

HIV Prevention 6



Coming to terms with complexity: a call to action for HIV prevention

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A quarter of a century of AIDS responses has created a huge body of knowledge about HIV transmission and how to prevent it, yet every day, around the world, nearly 7000 people become infected with the virus. Although HIV prevention is complex, it ought not to be mystifying. Local and national achievements in curbing the epidemic have been myriad, and have created a body of evidence about what works, but these successful approaches have not yet been fully applied. Essential programmes and services have not had sufficient coverage; they have often lacked the funding to be applied with sufficient quality and intensity. Action and funding have not necessarily been directed to where the epidemic is or to what drives it. Few programmes address vulnerability to HIV and structural determinants of the epidemic. A prevention constituency has not been adequately mobilised to stimulate the demand for HIV prevention. Confident and unified leadership has not emerged to assert what is needed in HIV prevention and how to overcome the political, sociocultural, and logistic barriers in getting there. We discuss the combination of solutions which are needed to intensify HIV prevention, using the existing body of evidence and the lessons from our successes and failures in HIV prevention.

Momentum for HIV prevention

Although the gap between what is needed in HIV prevention worldwide and what has so far been achieved is huge, we should not neglect the momentum which has been generated, especially over the past decade. HIV prevalence has declined substantially in a growing number of countries and regions: Zimbabwe, Côte d'Ivoire, Burkina Faso, Thailand, Cambodia, southern India, and urban Haiti and Kenya.¹ These reductions represent the payoff from investments made throughout the 1990s and into this century. Commitment of political capital and other resources has been translated into major increases in programmatic effort that are now bearing fruit in improved outcomes—infections averted and lives saved. But worldwide the current degree of effort is not yet sufficient: the epidemic continues to extend its reach, and new infections continue at a rate which puts unsustainable burdens on countries for decades to come.

To intensify HIV prevention, programme implementers need to know their epidemic, and to respond in at least three dimensions. The first—HIV rates and behaviours at a local level—is commonly used. The second—the state of HIV/AIDS spending and programming in relation to the levels of need, including in relation to each key subpopulation—is sometimes used. Bertozzi and colleagues in this Series² detail the mix of spending and programming required for an optimum response. The third—an appreciation of macro-level political, demographic, and economic changes—is rarely used, but unless responses take these changing social and cultural contexts into account, they will miss their mark. This combination of knowledge and context is what makes information strategic and the basis for action (panel 1). Only when it

is applied in a comprehensive AIDS programming cycle can it create an effective feedback loop between information, programming, assessment of programme effectiveness, and back to improved information and programming (panel 2).⁷

As Rao Gupta and colleagues note in this Series⁸ other public-health efforts have shown the consequences of not conducting adequate analysis of the social and political environment. One of the more extreme examples has been in the global polio-eradication initiative, in which an overly top-down effort neither adequately assessed local cultural and political contexts nor adequately engaged local communities early in the effort, leading to a state-wide boycott of polio vaccination in Northern Nigeria,⁹ community-level refusals in northern India, and pockets of refusals in other settings. To take another example, reproductive-health programmes have also recognised the need to understand social and cultural systems in planning any intervention—in-depth analysis from nine countries showed that “development entry points and constraints that derive from social and cultural systems and structures cannot be overlooked or underestimated”.¹⁰

The epidemic could continue to surprise us

As Bertozzi and colleagues argue in this Series,¹ HIV prevention responses must be informed by an analysis of where the next 1000 HIV infections are likely to come from in any given context. HIV/AIDS is highly dynamic. Initial HIV outbreaks in highly vulnerable populations might be followed by a slower spread which could nevertheless affect large numbers of people:¹¹ in Thailand or Uganda, for example, a large proportion of transmission is among serodiscordant long-term couples. Epidemics could resurge—as among gay men in western

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Panel 1: Strategic reorientation of responses in Lesotho

An in-depth analysis of data from the 2004 Demographic Health Survey in Lesotho showed prevalence of HIV was 6.1% among young women aged 15–17 years, and 10.7% in 18–19 year-old women.³ HIV prevalence was higher in young women with a regular partner than in those without, higher in urban than in rural areas, and around the same for girls with and without secondary education. On this basis, a 2007 joint UN system mission was able to argue that current efforts by both the UN system and Lesotho's government that were directed towards out-of-school youth in rural areas might be better reoriented to national efforts towards girls in schools, and to making the link with adult sexual behaviour.

Panel 2: Using strategic information to reorient responses in Bangkok

In Bangkok, Thailand, rates of HIV infection in men who have sex with men rose from about 10% at the beginning of the decade to 28% in 2005.⁴ This upsurge was associated with public-order campaigns that closed bars and sex venues, and forced men into street-based or illegal settings for sex; weak community organisation; and policy attention centred on access to treatment.⁵ Creditably, the resurgence led to a direct response in both policy and action: a national target to reduce new infections by half, extension of focused activities and services for gay men, and launch of a massive safe-sex campaign.⁶ Equally, acting on new or persistent epidemics among injecting drug users or other groups at most risk needs to be grounded in an analysis of their socioeconomic and political contexts: what effect, for example, do “wars on drugs” have on HIV rates?

Europe and Australia, or the higher than expected incidence in the USA—or move into new areas, such as the apparently unchecked growth in many of the cities of Asia of HIV in men who have sex with men and injecting drug users, where synthetic-drug use is further catalysing wider sexual spread (figure 1).

Past history shows we have failed to heed early warning signs of these changing dynamics. In the early 1990s, eastern Africa was regarded as the epicentre of the pandemic. The explosive growth of HIV/AIDS in southern Africa did not come until the second decade of the pandemic. Southern and eastern Africa are now the regions with the world's second highest growth in opiate use, since use follows the evolution of heroin trafficking routes. Responses are as yet ill-prepared for this new twist on the HIV threat.^{12,13} West Africa has emerged as a major cocaine trafficking route, and now opiates are starting to be trafficked through the same networks.¹⁴ Russia's 1 million HIV infections have occurred since 1990—largely as a result of explosive growth of HIV transmission among injecting drug users. More recently the epidemic has emerged in that

region much more strongly in women, both as injecting drug users and partners of injecting drug users: women account for 42% of newly reported HIV cases in Moldova, 46% in Belarus, and 44% in Ukraine and Russia.¹⁵

Demographic, technological, sociopolitical, and economic change will fundamentally shape the future epidemic, but the Asian Development Bank's systematic incorporation of HIV/AIDS-related considerations into large-scale infrastructure projects in the region and the AIDS in Africa *Three Scenarios to 2025* project are among the few attempts to incorporate such analysis into planning.¹⁶ Both the internet and mobile telephony have reshaped sexual conduct at its roots: for example, mobile connections overtook the number of fixed lines in Africa at the end of the 1990s, but few national-scale campaigns have played on this change (Swaziland's bold if controversial “secret lover” campaign in 2006–07 was a notable exception). Economic development also changes the nature of transactional sex: Cambodia has been actively realigning its HIV/AIDS response in the light of evidence that economic growth has changed the traditional pattern of sex work into a much more fluid mode of sexual exchanges around new entertainment venues.

Meeting the challenges of an expanded prevention response

Expanded HIV prevention grounded in a strategic analysis of the epidemic's dynamics in local contexts is the *sine qua non* of getting ahead of the epidemic. Shortcuts are tempting, but illusory. Every time a magic-bullet solution has been proposed for HIV/AIDS it has been found wanting, as Padian and colleagues argue in this Series⁷ in relation to biomedical interventions. The latest candidates for the single intervention which could stop the spread of HIV have been circumcision for adult men and, more recently, stopping concurrent partnerships. However, from the point of view of those who implement programmes and make policy, no one-dimensional HIV/AIDS solution has ever become available. “Combination prevention” is as necessary as “combination treatment” when it comes to stopping the pandemic.

An impressive range of both individuals¹⁸ and states¹⁹ subscribe to the global consensus that effective HIV prevention requires locally contextualised approaches that address both individuals and social norms and structures, and are grounded in human rights. Furthermore, HIV prevention must be one of the most studied fields of health promotion: nearly 35 000 citations on HIV prevention have been published internationally in scientific research alone (compared with 27 000 about prevention of smoking or tobacco use). But despite both the broad consensus on what needs to be done and the evidence base, we have only partial understanding of what facilitates systematic implementation of prevention

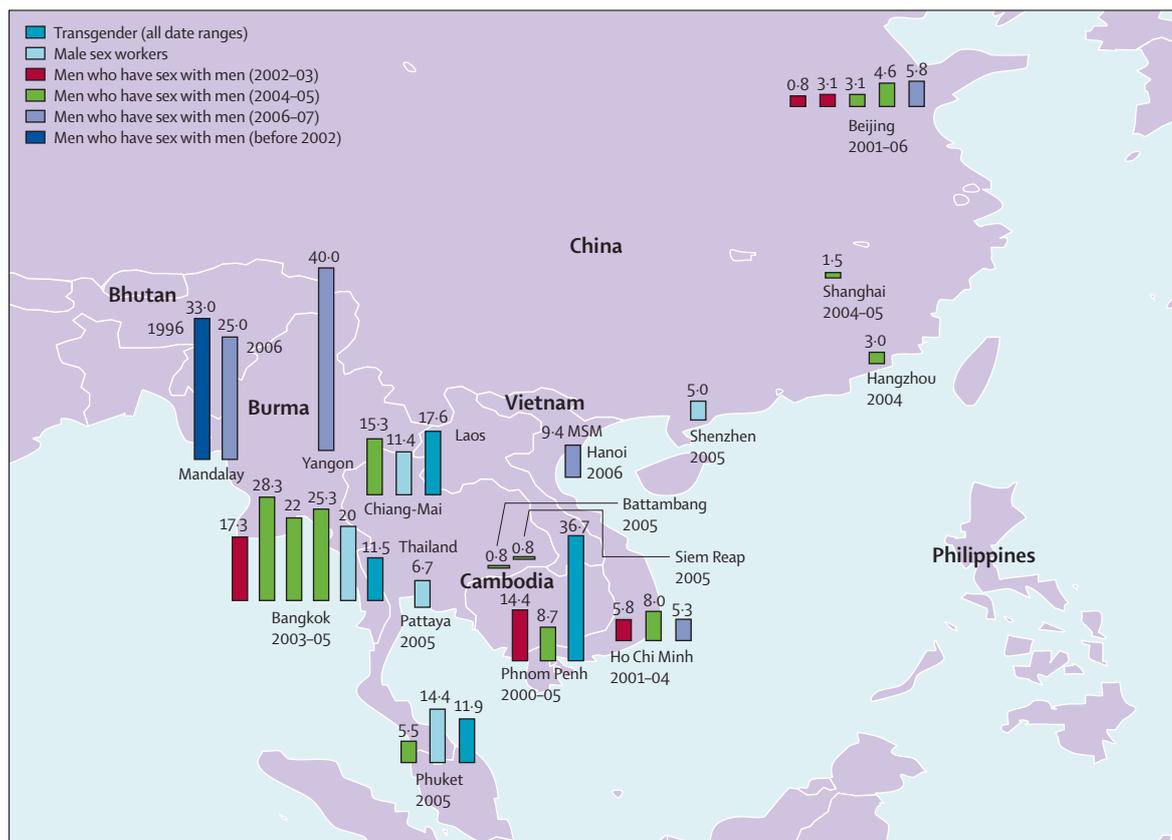


Figure 1: HIV prevalence in men who have sex with men in 17 cities of east and southeast Asia. Data are HIV-positive people per hundred. Adapted from data in reference 4.

programmes, what bottlenecks hold up progress, and what strength of effort will be necessary.

Here, we discuss four of the core challenges which stand in the way of fully effective combination prevention: inadequacy of attempts to tackle sexual transmission, unwillingness to be frank with young people, difficulties of dealing rationally with drug use, and the failure to yet eliminate mother-to-child transmission.

Tackling sex in the right way

About 85% of HIV transmission is sexual. If the pandemic has proved nothing else, it is that a diverse sexual life is part of being human. But despite the vast increase in the awareness of sexual diversity which has come in the wake of HIV/AIDS-driven research and community action, programming responses still find it hard to tackle sexual transmission in the right way or in the right populations.

Programming efforts that focus on sexual transmission have been plagued by insufficient confidence in their efficacy and hence inconsistency in their targets. As Coates and colleagues point out in their contribution to this Series,²⁰ behavioural research on HIV prevention has been too focused on single interventions and individual behaviours. In the USA, for example, the only best-evidence

interventions for HIV prevention that are recommended by the Centers for Disease Control and Prevention to guide prevention programming domestically are a series of variants on intensive one-to-one counselling or

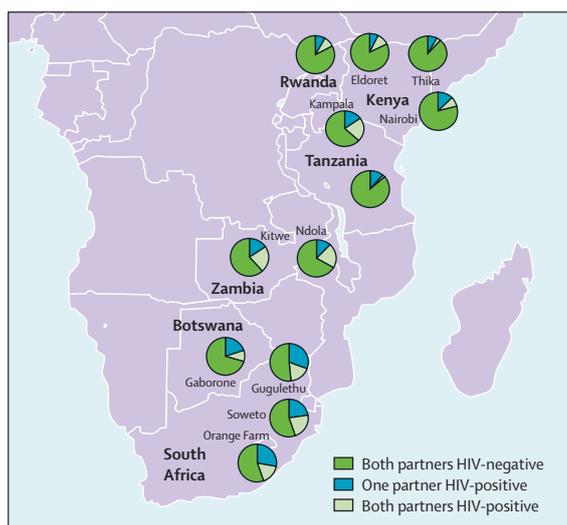


Figure 2: Couples with and without HIV in selected African countries. Adapted from data in reference 25.

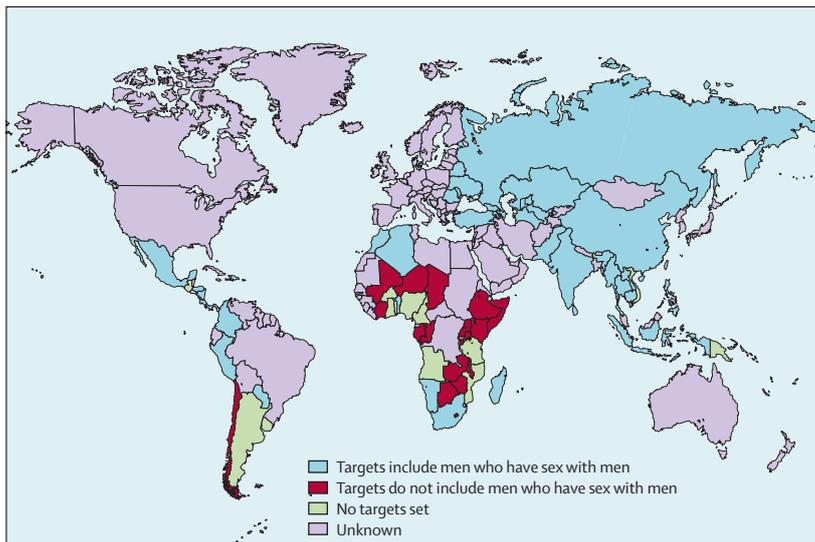


Figure 3: Global map showing low-income and middle-income countries with targets for universal access to HIV prevention, care, and treatment include men who have sex with men
Adapted from data in reference 37.

small-group discussion interventions.²¹ The synergies between interventions and action at the community level have been neglected and are not amenable to proof via randomised controlled trials, since this method is designed precisely to eliminate synergies as confounders. As a result, although data on behaviours and HIV transmission show sustained positive change in dozens of settings on all continents, precise assessment of what has brought about the change has proved difficult, given that it has almost certainly come from interactions between the individual, community (or environmental), and structural (population or national) levels, as described by Rao Gupta and colleagues in this Series.⁸

Much of the history of preventing sexual transmission of HIV has concentrated on reducing multiple partnerships or adopting condom use in casual sex. However, especially as epidemics mature, a higher proportion of HIV infections take place within marriages or other long-term partnerships.²² In Uganda, for example, HIV is present in 8% of all married or cohabiting couples, and in only about half the cases are both the partners infected with HIV.²³ Similarly, across Burkina Faso, Cameroon, Ghana, Kenya, and Tanzania, two-thirds of couples in which HIV is present are serodiscordant, and in 30–40% of these cases the female partner is infected.²⁴ A large-scale HIV-prevention trial focusing on serodiscordant couples in eastern and southern Africa reported that serodiscordancy varied between 8% and 31% (figure 2).²⁵ In both Thailand and Cambodia, a substantial proportion of HIV transmission has occurred in the context of serodiscordant marriages. The challenge for HIV-prevention programming is to address couples: for example, the positive benefits of HIV testing are promoted when couples are tested

together, and negative consequences, such as violence or exclusion, are reduced. Many couples will also want to conceive, and to find effective strategies for condom use and other risk-reduction strategies. Effective HIV treatment also modifies the risk of HIV transmission, and Switzerland's national HIV/AIDS organisation has recently gone as far as to advise that serodiscordant couples can forego condom use if the viral load of the HIV-positive partner has been suppressed to undetectable levels and in the absence of sexually transmitted infections.²⁶ The applicability of such a policy in settings where viral-load testing is not readily available has yet to be established.

One particular subset of serodiscordant established partnerships which has been discussed for more than a decade as a major source of HIV transmission is concurrent partnerships. High rates of concurrency probably facilitate the spread of HIV, but we do not know to what extent concurrency acts alone or in concert with other factors, such as low rates of male circumcision,^{27,28} mobility, family separation, religion, and other cultural factors. To date, comparative data on rates of concurrency across different global regions are scarce, although more are starting to be collected; for example the Demographic and Health Surveys are introducing a set of concurrency questions. Rates of multiple partnership (which includes concurrent partnerships, serial partners, and sex with many casual partners) vary widely in different countries; but in general, highly developed nations have the highest rates.²⁹ However, national aggregate rates of multiple partnership are not correlated with national rates of HIV infection. At an individual level, relationships with multiple partners remain a strong predictor of HIV infection³⁰—a reminder that individual risk patterns do not translate easily into explanations of national differences in HIV prevalence.

In any event, although the question of the role of concurrent partnerships in explaining different epidemic patterns is undoubtedly important, even more important is what ought to be the HIV-prevention response to concurrency, given that effective responses to HIV risk within established intimate relationships has always been the hardest of prevention challenges.³¹ In response to the declaration of prevention priorities made by the Southern African Development Committee (SADC) in 2006, work in that region has started to elaborate a programmatic response to concurrency in southern Africa. Formative research conducted in nine countries of southern Africa in the second half of 2007 reported very similar reasons across the subregion for multiple and concurrent partnerships: dissatisfaction with main relationships; social norms (cultural, gender, and peer-pressure issues); poverty and materialism; male domination; and alcohol use. On the basis of these results, regional stakeholders have proposed a communication campaign throughout the subregion to tackle: communication between children and parents,

Panel 3: Opiate substitution therapy

Methadone is used in the treatment of opiate addiction in many countries, including pilot programmes: Albania, Andorra, Australia, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Canada, China (including Hong Kong), Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Indonesia, Iran, Ireland, Israel, Italy, Kyrgyzstan, Latvia, Liechtenstein, Lithuania, Luxembourg, Macedonia, Malaysia, Malta, Mexico, Moldova, Nepal, Netherlands, New Zealand, Norway, Poland, Portugal, Romania, San Marino, Serbia, Slovakia, Slovenia, South Africa, Spain, Sweden, Switzerland, Thailand, Ukraine, UK (plus overseas territories and dependencies), and the USA. Buprenorphine treatment (including pilot programmes) is available in: Australia, Austria, Belgium, Canada, China (including Hong Kong), Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Iceland, India, Indonesia, Israel, Italy, Lithuania, Luxembourg, Malaysia, Norway, Portugal, Singapore, Slovakia, Slovenia, South Africa, Sweden, Switzerland, Ukraine, UK, and the USA.

and between partners; gender disparities (including dimensions of male domination and women's empowerment); and socialisation and peer pressure.³²

The focus on sexual transmission has also been diluted as a result of stigma. In both Latin America³³ and Asia and the Pacific³⁴ the mismatch between the high proportion of the epidemic in men who have sex with men and the low level of funding and programming efforts directed to this population has been repeatedly observed.³⁵ Men who have sex with men account for a larger proportion of the epidemic than hitherto assumed, even where heterosexual transmission predominates, such as in sub-Saharan Africa.³⁶ The most recent collection of national reports that use the indicators agreed after the UN General Assembly Special Session in 2001 showed that only 40% of men who have sex with men in 17 reporting countries were reached by prevention services.¹ Similarly, in the annual analysis of national responses conducted by UNAIDS country offices, of 90 responding countries, 54 had included men who have sex with men as a target population within their national HIV/AIDS action framework; these countries were mainly in the Asia-Pacific region, the Caribbean, eastern Europe, and Latin America (figure 3).³⁷ Representatives of men who have sex with men were regarded as full participants in national AIDS planning in 23 countries.³⁷ We hope that attempts to improve attention to this population in national policy making will cause this gap to be better addressed in the future.³⁷ The paucity of effective attention to sexual diversity is especially magnified in the case of transgender populations, which are among the most marginalised, abused, and HIV-affected populations anywhere, but which nevertheless receive scant programming attention.

Panel 4: Scaling up services for injecting drug users in the world's largest countries

China, India, and Indonesia, with more than 40% of the world's total population between them, provide good examples of large-scale programmatic responses to HIV among injecting drug users. The fragmented approach to HIV responses among users of such drugs in India reported only 3 years ago⁴² is giving way to implementation of full-scale approaches through the new National AIDS Control Programme and other key partners such as the Avahan project.⁴³ China had about 50 needle and syringe exchange sites in 2004;⁴⁴ by the end of 2006 this had risen to 729, with 320 methadone clinics. By 2010, China plans to double the number of needle and syringe exchanges and to reach 70% of all heroin users with methadone clinics.⁴⁵ In Indonesia, harm reduction has been progressively incorporated into national policy and implementation.⁴⁶ Despite the impressive commitment to scale up services for injecting drug users, policy remains inconsistent. For example, methadone remains illegal in India (where substitution therapy relies on buprenorphine), and inconsistencies are also widespread in other regions.⁴⁷ One example is southern Guangxi province in China, where although police and local authorities have supported needle and syringe exchange, police have also committed growing numbers of injecting drug users to detoxification centres and labour camps, which has driven many drug users underground—as a result, the average number of needles provided by the service has dropped from 12 000 every month in 2003 to 8000 in 2005.⁴⁸

Educating young people frankly about sex

Any sustainable effect on the future of HIV/AIDS will depend on the behaviour of young people, the adults of tomorrow. The tragic reality is that we have not provided a clear focus to ensure that all young people have the information they need before and while they are engaging in sex, especially in light of the high infection rates in young people, especially girls, and the early ages of sexual initiation—in many countries, 14–15 years is the median age of first sexual intercourse.

Even in settings where the epidemic is most concentrated, we still need to ensure that all young people have the information they need to prevent infection with HIV, given that the epidemic is dynamic, changing, and rarely stays in any one risk group. Yet as Coates and colleagues discuss in this Series,²⁰ young people's knowledge is still far short of the global targets set in 2001. The fact is that systematic HIV/AIDS education, starting with young people before they become sexually active, has not been made available. Even in the city of New York, where rates of infection with HIV among 13–19 year-old boys have doubled in the past 5 years, and one in four teenagers across the USA has at least one sexually transmitted disease, many schools block access to websites about HIV/AIDS and

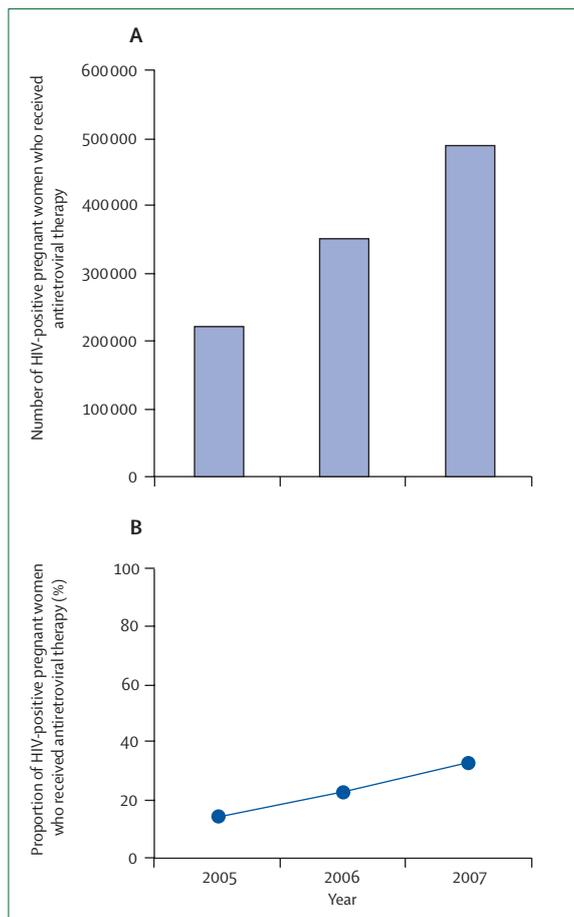


Figure 4: Number and proportion of HIV-positive pregnant women who received antiretroviral therapy in 2005-07

Data are sourced from reference 50.

sex education. In much of the world, HIV/AIDS education is not integrated into primary school curricula. Less than 70% of countries with generalised epidemics deliver school-based education about HIV/AIDS in most or all districts.

The tremendous diversity in the personalities and circumstances of young people drive their choices. If we focus education efforts only on defined risk groups, such as men who have sex with men or injecting drug users, and neglect efforts which could reach young people before they make life choices, we could miss important opportunities to affect the course of the pandemic over the next generation. Age-appropriate universal sex education is clearly needed from primary-school age, taking into account all sexual choices. Sex education has never been shown to encourage promiscuity, as is sometimes claimed. In fact, the weight of evidence shows that it encourages both the delay of first sexual activity and higher rates of protected sex.³⁸

Sex education should be a core part of education budgets and not be a separate HIV/AIDS-related line in

the budget. HIV/AIDS budgets should also support specific campaigns, such as those designed to reach young people, from MTV to Uganda's "straight talk". Equally, the full range of new communications technologies ought to be deployed to mobilise youth networks, as for example, in Kenya's Partnership for an HIV-Free Generation—a partnership of government, PEPFAR, MTV, businesses, and youth groups.

If social norms need to change, which in the absence of a vaccine might be the only truly sustainable way to change the course of the pandemic and its effects, it must start with young people. For young people, the issue is not about behaviour change—it is about motivating informed, safer behaviour from the start.

Dealing rationally with drug use

The one issue that is more controversial than prevention of transmission through sex is prevention of transmission through injecting drug use. Scientific consensus has been achieved on the effectiveness of harm-reduction approaches to HIV among such users³⁹ and its component elements have been fleshed out: needle and syringe programmes; opioid substitution therapy; voluntary counselling and testing; antiretroviral therapy; prevention of sexually transmitted infections; condom programming for users and their sexual partners; targeted information provision; hepatitis diagnosis and treatment; and tuberculosis prevention, diagnosis, and treatment.⁴⁰ Nevertheless, countries still struggle to balance minimisation of harms to injecting drug users with the goal of reducing supply and demand of illicit drugs, which remains a complex regulatory task.

Methadone is available in only 52 countries worldwide and buprenorphine in 32 (panel 3).⁴¹ In most countries where it is not available, possession is illegal. In Russia and most countries of eastern Europe and central Asia, despite the fact that use of injected drugs constitutes the most important route of HIV transmission, access to substitution therapy remains poor (panel 4).

Given these inconsistencies in policy and practice, rates of HIV infection among injecting drugs users in many parts of the world have remained stubbornly high or been resurgent. In other places, new infections have started to emerge in the wake of drug trafficking routes, as has been reported in eastern Africa. One weak link in a chain of responses can cause the whole HIV-prevention apparatus to fail. A positive cycle needs to address injecting drug users and their sexual partners; respond to the links between injecting and the sale of sex; deal with prison and rehabilitation settings; and tackle HIV/AIDS, hepatitis, tuberculosis, and sexually transmitted infections.

Although use of injected drugs has been the principal focus of much of the drugs-related HIV/AIDS response, other illicit-drug use also raises key issues. Subcultures within the gay community which use amphetamines have been a particular concern in relation to spread of

HIV in the USA and to some extent Australia and Canada, and more recently the spread of amphetamine use in southeast Asia has posed similar concerns. HIV risk has been strongly associated with both the use of illicit drugs and with alcohol use, especially in settings where sexual contacts are also made. Alcohol and drug use might not be the straightforward causes of risky behaviour, but they do seem to sustain subcultures of risk.⁴⁹

Eliminating mother-to-child transmission

High-income countries have almost eliminated transmission of HIV from mother to child (figure 4). Several middle income-income and lower middle-income countries have done the same—in El Salvador for example, in about 2003, some 150 infants were born HIV-positive, but within 3 years after the introduction of a nationwide programme to prevent mother-to-child transmission the numbers were reduced to below 20. Botswana had the distinction of being the first country in sub-Saharan Africa to achieve practically universal coverage of such programmes. But despite concerted advocacy in every part of the world, the results are variable.⁵¹

Notably, of the 12 countries which contain three-quarters of the world's HIV-positive pregnant women, only Kenya and South Africa have programmes to prevent mother-to-child transmission of HIV that reach at least half those in need. Global partners from both government and non-government sectors have agreed that successful programmes need: strong government commitment able to rally partners around one national plan; strong national management and coordination, including non-governmental stakeholders; provider-initiated HIV testing and counselling in antenatal care settings; lay counsellors to alleviate shortages of health-care workers; and a comprehensive set of services including family-centred HIV/AIDS care; maternal, newborn, and child health; and sexual and reproductive health care.⁴⁸

In November, 2007, when global partners considered progress in implementation of programmes with these characteristics, they concluded that the reasons only 17 countries globally were on track included poor coordination of efforts between programmes for maternal and child health and HIV/AIDS; insufficient resources; stigma; insufficient engagement by men; and a failure to tackle gender violence.⁵²

Politics, leadership, and demand generation

Whereas leadership on HIV treatment in a growing number of countries has been exemplary, and has achieved clear results, leadership has been very uneven for HIV prevention. Some of this lack of explicit leadership relates to the controversial nature of what works in terms of HIV prevention, such as reduction of harm for injecting drug users, sex education for children, promotion of condom use, and societal norms about sexuality, in particular homosexuality.⁵³ Overcoming

reluctance to deal with difficult issues can be an act of enlightened top leadership; for example, in Thailand, Uganda, and Brazil in the 1990s. However, such leadership rarely happens by coincidence, and requires a well designed political strategy that is embedded in scientific evidence and that engages a broad set of sectors and opinion groups in society.

Activism by those primarily affected by AIDS has played an essential role throughout the history of the AIDS response, whether by gay men in developed countries or Brazil, sex workers in Calcutta, or the Treatment Action Campaign in South Africa.⁵⁴ However, in general, activism for HIV prevention is much less than what it was in the early days of the epidemic in the gay community, and less than activism for HIV treatment, which has been so successful around the world.

HIV prevention must now come out of the closet of prevention experts. Building a strong constituency for HIV prevention should be a top priority. A broad-based coalition from youth, women's, and religious organisations to business leaders and HIV/AIDS activists is what is needed.⁵⁵

The need for strong and well directed leadership to keep HIV prevention at the forefront of social policy and action is especially crucial because of the many controversies associated with sex and drug use, the long time lag between HIV infection and the appearance of illness, and the pressing need to provide treatment to those who live with HIV/AIDS. As illustrated in our discussion of sex education and harm reduction, so-called good politics provides the necessary leadership based on scientific evidence and human rights, whereas bad politics, including the absence of leadership, is one of the main obstacles to effective HIV prevention.⁵³ The cost of such bad politics is measured in human lives. Political leadership and courage also underpin the will to change laws that hinder HIV prevention and could even promote the spread of the virus (such as anti-sodomy laws, laws that criminalise prostitution and sex workers, barriers to the legalised distribution of methadone and uncontaminated injecting equipment, and the criminalisation of HIV transmission). Such laws are key structural barriers to prevention, as analysed by Rao Gupta and colleagues in this Series.⁸

The leadership that is needed is not only political in nature, but in many settings also requires complementary technical leadership in HIV prevention, which has too often been lacking, especially by contrast with the strong technical leadership for extending HIV treatment. Unfortunately, weak technical leadership in prevention areas is more often the rule than the exception, both in public health and across other sectors which need to be involved, including humanitarian responses, social protection, and poverty alleviation, and Bertozzi and colleagues² make a compelling case in this Series for the mix of technical and managerial capacity which is needed for optimal responses.



Figure 5: Prevention march by South Africa's Treatment Action Campaign
5000 people marched through the streets of Cape Town at the start of the 38th Annual Union World Conference on Lung Health in November, 2007, organised by the Treatment Action Campaign and the AIDS and Rights Alliance of Southern Africa. Reproduced with permission of the photographer, Damien Schumann.

The reasons that appropriate leadership has not emerged are not hard to divine. First, HIV prevention, by its nature, requires the engagement of many sectors. Second, the solutions required can challenge personal values (including the values held by implementers and those needed to champion prevention). Third, as with prevention of any disease or ill, treatment of the acute crisis can produce immediate results, compared with prevention of the root cause, which achieves results over years and decades. Overcoming the deficit of leadership in HIV prevention will require much more systematic investment than has been provided up to now.

Over the history of HIV/AIDS, political processes have often come together to create a mass popular demand for HIV prevention. In many instances, this demand has coincided with periods of social and political transformation. So, for example, Brazil's HIV/AIDS movement emerged hand in hand with the flowering of a strong civil society in creative tension with the state, after the repressive period of the military dictatorship.⁵⁶ The early and vigorous responses to HIV/AIDS by gay communities in most developed countries were in part mobilised by a desire to protect recently gained freedoms and social recognition.⁵⁷ Uganda's social mobilisation against HIV/AIDS came as the country emerged from civil war, and both civil society and the state were determined that the peace dividend should not be undermined by this new threat. In South Africa, civil society organised a militant approach to HIV/AIDS that was grounded in the struggle against apartheid and the conviction that the dividend of political transition was in danger of being wiped away by HIV/AIDS. Thailand saw a strong political and community response at the

beginning of the 1990s in the middle of its decade of spectacular economic growth and integration into the world economy.⁵⁸ Cambodia's response was galvanised by the appeal for HIV/AIDS not to be a second genocide.

However, we cannot rely on the hope that an effective movement to demand HIV prevention will emerge spontaneously. Social mobilisation has been recognised as a key technique for national HIV/AIDS responses since at least the late 1980s,⁵⁹ and has been a part of many government, multilateral, donor, and non-governmental efforts. These efforts at social mobilisation are increasingly implemented at the scale of whole nations. For example, Ethiopia's HIV/AIDS Prevention and Control Office has given priority to cross-cutting efforts to mobilise Ethiopian society from the level of local kebeles upwards in its road map towards universal access to HIV prevention, care, and treatment, and a collective effort to generate community conversations on HIV/AIDS is being rolled out across the country.⁶⁰

Religious organisations have also been a source of mass mobilisation in HIV prevention, including both systematic efforts led by international faith-based organisations (such as World Vision, the Ecumenical Advocacy Alliance, Caritas, Saddleback Church, Islamic Relief, and the Sangha Metta Project), and local efforts by religious leaders from various faiths. Many youth organisations have also mobilised against HIV/AIDS, with interesting examples of the confluence of youth marketing, social networking, and corporate social responsibility. These are best exemplified by MTV's "Staying Alive" initiative, which began as HIV/AIDS-related broadcasts for World AIDS Day in 1998, but has now spawned a mix of music and television programming and web-based networking with mass youth participation.

Finally, although the HIV/AIDS activist movement is today most often associated with access to treatment, we should remember that the iconic movement of direct AIDS activism, ACT-UP, took as its most recognisable slogan "silence=death", and at its founding in 1987 was as much concerned about the silencing of effective HIV/AIDS education as it was to accelerate processes for drug development and approval.⁶¹ More recently, as Merson and colleagues⁶² note, one of the world's most successful national HIV/AIDS activist organisations, South Africa's Treatment Action Campaign, has used its methods and organisational capacity in direct support of HIV prevention, with a series of advocacy efforts and marches that demand intensified HIV prevention (figure 5).⁵⁴

Although each of these sectors can justifiably claim to having successfully generated demand for HIV prevention, the challenge has been to join these efforts into a coherent movement that is able to shift social norms and sexual and drug-use practices. Instead, the demands of these sectors have been competing or contradictory: community versus state, religious versus secular, local versus international, private versus public,

and medical versus social. The extent of the pandemic has made the need to overcome these differences in the creation of an effective movement to demand HIV prevention even more compelling. Such a movement must be underpinned by several core priorities: full-scale emergency mobilisation in the worst-affected countries, attempts to reach all those in need, and taking a long-term perspective.

HIV hyperendemic countries: a full-scale emergency

Southern Africa, and to a lesser extent eastern Africa, is experiencing an unparalleled epidemic, with a prevalence of HIV/AIDS that until the mid-1990s was thought to be impossible in the population at large. Up to 25% of 15–49 year-olds are HIV positive,⁶⁵ and the annual incidence in young women is 4–6%, which is worse than the cumulative prevalence in the whole population after 30 years almost anywhere else in the world.

Although some real reductions in HIV prevalence in the region have been achieved by changes in sexual behaviour, such as in Zimbabwe,⁶³ and HIV prevalence in young attendees of antenatal clinics has started to decline in most countries, HIV incidence continues to be high (eg, half a million new infections per year in South Africa alone), and could be even rising (eg, in Mozambique, which could have a younger epidemic).

What makes these societies unique from the HIV/AIDS perspective is that HIV transmission is far more diffuse than elsewhere, and occurs mostly within long-term and occasional heterosexual partnerships, often transgressing traditional concepts of high or low risk. Multiple vulnerability and risk factors (such as mobility, gender-based violence, or concurrent partnerships), which individually exist to an even greater extent in other regions (eg, low rates of male circumcision in Europe), converge to act synergistically in these societies. In other words, southern Africa seems to be experiencing a perfect storm of HIV-related risks. Any explanation based on a single risk factor for this very high HIV endemicity ignores the realities of complex societies and human behaviour. A complex and diffuse epidemic should be addressed by an equally nuanced and multipronged response.

Even if greater coverage of all effective interventions for HIV prevention is a priority in high-prevalence societies, and would most probably result in large reductions in HIV incidence, as argued in this Series,^{5,21} individual behaviour change alone is unlikely to stop the spread of HIV in a sustainable way. Comprehensive HIV prevention should urgently include programmes that address the key drivers of the epidemic in the region, in particular those that change societal norms and create safer sexual environments—eg, working towards the elimination of sexual coercion and violence—and those that reduce the vulnerability of communities and individuals, such as food security

programmes or adjustments to labour migration to minimise family disruption.⁶⁴

In communities that are heavily affected by HIV/AIDS, HIV-prevention activities must also go hand in hand with HIV treatment and strategies to mitigate effects on individuals, households, and communities. Promotion of HIV prevention without mitigating the overwhelming consequences of the epidemic has little credibility and provides few incentives for safe sexual behaviour.^{65,66} These principles have been put into practice in many settings. For example, in Zambia, the Antiretroviral Community Education and Referral Project, ACER, aimed to bolster positive attitudes to treatment and prevention in communities by employing treatment-support workers and treatment mobilisers.⁶⁷ The project has since been extended to Uganda and within Zambia on the basis of its generally positive effects (although project sites and comparisons sites did not differ on most measures, including sexual behaviours).⁶⁸ Both operational research and systematic evaluation should urgently try to not only capture the ways in which integrated interventions which tackle social vulnerability can be made more effective, but also measure their effect on HIV-related outcomes, such as quality of life, mortality, and HIV transmission.

The challenge in the hyperendemic context is not so much to specify the content of HIV-prevention programmes (with some exceptions such as interventions for serodiscordant couples) but to identify the mechanisms by which these programmes will be implemented at sufficient scale. The substance of HIV prevention has been well developed in the region itself.⁶⁹ The difficult challenges are to elevate HIV prevention as a national emergency,⁷⁰ and to deliver on leadership, governance, institutional and community capacity, accountability, and implementation in general. Initiation of such a nationwide emergency response has at least three major policy implications: (1) HIV prevention must be an integral part of a country's development plan; (2) multiple sectors in government and civil society must be actively engaged; and (3) the effort must be effectively led at the highest level of the state, as is the case in Botswana.

Reaching all those in need: the implementation science of HIV prevention

Most published work on HIV prevention focuses on debates about which discrete interventions should be used for HIV prevention. Surprisingly little attention focuses on how they should be used, which is where our biggest challenges lie.⁷¹ HIV prevention must be able to deal with complexity: what makes the difference between a growing and a diminishing HIV epidemic is not merely net changes in individual behaviours, but dynamic shifts in sexual and social networks. Analytical tools need to be designed to capture these dynamics. Agent-based models are increasingly being used to

understand the dynamic characteristics of complex systems, such as sexual networks. The analytical tools which have led to the identification of characteristics which make complex systems more able to adapt positively to change and diffuse innovation⁷² could have much to offer efforts to implement HIV-prevention programmes.

Attention to the how of HIV prevention must also entail attention to issues of scale: with the goal of optimising programme settings (panel 5).² A different set of operational issues come to the fore when full-scale responses are attempted as opposed to pilot schemes or research projects, but very little operational research has investigated the means of going to scale, and correspondingly lessons learnt in scaling up have not been disseminated. The Avahan initiative in India (see Bertozzi and colleagues)² has taken scale-up as one of the key elements of its business model and has an explicit strategy to achieve scale-up through partnerships among four sectors: government, networks of non-governmental and community organisations, business, and donors.⁷³ Another example of a very large country attempting to reach full national coverage is Ethiopia and the ambitious targets of its Millennium AIDS Campaign (commenced in 2007, at the turn of the new millennium under the Julian calendar used in Ethiopia).⁷⁴

Reaching all those in need: going beyond health services

Whereas provision of HIV treatment and the prevention of HIV transmission from mother to child are the primary responsibility of the health-care system, prevention of sexual transmission of HIV and of transmission through sharing of needles largely happens outside the health sector and medical services. Therefore the much-needed strengthening of health services in developing countries might only be marginally beneficial for HIV prevention. For this and other reasons, the debate in some public-health and political circles that polarises so-called vertical HIV/AIDS programmes versus horizontal strengthening of health services is the wrong agenda, and is unhelpful for the HIV/AIDS response. The needs of individuals or communities do not come packaged into sectoral boxes, and an activist HIV/AIDS movement, focused on meeting real needs effectively, will not only be the strongest weapon against the inefficiencies of 20th century verticality, but also a corrective to system strengthening without clearly defined objectives.

Clear and simple criteria for managing performance within countries and between them is crucial to success—if we can measure it, we can manage it. Such criteria allow us to highlight successes as best practice and to identify underperformers for intensive interventions. Positive competition can lead countries to review and raise their performances. Other sectors provide important

Panel 5: The programming cycle for HIV prevention

- “Know your epidemic”, and create a situation analysis that sets programmatic targets where new HIV infections are occurring
- “Know your response”, and ensure the response addresses both the immediate risks and underlying drivers of the epidemic
- Allocate resources where they will make the biggest difference in the country, for reduction of both risk and vulnerability
- Implement in a very systematic way a business plan for HIV prevention, with clear responsibilities and deliverables for all actors, and address not only the individual dimensions of HIV prevention but also the legal, cultural, and social environment
- Invest in the management capacity of both governmental and non-governmental organisations
- Use the integrated tools of social-change advocacy, communication, and community mobilisation to generate a prevention constituency and support development of community capacity
- Carefully design methods to assess effectiveness, measure progress, and review implementation; hold people at all levels of the response publicly accountable for their performance and ensure that programmes are adapted in the light of reviews

lessons. Positive performance towards universally respected goals, including increased immunisation, education, or coverage of HIV/AIDS treatment, enhances international confidence in development in a way that capacity or systems-building initiatives alone cannot do. The delivery of immunisation (spearheaded by the Global Alliance for Vaccines and Immunisation [GAVI Alliance]), the international commitment to Education for All and the associated Fast Track Initiative, and the roll-out of antiretroviral therapy share some common and important lessons. First, all set important ambitious goals that were considered unattainable when first proclaimed. Such goals lift our vision of what is possible and lead to far higher achievement than is possible in the absence of such aspirational goals. Second, if we focus on crucial development challenges with laser-like intensity, we can achieve exceptional progress. Third, and relatedly, even in an age of budget support, sector-wide approaches, and health-systems development, special initiatives are needed, supported by distinct goals, technical teams, financing, management, and monitoring mechanisms: both system-wide and focused initiatives are needed.

Effective and large-scale HIV prevention requires the active engagement of many state and non-state actors, and has been a hallmark of successful AIDS programmes. By contrast with some claims, such pluralism in action is not a bad thing. Maximal effectiveness is achieved when all entities working on HIV prevention in a given country

commit to work towards the realisation and continuous improvement of nationally and locally defined goals, along the principles of the Three Ones (panel 6).⁷⁵ These principles—a coherent AIDS response guided by one national authority, one strategic plan, and a single monitoring and assessment framework—have been almost universally embraced.

The Three Ones have greatly strengthened the partnership between developing countries and those who provide financial assistance to HIV/AIDS programmes. However, embracing these principles has not yet realised the practical benefits of a reduced reporting burden; nor has it produced predictability in funding or increased investment in capacity building. These are precisely the outcomes that are most needed in the context of HIV/AIDS, since in the worst-affected countries, national administrative and management capacities, which are already often in a weak state, have been further depleted by the epidemic.⁷⁶

Implementation of the HIV-prevention actions proposed in this paper and Series will require a substantial boost in spending, from both global and domestic sources. As important as the level of funding is its predictability. Many of the actions we have called for need sustained long-term investment—building prevention capacity, for example, or developing the community infrastructure that is essential to support demand for HIV prevention.

About 40% of the US\$10 billion spent on HIV/AIDS in low-income and middle-income countries in 2007 went to prevention. The recent UNAIDS estimate of global resource needs estimated that HIV prevention activities and services will cost US \$11.6 billion by 2010 and US \$15.3 billion by 2015 as programmes phase up to reach universal access.⁷⁷ That calculation was made on the basis of several elements that are commonly used in HIV-prevention programmes. The proposals we have made here differ in emphasis but are unlikely to cost more: our argument is as much about spending smarter, once the threshold for universal access is met. Implementing HIV prevention in this way would have a major effect on the epidemic—more than half of the new infections between now and 2015 would be averted. In other words, if combination prevention is intensified as rapidly as possible from today, then some 12 million HIV fewer infections will occur between now and 2015 than will occur if incidence at today's levels remains constant, and the annual number of new infections in 2015 will have reduced by two-thirds.^{1,78}

The long-term view

A quarter of a century into the pandemic, with no vaccine in sight and the number of new infections outpacing the progress in access to treatment, we clearly need to take a long-term view in planning our actions.⁷⁹ The HIV/AIDS response environment cannot be taken for granted: the pandemic is dynamic and moving; populations are

dynamic and mobility only increasing; leadership at both state and non-state levels changes; the availability of resources and the demands upon them are highly variable; the geopolitical environment around HIV/AIDS could take positive (or not so positive) turns in affecting the legislative environment, buffeted by the winds of xenophobia and religious and other fundamentalisms; and leaders and public opinion are prone to complacency and fatigue.

The state of HIV/AIDS is at a highly vulnerable point. Although we have made progress in some areas, the gains made can be lost quickly if we are not vigilant in sustaining—and building on—areas that already show results. Beyond sustaining our gains, we need to keep our eyes on the horizon, build in a readiness and flexibility to manage uncertainty and surprises, and

Panel 6: The Three Ones in India

The Indian Government's National AIDS Control Programme is now in its third 5 year cycle, and is demonstrably reducing HIV infection in India's southern and western states, which have the highest prevalence of HIV. The key strengths of the programme are:

- An institutional framework that supports central leadership and harmonisation, combined with a sustained, decentralised response consisting of: a legislatively-based National AIDS Control Authority (NACO), with senior Indian Administrative Service leadership; a National AIDS Commission, chaired by the Prime Minister; and independent state AIDS-control societies, established under the Societies Act and functioning under the leadership of NACO. India's robust approach to donor harmonisation, and its 2003 policy to eliminate small bilateral programmes in favour of programmes consolidated through multilateral donors or non-governmental organisations (NGOs), is both a consequence of clear national leadership and a cause of increased effectiveness of aid
- Clear scientific leadership: India's surveillance and research programme, supported by local and international partners, decisively established that India faces a concentrated epidemic
- Translation of scientific vision into implementation systems and procedures: for example implementation, funding, costing, performance, and monitoring systems developed by NACO for sex-worker interventions enabled it to support thousands of targeted interventions, and to better coordinate development partners
- Recognition of what government can and cannot do: India recognised that the private sector is better placed than government to develop media campaigns to change behaviour and to socially market condoms and that NGOs are far better placed than government to work with vulnerable groups of sex workers, men who have sex with men, and injecting drug users. The Indian government recognised and partnered with excellence outside government; for example, steps taken to ensure that expertise from the Avahan programme, funded by the Bill & Melinda Gates Foundation, would flow back into the national programme
- Focus and prioritisation: as the character of India's epidemic became clearer with improved national surveillance, the HIV programme became more focused, resisting the tendency for mission spread or for it to drift into low-priority activities

The achievements of India's coordinated HIV response should not disguise the ongoing challenges: in a large federal nation, some states lag far behind others in the scale and effectiveness of their response. Some vulnerable groups have been neglected in the response: for example, national efforts in relation to men who have sex with men were only fully embraced in the most recent (third) National AIDS Control Programme, and were also initially neglected by the Avahan programme.

develop resilience to negative changes that could undermine our progress to date.

We need resilience at many levels. We need predictability in funding flows—moving from short-term to long-term

funding commitments. We need resilience in leadership—building coalitions that will not wane when individual leaders change. We need resilience in public awareness about the state of HIV/AIDS to ensure an

Call to action

We urge governments, communities and scientists to fully implement combination HIV prevention, and urge the international community to mobilise all the support necessary for this effort

- Every HIV/AIDS programme must know its epidemic and its response, by an analysis of where the epidemic is, where the next 1000 HIV infections are likely to come from, and where socioeconomic change suggests they could come from in 10 years time
- Focus on an optimal mix of quality efforts in terms of what is most needed for the populations most affected and most at risk, respecting different types of evidence, and connecting HIV prevention with treatment efforts
- Scale up coverage to optimal levels to ensure universal access to HIV prevention, starting by using what we have more effectively and giving access to basic programmes for HIV prevention (eg, condoms and prevention of mother-to-child transmission)
- Set specific, ambitious, and actionable targets to reach universal access to HIV prevention
- Generate systematic social change to prevent the spread of HIV and reduce vulnerability to it, by using the full range of contemporary media, reforming discriminatory laws, supporting access to justice, creating safe spaces away from gender-based violence, and prosecuting sexual violence

We call for sustained political and technical leadership for the AIDS response

- Adopt HIV prevention as a national cause, and rally support for the cause in every possible context, including workplaces, schools, communities, and places of worship
- Establish clear responsibility and accountability for HIV prevention efforts, and make sure that national prevention taskforces are established to push prevention goals
- Muster the political courage to advocate scientifically sound approaches in sensitive areas of sexuality, gender, and drug use, including the full set of effective harm-reduction methods in relation to HIV and injecting drug use, addressing sex education to children before they become sexually active, and including sexual minorities in HIV programmes
- Support governments and donors to deliver on a shared commitment to predictable and sustained financing for HIV prevention that eliminates duplication and minimises transaction costs
- Guide AIDS responses in a spirit of pragmatism and science, instead of using HIV/AIDS as a vehicle to advance dogma of any kind

We urge international institutions, national governments, and community activists to work together to build demand for HIV prevention

- Develop a broad HIV-prevention movement, grounded in the strengthening of natural constituencies for HIV prevention in the communities of those who are most vulnerable and affected
- Support HIV-prevention literacy at all levels, linked to the successful scaling up of treatment literacy
- Identify and promote bold advocates and public models for changing harmful social, behavioural, and legal norms and practices
- Create an active coalition between the movement for HIV prevention and the movement of people living with HIV/AIDS, and link this coalition with other motors of social change, including treatment activists, entrepreneurs, rights activists, and women's and youth activists

We urge scientists, research funders, and programme planners to broaden the HIV-prevention research agenda

- Create an agenda for operations research and evaluation and ensure its funding, focused on what strategies work best under what circumstances and how best to deliver them
- Research novel approaches to implementation science and interdisciplinary applications to elucidate ways to tackle the structural drivers of the epidemic
- Continue the concerted and coordinated search for an HIV vaccine
- Invest in research on many potential HIV-prevention technologies, including microbicides and antiretroviral prevention

We call for immediate investment in building capacities at all levels for HIV-prevention efforts

- Invest in managerial, technical, and implementation capacity for national HIV/AIDS authorities, to allow them to direct the HIV-prevention response with confidence
- Invest equally in capacity building in the community sector, which has the lion's share of responsibility for HIV prevention
- Adopt a combination approach to capacity building in governmental and non-governmental sectors, by developing a cadre of competent HIV-prevention personnel in the range of professional disciplines that are needed to make up a strong HIV-prevention response
- Invest in the capacity for HIV-prevention policy, research, and assessment

honest understanding of real risks rather than complacency due to a perception that things are somehow “ok”. And we need resilience in programmes and research—recognising that effective implementation does not achieve, and cannot demonstrate, its results over the short term.

We need to be thinking ahead, not only to anticipate the next technologies in the pipeline, but also the issues around their introduction. Experience with introduction of other vaccines to target populations of reproductive age, such as human papillomavirus and tetanus, represents lessons that we can draw from. The introduction of new technologies will not only need long-term thinking in terms of the policy environment and building community acceptance, but also the long-term financial implications.

In terms of a research agenda, in the same way that we need to take multiple combination approaches to prevention programming, we need to take a combination approach to the development of new technologies and build a research agenda that not only anticipates new needs but addresses known needs, and encompasses the full range of factors which affect the epidemic.

Ultimately, we need to come to terms with addressing the underlying social drivers of HIV/AIDS. Prevention work takes the longest time, is largely outside of health services, and has no “quick win”. If not tackled, prevention work will also continue to undermine all the other gains. On the other hand, progress in addressing social drivers will accelerate access to, and long-term effects of, other prevention technologies and interventions. The AIDS 2031 project aims to address many of these issues through the lens of looking at the longer term implications of not analysing, anticipating, and dealing with key drivers of the epidemic now. Its report *An Agenda for the Future* will be delivered by the end of 2009 with recommendations intended to guide decision makers and activists as they plan for the future response to HIV/AIDS.⁸⁰

A call to action on HIV prevention

A quarter of a century into the response to HIV/AIDS, we consider that our call for an all-out, unprecedented effort towards HIV prevention—as has been successfully made towards HIV treatment—is imperative. We have learnt much and we know much about this epidemic that can be harnessed to prevent more infections: we need to invest now in scaling up and building on our learnings and the results we are seeing. Global commitments have already been made: specific prevention targets set at the historic UN General Assembly Special Session on AIDS in 2001, together with the political declaration adopted by the UN General Assembly in 2006 that committed to coming as close as possible towards universal access to HIV prevention, treatment care, and support by 2010.⁸¹ If access to HIV-prevention knowledge and tools is recognised as a

basic human right, resources will have to be made available and an enabling environment created so that everyone has such access. This investment in our future would make ethical and economic sense in terms of the enormous dividends it will provide. The articles in this Series point to some of the key action areas in HIV prevention in which we need to make such an unprecedented investment (see Call to Action panel).

None of the successes in HIV prevention over the past quarter of a century have been easily won. They have required taboos to be broken, pleasures foregone, and resources reallocated. When HIV/AIDS was brand new and seen clearly as an emergency, these costs seemed easier to bear. The challenge for HIV prevention today is to sustain a momentum for effective, complex, combination efforts over the long haul. A failure of confidence now in our collective capacity to deliver full-scale and effective HIV prevention would be devastating, and its effect would be felt for generations. We cannot expect that miraculous results will be universally evident over the current political or funding cycle, or even over the next one. But we must have the courage to press ahead, because if we fail the challenge of HIV prevention, HIV/AIDS will relentlessly undermine human progress. An energised HIV-prevention movement, marching hand in hand with the movement to make access to treatment universal, is a goal truly worth the effort it will take.

Conflict of interest statement

We declare that we have no conflict of interest.

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