Saharan Africa: from discord to harmony. *Journal of International Development* 2001; 13:467-485.
23. Campbell C. Migrancy, masculine identities and AIDS: the psychosocial context of HIV transmission on the South African gold mines. *Soc Sci Med* 1997; 45:273-281.

4 Mobility and HIV in Tanzanian couples: both mobile persons and their partners show increased risk

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Abstract

Objective To investigate how mobility is related to sexual risk behavior and HIV infection, with special reference to the partners who stay behind in mobile couples.

Methods HIV status, sexual behavior and demographic data of 2,800 couples were collected in a longitudinal study in Kisesa, rural Tanzania. People were considered short-term mobile if they had slept outside the household at least once the night before one of the five demographic interviews, and long-term mobile if they were living elsewhere at least once at the time of a demographic round.

Results Overall, whereas long-term mobile men did not report more risk behavior than resident men, short-term mobile men reported having multiple sex partners in the last year significantly more often. In contrast, long-term mobile women reported having multiple sex partners more often than resident women (6.8 versus 2.4%; p=0.001), and also had a higher HIV prevalence (7.7 versus 2.7%; p=0.02). In couples, men and women who were resident and had a long-term mobile partner both reported more sexual risk behavior and also showed higher HIV prevalence than people with resident/short-term mobile partners. Remarkably, risk behavior of men increased more when their wives moved than when they were mobile themselves.

Conclusions More sexual risk behavior and an increased risk of HIV infection were seen not only in mobile persons, but also in partners staying behind. Interventions aiming at reducing risk behavior due to mobility should therefore include partners staying behind.

Introduction

Mobility is one of the many factors that have contributed to the AIDS epidemic [1-3]. Several studies have shown that people who travel or who have recently migrated tend to be at higher risk for HIV and other sexually transmitted diseases (STD) [4-8]. The role of migration in the spread of HIV has been described primarily as the result of men who become infected while they are away from home, and infect their wives or regular partners when they return [1,4,9]. Married men often travel without their spouses. Being away from their families and communities, and thus from social and sexual control, may cause mobile men to change their behavior. They may have sex with more women than if they had stayed at home [10]. On the other hand, due to differences in languages and culture, sexual partnerships with local women in the destination area may be difficult. This leads mobiles to have sex with commercial sex workers, who often have high rates of HIV and other STD infections.

Most studies tend to give a one-sided view which only takes mobile people into account and do not consider those who stay behind. Due to a number of factors, such as loneliness, peer pressure, and lack of financial support, partners who stay behind may also engage in riskier sexual behavior. Consequently, people are not only vulnerable to HIV infection by the risk behavior of their partners, but also by their own risk behavior when left behind.

A South African study investigated HIV infection among migrants and their partners staying behind and among non-migrant couples in which both partners stayed at home [11]. This study showed that HIV discordance was 2.5 times more likely in migrant couples than in non-migrant couples. Men and women in a migrant couple were both more likely to be infected from outside the relationship than by their spouse. This study also found that in one-third of the couples with only one HIV-positive partner, the wife who stayed at home, was infected [11]. Therefore, understanding the sexual behavior of both partners within a couple is essential for the successful implementation of targeted interventions.

This study was carried out in Tanzania, where the HIV epidemic is spreading at an alarming pace since the first three AIDS cases were reported in 1983. In the period 1990 to 2000, surveillance reports indicated an increase in the HIV prevalence from 8.9 to 12.2% among pregnant women in antenatal clinics [12]. By the end of 2003, it was estimated that about 1.6 million people in Tanzania were living with HIV/AIDS [12]. HIV prevalence in the sexually active population (15–49 years) was estimated at 8.8% in 2003 [12]. AIDS is now the major cause of illness and death in all economic sectors and at all social levels [13].

Our study aimed to establish whether men and women who are part of couples in which one of the partners is mobile show more sexual risk behavior and a higher HIV prevalence than continuously co-resident men and women. In particular, we were interested whether absence of the mobile partner increased the risk behavior of the partner staying behind.

Methods

Study site and data collection procedure

Data were available from a longitudinal cohort study in Kisesa Ward in Mwanza Region, Tanzania [14,15]. The main objective of this study was to monitor the spread and impact of the HIV/AIDS epidemic in the Kisesa community and to identify possible risk factors (including mobility). It started in 1994 and is still ongoing. The ward has a population of about 28,000 people and is administratively divided into six villages, three of which are located along one of the main roads connecting Tanzania and Kenya. The main economic activity among the residents of the area is farming (97%).

Between 1994 and the end of 2003, 16 demographic surveillance rounds were completed. Per round, information was collected from each household (defined as a group of people who regularly eat together from the same pot) on the residence and survival status of all household members, on pregnancies in women, on mobility behavior and on new arrivals (migrants and new-borns). A new person was listed as a household member if the household respondent had indicated that this person was intending to stay in the household. Returning household members were re-listed, keeping their original line number on the household card.

Between 1994 and 2000, three rounds of epidemiological and behavioral surveys were conducted: the first in 1994/95, the second in 1996/97, and the third in 1999/2000. In all three surveys, participants were interviewed using standardized questionnaires (in Swahili). Socio-demographic characteristics, birth and marital history, family planning, sexual behavior, STD history, HIV/AIDS awareness, and risk perception were asked. Participants were also asked to provide a blood sample for HIV screening. Blood samples were tested using two independent enzyme-linked immunosorbent assay (ELISA) tests: Vironostika HIV-MIXT (Organon, Boxtel, the Netherlands) and Enzygnost HIV1/HIV2 (Behring, Marburg, Germany). Only samples with two positive ELISA results were considered to be HIV positive. All participants were given study numbers to guarantee anonymity.

Data analysis

Men and women in long-term relationships or marriages (marital units) were identified in 1996 and again in 2002. For all marital units, demographic interview information was used to identify the period of co-residence. Marital units were only included in our analyses if they had been living together before or during the studied demographic rounds and if at least one of the partners had been tested for HIV infection at survey 2 or 3. Those marital units with members who moved, separated or died before the identification were not included.

Two indicators, both asked in demographic surveillance rounds, were used to define the mobility status: 'slept outside the household on the night before the demographic round' and 'lives in another household since the last demographic round'. We used data from the five demographic rounds between survey 1 and 2 to define the mobility status of people attending survey 2. For people in survey 3, we used the five rounds between survey 2 and 3. A person was considered to be *short-term mobile* if he or she had slept outside the household at least once the night before one of the five demographic rounds, and considered to be *long-term mobile* if he or she had been living elsewhere at least once. *Residents* were all people that did not sleep outside the household nor lived elsewhere at the time of the demographic rounds. Long-term mobiles were defined first, followed by short-term mobiles. This procedure led to exclusive mobility categories.

For men and women all analyses were done separately. Polygamous marriages with men married to two or three women were included in our study. However, in our analyses a couple is defined as one man married to one woman. Therefore, for the analyses of men we kept only one record in case of a polygamous marriage and we randomly chose one of his wives. For the analyses of women, we included all women of whom some share the same man.

For each of the three mobility strata, proportions were calculated for different indicators of sexual risk behavior and of STD/HIV status. The sexual risk indicators were: having a regular non-spousal partner in the last year (i.e. long-term relation with someone besides the husband/wife), and having a casual partner in the last year (i.e. short-term relation). In addition, the number of sex partners in the last year was asked. STD/HIV indicators were reported ulcers in private parts in the last year, and prevalence and incidence of HIV. To adjust for the confounding effect of age, proportions were standardized using the age distribution of the total number of men or women. To test whether short-term or long-term mobile people differed from residents, we used logistic regression modeling, adjusting for age (which was the only significant demographic confounder).

After these analyses based on the participant's own mobility, we studied the effects of the mobility status of their partners. We further stratified the groups of men and women according to the mobility status of their partners, and calculated age-adjusted proportions. As there was only one long-term mobile man with a short-term mobile wife, and because earlier analyses yielded only minimal differences between short-term and long-term mobile men, we decided to combine these two groups into one. In a second analysis, we formed groups based on the mobility status of both partners and studied the differences between these groups with logistic regression analysis adjusting for age. The groups were divided as follows: both resident; being short-term or long-term mobile yourself with a partner at home; being at home with a short-term or long-term mobile partner; and both being short-term or long-term mobile. We combined the groups of short-term and long-term mobile people in the analyses of women, because some categories did not have enough observations to perform logistic regression analyses.

We determined the HIV incidence using two successive surveys (i.e. survey 1 and 2, or survey 2 and 3). Since not all people attended two successive surveys, the number of people in the analyses of HIV incidence were lower.

The results of survey 2 and 3 were combined to increase power. Therefore, individuals who attended both surveys were included twice. We applied generalized estimation equation (GEE) techniques for logistic regression to account for dependencies between repeated observations and for dependencies resulting from inclusion of polygamous marriages [16]. All analyses were performed using Stata version 8.0 (Stata Corporation, College Station, Texas, USA).

Results

In total, we identified 2,800 marital units in which at least one of the partners was tested for HIV. These marital units consisted of 2,614 monogamous relationships, 175 men with two wives, and 11 men with three wives. Basic demographic information was available for all of the individuals involved in these partnerships, but HIV status, sexual risk behavior, and mobility characteristics were known for 1,675 out of 2,800 men (59.8%) and 2,185 out of 2,997 women (72.9%). The analyses that also involved the mobility status of the partner, were limited to 1,541 men and 2,157 women, respectively. Most long-term mobiles (60%) temporarily lived elsewhere and returned to their original households in the next demographic rounds. Others lived in a place nearby and were still able to attend the next survey round.

Of the men, 1,049 were resident, 474 short-term mobile (i.e. slept outside the household at least once) and 152 long-term mobile (i.e. lived elsewhere at least once). Of the women, 1,534 were resident, 444 short-term mobile, and 207 long-term mobile. Age distribution of men and women and the mobility status of their partners is shown in Table 4.1. Long-term mobile men were considerably younger than short-term mobile or resident men. The majority of resident men also had a resident partner (70.2%), and most long-term mobile men had a long-term mobile partner (81.6%). Half of the short-term mobile men had a resident wife, and about one-third had a short-term mobile wife. Women showed a similar age pattern as men. About two-thirds of the resident women and two-thirds of the long-term mobile women had a husband with the same mobility status. Almost half of the short-term mobile women had a resident husband and another 50% a short-term mobile one.

Table 4.1 Age group and partner's mobility status, by gender and mobility status.

	Men			Women		
	Resident n=1049	Short-term mobile n=474	Long-term mobile n=152	Resident n=1534	Short-term mobile n=444	Long-term mobile n=207
Age group (years)						
15–24	5.2	2.7	6.6	8.9	11.9	24.6
25–34	26.7	29.3	50.0	39.0	40.1	48.8
35–44	38.6	35.9	28.9	34.8	32.4	22.2
45+	29.5	32.1	14.5	17.4	15.6	4.3
Mobility status partner						
Resident	70.2	54.6	9.2	68.0	47.3	13.5
Short-term mobile	17.0	31.4	0.7	28.9	49.3	14.5
Long-term mobile	4.5	7.0	81.6	1.8	1.8	71.0
Unknown	8.4	7.0	8.6	1.2	1.6	1.0

Values represent percentages.

The proportion of men having sex with regular non-spousal or casual partners did not consistently differ between the three mobility groups (Table 4.2). However, short-term mobile men reported significantly more often than resident men that they had more than two sex partners in the last year (47.8 versus 40.0%; p=0.006). The proportion reporting ulcers in private parts was somewhat higher for short-term (6.7%) and long-term mobiles (5.7%), but this did not differ significantly from resident men (4.6%). The HIV status did not differ significantly between the three mobility groups, although short-term and long-term mobile men had a slightly lower prevalence and incidence of HIV.

Table 4.2 Relation between mobility status and sexual risk behavior and sexually transmitted diseases (STD)/ HIV status, by gender.

	Men			Women		
	Resident n=1049	Short-term mobile n=474	Long-term mobile n=152	Resident n=1534	Short-term mobile n=444	Long-term mobile n=207
Sexual risk behavior[a]						
Regular non-spousal partner	13.6	14.7	11.5	2.0	1.1	8.3 **
Casual partner	26.7	28.7	29.7	1.8	1.1	5.2 **
Two or more sex partners	40.0	47.8 **	45.2	2.4	1.7	6.8 **
Three or more sex partners[b]	17.2	19.2	22.6	–	–	–
STD/HIV status						
Ulcers in private parts[a]	4.6	6.7	5.7	3.1	1.8	3.5
HIV prevalence	5.7	4.0	2.8	2.7	2.7	7.7 *
HIV incidence[c]	2.1	1.5	1.7	0.7	1.2	1.8

Values represent age-adjusted percentages. Differences between groups were tested using generalized estimation equation (GEE) logistic regression adjusting for age.
* p<0.05 in relation to resident men or women.
** p<0.01 in relation to resident men or women.
[a] Reported over the last year.
[b] Only reported by men.
[c] HIV incidence based on lower numbers of individuals. For resident, short-term mobile and long-term mobile men these were 727, 320 and 123. For resident, short-term mobile and long-term mobile women these were 1200, 343, and 163.

Sex with a regular non-spousal partner was more common among long-term mobile women than among resident women (8.3 versus 2.0%; p<0.001) (Table 4.2). Long-term mobile women also reported sex with casual partners (5.2 versus 1.8%; p=0.004) and with multiple partners in the last year (6.8 versus 2.4%; p=0.001) more often than resident women. The increased risk behavior among long-term mobile women was accompanied by a significantly higher HIV prevalence than in resident women (7.7 versus 2.7%; p=0.02), and a slightly higher HIV incidence. There were no particular differences in sexual risk behavior and HIV status between short-term mobile and resident women.

After looking at participants' own mobility, we studied the effects of the mobility behavior of the partner. For resident men, the mobility status of their wives was strongly associated with their own sexual risk behavior and HIV/STD status (Tables 4.3 and 4.5). The overall test on the mobility status of couples was for most outcomes either significant or borderline significant (see p-values in Table 4.5). Resident men with long-term mobile wives reported significantly more regular non-spousal (30.9 versus 11.7%; odds ratio [OR]=2.65), casual (36.3 versus 23.0%; OR=2.15) or multiple sex partners (62.4 versus 36.7%; OR=2.76) in the last year than resident men with resident partners. These men also had a higher proportion of ulcers in private parts (11.9 versus 3.8%; OR=3.95)

Table 4.3 Relation between mobility status and sexual risk behavior and sexually transmitted diseases (STD)/ HIV status for men, by the mobility status of their wives.

	Resident men			Short- or long-term mobile men		
	Resident wives n=736	Short-term mobile wives n=178	Long-term mobile wives n=47	Resident wives n=273	Short-term mobile wives n=150	Long-term mobile wives n=157
Sexual risk behavior[a]						
Regular non-spousal partner	11.7	16.9	30.9 **	13.0	14.5	10.4
Casual partner	23.0	29.7	36.3 *	25.7	28.0	29.0
Two or more sex partners	36.7	43.3	62.4 **	47.2	43.3	44.9
Three or more sex partners	15.1	17.5	25.1 **	16.8	18.0	18.7
STD/HIV status						
Ulcers in private parts[a]	3.8	4.4	11.9 **	4.7	8.3	5.2
HIV prevalence	5.5	4.5	11.2 **	3.5	2.6	2.6
HIV incidence[b]	2.0	0.7	6.0 *	1.6	0.0	0.5

Values represent age-adjusted percentages. Differences between groups were tested using generalized estimation equation (GEE) logistic regression adjusting for age.
* p<0.05 in relation to resident men with resident wives.
** p<0.01 in relation to resident men with resident wives.
[a] Reported over the last year.
[b] HIV incidence based on lower numbers of individuals. These were 501, 128, 37, 178, 102 and 134, respectively.

Table 4.4 Relation between mobility status and sexual risk behavior and sexually transmitted diseases (STD)/ HIV status for women, by the mobility status of their husbands.

	Resident women		Short-term mobile women		Long-term mobile women	
	Resident husbands n=1043	Mobile[a] husbands n=472	Resident husbands n=210	Mobile[a] husbands n=227	Resident husbands n=28	Mobile[a] husbands n=177
Sexual risk behavior[b]						
Regular non-spousal partner	1.8	3.1	1.0	1.3	7.4	8.6
Casual partner	1.3	3.0 *	1.3	0.5	1.2	5.9
Two or more sex partners	2.3	2.6	1.7	1.4	6.2	7.2
STD/HIV status						
Ulcers in private parts[b]	3.1	3.3	2.2	1.4	5.0	3.5
HIV prevalence	2.4	3.5	3.6	1.7	0.0	8.6
HIV incidence[c]	0.6	1.3	1.1	1.1	0.0	2.2

Values represent age-adjusted percentages. Differences between groups were tested using generalized estimation equation (GEE) logistic regression adjusting for age.
* p<0.05 in relation to resident women with resident husbands.
[a] Both short-term and long-term mobile husbands.
[b] Reported over the last year.
[c] HIV incidence based on lower numbers of individuals. These were 820, 366, 161, 176, 18 and 144, respectively.

Table 4.5 The effect of mobility status of a couple on sexual behavior and sexually transmitted diseases (STD)/HIV outcomes.

	Regular non-spousal partner[a]	Casual partner[a]	Two or more sex partners[a]	Three or more sex partners[a,b]	Ulcers[a]	HIV prevalence	HIV incidence[c]
MEN (n=1541)							
Mobility of couples[d]	p=0.07	p=0.07	p=0.002	p=0.2	p=0.02	p=0.05	p=0.05
Res – Res	1	1	1	1	1	1	1
ST mob – Res	1.04 (0.66-1.64)	1.19 (0.84-1.68)	1.59 (1.19-2.13) **	1.12 (0.75-1.67)	1.13 (0.53-2.39)	0.64 (0.33-1.25)	0.59 (0.13-2.73)
LT mob – Res	0.52 (0.07-4.14)	0.83 (0.22-3.11)	1.69 (0.58-4.95)	2.11 (0.63-7.05)	3.75 (0.76-18.53)	1.39 (0.23-8.54)	4.65 (0.54-40.24)
Res – ST mob	1.52 (0.96-2.41)	1.42 (0.98-2.08)	1.30 (0.93-1.81)	1.15 (0.74-1.79)	1.13 (0.50-2.57)	0.91 (0.46-1.79)	0.38 (0.05-3.01)
Res – LT mob	2.65 (1.31-5.34) **	2.15 (1.13-4.07) *	2.76 (1.47-5.16) **	2.18 (1.10-4.32) *	3.95 (1.55-10.07) **	2.79 (1.18-6.56) *	4.22 (1.03-17.33) *
Mob – Mob	1.14 (0.76-1.70)	1.41 (1.03-1.92) *	1.32 (1.00-1.74)	1.37 (0.97-1.94)	1.90 (1.08-3.35) *	0.62 (0.33-1.17)	0.20 (0.02-1.56)
WOMEN (n=2157)							
Mobility of couples[d]	p=0.008	p=0.08	p=0.3		p=0.9	p=0.5	p=0.5
Res – Res	1	1	1		1	1	1
Res – Mob	1.60 (0.76-3.37)	2.45 (1.12-5.35) *	1.08 (0.52-2.22)		1.14 (0.61-2.15)	1.29 (0.70-2.36)	1.81 (0.48-6.77)
Mob – Res	1.10 (0.40-3.01)	1.23 (0.40-3.80)	1.01 (0.41-2.50)		0.77 (0.32-1.88)	1.29 (0.61-2.73)	1.83 (0.35-9.56)
Mob – Mob	2.93 (1.54-5.56) **	2.31 (1.06-5.05) *	1.78 (0.95-3.33)		0.62 (0.49-1.87)	1.58 (0.87-2.87)	2.57 (0.73-9.00)

Values represent odds ratios (95% confidence intervals). Differences between groups were tested using generalized estimation equation (GEE) logistic regression adjusting for age.

* p<0.05 in relation to both resident partners.

** p<0.01 in relation to both resident partners.

[a] Reported over the last year.

[b] Only reported by men.

[c] HIV incidence based on lower numbers of individuals. These were 1080 for men and 1685 for women.

[d] Res, resident partner; ST mob, short-term mobile partner; LT mob, long-term mobile partner; Mob, short- or long-term partner. For the analyses of men, the male partner is mentioned first. For the analyses of women, the female partner is mentioned first.

and a higher HIV prevalence (11.2 versus 5.5%; OR=2.79) and incidence (6.0 versus 2.0%; OR=4.22). Resident men with short-term mobile wives reported more casual sex partners, more regular non-spousal partners and multiple sex partners in the last year than those with resident wives, although the differences were not significant. Surprisingly, men's sexual behavior seemed to be more risky if their wives moved than if they were mobile themselves. Short-term mobile men with a partner at home had an odds ratio of 1.59, in comparison with resident men with resident wives, of reporting two or more sex partners in the last year. If both partners were mobile, men reported more casual partners (OR=1.41; 95% confidence interval [CI] 1.03-1.92) and more ulcers in private parts (OR=1.90; 95% CI 1.08-3.35) than if both partners were resident.

Table 4.4 shows sexual behavior data and STD prevalences of women with partners in different mobility groups. The overall test on the mobility status of couples was only significant for having a regular non-spousal partner in the last year (see p-values in Table 4.5). Resident women reported markedly more casual partners if their husbands were mobile (3.0 versus 1.3%; OR=2.45); they also had a higher, although not significant, HIV prevalence and incidence than resident women with resident partners (Tables 4.4 and 4.5). In contrast to resident women, the mobility status of the partners did not have much influence on the sexual behavior or STD status of short-term mobile women. If both partners were mobile, women had an odds ratio of 2.93 compared with resident women with resident husbands to report sex with a regular non-spousal partner (Table 4.5). These women also reported more casual partners (OR=2.31; 95% CI 1.06-5.05). Overall, long-term mobile women with mobile partners showed the highest HIV prevalence (8.6%).

Discussion

The mobility status of men did not greatly influence their sexual risk behavior or STD status. In contrast, long-term mobile women reported more often than resident women that they had non-spousal, casual or multiple partners in the last year and they had a higher HIV prevalence. The risk behavior of men was influenced more by the mobility of their partner than by their own mobility. Long-term mobile women with mobile partners reported more sexual risk behavior, which was also reflected in a higher HIV prevalence.

There are some limitations in our study design. The indicator 'slept outside the household the night before the demographic round' is a good indicator for population mobility, but a relatively poor indicator at the individual level. For instance, people who often sleep outside the household may, by chance, be found at home during a demographic round,

and thus be classified in the study as a resident. A similar reasoning can be followed for people who rarely sleep elsewhere but were not found at the time of the demographic round, and consequently classified as short-term mobile. In spite of this, our results show that being short-term mobile or having a short-term mobile partner is a risk factor for increased sexual risk behavior and HIV infection. With the use of more precise indicators of mobility this pattern may well become stronger. Such an alternative indicator could be 'the number of nights spent outside the household during the last month', but this has the limitation of recall bias.

Another limitation was the couple identification, which occurred after the study period. It is possible that some couples were not included due to HIV/AIDS-related causes. Some people might have lost their partner due to AIDS. Other couples might have split up when one of the partners found out that their husband/wife was HIV-positive. It is therefore possible that the number of HIV cases in our study is biased towards a lower value.

About 60% of the men and 70% of the women were included in our analyses. Men who were included were somewhat younger, but included women were slightly older than persons not included. Mobile people were relatively often not included in the analyses, because they did not attend the survey rounds.

Male circumcision could be a potential confounder in the association between mobility and HIV infection. The circumcision status was known for 80% of the men in our analyses and mobile men were slightly more often circumcised than resident men (24 versus 19%). Adjusting for male circumcision did not change the association between mobility and sexual risk behavior or HIV infection.

Our study demonstrated an association between people's mobility behavior, their sexual risk behavior and their HIV status. This is consistent with earlier findings that migration and travel are affecting the spread of HIV [4-8]. A study in South Africa showed that migrant women were significantly more likely than non-migrant women to have had two or more partners in the last year and to have had sexual contact with a partner other than the regular partner [17]. This was accompanied by a higher HIV prevalence in migrant women [17]. In addition to this, long-term mobile women in our study also showed increased sexual risk behavior and had a higher HIV prevalence than resident women.

Resident women with mobile partners reported more casual partners in the last year than those with resident partners. A possible explanation could be that women with mobile partners have more opportunity to engage themselves in sexual relationships with other men. This may not always be out of free choice. Sometimes men who travel or move do not leave money for their wives. In a South African study only half of the migrant men

did send money back home [18]. Some women who stay behind may be compelled to engage in transactional sex for food and other living expenses.

Most studies have focused on one type of mobility. Some studies looked at seasonal migration, circular migration or migration in relation to work [4,9,19]. Studies in Cameroon and Uganda investigated the relation between traveling, sexual behavior, and HIV infection [8,20]. We compared resident people with both short-term and long-term mobiles. This enabled us to study differences in sexual behavior and HIV status as a result of different types of mobility. As in an earlier study in South Africa, we followed both the partner moving away and the one staying behind [11,18]. The South African study was restricted to men, while we also examined mobile *women* and their partners. We saw that long-term mobile women, in particular, showed more risky sexual behavior and had a higher HIV prevalence. Since moving rates of women in Kisesa are high (70% lived elsewhere at least once in their life), these results indicate that long-term mobile women play an important role in the spread of HIV [21].

We conclude that both partners, namely the one moving away and the one staying behind, showed more sexual risk behavior and had a higher risk of HIV infection. Current interventions mainly target mobile people (e.g. miners) and places where they gather (e.g. truck stops), and consist of STD services, condom distribution and education [22,23]. This study shows that policy makers should be aware of partners staying behind. They should aim their HIV interventions not only at mobiles, but also at partners at home. A first option could be health education or condom distribution focused at partners staying behind in rural areas. In case that this is too costly, another option might be to encourage partners to move to the new area together, by creating the right circumstances for housing, employment and schooling opportunities for children. However, moving with your partner may not always be practical in Tanzania. Most people who move to seek casual employment can not risk bringing their family, because they will often share a room with relatives, who may tolerate one person but not a whole family. In other areas moving together could be a practical intervention. If partners move together, they may be less prone to engage in risky sexual behavior, and may therefore be less likely to acquire an HIV infection.

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References

1. Decosas J, Adrien A. Migration and HIV. *AIDS* 1997; 1 (Suppl. A):S77-84.
2. Mabey D, Mayaud P. Sexually transmitted diseases in mobile populations. *Genitourin Med* 1997; 73:18-22.
3. Quinn TC. Population migration and the spread of types 1 and 2 human immunodeficiency viruses. *Proc Natl Acad Sci U S A* 1994; 91:2407-2414.
4. Pison G, Le Guenno B, Lagarde E, Enel C, Seck C. Seasonal migration: a risk factor for HIV infection in rural Senegal. *J Acquir Immune Defic Syndr* 1993; 6:196-200.
5. Nunn AJ, Wagner HU, Kamali A, Kengeya-Kayondo JF, Mulder DW. Migration and HIV-1 seroprevalence in a rural Ugandan population. *AIDS* 1995; 9:503-506.
6. Lagarde E, Pison G, Enel C. A study of sexual behavior change in rural Senegal. *J Acq Immune Defic Syndr Hum Retrovirol* 1996; 11:282-287.
7. Barongo LR, Borgdorff MW, Mosha FF, Nicoll A, Grosskurth H, Senkoro KP*, et al.* The epidemiology of HIV-1 infection in urban areas, roadside settlements and rural villages in Mwanza region, Tanzania. *AIDS* 1992; 6:1521-1528.
8. Lydie N, Robinson NJ, Ferry B, Akam E, De Loenzien M, Abega S. Mobility, sexual behavior, and HIV infection in an urban population in Cameroon. *J Acquir Immune Defic Syndr* 2004; 35:67-74.
9. Lurie M, Harrison A, Wilkinson D, Abdool Karim S. Circular migration and sexual networking in rural KwaZulu/Natal: implications for the spread of HIV and other sexually transmitted diseases. *Health Transition Review* 1997; 7 (Suppl. 3):17-27.
10. Mbizvo MT, Machekano R, McFarland W, Ray S, Bassett M, Latif A, Katzenstein D. HIV seroincidence and correlates of seroconversion in a cohort of male factory workers in Harare, Zimbabwe. *AIDS* 1996; 10:895-901.
11. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sweat MD*, et al.* Who infects whom? HIV-1 concordance and discordance among migrant and non-mirant couples in South Africa. *AIDS* 2003; 17:2245-2252.
12. UNAIDS. Tanzania epidemiological fact sheet on HIV/AIDS and sexually transmitted infections. Geneva: UNAIDS, 2004.
13. TACAIDS. National Multi-sectoral strategic framework on HIV/AIDS 2003 - 2007. Dar es Salaam, Tanzania: TACAIDS, 2003.
14. Boerma JT, Urassa M, Senkoro K, Klokke A, Ng'weshemi JZL. Spread of HIV infection in a rural area of Tanzania. *AIDS* 1999; 13:1233-1240.
15. Mwaluko G, Urassa M, Isingo R, Zaba B, Boerma JT. Trends in HIV and sexual behaviour in a longitudinal study in a rural population in Tanzania, 1994-2000. *AIDS* 2003; 17:2645-2651.
16. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *BMKA* 1986; 73:13-22.

17. Zuma K, Gouws E, Williams B, Lurie M. Risk factors for HIV infection among women in Carletonville, South Africa: migration, demography and sexually transmitted diseases. *Int J STD AIDS* 2003; 14:814-817.
18. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sturm AW*, et al.* The impact of migration on HIV-1 transmission in South-Africa: a study of migrant men and non-migrant men and their partners. *Sex Transm Dis* 2003; 30:149-156.
19. Ramjee G, Gouws a EE. Prevalence of HIV among truck drivers visiting sex workers in KwaZulu-Natal, South Africa. *Sex Transm Dis* 2002; 29:44-49.
20. Morris M, Wawer MJ, Makumbi F, Zavisca JR, Sewankambo N. Condom acceptance is higher among travelers in Uganda. *AIDS* 2000; 14:733-741.
21. Isingo R, Urassa M, Kishamawe C, Knoops E, Voeten H, Mwaluko G*, et al.* Mobility is an important risk factor for HIV infection in rural Tanzania [abstract ThOrC1485]. *XIV International AIDS Conference*. Barcelona, Spain, July 2002.
22. Robinson ET. Reaching men: at work and in social settings. *Network* 1991; 12:15-16.
23. Nyamuryekung'e KM, Laukamm-Josten U, Vuylsteke B, Mbuya C, Hamelmann C, Outwater A*, et al.* STD services for women at truck stop in Tanzania: evaluation of acceptable approaches. *East Afr Med J* 1997; 74:343-347.

5 Separation of spouses due to travel and living apart raises HIV risk in Tanzanian couples

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Abstract

Background Persons with absent partners may be more vulnerable to risky sexual behavior and therefore HIV. Partner absence can be due to traveling (e.g. family visits or funerals) or to living apart (e.g. work-related or in polygamous marriages). We investigated to what extent partner absence leads to more risky sexual behavior in Tanzanian couples.

Methods We compared 95 men and 85 women living apart with 283 men and 331 women living together. Only persons who were still married were included, either living apart or cohabiting at the time of the interview. Subjects were classified into four groups: co-residents being either non-mobile or mobile, and people living apart either frequently or infrequently seeing each other.

Results Most people living apart were polygamously married. Men living apart did not report more extramarital sex than co-resident men. However, among co-resident men, extramarital sex was reported by 35% of those being mobile compared to 15% of those non-mobile. Among women, those living apart reported extramarital sex more often than co-residents (14 versus 7%), and this was mainly due to women living apart who infrequently saw their husbands.

Conclusions Risky sexual behavior occurs more often in mobile co-resident men, and in women living apart infrequently seeing their spouses. These groups are relatively easy to identify and need extra attention in HIV prevention campaigns.

Introduction

Unsafe sexual behavior increases the risk of getting HIV infected. In couples, absence of one of the spouses may lead to more risky sexual behavior in both partners. There are many reasons for absence: work such as seasonal migration or truck driving [1,2], visiting family and relatives, or attending funerals and other ceremonies. Polygamy is also a common reason in the area of Tanzania where this study took place, because the usual arrangement is that a polygamously married man lives alternately with his co-wives.

Most previous studies looking at separation of married partners focused on occupational migration or travel. For example, studies involving work-related migration of the male partner were done in South Africa and Bangladesh. In South Africa, HIV infection of one or both partners occurred twice as often in migrant couples than in non-migrant couples [3]. In Bangladesh, persons who had lived apart reported 2 to 3 times more often that they had extramarital sex than those who had not lived apart [4]. In an earlier study in Tanzania, we found that not only mobile persons but also the partners left behind reported more sexual risk behavior [5]. In Tanzania and Zimbabwe, women whose partners traveled frequently were more likely to be HIV-positive [6,7].

To our knowledge there are only two studies that looked into the effect of polygamy, absence of the partner, and the related risk of HIV. In both Kenya and Tanzania, women in polygamous marriages were more likely to report multiple partners [8,9].

Risky sexual behavior such as multiple partners and concurrent relationships are associated with an increased risk of HIV infection [10,11]. Especially classic sexually transmitted diseases (STDs), which have a short natural history, may be transmitted through concurrent relationships. These STDs enhance the transmission of HIV [12,13]. Condoms may decrease the per-contact probability of male-to-female transmission with 95% [14], but are often not used.

In this study, we investigated whether partner absence due to travel or living in separate households leads to more extramarital sex in couples in rural northwestern Tanzania. If so, more information about these specific groups may help to develop new strategies to prevent HIV infection. Implementation of new interventions for couples with an absent partner is feasible, because they are relatively easy to identify. Mobile persons, for example, can be identified along roads, at bus-stops or lodges, and maybe at special ceremonies, like marriages or funerals.

Methods

Data

Data were collected in an HIV cohort study in Kisesa Ward in the Mwanza region of northwest Tanzania. Kisesa is situated 20 km east of Mwanza city, the regional capital and second largest city in Tanzania. The ward consists of six villages and had about 21,000 inhabitants in 2003. The ward includes Kisesa trading center located on the main road from Mwanza to Kenya.

The HIV cohort was established in 1994. Demographic data for all residents have been collected yearly. Every three years, adults have been invited to come to serological surveys to provide information about their sexual behavior and give blood for HIV testing [15,16]. From July to September 2003, additional data were collected on a purposively selected subsample of the Kisesa cohort. The subsample for this "Couples Apart Study" consisted of couples living apart, and a comparison group of cohabiting couples.

The subsample was based on couples who had been co-resident in 1996. In the demographic round in 2002, it was checked whether they still lived together. Couples who no longer lived together were designated as living apart. Couples for comparison were randomly selected from those who were still living together, distributed across the study villages in the same proportion as the original residences of the people living apart. In polygamous marriages, only one wife was selected for interview. The members of the couples living apart who had stayed in the marital home were interviewed in 2003. They were asked to provide the name and village of their formerly cohabiting spouse (i.e. partner who moved). Most of them were still living in Kisesa area, but some were living further away. Only those living within 60 km from Kisesa were followed up for interview. If partners who moved were found and agreed to be in the study, they were interviewed. The aim was to interview both partners in couples living apart and in co-resident couples, but this was not always possible, because some partners were absent due to work.

Data collected in the Couples Apart Study included age, education, marital status, partner visiting details for those living apart, travel behavior, sexual risk behavior, and self-reported symptoms of STDs. HIV testing was not part of the Couples Apart Study. However, the data were linked to HIV status ascertained in the routine serological surveys within the Kisesa cohort. Since not all respondents in the Couples Apart Study attended the serological surveys, HIV status was only available for 65% of women and 56% of men.

Respondents

The original aim was to interview 300 couples currently living apart and 300 cohabiting couples. However, fewer people in the group living apart could be interviewed because of difficulties in tracing them or refusal. Persons were only included in the analyses if they were part of a married couple (Figure 5.1). Couples in which one or both of the spouses claimed to be an ex-spouse, (ex-)regular partner, or merely a boyfriend/girlfriend at the time of interview were excluded. Some persons classified as living apart according to the demographic round in 2002 actually turned out to have re-united, and were cohabiting with their partner at the time of the interview. These persons were also left out of the analyses. Because women who moved (n=18) and men who stayed (n=40) both concerned relatively small numbers, we focused only on men who moved and women who stayed.

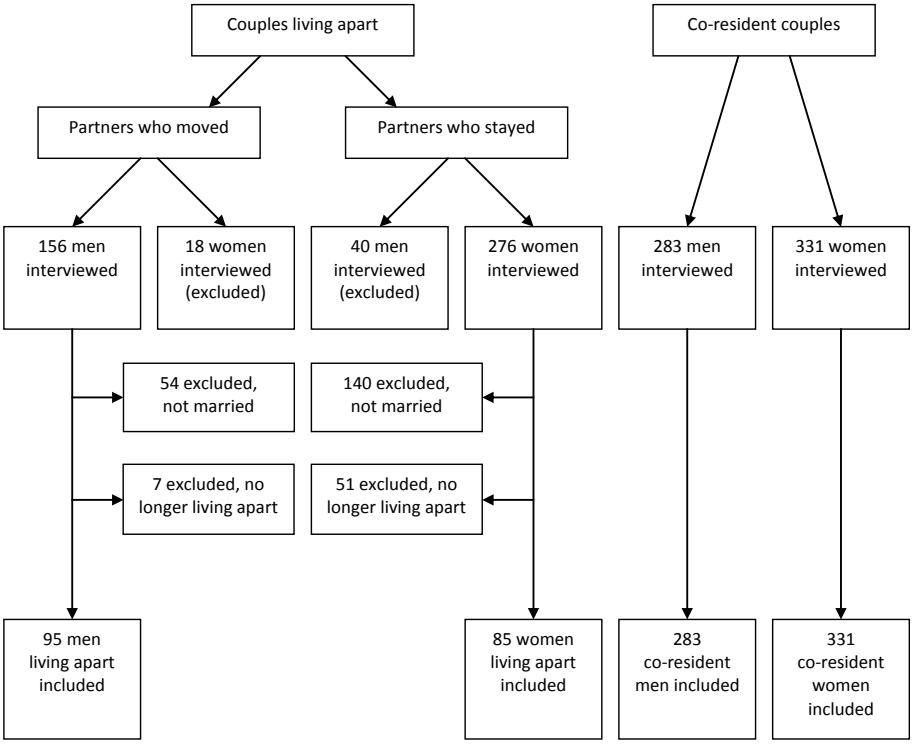

Figure 5.1 Exclusion criteria and number of study subjects.

Statistical analyses

Partners living apart were divided into two categories based on visiting frequency, in which visits by both the man and the woman were taken into account. Partners living apart who visited each other two or more times per week were defined as frequently seeing each other, whereas those who visited each other less than two times per week were defined as infrequently seeing each other. This cutoff point of two times per week was chosen to obtain groups of approximately equal size. Co-resident persons were stratified into mobile and non-mobile. Mobile co-residents were members of co-resident couples who slept outside the household more than ten times in the last year. Non-mobile co-residents slept outside the household at most ten times in the last year.

Analyses were done for men and women separately. For each category, we calculated proportions of persons per socio-demographic or travel characteristic. To test for differences we used a chi-square test or a Fisher exact test. Statistical significance was conventionally based on p-values ≤ 0.05. We calculated age-adjusted proportions for unprotected extramarital sex in the last year, self-reported STD symptoms in the last year and HIV prevalence. In polygamous marriages, extramarital sex was sex with a woman other than the wives in the marriage. Unprotected extramarital sex was defined as not using a condom during the last sex act with an extramarital partner. Differences were tested using logistic regression adjusting for age, because age distribution differed significantly between co-residents and people living apart ($p<0.001$). Finally, we used logistic regression analyses to determine whether category was associated with extramarital sex, adjusting for age and type of marriage. All analyses were done using Stata version 8.0 (Stata Corporation, College Station, Texas, USA).

Results

Our statistical analysis focused on 794 people: 95 men living apart, 85 women living apart, 283 male co-residents, and 331 female co-residents (Figure 5.1). Men living apart were significantly older than co-resident men (Table 5.1). The majority of men living apart were polygamously married (92%), whereas most co-resident men were monogamously married (87%, $p<0.001$). Furthermore, men living apart traveled more often within Kisesa ward during their most recent travel than co-resident men (38 versus 21%; $p=0.001$). The most common reason for the most recent travel was attending a funeral or other ceremony, e.g. marriage or traditional dancing after harvest season. Men living apart reported visiting a spouse/extramarital partner during their most recent travel more often than co-resident men. This was related to men living apart being more often polygamously married. Mobile

Table 5.1 Socio-demographic and travel characteristics of men and women by cohabiting status, further stratified by mobility behavior for co-residents and by partner visiting frequency for people living apart.

	Men						Women					
			Co-resident		Living apart				Co-resident		Living apart	
	Co-residents[a]	Living apart[a]	Non-mobile[a]	Mobile[a]	Many visits[a]	Few visits[a]	Co-residents[a]	Living apart[a]	Non-mobile[a]	Mobile[a]	Many visits[a]	Few visits[a]
	n=283	n=95	n=171	n=112	n=57	n=38	n=331	n=85	n=211	n=120	n=36	n=49
Age (years)		***										
15–24	8	5	8	7	4	8	22	21	24	17	17	27
25–34	31	12	27	38	12	10	27	37	35	39	25	28
35+	61	83	65	55	84	82	51	42	41	44	58	45
Education								**				
None	15	24	17	12	30	16	27	47	26	30	53	43
Primary	76	64	75	79	60	71	69	52	70	66	47	55
Secondary/higher	9	12	8	9	10	13	4	1	4	4	0	2
Type of marriage		***		***				***				***
Monogamous	87	7	92	79	4	14	85	20	86	85	3	33
Polygamous	13	93	8	21	96	86	15	80	14	15	97	67
Reason for most recent travel[b,c]												
Work	13	12	8	19	15	8	1	3	1	1	0	4
Visit relatives	21	19	21	21	17	22	31	29	25	38	30	29
Visit spouse/extramarital partner	8	26	4	12	28	22	2	8	2	1	0	13
Funeral/other ceremony	53	40	65	39	38	43	63	56	70	54	70	47
Other reason	10	10	9	12	8	14	9	8	5	14	10	7
Duration of most recent travel[c]								*				
1–5 days	63	65	60	69	63	68	53	67	55	48	69	65
> 5 days	37	35	40	31	37	32	47	33	45	52	31	35
Destination of most recent travel[c]		***		*								
Kisesa area	21	38	17	27	37	39	21	32	24	18	33	31
Elsewhere	79	62	83	73	63	61	78	68	76	82	67	69

Values represent percentages. Differences between groups were tested using Chi-squared test or Fisher exact test when appropriate.
* p≤0.05, ** p≤0.01, *** p≤0.001.
[a] We defined the following groups: *co-resident*, man and woman live in the same household; *living apart*, man and woman live in separate households, because the husband has left the household and the wife was left behind; *non-mobile*, person slept outside the household ≤ 10 times in the last year; *mobile*, person slept outside he household > 10 times in the last year; *many visits*, couples living apart seeing each other ≥ 2 times per week; *few visits*, couples living apart seeing each other < 2 times per week.
[b] Multiple answers possible.
[c] Only answered if persons traveled at least once in the last year: 232 co-resident men, 90 men living apart, 267 co-resident women, and 75 women living apart.

co-resident men were significantly more often polygamously married than non-mobile co-resident men (21 versus 8%; p=0.001). The destination of their most recent travel was significantly more often in Kisesa ward compared to non-mobile co-resident men. There were no differences in socio-demographic and travel characteristics within the subgroups of men living apart.

Women living apart were significantly less educated and more often polygamously married than co-resident women (Table 5.1). The duration of the most recent travel was significantly longer for co-resident women than for women living apart. About 60% of the women, both co-resident and living apart, traveled to attend a funeral or other ceremony, followed by 30% who traveled to visit relatives. Non-mobile co-resident women did not differ from mobile co-resident women with regard to socio-demographic and travel characteristics. Within the group of women living apart, those who saw their partner frequently were more often polygamously married than those who saw their partner less than twice a week (92 versus 67%; p=0.001).

More than 80% of the men living apart still lived in close proximity of their wife, i.e. within Kisesa ward. In women, the distance between the partners differed between the subgroups: 92% of the women living apart who frequently saw their partners lived close to their husbands, i.e. both in Kisesa ward, compared with 43% of the women living apart who saw their partners infrequently (p<0.001). The main reason for couples to live apart was that the man had a polygamous marriage and was living with another woman. Other reasons were work-related, including farming, or family-related (e.g. taking care of relatives).

Table 5.2 shows extramarital sex in the last year and STD/HIV status of co-residents and people living apart. After age-adjustment, there were no differences in unprotected extramarital sex, self-reported STD symptoms in the last year or HIV prevalence between co-resident men and men living apart. Mobile co-resident men reported significantly more extramarital sex in the last year than non-mobile men (35 versus 15%; p<0.001). However, this difference in risk behavior did not lead to differences in self-reported STD symptoms or HIV prevalence between non-mobile and mobile co-resident men. Overall, reported condom use with extramarital sex partners was low. Condom use in the last extramarital sex act varied from 0% in men living apart who frequently saw their spouse to 43% in non-mobile co-resident men (data not shown).

In women, the pattern of sexual risk behavior and STDs is not consistent. Women living apart reported significantly more extramarital sex in the last year than co-resident women (13 versus 7%; p=0.05) (Table 5.2), but they reported significantly fewer STD symptoms in the last year (7 versus 17%; p=0.04). The HIV pattern in women is similar to the

Table 5.2 Extramarital sex in the last year, sexually transmitted disease (STD) and HIV status of men and women by cohabiting status, further stratified by mobility behavior for co-residents and by partner visiting frequency for people living apart.

	Men						Women					
			Co-resident		Living apart				Co-resident		Living apart	
	Co-residents[a]	Living apart[a]	Non-mobile[a]	Mobile[a]	Many visits[a]	Few visits[a]	Co-residents[a]	Living apart[a]	Non-mobile[a]	Mobile[a]	Many visits[a]	Few visits[a]
	n=283	n=95	n=171	n=112	n=57	n=38	n=331	n=85	n=211	n=120	n=36	n=49
Extramarital sex in last year	23.4	24.0	15.0	35.4***	22.4	22.3	6.9	13.6*	6.0	9.1	8.0	16.0
Unprotected sex at last extramarital sex act[b]	67.8	86.6	57.2	76.6	100	64.4	84.5	80.0	85.7	82.8	78.0	94.7
STD symptoms in last year[c]	15.4	16.3	16.0	14.8	18.2	15.5	16.8	6.9*	14.4	21.0	11.0	3.5
HIV prevalence[d]	5.0	4.5	5.1	5.0	5.1	0.0	4.9	10.2	5.4	3.8	9.9	9.7

Values represent age-adjusted percentages. Differences between groups were tested using logistic regression analysis adjusting for age.
* p≤0.05, ** p≤0.01, *** p≤0.001.

[a] We defined the following groups: *co-resident*, man and woman live in the same household; *living apart*, man and woman live in separate households, because the husband has left the household and the wife was left behind; *non-mobile*, person slept outside the household ≤ 10 times in the last year; *mobile*, person slept outside the household > 10 times in the last year; *many visits*, couples living apart seeing each other ≥ 2 times per week; *few visits*, couples living apart seeing each other < 2 times per week.

[b] Only answered by persons who reported an extramarital partner in the last year: 70 co-resident men, 19 men living apart, 23 co-resident women, and 11 women living apart.

[c] Only answered by persons who had heard of STDs: 258 co-resident men, 92 men living apart, 282 co-resident women, and 65 women living apart.

[d] HIV status is only known in part of the respondents: 168 co-resident men, 42 men living apart, 205 co-resident women, and 59 women living apart.

Table 5.3 Extramarital sex in the last year in relation to important risk factors in multivariate analyses, for men and women.

	Men					Women				
	n	% extra-marital sex	OR	95% CI	p-value	n	% extra-marital sex	OR	95% CI	p-value
Age (years)										
15–24	27	44.4	4.2	1.7-10.3	0.002	89	15.7	5.8	2.1-16.0	0.001
25–35	100	39.0	3.2	1.8-5.7	<0.001	144	9.7	3.1	1.1-8.5	0.03
35+	251	15.2	1	–	–	183	3.3	1	–	–
Type of marriage										
Monogamous	253	25.7	1	–	–	299	7.7	1	–	–
Polygamous	124	18.5	0.7	0.3-1.6	0.4	111	9.0	1.2	0.4-3.2	0.8
Category										
Co-residents, non-mobile[a]	171	15.2	1	–	–	211	6.2	1	–	–
Co-residents, mobile[a]	112	39.3	3.7	2.0-6.7	<0.001	120	8.3	1.5	0.6-3.7	0.3
Living apart, many visits[a]	57	19.3	2.5	0.8-7.4	0.10	36	8.3	1.0	0.2-6.0	0.9
Living apart, few visits[a]	38	21.1	2.3	0.7-7.3	0.16	49	16.3	3.2	1.1-9.6	0.036

OR, odds ratio; 95% CI, 95% confidence interval

[a] We defined the following groups: *co-resident*, man and woman live in the same household; *living apart*, man and woman live in separate households, because the husband has left the household and the wife was left behind; *non-mobile*, person slept outside the household ≤ 10 times in the last year; *mobile*, person slept outside the household > 10 times in the last year; *many visits*, couples living apart seeing each other ≥ 2 times per week; *few visits*, couples living apart seeing each other < 2 times per week.

pattern of extramarital sex: 10% in women living apart versus 5% in co-resident women, although the difference is not significant (p=0.16). Reported condom use during the last extramarital sex act varied from 20% in women living apart to 15% in co-resident women (data not shown). There were no significant differences in sexual behavior or STD/HIV status within the different subgroups of women.

Table 5.3 gives the results of the multivariate analyses for extramarital sex in the last year. Mobile co-resident men were significantly more likely than non-mobile co-resident men to have had extramarital sex (odds ratio [OR]=3.7; 95% confidence interval [CI] 2.0-6.7). The odds of having had extramarital sex was 3.2 times higher in women living apart who saw their partner infrequently than in non-mobile co-resident women (95% CI 1.1-9.6). Men living apart in both subgroups and mobile co-resident women had higher odds of having had an extramarital sex partner than non-mobile co-residents, but results were not significant. Polygamously married men were less likely to report extramarital sex (OR=0.7; 95% CI 0.3-1.6), whereas women in polygamous marriages were slightly more likely to report extramarital sex (OR=1.2; 95% CI 0.4-3.2).

Discussion

In this rural area in northwestern Tanzania, most couples living apart were part of polygamous marriages, which led to a relatively low prevalence of reported extramarital sex in men.However, women living apart from their husbands reported more extramarital sex than women who lived with their husbands. More specifically, those living apart and infrequently seeing their spouse were most at risk. Being mobile was a risk factor for unprotected extramarital sex in men, but not in women.

Men and women may have different perceptions about their relationship and may sometimes report differently. Men who see their wives infrequently may report this relationship has ended, whereas the women may still report the marriage as ongoing because they are sometimes visited by their husbands. Women in Tanzania were more likely than men to report a relationship, that started a relatively long time ago, as ongoing [9]. Because we were only interested in risky behavior of married couples, we restricted our analyses to couples in which both partners still reported to be married. In this way, dilution of the study effect due to misclassification of married people was not possible.

Furthermore, most polygamous couples were included in the group living apart. However, some polygamous individuals were by chance included as being co-resident. Polygamous marriages in Tanzania consist of a man married to two or more women. In general, this man will alternately live with one of his wives, which means that whenever he is co-

residing with one, he is living apart from the other(s). Whether polygamous individuals were classified as co-residing or living apart at the time of the interview was therefore accidental. This probably diluted the effects found in our study.

Men living apart outside Kisesa or even abroad were underrepresented due to tracing difficulties. It is plausible that men living further away will see their wives less frequently. We found that men living apart and seeing their wives infrequently reported considerably more extramarital sex, but results were not significant (OR=2.3; p=0.16), due to small numbers and because the effect is most likely diluted because our sample did not include enough men living further away.

We only investigated reported extramarital sex in the last year, which has proven to be a good indicator of HIV infection [10,17]. Other indicators such as the number of lifetime sex partners or involvement in commercial sex were not asked. However, these indicators are more subject to recall and reporting bias than extramarital sex. Moreover, commercial sex questions are limited to men.

HIV status was obtained by linking with the overall cohort study. Being mobile or absent is a risk factor for HIV infection, but also a reason for not attending HIV surveys. Therefore, we could have underestimated the HIV prevalence in these persons. STD symptoms were only asked in a subgroup who had heard of STDs, and symptoms were self-reported and not confirmed by a physical examination and/or laboratory testing. Women living apart had heard of STDs slightly less often than co-resident women (76 versus 85%; p=0.05). Less knowledge about STDs and their symptoms may explain the conflicting results in women living apart reporting more extramarital sex, but less STD symptoms in the last year. Moreover, STD symptoms in women can be very asymptomatic and can also be related to other diseases. We would expect a higher STD prevalence in our study because high prevalences of STDs were found in both men and women in the Mwanza trial, which study area is near to Kisesa [18].

Women living apart and seeing their husbands infrequently reported more extramarital sex than those who saw their partners frequently. It seems likely that women who are left alone for a longer period are more vulnerable to risky behavior. By seeing their husband less often their sexual needs may not be fulfilled [19,20]. Furthermore, there is also less social control from their husbands. Both conditions facilitate women to actively start new sexual relationships. On the other hand, some women may not be supported financially by their absent husbands and may therefore need to engage in sex in exchange for money or food [21]. Before effective prevention programmes can be developed, more understanding of the determinants of sexual risk behaviour of women left behind is needed.

Other studies reported more extramarital sex and more HIV infections in men living apart due to work-related migration [3,4]. However, migration for work is not a common reason for living apart in this rural area in Tanzania. We found that being polygamously married was the most common reason for living apart, but for men this was not associated with more risky sexual behavior. Possible explanations are that polygamously married men need all their time and energy for their wives, have less opportunities to start other sexual relationships, and have less unmet sexual needs. Furthermore, most men living apart in our study still lived in close proximity to their wives and were able to see them often. In contrast, migrant men in South Africa and Bangladesh lived relatively far away and were not able to visit their rural homes often [3,4].

Our finding that mobile co-resident men more often report an extramarital sex partner than non-mobile co-resident men is consistent with studies in Cameroon and Senegal. In Cameroon, mobile men were significantly more likely to report having nonspousal partners and one-off contacts than men who were not mobile [22]. In Senegal, short-term mobility was associated with having more casual sex partners [23].

We conclude that couples who are temporarily separated due to travel or living apart reported more risky behavior and are therefore at increased risk of acquiring an HIV infection. The main reasons for temporary separation from a spouse were attending funerals or other ceremonies, visiting relatives, and in particular being polygamously married. Changing these patterns is neither straightforward nor likely to happen in the near future. Therefore, the best prevention strategy might be to make sexual risk behavior as safe as possible. Because condom use within marriages is unpopular [24,25], condom use with extramarital partners should be emphasized. Individuals most at risk, namely mobile co-resident men, and women living apart and infrequently seeing their husbands, which can readily be identified, need extra attention in HIV prevention campaigns.

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References

1. Lagarde E, Pison G, Enel C. A study of sexual behavior change in rural Senegal. *J Acq Immune Defic Syndr Hum Retrovirol* 1996; 11:282-287.
2. Rakwar J, Lavreys L, Thompson ML, Jackson D, Bwayo J, Hassanali S*, et al.* Cofactors for the acquisition of HIV-1 among heterosexual men: prospective cohort study of trucking company workers in Kenya. *AIDS* 1999; 13:607-614.
3. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sweat MD*, et al.* Who infects whom? HIV-1 concordance and discordance among migrant and non-mirant couples in South Africa. *AIDS* 2003; 17:2245-2252.
4. Mercer A, Khanam R, Gurley E, Azim T. Sexual risk behavior of married men and women in Bangladesh associated with husbands' work migration and living apart. *Sex Transm Dis* 2007; 34:265-273.
5. Kishamawe C, Vissers D, Urassa M, Isingo R, Mwaluko G, Borsboom GJJM*, et al.* Mobility and HIV in Tanzanian couples: both mobile persons and their partners behind show increased risk. *AIDS* 2006; 20:601-608.
6. Mbizvo EM, Msuya SE, Stray-Pedersen B, Sundby J, Chirenje MZ, Hussain A. HIV seroprevalence and its associations with the other reproductive tract infections in asymptomatic women in Harare, Zimbabwe. *Int J STD AIDS* 2001; 12:524-531.
7. Msuya SE, Mbizvo E, Hussain A, Uriyo J, Sam NE, Stray-Pedersen B. HIV among pregnant women in Moshi Tanzania: the role of sexual behavior, male partner characteristics and sexually transmitted infections. *AIDS Res Ther* 2006; 3:27.
8. Hattori MK, Dodoo FN. Cohabitation, marriage, and 'sexual monogamy' in Nairobi's slums. *Soc Sci Med* 2007; 64:1067-1078.
9. Nnko S, Boerma JT, Urassa M, Mwaluko G, Zaba B. Secretive females or swaggering males? An assessment of the quality of sexual partnership reporting in rural Tanzania. *Soc Sci Med* 2004; 59:299-310.
10. Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. *AIDS* 1997; 11:641-648.
11. Halperin DT, Epstein H. Concurrent sexual partnerships help to explain Africa's high HIV prevalence: implications for prevention. *Lancet* 2004; 364:4-6.
12. Laga M, Nzila N, Goeman J. The interrelationship of sexually transmitted diseases and HIV infection: implications for the control of both epidemics in Africa. *AIDS* 1991; 5:S55-63.
13. Plummer FA, Simonsen JN, Cameron DW, Ndinya-Achola JO, Kreiss JK, Gakinya MN*, et al.* Cofactors in male-female sexual transmission of human immunodeficiency virus type 1. *J Infect Dis* 1991; 163:233-239.
14. Pinkerton SD, Abramson PR. Effectiveness of condoms in preventing HIV transmission. *Soc Sci Med* 1997; 44:1303-1312.
15. Boerma JT, Urassa M, Senkoro K, Klokke A, Ng'weshemi JZL. Spread of HIV infection in a rural area of Tanzania. *AIDS* 1999; 13:1233-1240.
16. Mwaluko G, Urassa M, Isingo R, Zaba B, Boerma JT. Trends in HIV and sexual behaviour in a longitudinal study in a rural population in Tanzania, 1994-2000. *AIDS* 2003; 17:2645-2651.
17. Slaymaker E. A critique of international indicators of sexual risk behaviour. *Sex Transm Infect* 2004; 80 Suppl 2:ii13-21.

18. Orroth KK, Korenromp EL, White RG, Gavyole A, Gray RH, Muhangi L*, et al.* Higher risk behaviours and rates of sexually transmitted diseases in Mwanza compared to Uganda may help explain HIV prevention trial outcomes. *AIDS* 2003; 17:2653-2660.
19. Tawfik L, Watkins SC. Sex in Geneva, sex in Lilongwe, and sex in Balaka. *Soc Sci Med* 2007; 64:1090-1101.
20. Kesby M. Participatory diagramming as a means to improve communication about sex in rural Zimbabwe: a pilot study. *Soc Sci Med* 2000; 50:1723-1741.
21. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sturm AW*, et al.* The impact of migration on HIV-1 transmission in South-Africa: a study of migrant men and non-migrant men and their partners. *Sex Transm Dis* 2003; 30:149-156.
22. Lydie N, Robinson NJ, Ferry B, Akam E, De Loenzien M, Abega S. Mobility, sexual behavior, and HIV infection in an urban population in Cameroon. *J Acquir Immune Defic Syndr* 2004; 35:67-74.
23. Lagarde E, Schim Van Der Loeff M, Enel C, Holmgren B, Dray-Spira R, Pison G*, et al.* Mobility and the spread of human immunodeficiency virus into rural areas of West Africa. *Int J Epidemiol* 2003; 32:744-752.
24. Bond V, Dover P. Men, women and the trouble with condoms: problems associated with condom use by migrant workers in rural Zambia. *Health Transit Rev* 1997; 7 (Suppl):377-391.
25. Chimbiri AM. The condom is an 'intruder' in marriage: evidence from rural Malawi. *Soc Sci Med* 2007; 64:1102-1115.

6 The impact of non-participation of mobile groups on HIV control: a modeling study

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Abstract

Background Mobility (migration and travel) is associated with HIV infection due to risky sexual behavior. Limited participation of mobile groups may therefore reduce the effectiveness of HIV interventions disproportionally. We investigated how much mobility may affect HIV control.

Methods We used the STDSIM model, which simulates transmission and control of HIV and sexually transmitted diseases (STDs) in a population consisting of individuals with various types of sexual relationships. STDSIM was extended to simulate migration and travel in detail. In the baseline situation, we modeled mobility patterns based on data from Kisesa area in Tanzania. Simulated interventions were condom promotion, STD treatment, and health education. We explored the impact of non-participation of immigrants and/or travelers on the effectiveness of interventions.

Results With our assumptions, immigrants and travelers who were more often away from home had more HIV infections than non-migrants and people who traveled less often. This was primarily caused by more casual sex partners, and more sex with one-off and commercial sex contacts. If both mobile groups do not participate, the effectiveness of condom promotion and health education could be reduced by 40%.

Conclusions Non-participation of mobile groups can considerably reduce the effectiveness of HIV control strategies. It is worth to monitor interventions with respect to participation of migrants and travelers. If non-participation is substantial, impact of HIV interventions can be improved by actively approaching these people.

Introduction

Mobility exists in different forms: people can move to another area or country [1,2], they can visit relatives and ceremonies, and they can undertake work-related travel, such as trading, truck driving, and seasonal work [3-5]. Mobility is often related to risky sexual behavior, and consequently to the spread of HIV and other sexually transmitted diseases (STDs) [1,6,7]. Studies in Senegal and South Africa found that seasonal or temporary migrants reported more sexual partners [5] and had a higher HIV prevalence than residents [6]. In a recent study in rural Tanzania, immigrants had more risky behavior than people who were born in the area, also when they had immigrated longer ago [8]. Most of the long distance truck drivers in Kenya reported having sex with commercial sex workers (CSW), and one quarter was infected with HIV [4]. Social and living conditions make migrants and travelers more prone to casual and commercial sex [9,10]. Partners staying behind also reported more casual partners [11]. Mobile groups may form a small part of the population, but due to their high-risk behavior and increased HIV prevalence, they may play an important role in the spread of HIV.

The role of condom promotion and health education in reducing HIV transmission has been established since a long time [12-15]. Although there is no available data, we may speculate that mobile people may often not be reached in these interventions. Immigrants who recently arrived in an area may not know where to buy condoms or where to find health clinics. Travelers away from home may not use condoms and may easier engage in sex with a new partner.

Spread and control of HIV can be studied with dynamic modeling [16]. Two models have incorporated the relationship between migration and HIV infection [17,18]. To our knowledge there are no models that explicitly model travel. The microsimulation model STDSIM [19,20] has been used among others to study the results of the Mwanza and Rakai trials [21,22], to explore the contrasting HIV epidemics in east and west Africa [23,24], and to study the possible impact of male circumcision [25]. In the current study, we used STDSIM to explore the importance of mobile groups on HIV spread, and to what extent non-participation of mobile groups may decrease the impact of interventions.

Methods

Modeling mobility in STDSIM

We used the microsimulation model STDSIM, which simulates the natural history and transmission of HIV and other STDs in a population over time [19,26]. In STDSIM,

individuals are part of heterosexual networks consisting of (steady and casual) sexual relationships, one-off contacts, and contacts of men with commercial sex workers (CSWs). Different interventions to control the spread of HIV and other STDs can be modeled in STDSIM. In earlier simulations with STDSIM, mobility was not considered [22,27]. For the present study, we included migration and travel to model mobility in detail. Mobility parameters were based on data or, if this was lacking, on assumptions based on expert opinion.

We simulated an HIV epidemic in Kisesa, a rural area in Mwanza region in Tanzania [28]. Starting from an existing quantification of STDSIM for the HIV epidemic in another part of Mwanza region [22,27], almost all parameters on demography, STD biology and sexual behavior could be kept the same. However, to compensate for the higher risk due to the new mobility patterns, the overall rate of starting new sexual relationships and the level of CSW-visiting needed to be downward-adjusted with 20% to arrive at the same HIV prevalence. Furthermore, quantifications for condom use were changed, since condom use had increased by the early nineties. In Kisesa, 8% of men reported always using a condom during sex with a casual partner, and an additional 17% sometimes used a condom [29]. In women, these figures were 7% and 6%, respectively. We therefore set condom use during casual sex at 10% from 1990 onwards. Condom use in commercial sex contacts was assumed to be twice as high (20%). Data from Kenya from 1999 showed that 34-56% of clients and 75% of sex workers reported always or usually using condoms during commercial sex [30]. Therefore, we assumed that condom use increased to 50% in 2000. Analogously, we assumed that condom use during casual sex increased from 10% in 1990 to 25% in 2000.

As source for immigrants, visitors and sexual partners for travelers, we created an 'outside' population with STDSIM. This outside population was also defined as a rural population with the same risk behavior as the study population, and the parameters for those of the existing Mwanza quantification without mobility [22,27]. HIV prevalence in men and women in the outside population was pre-set to be identical to the simulated HIV prevalence in the study population. Individuals of this population were stored in a database system from which STDSIM could sample immigrants, visitors and sexual partners for travelers. The database system contains information for each year of the simulation.

Mobility defined and quantified

Two mobile groups were defined: *immigrants* (people from the outside population who recently moved into the study population), and *travelers* (people living in the study

population traveling to the outside population). These mobile groups are non-exclusive: immigrants can be travelers, and vice versa.

We modeled 10% immigration annually, based on migration rates found in Kisesa [29]. Migration was concentrated in young adults [31]. Based on the study by Mmbaga *et al.* [8], we assumed that immigrants who move into the study population, have more risky behavior in the first five years after immigration: i.e. all immigrants had a 20% higher tendency to engage in steady and casual relationships and male immigrants were 20% more likely to visit CSWs. During these first five years the chance for recent immigrants to leave the population again was twice as high as for non-migrants. We further assumed that after five years, immigrants adapted to the existing sexual behavior norms of the study population they started to live in.

Based on data from Kisesa [29], we defined the following three travel profiles: firstly, those who visit family and relatives (77%), traveling for a period of one week followed by half a year at home. Secondly, traders who go to markets and towns nearby to sell their products and people who attend ceremonies (20%). They are away from home for one week followed by 3 weeks at home. Thirdly, highly mobile people (3%), such as truck drivers, who are away from home for three weeks followed by one week at home. These assumptions imply 8% traveling (28 nights per year) divided over three travel profiles. People were assumed to be in one travel profile during their lifetime. Both men and women, aged 15 to 55 years, traveled according to one of these profiles. Travelers had sexual contacts with steady or casual partners while being at home, just like the rest of the study population, but one-off contacts with persons from the outside population while traveling. We assumed that the average interval for one-off contacts was two weeks for each group following a Poisson process. Besides this, male travelers could also visit CSWs during travel, with 6 visits per year for highly mobile men and 1 visit per year for other travelers.

Besides immigration and traveling, there are two other forms of mobility in our model: out-migration (people who leave the study population), and visiting (people from the outside population that have sexual contacts with random persons in the study population). Based on Kisesa data [29], 12% out-migration was modeled per year. Furthermore, we assumed an average of one sex contact per person per year with a visitor from the outside population for the age group 15 to 55 years. Visitors had sexual contact with persons of the same age group and both men and women were at risk of having sexual contacts with visitors (based on a fully random process).

HIV interventions

We simulated three interventions, all starting in 2009. Firstly, condom promotion campaigns: we assumed that condom promotion increased condom use from 25% to 50% in casual contacts and from 50% to 75% in CSW contacts from 2009 onwards. The second intervention consisted of improving health seeking behavior and quality of care, leading to an increased proportion of cured STDs. Before 2009, 5% of symptomatic STDs were cured [32,33]. From 2009 onwards, the proportion of symptomatic STDs cured increased to 25% per year, comparable to assumptions in previous STDSIM applications [32,33]. The third intervention was health education aimed at partner reduction. From 2009 onwards, health education was assumed to reduce the number of sexual partners and CSW visits by 25%.

To study the impact of non-participation of mobile people, we modeled four scenarios for each intervention. In the first scenario, both immigrants and travelers participated in the intervention of interest, similar to the rest of the population. In the second and third scenario, either immigrants during their adaptation period of five years or travelers while away from home did not participate at all, while the other group participated as in the first scenario. In the fourth scenario, both mobile groups did not participate. Non-participation of travelers when away from home was defined as non-adherence to the intervention when traveling; travelers did participate in the intervention of interest when at home. In a sensitivity analysis, we explored the impact of travelers having a two to four times more risky behavior than in the baseline assumptions. Results of each scenario were averaged over 100 runs to reduce the influence of random fluctuations associated with stochastic modeling. All results concern the general adult population aged 15 to 55 years, except Figure 6.1, where the available data reported HIV prevalence in 15 to 45 years.

Results

In Figure 6.1, data for adults aged 15 to 45 years is shown for both simulated and empirical data. Simulated HIV prevalence in men and women reasonably fitted data from Kisesa [28]. After the increase in condom use in 2000 the HIV prevalence showed a slightly downward trend. This trend continued until the end of the simulation period in the baseline situation without HIV interventions (Figure 6.2).

The sexual risk behavior and HIV prevalence per mobile group resulting from our assumptions is presented in Table 6.1. Men aged 15 to 55 years had on average 41 sex acts per year. For women, this number was 40. About one fifth of the population consisted of immigrants. Young male immigrants (15 to 25 years) had more often casual

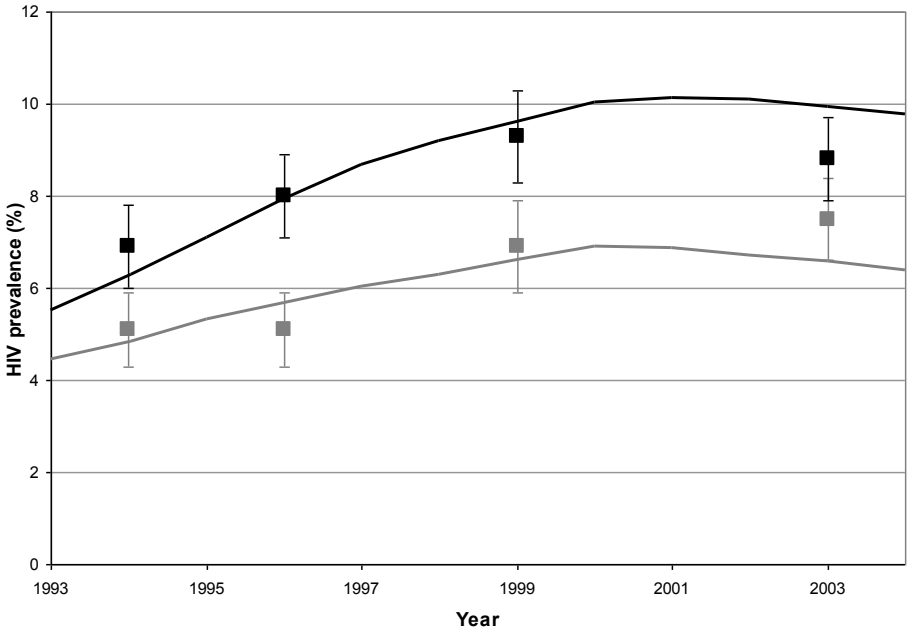

Figure 6.1 Simulated and observed HIV prevalence (%) in men and women aged 15 to 45 years in Kisesa, Tanzania. Black, women; grey, men; markers, observed data with 95% confidence intervals; lines, model prediction in study population.

sex than young non-migrants, resulting in a higher HIV prevalence. After age 25, most men had steady relationships. Immigrants aged 25 years and older still had a higher HIV prevalence, due to slightly more casual sex and CSW visits. Female immigrants showed similar patterns, although young immigrant women were more often married. At age 25 and above, HIV prevalence was similar for recent immigrant and non-migrant women. Mobile groups are non-exclusive: migrants and non-migrants can also travel, and are on average 8% of the time away. Migrants and non-migrants had on average 2 one-off contacts while away from home, and 0.14 CSW contact if male. The number of sex contacts was lowest in the group of travelers most often away (Table 6.1). However, their sexual behavior was more risky, since sexual contacts within steady relationships occurred less often and contacts with one-off and CSW partners increased. This leads to the highest HIV prevalence in people who travel most: 8.1% in highly mobile men and 11.4% in highly mobile women.

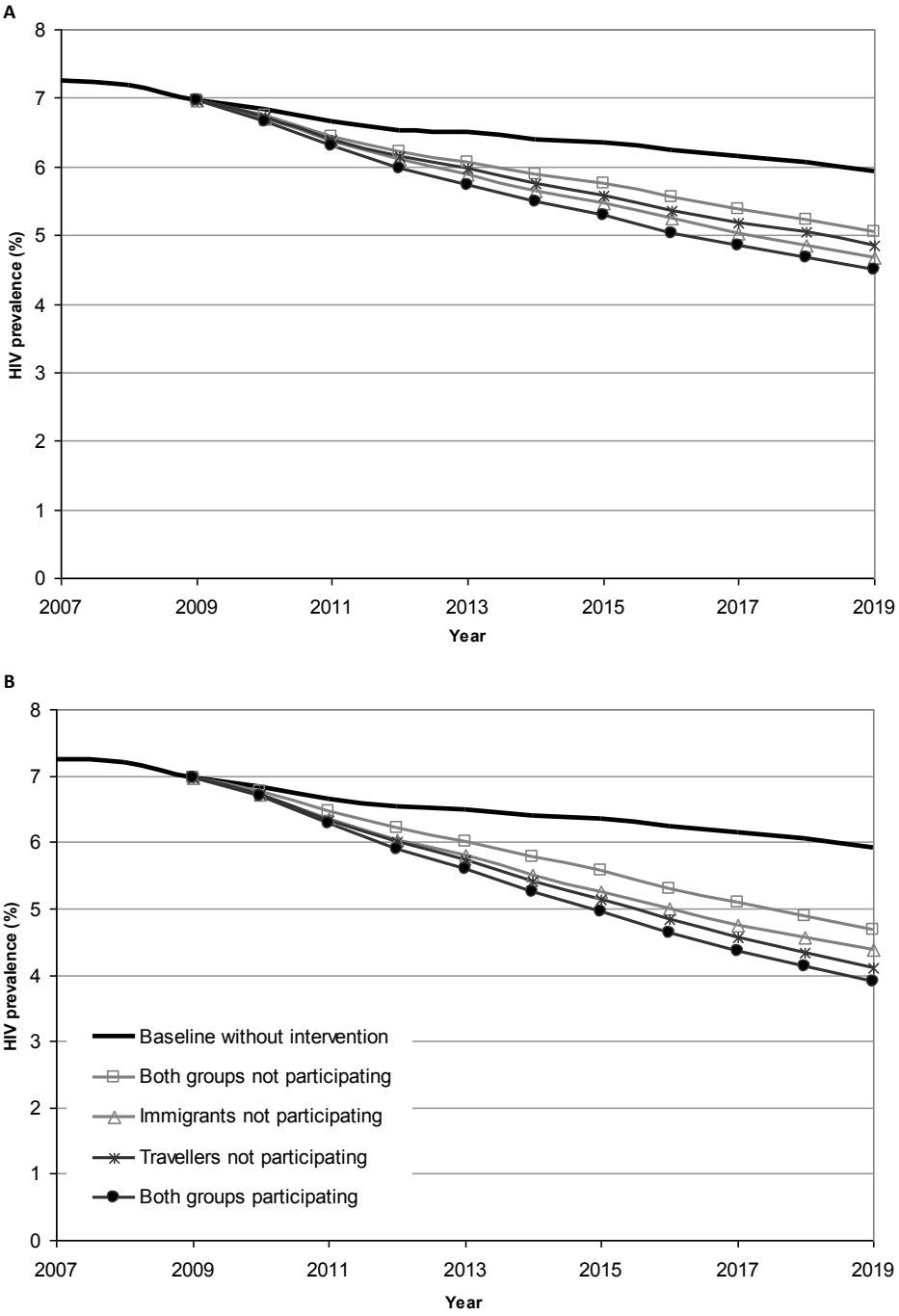

Figure 6.2 Impact of participation and non-participation of mobile groups on the effectiveness of the condom promotion intervention (A) and the health education intervention (B). HIV interventions started in 2009.

Table 6.1 Sexual risk behavior and HIV prevalence for men and women in 2009, grouped by mobility status.

	Group size	Number of sex acts while being at home				Number of sex acts while traveling		Total number of sex acts	HIV prevalence
		In steady relations	In casual relations	With CSWs	With visitors	One-off	With CSWs		
MEN (n=7201)									
Migration status									
Immigrants 15-24y	9.5%	13.9	4.8	0.41	1.1	2.0	0.14	22.3	2.3%
Immigrants 25-54y	12.1%	53.6	1.7	0.56	1.1	2.0	0.14	59.1	9.6%
Non-migrants 15-24y	39.1%	12.2	4.2	0.28	1.1	2.0	0.14	19.9	1.5%
Non-migrants 25-54y	39.3%	54.7	1.3	0.38	1.1	2.0	0.14	59.6	8.8%
Travel profile									
Family visitors	77.4%	35.8	2.9	0.43	1.2	1.0	0.04	41.4	5.3%
Market traders*	19.7%	29.7	2.4	0.36	1.1	4.9	0.19	38.7	5.7%
Highly mobile men	2.9%	21.4	1.8	0.26	0.8	10.7	2.46	37.4	8.1%
WOMEN (n=7511)									
Migration status									
Immigrants 15-24y	11.5%	30.0	4.2	N/A	1.1	2.1	N/A	37.4	8.1%
Immigrants 25-54y	9.6%	44.3	0.6	N/A	1.1	2.1	N/A	48.1	10.6%
Non-migrants 15-24y	37.3%	27.4	3.9	N/A	1.1	2.1	N/A	34.5	5.4%
Non-migrants 25-54y	41.6%	39.7	0.5	N/A	1.1	2.1	N/A	43.4	10.5%
Travel profile									
Family visitors	77.1%	36.1	2.3	N/A	1.2	1.0	N/A	40.6	8.0%
Market traders*	20.1%	30.3	1.9	N/A	1.1	4.9	N/A	38.2	9.3%
Highly mobile women	2.8%	22.1	1.4	N/A	0.8	10.7	N/A	35.0	11.4%

N/A: non applicable; * This group of travelers also includes those visiting ceremonies such as marriages and funerals.

Table 6.2 gives the overall number of averted HIV cases in a 10-year period for the different interventions. The effectiveness of condom promotion and health education if both mobile groups participated was estimated at 19% and 26% prevented HIV cases, respectively. Non-participation of immigrants and travelers while away from home could reduce the impact of both interventions by about 40% (Table 6.2). Figure 6.2 illustrates the HIV prevalence over time for the different scenarios for condom promotion (A) and health education (B). HIV prevalence in 2019 could decrease from 5.9% without intervention to 4.5% with condom promotion and to 3.9% with health education. Non-participation of one or both mobile groups led to reduced effectiveness of these interventions (Figure 6.2). STD treatment hardly had an impact on the number of averted HIV cases. The effectiveness if both mobile groups participated was estimated at only 2% prevented HIV cases, making a reduction of this intervention due to non-participation of mobile groups negligible (not shown).

Table 6.2 Averted HIV cases per 100,000 HIV-negative adult person years in the period 2010 to 2019, and the impact of non-participation of mobile groups. The baseline situation without any intervention results in 1,538 HIV cases in the period 2010 to 2019. Non-participation of mobile groups means that immigrants do not participate in the 5-years after immigration, and that travelers do not adhere to the intervention when being away from home.

Intervention	Both groups participate	Non-participation of mobile groups		
		Immigrants	Travelers	Both groups
Condom promotion	295 * (100%)	254 (86%)	217 (74%)	177 (60%)
Health education	401 * (100%)	303 (75%)	351 (88%)	235 (59%)

* 295 corresponds to a 19% decrease in HIV cases; 401 corresponds to a 26% decrease in HIV cases.

The sensitivity analysis showed that condom promotion was more sensitive to the risk behavior of travelers than health education. Due to non-participation of both mobile groups condom promotion effectiveness was reduced by 40% in the baseline situation, by 47% with two times more risky behavior, and by 56% when risk behavior was four times more risky. The effectiveness of health education was reduced by 41%, 43%, and 45%, respectively. Overall, results did not change drastically if risk behavior of travelers while away from home was increased.

Discussion

With our assumptions, immigrants and travelers who were more often away from home had considerably more HIV infections than non-migrants and people who traveled less often. This was mainly due to young immigrants having more often casual sex, and frequent travelers being more engaged in risky sex with one-off contacts and CSWs.

We also showed that mobility could considerably reduce the effect of different HIV intervention strategies. If both mobile groups do not participate in the intervention of interest, the effectiveness could be reduced by 40%.

Since mobility is an important risk factor for HIV infection, it should not be neglected in modeling studies [1,34,35]. Until now, only a few modeling studies simulating HIV infection or other STDs took migration into account [17,18]. Coffee *et al*. [17] used a deterministic model to evaluate the interactions between migration, sexual behavior and HIV infection in South Africa. They showed that migration increases HIV prevalence by enhanced risk behavior, and less so by linking geographically separate epidemics. Walker *et al*. [18] used a deterministic model to study the impact of migration on declining HIV epidemics. They found that trends in HIV prevalence are influenced when migration rates changes and when those migrating have different HIV risk compared to the rest of the population. Our study is the first that explores both migration and traveling behavior.

The impact of non-participation of mobile groups on the effectiveness of HIV interventions may be explained by the simple fact that this relatively large group of persons is non-participating, and not by their increased risk. To study how much is explained by random non-participation of people, we compared this random non-participation with non-participation of immigrants. Results for condom promotion could be fully explained by non-participation per se. In contrast, for health education it does matter who is non-participating: reduction in effectiveness was more than two times higher if immigrants were non-participating (25% versus 11%). This can be explained by the increased risk behavior of immigrants in the first five years.

It is less straightforward to compare non-participation of travelers with equal-sized random non-participation, since travelers only keep to their pre-intervention behavior when they are away from home. Although not modeled, it is expected that it does matter who is non-participating. The main reason is the type of sex partners when away from home. These are one-off contacts and CSW visits (for male travelers). CSWs are more often HIV infected, so chances of getting HIV are higher. One-off contacts may also form a risk, since each sex contact will be with a different partner and having multiple sex partners is a risk factor for HIV infection [36].

In most HIV prevention strategies, health education campaigns will be combined with condom campaigns, and maybe with other strategies such as voluntary counseling and testing. In our model simulations, interventions were kept separate to calculate the impact of non-participation per intervention. Furthermore, the effectiveness of the STD treatment intervention was relatively small in our model simulations, due to the already advanced stage of the HIV epidemic in Kisesa [28].

Mobile groups can be missed in HIV surveys and prevention programs. These persons are highly vulnerable to getting HIV infected due to their sexual risk behavior and social circumstances. Prevention programs can be expanded by making antiretroviral treatment and condoms available and easy to find and affordable for all people in an area, including new immigrants. Another option is to specifically target mobile groups. Often it will not be possible to reduce mobility behavior, so interventions should try to change risk behavior of travelers and immigrants. Examples of such targeted interventions are condom distribution and education activities at truck stops [37].

In conclusion, this study shows that non-participation of mobile groups can considerably reduce the effectiveness of HIV control strategies. It is worthwhile to further explore to what extent migrants and travelers are non-participating in prevention programs. In areas with high levels of mobility and substantial non-participation of mobile people, impact of HIV interventions may considerably be improved by actively addressing these people. Moreover, specific targeting of these groups may form an interesting prevention strategy.

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References

1. Nunn AJ, Wagner HU, Kamali A, Kengeya-Kayondo JF, Mulder DW. Migration and HIV-1 seroprevalence in a rural Ugandan population. *AIDS* 1995; 9:503-506.
2. Decosas J, Kane F, Anarfi JK, Sodji KDR, Wagner HU. Migration and AIDS. *Lancet* 1995; 346:826-828.
3. Pickering H, Okongo M, Bwanika K, Nnalusiba B, Whitworth J. Sexual mixing patterns in Uganda: small-time urban/rural traders. *AIDS* 1996; 10:533-536.
4. Bwayo J, Plummer F, Omari M, Mutere A, Moses S, Ndinya-Achola J, *et al.* Human immunodeficiency virus infection in long-distance truck drivers in east Africa. *Arch Intern Med* 1994; 154:1391-1396.
5. Lagarde E, Pison G, Enel C. A study of sexual behavior change in rural Senegal. *J Acq Immune Defic Syndr Hum Retrovirol* 1996; 11:282-287.
6. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sturm AW, *et al.* The impact of migration on HIV-1 transmission in South-Africa: a study of migrant men and non-migrant men and their partners. *Sex Transm Dis* 2003; 30:149-156.
7. Lydie N, Robinson NJ, Ferry B, Akam E, De Loenzien M, Abega S. Mobility, sexual behavior, and HIV infection in an urban population in Cameroon. *J Acquir Immune Defic Syndr* 2004; 35:67-74.

8. Mmbaga EJ, Leyna GH, Hussain A, Mnyika KS, Sam NE, Klepp KI. The role of in-migrants in the increasing rural HIV-1 epidemic: results from a village population survey in the Kilimanjaro region of Tanzania. *Int J Infect Dis* 2008; 12:519-525.
9. Chirwa WC. Migrant labour, sexual networking and multi-partnered sex in Malawi. *Health Transit Rev* 1997; 7 (Suppl 3):5-15.
10. IOM. HIV/AIDS, population mobility and migration in Southern Africa; defining a research and policy agenda. Geneva; 2005. Available at: http://www.reliefweb.int/library/documents/2005/iom-souafr-30jun.pdf.
11. Kishamawe C, Vissers D, Urassa M, Isingo R, Mwaluko G, Borsboom GJJM*, et al.* Mobility and HIV in Tanzanian couples: both mobile persons and their partners behind show increased risk. *AIDS* 2006; 20:601-608.
12. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* 2002:CD003255.
13. Pinkerton SD, Abramson PR. Effectiveness of condoms in preventing HIV transmission. *Soc Sci Med* 1997; 44:1303-1312.
14. Shelton JD, Halperin DT, Nantulya V, Potts M, Gayle HD, Holmes KK. Partner reduction is crucial for balanced "ABC" approach to HIV prevention. *BMJ* 2004; 328:891-893.
15. Stoneburner RL, Low-Beer D. Population-level HIV declines and behavioral risk avoidance in Uganda. *Science* 2004; 304:714-718.
16. Anderson RM, Garnett GP. Mathematical models of the transmission and control of sexually transmitted diseases. *Sex Transm Dis* 2000; 27:636-643.
17. Coffee M, Lurie MN, Garnett GP. Modelling the impact of migration on the HIV epidemic in South Africa. *AIDS* 2007; 21:343-350.
18. Walker PT, Hallett TB, White PJ, Garnett GP. Interpreting declines in HIV prevalence: impact of spatial aggregation and migration on expected declines in prevalence. *Sex Transm Infect* 2008; 84 (Suppl 2):ii42-48.
19. Van der Ploeg CPB, Van Vliet C, De Vlas SJ, Ndinya-Achola JO, Fransen L, Van Oortmarssen GJ*, et al.* STDSIM: a microsimulation model for decision support on STD control. *Interfaces* 1998; 28:84-100.
20. Korenromp EL, Van Vliet C, Bakker R, De Vlas SJ, Habbema JDF. HIV spread and partnership reduction for different patterns of sexual behaviour - a study with the microsimulation model STDSIM. *Math Popul Studies* 2000; 8:135-173.
21. Korenromp EL, Bakker R, Gray R, Wawer MJ, Serwadda D, Habbema JD. The effect of HIV, behavioural change, and STD syndromic management on STD epidemiology in sub-Saharan Africa: simulations of Uganda. *Sex Transm Infect* 2002; 78 (Suppl 1):i55-63.
22. White RG, Orroth KK, Korenromp EL, Bakker R, Wambur M, Sewankambo NK*, et al.* Can population differences explain the contrasting results of the Mwanza, Rakai, and Masaka HIV/sexually transmitted disease intervention trials? A modeling study. *J Acquir Immune Defic Syndr* 2004; 37:1500-1513.
23. Freeman EE, Orroth KK, White RG, Glynn JR, Bakker R, Boily MC*, et al.* Proportion of new HIV infections attributable to herpes simplex 2 increases over time: simulations of the changing role of sexually transmitted infections in sub-Saharan African HIV epidemics. *Sex Transm Infect* 2007; 83 (Suppl 1):i17-24.

24. Orroth KK, Freeman EE, Bakker R, Buve A, Glynn JR, Boily MC, *et al.* Understanding differences between contrasting HIV epidemics in East and West Africa: results from a simulation model of the Four Cities Study. *Sex Transm Infect* 2007; 83 (Suppl 1):i5-16.
25. White RG, Glynn JR, Orroth KK, Freeman EE, Bakker R, Weiss HA, *et al.* Male circumcision for HIV prevention in sub-Saharan Africa: who, what and when? *AIDS* 2008; 22:1841-1850.
26. Korenromp EL, Bakker R, De Vlas SJ, Robinson NJ, Hayes R, Habbema JDF. Can behaviour change explain increases in the proportion of genital ulcers attributable to herpes in sub-Saharan Africa? A simulation modelling study. *Sex Transm Dis* 2002; 29:228-238.
27. Korenromp EL, White RG, Orroth KK, Bakker R, Kamali A, Serwadda D, *et al.* Determinants of the impact of sexually transmitted infection treatment on prevention of HIV infection: a synthesis of evidence from the Mwanza, Rakai, and Masaka intervention trials. *J Infect Dis* 2005; 191 (Suppl 1):S168-178.
28. Wambura M, Urassa M, Isingo R, Ndege M, Marston M, Slaymaker E, *et al.* HIV prevalence and incidence in rural Tanzania: results from 10 years of follow-up in an open-cohort study. *J Acquir Immune Defic Syndr* 2007; 46:616-623.
29. Boerma JT, Urassa M, Nnko S, Ng'Weshemi J, Isingo R, Zaba B, *et al.* Socio-demographic context of the AIDS epidemic in a rural area in Tanzania with a focus on people's mobility and marriage. *Sex Transm Infect* 2002; 78:i97-105.
30. Voeten HACM, Egesah OB, Ondiege MY, Varkevisser CM, Habbema JDF. Clients of female sex workers in Nyanza province, Kenya: a core group in STD/HIV transmission. *Sex Transm Dis* 2002; 29:444-452.
31. Orroth KK, Korenromp EL, White RG, Gavyole A, Gray RH, Muhangi L, *et al.* Higher risk behaviours and rates of sexually transmitted diseases in Mwanza compared to Uganda may help explain HIV prevention trial outcomes. *AIDS* 2003; 17:2653-2660.
32. Grosskurth H, Mwijarubi E, Todd J, Rwakatare M, Orroth K, Mayaud P, *et al.* Operational performance of an STD control programme in Mwanza Region, Tanzania. *Sex Transm Infect* 2000; 76:426-436.
33. Buve A, Changalucha J, Mayaud P, Gavyole A, Mugeye K, Todd J, *et al.* How many patients with a sexually transmitted infection are cured by health services? A study from Mwanza region, Tanzania. *Trop Med Int Health* 2001; 6:971-979.
34. Decosas J, Adrien A. Migration and HIV. *AIDS* 1997; 11 (Suppl A):S77-84.
35. Quinn TC. Population migration and the spread of types 1 and 2 human immunodeficiency viruses. *Proc Natl Acad Sci U S A* 1994; 91:2407-2414.
36. Malamba SS, Wagner HU, Maude G, Okongo M, Nunn AJ, Kengeya-Kayondo JF, *et al.* Risk factors for HIV-1 infection in adults in a rural Ugandan community: a case-control study. *AIDS* 1994; 8:253-257.
37. Nyamuryekung'e KM, Laukamm-Josten U, Vuylsteke B, Mbuya C, Hamelmann C, Outwater A, *et al.* STD services for women at truck stop in Tanzania: evaluation of acceptable approaches. *East Afr Med J* 1997; 74:343-347.

7 The impact of pre-exposure prophylaxis (PrEP) on HIV epidemics in Africa and India: a simulation study

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Abstract

Background Pre-exposure prophylaxis (PrEP) is a promising new HIV prevention method, especially for women. An urgent demand for implementation of PrEP is expected at the moment efficacy has been demonstrated in clinical trials. We explored the long-term impact of PrEP on HIV transmission in different HIV epidemics.

Methods We used a mathematical model that distinguishes the general population, sex workers and their clients. PrEP scenarios varying in effectiveness, coverage and target group were modeled in the epidemiological settings of Botswana, Nyanza Province in Kenya, and Southern India. We also studied the effect of condom addition or condom substitution during PrEP use. Main outcome was the number of HIV infections averted over ten years of PrEP use.

Results PrEP strategies with high effectiveness and high coverage can have a substantial impact in African settings. In Southern India, by contrast, the number of averted HIV infections in different PrEP scenarios would be much lower. The impact of PrEP may be strongly diminished or even reversed by behavioral disinhibition, especially in scenarios with low coverage and low effectiveness. However, additional condom use during low coverage and low effective PrEP doubled the amount of averted HIV infections.

Conclusions The public health impact of PrEP can be substantial. However, this impact may be diminished, or even reversed, by changes in risk behavior. Implementation of PrEP strategies should therefore come on top of current condom campaigns, not as a substitution.

Introduction

Behavioral changes, such as reduction in the number of sex partners and the use of barrier methods in high-risk contacts, have slowed down the HIV epidemic in many places in the world [1,2] and will be of importance as long as no vaccine is available. Condom use, the main barrier method, is mainly male-controlled. Although condoms could, potentially, stop sexual HIV transmission almost completely, new intervention strategies are still urgently needed, especially those that can help women protect themselves. A recent microbicides trial testing cellulose sulphate was stopped prematurely because the gel was not only ineffective, but actually increased HIV risk [3,4]. Furthermore, recent trials with a diaphragm intervention method or with an HIV vaccine did not show any benefit [5,6]. Pre-exposure prophylaxis (PrEP) seems a promising new intervention [7-9] to fill the gap in female-controlled prevention, but the method may be equally effective for males.

PrEP means that HIV-negative people regularly take antiretroviral (ARV) drugs to prevent infection [8,10,11]. The concept of using ARV as a preventive method has been tested and proven successful in prevention of mother-to-child transmission of HIV [12]. Perhaps more significantly, post-exposure prophylaxis (PEP) in health care workers immediately after accidental exposure to HIV is common practice and may prevent 80% of the HIV infections due to needle accidents [13].

Animal HIV challenge studies provided preliminary evidence that PrEP might be partially effective in preventing HIV infection [14-16]. The ARV drug tenofovir prevented simian immunodeficiency virus (SIV) infection in macaques, when given 48 hours before an intravenous exposure to SIV [14]. Yet, while delaying SIV infection, tenofovir could not fully prevent infection after repeated viral challenges [15]. A combination of tenofovir and emtricitabine (FTC) however provided a high level of protection in humanized BLT mice [16].

To determine safety and efficacy of tenofovir and tenofovir/FTC in humans, clinical trials are currently ongoing in young adults (Botswana), injection drug users (Thailand), and men who have sex with men (United States, Peru/Ecuador) [17]. Preliminary results of a phase II safety trial among female sex workers in Ghana, Nigeria and Cameroon showed that the use of tenofovir was not associated with adverse events [18]. However, efficacy could not be determined due to the low number of HIV infections. Other trial results are expected at the earliest in 2008-2009 [17,19].

Some fear that the use of PrEP may lead to more risky sexual behavior because people may feel protected against HIV infection [20,21]. This increase, which is called behavioral

disinhibition or risk compensation [22], would to some extent reduce the effect of PrEP. Persons taking PrEP may feel protected against HIV infection and consequently use fewer condoms. On the other hand, PrEP users may be extensively counselled, be more aware of their risk behaviour and the risks of unprotected sex, and may therefore be more likely to use condoms. Nevertheless, whether or not PrEP will lead to changes in risk behavior remains uncertain especially if upscaling of services would lead to less effective counselling.

PrEP will directly protect individuals taking it, but may also have an indirect effect on non-PrEP users since reduced numbers of HIV infections will lead to decreased transmission. Mathematical models can be used to estimate these indirect effects. Accurate projections of the effect of PrEP on populations may help policy makers in their decision process and planning of PrEP services in AIDS control programmes. A demand for implementation of such programmes is expected at the moment efficacy of tenofovir or tenofovir/FTC against HIV transmission is proven in the different clinical trials [19]. We used a mathematical model that has previously been used to study the effect of HIV vaccines and male circumcision [23,24]. In this study, we examined the long-term effect of different levels of PrEP effectiveness on HIV transmission in populations differing in HIV epidemiology.

Methods

HIV model

We adapted an existing compartmental HIV transmission model to study the impact of PrEP on HIV epidemics in three different regions, namely Botswana, Nyanza Province in Kenya and Southern India [23,24]. This model divides the population in groups of low-risk persons (not involved in sex work) and high-risk persons (male clients and female sex workers), further subdivided into compartments by HIV infection status, stage of infection, and PrEP use. HIV infection was defined as early in the first four years of infection and as late in the last four years. Per gender and risk group, five compartments are distinguished in our model: HIV-negative not using PrEP; HIV-negative using PrEP; HIV-early not using PrEP; HIV-early using PrEP; and HIV-late not using PrEP. AIDS and death are endpoints of the model.

Low-risk persons can become high-risk persons, and vice versa. We only modeled heterosexual transmission. HIV can spread from infected to uninfected persons by three relationship types. First, HIV transmission can occur in sexual contacts between female sex workers and their clients. Second, transmission can occur through marriage-like

relationships. Third, "leakage" from infected individuals can occur reflecting all non-paid casual sex. HIV transmission through marriage and "leakage" only occurs in low-risk groups. Condom use is assumed in client-sex worker contacts, but not in other types of sexual relationships.

All other assumptions underlying the original model can be found elsewhere [23,24]. A technical description of the model including compartments, flows, variables and parameters can be found in the Appendix 1 and Figure A1. ModelMaker® (version 3.0.3) was used to implement and run the model.

Parameter values to model HIV epidemics in Botswana and Nyanza were based on recent modeling work of Nagelkerke *et al.* [24], who explored the effect of male circumcision. In our model, circumcision was not taken into account. We slightly lowered the former female-to-male transmission risk to adjust for the protective effect of male circumcision. In earlier modeling work, condom use in commercial sex was set at 20%. Data of Nyanza province from 1999 showed that 34-56% of clients and 75% of sex workers reported that they always or usually used condoms during commercial sex [25]. Therefore, we assumed that condom use in commercial sex increased to 50% from 2000 onwards. All other parameter values were kept identical to earlier values [24]. The main difference between Botswana and Nyanza was the higher "leakage" in Botswana, reflecting an assumed higher number of casual contacts in this country (see Appendix 1).

These parameter choices yielded approximate equilibrium HIV prevalence levels of 33% in Botswana and 16% in Nyanza. In Botswana, as the actual reported national HIV prevalence was 24% in 2005 [26], our model therefore probably only reflects the worst affected parts of the country. In Nyanza, HIV prevalence was estimated at 15% in 2003 [27], similar to the model's prediction.

In India, the southern states are the most affected area [28]. Condom use during commercial sex is more than 85% since 2000 [29]. We assumed that condom use in commercial sex was 60% in 1994 and increased to 90% from 1998 onwards. Besides the level of condom use, the main difference between Botswana/Nyanza and Southern India was a lower "leakage", reflecting an assumed lower frequency of casual contacts in India (see Appendix 1).

Our modeled HIV prevalence in India was based on two data sources. First, we used antenatal clinic (ANC) sentinel surveillance data from Southern India, which showed a decline in HIV prevalence from 1.8% in 1998 to 1.3% in 2004 [30,31]. Second, we used a large, representative population based prevalence survey in a rural area in South India which found an overall prevalence of 2.9% in 2003 [32]. Because the latter study had a

larger sample size and included the whole population instead of only pregnant women, it might be more representative for Southern India than the ANC data. Therefore, we simulated the decreasing trend of ANC data, but ended slightly higher at a 1.3% prevalence in 2007.

Modeling PrEP

Only uninfected persons start taking PrEP. HIV-negatives can be identified by either Client-Initiated Testing and Counselling (CITC, formerly known as Voluntary Counselling and Testing) or Provider-Initiated Testing and Counselling (PITC) [33]. The coverage of PrEP is based on HIV-negative persons taking PrEP. Some will stop taking pills (non-adherence). Since PrEP will most likely not fully protect against HIV infection, persons may still get infected, but at a lower rate than those not on PrEP. We assumed that persons taking PrEP pills who get HIV infected, continue to use PrEP on average for one year.

The use of a single drug, such as tenofovir, could promote HIV resistance. However, a modeling study of the Botswana trial estimated that of 600 participants receiving tenofovir, 45 persons would seroconvert and less than one participant was expected to acquire or develop a resistant HIV strain [34]. Therefore, we assumed that taking PrEP pills will not lead to any resistance.

We assumed that PrEP would become available in 2012. We predicted the effect of two strategies: targeting only sex workers or targeting both sex workers and clients. This latter strategy resembles a general population intervention with high-risk individuals coming to clinics for PrEP. The efficacy of PrEP is not known yet. We thus, somewhat arbitrarily, assumed a 50% or 90% effectiveness (i.e. reduced HIV susceptibility of those taking PrEP). Coverages of persons taking PrEP varied per targeting strategy. For Botswana/Nyanza, we explored a low (25%) or high (75%) coverage. For Southern India, we assumed that targeting with PrEP would result in higher coverage rates, since condom use is also very high in commercial sex [29]. As taking one pill per day might be as easy, or easier, than using a condom in each sex act, we assumed that PrEP coverage rates in Southern India were 50% and 95%, respectively.

We supposed that when sex workers and clients who use PrEP pills stop their high-risk behaviour and become low-risk individuals, they will also stop taking PrEP pills (i.e. they are no longer part of the target group). Main outcomes were HIV prevalence, number of HIV infections averted over ten years of PrEP use (i.e. in 2022), and amount of PrEP

needed in ten years. Both averted infections and amount of PrEP were calculated per 100,000 HIV-negative adult person years.

To explore alternatives to PrEP, we also modelled an intervention resulting in increased condom use in client-sex worker contacts. In this intervention, condom use was assumed to increase in 2007 (and not in 2012 like the PrEP strategies, since it is already available) from 50% to 75% in Botswana/Nyanza, and from 90% to 95% in Southern India. Thus, in both situations we assumed that the number of non-users was halved. Furthermore, we explored the effect of less (i.e. condom substitution) or more (i.e. condom addition) condom use during PrEP interventions. In substitution scenarios, the level of condom use was assumed to be 15% lower, 35% in Botswana/Nyanza and 75% in India (i.e. halfway the levels in 2007 and 2000 or 1998, respectively). In addition scenarios, condom use was assumed to be halfway that of the condom intervention level, 62.5% in Botswana/Nyanza and 92.5% in India.

Results

The impact of different PrEP strategies and the condom intervention on HIV prevalence in Botswana and Nyanza over the period 2006-2022 is shown in Figure 7.1. PrEP strategies with high coverage and high effectiveness targeting only sex workers or both sex workers and clients have a substantial impact on HIV prevalence. In both settings, the condom intervention and the high PrEP scenario targeting both sex workers and clients resulted in comparable HIV prevalences in 2022.

Figure 7.2 shows the baseline fit in Southern India. A PrEP scenario with 50% coverage and 50% effectiveness targeting only sex workers with three different condom options is also depicted. Condom substitution (i.e. 15% less use) during the PrEP scenario, resulted in a higher HIV prevalence, however, the prevalence was still decreasing. HIV prevalence no longer decreased if condom use during PrEP was reduced to 60% (i.e. 30% less use).

Results of different PrEP strategies and condom substitution or condom addition during PrEP are given in Table 7.1. The number of infections averted varied from 26 to 785 per 100,000 uninfected adult person years in Botswana, and from 44 to 733 per 100,000 person years in Nyanza. The number of averted infections was, even with higher coverages, considerably lower in Southern India: only 0.9 to 6.0 averted infections per 100,000 person years. The amount of PrEP pills needed in a 10-year period varied from around 50,000 to around 2 million pills per 100,000 person years in the African settings. Slightly more PrEP pills were needed in Southern India (Table 7.1).

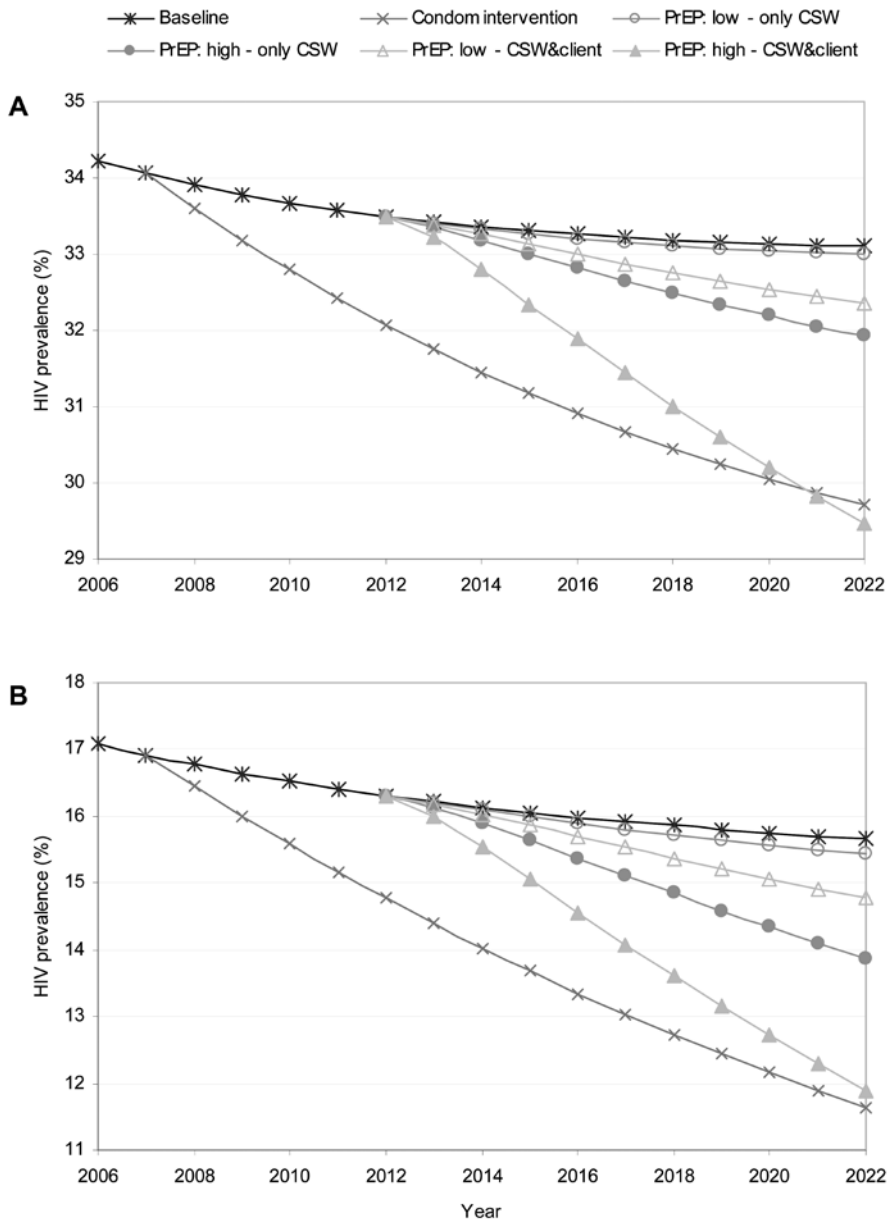

Figure 7.1 Effect of different PrEP scenarios and condom use on HIV prevalence in Botswana (A) and Nyanza province, Kenya (B). 'PrEP low' means 25% coverage and 50% effectiveness; 'PrEP high' means 75% coverage and 90% effectiveness; 'Only CSW' means target group is sex workers; 'CSW&client' means target group is sex workers and clients.

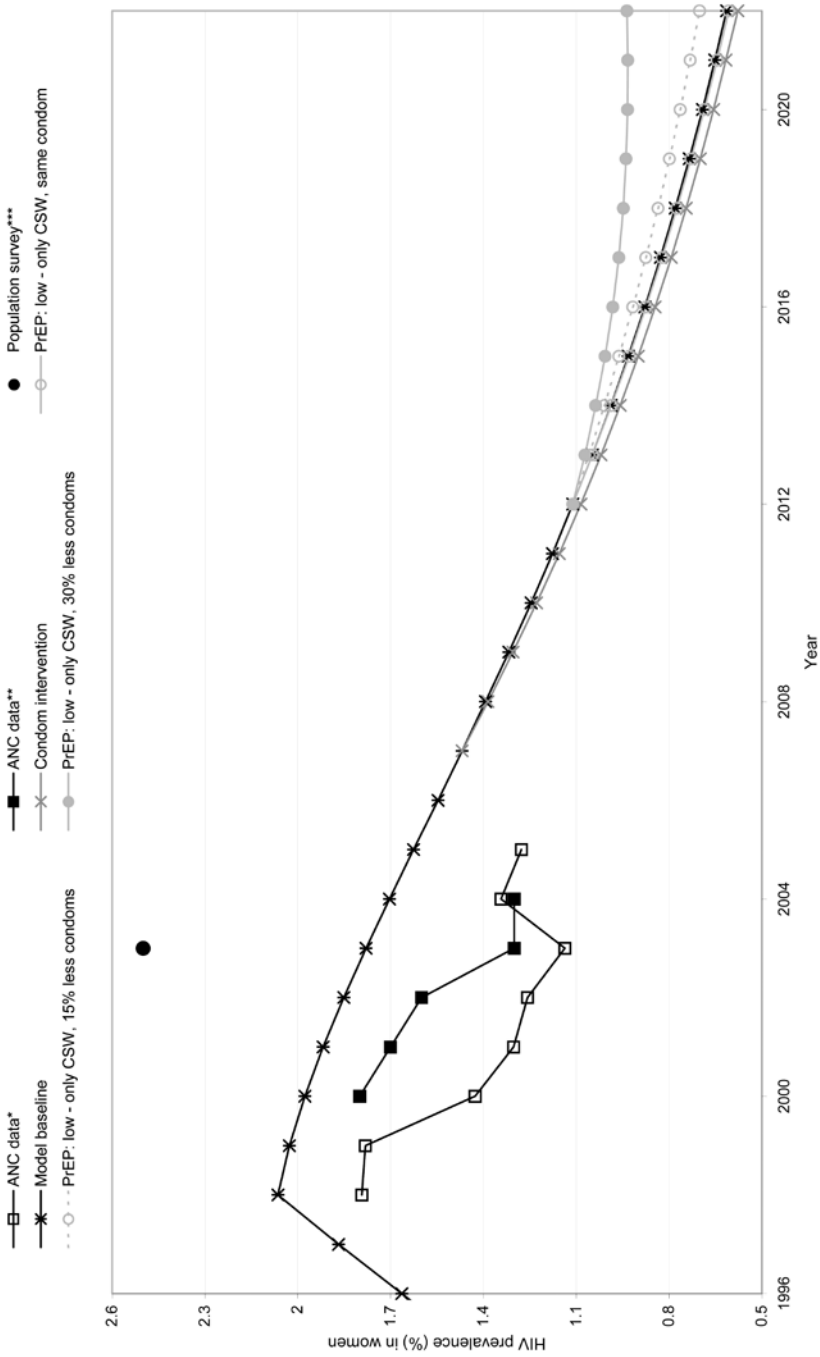

Figure 7.2 HIV prevalence in women in Southern India. Depicted are the baseline fit and the effect of different PrEP scenarios and condom use. *NACO, 2005 [30]; **Kumar *et al.*, 2006 [31]; ***Becker *et al.*, 2007 [32]. 'PrEP low' means 50% coverage and 50% effectiveness; 'Only CSW' means target group is sex workers; 'Same' means unchanged condom use during PrEP (90%); 'Less' means condom substitution during PrEP (condom use is 75% or 60%).

Table 7.1 Impact of different PrEP scenarios in Botswana, Nyanza and Southern India.

Setting – PrEP scenarios[a]	PrEP efficacy (%)	PrEP coverage (%)	PrEP pills[c] (x10[6])	Averted HIV cases[d] in case condom use was:		
				Same 50/90%[e]	Less 35/75%[e]	More 62.5/92.5%[e]
Botswana (n=516,000[b])						
Low – sex workers	50	25	0.04	26	-221	288
High – sex workers	90	75	0.18	251	- 14	503
Low – sex workers/clients	50	25	0.83	159	- 80	403
High – sex workers/clients	90	75	2.11	785	640	909
Nyanza (n=837,000[b])						
Low – sex workers	50	25	0.06	44	-236	325
High – sex workers	90	75	0.23	342	75	564
Low – sex workers/clients	50	25	0.77	166	-100	419
High – sex workers/clients	90	75	1.92	733	610	831
Southern India (n=235,000,000[b])						
Low – sex workers	50	50	0.25	0.9	-16.5	2.7
High – sex workers	90	95	0.51	3.8	- 2.2	4.6
Low – sex workers/clients	50	50	1.50	1.8	-11.4	3.3
High – sex workers/clients	90	95	2.66	6.0	4.4	6.2

[a] All PrEP scenarios started in 2012. 'Low' and 'High' refer to PrEP effectiveness and PrEP coverage; 'sex workers' and 'sex workers/clients' refer to the different target groups.

[b] Adult population size in 2012.

[c] Number of PrEP pills per 100,000 uninfected adult person years needed in the period 2013-2022 in scenarios in which condom use was unchanged.

[d] Number of averted HIV infections per 100,000 uninfected adult person years in the period 2013-2022.

[e] 'Same' means unchanged condom use during PrEP: 50% in Botswana/Nyanza and 90% in Southern India; 'Less' means condom substitution during PrEP (i.e. less condom use): 35% in Botswana/Nyanza and 75% in Southern India; 'More' means condom addition during PrEP (i.e. more condom use): 62.5% in Botswana/Nyanza and 92.5% in Southern India.

Condom substitution (i.e. 15% less condom use during PrEP scenarios) reduced the number of infections averted in all three settings in all four PrEP scenarios (Table 7.1). In PrEP scenarios with both low coverage and low effectiveness, condom substitution even led to an increase in the number of HIV infections in all three settings. In Botswana and in Southern India, the impact of the high PrEP scenario targeting only sex workers was also nullified by condom substitution. The effect of the high PrEP scenario targeting both sex workers and clients was substantially reduced, but not nullified, by condom substitution.

In African settings, the effect of condom addition (i.e. 15% more condom use during PrEP scenarios) was highest in low PrEP scenarios targeting sex workers only (Table 7.1). Additional condom use during the low PrEP scenarios targeting both sex workers and clients more than doubled the number of averted HIV infections. Condom addition in the high PrEP scenarios resulted in 10 to 100% more averted infections.

The impact of condom addition in Southern India (i.e. 2.5% more condom use during PrEP scenarios) was high in low PrEP scenarios (80 to 300% more averted infections). In high PrEP scenarios, condom addition resulted in 3 to 20% more averted HIV infections.

Discussion

PrEP strategies with high efficacy and high coverage can have a substantial impact in African settings. In Southern India, by contrast, the number of averted HIV infections in different PrEP scenarios would be much lower. The impact of PrEP may be strongly diminished or even reversed by behavioral disinhibition, especially in scenarios with low coverage and low effectiveness. However, additional condom use during low coverage and low effective PrEP doubled the amount of averted HIV infections.

We did not model ART treatment in the different epidemics. Since ART and PrEP could be the same drugs and ART is being scaled-up in many resource-poor countries, it is very unlikely that in reality PrEP would be introduced in an area without ART. ART coverage among HIV-infected adults in need of ART according to WHO criteria was estimated to be 79% in Botswana, 33% in Kenya and 4-9% in India by the end of 2006 (www.who.int/globalatlas/default.asp). Furthermore, we ignored the effect of PrEP on onward transmission, although an approximate 80% reduction in HIV transmission was shown in discordant couples where HIV-positive partners were taking ART [35]. PrEP users who become infected may also have reduced infectivity. Arguably, we may thus have underestimated the overall effect of PrEP use on HIV spread.

In our model, PrEP users who got HIV infected remained on PrEP on average for one year. This was done to reflect the reality that persons taking PrEP who get infected will be unaware of their changed HIV status until being tested again. Thus, in our model, condom substitution also affects such HIV-positive individuals making the effect of such substitution worse. Frequent HIV testing would moderate this adverse effect, but also put a heavy additional burden on health care resources.

We found that PrEP strategies could have a substantial impact in African settings. Another recent modeling study estimated a comparable impact of PrEP in sub-Saharan Africa [36]. In Botswana, we found 29,399 averted infections and 3,745,054 HIV-negative adult person years resulting in 785 averted infections per 100,000 person years (Table 7.1). The number of person years on PrEP was 216,541. Converting our result in averted infections per person year on PrEP, like Abbas *et al.* did, we found 0.14 averted infections per person year. They found 0.33 averted HIV infections in a similar PrEP scenario (i.e. 90% effectiveness, 75% coverage, targeting high-risk individuals) [36]. The difference might be explained by the different model assumptions. We modeled high-risk behavior explicitly by including sex workers and clients, who were in these compartments for a certain period (on average four years for sex workers and ten years for clients) and afterwards changed to low-risk individuals. Abbas *et al.* used four different sexual activity levels, that lasted lifelong. Moreover, they also included reduced infectivity when a PrEP user got infected with HIV, which was not in our model.

We performed sensitivity analyses of PrEP coverage in all three settings. We changed PrEP coverage in steps of 5% with both PrEP efficacy levels (50% and 90%) and both target groups (CSW only and CSWs & clients), ranging from 15-35% and 65-85% in African settings and from 40-60% and 80-99% for Southern India. In Southern India, we also looked at low coverage varying from 15% to 35%, which is comparable to the African settings. We found that the number of averted HIV infections in the period 2012-2022 was almost proportional to the coverage of PrEP. For the interventions directed at CSW only, there was a modest additional effect with higher PrEP coverage due to a slightly reduced level of transmission within the population (results not shown).

One of the added values of our study is that we also modeled the impact of PrEP in Southern India. The number of HIV infections averted was much lower than in the African settings. This is primarily due to the high levels of condom use during commercial sex in Southern India that have resulted in a steeply decreasing HIV trend since 2000 [29-31]. If PrEP would even slightly decrease current condom use levels in India, its impact would be negative. Furthermore, India is a densely populated country where about 300 million people live in the Southern states at this moment (www.censusindia.gov.in). The population grows with 1.4% per year, resulting in about 370 million people in 2022. On a population level, around 2,700 HIV infections can be averted in Southern India in a 10-year PrEP scenario targeting 50% of the sex workers and with 50% effectiveness. However, if during this PrEP scenario 15% less condoms are used, this leads to an additional 51,000 HIV infections, and even 180,000 more infections if condom use goes down to 60%. Thus, in India introduction of new prevention methods such as PrEP must

be done very carefully in order not to compromise the benefits gained through condom use.

Prophylaxis can be a useful method to prevent HIV infection, especially for women. However, large-scale PrEP use might encounter problems such as poor adherence and resistance. In a study in Zambia, 30% of tuberculosis patients in a Directly Observed Therapy programme stopped medication prematurely, before the completion of the scheduled 8-month treatment course [37], and adhering to pills for disease prevention might even be more difficult than for treatment. Clearly, assuring long-time adherence might be one of the tremendous difficulties facing PrEP services.

One of the problems of intermittent use, besides reduced effectivity, is possible emergence of resistant viruses. We assumed that PrEP use would not lead to resistance to ART drugs, based on the modeling work of Smith *et al.* for a clinical trial situation in Botswana [34]. PrEP use on a wider scale outside trial settings with more people taking PrEP, a higher risk of non-adherence, and possible changes in risk behavior due to less extensive counseling may well lead to the emergence of resistant strains. Although usage of PrEP pills that contain two or more different ARV drugs may decrease the risk of development of resistance, it may not ultimately prevent it.

We have demonstrated that disinhibition during PrEP services is important and may have a considerable effect on HIV epidemics. To what extent disinhibition will actually occur is still uncertain. Earlier studies of the effect of PEP or ART on disinhibition reported conflicting results. Studies of PEP in homosexual men in the US did not demonstrate an increase in risky sexual behavior [38,39]. Similarly, a meta-analysis on sexual behavior and ART in industrialized countries did not reveal an increase in risky behavior of persons receiving ART compared to those who did not, except in those who believed that therapy prevented transmission [40]. Providing ART and counseling was even associated with reduced sexual risk behavior in Uganda [41]. In South Africa, by contrast, high levels of unprotected sex were reported both by persons on ART and by those not yet eligible for ART [42].

Condom addition had a substantial impact on the number of averted HIV infections in the different PrEP scenarios. People coming for HIV-testing and PrEP should be extensively counseled about the necessity to continue or enhance habits of safe sex, such as use of condoms. Furthermore, PrEP pills could be distributed in combination with condoms. Changes in risk behavior can be assessed by repeated sexual behavior surveys or by STD screening when people visit clinics for scheduled PrEP pills collections.

We conclude that PrEP can have a substantial impact in the reduction of HIV. Targeting high-risk groups is relatively easy and inexpensive and would result in comparable HIV prevalences as successful condom interventions. However, policy makers should be aware of changes in risk behavior. Especially in Southern India, where condom use is already very high during commercial sex, small changes could have strong negative effects. Implementation of PrEP strategies should come on top of current condom campaigns, not as a substitution.

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References

1. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* 2002:CD003255.
2. Hallett TB, Aberle-Grasse J, Bello G, Boulos LM, Cayemittes MP, Cheluget B*, et al.* Declines in HIV prevalence can be associated with changing sexual behaviour in Uganda, urban Kenya, Zimbabwe, and urban Haiti. *Sex Transm Infect* 2006; 82 (Suppl 1):i1-8.
3. Ramjee G, Govinden R, Morar NS, Mbewu A. South Africa's experience of the closure of the cellulose sulphate microbicide trial. *PLoS Med* 2007; 4:e235.
4. Trial and failure. *Nature* 2007; 446:1.
5. Padian NS, van der Straten A, Ramjee G, Chipato T, de Bruyn G, Blanchard K*, et al.* Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. *Lancet* 2007; 370:251-261.
6. Cohen J. AIDS research. Did Merck's failed HIV vaccine cause harm? *Science* 2007; 318:1048-1049.
7. Youle M, Wainberg MA. Pre-exposure chemoprophylaxis (PrEP) as an HIV prevention strategy. *J Int Assoc Physicians AIDS Care* 2003; 2:102-105.
8. Smith SM. Pre-exposure chemoprophylaxis for HIV: it is time. *Retrovirology* 2004; 1:16.
9. Stephenson J. New HIV prevention strategies urged: averting new infections key to controlling pandemic. *JAMA* 2004; 292:1163-1164.
10. Youle M, Wainberg MA. Could chemoprophylaxis be used as an HIV prevention strategy while we wait for an effective vaccine? *AIDS* 2003; 17:937-938.
11. Grant RM, Buchbinder S, Cates W, Jr., Clarke E, Coates T, Cohen MS*, et al.* AIDS. Promote HIV chemoprophylaxis research, don't prevent it. *Science* 2005; 309:2170-2171.
12. Lallemant M, Jourdain G, Le Coeur S, Mary JY, Ngo-Giang-Huong N, Koetsawang S*, et al.* Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *N Engl J Med* 2004; 351:217-228.
13. Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D*, et al.* A case-control study of HIV seroconversion in health care workers after percutaneous exposure.

Centers for Disease Control and Prevention Needlestick Surveillance Group. *N Engl J Med* 1997; 337:1485-1490.
14. Tsai CC, Follis KE, Sabo A, Beck TW, Grant RF, Bischofberger N, *et al.* Prevention of SIV infection in macaques by (R)-9-(2-phosphonylmethoxypropyl)adenine. *Science* 1995; 270:1197-1199.
15. Subbarao S, Otten RA, Ramos A, Kim C, Jackson E, Monsour M, *et al.* Chemoprophylaxis with tenofovir disoproxil fumarate provided partial protection against infection with simian human immunodeficiency virus in macaques given multiple virus challenges. *J Infect Dis* 2006; 194:904-911.
16. Denton PW, Estes JD, Sun Z, Othieno FA, Wei BL, Wege AK, *et al.* Antiretroviral Pre-exposure Prophylaxis Prevents Vaginal Transmission of HIV-1 in Humanized BLT Mice. *PLoS Med* 2008; 5:e16.
17. Clearinghouse AV. PrEP Watch. http://www.prepwatch.org. *Accessed 22 May 2007*.
18. Peterson L, Taylor D, Roddy R, Belai G, Phillips P, Nanda K, *et al.* Tenofovir Disoproxil Fumarate for Prevention of HIV Infection in Women: A Phase 2, Double-Blind, Randomized, Placebo-Controlled Trial. *PLoS Clin Trials* 2007; 2:e27.
19. Paxton LA, Hope T, Jaffe HW. Pre-exposure prophylaxis for HIV infection: what if it works? *Lancet* 2007; 370:89-93.
20. Grant RM, Wainberg MA. Chemoprophylaxis of HIV infection: moving forward with caution. *J Infect Dis* 2006; 194:874-876.
21. Liu AY, Grant RM, Buchbinder SP. Preexposure prophylaxis for HIV: unproven promise and potential pitfalls. *JAMA* 2006; 296:863-865.
22. Cassell MM, Halperin DT, Shelton JD, Stanton D. Risk compensation: the Achilles' heel of innovations in HIV prevention? *BMJ* 2006; 332:605-607.
23. Nagelkerke NJ, Jha P, de Vlas SJ, Korenromp EL, Moses S, Blanchard JF, *et al.* Modelling HIV/AIDS epidemics in Botswana and India: impact of interventions to prevent transmission. *Bull World Health Organ* 2002; 80:89-96.
24. Nagelkerke NJ, Moses S, de Vlas SJ, Bailey RC. Modelling the public health impact of male circumcision for HIV prevention in high prevalence areas in Africa. *BMC Infect Dis* 2007; 7:16.
25. Voeten HACM, Egesah OB, Ondiege MY, Varkevisser CM, Habbema JDF. Clients of female sex workers in Nyanza province, Kenya: a core group in STD/HIV transmission. *Sex Transm Dis* 2002; 29:444-452.
26. UNAIDS. Report on the global AIDS epidemic. 2006
27. Marum L, Muttunga JN, Munene FM, Cheluget BK. Kenya, Demographic and Health Survey. Chapter 13. HIV prevalence and associated factors. 2003
28. UNAIDS/WHO. India epidemiological fact sheet on HIV/AIDS and sexually transmitted infections, update 2004.
29. NACO. Behavioral Surveillance Survey report, Tamil Nadu Wave X. 2005
30. NACO. National AIDS Control Organization: facts and figures. 2005
31. Kumar R, Jha P, Arora P, Mony P, Bhatia P, Millson P, *et al.* Trends in HIV-1 in young adults in south India from 2000 to 2004: a prevalence study. *Lancet* 2006; 367:1164-1172.
32. Becker ML, Ramesh BM, Washington RG, Halli S, Blanchard JF, Moses S. Prevalence and determinants of HIV infection in South India: a heterogeneous, rural epidemic. *AIDS* 2007; 21:739-747.

33. WHO, UNAIDS. Guidance of provider-initiated HIV testing and counselling in health facilities. 2007
34. Smith D, Kebaabetswe P, Disasi K, Fleming D, Paxton L, Davis M. Antiretroviral resistance is not an important risk of the oral tenofovir prophylaxis trial in Botswana: a simple mathematical modeling approach [abstract THAX0105]. *XVI International AIDS conference*. Toronto, Canada, 2006.
35. Castilla J, Del Romero J, Hernando V, Marincovich B, Garcia S, Rodriguez C. Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV. *J Acquir Immune Defic Syndr* 2005; 40:96-101.
36. Abbas UL, Anderson RM, Mellors JW. Potential impact of antiretroviral chemoprophylaxis on HIV-1 transmission in resource-limited settings. *PLoS ONE* 2007; 2:e875.
37. Kaona FA, Tuba M, Siziya S, Sikaona L. An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. *BMC Public Health* 2004; 4:68.
38. Martin JN, Roland ME, Neilands TB, Krone MR, Bamberger JD, Kohn RP*, et al.* Use of postexposure prophylaxis against HIV infection following sexual exposure does not lead to increases in high-risk behavior. *AIDS* 2004; 18:787-792.
39. Schechter M, do Lago RF, Mendelsohn AB, Moreira RI, Moulton LH, Harrison LH*, et al.* Behavioral impact, acceptability, and HIV incidence among homosexual men with access to postexposure chemoprophylaxis for HIV. *J Acquir Immune Defic Syndr* 2004; 35:519-525.
40. Crepaz N, Hart TA, Marks G. Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review. *JAMA* 2004; 292:224-236.
41. Bunnell R, Ekwaru JP, Solberg P, Wamai N, Bikaako-Kajura W, Were W*, et al.* Changes in sexual behavior and risk of HIV transmission after antiretroviral therapy and prevention interventions in rural Uganda. *AIDS* 2006; 20:85-92.
42. Eisele TP, Mathews C, Chopra M, Brown L, Silvestre E, Daries V*, et al.* High Levels of Risk Behavior Among People Living with HIV Initiating and Waiting to Start Antiretroviral Therapy in Cape Town South Africa. *AIDS Behav* 2007.

Appendix 1: Formal structure of the model

A schematic overview of the model can be found in Figure A1. Boxes represent compartments, i.e. the states males or females can be in. Arrows represent flows of individuals between compartments. High-risk groups are male clients and female sex workers. Disease progression is subdivided into 2 stages: early and late, including AIDS. Individuals move to the PrEP box when PrEP is initiated. Symbols refer to compartments and flows formally defined below.

Names of compartments and flows were chosen as follows. Compartments: G = gender (where M = male or F = female); i = first subscript with 1 = low-risk group, 2 = high-risk group; j = second subscript with 1 = uninfected, 2 = early HIV, 3 = late HIV, 4 = taking PrEP and uninfected, 5 = taking PrEP and early HIV. Flows: a = from low-risk to high-risk group, b = from high-risk to low-risk group, t = start taking PrEP, u = stop taking PrEP, i = infection, p = progression (to late stage HIV infection), q = death.

PrEP use can be modelled in the general population and in high-risk groups. Only the latter was used in the main article. Parameters names are in *italics,* variable names are in normal font. Parameter values that are identical for all three settings are only shown once.

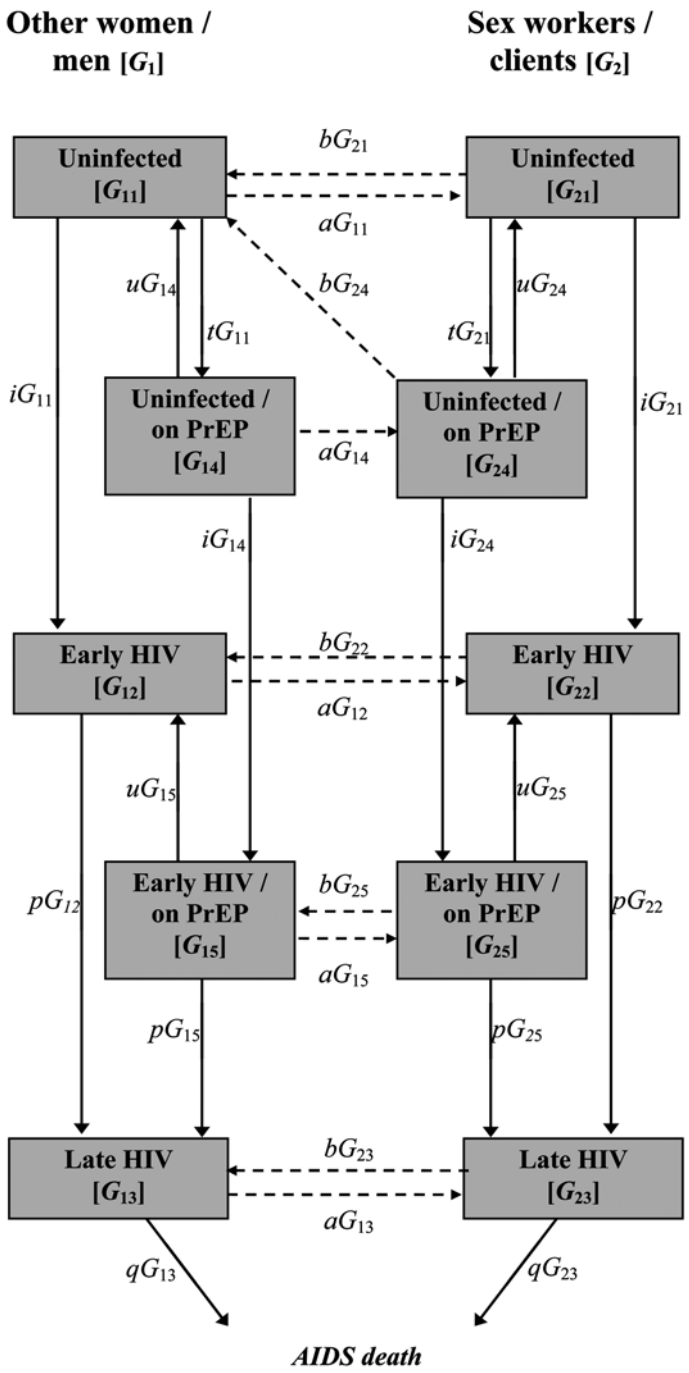

Figure A1. Structure of the compartmental model.

Compartments

Symbol Figure A1	Equation
G_{11}	In women: -*mu_neg*$*F_{11}$ - aG_{11} + bG_{21} + bG_{24} - tG_{11} + uG_{14} - iG_{11} + population**femgr* In men: -*mu_neg*$*M_{11}$ - aG_{11} + bG_{21} + bG_{24} - tG_{11} + uG_{14} - iG_{11} + population**malegr*
G_{12}	-*mu_pos*$*G_{12}$ - aG_{12} + bG_{22} + uG_{15} + iG_{11} - pG_{12}
G_{13}	-*mu_pos*$*G_{13}$ - aG_{13} + bG_{23} + pG_{12} + pG_{15} - qG_{13}
G_{14}	-*mu_neg*$*G_{14}$ - aG_{14} + tG_{11} - uG_{14} - iG_{14}
G_{15}	-*mu_pos*$*G_{15}$ - aG_{15} + bG_{25} - uG_{15} + iG_{14} - pG_{15}
G_{21}	-*mu_neg*$*G_{21}$ + aG_{11} - bG_{21} - tG_{21} + uG_{24} - iG_{21}
G_{22}	-*mu_pos*$*G_{22}$ + aG_{12} - bG_{22} + uG_{25} + iG_{21} - pG_{22}
G_{23}	-*mu_pos*$*G_{23}$ + aG_{13} - bG_{23} + pG_{22} + pG_{25} - qG_{23}
G_{24}	-*mu_neg*$*G_{24}$ + aG_{14} - bG_{24} + tG_{21} - uG_{24} - iG_{24}
G_{25}	-*mu_pos*$*G_{25}$ + aG_{15} - bG_{25} - uG_{25} + iG_{24} - pG_{25}
AIDS death	qG_{13} + qG_{23}

Variables

Variable name	Defining equation
non_csw	F_{11} + F_{12} + F_{13} + F_{14} + F_{15}
non_clients	M_{11} + M_{12} + M_{13} + M_{14} + M_{15}
csw	F_{21} + F_{22} + F_{23} + F_{24} + F_{25}
clients	M_{21} + M_{22} + M_{23} + M_{24} + M_{25}
females	non_csw + csw
males	non_clients + clients
population	females + males
annualCSWcontacts	*cont_rate* * clients / csw
leakwomen	*leak* * 2 * *fm_risk* / (*fm_risk* + *mf_risk)*
leakmen	*leak* * 2 * *mf_risk* / (*fm_risk* + *mf_risk)*
marrate_female	*marrate_male* * non_clients / non_csw
female_prevalence	(females - F_{11} - F_{21} - F_{14} - F_{24}) / females
male_prevalence	(males - M_{11} - M_{21} - M_{14} - M_{24}) / males
uninf_on_PrEP	F_{14} + F_{24} + M_{14} + M_{24}
HIV_on_PrEP	F_{15} + F_{25} + M_{15} + M_{25}
total_on_PrEP	uninf_on_PrEP + HIV_on_PrEP

Flows (transitions between compartments)

Symbol Figure A1	Equation
aG_{1j} (j=1,…,5)	In women: *prof* * F_{1j} * exp (annualCSWcontacts / *mkt* - 1) In men: *cust* * M_{1j}
bG_{2j} (j=1,…,5)	In women: *unprof* * F_{2j} In men: *uncust* * M_{2j}
iG_{11}	In women: leakmen * (M_{12} + M_{13} + M_{15} + M_{22}+ M_{23} + M_{25}) * F_{11} / non_csw + F_{11} * *stabfactor* * *mf_risk* * marrate_female * (M_{12} + M_{13} + M_{15}) / non_clients In men: leakwomen * (F_{12} + F_{13} + F_{15} + F_{22} + F_{23} + F_{25}) * M_{11} / non_clients + M_{11} * *stabfactor* * *fm_risk* * *marrate_male* * (F_{12} + F_{13} + F_{15}) / non_csw
iG_{14}	In women: (1 – *PrEP_efficacy*) * (leakmen * (M_{12} + M_{13} + M_{15} + M_{22} + M_{23} + M_{25}) * F_{14} / non_csw + F_{14} * *stabfactor* * *mf_risk* * marrate_female * (M_{12} + M_{13} + M_{15}) / non_clients) In men: (1 – *PrEP_efficacy*) * (leakwomen * (F_{12} + F_{13} + F_{15} + F_{22} + F_{23} + F_{25}) * M_{14} / non_clients + M_{14} * *stabfactor* * *fm_risk* * *marrate_male* * (F_{12} + F_{13} + F_{15}) / non_csw)
iG_{21}	In women: F_{21} * annualCSWcontacts * *mf_risk* * (1 – *condom_prot*) * (M_{22} + M_{23} + M_{25}) / clients In men: M_{21} * *cont_rate* * *fm_risk* * (1 – *condom_prot*) * (F_{22} + F_{23} + F_{25}) / csw
iG_{24}	In women: (1 – *PrEP_efficacy*) * F_{24} * annualCSWcontacts * *mf_risk* * (1 – *condom_prot*) * (M_{22} + M_{23} + M_{25}) / clients In men: (1 – *PrEP_efficacy*) * M_{24} * *cont_rate* * *fm_risk* * (1 – *condom_prot*) * (F_{22} + F_{23} + F_{25}) / csw
pG_{ij} (i=1,2; j=2,5)	*hivprog* * G_{ij}
qG_{i3} (i=1,2)	*mu_aids* * G_{i3}
tG_{i1} (i=1,2)	*PrEP_rate* * G_{i1}
uG_{ij} (i=1,2; j=4)	*rate_stop_PrEP* * G_{ij}
uG_{ij} (i=1,2; j=5)	*rate_stop_PrEP_early* * G_{ij}

Model parameters (values)
Values that are identical for all settings are only shown once.

Parameter name	Parameter description / interpretation	Botswana	Nyanza province	Southern India
femgr	Annual growth rate adult female population		0.04	
malegr	Annual growth rate adult male population		0.04	
mu_neg	Annual mortality rate HIV negatives		0.026	
mu_pos	Annual mortality rate (non-AIDS) HIV positives		0.028	
mu_aids	Annual rate of AIDS death among late stage HIV infected		1	
fm_risk	Probability of female-to-male transmission per high-risk contact		0.0125	
mf_risk	Probability of male-to-female transmission per high-risk contact		0.03	
hivprog	Annual rate of developing late stage HIV among early stage HIV infected		0.25	
marrate_male	Annual rate of establishing stable relationships (men)		0.232	
stabfactor	Multiplier for stable relationships		25	
leak	Annual HIV transmission to non-commercial and non-marital partners	0.11	0.065	0.04
cust	Annual rate of becoming CSW client		0.025	
uncust	Annual rate of becoming low-risk male among clients		0.1	
prof	Annual rate of becoming CSW, when CSW have *mkt* clients annually		0.025	
unprof	Annual rate of becoming low risk female among CSW		0.25	
cont_rate	Annual number of CSW contacts per client (rate)		26	
mkt	Parameter controlling the rate of becoming CSW in response to demand		1000	
condom_prot	Effective condom use (%) in CSW client contacts at different time points	20% 50%		60% 90%
condom_after	Effective condom use (%) in CSW client contacts during condom intervention	75%		95%
PrEP_efficacy	Level of protection by PrEP: Low scenarios (50%) High scenarios (90%)		 0.5 0.9	
PrEP_rate	Annual rate of starting PrEP to obtain correct coverage: Low scenarios (25% or 50%) High scenarios (75% or 95%)	 0.22 1.1		 0.37 6.0
rate_stop_PrEP	Annual rate of stopping PrEP if uninfected		0.04	
rate_stop_PrEP_early	Annual rate of stopping PrEP if HIV early		1	

8 General discussion

In this chapter, the research questions formulated in Chapter 1 are answered and discussed (Section 8.1). Furthermore, some preliminary explorations on the effectiveness of targeting interventions at travelers is presented (Section 8.2). We conclude by formulating the main conclusions and recommendations of this thesis (Section 8.3).

8.1 Answering the research questions

1. **Can migration explain differences in spread of HIV in Africa?**
   Migration is an important determinant of differences in HIV spread, especially in rapidly increasing epidemics.

We found a strong association between the proportion of recent female immigrants and HIV prevalence in urban areas, especially in the late eighties and early nineties, when HIV epidemics rapidly increased in many African countries (Chapter 2). More recently, HIV prevalence started to level off due to interventions and AIDS-related mortality, making the association less prominent.

The main limitation of an ecological analysis like this one is the impossibility of making a causal interpretation. It has been demonstrated before that migration causes an increased risk of getting HIV infected by an increased risk of unsafe sexual behavior among migrants [1-5]. On the other hand, in some parts of Africa, HIV-positive people migrate back to their home villages when they become ill in the late stages of disease [6,7]. Family and relatives will take care of the terminal patients and assist in burial of the deceased.

Migration may also play an important role in other areas with rapidly increasing HIV epidemics such as China. In 2008, the HIV prevalence was estimated to be 0.1% in China, corresponding to 700,000 people living with HIV/AIDS [8]. Economic development and urbanization led to massive migration from rural to urban areas. There are an estimated 150 million migrant workers in China who moved to cities, sometimes as sex workers [9,10]. Chinese migrants were more often engaged in risky sexual behavior, including unprotected sex and multiple sex partners, in comparison to residents [9-12]. With the still ongoing economic development and industrialization of China, it is worth to explore the effect that rural to urban migration may continue to have on the Chinese HIV epidemic.

2. Are migrants a selection of high-risk individuals?
In rural Zimbabwe, migrants do not differ in their sexual risk behavior from other people, nor do they have higher levels of HIV infection.

In 12 communities in rural Manicaland, Eastern Zimbabwe, out-migrants were compared with residents before and after they moved out of the area (Chapter 3). There were no differences in reported sexual behavior or HIV prevalence between migrants and residents. This suggests that out-migration from rural areas plays a minor role in HIV transmission at this stage of the epidemic in Zimbabwe. However, not all migrants could be traced. Only those who had moved to the cities Harare and Mutare or to places nearby the 12 study communities were followed up. Therefore additional research is needed to assess the generalizability of these findings.

Many of the migrants went to stay with relatives. This may lower their longing for sexual contacts, since they may receive social, emotional and financial support, and may feel less lonely. Moreover, staying with relatives may limit risky sexual behavior due to more social control. In contrast with this Zimbabwean population, the circumstances and conditions in the migration process in comparable studies in Kenya and South Africa created opportunities for more sexual risk behavior [5,13]. For example, migrant men in South Africa were more likely to have casual sex partners and to be HIV-positive [5]. Labor migration in South Africa is associated with separation of families and social disruption due to repeated relocation [5].

In our ecological analysis (research question 1), we found that female recent immigration was associated with HIV prevalence in urban areas in sub-Saharan Africa. This is in contrast with the finding that HIV prevalence and risk behavior of out-migrants in rural Zimbabwe were not different from that of residents. But there are differences between studies; most importantly, the HIV epidemic was more generalised in Zimbabwe than in most sub-Saharan countries at the time of the surveys in the ecological study. AIDS-related mortality in rural Zimbabwe rose substantially since the early nineties: 60% of mortality in adult men and 71% in adult women could be attributed HIV in the period 1998 to 2003 [14]. It is likely that being testimony of so many AIDS deaths influenced people to down-tune their risk behavior. Moreover, HIV prevention activities were considerable in all study communities [15]. Finally, the ecological study only looked at urban immigrants, while the study in rural Zimbabwe also studied out-migrants that moved into other rural areas.

3. Is mobility associated with sexual risk behavior?

In Tanzania, travelers and their partners staying behind reported increased sexual risk behavior. In couples living apart, only women infrequently seeing their spouses reported increased risk behavior.

The sexual risk behavior of both partners of married couples was studied in Kisesa ward in rural Tanzania. In Chapter 4, people were classified as migrants, travelers or residents, and risk behavior was studied taking into account people's own mobility and the mobility status of their partners. The sexual risk behavior of men was not much influenced by their mobility status. In contrast, migrant women reported more sexual risk behavior than resident women. Resident men and women reported more casual sex partners when they had migrant partners. In Chapter 5, couples living apart were subdivided into frequently and infrequently seeing each other, and cohabiting couples into traveling or not. Co-resident men who travel and women living apart infrequently seeing their spouse reported increased risky sexual behavior.

Most studies on mobility evaluated work-related long-term mobility and focused on the sexual behavior and HIV risk of the partner who was away from home [16,17]. In the studies in Chapters 4 and 5, sleeping elsewhere and polygamy were also taken into account, and the behavior and risk of the partner staying behind was considered. It should be noted that in Chapter 5, living apart most often occurred for people in a polygamous marriage (93%).

In a recent analysis of Demographic and Health Survey (DHS) data, duration and times away from home (frequency) and HIV data from 15 developing countries were analyzed [18]. The majority of the countries were sub-Saharan African (11 countries), although Tanzania was not included due to unavailability of data. They concluded that frequency, but not the duration of time away from home was related to higher HIV prevalence in men [18]. In our study in Chapter 5, we found that men being frequently away from home (more than 10 times per year) reported more extramarital sex, although HIV prevalence was not increased.

The results for Kisesa ward may apply to the rest of Tanzania and even to other African countries. However, mobility patterns and sexual behavior norms, in particular the presence of polygamous marriages, may differ per area and country.

Increased HIV prevalence in mobile groups has been frequently reported in sub-Saharan Africa [2,4,19], and was also found in our study in Tanzania (Chapter 4). Mobile people may also have been missed in surveys when they were not at home. Marston *et al*. estimated

the bias caused by mobility in national estimates of HIV prevalence in population-based surveys, and concluded that mobility does not substantially bias HIV prevalence [20].

In Chapter 5 sexual risk behavior was used as a proxy for HIV risk, since HIV data was not available in 44% of men and 35% of women. A reason that HIV data were lacking is unavailability of antiretroviral treatment (ART) in the study area. Without possibilities for treatment, knowing that you are HIV-positive will only lead to the risk of stigma and discrimination. With ART coverage increasing worldwide [21], HIV counseling and testing are likely to increase as well.

Resident women with mobile husbands were more likely to have casual sex partners than other women (Chapter 4). Interventions to reduce the risk behavior of women who stay behind include health education, improvement of economic independence and support from peers. Education may make women aware of their risk of getting HIV and can inform them on ways to protect themselves (e.g. using condoms, or possible future use of pre-exposure prophylaxis). Sometimes women engage in transactional sex for economic reasons, for instance when they are in need of money for food or school fees for their children and their husbands are not sending money home [5]. Micro-credit or free schooling systems may be solutions, and again education can help women in their development and autonomy. Programs can also be started to help women to support each other. Advice and support from women in their community who have experience with the same problems could be useful. Moreover, peer contact can reduce loneliness and increase social control, both of which may reduce risky sexual behavior. Finally, facilitating the possibility to move with the partner may be worth to be explored. However, this is only feasible when the partner is living elsewhere for a longer period of time and when living apart is not related to polygamous marriages, since having more than one woman in the same compound is not customary in the African culture.

Terms such as migrants, travelers, seasonal workers, short-term or long-term mobiles, are used in the literature alongside many others, making comparisons and reviews complex. In the DHS, the highest category in times spent away from home was 5 nights or more per year [18]. In our study (Chapter 5), we defined being mobile as sleeping elsewhere more than 10 nights per year. Moreover, the boundary between travel and migration is vague: Where does travel stop and become migration, and vice versa? Migrants who decide to return home could be called travelers who move with a low frequency; and travelers who stay in another place for a longer time could be called migrants. Differences in definition can include frequency, duration and destination, and complicate comparisons between studies. It would be useful to standardize mobility indicators.

4. **How much do mobile groups reduce the effect of HIV interventions?**
   Non-participation of mobile groups in HIV interventions can considerably reduce the effect of condom promotion and health education interventions.

In our simulation studies with STDSIM, non-participation of travelers and immigrants reduced the impact of both condom promotion and health education interventions by 40% (Chapter 6). In our simulations, we assumed that immigrants do not participate during the first five years after migration and travelers do not adhere while being away from home. In practice, the impact of mobile groups will be less, since some immigrants may rapidly adhere to HIV interventions in their new living environment. Still, we expect that some non-participation will remain and will need attention in the development and implementation of HIV prevention campaigns.

It is important to identify the amount of mobility, which may form a proxy for non-participation. One way to identify mobility in an area can be by asking household members about absent persons. Moreover, it is important to create awareness in people involved in surveys and prevention activities that mobility can have an influence, including reduced effectiveness of HIV interventions. It can be worthwhile to make efforts to involve mobile groups in these interventions. Target sites to approach mobile people include main roads, markets or truck stops, and ceremonies such as burials and marriages.

Once mobile people are contacted and aware of HIV interventions, it may still be difficult for them to adhere to an intervention. Adherence to consistent condom use can be difficult in areas that they do not know well. Negotiating condom use with a new partner may also be difficult. Moreover, there may be less social control on someone's behavior when away from home. Engaging in sexual contacts may therefore be relative easy. The involvement of mobile people in HIV interventions is illustrated below with pre-exposure prophylaxis.

Pre-exposure prophylaxis (PrEP)

Research is ongoing to define the best dosing regimen for PrEP regarding adherence, efficacy and safety. Alternatives are daily dosing, intermittent dosing and dosing related to coitus. People who travel may run out of daily PrEP pills before returning home. If intermittent dosing proves effective, this may not be problematic. However, poor adherence due to mobility may lead to suboptimal protection and the risk of developing resistance. When implementing PrEP programmes, full attention should be given to adherence in mobile people.

People who feel protected against HIV infection by using PrEP may increase their risk behavior [22,23]. This risk compensation can have a considerable effect on the HIV epidemics (Chapter 7). It is not expected that mobile persons taking PrEP will act differently regarding risk compensation than non-mobile persons taking PrEP. However, mobile people on PrEP may continue their sexual behavior, which can be more risky than the behavior of residents. Risk behavior should therefore be monitored when PrEP services are rolled out. Counseling of high-risk groups, including mobiles, on the risk of getting HIV remains important and should be part of PrEP programs, especially if PrEP efficacy proves to be limited.

8.2 Targeting of travelers, an exploration

In Chapter 6, we modeled the impact of non-participation of mobile groups, including travelers when they were away from home, on HIV interventions. Although frequent travelers usually form a minority in a population, their increased risk behavior can considerably accelerate the spread of HIV. Targeting of interventions at travelers may therefore be a useful way to prevent HIV transmission, especially in areas with high mobility. We used the STDSIM model as described in Chapter 6 to explore the potential impact of interventions targeted at specific travel profiles. As in Chapter 6, the HIV epidemic and mobility patterns are assumed to reflect the situation in Kisesa ward in Tanzania [24,25].

In our explorations, HIV interventions are targeted at two travel groups in our model: highly mobile people (3%) and market traders / visitors of ceremonies (20%). The interventions start in 2009 for both men and women. Targeting is by definition adapted to a certain group and is likely to result in higher participation than general population interventions. We therefore model a combined intervention campaign, consisting of health education and condom promotion, in travel groups. We assume that health education results in 50% reduction in the average number of sexual partners and sex worker visits. Condom promotion increases condom use to 75% during casual contacts and to 95% during commercial sex while being away from home. This targeted combination campaign is compared with HIV interventions in the general population that are similar to HIV interventions modeled in Chapter 6. In one scenario, the number of sexual partners and commercial sex visits is reduced by 25%. In a separate scenario, condom use is increased to 50% in casual contacts and 75% in commercial sex in the general population. Both recent immigrants and travelers away from home are assumed not to participate in general population interventions, as in Chapter 6.

Table 8.1 shows the impact of the combined targeted intervention in travel groups in comparison to the HIV interventions in the general population. The targeted intervention reduced the number of new HIV cases in the period 2010 to 2019 by 11%. This is only slightly less than campaigns with health education or condom promotion in the general population (15% and 12%, respectively).

Table 8.1 Impact of interventions on HIV incidence in adult people from 2010 to 2019.

Type of intervention	Reduction in HIV
Condom promotion in general population *	12%
Health education in general population *	15%
Condom promotion and health education targeted at the two travel groups with highest risk	11%

* Mobile groups are non-participating in general population interventions (see Chapter 6).

We have assumed in our model that travelers who are targeted to reduce their number of sexual partners and to increase condom use in risky contacts will only do so when they are traveling, and not when they are at home (comparable to simulations in Chapter 6). It is however likely that they will also change their behavior while being at home. Therefore, the expected impact of targeting may even be higher than the 11% found.

Thus, this intervention involving 23% of the population may have a considerable impact, and it may costs less than general interventions since fewer people need to participate. The main challenge will be to reach these people. Options to involve travelers include the provision of health education at truck and bus stops, or along main routes. A study along the trans-African highway in Kenya and Uganda showed that availability of condoms along the route may increase uptake [26]. Another possibility to get into contact with travelers may be at ceremonies such as funerals or marriages. These ceremonies may involve big groups of people and can take several days, for example disco funerals in Kenya [27]. These disco funerals provide opportunities to engage in risky sex, involving casual sex, sometimes with multiple partners and mostly without condoms. Although privacy of the family of the deceased should of course be respected, it may be good to discuss HIV risks and prevention strategies in these settings. DJs can be used as peer educators and condoms may be freely available [27].

We conclude that targeting of interventions towards mobile groups may have a considerable impact on the HIV epidemic, and is worth considering in areas with high mobility.

8.3 Conclusions and recommendations

Conclusions

- Urban immigration explains much of the differences between countries in the African HIV epidemic.
- Out-migrants do not constitute a high-risk group in rural Zimbabwe.
- Risky sexual behavior is seen in both mobile persons and in their partners staying behind.
- Non-participation of mobile groups can strongly reduce the impact of HIV interventions, and targeting them is a promising additional option in the control of HIV.

Recommendations

- Mobility indicators should be standardized to facilitate comparison between studies.
- Mobile groups should be given special attention in surveys and HIV intervention campaigns.
- Interventions aiming at reducing risk behavior in mobile people should include partners staying behind.
- There is a need to explore the feasibility and efficacy of interventions targeting mobile groups.

References

1. Hunt CW. Migrant labor and sexually transmitted disease: AIDS in Africa. *J Health & Soc Behav* 1989; 30:353-373.
2. Pison G, Le Guenno B, Lagarde E, Enel C, Seck C. Seasonal migration: a risk factor for HIV infection in rural Senegal. *J Acquir Immune Defic Syndr* 1993; 6:196-200.
3. Quinn TC. Population migration and the spread of types 1 and 2 human immunodeficiency viruses. *Proc Natl Acad Sci U S A* 1994; 91:2407-2414.
4. Nunn AJ, Wagner HU, Kamali A, Kengeya-Kayondo JF, Mulder DW. Migration and HIV-1 seroprevalence in a rural Ugandan population. *AIDS* 1995; 9:503-506.
5. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sturm AW*, et al.* The impact of migration on HIV-1 transmission in South-Africa: a study of migrant men and non-migrant men and their partners. *Sex Transm Dis* 2003; 30:149-156.
6. Hosegood V, Preston-Whyte E, Busza J, Moitse S, Timaeus IM. Revealing the full extent of households' experiences of HIV and AIDS in rural South Africa. *Soc Sci Med* 2007; 65:1249-1259.

7. Welaga P, Hosegood V, Weiner R, Hill C, Herbst K, Newell ML. Coming home to die? The association between migration and mortality in rural South Africa. *BMC Public Health* 2009; 9:193.
8. UNAIDS. China epidemiological fact sheet on HIV and AIDS. 2008 update. Available at: http://apps.who.int/globalatlas/predefinedReports/EFS2008/full/EFS2008_CN.pdf
9. Li X, Zhang L, Stanton B, Fang X, Xiong Q, Lin D. HIV/AIDS-related sexual risk behaviors among rural residents in China: potential role of rural-to-urban migration. *AIDS Educ Prev* 2007; 19:396-407.
10. Li S, Huang H, Cai Y, Xu G, Huang F, Shen X. Characteristics and determinants of sexual behavior among adolescents of migrant workers in Shangai (China). *BMC Public Health* 2009; 9:195.
11. Hu Z, Liu H, Li X, Stanton B, Chen X. HIV-related sexual behaviour among migrants and non-migrants in a rural area of China: role of rural-to-urban migration. *Public Health* 2006; 120:339-345.
12. He N, Detels R, Chen Z, Jiang Q, Zhu J, Dai Y*, et al.* Sexual behavior among employed male rural migrants in Shanghai, China. *AIDS Educ Prev* 2006; 18:176-186.
13. Brockerhoff M, Biddlecom A. Migration, sexual behavior, and HIV diffusion in Kenya. *International Migration Review* 1998; 33:833-856.
14. Lopman BA, Barnabas R, Hallett TB, Nyamukapa C, Mundandi C, Mushati P*, et al.* Assessing adult mortality in HIV-1-afflicted Zimbabwe (1998 - 2003). *Bull World Health Organ* 2006; 84:189-197.
15. Gregson S, Adamson S, Papaya S, Mundondo J, Nyamukapa CA, Mason PR*, et al.* Impact and process evaluation of integrated community and clinic-based HIV-1 control: a cluster-randomised trial in eastern Zimbabwe. *PLoS Med* 2007; 4:e102.
16. Lurie M, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sweat MD*, et al.* Who infects whom? HIV-1 concordance and discordance among migrant and non-mirant couples in South Africa. *AIDS* 2003; 17:2245-2252.
17. Mercer A, Khanam R, Gurley E, Azim T. Sexual risk behavior of married men and women in Bangladesh associated with husbands' work migration and living apart. *Sex Transm Dis* 2007; 34:265-273.
18. Mishra V, Medley A, Hong R, Gu Y, Robey B. Levels and spread of HIV seroprevalence and associated factors: evidence from national household surveys. 2009. Available at: http://www.measuredhs.com/pubs/pdf/CR22/CR22.pdf
19. Lydie N, Robinson NJ, Ferry B, Akam E, De Loenzien M, Abega S. Mobility, sexual behavior, and HIV infection in an urban population in Cameroon. *J Acquir Immune Defic Syndr* 2004; 35:67-74.
20. Marston M, Harriss K, Slaymaker E. Non-response bias in estimates of HIV prevalence due to the mobility of absentees in national population-based surveys: a study of nine national surveys. *Sex Transm Infect* 2008; 84 (Suppl 1):i71-i77.
21. WHO, UNAIDS, Unicef. Towards universal access - Scaling up of priority HIV/AIDS interventions in the health sector. 2008. Available at: http://www.searo.who.int/en/Section10/Section18/Section2008_13202.htm
22. Grant RM, Wainberg MA. Chemoprophylaxis of HIV infection: moving forward with caution. *J Infect Dis* 2006; 194:874-876.

23. Liu AY, Grant RM, Buchbinder SP. Preexposure prophylaxis for HIV: unproven promise and potential pitfalls. *JAMA* 2006; 296:863-865.
24. Wambura M, Urassa M, Isingo R, Ndege M, Marston M, Slaymaker E*, et al.* HIV prevalence and incidence in rural Tanzania: results from 10 years of follow-up in an open-cohort study. *J Acquir Immune Defic Syndr* 2007; 46:616-623.
25. Boerma JT, Urassa M, Nnko S, Ng'Weshemi J, Isingo R, Zaba B*, et al.* Socio-demographic context of the AIDS epidemic in a rural area in Tanzania with a focus on people's mobility and marriage. *Sex Transm Infect* 2002; 78 (Suppl 1):i97-105.
26. Morris CN, Morris SR, Ferguson AG. Sexual behavior of female sex workers and access to condoms in Kenya and Uganda on the trans-Africa highway. *AIDS Behav* 2008; 82:368-371.
27. Njue C, Voeten HA, Remes P. Disco funerals: a risk situation for HIV infection among youth in Kisumu, Kenya. *AIDS* 2009; 23:505-509.

Summary

Samenvatting

Summary

This thesis investigates the relationships between mobility, sexual risk behavior and HIV infection.

Chapter 1 is an introduction to HIV/AIDS and HIV-interventions. Worldwide, more than 33 million people were infected with HIV in 2007. The majority of infections are due to heterosexual transmission. HIV prevention strategies include health education, condom promotion, treatment of curable sexually transmitted diseases (STDs), male circumcision, and pre-exposure prophylaxis (PrEP). Mobility is described in detail. *Migration* is defined as moving to a new community and includes both immigration and out-migration. *Travel* includes all types of travel with one or more nights away from home. Mobility is a risk factor for the transmission of HIV and is linked through sexual risk behavior. Understanding the risk behavior in couples in which one of the partners is mobile may help in designing feasible HIV interventions. Mobility can also reduce the effectiveness of HIV interventions, but it is not known to what extent this happens.

The overall aim of this thesis was to investigate the role of mobility on HIV transmission and control. The following questions were addressed in this thesis: 1. Can migration explain differences in HIV transmission in Africa? 2. Are migrants a selection of high-risk individuals? 3. Is mobility associated with sexual risk behavior? and 4. How much do mobile groups reduce the effect of HIV interventions?

Chapter 2 describes an ecological study that analyzed the association between female immigration and HIV prevalence in 28 sub-Saharan countries. Migration explains much of the variation in HIV spread in urban areas of sub-Saharan Africa, especially before the year 2000, after which HIV prevalence started to level off in many countries. Our findings suggest that migration is an important factor in the spread of HIV, especially in rapidly increasing epidemics.

In **Chapter 3,** we investigated whether out-migrants were a selection of high-risk individuals. Before and after moving, out-migrants in rural Zimbabwe were compared with residents. No differences were found in sexual behavior and HIV infection at both time points. These findings may be related to the mature stage of the HIV epidemic in Zimbabwe and the social and living conditions of migrants in cities in Zimbabwe.

Chapter 4 presents how mobility is related to sexual behavior and HIV infection in couples in rural Tanzania. People were considered travelers if they had slept outside the household at least once, and migrants if they were living elsewhere at least once. Sexual risky behavior and an increased risk of HIV infection were seen in both mobile persons

and in partners staying behind. Interventions aiming at reducing risk behaviour due to mobility should therefore include partners staying behind.

In **Chapter 5**, we describe to what extent partner absence leads to more risky sexual behavior in couples in rural Tanzania. People living apart (mostly due to polygamous marriages), divided into frequently and infrequently seeing each other, were compared with co-resident couples, divided into traveling or not. Risky sexual behavior occurred more often in mobile co-resident men and in women living apart infrequently seeing their spouses. These groups are relatively easy to identify and need extra attention in HIV prevention campaigns.

Chapter 6 presents modeling results using STDSIM, a microsimulation model for HIV and STD transmission and control in a network of people with different sexual risk patterns. The impact of non-participation of mobile groups on several HIV interventions was studied in an HIV epidemic in rural Tanzania. Mobility patterns were modeled in detail, including recent immigration and travel profiles with concomitant risk behavior. If both immigrants and travelers when away from home were not participating, effectiveness of condom use and health education could be reduced by 40%. It is worth to explore to what extent migrants and travelers are non-participating in different settings. If non-participation is substantial, impact of HIV interventions can be improved by actively approaching mobile people.

Chapter 7 studies the long-term impact of pre-exposure prophylaxis (PrEP) on HIV transmission in Botswana, Kenya and Southern India. Different PrEP scenarios varying in effectiveness, coverage and target group were modeled using a deterministic HIV transmission model. Effects of changes in condom use (e.g. more or less condoms) during PrEP use were also studied. The public health impact of PrEP can be substantial. This impact, however, can be diminished or even reversed, by increases in sexual risk behavior. PrEP should therefore be implemented in addition to current HIV interventions.

Chapter 8 is a general discussion of the findings and provides answers to the research questions. The conclusions and recommendations that follow from the research in this thesis are given below.

Conclusions

- Urban immigration explains much of the differences between countries in the African HIV epidemic.
- Out-migrants do not constitute a high-risk group in rural Zimbabwe.
- Risky sexual behavior is seen in both mobile persons and in their partners staying behind.
- Non-participation of mobile groups can strongly reduce the impact of HIV interventions, and targeting them is a promising additional option in the control of HIV.

Recommendations

- Mobility indicators should be standardized to facilitate comparison between studies.
- Mobile groups should be given special attention in surveys and HIV intervention campaigns.
- Interventions aiming at reducing risk behavior in mobile people should include partners staying behind.
- There is a need to explore the feasibility and efficacy of interventions targeting mobile groups.

Samenvatting

In dit proefschrift worden de relaties tussen mobiliteit, seksueel risicogedrag en HIV infectie in Afrika onderzocht.

Hoofdstuk 1 introduceert hiv/aids en de verschillende interventies gericht op het voorkomen van hiv. In 2007 waren er wereldwijd meer dan 33 miljoen mensen geïnfecteerd met het hiv virus. De meeste infecties in Afrika komen door heteroseksuele transmissie. Hiv preventie strategieën bestaan uit gezondheidsvoorlichting, promotie van condooms, behandeling van seksueel overdraagbare aandoeningen (soa), besnijdenis van mannen en pre-exposure prophylaxis (PrEP; antiretrovirale pillen om hiv infectie te voorkomen). Ook mobiliteit wordt hier in detail beschreven. *Migratie* wordt gedefinieerd als verhuizen naar een nieuwe woonplaats en bestaat uit zowel immigratie als emigratie. *Reizen* omvat alle vormen van reizen waarbij een of meer nachten elders wordt geslapen. Mobiliteit vormt via extra seksueel risicogedrag een risicofactor voor hiv transmissie. Inzicht in het risicogedrag van paren waarin een van beide partners afwezig is, kan helpen in de ontwikkeling van bruikbare hiv interventies. Mobiliteit kan ook het effect van HIV interventies verminderen, maar vooralsnog is onbekend in welke mate dit gebeurt.

De algemene doelstelling van dit proefschrift was de rol van mobiliteit in de transmissie en bestrijding van hiv te onderzoeken. De volgende onderzoeksvragen werden in dit proefschrift beantwoord: 1. In hoeverre kunnen verschillen in hiv transmissie in Afrika verklaard worden door migratie? 2. Zijn migranten een selectie van hoog-risico individuen? 3. Is er een associatie tussen mobiliteit en seksueel risicogedrag? en 4. In welke mate reduceren mobiele groepen het effect van hiv interventies?

Hoofdstuk 2 betreft een ecologische studie van 28 landen ten zuiden van de Sahara, waarin de associatie tussen immigratie van vrouwen en hiv prevalentie wordt beschreven. Migratie kan een groot deel van de variatie in de verspreiding van hiv in de stedelijke gebieden in sub-Sahara Afrika verklaren, en dan met name voor het jaar 2000. Na dat jaar begon de hiv prevalentie in veel landen af te nemen. Onze gegevens ondersteunen dat migratie een belangrijke factor is voor de verspreiding van hiv, met name in epidemieën die snel toenemen.

In **Hoofdstuk 3** onderzoeken wij of emigranten een selectie van hoog-risico individuen vormen. Op het platteland van Zimbabwe werden emigranten, voor en na vertrek, vergeleken met de vaste inwoners van het gebied. In tegenstelling tot eerdere studies werd op beide tijdstippen geen verschil gevonden in het seksueel risiscogedrag of in hiv infectie. Dit zou kunnen komen door het vergevorderde stadium van de hiv epidemie in Zimbabwe.

In **Hoofdstuk 4** wordt de relatie tussen mobiliteit, seksueel gedrag en hiv infectie in paren op het platteland van Tanzania onderzocht. Mobiele mensen werden als reizigers gedefineerd als zij minimaal één keer elders hadden geslapen en als migranten als ze minimaal één keer elders hadden gewoond tijdens 5 interviewrondes over een periode van 3 jaar. Zowel mobiele mensen als partners die achterbleven hadden seksueel risicogedrag en een verhoogd risico op hiv infectie. Interventies gericht op het verminderen van risicogedrag door mobiliteit zouden daarom ook partners die achterblijven moeten omvatten.

In **Hoofdstuk 5** beschrijven we in welke mate afwezigheid van de vaste partner op het platteland van Tanzania tot meer riskant seksueel gedrag leidt. Mensen die apart van elkaar wonen (met name door polygame huwelijken) werden opgedeeld in mensen die elkaar vaak bezoeken en mensen die elkaar minder vaak bezoeken. Deze groepen zijn vergeleken met samenwonende mensen, verdeeld in reizigers en niet-reizigers. Riskant seksueel gedrag werd vaker gevonden in samenwonende mannen die reizen en in vrouwen die apart wonen en hun echtgenoten minder vaak zien. Deze groepen kunnen relatief makkelijk geïdentificeerd worden en zouden extra aandacht moeten krijgen in campagnes gericht op hiv preventie.

Resultaten van het STDSIM model worden gepresenteerd in **Hoofdstuk 6**. STDSIM is een microsimulatie model waarin de transmissie en bestrijding van hiv en soa in een netwerk van mensen met verschillende seksuele risicopatronen wordt gemodelleerd. We onderzochten op het platteland van Tanzania de invloed van het niet-deelnemen van mobiele groepen op verschillende hiv interventies. Mobiliteitspatronen, waaronder recente immigratie en reizigersprofielen met bijbehorend risicogedrag, werden in detail gemodelleerd. Het effect van condoomgebruik en van gezondheidsvoorlichting bleek met 40% gereduceerd, als zowel immigranten als reizigers, wanneer ze van huis waren, niet deelnamen aan de interventies. Het is belangrijk om uit te zoeken in welke mate migranten en reizigers niet deel nemen aan interventies in verschillende gebieden. Als niet-deelname substantieel is, dan zou de impact van hiv interventies verbeterd kunnen worden door actief mobiele mensen te benaderen.

In **Hoofdstuk 7** wordt het lange termijn effect van PrEP op de hiv transmissie in Botswana, Kenia en Zuid-India bestudeerd. Verschillende PrEP scenario's variërend in effectiviteit, dekkingsgraad en doelgroep werden gemodelleerd met behulp van een deterministisch hiv transmissiemodel. Veranderingen in condoomgebruik (meer of minder condooms) tijdens het gebruik van PrEP werden ook bestudeerd. De maatschappelijke impact van PrEP kan aanzienlijk zijn. Maar dit effect kan afnemen, of zelfs omkeren, als seksueel risicogedrag toeneemt. Implementatie van PreP zou daarom niet in plaats van, maar samen met bestaande hiv interventies moeten gebeuren.

Hoofdstuk 8 is een algemene discussie en geeft antwoord op de onderzoeksvragen. De conclusies en aanbevelingen zijn hieronder weergegeven.

Conclusies

- Immigratie in steden kan het verschil in de hiv epidemie van Afrikaanse landen voor een groot deel verklaren.
- Emigranten vormen geen hoog-risico groep op het platteland van Zimbabwe.
- Riskant seksueel gedrag wordt relatief veel gerapporteerd door zowel mobiele mensen, als hun partners die achterblijven.
- Het niet-deelnemen van mobiele groepen kan de impact van hiv interventies sterk reduceren; het speciaal richten van maatregelen op deze mensen lijkt een veelbelovende extra optie in de bestrijding van hiv.

Aanbevelingen

- Om vergelijkbaarheid tussen studies te vergemakkelijken zouden mobiliteitsindicatoren gestandaardiseerd moeten worden.
- In onderzoeken naar en campagnes met hiv interventies zou er speciale aandacht aan mobiele groepen gegeven moeten worden.
- Interventies gericht op het reduceren van risicogedrag in mobiele mensen zouden ook betrekking moeten hebben op partners die achterblijven.
- Het is noodzakelijk om de uitvoerbaarheid en de effectiviteit van interventies gericht op mobiele groepen te onderzoeken.

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Dankwoord

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Dankwoord

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Curriculum vitae

Curriculum vitae

Debby Vissers was born on August 3, 1979 in Prinsenbeek. In 1997, she passed her secondary school exam in Breda, and moved to Leiden to study Biomedical Sciences. During her main internship on schistosomiasis, she lived and studied five months in Malawi. She also followed an extra-curricular year in Science Based Business, in which she did an internship at Pfizer. From 2003 to 2007, Debby has worked as a PhD student at the Department of Public Health, Erasmus MC, University Medical Center Rotterdam. She worked on the project on HIV and mobility, described in this thesis. In 2006, she obtained a Master of Science degree in Epidemiology at the Netherlands Institute of Health Sciences (NIHES) in Rotterdam. Debby was also a board member of Promeras, the PhD association of Erasmus MC, for three years. She received the award "PhD of the year 2006" for this board membership. Since September 2007, Debby works as a Senior Research Associate at Mapi Values in Houten, a strategic consultancy company for the pharmaceutical industry.

Debby Vissers werd op 3 augustus 1979 geboren in Prinsenbeek. Zij haalde in 1997 haar VWO diploma aan het Mencia de Mendoza Lyceum in Breda, waarna zij naar Leiden verhuisde om Biomedische Wetenschappen te studeren. Voor haar afstudeerstage over schistosomiasis bracht ze vijf maanden in Malawi door. Ook deed zij een extra jaar Science Based Business, waarin zij kennis maakte met het bedrijfsleven door een stage bij Pfizer. In de periode 2003-2007 was Debby als AIO werkzaam bij de afdeling Maatschappelijke Gezondheidszorg van het Erasmus MC in Rotterdam. Zij heeft daar gewerkt aan het project over hiv en reisgedrag, beschreven in dit proefschrift. In 2006 haalde zij een mastergraad in de Epidemiologie bij het NIHES (Netherlands Institute for Health Sciences) in Rotterdam. Daarnaast heeft Debby zich ruim 3 jaar als bestuurslid ingezet bij Promeras, de belangenvereniging voor promovendi in het Erasmus MC. Voor dit bestuurswerk ontving zij de prijs voor "Promovendus van het jaar 2006". Vanaf september 2007 is Debby als senior onderzoeker werkzaam bij Mapi Values, een strategisch onderzoeks- en adviesbureau voor de farmaceutische industrie, in Houten.

PhD portfolio summary

PhD Portfolio Summary

Name PhD student	Debby C.J. Vissers
Erasmus MC Department	Public Health
PhD period	2003 – 2007
Promotor	Prof.dr. J.D.F. Habbema
Supervisor	Dr. S.J. de Vlas

1. PhD training	Year	Workload
General academic skills		
- Short course Biomedical English Writing and Communication	2005	24 hours
- Basic didactic skills	2006	24 hours
In-depth courses		
- Master of Epidemiology, Netherlands Institute for Health Sciences (NIHES), Rotterdam, the Netherlands		
o Erasmus Summer Programme		
• Principles of research in medicine and epidemiology	2004	20 hours
• Methods of public health research	2004	20 hours
• Topics in evidence-based medicine	2004	20 hours
• Introduction to public health in the changing global context	2004	20 hours
• Methods of health services research	2004	20 hours
• Prevention research	2004	20 hours
o Core curriculum		
• Study design	2004	64 hours
• Classical methods for data-analysis	2003	96 hours
• Public health research	2005	96 hours
• Methodological topics in epidemiologic research	2004	32 hours
• Modern statistical methods	2005	64 hours
o Advanced short courses		
• Epidemiology of infectious diseases	2004	40 hours
• Quantitative models for evaluation of tropical disease control	2004	72 hours
• Health services: research and practice	2004	24 hours
Presentations		
- Oral presentation “Mobility and HIV risk in Tanzanian couples: when the cat’s away, the mice will play” at the IUSSP XXV International Population Conference in 2005 in Tours, France	2005	25 hours
- Poster presentation “Mobility and HIV risk in Tanzanian couples: when the cat’s away, the mice will play” at the 16th biennial meeting of ISSTDR in 2005 in Amsterdam, the Netherlands	2005	25 hours
Seminars and workshops		
- Attending seminars of the department of Public Health	2003-2007	70 hours
- Workshop “The role of mobility in the spread and control of HIV” preceding the XV AIDS conference in 2004 in Bangkok, Thailand	2004	10 hours

International conferences		
- The XV AIDS conference in 2004 in Bangkok, Thailand	2004	36 hours
- National congress STD-HIV in 2004 and 2005 in Amsterdam, the Netherlands	2004-2005	16 hours
- The IUSSP XXV International Population Conference in 2005 in Tours, France	2005	28 hours
- The 16th biennial meeting of ISSTDR in 2005 in Amsterdam, the Netherlands	2005	24 hours
- The XVI AIDS conference in 2006 in Toronto, Canada	2006	32 hours
2. Teaching activities	**Year**	**Workload**
- Lecturing in NIHES course on quantitative models for evaluation of tropical disease control	2006	10 hours
- Supervising and coordinating STOLA tropical course, STOLA foundation, Rotterdam, the Netherlands	2004-2006	150 hours
- Revising essays of STOLA tropical course, STOLA foundation, Rotterdam, the Netherlands	2004-2006	125 hours
3. Other activities	**Year**	
- 3-week field visit to the National Institute for Medical Research (NIMR), Mwanza, Tanzania	2006	
- Board member of Promeras, the PhD association for Erasmus MC. Main activities:	2004-2006	
o Representation of PhD students within Erasmus MC (regular meetings with the Dean, the Department of Research and Policy, and the Department of Human Resources; providing feedback to the PhD students).		
o Composition of a central database with potential employers for PhD students after their thesis.		
o A survey among former PhD students about the printing costs of a thesis.		
o Being a member of the PhD committee of Erasmus MC.		
o Organisation of the “PhD Education Day” and the “Information Market for PhDs”.		