FT Health Combating Aids

Friday November 30 2012

www.ft.com/reports | twitter.com/ftreports

Biggest obstacle is human behaviour

Scientific advances and unprecedented funding run up against political sensitivities and rising complacency, writes *Andrew Jack*

Chain reaction: volunteers in Taipei form a red ribbon in support of better care for those living with HIV and Aids Getty

As Elton John's band played on during the latest International Aids Society conference in July in Washington, President Barack Obama kept his distance, hosting a select political gathering a short distance away in the White House.

It was perhaps not surprising, since HIV remains a touchy topic that could have erupted unpredictably during the febrile US election campaign. His cautious approach highlighted the continuing sensitivity about one of the globe's most lethal infectious diseases, even in the capital of the world's richest nation.

Despite growing rhetoric about "the end of Aids" and "an Aids-free generation", the disease continues to impose a heavy toll more than 30 years since it was first identified by US researchers. Human behaviour, including political sensitivities and rising complacency, remain among the greatest obstacles to further progress.

The latest calculations from UNAids released this month estimate that 34m people are living with HIV and 1.7m died from its complications in 2011. A further 2.5m were newly infected during the year, albeit on a declining trajectory, while treatment for those diagnosed has been steadily rising.

For Mitchell Warren, head of Avac, an HIV prevention advocacy group, the calculations signal a "tipping point" at which, unless there are accelerated efforts to stem the epidemic, advances risk being lost. "Current models tell us that the next 12 to 24 months are a critical window," he says.

Much of the progress to date in sustaining life – saving 14m people since the mid 1990s – has been the result of remarkable scientific advances in understanding HIV and unusually rapid progress in accelerating the development of new drugs. Backed by unprecedented funding, a record 8m people now receive treatment. At the same time, that is only half of those around the world who need it.

Most of the billions of dollars invested in new "tools" – notably for the prevention of infection – have failed to deliver.

A vaccine still appears to be many years away at best. More promising results with experimental vaginal and anal microbicide gels to kill the virus have yielded mixed results.

> UNAids estimates that 34m people are living with HIV, and 1.7m died from its complications in 2011

Instead, making better use of cheap technologies that already exist offers greater short-term promise. That starts with intensified distribution of condoms and clean syringes for injecting drug users; drugs for pregnant mothers with HIV to prevent transmission to their children; rapid diagnostics; and simple devices for adult male circumcision – a technique long anecdotally shown to reduce infection.

The reality is that there is a lack of better targeting of stretched funds to programmes in groups at the greatest risk. Conservative politicians have proved reluctant to support evidence-based programmes to reduce infection among drug users, gay and transsexual people and even young people where the programmes may be seen to be promoting sex.

That helps explain why HIV continues to rise in eastern Europe, Russia and Central Asia, notably the result of drug abuse, and in the Middle East and north Africa, where homosexuality is taboo. Elsewhere, the "mature epidemics" of North America and western Europe, let alone Uganda, point to the need for more imaginative behaviour change campaigns.

UNAids has highlighted a significant mismatch of resources, with much money still wasted on general HIV programmes while far better returns would come from focusing particular proven interventions on those groups at greatest risk. "We need to put resources where we have the maximum benefit," says Michel Sidibé, head of the agency.

The decriminalisation of homosexuality, and policies to remove economic and social barriers exposing women to infection, are also important.

Continued on Page 2

Inside »

Reforms to support regions
Revamped grant system offers hope to millions
Page 2

Medicinal benefits
Pre-emptive strike to help stave off infection
Page 3

Treatment
Discoveries revolutionise outcomes for patients
Page 3

Campaign to tackle epidemic
Washington struggles to raise HIV awareness
Page 4

Tolerance is key
Stigmatising people with HIV or Aids will only deepen the epidemic
www.ft.com/reports

WE AGREE.

We see a world where AIDS will
stop stealing our friends.
Threatening our employees.
And harming newborn babies.
From San Francisco to West Africa,
AIDS attacks us where we work and live.
At Chevron, we've fought back with
testing, education, care, and support.
Our employees and partners are working
side by side to end mother-to-child transmission.
And we're winning.
In Nigeria, where the grip of HIV is fierce,
our children haven't had a reported case in 12 years.
AIDS is strong.
But, together, we are stronger.

Lend your voice at
chevron.com/aids #aidswilllose

Human Energy®

CHEVRON, the CHEVRON Hallmark and HUMAN ENERGY are registered trademarks of Chevron Intellectual Property LLC. © 2012 Chevron U.S.A. Inc. All rights reserved.

Reforms offer chance of more support for regions in need

Global Fund New leader Mark Dybul will oversee fresh grant system after board feud and anomalies in awards, writes *Andrew Jack*

Rarely have international politics, big money and global health been so closely linked – and with such consequences for human life – as in the recent growing pains of the Global Fund to Fight Aids, Tuberculosis and Malaria.

A year ago, as the UN-backed organisation moved into its second decade of existence, there was scant sign of celebration. Instead, the mood among the feuding members of the governing board of the world's largest conduit of multilateral aid for health resembled that of a wake. The conflict really did end in tears, as well as the departure of Michel Kazatchkine, its executive director, not long after.

But now, fresh from the selection this month of Mark Dybul as his replacement, many participants see grounds for renewed optimism. "There was truly a crisis at the Global Fund but now donor confidence is high," says Alvaro Bermejo, director of the International HIV/Aids Alliance, a non-profit umbrella group.

More than 10 years since its creation, the Global Fund has made its mark. It was a new entity: a multilateral agency outside the heavy strictures and bureaucracy of the UN, committed to transparency and operating under the supervision not only of donors, but also of recipient countries and non-profit and business representatives. Yet those strengths provided ammunition for its critics.

It raised nearly $23bn, primarily from the governments of richer countries, but also with some corporate and philanthropic support. It provided an unprecedented boost to tackling the world's three leading fatal infectious diseases, funding prevention and treatment programmes that it estimates saved 1m lives in 2011 alone through grants of nearly $3bn.

Yet the fund's fast growth created managerial strains, while the historic surge in funding had overextended expectations at a time when donors, squeezed by domestic austerity, were looking for excuses to cut back their aid. Staff numbers grew rapidly, but employees were not always best deployed to scrutinise grants.

Over-optimistic objectives for fundraising were dashed and the organisation's board, with its competing interests, proved dysfunctional and unable to delegate or to agree where reductions in funding should be made. There were sharp anomalies in disbursements to richer middle-income countries and to disease programmes that did not offer the best returns for the money available.

Meanwhile, in the absence of more aggressive scrutiny by the fund's auditors in each recipient country, an overenthusiastic inspector-general at its Geneva headquarters gained free rein. He launched and made public aggressive inspections that gave an exaggerated impression of mismanagement and corruption.

Furthermore, miscommunication – if not misjudgment – in fees paid to a friend of the fund's high-profile ambassador, Carla Bruni – wife of then French president Nicolas Sarkozy – provided grist to the mill for domestic and international political feuds alike.

Bernard Rivers, ex-head of Global Fund Observer, a newsletter published by Aidspan, a watchdog for the fund, says: "It had a terrible 2011 and if 2012 were as bad it probably would have been the end of the fund. But that did not happen. It is in a stronger position than a year ago because of its very committed acceptance of the need for reform. It is time for version 2.0."

With the fund's interim appointment as general manager of Gabriel Jaramillo, a Colombian banker who took part in a commission that reviewed the fund in 2011, internal reforms were launched to strengthen management and refocus staff on the organisation's priorities.

The board itself has adopted a new governance approach and delegates more decision-making on grant management. Renewed emphasis is on targeting the poorer countries most in need and the programmes most likely to make a difference.

As important was that the fund agreed the appointment of a new executive director from a shortlist of four, in far less acrimonious circumstances than in the past. Mr Dybul brings experience as a doctor, scientist and manager, notably as a previous head of Pepfar, former US president George W. Bush's bilateral Aids programme focused primarily on Africa.

> Dybul has to prepare for a fresh round of fundraising while global austerity continues

"I am very excited," Mr Dybul says. "If we use the tools we have today in a very strategic way, focus on high-risk populations and in hotspots of the epidemic geographies, we can make a difference."

His challenges are far from over. Mr Dybul triggered opposition from some activists, notably for having to implement US policy at Pepfar that undermined organisations best equipped to tackle some aspects of HIV by requiring them to condemn prostitution.

He needs to prepare for a fresh round of fundraising – set for autumn 2013 after two delays – of $10bn-$15bn, while global austerity continues and governments with shallow pockets and short attention spans look elsewhere in the faddish world of development.

He inherits a new grant system that relies on external partners to help prepare and scrutinise applications and will have to make unpopular decisions over how best to spread limited resources. The task will not be easy, but at least the fund has bought Mr Dybul a little time to deliver.

Innovative aid Tracing a path to recovery in rural South Africa

Sisa Dyantyi, right, is a 'tracer' who looks in rural areas for patients who fail to continue taking medication that could save their lives – people such as Ntombencinci Duma, left, a young mother who stops her treatment when she feels better. Tracing is an important part of the work of the Donald Woods Foundation (www.DonaldWoodsFoundation.org) and has ensured that 93.6 per cent who start treatment continue with it. Susan Winters Cook

Technology offers hope for rich and poor

Diagnostics

Speeding up market entry will help save thousands of lives, says *Sarah Murray*

While access to antiretroviral medicines across the world has transformed life for millions of infected individuals, attention is focusing on the potential of improved diagnostic technologies to slow the spread of the disease.

There is plenty of catching up to do. "Diagnostics is the most undervalued intervention," says Renuka Gadde, senior director of global health at Becton Dickinson, the medical devices company. "Funding is typically a fraction of healthcare spending even though the results of diagnostics tests influence 60 to 70 per cent of patient management decisions."

However, given the dramatic shifts in the disease and its treatment over the past decade, the issue of testing is attracting increasing attention.

"In the past eight years, diagnostics has moved up the agenda massively and is seen as one of the key interventions," says Yusef Azad, director of policy and campaigns at the UK's National Aids Trust.

First, new technologies are making testing cheaper and easier. And because treatment of the disease is now effective, there is less resistance among individuals to being tested.

"In the early days, testing was treated with suspicion because there was no gain," says Mr Azad. "Now, it's become immensely important."

This is because the earlier an individual who is HIV positive can be diagnosed and started on treatment, the better are his or her chances of living longer and more healthily.

"If you're diagnosed late, you're 10 times more likely to die in the first year and if not, your immune system is permanently impaired," says Mr Azad.

However, the importance of HIV goes beyond helping infected individuals to get treatment early. Increased testing offers a broader public benefit because, once on therapy, individuals are far less likely to transmit their infection.

The technology has moved ahead rapidly. Tests are now able to identify infection far earlier, with the time during which HIV cannot be detected falling from three months from infection to a month.

At the same time, rapid point-of-care testing means individuals no longer have to wait for blood samples to be sent to a lab before getting the results but can get them in as little as 20 minutes.

A further step has been taken in the US, where home testing kits – which operate in a similar way to home pregnancy tests – have been approved for use.

Concerns have been raised about home testing. Some have questioned their accuracy and the increased room for error when testing is no longer in the hands of healthcare professionals.

Others worry about the potential for individuals to coerce their partners into taking the test – or even test them surreptitiously – as well as the risk of suicide among individuals who find they are HIV positive but have no psychological support at hand.

Mr Azad believes that such risks are outweighed by the benefits of home testing. He would like to see the kits approved for use in the UK.

"This technology is out there and is being accessed. We can't pretend it doesn't exist," he says. "It would be better to regulate it and explain it – rather than letting people go online and take up kits with no regulatory approach."

Mr Azad stresses, however, that home testing kits – as do pregnancy tests – should come with a clear message that the home test is only a first step.

"I don't want to dismiss the concerns about accuracy," he says. "And there are challenges. But none of these reasons, from a statistical point of view alone, are enough for us not to provide people with an effective technology to reduce the harms of HIV."

Efforts to offer rapid and accessible testing more widely are not limited to developed countries. Several companies are developing affordable point-of-care testing for the developing world.

Next year, for example, Becton Dickinson is launching a technology it calls FACSPresto, designed for use in places with limited healthcare resources.

With a touch screen interface that is very easy for a technician to use, the solar powered device comes with an integrated micro-printer and has data transfer capabilities. It uses dried reagents that, unlike liquid versions, have a longer shelf life and do not require refrigeration.

> 'If you're diagnosed late, you're 10 times more likely to die in the first year'
> **Yusef Azad, National Aids Trust**

The global public sector is directing more investment into promoting affordable point-of-care-testing and decentralised diagnostic products for the developing world.

In July, $140m in funding for the development of such technologies was announced by Unitaid, a multi-government health initiative that directs funds towards initiatives combating HIV/Aids, malaria and tuberculosis.

The idea is to create incentives to develop new products and to speed up market entry for manufacturers with tests that are in late-stage development.

Ms Gadde believes such initiatives are critical when it comes to tackling the spread of HIV-Aids in low-income countries.

"In the developing world, everyone is talking about point of care technologies," says Ms Gadde. "Because this is the only way to increase access in semi-urban and rural settings."

Death toll could be reduced by going after TB

Tuberculosis

Health experts see co-ordinating treatment as crucial, reports *Andrew Jack*

When it comes to tracking down people infected with one of the world's most lethal diseases, it is starting to seem as though the lawyers are doing a better job than the doctors.

With decades of tuberculosis infections in miners sparking intensifying court actions for compensation – notably in southern Africa – legal experts are eager to find plaintiffs to recruit for lawsuits.

Companies and governments are only belatedly starting to respond.

Miners with TB, frequently also struck with HIV and lung-crippling silicosis, return to their families rather than being diagnosed and treated close to their employers.

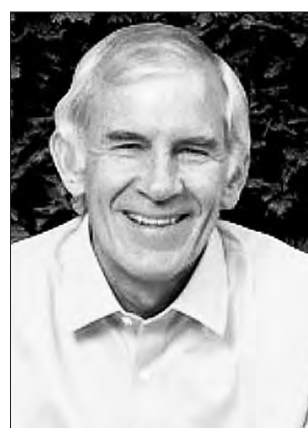
Many fall through the holes in fragile health systems and struggle to obtain compensation, especially if they work for subcontractors. Meanwhile, they spread the disease.

Infection in mines is at the centre of the epidemic of TB in sub-Saharan Africa, which is itself at the core of problems linked to HIV. Mine-related TB infections account for an estimated third of all TB in South Africa.

Yet compared with malaria and above all HIV, TB seems the most neglected and orphaned of the "big three" diseases and puts other people at greater risk than the rest.

Brian Brink, chief medical officer at AngloAmerican, will not talk directly about the mining litigation, but has no qualms about expressing his concerns over TB in South Africa.

"It's the face of the Aids epidemic," says Mr Brink. "It is difficult to diagnose and treat and if you get multi-drug resistant TB, it's a nightmare. With 16 people often sharing a taxi, you only need one person to cough and everyone is exposed to a resistant bug. It's scary."



Brian Brink, AngloAmerican

UNAids estimates that 430,000 deaths of people with HIV last year were linked to TB, as their failing immune systems made them more vulnerable to other infections. Of the 8.7m new cases of TB worldwide in 2011, 1.1m had HIV.

Only 48 per cent of people globally – and 46 per cent in sub-Saharan Africa – who have HIV and TB are receiving antiretroviral therapy, even though the medicines cut the risk of TB by two-thirds. Many go undiagnosed until it is too late for treatment or the prevention of infection.

Lucica Ditiu, head of the Stop TB Partnership, which brings together a range of multilateral agencies, non-profit groups and business, says: "The tools are there, we have the guidelines at the global level but we lack the implementation. There is very slow uptake."

A starting point is poor quality data to track progress. The World Health Organisation's latest annual report on TB gave global figures on the disease but did not break down the co-infection of TB and HIV by individual country in Africa, which is at the epicentre of the crisis.

Funding is insufficient. Many donors, including the US bilateral agency Pepfar, focus on HIV.

While Pepfar and others increasingly pay lip service to integration with TB, critics argue that most of those agencies giving money – or their implementing partners – remain too targeted on "vertical" HIV programmes.

Even the UN-backed Global Fund to Fight Aids, TB and Malaria has earmarked just 16 per cent of its nearly $3bn in annual disbursements for TB in the months ahead, significantly punching beneath the weight of support for the other two infections.

Ms Ditiu says this reflects poor advocacy, with TB patients' organisations – often the most marginalised groups in society and the most difficult for whom to garner external support and sympathy – less vocal and more ineffective in lobbying for more aid.

"It's very time consuming but we must negotiate to bring HIV and TB together like a forced marriage," she says, even while expressing fears that new funding structures just agreed for the Global Fund risk moving in the opposition direction.

A number of important things could be done. One would be mandatory TB testing of people with HIV.

A second would be to provide preventive treatment with the drug isoniazid for those without active TB, to reduce the risk of the infection developing. A third would be to ensure those with both infections receive antiretroviral therapy immediately, even if they still have a relatively strong immune system.

There are signs of change. In August, heads of state and governments of the South African Development Community signed a declaration on TB within the mining community.

The International Council on Mines and Metal is convening its member companies to take stronger steps.

More broadly, a dozen heads of state recently pledged to meet a target of "zero deaths" from TB.

With vaccines ancient and inefficient, and drug treatment painful, lengthy and cumbersome, more research is required.

That said, more aggressive prevention, diagnosis and treatment could do more even with the crude instruments available.

Biggest obstacle is human behaviour

Continued from Page 1

Yet Alvaro Bermejo, director of the International HIV/Aids Alliance, a non-profit umbrella group, argues that, despite the UK Department for International Development's strong financial support for Aids prevention, it has abandoned its leadership role on such issues. "It needs to put its mouth where its money is," he says.

Much – perhaps too much – scientific excitement has focused on clinical trials and mathematical models pointing to enhanced value through new uses of existing antiretroviral medicines. One is "treatment as prevention", with use of drugs earlier after HIV is detected while the body's immunity remains higher.

That has demonstrated both improved patient health and reduced risk of infecting others, with potential for long-term savings in lives and costs. The downside, particularly in developing countries, is the greater up-front investment required in both drug delivery and diagnosis.

The second new use of existing approaches which has sparked much excitement is "pre-exposure prophylaxis", or giving drugs currently used for treatment to those without HIV, but at high risk of infection. The US Food & Drug Administration this year extended approval of Gilead's combination treatment Truvada for use in the US in this way.

Doctors will need to study how this works in practice. If it proves highly effective, there is a danger of "disinhibition", with individuals taking greater risks of infection in the belief that they are protected.

Giving medicines with side effects to healthy individuals also creates a different balance of risk against benefit. Poor compliance could spark resistance, increasing the difficulties in tackling treatment in the future. In poorer countries with limited access to drugs, it could create tensions between those with and those without HIV.

As the latest UNAids report indicates, five years into treatment, retention rates have fallen as low as 50 per cent in Malawi. That highlights broader concerns over the difficulties of patients receiving, taking and having support while on medication.

Brian Brink, chief medical officer at AngloAmerican, the mining group active in South Africa, says: "It's now down to implementation. We can have drugs, but if the health systems are not functioning well, the response will be compromised."

A remaining issue is funding. As Mark Dybul, the newly appointed head of the Global Fund to fight HIV, TB and Malaria, the multilateral financing agency, argues: "We have the tools within our grasp. If we don't act now, infection rates will go back up and the costs may not be affordable. Not to use them right now is unconscionable."

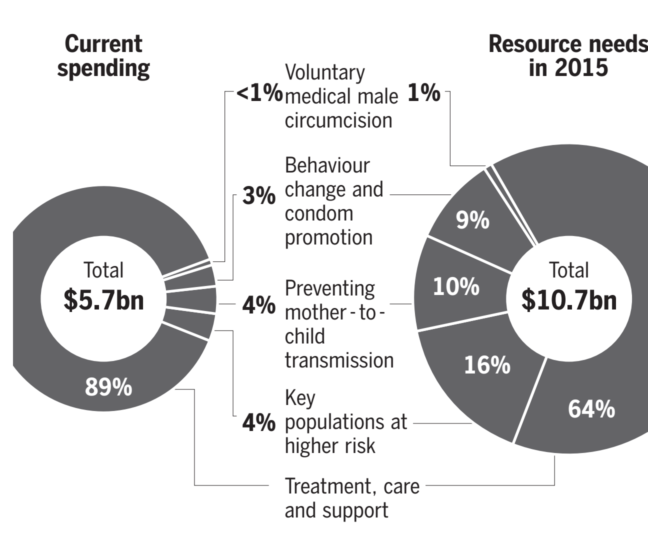
He is bracing for a new round of fundraising next year from donors of $15bn or more over three years. He points to middle income countries such as China, Nigeria and South Africa taking more responsibility for funding programmes themselves. He sees potential for innovative financing such as matching funds from regional development banks, companies and even social impact bonds to tackle HIV.

Mr Sidibé warns of the need to integrate HIV programmes with TB and chronic diseases to sustain momentum as leaders mull over replacements to the Millennium Development Goals in 2015, which have helped mobilise support.

The mere fact that this year's Aids conference could be held in the US reflected President Obama's first-term achievements, including removal of a travel ban on those with HIV and sustained commitment to foreign funding, despite financial pressures.

Much more work lies ahead. Getting the right prevention and treatment programmes along that "last mile" to the remaining 8m people with HIV, especially in developing countries – and the many millions more who are at risk – will yet prove the hardest obstacle to overcome. The Aids-free generation has yet to be born.

Mismatch: spending and needs on people-centred programming in low and middle-income countries



Source: UNAids Global Report 2012

Researchers explore avenues to flush out HIV

Treatment Stunning discoveries have revolutionised outcomes for patients but doctors say prevention is still best strategy, writes *Alan Rappeport*

Hopes of finding a cure for HIV were raised two years ago, when it was revealed that a patient being treated in Germany had been cleared of the virus after receiving a bone-marrow transplant in 2007. This raised the possibility that defeating Aids was a step closer.

Known as the "Berlin patient", Timothy Brown, who had leukaemia and HIV, received the transplant from a donor who had a rare genetic mutation that made him resistant to HIV.

Mr Brown remains free of HIV, and his case has opened the possibility of replicating that success through gene therapy in other infected patients without the risks of bone-marrow transplants.

"It is extremely expensive and risky and not easy to get that resistant bone marrow, but it is a proof of the principle that it is possible to cure somebody," says Ned Landau, a microbiologist at the New York University School of Medicine.

HIV has been among the most challenging diseases to control because it can be transmitted sexually, during birth, through blood transfusions or through the sharing of needles. However, better drugs and improved access to treatment helped to reduce Aids-related deaths globally by 25 per cent between 2005 and 2011, according to the UN.

In Mr Brown's case, the donor was a rare person who lacked a protein known as CCR5, which sits on immune cells and acts as a gateway for HIV. "Gene therapy means introducing DNA into the cells of a person to instruct the cells to make different proteins they need," Dr Landau says. "Proteins can target a gene in the genome and destroy it."

Survivor: Timothy Brown, the 'Berlin patient', with German oncologist Gero Hütter, right, answering questions at a symposium in Marseille this summer Getty

Other potential avenues for curing HIV include attacking "latent reservoirs" of the virus that hide when a patient is being treated with antiretroviral drugs.

Such drugs have been very successful at turning HIV, which was once a death sentence, into a chronic illness. However, when a patient stops taking the costly cocktail of drugs, latent pools of T-cells infected with HIV re-emerge. Researchers are looking for ways to coax these infected cells out of hiding so that the immune system can fully attack the virus.

Scientists in Australia are investigating the ability of a drug – disulfiram – used to treat alcoholism to flush out latent HIV-infected cells. "This study will increase our knowledge of the potential for this strategy – reversing HIV latency and targeting resulting virus outgrowth with antiretroviral therapy – to cure HIV," says the Foundation for Aids Research, amfAR.

Progress is also being made in antiretroviral therapies. ViiV Healthcare, which is owned by GlaxoSmithKline and Pfizer, recently reported encouraging phase-three trial results for dolutegravir, which is designed to block viral DNA from integrating with T-cells, a key step in the HIV replication cycle.

In August, the US Food and Drug Administration approved a drug from Gilead Sciences to be sold under the brand name Stribild. It is a cocktail of four components, reducing the need for patients to take multiple doses of the individual ingredients.

Despite such signs of breakthroughs, a 2011 report by the Treatment Action Group, an Aids research policy organisation, said drug trials were a difficult proposition for infected patients: "If treatment interruptions are necessary, how can they be conducted safely in research participants when prevailing data suggest even relatively short treatment interruptions can be harmful for some?"

Dr Landau suggests a cure for HIV is still many years away. Due to the risks associated with drug discovery and the virus's continued elusiveness, Aids advocates continue to suggest prevention is the best policy.

An advisory group to the FDA recommended in November that all Americans between 15 and 65 should be tested for HIV. Because earlier treatment with antiretrovirals reduces the chances of the virus spreading between sexual partners, testing for a broader swath of the population could be in the interest of public health.

"Targeted screening misses a substantial proportion of cases, and treatments are effective in patients with advanced immunodeficiency," according to a new study in the Annals of Internal Medicine. "New evidence indicates ART [antiretroviral therapy] reduces risk for Aids-defining events and death in persons with less advanced immunodeficiency and reduces sexual transmission of HIV."

Pre-emptive strike to help stave off infection

Prevention

Truvada has caused controversy but it has many benefits, says *Sarah Murray*

Taken daily, Truvada is among the treatment options available to those with HIV-Aids. However, following its approval in the US to pre-emptively reduce the risk of infection, the question is how to maximise the drug's potential to fight the disease and minimise the risk of increasing infection rates.

The US Food and Drug Administration's approval of Truvada – made by Gilead Sciences – for pre-exposure prophylaxis (PrEP) has not come without controversy.

Some, such as the Aids Healthcare Foundation, have questioned whether healthy individuals should be given a drug whose side effects include liver and bone problems, and have suggested that pre-emptive use of the drug would increase risky behaviour.

Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, admits that risks do exist. "To think that there's no risk when you have an intervention for something as serious as this is not being realistic," he says.

Dr Fauci points out that during trials of the drug as a prophylactic, participants were closely monitored for changes in sexual behaviour. "You could assume that it could happen and you've got to be alert for it," he says. "But we did not see it in the studies."

It remains to be seen whether the results of the trials, in which sexual acts were self-reported, are mirrored in the real world.

"We know that self-reporting isn't great," says Howard Jaffe, president of the Gilead Foundation. "So that's still something that needs to be monitored." Moreover, for the drug to play a role in combating HIV transmission, it needs to be deployed in combination with other methods. "It's not a substitute for other modalities, such as the proper use of condoms," says Dr Fauci.

He stresses that individuals need to be regularly tested for HIV. "If you're already infected, you could have the unintended effect of selecting for a resistant virus that you already have," explains Dr Fauci.

And because effective protection depends on maintaining levels of medicine in the body, it must be taken consistently.

This is easier said than done. Certainly, Truvada is a relatively simple drug to take. A once-daily pill, it comes with no restrictions as to the time of the day or circumstances under which it should be taken.

> 'You're asking people to take medications for something they can't feel'

However, taking PrEP is not motivated by the desire to reduce pain or discomfort, as with treatment medications.

"You're asking people to take medications for something they can't feel – and they might even feel a little worse – for some future benefit," says Dawn Smith, a medical officer in the division of HIV-Aids prevention at the US's Centers for Disease Control and Prevention (CDC). "That's more of a challenge."

Despite the obstacles, some argue that the PrEP approach could have a significant impact in slowing the spread of the disease.

"If properly used, and people are educated to make it clear that it's not a substitute for other prevention modalities, the potential for this approach to have a beneficial effect in selected groups far outweighs the risks," says Dr Fauci.

And protecting high-risk individuals against infection has a knock-on effect – while they are not infected there is no risk of their passing on the disease.

Two major groups are seen as appropriate candidates for the drug – men who have sex with men and practise high-risk behaviour, and people in heterosexual relationships in which one partner is HIV positive and will not or cannot take medication for the condition – including those trying to start a pregnancy.

Healthcare providers will play a crucial role in selecting candidates for PrEP, testing them for HIV and encouraging them to take their pills regularly. And since the PrEP approach is designed for people who are not HIV positive, general healthcare practitioners need to be educated to help them.

"Uninfected people don't go to the HIV clinic – they go to a general care provider," says Dr Smith. "So we're in the very early days in figuring this out."

Guidelines produced by the CDC explain how healthcare professionals should go about determining patients' eligibility, and ensuring that they keep taking the drugs and submit to regular testing.

But, since healthcare providers can only advise people who come to them, the question for policymakers is how to encourage high-risk individuals to enter the healthcare system and take the medication.

"That's very difficult," says Mr Jaffe. "In the US there's access to local community clinics, but whether you go or not is a personal decision. How you change that is going to be important in moving the needle."

Contributors »

Andrew Jack
Pharmaceuticals Correspondent

Alan Rappeport
US Consumer Correspondent

Amy Kazmin
South Asia Correspondent

Clive Cookson
Science Editor

Sarah Murray
FT Contributor

Aban Contractor
Commissioning Editor

Steven Bird
Designer

Andy Mears
Picture Editor

For advertising details, contact: **Ian Edwards** on +44(0)20 7873 3272; email Ian.Edwards@FT.com or your usual FT representative

All FT Reports are available on FT.com at ft.com/reports

STARBUCKS Coca-Cola beats by dr.dre BELVEDERE VODKA CONVERSE GAP mophie DELL SHAZAM TOURNEAU FEED fatboy U2 BOTTLETOP Microsoft Hallmark TOUS NANDA HOME

The Global Fund
To Fight AIDS, Tuberculosis and Malaria

THANKS (RED)™ PARTNERS FOR
$200 MILLION TO FIGHT AIDS

Help us deliver an
AIDS FREE GENERATION by 2015.
It's time for #thebigpush

SAP EMPORIO ARMANI bugaboo AMERICAN EXPRESS Penfolds telcel Damien Hirst & the (RED) Auction Supporters Claro

Scientists turn attention to prevention and cure

Research

Focus is on vaccines over antiretrovirals, writes *Clive Cookson*

"Getting to zero" – meaning no new infections or deaths from HIV – is the slogan for World Aids Day. Until recently such a target would have seemed absurdly ambitious. Even now, with 1.7m people dying of Aids and 2.5m newly infected with HIV in 2011, we are years from being close to achieving it.

But researchers are more optimistic about the prospects for preventing infection of people who are HIV-free and eventually eradicating the virus from those who are infected – "curing" them.

Drug combinations known as highly active antiretroviral therapy, or HAART, are keeping millions of people with HIV in reasonable health and free of serious Aids symptoms. Such treatment, which for most people must continue for life to keep the disease at bay, comes at a cost – not just the financial cost of the drugs, but also their side-effects. For example, a recent study by Johns Hopkins University suggests an important component of HAART – efavirenz (sold by Bristol-Myers Squibb, the pharmaceutical company, as Sustiva) – may contribute to cognitive impairment by damaging brain cells. Almost half of people with HIV will eventually develop mild neural damage.

It had been assumed that the infection itself was causing the trouble, but Norman Haughey, the study leader, says the drug may play a key role.

"Some people seem to have the attitude that HIV is no longer a death sentence," he says. "But even with antiretroviral treatments people infected with HIV have a shorter lifespan and the chance of cognitive decline is high."

Such research highlights the importance in the long run of moving beyond lifelong drug treatment to prevention and cure.

While traditional non-pharmaceutical methods to prevent infection, such as safe sex, remain important, HIV vaccine development is still agonisingly slow. Even though $845m was spent on HIV vaccine research and development in 2011, according to UNAids, only one vaccine is undergoing a clinical trial beyond early-stage safety testing.

The largest HIV vaccine trial to date, the RV144 trial, which tested a combination of two vaccines in Thailand, reported a modest 31 per cent efficacy in 2009. Subsequent analysis of the results is teasing out clues about what worked, and what didn't, but follow-up trials with an improved version of RV144 are unlikely to start before 2014.

Participants in the Aids Vaccine 2012 conference in Boston, Massachusetts, in September agreed large-scale production of a prophylactic HIV vaccine was well over a decade away under best assumptions.

There is, therefore, renewed scientific emphasis on pharmaceutical prevention, either through treating people with HIV to stop

> Antiretrovirals come at a cost – not just the financial cost of the drugs but also their side-effects

them passing on the virus or by treating uninfected people. Here, the news is better.

The journal Science named "HIV treatment as prevention" as its "breakthrough of the year" for 2011 in all fields of research. A $73m clinical trial by the HIV Prevention Trials Network demonstrated that early initiation of antiretroviral therapy in people infected with HIV reduces transmission of the virus to their partners by 96 per cent – a far larger impact than virologists had expected.

Then, in July 2012, the US Food and Drug Administration approved the first HIV-prevention pill. The FDA said Truvada, produced by Gilead Sciences and used for years to treat HIV-positive patients, could be prescribed for uninfected people at high risk of acquiring HIV from infected partners.

There had been concern that Truvada would be less effective in the real world than in clinical trials at preventing transmission, because people would not stick to a regimen of one pill a day. But further research published in September showed rigid adherence was not necessary.

"Even in patients who didn't adhere perfectly, their risk of contracting HIV still dropped by more than 90 per cent, offering a high level of prevention," says Robert Grant, professor of medicine at the University of California San Francisco.

Meanwhile, scientists continue their quest for a cure that would eradicate HIV or at least ensure the virus remains so deeply buried in a patient's genome that it does not reappear when he or she stops taking antiviral medication.

The famous "Berlin patient" Timothy Ray Brown demonstrated the possibility of a cure by undergoing a bone-marrow transplant from a donor with a rare genetic mutation that made him immune to HIV infection; Mr Brown has been HIV-free for five years off drugs.

Such transplants are too complex and costly to become a routine cure, so scientists are seeking to achieve the same effect pharmaceutically, perhaps with one drug to dislodge dormant HIV hidden in the immune system and the other to kill the virus.

Budget shifts raise fear of lost momentum

India

Focus switches to general campaigns, says *Amy Kazmin*

In the global battle against HIV and Aids, India is an unlikely success story.

After years of denial and squabbling with the world over the magnitude of its Aids epidemic, India launched a pragmatic campaign targeting high-risk groups with information and services to stop the spread of the virus.

Despite its deep social conservatism, India reached out aggressively to spread the message about Aids, and encourage condom use among sex workers and their clients, injecting drug users, and men having sex with men. These programmes – mostly internationally funded and many implemented by members of the affected communities – paid off.

India is one of just 25 countries that has turned the tide of its Aids epidemic, reducing its annual rate of new infections by more than 50 per cent over the past decade – from some 270,000 in 2001 to 120,000 now.

Aids prevalence has dropped to about 0.3 per cent, and the epidemic has remained concentrated largely in high-risk groups. In the past few years, India has also scaled up its treatment programme and now has about 400,000 patients receiving free antiretroviral drugs at special clinics.

Yet India's battle against Aids is far from won. With an estimated 2.1m people still living with HIV – one of the biggest Aids burdens of any country – India faces a threat from the virus for years to come. But, as international funds for its Aids programme taper off, the country is now shouldering most of the cost itself.

This dramatic shift in funding – combined with an apparent new aloofness, and change in priorities, by the National Aids Control Organisation (NACO) – has raised anxiety among many public health professionals, who fear India's impressive gains against the virus are in danger of being lost.

"The danger with HIV is that if you stop investing heavily in prevention, it will rebound – and it could rebound very badly," says Charles Gilks, UNAids country co-ordinator for India.

Over the past five years, international donors and the government together have spent about $2bn on prevention and treatment of Aids. New Delhi plans to allocate an equal amount, from its own coffers, for its Aids programme over the next five years.

But treatment costs are rising sharply, as more people who have been living with the virus for years fall sick and require life-saving drugs. India is also changing treatment protocols so HIV patients receive antiretrovirals at an earlier stage of the illness.

That means up to 1m people could be on treatment within the next few years. But, with the budget designated for Aids being flat, health professionals worry that a much-needed expansion of treatment will inevitably be at the expense of prevention efforts.

"I am worried about complacency and losing political drive," says Dr Gilks. "As soon as politicians think Aids is beaten, they will cut back."

K Sujatha Rao, former head of NACO, is upset authorities are reducing their once intense strategic focus on high-risk groups – where the epidemic remains concentrated – and appear more interested in mounting public awareness campaigns for the wider population.

"There is a change in direction, emphasising general information rather than focusing hard on the vulnerable groups, and pushing them hard for behavioural change," Ms Rao says.

Yet, she says, such a loss of strategic focus is likely to backfire badly. "We did general information campaigns for 10 years and failed to have an impact."

New Delhi is also planning to shift some of the burden for its fight against Aids to other parts of its public health system,

> There is concern rural volunteers are ill-prepared to deal with marginalised high-risk groups

including the National Rural Health Mission, an initiative to strengthen its crumbling public health system in rural areas.

But activists are concerned that volunteer rural health workers, trained in basic issues such as sanitation, hygiene and promoting immunisation, are ill-prepared to deal with marginalised high-risk groups or people living with Aids.

"I don't think there has been enough sensitisation," says Anjali Gopalan, founder of the Naz Foundation, a New Delhi-based Aids campaign group that works with men who have sex with men, and other sexual minorities. "There is still huge stigma around HIV," she says.

Meanwhile, civil society groups, once considered crucial partners in fighting Aids, complain of being excluded from preparing India's new national Aids control strategy for the next five years.

All told, Ms Rao fears the government is losing its sense of urgency and momentum in the battle against Aids, as international interest and funds wane.

"The passion is lacking, as is the commitment to see the end of the road of HIV and Aids," she says. "Globally there is a reduction of interest in HIV, but we have a huge burden of 2m people living with the virus. We cannot let down our guard."

US capital goes on campaign trail to tackle its epidemic

Washington DC By raising HIV awareness, the city aims to lose its tag of being on a par with a developing country, reports *Alan Rappeport*

Washington may be the US capital, but when it comes to the prevalence of HIV, the city's problem has been compared with a developing country.

Nearly 3 per cent of Washington residents are living with HIV and the city has a higher Aids diagnosis rate than any state in the country. The rate of infection exceeds those in some African nations, casting a blemish on the ability of the world's richest country to deal with its own public health epidemic.

"Washington is one of the areas hardest hit by HIV in the US, with an epidemic on par with some developing nations," the Henry J Kaiser Family Foundation, the health policy analysis organisation, said in a recent report.

While HIV prevalence in the US has improved in recent years, it remains a stubborn problem. The Centers for Disease Control and Prevention, the US federal agency, estimates 1.2m people are living with the disease and 20 per cent of those are unaware they are infected. The number of new infections each year has stabilised, according to the CDC, but still hovers around 50,000 cases a year.

The HIV problem in Washington is usually attributed to the city's high poverty rate, a relatively small population, a growing gay population and widespread drug use. These factors have been coupled with inadequate infrastructure for HIV testing and prevention services in high-risk areas. Aids activists also blame weak data about the severity of the problem, combined with poorly directed funding, for exacerbating the epidemic.

"The local public health and policy response has not controlled the HIV epidemic in the District of Columbia," according to a 2009 study in the journal Health Affairs.

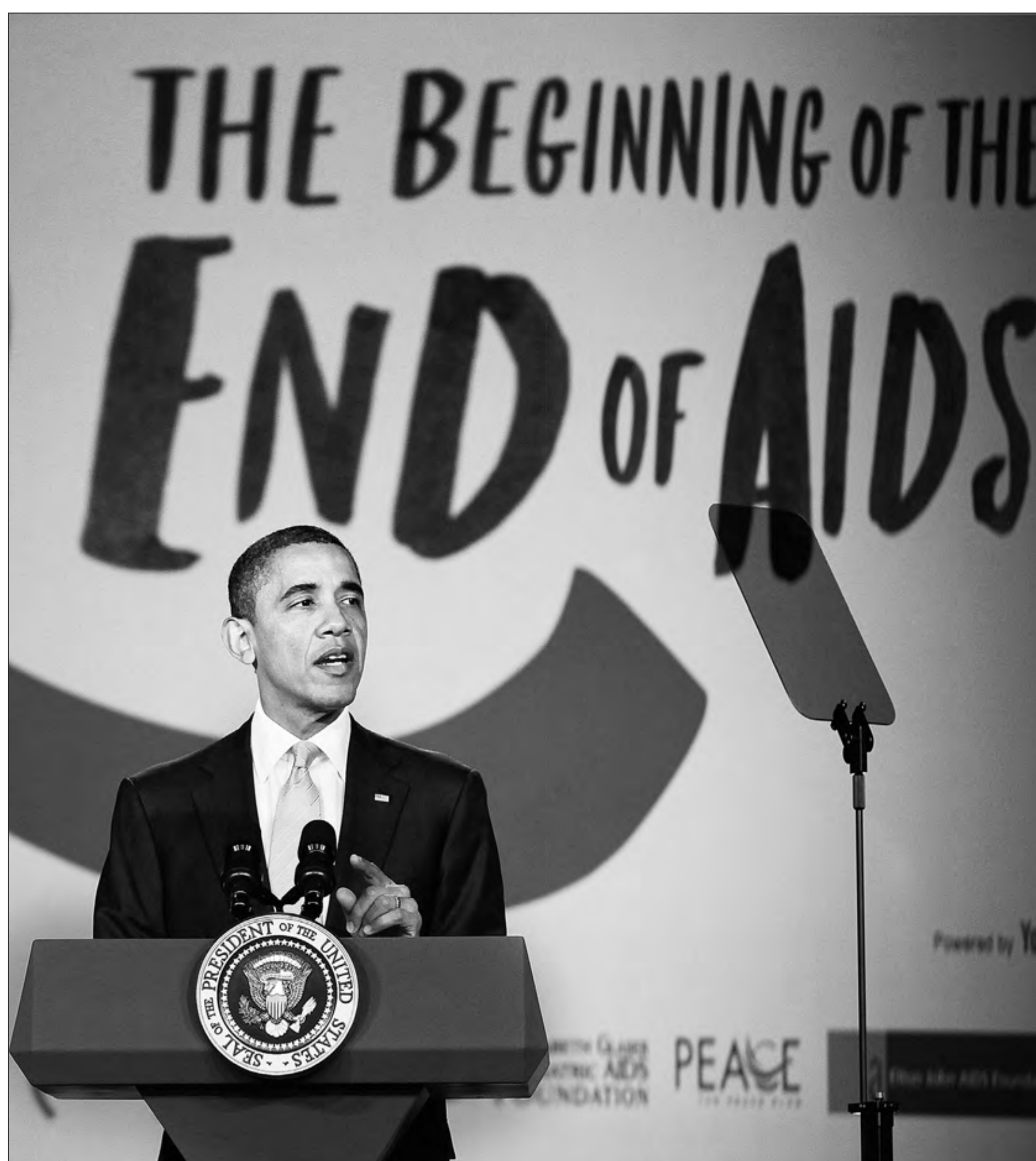
At the time, Washington's Aids problem was on a scale similar to that faced by San Francisco in the 1990s. The virus was most prevalent among African-Americans, who had an infection rate of 7 per cent. Homosexual transmission between men, followed by intravenous drug users sharing needles, was the most common way in which HIV spread.

The picture has improved in recent years, as HIV has became a priority for the city's past two mayors and public spending on testing and prevention has increased. Washington has implemented automatic HIV testing in hospital emergency departments and prisons, and has launched an aggressive campaign with the slogan "DC takes on HIV".

Beyond awareness, Washington has ramped up distribution of condoms in the highest-risk parts of the city. It became the second city to launch a major condom distribution programme, giving out millions of condoms at places such as liquor stores, malls and hair salons. Washington has also started using public funding to promote needle exchange programmes, which aim to give drug users access to clean needles.

Drugs companies have also pitched in, raising awareness of the HIV problem with local physicians. Medical schools, such as the one at George Washington University, have made

> Health experts warn that many HIV patients are still not getting proper treatment



View from the top: Barack Obama, US president, speaks at George Washington University on World Aids Day, 2011 Getty

HIV prevention a more central part of the curriculum. A report last summer from the District of Columbia Department of Health showed signs of improvement. From 2006 to 2010, the number of new Aids cases fell 32 per cent to 477 and the number of deaths among people with HIV halved to 207.

"We are getting people diagnosed with HIV infection earlier and directly into care with our treatment-on-demand policy," Vincent Gray, Washington's mayor, said in June. "Through uniting government agencies with private-sector health experts and community organisations – via vehicles like the Mayor's Commission on HIV/Aids – we are creating solutions to curb the HIV infection rate in our city."

Despite that progress, health experts warn many HIV patients are still not getting proper treatment and hundreds of residents are still contracting the virus each year.

"Seven in 10 DC residents diagnosed with HIV have a high level of HIV in their blood, often due to not being on HIV medications, which means they can more easily infect other people," says Raymond Martins, chief medical officer at Whitman-Walker Health, the healthcare provider. "We have a long way to go to reach the ultimate goal of having every HIV-positive resident on medications to maintain their health and prevent transmission."

The US National Institutes of Health, the research centre, is working with the DC health department to extend the city's recent gains. NIH has spent more than $11m on the programme so far, which aims to ascertain why HIV is so prevalent in black communities. The investment is also being used to collect information electronically about HIV monitoring at clinics throughout the city and to understand better which prevention measures are working.

"The District of Columbia still has one of the highest HIV prevalence rates in the country, with roughly 2.7 per cent of adults and adolescents infected," says Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases.

"Our ongoing research collaboration with the District is a commitment to find and improve the methods that work on a community level by funding studies designed to ease the HIV/Aids burden for the residents of this city – and potentially other communities."

Change in attitude is needed to prevent unnecessary human tragedy

Opinion
Michel Kazatchkine

UNAids figures released last week on the global HIV/Aids epidemic confirm the very encouraging trend of the past five years: fewer new infections, fewer deaths and increasing coverage (55 per cent globally) of those in need receiving antiretrovirals.

In many parts of the world we are "getting to zero" HIV and Aids (the slogan for World Aids Day), but the UN figures offer unsettling evidence that achieving this target will require the world's fastest growing epidemic, in eastern Europe and central Asia, to be overcome.

Only a decade ago some 150,000 people in this region were living with HIV. Today, that figure is 1.4m, with Russia and Ukraine accounting for 90 per cent of infections. Aids-related deaths have almost quadrupled in the past 10 years and the number of people receiving treatment is a lowly 23 per cent.

If urgent and measured action, based on scientific evidence is not taken here, we will be heading for a major human tragedy.

The epidemic is characterised by escalating HIV infection and startling hepatitis C, tuberculosis and multi-drug-resistant TB prevalence.

The region has the highest rate of injecting drug use in the world, accounting for two-thirds of new HIV infections there. It is mainly heroin-based, but increasingly involves the use of cocaine, amphetamine-type stimulants, psychotropic substances and home-made cocktails such as krokodil (desomorphine), a mixture of codeine-based painkillers and other cheap household ingredients.

Drug users in the region are often stigmatised and criminalised. Fear of arrest drives people away from testing and services. There are almost no needle exchange programmes and opioid substitution therapy (OST) with methadone or buprenorphine is illegal in several countries.

There is a high HIV prevalence among prisoners, particularly those with a history of injecting drug use, and women who, in the main, are the sexual partners of injecting drug users.

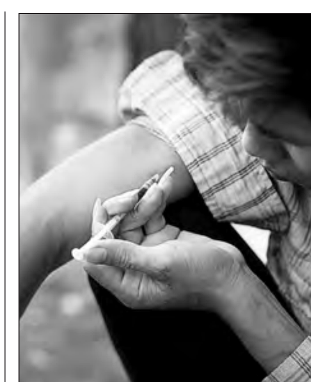
The scenario is bleak – but not hopeless. We have known that, over the past three decades, four major factors have determined our success in the fight against Aids worldwide: political commitment, adequate resourcing, strong involvement of civil society and affected communities; and the implementation of policies and practice based on evidence and science as opposed to prejudice and criminalisation.

We have known since the 1980s that the simple and cost-effective provision of clean needles and methadone prevents HIV and Aids from spiralling out of control among drug-using communities.

Encouragingly, several countries, including Ukraine, Kyrgyzstan, Moldova, Kazakhstan and Tajikistan, have engaged in harm-reduction programmes around clean needles and OST, leading to a decrease in new HIV infections.

In the past five years, the Global Fund to Fight Aids, Tuberculosis and Malaria has played a key role in the region, funding needle exchange programmes, OST and access to Aids treatment.

These programmes may be at risk soon if countries in the region, particularly those that are middle income, faced restrictions in access to international funding. Funding cuts would also reduce civil society's important role in promoting advocacy, legislative changes, and programme implementation.



Drug use spreads HIV

On the whole, however, leaderships in eastern Europe and central Asia remain silent on the epidemic. Civil society organisations and communities face increasing logistical, political and legal challenges. And resources from the international community are decreasing as many countries move to being middle income and therefore ineligible for programmes from organisations such as the Global Fund to Fight Aids, Tuberculosis and Malaria.

National governments have failed to pick up the financial slack and, too often, the investments that do happen, particularly in prevention, fail to reach communities at greatest risk of infection. The result is woefully inadequate coverage of the most vulnerable in terms of treatment and prevention, accompanied by an equally low return on investment.

The treatment of HIV and Aids in eastern Europe and central Asia is at a tipping point. We are barely three years from fulfilling the UN Millennium Development Goals of getting 15m people on treatment globally and reducing new infections among injecting drug users by 50 per cent. Eastern European and central Asian countries recommitted to these targets at the UN in 2011.

Only a change in mindset among the region's political classes towards a public health policy approach will save the region from a human tragedy.

Michel Kazatchkine is the UN special envoy for HIV/Aids in eastern Europe and central Asia.