

The effectiveness of HIV prevention and the epidemiological context

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Abstract Planning an intervention to prevent infections with the human immunodeficiency virus (HIV) should be guided by local epidemiological and socioeconomic conditions. The socioeconomic setting and existing public service capacity determine whether an intervention can have a significant outcome in terms of a reduction in a defined risk. The epidemiological context determines whether such risk reduction translates into a measurable impact on HIV incidence. Measurement of variables describing the epidemiological context can be used to determine the local suitability of interventions, thereby guiding planners and policy-makers in their choice of intervention. Such measurements also permit the retrospective analysis of the impact of interventions where HIV incidence was not recorded. The epidemiological context is defined for four different categories of intervention, shown to be effective in lower-income countries by randomized controlled trials. Appropriate indicators for the epidemiological context and methodological guidelines for their measurement are proposed. Their use in the transfer of a successful intervention from one context to another and in scaling up the effort to control HIV infection is explored. These indicators should provide a useful resource for those involved in planning HIV prevention interventions.

Keywords HIV infections/ prevention and control/transmission; Disease transmission/prevention and control; Communicable disease control/methods; Epidemiologic factors; Epidemiologic measurements; Randomized controlled trials; Logistic models; Developing countries (*source: MeSH*).

Mots clés HIV, Infection/prévention et contrôle/transmission; Transmission maladie/prévention et contrôle; Lutte contre maladie contagieuse/méthodes; Facteurs épidémiologiques; Mesures épidémiologiques; Essai clinique randomisé; Modèle logistique; Pays en développement (*source: INSERM*).

Palabras clave Infecciones por VIH/prevenición y control/transmisión; Transmisión de enfermedad/prevenición y control; Control de enfermedades transmisibles/métodos; Factores epidemiológicos; Mediciones epidemiológicas; Ensayos controlados aleatorios; Modelos logísticos; Países en desarrollo (*fuentes: BIREME*).

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Voir page 1130 le résumé en français. En la página 1130 figura un resumen en español.

Introduction

Public health interventions to prevent new human immunodeficiency virus (HIV) infections can be targeted at different risk behaviours (e.g. heterosexual sexual intercourse, injecting drug use), different aspects of a given risk behaviour (e.g. heterosexual sexual intercourse: age at sexual debut, levels of pre-

and extramarital sexual intercourse, condom use, etc.), and different at-risk populations (e.g. prostitutes, adolescents and school youth, young women). Interventions can range from education to promote behaviour change, to treatment of bacterial sexually transmitted infections (STIs) that enhance HIV transmission, to social marketing of condoms. The impact of such interventions depends very much upon the local context, in terms of risk behaviour, attitudes to risk, prevalence of cofactor STIs, stage of the HIV epidemic, existing health services, etc. Intervention design must take the local context into account.

Implementation of interventions

The implementation of an intervention to prevent the spread of HIV can be considered to have an immediate 'outcome' in terms of a change in risk behaviour or the riskiness of that behaviour, and a consequent 'impact' on HIV incidence (Fig. 1). The likelihood of a significant outcome in this sense is determined by the socioeconomic, cultural and legislative context, and the existing public health service infrastructure.

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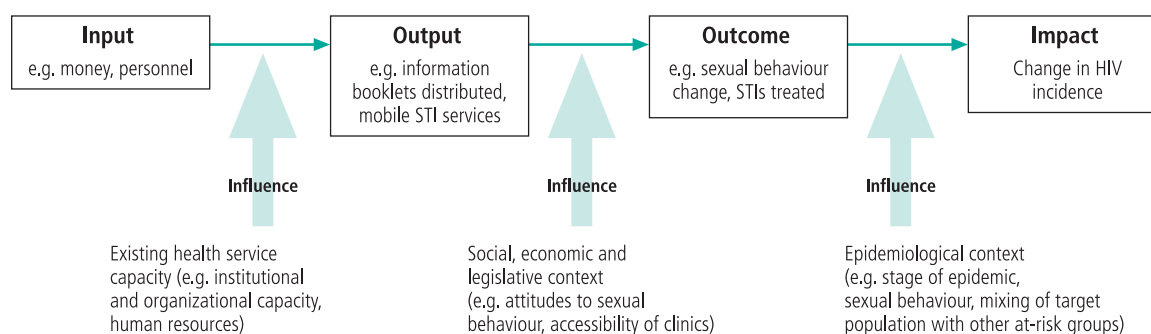
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Fig. 1. **Contextual factors that determine the impact of a human immunodeficiency virus (HIV) prevention intervention** (The epidemiological context determines whether the outcome of an intervention translates into a reduction in HIV incidence. Often overlooked by policy-makers, it is the ultimate determinant of the success of HIV prevention interventions.)



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For example, an intervention that promotes access to educational material about safer sex may have different outcomes, in terms of changes in sexual risk behaviour, in different localities depending on community attitudes to sex. Whether or not the outcome of an intervention translates into an impact on HIV incidence depends on the epidemiological context. Although a significant programme outcome implies a relative reduction in HIV incidence, the relations between these two parameters are complex and non-linear (1, 2). Even an intervention with a large outcome may have minimal impact on HIV incidence if implemented late in the HIV epidemic or targeted at the wrong people (3). Dramatic increases in condom distribution may have very little impact on HIV spread until use during sexual intercourse is close to 100% in high-risk partnerships (4). Researchers and policy advisers must therefore be very careful in advocating interventions that have been shown to be successful using only measures of programme outcome and not impact (7).

Epidemiological context

The epidemiological context will depend on the intervention of interest, but can be broadly defined as the current state and trends in the behavioural and biological factors that determine the transmission dynamics of a given disease and the impact of a specified intervention. The appropriateness of an intervention to the local context can be assessed by the use of intervention trials, most rigorously by randomized controlled trials (RCTs). However, for the majority of HIV/AIDS programme managers this is not an option, and intervention selection typically proceeds by a process of analogy: those interventions that have proved effective in similar socioeconomic and epidemiological contexts are taken as models for the local intervention. This process often results in the selection of those interventions shown to be effective by the few published and well-publicized RCTs. When the same intervention carried out in different contexts has different impacts, confusion can arise over its

appropriateness. For example, the reduction in HIV incidence resulting from an intervention offering improved syndromic treatment of cofactor STIs in the United Republic of Tanzania was not replicated by a community-wide STI treatment programme in Uganda (5, 6). Although these interventions implemented STI treatment in different ways, a significant cause of their different impacts is likely to have been the different contexts (7). In Uganda, the prevalence of one cofactor STI (herpes simplex virus type 2) was higher and the HIV/AIDS epidemic was at a later stage — a point at which the proportion of new HIV infections attributable to STI presence tends to be lower than earlier on, when core groups with high STI prevalence may be responsible for the more generalized spread of HIV.

This article describes the epidemiological contexts for different types of intervention aimed at preventing the spread of HIV in lower-income countries. Appropriate indicators are proposed, together with guidelines for their measurement. Ways of using these indicators to guide the choice of intervention and their role in the process of scaling up interventions to the national level are also considered. The relation between indicators recording the epidemiological context and national monitoring and evaluation indicators (8) is explored, and the complementary roles of national programme monitoring and evaluation, and local intervention planning are highlighted. The article begins with a review of selected interventions that have been shown to be effective at reducing HIV spread in lower-income countries by means of rigorous RCTs.

Randomized controlled trials

The “gold standard” for dealing with the influence of context is an assessment of specific interventions by means of an RCT prior to their widespread implementation (9). Randomization across individuals or communities is aimed at eliminating the influence that variation in contextual factors may have on apparent programme success or failure. In

practice, RCTs, especially those undertaken in the community, have to be carried out within reasonably narrow geographical and political bounds and may thus fail to control for broader contextual issues. This restricts the general applicability of results and can give conflicting outcomes for different RCTs (7). In addition, there may be design problems, such as contamination and insufficient documentation of implementation or difficulties in replication (9).

RCTs of interventions to prevent heterosexual and perinatal HIV transmission that have shown a statistically significant outcome or impact are illustrated in Table 1 (10–24). This updates the 1997 World Bank study of selected interventions to prevent HIV infection in developing countries (10), and focuses on studies published in the last three years. A recent review of interventions in developing countries that targeted heterosexual transmission and injecting drug users, which also includes prospective cohort studies and repeat cross-sectional surveys, with and without comparison groups, has been carried out by Merson et al. (11).

RCTs have identified a substantial number of interventions that have potential for wider implementation and also scaling-up. The interventions fall into four categories, based on their outcome: sexual behaviour change; improved STI service use and quality; increased number of mothers receiving antiretroviral therapy to prevent mother-to-child transmission; and increased use of safe alternatives to breastfeeding. A number of other trials are currently in progress, e.g. information, education and counselling (IEC) with and without STI treatment in rural Uganda (25), replacement feeding of infants and antiretroviral therapy of mothers to prevent mother-to-child transmission in Côte d'Ivoire (26), and peer education and STI management in rural Zimbabwe (S. Gregson, personal communication, 2001). A reduction in the relative incidence of HIV infections is the clear aim of interventions, and can be considered the ultimate measure of intervention success (see Fig. 1). However, measures of success other than intervention impact are typically recorded, such as a decline in average numbers of extramarital sexual partners, more consistent condom use, or an increase in the average age at sexual debut. Of the RCTs of behavioural interventions listed in Table 1, four recorded changes in sexual behaviour, three recorded knowledge and attitudes, and one recorded the impact on STI incidence — none recorded the impact on HIV incidence. This pattern reflects that seen by Merson et al. (11) and the World Bank (10).

The epidemiological context

The impact on HIV incidence of an intervention with a significant outcome in a particular location depends on the epidemiological context. It is therefore essential to assess the epidemiological context in order to predict the likely impact of an intervention

and determine whether it is potentially transferable to other locations. Proposed indicators describing the epidemiological context for the four previously identified intervention types are listed in Table 2 (27–35). Reasons for their inclusion, and how they determine the impact of an intervention on HIV incidence are described in the Annex (available at www.who.int/bulletin). The guidelines for their measurement are given, and this information is provided as a hypertext document with the relevant links (available at www.epidem.org/indicators.htm). Comments on the usefulness of the indicators and suggestions for improvement are welcomed and should be sent to the corresponding author.

If these indicators are measured in the appropriate way, the local suitability of an intervention can be assessed and its impact on HIV incidence estimated prior to implementation. Similarly, if an intervention has reduced a risk behaviour by a certain amount, but HIV incidence was not recorded, the impact of this intervention on the incidence can be estimated by a consideration of the relevant contextual indicators. For example, a national HIV/AIDS programme manager may be interested in determining whether a government education and condom distribution programme targeted at commercial sex workers has been successful in decreasing HIV incidence in the local population. The intervention has been evaluated in terms of the change in rates of condom use with clients and the average number of clients per day. The relevant epidemiological contextual indicators would therefore be the phase of the HIV epidemic, cofactor STI prevalence in the target and general population, sexual behaviour of the general population, and patterns of mixing of sex workers with the general population. It may emerge that, although HIV infection is reasonably prevalent throughout the population, cofactor STIs are concentrated among sex workers and their male clients, while self-reported sexual behaviour in the general population indicates a low intrinsic risk. This would suggest that many new HIV infections arise because of the high rate of transmission from sex workers to their clients (enhanced by cofactor STIs), and subsequently to the spouses and other sexual partners of the clients. Thus the intervention targeting commercial sex workers is likely to have been effective in reducing overall HIV incidence, and its continued implementation is therefore of key importance. Further, it may become clear that clients of sex workers disproportionately represent a particular section of society, such as migrant labourers, and that an intervention targeting these individuals would also be effective.

If the programme manager was subsequently to consider implementing this intervention elsewhere, the same contextual indicators should be recorded in the new location. If the epidemiological context is favourable, implementation of the intervention can follow. For example, the epidemic may be at an early stage in the new location, and so most new HIV infections in the general population will be

Table 1. **Randomized controlled trials (RCTs), published from 1998 onwards,^a demonstrating effective interventions to prevent heterosexual and perinatal transmission of HIV-1 in low-income countries^b**

Intervention	Author and year	Country	Randomization across	Measures of effectiveness	Outcome ^c
Education to alter sexual behaviour/condom distribution					
Face-to-face interviews with secondary school students to promote safer sex and sexual abstinence	Stanton et al. (12), 1998	Namibia	Individuals	HIV risk behaviour/ condom use; knowledge and attitudes	Increased sexual abstinence among baseline virgins in intervention vs those receiving no intervention for 12 months (17% vs 9% remained sexually inexperienced after 12 months, $P < 0.05$); increased knowledge of condom use (89% vs 72%, $P < 0.05$)
Education and role-play in schools	Fawole et al. (13), 1999	Nigeria	Schools	Mean number of sexual partners/ condom use; knowledge and attitudes	Greater knowledge of HIV transmission and prevention in intervention schools vs control schools with no intervention ($P < 0.05$); non-significant reduction in mean no. of sexual partners, 1.51–1.06 (vs control, 1.3–1.39); nonsignificant increase in condom use
Condom provision in motel rooms	Egger et al. (14), 2000	Nicaragua	Motels	Condom use	Increased use of condoms for commercial (OR = 1.31, CI = 1.09–1.75) and non-commercial sex (OR = 1.81, CI = 1.14–2.81)
Drama-in-education programme in high schools	Harvey et al. (15), 2000	South Africa	Individuals	Knowledge and attitudes; condom use	Increased knowledge in intervention group vs those receiving written information only ($P = 0.0002$); sexually active pupils reported an increase in condom use ($P < 0.01$)
Voluntary counselling and testing (VCT) among individuals and couples including STD treatment at first follow-up	The VCT Efficacy Study Group (16), 2000	Kenya, United Republic of Tanzania	Site, sex and couple or individual status	Levels of unprotected sex; STD incidence	Reduction in unprotected intercourse with non-primary partners for individuals receiving VCT vs health information only (OR = 0.68, CI = 0.56–0.82); non-significant decline in STD incidence in intervention group (OR = 0.8, CI = 0.53–1.20)
Improved STI treatment					
Education to promote STI knowledge and treatment-seeking behaviour of youth, and improved STI treatment facilities through retraining of providers	Coplan et al. (17), 2000	Nigeria	Schools	STI knowledge and condom use; STI treatment-seeking behaviour; STI prevalence	Improved STI knowledge; increased treatment by private physicians (OR = 2.1, CI = 1.1–4.0), and decreased treatment by untrained over-the-counter providers (OR = 0.44, CI = 0.22–0.88); reduction in STI prevalence in intervention schools (OR = 0.68, CI = 0.48–0.95)
Health worker training and STI syndrome packets to improve quality of STI case management in rural primary care clinics	Harrison et al. (18), 2000	South Africa	Primary health care clinics	Quality of case management; STI treatment-seeking behaviour	Increased use of recommended drugs (RR = 1.28, CI = 1.12–1.47); more patients received appropriate drugs (RR = 2.08, CI = 1.53–2.84);
Antiretroviral therapy to prevent mother-to-child transmission					
Short-course perinatal oral zidovudine	Wiktor et al. (19), 1999	Côte d'Ivoire	Individuals	HIV infection of infants; infant mortality	Efficacy in preventing transmission was 44% (CI = 1–69%) at age 4 weeks and 37% (CI = 5–63%) at 3 months in a breastfeeding population; mortality of infants aged 2–120 days was 8.8% in the placebo and 1.4% in the intervention arm ($P = 0.008$)
	Dabis et al. (20), 1999; DITRAME ANRS 049 Study Group (21), 1999	Côte d'Ivoire, Burkina Faso	Individuals	HIV infection of infants; infant mortality	Efficacy was 38% (CI = 5–60%) at 6 months and 30% (CI = 2–52%) at 15 months in a breastfeeding population; infant mortality not significantly different ($P = 0.16$), but higher neonatal mortality in intervention (4%) vs placebo (2%) arm ($P = 0.04$)
Short-course perinatal zidovudine and lamivudine	Saba (22), 1999	South Africa, United Republic of Tanzania, Uganda	Individuals	HIV infection of infants; infant mortality	Reduced transmission where pre-, intra- and postpartum antiretrovirals were administered (RR at 6 weeks = 0.396, CI = 0.248–0.632) (70% of population breastfeeding); decreased infant mortality in intervention arm

(Table 1, continued)

Intervention	Author and year	Country	Randomization across	Measures of effectiveness	Outcome ^c
Intrapartum and neonatal single-dose nevirapine	Guay et al. (23), 1999	Uganda	Individuals	HIV infection of infants; infant mortality	Relative efficacy of nevirapine vs zidovudine 47% (CI = 20–60%) (implying ca 50% reduction in transmission probability); 2 babies in the nevirapine arm and 4 in the zidovudine arm possibly died from drug toxicity
Breastmilk substitutes Formula feeding in infants of HIV-positive mothers	Nduati et al. (24), 2000	Kenya	Individuals	HIV infection of infants; infant mortality	At 2 years the cumulative probability of HIV infection was 36.7% (CI 29.4–44.0%) in the breastfeeding arm and 20.5% (CI 14.0–27.0%) in the formula arm ($P = 0.001$); although infant mortality was not significantly different in the two arms ($P = 0.3$) at any stage during the 2-year follow-up, HIV-free survival was higher in the intervention arm (70.0% vs 58.0%; $P = 0.02$)

^a For RCTs in lower-income countries published before 1998 refer to references 10 and 11; published studies were located using the AIDS abstract database and Medline available at <http://gateway.nlm.nih.gov>, and the Web of ScienceSM citation databases published by the Institute for Scientific Information, in July 2001.

^b Low-income countries are those with a per capita gross national product in 1999 of less than US\$ 755, as assessed by the World Bank.

^c CI = 95% confidence intervals; OR = odds ratio; RR = relative risk.

due to contact with sex workers who are likely to be HIV-positive. An intervention targeting sex workers should therefore be highly effective in reducing overall HIV incidence.

Measurement of the components of the epidemiological context allows the local suitability of an intervention with a predicted outcome in terms of risk reduction to be determined. Once we have identified a set of interventions with a suitable outcome, we need to assess whether and how they can be implemented to achieve this outcome. This is dependent on broader socioeconomic, cultural and legislative factors, such as determinants of an individual's ability to control his or her own HIV risk, existing maternal and child services, availability of voluntary counselling and testing facilities, vulnerability of those individuals revealing their HIV status, community attitudes to sexual risk behaviour, adherence to antiretroviral drug therapy, alcohol consumption, and logistic problems with programme implementation (31, 36). A discussion of these factors is beyond the scope of this paper (8, 36).

An unfavourable epidemiological context suggesting a low impact for a specific intervention does not necessarily rule out implementation of that intervention, particularly if the broader socioeconomic context is such that a large intervention outcome can be achieved at low cost. Rather, the unfavourable components of the epidemiological context can themselves be targets of another intervention. For example, high STI prevalence among the clients of commercial sex workers will make improved STI treatment of the sex workers alone ineffective in reducing overall HIV incidence. By targeting another STI treatment intervention at the clients, for example by offering workplace STI treatment and counselling, the epidemiological context for the original intervention may become favourable.

Broader determinants of socioeconomic, cultural and legislative contexts can also be the target of interventions. Such interventions are typically termed "structural" or "environmental", the former resulting in changes in laws, policies or administrative procedures, and the latter in living conditions, resources or opportunities (11, 37).

The use of epidemiological models

By assessing and recording indicators for the epidemiological context, programme managers and policy-makers will be able to identify those interventions likely to be effective in their local setting, subject to the constraints of implementation discussed above. The value of this process can be increased through the use of mathematical models that predict the impact of interventions on the number of new HIV infections, while including, explicitly and quantitatively, potentially important contextual variables. Models are particularly useful when determining the impact of an intervention that results not only from a decline in susceptibility of targeted individuals, but also from the decrease in transmission of HIV to other individuals.

Many mathematical models of interventions to prevent the spread of HIV and results obtained by applying them to particular scenarios have been reported in the literature (4, 38–42). Although mathematically complex, such models have recently been implemented as user-friendly software designed to assist policy-makers and national HIV/AIDS programme managers. Two such applications were demonstrated at the XIII International AIDS Conference in Durban, South Africa, 2000. The first, a suite of programs entitled HIVTools, has been designed to assess interventions targeted at different populations

Table 2. Proposed indicators for the epidemiological context and guidelines for their measurement^a

Intervention	Variables recording intervention outcome	Indicator	Recommended variable	Proxy variable	Methodological references and guidelines
Education to alter sexual behaviour/ condom distribution	Baseline and change in sexual behaviour in target population including condom usage (methodology ref. 27, 28)	1. Phase of HIV epidemic	Age/sex-stratified HIV prevalence for different risk groups over time	Available measures of current and past HIV prevalence	(29)
		2. Cofactor STI prevalence	STI seroprevalence for different risk groups	STI prevalence in an available population (the constitution of which is not affected by STI status); prevalence of STI symptoms	(30)
		3. Mixing of target population with other at-risk populations (including different age groups if intervention is age-specific)	Sexual networks with social and geographical detail		(27, 28)
		4. Sexual behaviour of populations not targeted by the intervention	Sexual behaviour in untargeted populations		(27)
Improved STI treatment	Baseline STI service use and quality, and subsequent improvement following intervention (methodology ref. indicator from 8)	1. Phase of particular STI epidemic	STI seroprevalence for different risk groups	STI seroprevalence in an available population (the constitution of which is not affected by STI status); prevalence of STI symptoms	(30)
		2. Phase of HIV epidemic	Age/sex-stratified HIV prevalence for different risk groups over time	Available measures of current and past HIV prevalence	(29)
		3. Prevalence of other cofactor STIs including genital herpes (HSV-2)	STI seroprevalence for different risk groups	Unbiased estimate of STI prevalence in an available population; prevalence of STI symptoms	(30)
		4. Mixing of target population with other at-risk populations (including different age groups if intervention is age-specific)	Sexual networks with social and geographical detail		(28, 30)
		5. STI prevalence in neighbouring populations and importance of reintroduction following treatment	STI seroprevalence	Prevalence of STI symptoms	(30)
ARV drugs to prevent mother-to-child transmission	No. of mother-child pairs receiving and adhering to drugs plus drug efficacy ^b	1. Level of breastfeeding vs artificial feeding	Proportions breast-feeding/ artificial-feeding/ mixed-feeding; average duration of breastfeeding.		(31, 32)
		2. Prevalence of HIV among treated women ^c	Age-stratified HIV seroprevalence		(29)

(Table 2, continued)

Intervention	Variables recording intervention outcome	Indicator	Recommended variable	Proxy variable	Methodological references and guidelines
Alternatives to breastfeeding^e	Baseline and increase in no. of mothers using safe formula feeding (methodology ref. 31, 32)	3. Viral load of mothers	Viral load of a sample of individuals in the intervention	CD4 levels/prevalence of HIV morbidity in a sample of individuals in the intervention	Quantitative PCR (FDA approves Roche but no standard method); flow cytometry (33)
		4. Mode of delivery and rates of premature delivery ^d	Rates of Caesarean section; average duration of gestation		(31, 32)
		5. STI prevalence ^d	Proportion with STI		(30)
		1. Viral load of mothers; availability of ARV drugs	Viral load of a sample of individuals in the intervention; availability of ARV drugs	CD4 levels/prevalence of HIV morbidity in a sample of individuals in the intervention	Quantitative PCR (FDA approves Roche but no standard method); flow cytometry (33); provision of ARV therapy indicator in (8)
		2. Levels of mastitis and severe vitamin A deficiency	Rates of subclinical mastitis; nutritional status of mothers		(34, 35)
		3. Mode of delivery and rates of premature delivery ^d	Rates of Caesarean section; average duration of gestation		(31, 32)
		4. STI prevalence ^d	Proportion with STI		(30)

^a ARV = antiretroviral; FDA = United States Food and Drug Administration; PCR = polymerase chain reaction.

^b Efficacy is the proportion of HIV-positive births that are prevented by the ARV drug when administered correctly with 100% adherence (cf. effectiveness, the actual proportion of HIV-positive births averted during an intervention).

^c Important if ARV therapy is provided to all women irrespective of HIV status (which is likely to be unknown) (cf. formula-feeding interventions, which will only be appropriate if targeted at HIV-positive women).

^d Where contextual factors are being used retrospectively to determine the success of an intervention without a control group in reducing mother-to-child transmission, the incidence of HIV at birth is likely to have been recorded. In such cases only rates of breastfeeding, mother's viral load/CD4 levels and, for formula-feeding interventions, levels of mastitis and severe vitamin A deficiency, need to be recorded to determine the relative role of postnatal vs perinatal transmission, and hence the impact of the intervention on the vertical transmission of HIV.

^e Although access to clean water is not an epidemiological contextual variable, it should be stressed that before considering the implementation of this intervention, it is vital for it to be assessed; child mortality will be increased by the promotion of formula feeding in the absence of clean water.

including sex workers, school youth, and injecting drug users (43). These programs include costing spreadsheets for the interventions modelled, and were recently used to assess a harm-reduction programme aimed at injecting drug users in Svetlogorsk, Belarus (44). The second application, AIDS Strategic Intervention Support Tool (ASIST), developed by the US National Institute of Mental Health, models interventions aimed at reducing heterosexual transmission of HIV. Interventions that can be modelled include condom distribution, education for sexual behaviour change, bacterial STI treatment, microbicide gel distribution, and antiretroviral therapy.

Both of these programs are able to deal explicitly with the epidemiological context as described by the indicators listed in Table 2 through entry of the relevant parameters, and can predict the

effectiveness of interventions under different scenarios. In ASIST, a simple “wizard” guides users through the process of setting parameters consistent with a broadly defined scenario. Two ways of using such programs are illustrated in Box 1.

Scaling up to the national level

To what extent can and should interventions that are successful at a local level be implemented at the national level? Can an intervention shown to be effective by an RCT in a different specific epidemiological context be taken as the model for a component of the national HIV/AIDS programme? These questions concern the process of scaling up.

Box 1. Use of the computer program ASIST to assess epidemiological context

Scenario A

A programme of improved syndromic management of bacterial STIs combined with periodic mass screening and treatment was implemented in 1982 in a small district in rural sub-Saharan Africa. The outcome was a significant decline in the mean duration of infection with a bacterial STI. Since the bacterial STIs treated can act as cofactors for HIV transmission, an AIDS programme manager is interested in the impact this programme may have had on the incidence of HIV in this community. How can the manager assess this impact?

Step 1

Contextual determinants of intervention effectiveness are identified (see Table 2), and the available recommended variables are recorded. (In cases where the recommended variables have not been measured, and the possible proxy variables are also unavailable, data from locations likely to have a similar epidemiological context can be used. In the program ASIST, such data is available through the use of certain predetermined scenarios, e.g. populations with significant/insignificant commercial sex work, adequate/inadequate bacterial STI treatment facilities, etc.)

Step 2

All relevant contextual variables are entered as parameters of the model. For example, sexual behaviour data can be entered into the program ASIST by specifying different sexual activity classes and the proportions of the population in each class. A significant female sex worker industry would imply a sexual activity class for women with high rates of sexual partner change and few sex acts per partnership. The model is then run and the expected HIV incidence in the absence of an intervention is produced.

Step 3

The outcome of the intervention (rates of recovery from bacterial STIs) is entered into the program, together with the date of intervention implementation (1982), so that the predicted impact of the intervention on HIV incidence can be assessed.

Projections

The programme is likely to have been successful in controlling the spread of HIV in this district. The incidence of HIV has been kept close to zero — a very different scenario from that expected in the absence of the programme. The prediction of the model in this situation could be evaluated by testing for HIV in the district.

Scenario B

The same programme manager wishes to assess whether similar STI treatment is likely to be an effective intervention to prevent HIV transmission in another district in 2002. This district has a bacterial STI prevalence similar to that in the first district prior to programme implementation and has an emerging HIV epidemic. However, it has a high prevalence (65%) of herpes simplex virus type 2 (HSV-2), which is a cofactor for HIV transmission. This contrasts with the first district where HSV-2 prevalence was low.

Steps 1 and 2

The relevant contextual indicators from Table 2 are identified for the new location and recommended variables are entered as parameters into the program ASIST. While the two locations are similar in most respects, there is a higher prevalence of HSV-2 in the new district.

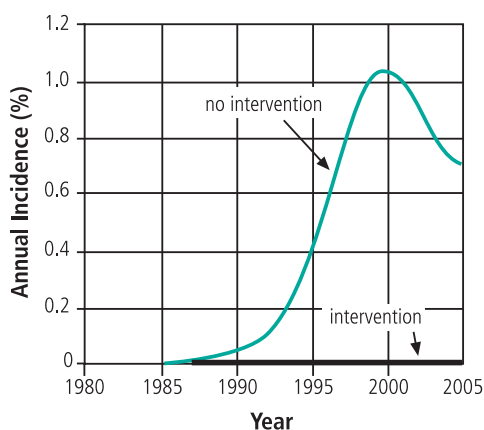
Step 3

An increase in rates of recovery from bacterial STIs is entered into the program, assuming that the intervention can be implemented with an equal outcome in the new location, and the proposed date of implementation of the intervention is specified (2002).

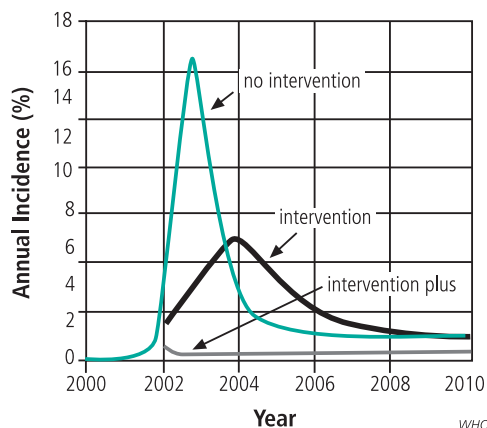
Projections

In the new location, the intervention is predicted to have a significant impact on HIV incidence, but is likely to be less effective than that in the first district, owing to the high prevalence of HSV-2 (which is not affected by the intervention). The intervention is also to be implemented one year after the HIV/AIDS epidemic has begun to spread, while in the first district implementation was at an earlier stage of the epidemic. STI treatment interventions to prevent the spread of HIV in areas with high HSV-2 prevalence should be supported by education and condom distribution, which can reduce transmission of both HIV and HSV-2. A combined approach is likely to have a large impact on HIV incidence (“intervention plus”).

Scenario A



Scenario B



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The effectiveness at the national level of an intervention targeted at a specific risk group is determined in part by the epidemiological context and how it varies across the country, for example, the mixing of the target population of the intervention (e.g. miners or truck drivers) with at-risk groups throughout the country. However, there are issues that are specifically relevant to the national level, such as the heterogeneous distribution of at-risk populations across the districts of a country, in terms of both type of risk and concentration. The most obvious distinctions in this case are rural/urban differences in HIV prevalence and risk behaviours. Such heterogeneity has implications both for HIV/AIDS surveillance (29), and for the impact of different types of intervention. For example, an intervention targeted at commercial sex workers may be more effective in urban areas, where sex work is a more clearly defined activity, and numbers of sex workers and their accessibility are often higher. The epidemiological context may also vary from one urban setting to another or from one rural area to another within the same country. For example, the relative roles of injecting drug use and commercial sex in the spread of HIV in India, and the interaction of these at-risk populations vary considerably from state to state (National AIDS Control Organisation of India, unpublished data).

A national HIV/AIDS programme should therefore allow regional approaches to the HIV/AIDS epidemic, and this naturally implies a certain amount of decentralization of the organization and financing of prevention activities. The use of flexible financing structures is crucial to such decentralization (45), permitting funds earmarked for HIV/AIDS prevention to be used for interventions reflecting local culturally adapted best practice (46). Local relevance can be established by examining the epidemiological context as well as broader structural and environmental factors, and by carrying out costing studies. Capacity to carry out analyses of costs and effectiveness may be centrally located or based within external organizations and accessible through technical assistance programmes. Alternatively, financing and aid instruments may be designed in such a way as to promote local capacity in carrying out such analyses. Organizational and institutional capacity-building for HIV/AIDS prevention activities can be made the explicit goal of financing arrangements. Indicators for the dimensions of this capacity have been designed and their performance examined (47).

Scaling up an intervention may produce economies of scale, not only in terms of costs, but also in terms of effectiveness. For example, in Rakai, Uganda, one of the problems with mass STI treatment was the rapidity of reinfection due to migration and contact with untreated infected individuals (7). An intervention that aims at improved STI treatment and is implemented at the national level would reduce this rate of reinfection.

In other words, the intervention has a “positive externality”. Scaling up those interventions that have positive externalities may result in increasing returns in terms of effectiveness. The logical conclusion of such interventions could be disease eradication, which is the rationale behind many accelerated health programmes (such as immunization against poliomyelitis). However, HIV eradication is not realistic given the maintenance of infection in difficult-to-reach groups such as commercial sex workers and injecting drug users, its long duration of asymptomatic infection, and the lack of an effective vaccine.

As an intervention programme is scaled up to the regional and national level, questions naturally arise about the possibility of targeting an expanded range of risk groups. For example, an STI and HIV/AIDS education programme targeted at commercial sex workers may be expanded to include all adult attendees of STI clinics. This concerns intervention design rather than scaling up. Prior to implementation, the relevant epidemiological context and socio-economic environment will need to be reassessed with respect to this new intervention with a different target population.

Although consideration of the epidemiological context may give some indication as to the likely effectiveness of a national intervention package, pilot programmes remain of fundamental importance. Pilot programmes differ from RCTs in that they tend not to include a matched control group. Although they are useful in clarifying the relative importance of different components of the epidemiological context, their key role is in identifying broader socioeconomic and financial constraints to effective programme implementation. The monitoring and evaluation of pilot programmes should therefore include indicators of programme outcome, costs and financial sustainability, in addition to those for the epidemiological context. For example, a list of indicators for the monitoring and evaluation of a pilot programme for the integrated prevention of mother-to-child transmission should include the epidemiological context, with indicators such as HIV prevalence in pregnant women, but also effectiveness indicators (e.g. receipt of antiretroviral drugs) and cost indicators (e.g. cost of drugs) (31).

Establishing the effectiveness of national AIDS control programmes

The importance of different levels of indicators, corresponding to programme input, output, outcome and impact, for the monitoring and evaluation of national HIV/AIDS programmes has recently been clarified (8, 48). This framework has been expanded to make clear the role of proximate determinants of HIV spread, which are the immediate biological and behavioural determinants of HIV spread, in other words the components of

the basic reproductive rate, R_0 ; the efficiency of transmission, the rate of exposure of a susceptible to an infectious person, and the duration of infectiousness (48–50). It is through these proximate determinants that the impact of the broader socio-economic context and the output of interventions on HIV incidence are seen.

Some of the indicators for these proximate determinants correspond to a subset of indicators for the epidemiological context for different interventions, as we have defined in this paper, while others correspond to those for the intervention outcome. For example, recommended indicators for monitoring the sexual behaviour of youth include sexual mixing by age, and the proportion of the population with multiple sex partners (8). The first of these can be compared with indicator 3 for the epidemiological context of interventions to promote sexual behaviour change and/or condom distribution (see Table 2). The second is a component of the variables recording the outcome of this intervention.

With the completion of recommendations for second-generation surveillance in 2000, some of these monitoring and evaluation indicators have been incorporated into the latest country-specific HIV fact sheets prepared by WHO/UNAIDS. They include indicators for proximate determinants, such as prevalence of curable STIs and self-reported sexual behaviour (including age at first sexual encounter and non-regular sexual partnerships), and context and outcome indicators, such as the

rate of STI treatment and counselling, general health service indicators for accessibility and blood safety, condom availability, and knowledge of methods of HIV protection.

At the national level, indicators recording proximate determinants are necessarily restricted, and therefore lack the detail that would permit the local relevance of interventions to be assessed. Indeed, this is not their role (8). Monitoring and evaluation of national HIV/AIDS programmes serve a different function to that of planning future interventions. However, the two processes are complementary. National monitoring and evaluation, together with appropriate costing studies, can guide the choice of interventions that should be assessed with respect to the epidemiological context at the local level. If the epidemiological context is favourable, consideration of the broader socioeconomic context and the use of pilot studies can lead to the appropriate choice of intervention. Once implemented, this intervention becomes part of the national monitoring and evaluation effort. ■

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Résumé

Effacité de la prévention du VIH et contexte épidémiologique

La planification d'une intervention destinée à la prévention des infections par le virus de l'immuno-déficience humaine (VIH) doit être guidée par les conditions épidémiologiques et socio-économiques locales. Le contexte socio-économique et la capacité des services publics existants détermineront si une intervention peut avoir un impact significatif en termes de réduction d'un risque déterminé. Le contexte épidémiologique déterminera si une telle réduction du risque est susceptible d'avoir un impact mesurable sur l'incidence du VIH. La mesure des paramètres décrivant le contexte épidémiologique peut être utilisée pour déterminer si une intervention peut convenir au niveau local, et guidera les planificateurs et les décideurs dans

leur choix. Ces mesures permettront également de procéder à l'analyse rétrospective de l'impact des interventions là où l'incidence du VIH n'a pas été enregistrée. Le contexte épidémiologique a été défini pour quatre catégories d'interventions dont l'efficacité dans les pays à faible revenu a été démontrée lors d'essais contrôlés randomisés. Des indicateurs appropriés pour le contexte épidémiologique sont proposés avec des directives méthodologiques pour leur mesure. Leur application au transfert d'une intervention réussie d'un contexte à un autre et au passage à une plus grande échelle de lutte contre l'infection à VIH est explorée. Ces indicateurs devraient constituer un outil précieux pour les responsables des choix politiques.

Resumen

Influencia del contexto epidemiológico en la eficacia de la prevención de la infección por el VIH

La planificación de una intervención de prevención de las infecciones por el virus de la inmunodeficiencia humana (VIH) debería hacerse en función de las condiciones epidemiológicas y socioeconómicas locales. La situación socioeconómica y la capacidad de la administración pública determinan si una intervención puede tener un

efecto importante de reducción de un riesgo definido, y el contexto epidemiológico determina si esa reducción del riesgo se traducirá en un impacto cuantificable en la incidencia de infección por el virus. Es posible medir las variables que caracterizan el contexto epidemiológico para establecer la idoneidad de las intervenciones a nivel

local y orientar la elección de las intervenciones por parte de los planificadores y los formuladores de políticas. Esas mediciones también permiten analizar retrospectivamente el impacto de las intervenciones en los casos en que no se registró la incidencia de infección por el VIH. Se define el contexto epidemiológico para cuatro categorías de intervención cuya eficacia en los países de bajos ingresos se ha demostrado mediante ensayos controla-

dos aleatorizados. Se proponen indicadores apropiados para el contexto epidemiológico, así como pautas metodológicas para su medición, y se analiza el empleo de esos instrumentos para transferir una intervención exitosa de un contexto a otro y ampliar las actividades de lucha contra la infección por el VIH. Estos indicadores deberían constituir un valioso recurso para los formuladores de políticas.

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Annex. Reasons for inclusion of the indicators of epidemiological context

Education to alter sexual behaviour/ condom distribution

1. Phase of the HIV/AIDS epidemic

The phase of the HIV/AIDS epidemic, as recorded by age- and sex-stratified HIV prevalence for different risk groups will determine the possible impact of a targeted intervention. Early on in a heterosexual HIV/AIDS epidemic, HIV infections tend to be concentrated in individuals with high rates of partner change, before spreading from such core groups to the general population. In other words, a generalized epidemic in which HIV prevalence exceeds 1% in the general population is usually preceded by a concentrated epidemic with >5% of core groups but <1% of the general population infected. An intervention targeting these core groups early in the epidemic can have a disproportionately greater effect than one implemented late on. A challenge in designing phase-specific interventions is in identifying core groups, since these will not always correspond with clearly defined social groups, such as commercial sex workers (1).

2. Cofactor STI prevalence

There is evidence that STIs such as syphilis, gonorrhoea, chlamydial infections, trichomoniasis, and genital herpes (HSV-2) act as cofactors, enhancing the probability of sexual transmission of HIV (2, 3). Likewise HIV-1 may act as a cofactor for the spread of HSV-2 by increasing viral shedding (4). In areas with high prevalence of untreated STIs, HIV prevalence is also often high. An education programme to alter sexual behaviour and promote condom use will result in a decline in both HIV and other STIs, each decline acting synergistically with the other. Thus in populations with high STI prevalence, the impact of such programmes on HIV incidence may be greater than in populations with low STI prevalence.

3. Mixing of target population with other at-risk populations or age-groups

If there is extensive mixing of the target population with other at-risk groups, the intervention can have a large impact on HIV incidence in the total population. This is the case if the target population corresponds to a spread network (a cause for a substantial number of new infections in other populations), with a large effective reproductive rate, R_e (2, 5). Conversely, if HIV incidence within the target population is mainly due to sexual contacts outside that risk group, and the intrinsic R_e is less than 1, an intervention targeting this group may have limited impact. Assessments of the mixing

patterns of the target population through social and geographical mapping, and sexual network questionnaires, and of baseline sexual behaviour (which determines R_e) allow the likely impact of an intervention on overall HIV incidence to be determined.

4. Sexual behaviour of populations not targeted by the intervention

The risk behaviour of untargeted populations determines the relative contribution of the targeted and untargeted populations to incident HIV infections. For example, if the target population is acting as a spread network, then assessment of sexual behaviour in untargeted populations can give an indication as to the likely impact on overall HIV incidence of a decline in this source of infection. If men who visit prostitutes are not using condoms with their regular sex partners (e.g. spouses), an intervention targeting prostitutes will have a bigger impact on overall HIV incidence than if these men use condoms all the time.

It may also be important to measure sexual behaviour in populations not targeted by the intervention if it is thought that the intervention may significantly affect the balance of supply and demand for sexual services. Thus an intervention that enables brothel-based female prostitutes to enforce condom use may reduce demand for brothel-based commercial sex and result in increased demand for commercial sex from non-brothel-based prostitutes — a group for which HIV prevention activities may not be in place.

Improved STI treatment

1. Phase of particular STI epidemic

As with HIV infection, interventions aimed at other STIs will be more or less appropriate at different phases of the STI epidemic (1).

2. Phase of HIV/AIDS epidemic

As for behavioural interventions described above.

3. Prevalence of other cofactor STIs including genital herpes (HSV-2)

Interventions to reduce HIV incidence by treating bacterial STIs, such as gonorrhoea, may be less effective if the prevalence of other untreated STIs is high. For instance, a high prevalence of viral STIs, such as HSV-2, may mean that the probability of HIV transmission remains high despite treatment of bacterial STIs (6). The prevalence of other STIs should therefore be measured and, if appropriate,

interventions to prevent and treat them should be implemented. The epidemiological context for one intervention may be the target of another. In this way interventions can act in synergy.

4. Mixing of target population with other at-risk populations and age-groups

As for behavioural interventions described above.

5. Prevalence of STIs in neighbouring populations and importance of reintroduction following treatment

If there is extensive mixing with other risk groups or sexual networks, as determined by indicator 4, then a high prevalence of STIs in these risk groups may result in rapid re-introduction of the STIs to the targeted population following treatment. This may make periodic mass treatment less effective than continuous symptomatic treatment in reducing STI prevalence and therefore HIV incidence.

Antiretroviral drugs to prevent mother-to-child transmission

1. Levels of breastfeeding compared to artificial feeding

The impact of antiretroviral (ARV) therapy on mother-to-child transmission (MTCT) will depend on levels of breastfeeding in the population. It is estimated that breastfeeding contributes between one-third and half of all cases of MTCT in breastfeeding populations (7, 8). In a breastfeeding population, therefore, ARV therapy that is only provided perinatally may be less effective in preventing MTCT than in a non-breastfeeding population, owing to this additional risk of vertical transmission. In recording modes of feeding it is important to distinguish mixed feeding from exclusive breastfeeding, since there is some evidence that the former may entail a higher risk of transmission than exclusive breastfeeding (9).

2. Prevalence of HIV infection in treated women

In countries with a very high prevalence of HIV infection, strategies to provide cheap one- or two-dose regimens of ARV drugs to pregnant women may be cost-effective. In these cases the prevalence of HIV infection in the women to be treated will be of key importance in determining the impact of the intervention on the incidence of perinatal cases of HIV infection.

3. Viral load of mothers

Viral load is a direct determinant of the probability of MTCT in the perinatal period and during breastfeeding (10, 11). If the average viral load of pregnant women varies between populations owing to the stage of the HIV/AIDS epidemic, or if genital

shedding of the virus varies because of differences in nutritional status (12), ARV therapy may be more effective in those populations with a higher mean maternal viral load. Measurement of the viral load or, as a proxy, CD4 levels in a sample of mothers may therefore give an indication of programme effectiveness. However, it is unclear whether there is likely to be significant variation between populations in terms of maternal viral load, in particular as prolonged HIV infection results in infertility (13).

4. Mode of delivery and rates of premature delivery

Perinatal transmission of HIV is on average more probable during vaginal delivery than Caesarean section, and is enhanced in pre-term delivery (14). ARV therapy to prevent MTCT may therefore be more effective in populations with low rates of Caesarean section and high rates of premature delivery — features of lower-income countries.

5. STI prevalence

The presence of certain STIs during labour may promote MTCT through increased genital shedding of HIV (12, 15). ARV therapy in populations with a high STI prevalence may therefore be more effective. Currently it is likely that STI treatment facilities will be in place prior to the existence of health services capable of supplying ARV drugs. However, this may change with the advent of cheap, one- or two-dose drug regimens, e.g. with nevirapine, to prevent MTCT (16).

Alternatives to breastfeeding

1. Viral load of mothers; availability of ARV drugs

The mother's viral load, determined by the natural history of the disease and the availability of ARV therapy, is a determinant of postnatal transmission (11). Thus interventions promoting alternatives to breastfeeding may be more effective in populations with high viral loads. As noted previously, the relevance of this indicator for the epidemiological context is not clear, since viral load may not vary at the population level for pregnant women.

2. Levels of mastitis and severe vitamin A deficiency

Mastitis and severe vitamin A deficiency may increase the probability of HIV transmission during breastfeeding (17, 18). If these factors vary significantly between populations, they will be important indicators for the epidemiological context of artificial feeding interventions.

3. Mode of delivery and rates of premature delivery; and STI prevalence

Mode of delivery, rates of premature delivery and prevalence of STIs have an impact on HIV

transmission during labour. They therefore determine rates of intrapartum compared to postpartum HIV transmission, and hence efficacy of measures

aimed at reducing postpartum transmission (the mother's viral load may also affect this balance). ■

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