FT HEALTH
Combating Aids

FINANCIAL TIMES SPECIAL REPORT | Thursday December 1 2011

A doctor writes . . .

Aids pioneer Michael Gottlieb looks back on 30 years tackling the disease and calls for fresh efforts **Page 4**

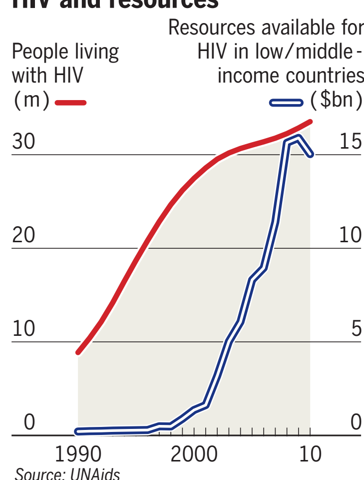
www.ft.com/aids-2011 | twitter.com/ftreports

Funding cuts put progress in peril

Research – led by the idea of 'treatment as prevention' – has made gains but results are coming more slowly, writes **Andrew Jack**

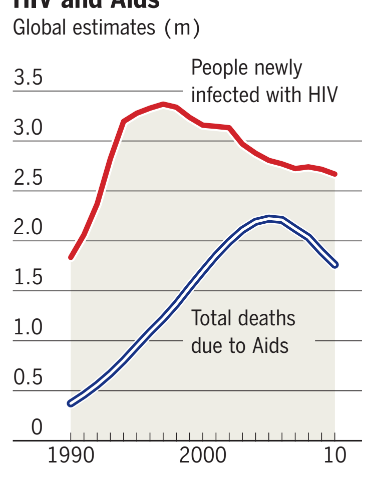
An HIV infected woman prepares her medicines Photo: Reuters

HIV and resources



HIV and Aids

Global estimates (m)



Estimated people living with HIV

By region, 2009 (m)*

Region	People living with HIV (m)
Sub-Saharan Africa	22.50
Middle East/North Africa	0.46
East Asia	0.77
South/South-East Asia	4.10
Oceania	0.057
Eastern Europe/Central Asia	1.40
Western/Central Europe	0.82
North America	1.50
Caribbean	0.24
Central/South America	1.40
Total	33.30

* Figures have been rounded

Three decades after the discovery of Aids, 2011 has been the best and the worst of times in tackling an epidemic that still kills 1.8m people every year.

It has marked a period of resurgent scientific advances, overshadowed by a backdrop of deep funding cuts that threaten continued progress and even a reversal in recent successes.

In a closely monitored speech last month, Hillary Clinton, the US secretary of state, talked about the possibility of "the end of Aids", stressing how fresh understanding offered the prospect for the first time to "get ahead of the pandemic" and put the world "on the path to an Aids-free generation".

After years of progress in developing and funding HIV drugs, patients – including for the first time almost half the 14m in need of treatment in developing countries – now have access to powerful antiretroviral medicines that are increasingly available in combinations as simple to take as a single daily pill to prolong life substantially.

Against that background, recent studies have reinvigorated the search for a cure, beginning with treatments that would need to be provided only every few months and eventually aiming to replicate more widely and cheaply the successful total elimination of the virus in Timothy Ray Brown, the "Berlin patient" *(see article on page 2)*.

Prevention research is also advancing steadily. Aside from continued gradual progress on an HIV vaccine, there has been a stream of positive findings on the use of antiretroviral medicines taken as both pills and gels to protect men and women from infection.

Most significant has been the idea of "treatment as prevention": putting patients on drugs also sharply reduces the risk of them infecting others. That has led to fresh calls for still earlier treatment, and the re-examination of life-long bans in many countries on professional practice by workers such as surgeons and dentists with HIV.

Yet implementation of research has proved disappointingly slow. One and a half years after the Caprisa study in South Africa suggested a nearly two-fifths reduction in infections in women using a microbicide gel, the prospect of the product being approved and distributed is at least two years away.

Professor Salim Abdool Karim at the University of KwaZulu-Natal, who ran the trial, says: "When you are constantly faced with failure, you don't plan for success. This is the period of greatest optimism. It would be really sad if governments and donors decided to pull back."

Yet the impact of the global economic slowdown is already being felt. For the first time in 15 years, 2010 marked a shift from fast growth to absolute decline in support for HIV in low and middle income countries, with total spending capped at $15bn and international assistance falling to $7.6bn.

Only last week in Ghana, at the most traumatic board meeting since its creation 10 years ago, the Global Fund to Fight Aids, Tuberculosis and Malaria, the largest multilateral supporter of HIV treatment and prevention programmes, resolved to postpone at least until 2014 its next "round" of funding.

That comes despite a renewed pledge from political leaders at the United Nations in New York in June to strive for "universal access" to treatment by 2015.

It threatens further momentum in many countries that were building capacity and expanding their efforts to tackle Aids, triggering fears of patients being turned away by clinics.

"Donors are really pulling the rug out from under people living with HIV/Aids at precisely the time when we need to move full steam ahead," warns Tido von Schoen-Angerer at Médecins sans Frontières, the medical charity, after the Global Fund decision.

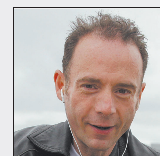
The new reality of austerity is sparking a long overdue debate on efficiency.

There are still some striking mismatches between spending and results. Male circumcision, for example, was shown to cut transmission by 60 per cent in the middle of the last decade, but since then only 500,000 procedures in sub-Saharan Africa have taken place, or less than 3 per cent of an initial optimistic goal.

Continued on Page 2

Inside this issue

Science A 'functional cure' has become the global target, inspired by 'Berlin Patient' Timothy Ray Brown (above) **Page 2**



Vaccines A broad approach is needed to counter HIV's variability **Page 2**

Circumcision Convincing Kenyan men to be circumcised can be an uphill battle **Page 2** In spite of evidence of the benefits, widespread adoption is yet to be achieved **Page 3**

Healthcare HIV treatment may conflict with family planning **Page 3**

Diagnostics The crucial role of testing is being stymied by high cost and poor access **Page 3**

Tranfusions Improved screening of donated blood can bring benefits far beyond the costs **Page 4**

Risk to patients Is a lifetime ban on HIV-infected doctors and dentists still fair? **Page 4**

Opinion The end of Aids is in sight, say Kenya's prime minister Raila Odinga (above), and Michel Sidibé, executive director of UNAids **Page 4**

Details of four more opinion articles on the battle to defeat Aids (available on FT.Com) on **Page 4**

At Chevron, we won't let up until the fight is won.
We'll continue our education and treatment programs.
Continue our support of The Global Fund to Fight AIDS, Tuberculosis and Malaria, whose programs have helped save 7.7 million lives so far.
We'll finish the fight we started 25 years ago.
Today, in Nigeria and Angola, we've gone seven years without one mother-to-child HIV transmission among our employees and their dependents.
And we recently committed $20 million to the new global plan spearheaded by UNAIDS and PEPFAR to eliminate new HIV infections among children and keep their mothers alive.
There is more to be done. And we're going to help do it.
Learn more at chevron.com/weagree

Proud Supporter of World AIDS Day

AIDS IS GOING TO LOSE.

WE AGREE.

Michel Sidibé
Executive Director
UNAIDS

Rhonda Zygocki
Executive Vice President, Policy and Planning
Chevron

A world first: Timothy Ray Brown, better known as the Berlin Patient, the first person to be cured of Aids through a medical procedure AP

'Functional cure' is global target

Science

The 'Berlin Patient' has become a living legend and inspired scientists to hunt for new solutions, says **Clive Cookson**

Even a couple of years ago, talk of "curing" Aids was regarded as dangerously over-optimistic. HIV was seen as a life-long infection that could be controlled by combinations of antiviral drugs but not cured.

Now a cure is on the agenda of every scientific meeting about HIV, and research funding agencies such as the Gates Foundation and US National Institutes of Health are providing grants explicitly to find ways for patients to stop taking drugs and live normally without medication.

The quest is personified by Timothy Ray Brown, better known as the Berlin Patient, who has become a living legend in the world of medical research as the first person to be cured of Aids through a medical procedure.

Doctors in Berlin eradicated HIV from Mr Brown, a 45-year-old American living in the city, through bone marrow transplants from a donor who was resistant to infection through a rare genetic mutation. This would not be practical for general use but its success, even in one case, has inspired scientists to look for ways to achieve the same effect without the risk, cost and complexity.

The Rome Statement for an HIV Cure, launched in July at this year's biggest scientific conference on Aids, called for a concerted international effort to achieve "at least a functional cure for HIV".

The term "functional" is crucial, because the way HIV can bury itself and lie dormant within the nuclei of human cells may make it impossible to remove all genetic traces of the virus from all parts of the body.

The important thing is permanently to remove enough of the virus and suppress viral replication, so that the patient's immune system works normally and symptoms of Aids never recur.

One approach, being developed by Calimmune, a Californian biotechnology company, is to replicate the natural resistance by treating the patient's cells through gene therapy. The idea is to remove a gateway protein called CCR5, which HIV uses to enter human T-cells, the primary target for viral infection.

This would be achieved by extracting and amplifying stem cells from the patient's blood, disabling their CCR5 genes through a genetic engineering technique called RNA interference, and then infusing them back into the patient.

> One approach is deliberately to activate the hidden reservoirs of HIV that lurk in immune cells

The treated stem cells will develop into new T-cells, resistant to viral attack, which will gradually take over the immune system as HIV kills off the original T-cells.

A clinical trial is due to start next year, with funding from the California Institute for Regenerative Medicine, to see whether gene therapy can reproduce the Berlin Patient cure. Even if this does not work, however, scientists are developing several alternative ways to rid the body – or at least the immune system – of HIV.

One popular approach is deliberately to activate the hidden reservoirs of HIV that lurk dangerously in patients' immune cells, temporarily suppressed by antiviral drugs but ready to come back to life when therapy stops. The idea is that, if the virus and/or infected cells are woken up, they can more easily be destroyed by drugs or the immune system.

A class of drugs called histone deacetylase inhibitors are the leading candidates to activate latent HIV, although extensive trials will be required to assess their safety and efficacy.

An alternative to activating the virus directly is to wake up infected cells. Interleukin-7, a natural promoter of T-cell proliferation in the body, is the favoured agent here. For example Orvacs, a French Aids research foundation, is running a clinical trial of interleukin-7 plus two antiviral drugs to see whether the combination can rid the immune system of HIV.

Then there are other proposals to target HIV-infected cells through gene therapy. For example Pin Wang and colleagues at the University of Southern California have created a viral vector that specifically targets HIV-infected cells and flags them for subsequent destruction by a drug.

The National Institutes of Health gave the field a boost in July. Its National Institute of Allergy and Infectious Disease announced three public-private partnerships aiming to develop HIV cures, which will receive $14m a year for up to five years.

- Fred Hutchinson Cancer Research Centre in Seattle, working with Sangamo BioSciences of California, will undertake five projects to develop proteins that directly attack HIV reservoirs and study whether a patient's immune cells can be made resistant to the virus.
- University of North Carolina working with Merck, the US pharmaceutical group, will undertake 15 scientific projects. The focus is to understand better how HIV persists in patients on antiviral therapy and to develop therapies to target the viral reservoirs.
- University of California, San Francisco, and the Vaccine & Gene Therapy Institute of Florida, also working with Merck, will have seven projects. They will define the nature and location of the cells where HIV hides and develop targeted treatments that eliminate HIV reservoirs without activating the whole immune system.

But Françoise Barré-Sinoussi, the French virologist who is president-elect of the International Aids Society, warns people not to expect too much too soon.

"While there is certainly a high level of interest being expressed about finding a functional HIV cure, it can only be achieved through an increased and concerted international effort engaging not only the scientific community but all stakeholders involved in the HIV/Aids response and global health," she says.

Vaccines Broad approach needed to counter HIV's variability

A current catchphrase in Aids vaccine research is "broadly neutralising antibodies" or bNAbs. These antibodies can protect cells from infection by many different strains of HIV, one of the most variable viruses known to science and therefore one of the most difficult targets for vaccine development.

Antibodies are large proteins that bind to pathogens such as HIV and flag them for destruction by the immune system.

The first bNAbs were isolated in 2009 from the minority of people infected with HIV whose immune system mounted a strong defence against the virus – and were recognised at once as a good basis for developing wide-ranging and effective Aids vaccines. Since then, scientists have isolated many more bNAbs, some of them much more powerful than the ones discovered originally.

The International Aids Vaccine Initiative, IAVI, is sponsoring a global search for bNAbs. In August its researchers published in the journal Nature a batch of 17 new antibodies isolated from the blood of HIV-positive volunteers in collaboration with the Scripps Research Institute, a non-profit US body engaged in biomedical science, and two US biotech companies, Theraclone Sciences and Monogram Biosciences. The best performers were 10 to 100 times more potent at blocking HIV infection of cells than bNAbs discovered previously.

"Most antiviral vaccines depend on stimulating the antibody response to work effectively," says Dennis Burton, director of the IAVI Neutralizing Antibody Centre at the Scripps Institute. "Because of HIV's remarkable variability, an effective HIV vaccine will probably have to elicit broadly neutralising antibodies."

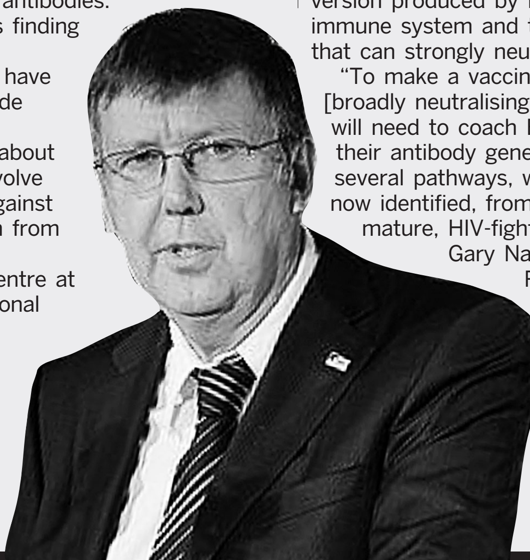
As well as finding new bNAbs, researchers have recently made important discoveries about how they evolve and work against HIV. A team from the Vaccine Research Centre at the US National Institute of Allergy and Infectious Disease (NIAID) found that a series of bNAbs all bind in the same way to the same spot on HIV.

This suggests that an HIV vaccine should contain a replica of this spot, known as the CD4 binding site, which has the huge advantage of being one of the few parts of the continuously mutating virus that remains unchanged in all variants.

The NIAID researchers also found that bNAbs evolve through an unusually large number of mutations – 70 to 90 – between the original version produced by B-cells in the immune system and the final version that can strongly neutralise HIV.

"To make a vaccine that elicits [broadly neutralising] antibodies, we will need to coach B-cells to evolve their antibody genes along one of several pathways, which we have now identified, from infancy to a mature, HIV-fighting form," says Gary Nabel, Vaccine Research Centre director.

Clive Cookson



Dennis Burton: it is important to stimulate antibodies

Uphill battle to overcome deep taboos

Case study
Kenya

Katrina Manson on efforts to win hearts and minds on circumcision

Since he was circumcised this year, 30-year-old Elisha Ouko is convinced he is a better lover. Keen to marry his long-term girlfriend, but all too aware he will never be faithful, he decided to undergo the procedure after health workers persuaded him it could reduce the risk of contracting HIV.

"It is difficult to stay monogamous; an open relationship is ideal for me; so this way I get to protect myself and my spouse. I'd hate to be the cause of her death," says Mr Ouko.

He used to sleep with one or two women a week in an arrangement he calls "hit-and-runs", and still sees three women regularly as well as the girlfriend he plans to marry next year, as soon as he can afford the 12 cows for her dowry. She is unaware she is in an open relationship.

Mr Ouko is among 323,479 Kenyan men who have been circumcised as part of an aggressive government-backed scheme promoting voluntary medical male circumcision since 2008. They account for more than half such circumcisions conducted in 13 target countries Africa-wide, including Botswana, Malawi and South Africa.

The World Health Organisation formally endorsed the practice in 2007, after indicative results from three medical trials in South Africa, Uganda and western Kenya, which showed circumcision may reduce male contraction of HIV from women by up to 60 per cent.

Several scientific studies since the 1980s argue the procedure removes Langerhans cell receptors that are densely packed into the inner foreskin and help the entry of the HIV.

Experts say circumcision also reduces the likelihood of open wounds that can absorb the virus during sex – by reducing abrasions and sexually transmitted infections that cause ulceration. It also hardens the remaining tissue, making it less sensitive and less easy for the HIV to penetrate.

"I'm a bit less sensitive than I used to be, but let's just say the game is better than before," says Mr Ouko.

A member of the Luo ethnic group, predominant in western Kenya's Nyanza province, he has overcome long-held taboos by agreeing to be circumcised.

Unlike 86 per cent of Kenyan men, who are often circumcised as part of initiation rites into adulthood, the Luo traditionally remove six lower teeth instead.

While Kenya's HIV prevalence rate stands at 12.9 per cent for uncircumcised men, it is 2.8 per cent for circumcised men.

Nationwide, the prevailing rate is 6.3 per cent for adults aged 15-49, but 20.2 per cent among the Luo. In Nyanza province, the traditional home of the Luo, it is 14 per cent.

Polygamous Kenyan men are more than twice as likely to have HIV as men married to one woman.

Hannington Onyango, field officer for Kenya's National Aids Control Council (NACC), also points out that "fish-for-sex" is widespread among Nyanza fishermen who rely on Lake Victoria.

As part of a rapid results initiative intended to reach 70,000 men during the long school holidays of November and December, mobile teams offer circumcisions by moonlight for daytime fishermen returning to shore. Sunrise procedures accommodate early-risers dodging city traffic, while clinics stay open all weekend. School rooms are commandeered; others work in mobile tents or jails.

Teams of "mobilisers" also seek out target groups. Lutgard Oluoch Oketch, for example, searches for Luos in Nairobi's garages, welding places and workshops.

"We might be doing well but we still have a long way to go – 500,000 more to do in two years," says Walter Obiero, director of the Nyanza Reproductive Health Society.

This year, he adds, 80 per cent of men the society has circumcised are 18-24, meaning it is not reaching enough men aged up to 49.

> 'It is difficult to stay monogamous; an open relationship is ideal for me'

The government has recruited prominent Luo role models to help overcome customary practice, including prime minister Raila Odinga, a Luo who openly says he is circumcised and will lead World Aids Day events in Nyanza.

Dr Obiero says many men worry about the pain of the procedure, abstinence required afterwards and whether it will affect sexual performance.

Long-term, the NACC hopes for a nationwide policy change to bring in circumcision at birth.

Studies show there is little benefit to women, so persuading wives and girlfriends to support their partners in what to some seems like a free card to play around can make the task harder.

Reducing the prevailing rate of HIV among men will help women in the long term, while circumcision also reduces the chance of infection with other sexually transmitted diseases, including the virus that causes cervical cancer.

Health workers hope there may be other reasons to persuade women. A 2011 survey found 92 per cent of Kenyan women preferred a circumcised partner, up from 72 per cent in 2009.

"We women, we take long: women are like slow cookers and men are like gas," says Ms Oluoch Oketch. "After circumcision, it takes a man some time, so a woman will at least enjoy."

Funding cuts put continued progress in peril

Continued from Page 1

Antiretroviral medicines to mothers and their newborn infants radically cut transmission to children, but remain woefully undersupplied. So do basic family planning services including the provision of condoms.

Testing remains insufficiently widespread, and is weakened where there is no integration with treatment programmes for those found to be infected with HIV. Cross-referrals with clinics handling TB – to which the virus is often linked – remain inadequate.

Such setbacks are not only problems of money, but reflect lack of political will, imagination or ability to focus on evidence.

With 2.7m new infections last year, the number of people living with HIV continues to rise, having reached 33.3m, even if the rate of growth has slowed in most countries.

As the UK gears up for the Olympic Games in 2012, for instance, condom donations have been arranged for visiting athletes. But Lisa Power, policy director at the Terrence Higgins Trust, says: "Many British people seem to think they are at risk from travellers, but they are at risk from [themselves]. The UK has one of the highest rates of sexually transmitted infections in western Europe."

Most worryingly, in the countries of eastern Europe and central Asia, treatment for those with HIV is less available than in most of Africa, while prevention programmes have failed to focus on the group in which the infection is concentrated in the region: injecting drug users. The result is one of the fastest-growing epidemics in the world.

UNAids, the specialist UN agency, has championed a new "investment framework" designed to target scarce resources more effectively in the coming years to save an estimated additional 7m lives and 12m infections by 2015. Michel Sidibé, its head, says: "We need a new paradigm. We need to be smarter using the resources we have."

Yet while models predict ambitious efficiencies from the framework, there is less information on or analysis of misallocation by countries and donors. That is essential to ensure money is spent better.

Stefano Bertozzi, head of the HIV programme at the Bill & Melinda Gates Foundation, says: "With funding flatlined, the only way to maintain and increase enrolment in programmes is by finding greater efficiencies."

His organisation was itself slow to focus on such issues, but is now examining cost-saving approaches. These range from long-lasting injectable reformulations and cheaper raw materials to cut drug costs, to more efficient procurement techniques and "task shifting" of treatment supervision to less costly community health workers.

A UN-backed "patent pool" has begun signing up academics and drug companies to share intellectual property, in the hope of reducing costs and stimulating different and child-friendly combinations.

Many activists continue to pin hopes on a Tobin-style financial transactions tax to raise more funds, while endorsing calls for richer middle-income countries to assume a greater share of HIV costs.

But with money tight, every new investment will require careful thought.

There is still as much wishful thinking as hard fact behind "treatment as prevention", and fresh findings last week undermined some of the potential of the Caprisa microbicide study.

As President Barack Obama gears up to host next year's International Aids conference in Washington, he will need all his political skills to focus not only on future dreams but also on current realities of doing more with existing approaches for less.

Contributors

Andrew Jack
Pharmaceuticals Correspondent

Clive Cookson
Science Editor

Katrina Manson
Nairobi Correspondent

George Cole
FT Contributor

Andrew Baxter
Commissioning Editor

Steven Bird
Designer

Andy Mears
Picture Editor

For advertising details, contact:

Julia Woolley
Phone +44 1473 652964
Fax +44 1473 652963
Email: julia.woolley@ft.com
or your usual FT representative

All FT Reports are available on FT.com. Go to: **www.ft.com/reports**
Follow us on twitter at **www.twitter.com/ftreports**

All editorial content in this supplement is produced by the FT.

Our advertisers have no influence over, or prior sight of, the articles or online material.

Potential yet to emerge in practice

Circumcision

Despite evidence of the health benefits, widespread adoption of the procedure is still to be achieved, writes **Andrew Jack**

Tzameret Fuerst whips two plastic rings out of her handbag and prises them together around her forefinger with a black rubber band, simulating a simple way to carry out male circumcision that she hopes will soon be widely adopted across Africa.

"This is a safe, simple, non-surgical device that needs no anaesthetic and is scaleable in resource-limited settings, using nurses to carry out the procedure in tents in rural areas," she says. "It's virtually painless, completely bloodless and does not require a sterile setting."

The PrePex device that her company Circ MedTech has developed is one of a growing number of experimental tools in search of a market that has the potential to help radically reduce HIV transmission.

But circumcision is also a practice that – despite the evidence – has yet to be adopted as much or as fast as experts had hoped.

Many years after observational studies indicated that circumcised cultures had lower HIV prevalence, progress remains extremely slow. In 2005, the results of the first carefully randomised controlled clinical trials in Orange Farm in South Africa demonstrated that sexual transmission was reduced by 60 per cent in men who were circumcised.

A recent estimate published by UNAids highlighted a jump in adult male circumcisions, especially in Kenya, South Africa and Zambia. But with 555,000 interventions in men aged 15-49 across sub-Saharan Africa by the end of last year, less than 3 per cent has been achieved of a target of 21m set for 2015 to reduce significantly new infections in the region.

"It's going to be a big challenge to reach this target," concedes Gottfried Hirnschall, head of the World Health Organisation's HIV programme.

International organisations have publicly endorsed the importance of circumcision, and a number of guidelines have been established, but the response so far has been haphazard and funding remains modest.

A mural promotes the benefits of circumcision at a clinic in Kenya AFP/Getty

> 'UN agencies called for the world to recognise circumcision as an important form of prevention but where are they now?'

Inon Schenker, who established Operation Abrahim as a joint project with Jewish and Muslim surgeons and nurses to provide technical support for the procedure across Africa, warns: "There is a big gap on the ground. UN agencies called for the world to recognise circumcision as an important form of prevention, but we aren't hearing from them now."

One reason has been that much government donor and philanthropic support for HIV prevention work was focused instead on more "high-tech" alternatives such as vaccines and microbicides.

Bertran Auvert, the French researcher who ran the Orange Farm trial, struggled to win funding, only latterly receiving a mea culpa from Bill Gates, whose Foundation has since begun to provide funds.

The absence of sufficient surgeons across Africa has acted as a brake, triggering belated experimentation with "task shifting" to nurses. There are cultural sensitivities, and a debate over "male mutilation" and human rights – something which observers say has slowed willingness by Unicef and other organisations to encourage wider use of the practice in young children to provide longer term protection.

Some African leaders such as Uganda's long-serving President Yoweri Museveni have questioned the benefits, sending a confusing message, despite previous prevention campaigns that he spearheaded, which helped his country make early progress against the epidemic.

Mr Auvert says: "The main problem is the fact that there is not enough political involvement in the scale-up of male circumcision. I suppose that prevention is not something politicians like to do. They don't have an immediate interest. They will do it only under pressure from their population."

Different groups and procedures have filled the void, but often without adequate guidance. PrePex is undertaking clinical trials of its device in Rwanda and Zambia, and has become the first manufacturer to submit for "prequalification" or approval by the WHO.

Others have marketed their equipment regardless, including Malaysia-based Tara KLamp, which was bought in large quantities by the KwaZulu Natal authorities in South Africa.

That was despite Mr Auvert advising against its use, after noting it was refused by many men in his study, and those who used the device reported higher rates of pain, bleeding, side-effects and cosmetic concerns than the alternative forceps-guided surgical technique.

Mr Hirnschall says he hopes the WHO will be able to issue recommendations on devices during 2012, while stressing that the agency does not recommend the Tara KLamp. "Any country using it needs to have mechanisms to monitor any side-effects very carefully," he cautions.

Eric Goosby, head of Pepfar, the US bilateral Aids programme, remains optimistic. "We are hitting an accelerating curve," he says. "It's a process of community awareness.

"It's not just a question of 'Put up a tent and they will come'. We have learnt the hard way that just telling men about the fall in infectivity doesn't win it.

"Female partners have been those bringing most men in. We cannot just go to implementing a programme without hitting the community. Now we have gone over that and done the preparation, circumcision will start to accelerate."

Healthcare 'Double whammy' for users of hormonal contraceptives

There are growing calls to integrate HIV prevention and treatment programmes with family planning and other health services, yet a recent study has sparked concern that the two may interact in dangerous ways.

Writing in the Lancet in October, Renee Heffron and colleagues at the University of Washington, Seattle, warned that women who used hormonal contraception in sub-Saharan Africa doubled their risk of contracting HIV.

Studying 3,790 mainly married "sero-discordant" heterosexual couples – one of whom had HIV and the other did not – they found a far higher chance of transmission to the "negative" partner when the woman had been using a contraceptive – above all if it was in the injectable form, DPMA, that is most widely used in the region.

Assuming there was no transmission through syringes, they suggest the drug may cause physiological changes in women that make them more susceptible to HIV – a phenomenon they also identified in women who are pregnant.

"Active promotion of DPMA in areas with high HIV incidence could be contributing to the HIV epidemic in sub-Saharan Africa, which would be tragic," wrote Charles Morrison and Kavita Nanda from FHI360, a family planning non-profit group in an accompanying editorial.

"Conversely, limiting one of the most highly used effective methods of contraception . . . would probably contribute to increased maternal mortality and morbidity and more low-birth-weight babies and orphans – an equally tragic result."

They point out that the trial was not explicitly structured to identify this link, and there are other reasons to question the findings. But it confirms previous "observational" studies, and has led to fresh calls for funders to support a study to address the link directly.

Mitchell Warren, head of Avac, a HIV prevention advocacy group, says: "This looks like another double whammy for women, who are on the front line of HIV infection and unintended pregnancy. But we must not rush to judgment in trying to help women and their health providers balance these risks. And we clearly need to provide women with more contraceptive and HIV prevention options."

Andrew Jack

Crucial role hampered by high cost and poor access

Diagnostics

Point-of-care tests are cheaper but can be hard to develop, writes **George Cole**

The Nyumbani children's home in Nairobi, Kenya, cares for more than 3,000 children and young adults with HIV.

The home has a sophisticated HIV test laboratory, but Sister Mary Owen, its executive director, says she has a big problem: "The cost of the test reagents is too high, and so many of those in our care can't receive the testing they need."

Of the 34m people around the world who are infected with HIV, more than two-thirds live in developing countries. The key to effective treatment is access to robust diagnostics systems, but such access is often unavailable.

"With the exception of South Africa, none of the high-HIV burden countries have access to routine virological monitoring," says Nathan Ford, medical co-ordinator, Médecins sans Frontières (MSF). As a result, the medical charity, "some patients are kept on a treatment regimen that does not work."

Steven Reid, programme manager for the CD4 Initiative, an HIV diagnostics project run by Imperial College London, says: "Diagnostics is vital, because someone with HIV can desperately need treatment without looking sick."

Diagnostics plays a pivotal role at all stages of HIV treatment. A test is used to identify people infected with HIV. An Early Infant Diagnosis (EID) test is used for children less than 18 months old. HIV-positive patients are monitored using another test, CD4, which counts T-cells in the blood.

T-cells help fight infection and are targeted by the HIV. When the T-Cell count falls below a threshold, the patient starts antiretroviral therapy (ART). During ART, another test, Viral Load (VL), is used to measure the amount of HIV in the blood, to monitor the treatment's effectiveness.

Bernard Branson, associate director for HIV laboratory diagnostics at the US Centers for Disease Control, says: "When people are on therapy, they are 96 per cent less likely to transmit infection, and so there's a huge movement to control the Aids epidemic by putting people on therapy. Improved monitoring not only helps the individual, but wider society."

Much progress has been made in developing rapid HIV diagnostic tests, suitable for low resource settings. Jason Warriner, clinical director at the Terrence Higgins Trust, a UK HIV and sexual health charity, explains: "Rapid diagnostic tests are cheap, quick and easy to use – you only need a drop of blood from a finger or a saliva sample, and some tests can be done in a minute."

Such tests can cost as little as 50 cents each and are easy to deploy at the point-of-care (POC), such as a clinic in a remote area.

Developing POC tests for other forms of HIV testing is more difficult. David Anderson, associate professor and deputy director at the Burnet Institute in Melbourne, Australia, says: "There's an enormous gulf between the rapid diagnostic tests and other tests in terms of cost. A CD4 test, for example, costs $6-$7."

Almost all sophisticated HIV tests require laboratories with clean water, electricity, air conditioning, test instruments (costing many thousands of dollars), and test reagents, which can cost as much as $70 per test. This technical complexity and high cost means that less than 5 per cent of the 170,000 HIV patients supported by MSF have had a VL test.

Test samples also have to be taken to a laboratory. Brenda Waning, co-ordinator of market dynamics for Unitaid, whose work includes helping children with HIV in developing countries, says: "You've got to send a blood sample to a lab that might be hundreds of kilometres away, and then wait for the results to be sent back. There's a huge follow-up loss – around half of the children [tested] are lost in this process."

Steven Reid: testing is 'vital'

> 'Many of the innovations are coming from new players in the market'

Maurine Murtagh, chief executive of The Murtagh Group, a consulting firm specialising in diagnostics for global health, says: "Manufacturers are aware that diagnostics for resource-limited settings need to be affordable."

Roche offers non-profit pricing for some HIV products supplied to least developed countries.

Becton Dickinson also offers low priced products, but Krista Thompson, its vice-president and general manager, says: "Affordability is very important, but so are things such as trained health workers and suitability for the work environment. Africa is littered with diagnostics equipment that hasn't produced a single result."

BD also runs laboratory training programmes for HIV workers in developing countries.

Alere, PointCare Technologies and Partec have launched CD4 test instruments designed for POC or near-POC testing.

Hardware prices range from $5,000-$25,000, but cheaper CD4 tests are under development. "Many of the innovations are coming from new players in the market," notes Ms Waning at Unitaid.

The Burnet Institute, along with Rush University, Chicago, and Duke University, North Carolina, has developed a CD4 test which uses a simple test stick costing about $2. The CD4 Initiative received $16m funding from the Bill & Melinda Gates Foundation for a low-cost CD4 test, now being developed by Californian company Zyomyx. BD has demonstrated a solar powered CD4 point-of-care test instrument.

The Diagnostics Development Unit (DDU) at Cambridge university is developing VL and EID point-of-care tests. Helen Lee, DDU director, says: "Of the 2.5m children infected with HIV worldwide, 90 per cent are in sub-Saharan Africa. Our Samba (Simple AMplification-Based Assay) EID test provides results within two hours, while the family are still on-site. We plan to launch it in 2013."

But barriers remain. Ms Murtagh says: "All diagnostic testing relies on strong health systems, including quality assurance. Generally, these systems are weak in resource-limited settings."

Ms Waning says introducing test products into countries runs into hurdles, which can create a bottleneck. "We have to help companies get their products into countries, and we need a global system for certification," she says.

And while Dr Lee is optimistic about the future of HIV diagnostics in developing countries from a technological point of view, she says: "It will be a real challenge to compete against the large companies with huge marketing power and resources, and overcome the inherent conservatism of the medical establishment."

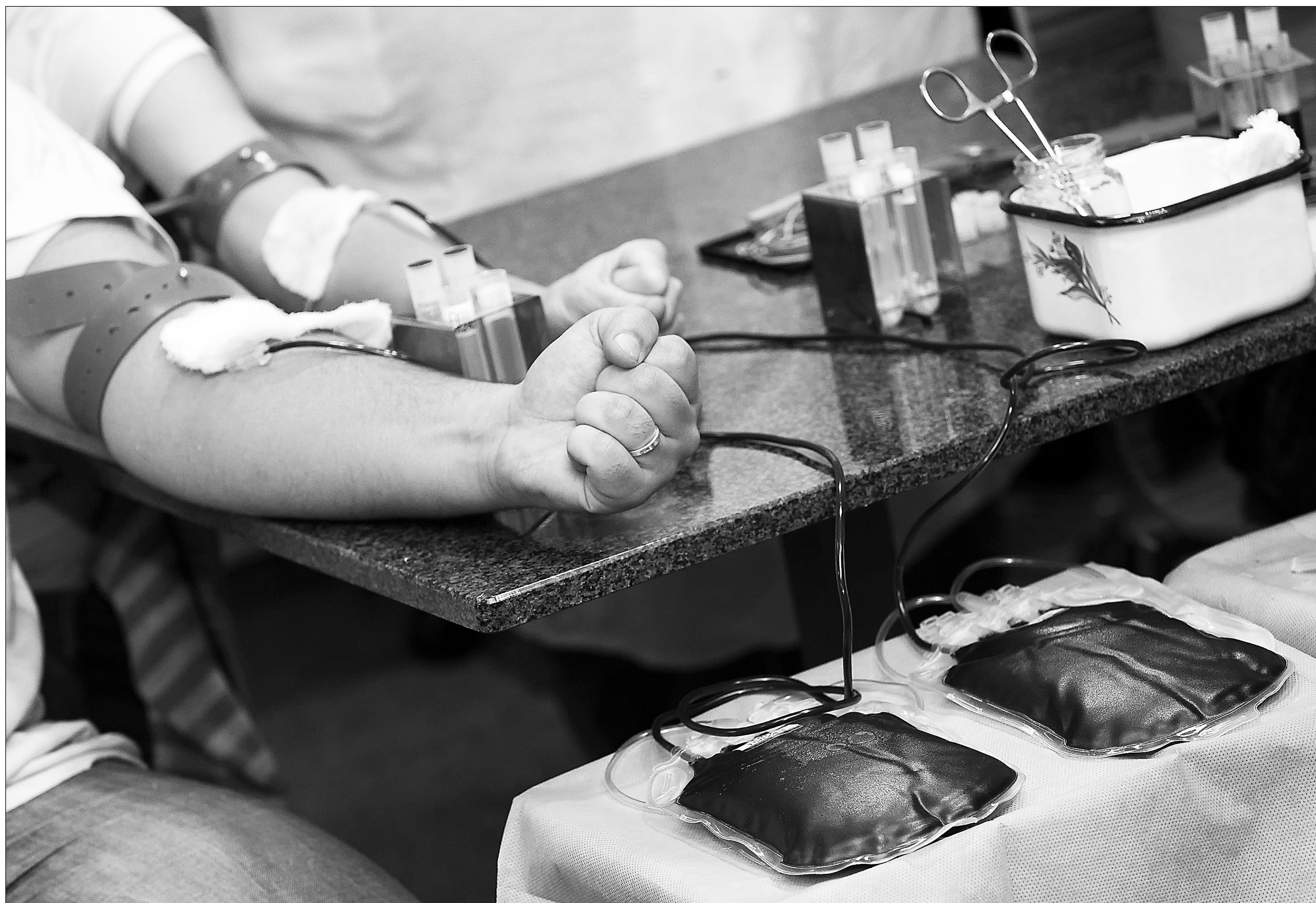
The International Rescue Committee works to provide hope, care, and comfort.

At Pearson, we're proud to support the work of the International Rescue Committee, a global humanitarian organization that helps uprooted people to survive and rebuild their lives. Since 1933, the IRC has helped children affected by conflict and disease in crisis zones around the world.

Their lifesaving work is critical in Sub-Saharan Africa, where an estimated 14.8 million children have been orphaned as a result of AIDS. Join us in helping the International Rescue Committee provide hope, care, and comfort to children affected by the AIDS epidemic. Find out more by visiting www.rescue.org.

Find out more about the ways in which the Pearson Foundation is helping people to live and learn. Visit www.pearsonfoundation.org

ALWAYS LEARNING PEARSON FOUNDATION



Strict rules: the US and Canada still have a lifetime ban on blood donations by gay men but in the UK the ban was lifted in September Dreamstime

Experts less than sanguine over risks from donated blood

Transfusions

Improved screening could bring benefits far beyond the costs, writes **Andrew Jack**

When a group of economists gathered this summer to debate how best to allocate scarce resources to tackle HIV, there was plenty of disagreement on priorities, but one recommendation that stood out as offering extraordinarily high returns: better protection of the blood supply.

Lori Bollinger, senior economist at the Futures Institute in Connecticut, concluded for the Rethink HIV project that 131,000 infections could be averted annually in sub-Saharan Africa for merely $2m in additional investments over the coming four years, providing benefits from avoided treatment and improved life expectancy more than 400 times the costs.

She pointed out that transfusions are particularly common in Africa, where anaemia is widespread, caused by factors including poor diet and malaria.

Yet while some countries such as South Africa have highly effective screening programmes, others, including Angola, Niger and Tanzania all report that less than a third of donated blood is tested for HIV contamination in a quality-assured manner.

Three decades into the epidemic, it seems extraordinary that transfusions – which bring the highest possible risks of transmission through the direct injection of large quantities of potentially infected blood – still continue to trigger cases of HIV each year.

Long after high profile cases of people contracting the disease from transfusions, the US calculates its current risk of infection at one in 1.5m. The chances are higher elsewhere, with periodic reports of contaminated blood transfusions highlighted in countries as diverse as India, Libya and Uzbekistan.

The World Health Organisation says there is no reliable information on the extent of transfusion-linked infections. It points out that there is no routine follow-up of either donors or patients receiving blood to help estimate figures. But it says just 53 per cent of blood across low income countries is adequately screened for HIV.

Paul DeLay from UNAids stresses that many developing countries do not even have significant blood banking from donations. With frequent stockouts occurring in rural areas, hospitals may rely on relatives and friends accompanying someone with an injury to hospital to provide a direct transfusion in emergency conditions.

If a low concentration of HIV is not detected during testing or screening, it will not subsequently be picked up during storage of blood ahead of transfusions.

That raises questions about intense scrutiny to ensure donors are not carriers, but also whether better screening techniques can be developed, or alternatives such as artificial blood promoted more widely.

For now, Mr DeLay says that if he were to have an accident near a rural hospital in some parts of Africa, he would seek a saline drip or other measures to defer the need for transfusion at least until arrival in a better resourced urban medical centre with greater chance of more effectively screened blood.

But if a problem in lower-income countries is inadequate screening, in richer nations campaigners are focusing their efforts on easing the rules on blood donation by those who risk carrying the infection where high quality techniques are more widely and systematically employed.

In the UK, where the last documented case of HIV transmission by transfusion was in 2002, the rules changed in September, lifting a lifetime ban imposed in 1984 on donations by men who had ever had oral or anal sex with other men, with or without a condom.

The new guidance, previously long "under review" but unchanged by SaBTO, the advisory committee on the safety of blood, states that donation is allowed more than one year after sex. Along with other donors, they must complete a questionnaire and their blood is subject to normal screening procedures.

As the National Health Service puts it: "Blood donation works on the principles of kindness and mutual trust and we ask all potential and existing donors to adhere to the blood donor selection criteria by providing completely honest answers to all the questions asked, both for the protection of their own health and that of others."

In most other countries, the rules remain much more strict. The US and Canada still have a lifetime ban on donations by men who have sex with men. Like the UK, Australia and Japan have a one-year deferral since sex among gay men, and South Africa has a shorter bar of six months.

The UK's one-year deferral period reflects scientific advice highlighting a "window" period of about a month during which HIV may not be detected in tests, and a much longer period to ensure the reliable detection of Hepatitis B, which is also disproportionately present in gay men.

As Yusef Azad, director of policy and campaigns at the UK's National Aids Trust, wrote recently in Gay Times: "This was an overdue and welcome step, ending discriminatory practice and establishing an evidence-based rule rather than one based on prejudice."

He argues that, with the advances in the science of testing and screening, keeping a ban in place limited the supplies of blood and fuelled an exaggerated stigma.

In the UK, the next debate is whether the easing of the lifetime ban should be extended to commercial sex workers. In other countries, far greater caution still remains.

Risk to patients Call for change in UK

When Allan Reid, a dentist practising in London, learnt in 2007 that he had HIV, he decided not to tell his employer because he knew what would happen.

After he was exposed in the Sun newspaper, his fears were confirmed: he was disciplined by his professional body and Lewisham primary care trust asked him to resign.

"It wasn't a question of: 'Don't ask, don't tell'," he says. "It was just: 'Don't tell'. It was pretty devastating. I had been a full-time dentist for 17 years, working six days a week. It took quite a bit of adjusting."

Mr Reid is one of a number of British healthcare specialists – among them surgeons, dentists and midwives – who have been forced to abandon their careers, despite strict rules on infection control and evidence worldwide of only four cases ever of HIV transmission to patients.

Longstanding UK guidance from the Department of Health, most recently updated in 2005, is stark. "HIV infected healthcare workers must not perform any exposure-prone procedures," it says, referring to any situation where a worker's blood could contaminate a patient's open tissues.

Yet that position – now just opened to a fresh consultation in the UK – comes despite a growing willingness to ease similar restrictions in other countries such as the US, Canada, New Zealand, Israel and France, as studies have shown that patients taking antiretroviral medicines have a very low risk of passing infection to others.

Yusef Azed, director of policy and campaigns at the National Aids Trust, says: "Now that we see the preventive value of treatment and all attention goes to how we can deploy it effectively, we should use it to end discrimination. It was never a good thing that dentists and surgeons had this terrible disincentive to find out their HIV status."

Professor Damien Walmsley, scientific adviser to the British Dental Association, says: "There is no evidence to suggest that a practitioner with HIV poses any danger to the health of their patients, providing appropriate precautions are taken. We believe the [UK] government should alter its approach."

That would be a relief to professionals such as Mr Reid, who says: "I think I would want to go back to dentistry because I can and I should."

Andrew Jack

Damien Walmsley: UK 'should alter its approach'

30 years on, disease's first doctor urges fresh impetus

Opinion
MICHAEL GOTTLIEB

Thirty years ago, a single patient threw a monkey wrench into my plans for a career in academic medicine.

He was 31 years old, homosexual, rail-thin, with platinum-dyed close-cropped hair, and a previously unknown immune deficiency.

When I reported his case and four others to the US Centers for Disease Control, I had no idea that the moment represented the beginning of a historic global HIV pandemic that over the next 30 years would ravage millions of lives.

I became the first Aids doctor and started talking about the new disease to anyone who would listen. Doctors took note of my first article; looking back, many remember exactly where they were when they read it. But years passed before the gravity of what was happening registered with the media and public. Once it did sink in, Aids was greeted with apathy and then fear and rejection.

In the early days, I was stunned by the silence of world leaders and the reluctance of academic institutions to get involved. They did not want to be associated with a "gay disease".

I experienced conflicting emotions, simultaneous sadness and anger. No one seemed to care that young men were dying and that all hell was breaking loose on big city hospital wards.

Four years later, I held a press conference to announce that Rock Hudson had Aids. It caused a sea-change in the public conversation about Aids. People started to feel empathy for those living with it. Celebrities – Dame Elizabeth Taylor, Diana, Princess of Wales, Sir Elton John, Elizabeth Glaser and Bono – used their prominence to put pressure on governments for research and treatment.

That first patient not only changed the course of my career, it changed me as a person. My early involvement produced an odd sense of responsibility. Treating young patients with what was then a fatal disease made me re-examine my life's priorities and reorder them.

I was grateful for the support and encouragement of my patients and allies in the gay community. Even as a doctor I had been insulated from the bigger picture of human suffering. The global nature of the pandemic opened my eyes to the extent of poverty and illness in resource-poor countries. I came to realise how irrational it is for empathy to stop at borders.

Thirty years ago I would never have imagined that today I would be passionate about people living in Africa.

My first patients with Aids died within a year of diagnosis. Since then I have witnessed the advent of life-saving treatment for a condition that was a death sentence.

I feel strongly that we have a responsibility to make these advances in treatment and prevention available to children, women and men in poor countries hard-hit by the virus.

It is a fact that Africa accounts for more cumulative deaths and current cases than anywhere else in the world, and today is home to two-thirds of the 34m people worldwide living with HIV/Aids. We have made substantial progress through remarkable humanitarian programs funded by the President's Emergency Plan for Aids Relief (Pepfar), and the Global Fund to Fight Aids, Tuberculosis and Malaria.

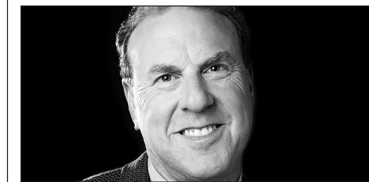
These initiatives fund prevention of mother-to-child transmission (PMTCT) and treatment – which also prevents transmission – for millions already infected.

Yet on this World Aids Day, and on every day in Africa, more than 1,000 children and some 6,000 adults will be newly infected with HIV.

In wealthy countries, the conversation today around HIV/Aids has changed.

The gay community, whose activism was largely responsible for making HIV a manageable medical condition, seems anxious to move beyond the epidemic. It is discouraging to note the decline of activism, media coverage, and sense of urgency about HIV/Aids.

In a positive development, many young people now volunteer to work on HIV, tuberculosis and malaria in Africa. The seeds of a movement to improve global health have put out roots.



'That first patient not only changed the course of my career, it changed me personally'
Michael Gottlieb

In November, the international HIV/Aids activist community was re-energised by a speech on Aids given by Hillary Clinton, the US secretary of state. As budget priorities are being debated in the US and around the world, we should unify around the historic opportunity proposed by Mrs Clinton to save both money and lives by investing in prevention.

We also should encourage donors – both private and public – not to retreat from supporting high yield interventions such as PMTCT that save tens of thousands of lives each year.

I have now worked on Aids for the life of the epidemic. I feel a responsibility to speak up about it. I am convinced that we have the know-how to curb the devastation and that we can do much better at implementing it. This is an auspicious moment to rekindle activism, shake off compassion fatigue, and intensify our efforts. It is our collective responsibility to act.

Michael Gottlieb is the Los Angeles immunologist who identified Aids as a new disease in 1981. He is a trustee of the Global Aids Interfaith Alliance (www.thegaia.org).

Aids-free world is no longer a distant dream

Opinion
RAILA ODINGA and
MICHEL SIDIBÉ

After 30 years, science, global solidarity and unprecedented commitment have led us confidently to a game-changing moment in the Aids epidemic. A point when we can now dare to say; the end of Aids is in sight.

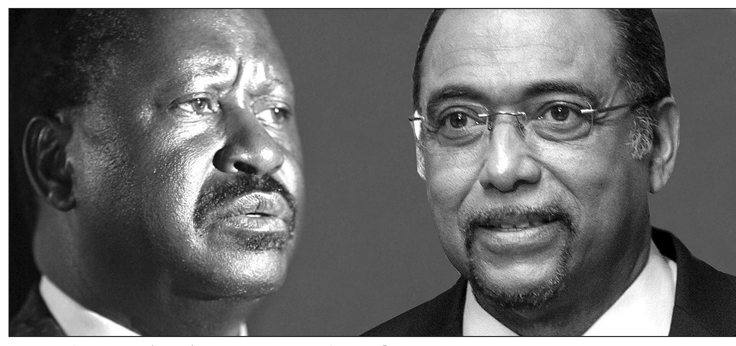
Science is offering promises of wide-scale reductions in new HIV infections and vibrant partnerships are delivering real results on the ground. Aids-related deaths have fallen 20 per cent in the past five years; new HIV infections dropped more than 20 per cent since the peak of the epidemic in 1997; and more people than ever before have access to lifesaving treatment.

The Aids response is making a return on investment and it is time to bolster the momentum.

World leaders are standing up to say that an Aids-free generation is possible and that no child should be born with HIV and no mother should die of Aids. This leadership is timely and critical.

At the United Nations High Level Meeting on Aids in June, countries agreed to a set of bold and ambitious targets to be met by 2015: eliminating new HIV infections in children, halving sexual transmission of HIV, providing treatment to 15m people by 2015 and increasing annual investments for Aids to $22bn-$24bn by 2015.

The global investment target which has been set is clearly a shared responsibility – of all countries, donors and others. Only together can we secure the future and provide greater and long-term dividends.



Raila Odinga (left) and Michel Sidibé: seize the science AP, Reuters

There are important milestones on the road to an Aids-free generation and getting there will evidently take a scaling up of joint efforts. All countries and their citizens are affected by Aids and must contribute to its end.

Kenya has based its response on joint accountability and has renewed its commitment to increase domestic resources for the response to HIV. It has already made huge gains in its response to HIV, notably through the widespread uptake of voluntary medical male circumcision.

Since 2008, more than 500,000 men have undergone medical male circumcision to prevent HIV in east and southern Africa, of which 40 per cent were in Kenya alone. Kenya took this bold step to promote the procedure as a key component of its national HIV response alongside other proven prevention options. In one province alone, Nyanza, voluntary male circumcision averted an estimated 2,000 HIV infections in 2010.

We are in tough economic times and to achieve our goals investments need to be made wisely. This means funding high-impact interventions with far-reaching ramifications.

Both money and lives can be saved by delivering a combination of scientifically proven prevention options for maximum effect. This includes treatment for prevention, where investments can be largely offset by savings in future treatment costs alone.

UNAids has developed an investment framework which shows how 12.2m new HIV infections and 7.4m HIV-related deaths can be averted between 2011 and 2020.

The key elements of this approach include scaling up basic, proven programme activities to maximum effect. This, combined with other smart investments, will also leverage progress more broadly for health and development.

By seizing the science and translating it into effective action, we can welcome an Aids-free generation. As we do, we will not only change the course of the epidemic, we will make Aids history.

Raila Odinga is prime minister of Kenya. Michel Sidibé is executive director of the Joint United Nations Programme on HIV/Aids and undersecretary-general of the UN

MORE ON FT.COM

Universal access to treatment for HIV/Aids will require more money from donors, not less, says **Bertrand Audoin** (right) of the International Aids Society

Hope should not get ahead of reality on Aids 'treatment as prevention', writes **Daniel Halperin** of the University of North Carolina

Javier Hourcade Bellocq, Latin America regional representative for the International HIV/Aids Alliance, makes a plea for global solidarity amid plans to cut funding

The Global Fund to Fight Aids has a credibility crisis, write **Vicky Hausman** (right), **Prashant Yadav, Daniella Ballou-Aares** and **Brad Herbert**
www.ft.com/aids-2011