

## Public health

## Can we reverse the HIV/AIDS pandemic with an expanded response?

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**HIV/AIDS has reached pandemic proportions, and is one of the leading causes of death worldwide. In 2001, the Declaration of Commitment on HIV/AIDS set out several aims with respect to reducing the effect and spread of HIV/AIDS, and an expanded response in low-income and middle-income countries was initiated. Here we examine the potential effect of the expanded global response based on analyses of epidemiological data, of mathematical models of HIV-1 transmission, and a review of the impact of prevention interventions on risk behaviours. Analyses suggest that if the successes achieved in some countries in prevention of transmission can be expanded to a global scale by 2005, about 29 million new infections could be prevented by 2010.**

Since the beginning of the epidemic, estimates suggest that more than 60 million people have become infected and more than 20 million people have died of HIV/AIDS, including 3 million deaths in 2001 alone. There are 14 million orphans because of AIDS and 40 million people with HIV/AIDS. AIDS is the leading cause of death in sub-Saharan Africa and the fourth leading cause of death worldwide.<sup>1</sup> The scale of this devastating epidemic is unprecedented in modern history and, in June, 2001, at the United Nations General Assembly Special Session on HIV/AIDS (UNGASS), the international community set global targets for reducing the spread of HIV/AIDS and alleviating its effect on the world. The Declaration of Commitment on HIV/AIDS<sup>2</sup> sets several aims, including a reduction in HIV-1 prevalence of 25% among young people, by 2005 in the most affected countries, and by 2010 globally. We previously estimated<sup>3</sup> that, by the year 2005, US\$9.2 billion would be needed annually to provide an expanded response to HIV/AIDS in low-income and middle-income countries. This response includes a package of 12 essential prevention interventions (table 1) and nine different care and support activities. Of this total, an estimated US\$4.8 billion is required for prevention. Our aim was to examine the potential effect of this programme by asking two key questions—namely, how many new infections can be averted by timely and effective implementation of this comprehensive prevention package, and will it be enough to reverse the epidemic and achieve the aims of the expanded response?

### Projections of spread of HIV-1

To answer these questions we projected the number of new adult HIV-1 infections that would arise through 2010 with and without the expanded prevention response for 126 low-income and middle-income countries, which we

characterised as having either concentrated or generalised epidemics (see webappendix 1 at <http://image.thelancet.com/extras/02art6114webappendix1.pdf> for list of countries). We made baseline projections, assuming no expanded response, using two approaches dependent on type of epidemic. (This method produced plausible projections for each country that are useful for this analysis. Obviously, all such projections are uncertain. Although further work with national experts is needed to refine the country projections, the regional and global totals are more robust. UNAIDS and WHO continue to work with national and international partners to increase the quality of data that can be used for assessments of the epidemic, and the methods used for modelling and projections.)

### Prevention interventions and care and support activities of the expanded response programme

#### Prevention interventions

- School-based AIDS education
- Peer education for out-of-school youth
- Outreach programmes for commercial sex workers and their clients
- Public sector condom promotion and distribution
- Condom social marketing
- Treatment for sexually transmitted infections
- Voluntary counselling and testing
- Workplace prevention programmes
- Prevention of mother-to-child transmission
- Mass media campaigns
- Harm reduction programmes
- Outreach programmes for homosexual men

#### Care and support activities

- Palliative care
- Treatment of opportunistic infections
- Diagnostic HIV-1 testing
- Prophylaxis for opportunistic infections
- Highly active antiretroviral treatment, treatment with three antiretroviral drugs
- Laboratory testing to monitor effect of highly active antiretroviral treatment monitoring
- Orphanage care
- Community support for orphans
- School fee support for orphans

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We simulated generalised epidemics, in which spread of HIV-1 is primarily through heterosexual contacts, using an epidemic projection package—a simple epidemiological model that was used to produce the UNAIDS/WHO estimates on the global epidemic.<sup>4</sup> In this model, the initial rate of spread of HIV-1 is ascertained by the reproductive potential  $r$  (the per capita rate of infection of susceptibles); the peak prevalence is identified primarily by the size of the population at risk of infection; and the final endemic prevalence is worked out with a variable that specifies the behavioural response of the population to the epidemic.<sup>4</sup> The model variables are estimated from sentinel site prevalence data (<http://www.census.gov>).<sup>5</sup> For each of the 41 countries with generalised epidemics, we used the model to produce an epidemic curve of adult prevalence (age 15–49 years), running from the start of the epidemic until 2010; we used all available surveillance data for each country.

For countries with epidemics concentrated in groups with higher risk behaviour—eg, homosexual men, intravenous drug users, sex workers and their clients—a three-step process was used to produce the current estimates (end 2001) of HIV/AIDS. First, for each country, we identified and estimated the size of groups at highest risk of acquiring HIV/AIDS. Second, estimates of point prevalence were made for these groups by application of the most up-to-date prevalence rates for these groups to the populations. Finally, we estimated prevalence in low-risk populations by allowing for transmission from high-risk to low-risk groups via sexual mixing.

Projections of these epidemics to 2010 were based on assumptions about degree of saturation for each of the high-risk groups, time to saturation, and spread from high-risk to low-risk populations over time. For each of the 85 countries, we compiled and combined trends in prevalence in high-risk groups.<sup>5</sup> We identified saturation levels for each risk group, and time to reach saturation, by review of available data country by country. The particular degree of, and time to, saturation were applied to the risk groups in each country based on current prevalence in the groups, rate of growth in the groups, and by comparisons to saturation levels and rates in neighbouring countries. This approach enabled us to project low growth for countries with long-running and

fairly stable epidemics—eg, Brazil, Myanmar. For countries with recent epidemics, but rapid rates of growth, the projections show much higher rates of increase—eg, China, Estonia. For all of these countries we have assumed limited spread from high-risk to low-risk populations, and no low-risk to low-risk transmission.

With these methods, we estimated adult prevalence over time for each country, assuming no behaviour change and no increase in intervention effort. We then used the epidemic projection package to estimate the variables of the baseline epidemic curves.

### Interventions to limit spread

The panel shows the interventions initiated to limit spread. Care and support programmes should also be introduced and scaled up, and provision of care can increase effectiveness of prevention programmes.<sup>6</sup> However, the effect of care programmes—eg, drug treatment—on new infections was not included in this exercise, because there is little empirical data available on the magnitude of the preventive effect of treatment (reduced viral load and hence infectiousness) and care. However, although our analyses do not address the possible effect of care and treatment on the spread of HIV-1 as such, we do believe that the substantial effects of prevention activities presented here will only be achievable in the presence of strong care and support programmes.

We assumed that coverage of the prevention package—ie, the proportion of the population in need of a service that has access to and uses that service—will increase linearly from 2001 to target values in 2005, based on need and feasibility, and then will remain constant through 2010. Target coverage values in 2005 are 100% for mass media, voluntary counselling and testing for HIV/AIDS, and safe blood; 60% for outreach programmes for commercial sex workers and homosexual men; and 75% for harm reduction and treatment of sexually transmitted diseases. Coverage targets vary in accord with prevalence from 16% to 100% for school-based education, 10% to 50% for out-of-school youths, 3% to 50% for workplace programmes, 20% to 60% for condom promotion and distribution, and 10% to 50% for prevention of mother-to-child transmission of HIV-1 (full details available from authors on request).

Intervention	Condom use (reduction in non-use)			Treatment for sexually transmitted disease (reduction in non-treatment)			Number of sexual partners (reduction in numbers of partners)			Age at first sexual intercourse (increase in age at first sexual intercourse)	Unsafe drug injections (increase in safe use of clean needles)
	High risk	Medium risk	Low risk	High risk	Medium risk	Low risk	High risk	Medium risk	Low risk	High risk	Low risk
Mass media campaigns	..	17%	17%	..	..	..	..	..	..	..	..
Voluntary counselling and testing programmes for HIV/AIDS	50%	34%	16%	..	..	..	..	..	..	..	..
Peer counseling—CSW	39%	42%	..	..	..	..	3%	..	..	..	..
School-based programmes	..	34%	..	..	..	..	..	33%	..	0-30	..
Programmes for out-of-school youths	..	..	..	..	..	..	..	..	..	..	..
Workplace programmes	39%	34%	1%	..	..	..	..	23%	..	..	..
Condom social marketing	21%	11%	5%	..	..	..	..	..	..	0-12	..
Public sector condom distribution	57%	10%	5%	11%	..	..	35%	..	..	..	..
Harm reduction programmes	..	..	..	..	..	..	33%	..	..	..	60%*
Peer outreach to homosexual men	33%	..	..	..	..	..	-17%	..	..	..	..
Treatment for sexually transmitted disease	54%	14%	..	47%	..	22%	50%	..	..	..	..
PMTCT	50%	34%	16%	..	..	..	..	..	..	..	..

CSW=commercial sex worker. PMTCT=prevention of mother-to-child transmission of HIV-1. \*We assumed a 60% decrease in the average number of partners with whom needles are shared and a 60% increase in the fraction of shared needles that are cleaned.

Table 1: Prevention interventions and their effect on behaviour

We define intervention effectiveness as the effect of prevention activities on five behaviours—namely, condom use, treatment seeking behaviour for sexually transmitted diseases, number of sexual partners, age at first sexual intercourse, and sharing of potentially infected needles. Intervention effectiveness was allowed to vary by degree of risk of the population (high risk, medium risk, or low risk). We did a systematic review of published work on the prevention of HIV/AIDS and sexually transmitted diseases in the developing world, and used 86 studies to ascertain the effectiveness of all interventions aimed at reducing sexual transmission (<http://www.tfgi.com>),<sup>7</sup> and several types of interventions for harm reduction in intravenous drug users, including needle exchange programmes and drug treatment programmes.<sup>8–12</sup> The effect for each activity was generated as a pooled estimate of study results (table 1).

We recognise that these estimates of effect could be overly optimistic, since only the best studies, showing significant results, are generally published. It may be difficult to achieve this level of impact as programmes are scaled-up to national level. The sensitivity of the results to these estimates is described below.

### Simulation of effects of interventions

We used three simulation models to estimate the effects of the comprehensive intervention package. The full details of the models are given elsewhere.<sup>13,14</sup> The models were used to estimate the change in the rate of infection ( $r$ ) over time as the interventions are implemented. The simulation models were used to ascertain the effects of changes in behaviour (due to the interventions) on the incidence of HIV-1 over time. The revised values of incidence were used to calculate the change in the rate of infection ( $r$ ). The new values of  $r$  were used in the epidemic projection package to project the number of infections averted for each country.

The Goals model ([www.tfgi.com](http://www.tfgi.com))<sup>13</sup> has been developed as a method for costing and resource allocation in the development of national HIV/AIDS strategic plans. This model uses the effect matrix in table 1 to estimate the effects of prevention interventions on behaviours for four risk groups: homosexual men, and high, medium, and low risk for heterosexual transmission. The amount of coverage of each intervention determines the proportion of the population that has the behaviour change shown in the effect matrix. These effects are aggregated across all interventions to ascertain the average change in each behaviour for each risk group (see webappendix 2 at <http://image.thelancet.com/extras/02art6114webappendix2.pdf> for full details). The probability of HIV-1 transmission is estimated for each risk group on the basis of these behaviours and current degrees of HIV-1 prevalence with an equation developed by Weinstein and colleagues<sup>15</sup> and validated against clinical trial data in a heterosexual population by Rehle and colleagues<sup>16</sup> (see webappendix 3 at <http://image.thelancet.com/extras/02art6114webappendix3.pdf> for details of calculation). From this information, the model calculates the number of new infections and the average rate of infection ( $r$ ) per year.

The effect of the interventions on new infections will depend on the stage of the epidemic (slow growth or rapid growth in prevalence); the four prevalence levels (very low, <0.5%; low, 0.5–1.0%; medium, 1–5%; and high, >5%), which determine the coverage of the interventions; and the type of epidemic (predominantly heterosexual, or predominantly homosexual or intravenous drug use). The two growth categories, four prevalence levels, and two transmission patterns yield 24 possible categories. Only 12

of these categories are required, since medium and high prevalence levels are only reached in countries where heterosexual spread is great. We applied the Goals model to a typical country in each of these categories to project the epidemic with, and without, the comprehensive interventions. These projections are used to calculate the reduction in per capita rate of infection over time as a result of the prevention interventions. The patterns of reduction were applied, for each country in the category, to the epidemic projection package projections, to estimate infections averted by country and by year. We separately modelled 51 countries, comprising 92% of all new infections, and combined the remaining countries into two groups (those with and without significant transmission via intravenous drug use).

We compared the effect of the expanded prevention interventions on the rate of HIV-1 infection ( $r$ ) estimated by the Goals model with the effect predicted by ASIST; a different model of HIV-1 spread.<sup>14</sup> These comparisons were used to validate the approach, and gave similar estimates for the effect of interventions on  $r$  when similar patterns of risk behaviour, intervention effectiveness, and coverage were specified.

Finally, we developed a simple model, describing transmission of HIV-1 in a population of intravenous drug users and an interconnected heterosexual population, to explore the effect of the package of interventions, which includes those targeted at a population of intravenous drug users, in a population in which a large fraction of infections are among users. In this ordinary differential equation model the risk of an intravenous drug user acquiring infection depends on the number of unclean needles shared and the number of people with whom they are shared. There is an additional hazard of sexual transmission within populations of intravenous drug users and their non-injecting sexual partners. A group with high-risk sexual behaviours was included in this model to allow for an independent sexually transmitted HIV-1 epidemic.

### Projections of effects of interventions

In the baseline projection of the global epidemic, the number of new infections among adults is expected to rise from 4 million in 2002 to more than 5 million in 2005, with a cumulative total of 45 million new infections between 2002 and 2010.

Implementation of the comprehensive prevention package by 2005 would reduce the total number of infections by 29 million (63%) between 2002 and 2010 (figure 1), lowering the annual incidence of new infections

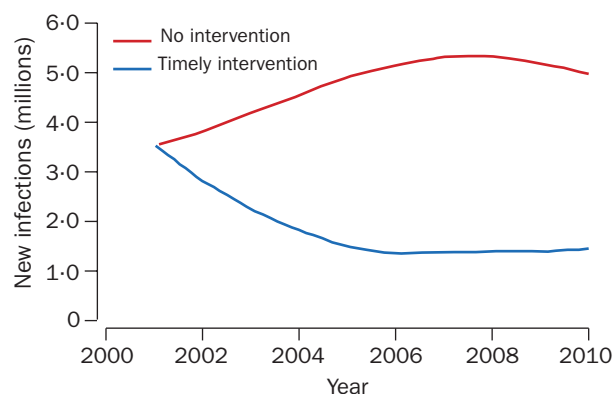


Figure 1: Projected new adult infections given current degree of intervention and a timely scale up of the comprehensive interventions package

	New infections, 2002–2010			
	Number of countries	Baseline (millions)	Expanded response (millions)	Proportion averted by expanded response
<b>All low-income and middle-income countries</b>	126	45.4	16.9	63%
<b>By region</b>				
Sub-Saharan Africa	38	21.0	8.8	58%
Eastern Europe and central Asia	24	2.8	1.3	54%
North Africa and Middle East	15	0.9	0.3	62%
South and southeast Asia	21	18.5	5.7	69%
Latin America and the Caribbean	28	2.3	0.7	67%
<b>By type of epidemic</b>				
Generalised	41	22.5	9.5	58%
Concentrated	85	22.9	7.4	68%
<b>By 2001 prevalence level</b>				
High (>5%)	24	16.6	6.2	63%
Medium (1–5%)	25	5.0	2.8	43%
Low (0.5–1%)	13	9.7	3.4	64%
Very low (<0.5%)	64	14.2	4.4	69%
<b>By projected incidence trend, 2001–2005</b>				
High ( $\geq$ 50% increases)	80	14.8	4.6	69%
Low (<50% increase)	46	30.6	12.3	60%

Table 2: Infections averted between 2002 and 2010

in adults to about 1.5 million per year once the package has been implemented fully.

The proportion of infections averted in different countries will vary in accord with the nature of the epidemic (generalised *vs* concentrated), the current level of prevalence, and the anticipated growth rate in incidence (table 2). The proportion of expected infections averted ranges from a low of 40% in countries with stable or declining prevalence, such as Senegal and Thailand, to a high of 70% in countries with rapidly growing epidemics, such as Cameroon and China. As noted in many analyses of intervention effect, efforts made early in the growth of an epidemic have a much greater effect in reducing the total size of the epidemic than similar efforts made late during the time course of its development.<sup>17,18</sup>

Overall, nearly one-third of all global benefits from the intervention package will accrue to two countries, India and China, and the countries of sub-Saharan Africa will contribute another 40% to the global total.

Delayed implementation of the prevention package would lead to a large reduction in total benefits in terms of instances of infection prevented (figure 2). For example, our analyses suggest that a 3-year delay in achieving full implementation would reduce the total number of new infections averted by 2010 by 50%. Any delay in the

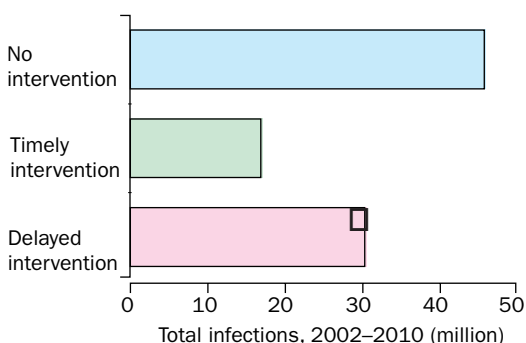


Figure 2: Number of adult infections prevented dependent on time of initiation of interventions

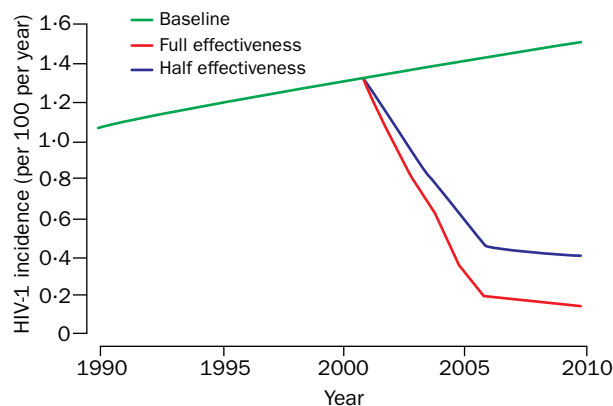


Figure 3: The simulated effect of interventions on the incidence of HIV-1 for scenarios in which prevalence exceeds 10% and is still rising

The effect of the proposed coverage and observed effectiveness from table 1 is compared with the same coverage but a halved efficacy.

implementation of the package shifts the benefit gained to a later time point, and concomitantly results in a much smaller benefit for each year of implementation.

The estimated number of averted infections is sensitive to varying assumptions about the effectiveness of the prevention interventions. Figure 3 shows the results of varying the effectiveness assumptions in a typical country. Different definitions of coverage can also affect the projected effect of interventions. If 50% coverage is interpreted to mean that 50% of people change their behaviour and the other 50% do not, then dependent on the precise pattern of the epidemic, the effect might be different than if it is interpreted to mean that all people change their behaviour by half as much (the assumption made in the simulations described by us).

## Discussion

Immediate implementation of a comprehensive set of interventions could avert a large number of future infections, and reverse the course of the AIDS epidemic. Without this response, we project 45 million new infections by 2010. Our analyses suggest that if the successes that have been achieved in some countries and communities can be expanded worldwide, then the course of the epidemic could be greatly altered in the coming decade.

The projections of any mathematical model of complex epidemiological and intervention processes must be interpreted with caution. Nevertheless, estimates have to be made, however imperfect, to assess global needs to combat this devastating epidemic. With this caveat in mind, we predicted that the implementation of the full package of interventions could prevent 29 million new infections by 2010. Furthermore, this package of prevention interventions is predicted to have the potential to reverse the growth of epidemics of all types, from the generalised to the newly emerging. These analyses, therefore, suggest that the aims of the UN Declaration of Commitment of reducing prevalence levels by 25% by 2010 can be met. In addition to averting new HIV-1 infections, this effort would also result in a better-educated youth, a reduction in the incidences of other sexually transmitted diseases, and fewer children infected through mother-to-child transmission.

We realise that the full implementation of this expanded response presents many challenges. However, we believe that the ambitious coverage levels of the interventions package used in our analysis are achievable given the effective mobilisation of the resources required. Human

capacity to deliver the required interventions needs to be scaled up greatly, and an improved infrastructure will need to be developed to meet the demand of expanded services. To meet these challenges, financial and political commitment will be needed.

The cost of the expanded prevention programme has been estimated to reach US\$4.8 billion annually by 2005.<sup>3</sup> Between 2001 and 2005, the scale-up costs are US\$8.4 billion and the full costs of scaling-up and sustaining the effort to 2010 are about US\$27 billion. This total implies a cost of about US\$1000 per infection averted. The true costs could be higher than this figure, since our estimates of the funding required are conservative and there is no guarantee that all of these funds would be used effectively in all countries. However, the net costs would be less if the savings from averted costs for care were included in the calculations.

Political commitment at all levels is essential if funds are to be effectively mobilised and used efficiently, and programmes implemented. Political commitment is also necessary to reduce other barriers to effective implementation. Governments and societies must acknowledge the scale of the HIV/AIDS problem and the need for a greatly increased response to this global disaster. Stigma associated with those living with HIV/AIDS must be reduced to remove barriers to accessing services. The provision of care and support to those who live with and are affected by HIV/AIDS provides hope and support and fosters prevention efforts by encouraging people to seek voluntary counselling and testing. The wide scale implementation of effective interventions can only take place when this commitment exists. The costs of scaling up prevention programmes are large, but any delay will be even more costly.

#### Contributors

All authors participated in study design and in writing of the report. G P Garnett, P D Ghys, N C Grassly, J A Salomon, K A Stanecki, J Stover, and N Walker were primarily responsible for work on national level projections and for production of models.

#### Conflict of interest statement

R M Anderson has been a paid consultant for Abbott pharmaceuticals and has shares in GlaxoSmithKline. G Garnett has been a paid consultant for Abbott Pharmaceuticals for work on the effect of antiretroviral drugs, and for GlaxoSmithKline for work on herpes simplex virus-2 vaccine impact.

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