

HIV treatment update

Issue 213
Autumn
2012

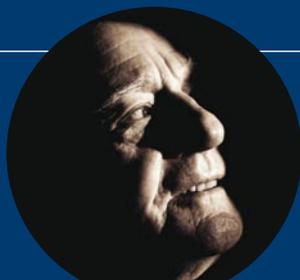


The generic generation

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HIV treatment update

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Printing Cambrian Printers

ISSN 17567890

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Charity number 1011220

HIV treatment update was

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Each feature in *HTU* is also reviewed in advance by a readers' panel of people living with HIV. We are grateful to our panel for their knowledge, attention and enthusiasm. If you would like to be a member of the *HTU* readers' panel, please email info@nam.org.uk.

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In this issue



Gus Cairns
Editor

What does the future hold? That seems to be the question that links the pieces in this autumn issue.

It wasn't too long ago in some memories that having HIV was a matter of staying alive right now, rather than planning for the future. Even for the newly diagnosed, finding you have HIV can have a paralysing effect on life plans, not least because – in the popular imagination – it often still means illness and early death.

The message is slowly getting through, though, that life expectancy in people on effective HIV treatment is approaching normal. Being positive for HIV can still allow you to be positive about your future.

One of the most fundamental decisions anyone makes about their life is whether and when to have children. Until recently, people with HIV faced daunting barriers to achieving this aim, especially people in different-status relationships, who would be put through – or put themselves through – a sequence of decidedly unsexy procedures – sperm washing, artificial insemination, test-tube fertilisation – in order to have a child but not infect their partner.

In the last two years we've discovered how successfully HIV treatment can prevent transmission; the chances of an HIV-positive person on effective treatment infecting their partner now really are pretty slim.

However, as Joanna Moss discovers on page 12, so-called discordant couples may be getting discordant advice from different specialists about how to reconcile safer sex with conception. Fertility help may still be needed more often for people with HIV, and some couples may want a 'belt and braces' prevention approach that adds in other measures, but the current situation is unsatisfactory and we are eagerly awaiting the publication of new fertility guidelines, which recognise the role of treatment as prevention.

In most of our futures is our old age – an old age many of us thought we would not see. *HTU* has reported before on research conducted with older people with HIV, which found high levels of isolation, poverty and depression in people who had never planned to get old. How can we fend off such miseries and ensure our autumnal years will be as long and happy as possible? On page 8 we talk to a couple of people who are over retirement age, and to their doctor, to get their advice on maintaining health and contentment.

On page 4 we discuss not our own future, but that of our treatments. The advent of cheaper, non-patented HIV drugs could be a tremendous opportunity to save a lot of money, to put that money into maintaining healthcare standards in the era of cuts, and even to spare some for research. All that will go to pot if the pressure to save money results in some people staying on regimens that don't really suit them. It's not that generic drugs are worse than branded ones – they are just as good – but that we must never let cost dictate inappropriate treatment.

One way to fend off that slippage of treatment standards is to try and formulate minimum ones. The new BHIVA standards for HIV care, summarised on page 16, are an attempt to set, in the hardest stone available, a set of minimum treatment standards that should be applicable for the next half-decade, no matter what contortions the NHS goes through and wherever we get our pills. We welcome this document as a contribution to, in an age of uncertainty, securing our future.

Upfront

Efavirenz and the brain: are we nearer to solving a mysterious side-effect?

by Gus Cairns

One of the most potent HIV drugs, efavirenz, unfortunately also causes mysterious and sometimes chronic disruptions of mood, thought and sleep. Researchers may have found the key to these side-effects,¹ and evidence that the drug may contribute to the subtle deficits in brain function usually attributed to HIV.

As *Sustiva* or *Stocrin*, or in the once-a-day pill *Atripla*, efavirenz is a staple part of many people's antiretroviral therapy (ART): in London last year, 53% of all people on ART took it. Yet ever since its introduction in 1999, the drug has been linked to vivid dreams, poor sleep, dizziness, lack of concentration and, in some cases, mood swings, anxiety and depression.²

It's accepted that these effects are common in the first month or so on the drug. What's disputed is whether these persist and, if so, whether they have real impact. While some studies found no evidence for long-term side-effects,³ others did^{4,5} – and some found that, even in people who had tolerated efavirenz for years, changing to other drugs, within⁶ or outside⁷ the NNRTI class, resulted in improvements in mood.

Early studies found that only 6% of people stopped efavirenz in the first year⁸ but a more recent study⁹ found that as many as 20% of people taking *Atripla* (efavirenz/tenofovir/FTC) stop taking it within a year, largely due to psychological side-effects.

There have been very few randomised, controlled studies to assess the extent to which these side-effects are peculiar to efavirenz, or which can provide any information about whether some of these effects might be due to HIV infection itself. One of these few¹⁰ found that people on efavirenz had slower reaction times and poorer decision-making skills than people on protease inhibitors. But most research has been in studies where participants knew they were on efavirenz – and the reputation

of the drug is such that they may have blamed mental distress on efavirenz when in fact had another cause.

The picture gets more complicated if you factor in HIV-associated neurocognitive disorder (HAND). This is the complex of deficits in mental performance that has been associated with HIV infection; it too tends to include deterioration of memory, co-ordination and concentration.

Marked brain impairment in people with HIV not taking antiretroviral therapy (ART) usually gets better if they start ART, but the mild version of HAND often persists. Some studies have found that people taking efavirenz have poorer HAND scores¹¹ and others have found that HAND may improve less in people taking efavirenz.¹²

Although mental disturbance, including psychosis and mania, has been linked to exceptionally high efavirenz levels,^{13,14} other studies have found no link with levels of efavirenz in blood.¹⁵ But higher drug levels and lower HIV viral load in the cerebrospinal fluid (CSF) that surrounds the brain were associated in one study with worse HAND symptoms,¹⁶ in another with nerve cell loss,¹⁷ and, in a third, HAND symptoms unexpectedly improved when patients stopped ARVs;¹⁸ these however were not efavirenz-specific effects.

The new research found that it might not be efavirenz itself that damages nerve cells but a metabolite, a chemical produced when the body acts on the efavirenz molecule.

In the body, efavirenz turns into two molecules called 7- and 8-hydroxy-efavirenz. The researchers incubated nerve cells taken from rats with efavirenz and these two compounds and found that, while all three were toxic to nerve cells, 8-hydroxy-efavirenz (8HE) was ten times more so. This additional toxicity appeared to have an independent mechanism; 8HE jammed open portals into nerve cells called voltage-operated calcium channels (VOCCs). When these gateways are

breached, calcium floods into nerve cells, unleashing a burst of brain signals, causing unpredictable effects.

With high drug levels this led to nerve cell death, but with lower levels the cells lost their 'dendritic spines': these are a nerve cell's 'input wires' and mean that the cell is less responsive to the signals reaching it. The typical level of 8HE seen in daily dosing of efavirenz is about three times the level sufficient to denude cells of dendritic spines.

This could explain why blood levels of efavirenz are not always related to side-effects: people who efficiently metabolise efavirenz may have lower blood efavirenz levels but higher peak levels of the 8HE compound.¹⁹

This research comes at a crucial time for efavirenz. The drug will be one of the first widely used ARVs to come off patent next year (see *The generic generation* on page 4). Generic efavirenz will be available cheaply and there will be cost pressures for people to stay on it if they can, rather than switch to costlier drugs.

The fact that a drug harms cells in a lab dish doesn't necessarily mean it will harm them in the body. Clearly, this line of research needs to be extended. We need to do the same experiments on neurones with metabolites of other drugs; we need to relate brain function in people to levels of 8HE; and there should be longitudinal research to look at how brain impairment improves or deteriorates in people with HIV on and off treatment, and to try to tease apart the symptomatic profiles of different kinds of neural damage.

Efavirenz has long been blamed, rightly or wrongly, for a subtle but pervasive deterioration in the quality of life of some people taking it and it would be good to find out whether the drug's benefits continue to outweigh this. The question is, with less money available as ARVs become generic, who will fund the research? **nam**

The **GENERIC**

In the next few years, some of the most widely used HIV drugs will come off patent in the UK. *Gus Cairns* asks: what are the implications for the tablets we take – and for our health?

From next year, if you're in the UK, your anti-HIV drugs may start to look different. One pill may be replaced by two or three and their appearance may change, even from one prescription to another. Names you are familiar with – *Atripla*, *Viramune*, *Sustiva* – may start to disappear.

You will still be getting the same drugs, but in a different guise. What you'll be getting are generics: different versions, but essentially the same things, without a brand name attached and cheaper to produce. A bit like supermarket cola versus Coca-Cola – though without anything 'secret' in the recipe.

When patents end

Why now? Because of patents. Patents are intellectual-property documents stating that a particular invention – whether it's a new drug or a gizmo in your computer – is the inventors' alone to profit from, usually for 20 years, and usually only in the specific country that issues the patent. A patent gives you the right to stop others from copying and selling your product. Increasingly, trade agreements are being forged that mean that a patent issued in one country will be honoured in others.

Trade agreements are controversial, usually because they involve rich countries such as the US getting poorer countries to adopt their patents. And so is patent law, which, some say, is increasingly abused to help companies grab unfair shares of a market, or help them maintain monopoly of a product longer than they should by

changing it in trivial ways.

It can also be very complex: the ongoing row between Apple and Samsung over their smartphones is an example. In medicines, the issues are (usually) simpler: whereas many different patented devices and programmes may go into a smartphone, what's patented in a drug is usually the active ingredient – a single molecule or combination of molecules.

Once something goes off patent, then any company can make a version of it and sell it without being guilty of selling a pirate copy. This is an issue in HIV because we're starting to reach that 20-year time limit.

Drug patents last for 20 years from the registration of the active ingredient. This has to happen before efficacy trials start in humans, so the actual time companies have to make a profit is only from when it's licensed to be sold, which may be only 12 to 15 years.

Name confusion

A patented drug gets a generic name or so-called INN (International Non-proprietary Name), which is registered with the World Health Organization. The INN is global, and permanent: it is the name doctors write on their prescription pads and ensures that wherever you get your prescription filled, you will be getting the same active drug. The same applies to over-the-counter medicines: they may contain all sorts of ingredients, but in small print somewhere on the packet they must list the active drug or drugs they contain.

Once drugs are licensed as safe and





generation

effective, they can only be sold under the company's brand name while the patent is in force. Drugs having two names can be very confusing, and some may have more than two, including several anti-HIV drugs. Take the oldest one as an example. It's best known as AZT. This stands for its chemical name, azidothymidine. Its generic (INN) name is zidovudine. And it was marketed by its manufacturers as *Retrovir*. To avoid confusion, NAM's convention, as above, is to always have brand names capitalised and in italics.

Patents don't always expire exactly 20 years after the INN was registered because patents are issued by individual countries. Thus zidovudine came off patent in September 2005 in the US and March 2006 in the European Union.

Since 2009, zidovudine has been available in generic form in the UK and if you're one of the few people who still use it, you will probably already be getting it as a little white pill instead of the old blue-striped capsules.¹ Several other HIV drugs have already come off patent, including didanosine (ddI) in May 2006, saquinavir in January 2011 and stavudine (d4T) in May 2011 (all these are European dates).

But these are hardly used these days. The first widely used drug to come off patent was lamivudine (3TC) in January 2011, and generic versions became available in the UK in July this year. Next year, a generic combination AZT/lamivudine pill will be out for the few people who still take this; it won't be called *Combivir*, the name of the patented combination pill.

What's going generic soon

From next year patents will start falling thick and fast.

Nevirapine (currently branded *Viramune*) comes off patent in June 2013 and four generic companies have applied to supply a version in the EU (there are already around ten in the US). Nevirapine has always been an alternative rather than first-choice drug though, because of rare but potentially serious side-effects.

Anna Brewster of *Viramune*

manufacturers Boehringer Ingelheim said she expected her company to continue making the drug, "but it would have to compete on price". In addition, there is a double-strength one-pill-a-day version of *Viramune* that is still on patent. Managing director, John Dixon, affirms "Boehringer Ingelheim has, for 15 years, been committed to providing high-quality innovative medicines to people living with HIV. Importantly, our commitment to our patients will not end after the patent for nevirapine expires in June 2013 as we will continue to produce and supply both *Viramune* and *Viramune prolonged-release*".

The first real blockbuster is efavirenz (currently *Sustiva* or, in some countries, *Stocrin*) in November 2013. Efavirenz, as well as being used in its own right, is an ingredient of *Atripla*, the once-a-day combination pill used by a large number of people as their first-line therapy. It's rumoured the Israeli generic manufacturer Teva will start shipping out generic efavirenz the day the patent expires.

The protease inhibitor booster ritonavir (*Norvir*) comes off patent around the same time. However, while the active substance comes off patent, the process that manufacturers Abbott devised to turn it from a capsule needing refrigeration to a heat-stable pill remains patented. The company's Dirk van Eeden told *HTU* that the World Health Organization had 'prequalified' pills made by several generic companies and was presumably satisfied as to their efficacy, so there should be no return to ritonavir capsules.

We'll have to wait longer for others; abacavir (*Ziagen*, and - with lamivudine - in the combination pill *Kivexa*) at the beginning of 2016; boosted lopinavir (*Kaletra*) at its end; and, in 2017, the biggest fish of all, tenofovir (*Viread*), the drug that's also in *Truvada* (along with emtricitabine [FTC], a drug easily substituted by lamivudine), *Atripla* and *Eviplera*.

How much do generics save?

Why will the NHS and other health systems start prescribing generics? Simple: cost.

Generic drugs cost a fraction of the price of brand-name drugs. This is largely because generic companies don't have to go through the costly process of drug discovery and approval, which involves an escalating series of randomised controlled trials (although it is striking how patent holders have been able to reduce prices for lower-income countries when there is generic competition).

All they have to show is that their formulation of the generic drug is pretty much as effective as the branded drug: they'll be allowed to sell their drug if their tests show it's up to 5% less – or more – effective than the branded drug.

A presentation² at the recent International AIDS Conference in Washington found that, even using very conservative estimates of efficacy, replacing Atripla with generic efavirenz and lamivudine, plus tenofovir, would save US\$4000 per quality-adjusted year of life (QALY) for each individual on treatment in the US, and would save the country \$920 million on its annual drugs bill.

That's just anti-HIV drugs. Overall savings from generic medicines in the US were estimated to be \$139 billion in 2009.³ That's one dollar in every \$18 saved of the \$2.5 trillion the US spends on health care, and whereas generics represent 70% of the drugs prescribed in the US, they comprise 83% of those prescribed in the UK.⁴

"By the end of 2013 I'd expect the price of a first-line regimen of Truvada [the branded tenofovir/emtricitabine combination pill] and generic efavirenz to come down by about a third, compared with Atripla," says Professor Brian Gazzard. Best known as an HIV consultant, Gazzard has also been a key member of the London Specialised Commissioning Group's Drugs and Treatments Subcommittee (LSCG DTSC), which provides clinical support for the negotiation of HIV drug prices for London.

The emtricitabine in *Truvada* could also be replaced by the closely similar lamivudine, he adds, which would cut the price by as much as two-thirds. The London group has calculated that adopting generic efavirenz alone could save the capital's NHS at least £2.6 million and possibly as much as £9 million. Add in generic nevirapine and you're talking about a potential saving of £13.3 million. This is without having to take controversial measures such as switching drugs, which London commissioners urged clinics to do last year in order to save £8 million.

Won't drug companies just put up the price of their branded drugs, which as yet still form an essential part of antiretroviral therapy regimens, to compensate, I ask. "No," says Gazzard, "because it's illegal in the UK to raise the price of a drug above the

“In the context of the English NHS's quality improvement programme, this represents an excellent opportunity not just to meet the target of finding £20 billion in savings in the NHS by 2015 but also to expand treatment to more patients, with higher CD4 counts, including patients who may be seeking treatment for reasons of prevention.”

Claire Foreman,
Assistant Director, London Specialised
Commissioning Group

list price set when it was originally licensed for sale. Locally, NHS trusts usually manage to negotiate discounts on the list price, but these are usually in the order of 10%. You'd still save money."

How will this be managed?

In England the move to using more generics will happen at the same time as changes in the NHS which will, amongst other things, see HIV treatment and care commissioned nationally from 1 April next year.

Claire Foreman, Assistant Director of the London Specialised Commissioning Group, says: "In the context of the English NHS's quality improvement programme, this represents an excellent opportunity not just to meet the target of finding £20 billion in savings in the NHS by 2015 but also to expand treatment to more patients, with higher CD4 counts, including patients who

may be seeking treatment for reasons of prevention."

I ask whether national commissioning presents a possible threat to patients, as well as an opportunity. Will generics be so much cheaper that there will be pressure to put or keep people on regimens that are less easy to tolerate, are marginally more likely to fail, or that have worse side-effect profiles (especially ones that don't show up in tests, like psychological unease) when newer, on-patent drugs might be better? Will the new NHS Commissioning Board mandate rigid treatment protocols and budgets that won't take into account the differing needs of individuals?

"I don't think national commissioning will involve producing a new set of treatment guidelines," she says. "We already have those. You could have a general set of guidelines, but allow for local variations."

Simon Collins, editor of HIV Treatment Bulletin at i-Base, and like me, a patient rep on the DTSC, does worry that there may be pressure to adopt cheaper regimens.

"Most combinations in the UK are now £6000 to £7000 a year. Though highly cost effective, to a funder £3000 to £4000 for a generic regimen looks a lot better. There may be underlying pressure for preferential use of drugs [that are generic] such as efavirenz that have a subtle side-effects profile. There are already incentives in the latest agreements to prescribe cheaper drugs for relatively small cost differences and if potential savings increase, the pressure might increase." Switching for tolerability, rather than outright virological failure, might get that bit more difficult, in other words.

Different kinds of changes to your pills

Changing to generics may involve different levels of change that people may be more, or less, happy with. There is no implication that people who need the branded drugs for medical reasons will have to take generics.

The first is that the appearance of your drugs may change. This, which may sound trivial, may be the thing that matters most to some people.

Douglas Kamerow, associate editor of the British Medical Journal, commented in an article last year: "Confusion may arise in patients when they find that their dependably round yellow pill is now a green oblong. Patients, especially elderly patients, use colour to identify their pills, and report great concern when the appearance, packaging and labelling change. This...may lead to a decrease in adherence."⁵

Secondly, one pill once a day may become two or more, either because the new suppliers, as with nevirapine, do not

make the higher-dose version, or because a combination pill is split into its components. (Or two could become one: generic companies already make combinations for the low-income countries that you won't find in the UK, and there's no reason a company couldn't make, say, an efavirenz/lamivudine pill for the UK market from 2014.)

People are often concerned that splitting combination pills into their components will result in lower adherence. While combination pills are undoubtedly popular amongst both physicians and patients, especially in situations where patients pay and a combination pill counts as a single medicine, there's little evidence that there's any difference in outcome or adherence.

One study presented at the Glasgow HIV drug therapy conference two years ago (funded by *Atripla* manufacturers Gilead) found that people who took one pill a day were 60% more likely to miss fewer than one in 20 doses than those taking three or more pills a day.⁶ But that study purely compared numbers of pills. People on one pill a day could only have been on *Atripla*, but those on three or more could have been on all sorts of combinations and would include a much higher proportion of people who were treatment-experienced and had drug-resistant HIV.

A more recent study presented at the International AIDS Conference in July⁷ found no difference in adherence between people using single-tablet regimens and multiple-tablet ones, as long as the regimen was a once-a-day one. Even this, however, did not directly compare a fixed-dose pill with its component drugs.

A study last month⁸ found that patients prescribed single-pill regimens were no more likely to take them than multi-pill ones. Eight per cent of patients prescribed single pills failed to even fill their prescriptions compared with 10 to 12% taking other regimens (not a significant difference). This was, however, in the USA, where patients are more likely to be non-adherent for financial reasons.

Some researchers in the UK are looking for funding to conduct a trial comparing adherence rates and outcomes between people starting ART with *Atripla* and those starting on the component drugs tenofovir, emtricitabine and efavirenz.

Others argue that comparing people starting on the two different formulations doesn't account for the fact that switching in itself may exact some penalty, and instead suggest a trial design in which 50% of participants are randomised to switch away from their existing *Atripla* to the component drugs.

The third level of generic switching is

“Most combinations in the UK are now £6000 to £7000 a year. Though highly cost effective, to a funder £3000 to £4000 looks a lot better. There may be underlying pressure for preferential use of [generic] drugs.”

Simon Collins,
HIV Treatment Bulletin, HIV i-Base

to substitute one drug for another that is closely equivalent: an example from outside the HIV field would be the cholesterol-lowering statins, where one of the most powerful, rosuvastatin, is still on patent as *Crestor* but the others are all available as generics. Inside HIV, one example would be switching branded emtricitabine, as *Emtriva* or in *Truvada*, *Atripla* or *Eviplera*, for generic lamivudine. These drugs are thought to be closely similar in efficacy.

They're not identical, though. One recent study from France⁹ compared people on regimens including tenofovir/emtricitabine with ones taking tenofovir/lamivudine. It found that although the two drugs were comparably effective, if lamivudine-containing regimens stopped working, people's HIV was more likely to develop drug resistance than if emtricitabine-based regimens failed, even though resistance to these two drugs is conveyed by the same mutation in HIV.

More controversial would be a switch already done in some areas for reasons of cost: using abacavir instead of tenofovir in people's first regimen. We have previously covered the decision in London (see *HTU 205* and *212*) to offer patients abacavir as first preference; as yet we don't have the results from audits to know whether there has been any change in the efficacy, tolerability or adherence to first-line regimens as a result. There is still argument as to whether abacavir is less efficacious in

people with high viral loads, or associated with more heart attacks. Actually switching people to generic abacavir once it became available, says Brian Gazzard, "would need to be re-discussed in some detail"; he isn't sure how acceptable it would be.

Finally, there's the option of switching from a once-daily regimen to a twice-daily one. Here the data are clear: taking pills twice a day is associated with significantly poorer adherence. In the study quoted above,¹⁰ adherence was 3% higher in people on once-a-day compared to twice-a-day regimens, 4% higher if they were new to ART and 7% higher if they had already experienced treatment failure on one regimen with a detectable viral load. In terms of clinical efficacy, there was no difference, but it's clear a lot of people wouldn't like it.

Will generics stifle innovation?

Finally, will the switch to generic medicines stifle innovation and starve the pharmaceutical industry of money to develop new drugs?

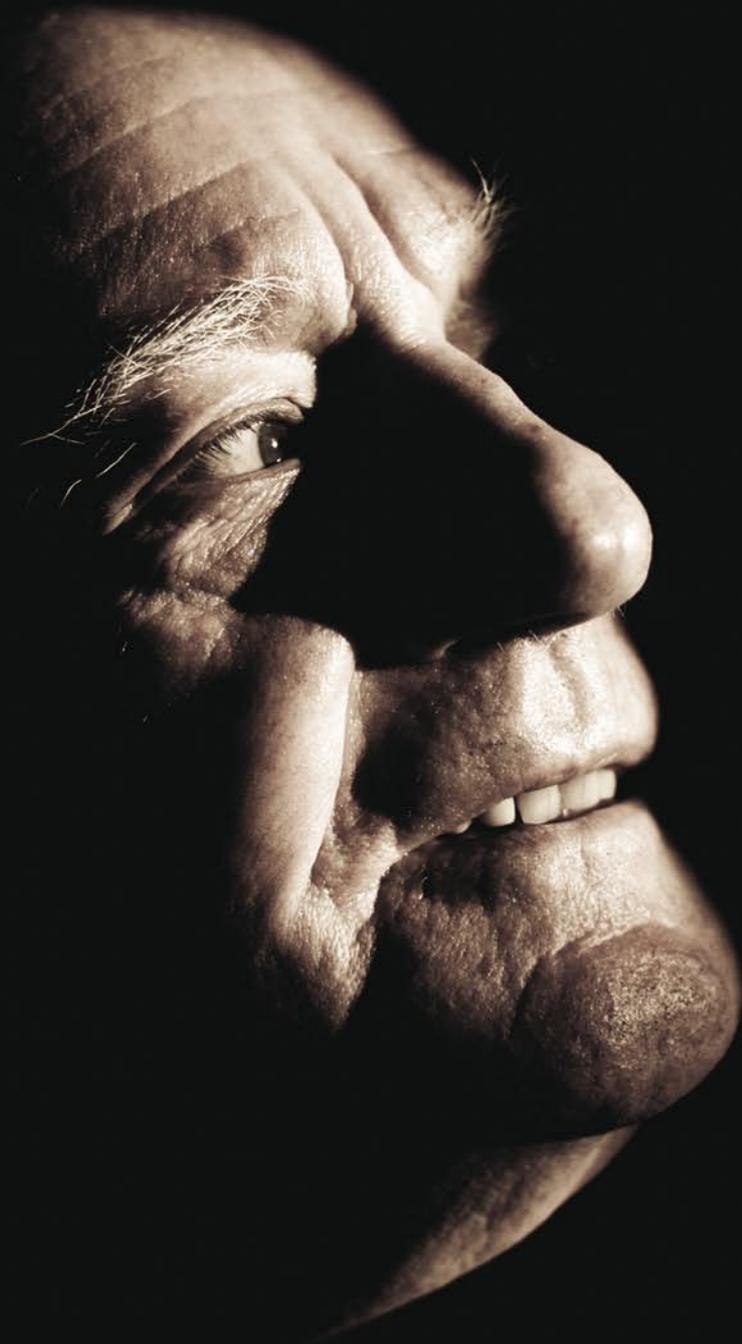
Claire Foreman notes drily that "it's not entirely accurate to suggest the NHS should forego the opportunity of cheaper drugs in order to ensure drug companies can innovate", and Simon Collins says: "Forecasts suggest that the financial potential for developing new HIV drugs will be lucrative for at least the next ten years."

The bar for new HIV drugs will get ever higher though; any new drug would have to be so clearly superior for a significant number of people, so that spending anything up to ten times as much on each prescription would be justifiable to the bodies that regulate these decisions.

We are already running into a situation where the prices charged for new HIV drugs are meeting more criticism than ever before. This is seen in the case of Gilead's new three-drug-plus-booster 'Quad' pill (marketed as *Stribild* in the US, approval is still pending in the European Union), which in the US has been set at 36% more expensive than *Atripla* (the equivalent of about £18,000 a year; UK prices have not yet been determined but are usually cheaper – see i-Base's piece on *Stribild* for more information¹¹).

Drug companies may be gambling on there being enough providers, especially in the US, willing to pay for innovative but expensive drugs before the window of opportunity closes and the economic argument for generics becomes overwhelming. In the UK, it may become increasingly difficult to demonstrate clear medical need for something so much pricier than its near-equivalents. Watch this space, as they say, and keep an eye on your pills too. [nam](#)

A healthy – and happy – old age with HIV



At least one-in-five people with HIV in the UK is now over 50.¹
Gus Cairns asks: What's the recipe for staying fit and happy as we age?

"I've been getting very cross with articles – including one I read in *HTU* – that emphasise how people with HIV are going to die 10 to 15 years younger," says John, 70.

"My recipe for long life is always to think positive and to refuse to be a victim of HIV," he adds.

John is referring to the oft-cited assertion that people with HIV age 10 to 15 years in advance of other people² – in other words that a 60 year-old with HIV has a biological age of 75.

Is this inevitable? Or does it involve factors we can control?

Will we age quicker?

People diagnosed in the last few years who start antiretroviral therapy (ART) at a sufficiently high CD4 count, and stay on it, are likely to have a normal lifespan. One recent UK study found that a non-smoking, 30-year-old gay man, whose HIV is diagnosed promptly, could expect to live until he is 78, the same age as the average UK male.³

This doesn't hold for everyone with HIV, though. Another recent study of life expectancy in people on ART found that, compared to the general UK population, life expectancy at age 20 was 18.3 years less for men and 11.4 years less for women.⁴ That means that, on average, life expectancy for someone aged 20 would be 59 if a man and 71 if a woman. Why the disagreement between studies?

On the one hand, excluding AIDS-defining illnesses – which now cause only a small minority of deaths in people taking ART⁵ – people with HIV also have higher rates of many other illnesses. They have about twice as much cardiovascular disease and 60% more heart attacks than the general population,⁶ are much more likely to get bacterial pneumonia⁷ and are at raised risks of many cancers.

On the other hand, this life expectancy deficit is overwhelmingly concentrated in people who are diagnosed late, and most of the deaths that bring the average life expectancy down occur in the first year after diagnosis.⁸ Also, life expectancy is an estimate of how long we might expect to live given current conditions and no further medical advances.

Anyway, who says *you* are average? If you're reading *HTU*, you're probably not. Half of *HTU*'s readers are over 50 – over twice the proportion in the general HIV-positive population. If you've already got that far, your life expectancy will now extend beyond 59 – and a lot of you will have reached that age already.

“Exercise and diet are key ... [HIV] can be exacerbated by an unhealthy lifestyle, but the burden of disease [it] impose[s] can be reversed by adopting a healthier one.”

**Dr Mike Youle,
HIV Consultant, Royal Free London
NHS Foundation Trust**

Medical issues in older people with HIV

Dr Mike Youle is an HIV doctor with a particular interest in the health of older people.

"Some changes are inevitable natural processes," he says. "Take high blood pressure. It's not good for you, but given that it rises in virtually everyone as they age, is it an 'illness' or just a consequence of ageing that develops at different rates in different people?"

He thinks a lot of the observed deficit in life expectancy and overall health is due to the legacy of untreated AIDS in the pre-ART era.

"A person who's had zero T-cells at some point in their life may never repair the gaps in their immune system," he says. "Their vulnerability to illness may be very different from someone who was treated soon after infection." This is borne out by studies that show that the likelihood of developing cancer⁹ or HIV-related brain impairment¹⁰ is related much more strongly to a person's lowest-ever CD4 count than to their current one. "There is also some evidence HIV directly ages cells," he adds.

So if we take ART, we should stop ageing faster? No, unfortunately. The one class of HIV drugs that virtually everyone on ART has taken are the NRTIs – the nucleoside reverse transcriptase inhibitors. NRTIs prevent HIV's DNA copying its genes. To a lesser extent, they also interfere with our own genes, especially those in our mitochondria.

Mitochondria are little capsules inside our cells that supply energy. Their genes are vulnerable to drug damage because they lack the error-correction mechanisms of the DNA in our cell nuclei. We've largely stopped using the drugs most toxic to mitochondrial DNA – ddI, ddC, d4T and, to a lesser extent, AZT – but the damage may be persistent, and all NRTIs may cause some mitochondrial toxicity.

Mitochondrial toxicity causes a whole range of effects seen in people with HIV – fat redistribution, type 2 diabetes, liver malfunction, nerve damage, damage to blood vessels.

What to do about it

By now, you may be feeling anxious. But there are things you can do to reduce the likelihood of age-related conditions.

"Exercise and diet are key," says Mike. "In many ways, treated HIV and type 2 diabetes resemble each other. They can be exacerbated by an unhealthy lifestyle, but the burden of disease they impose can be reversed by adopting a healthier one."

Our capacity for aerobic exercise is reduced when our mitochondria are damaged,¹¹ but, on the other hand, exercise can actually gee-up slow mitochondria,¹² at least in people with diabetes.

These are not the only risk factors that are under our control. One study in 2009,¹³ and others since, have estimated that the disease burden in people with HIV with undetectable viral loads could be halved if people maintained a healthy weight; controlled their carbohydrate intake and avoided diabetes; had their blood pressure monitored and took medication if it was too high; avoided hepatitis C and were vaccinated against hepatitis B; and stopped smoking. These measures would make even more difference in the over-50s.

So that's what your doctor would prescribe. But what can you do if you're the patient?

Always double-check what the doctors say

David is 67, a retired antiques dealer. He has had health scares, and he thinks that people like him need to monitor their health more closely than HIV-negative people might – and to learn how to get what they want out of the NHS.

"I do believe that people with HIV may present with diseases of ageing in advance of others: I think our health is often a little 'off-colour', he says. "I also think however that older people with HIV, far from being vigilant, may present with symptoms later, because they think, 'It's just HIV'."

In his case, anal screening had established he had AIN stage 2 – anal intraepithelial neoplasia, a change in the cells lining the anus that may, if left unchecked, develop into cancer.

"I felt things weren't right down there," he says. "The pathologist scheduled me for a biopsy but told no one he was on leave and further appointments kept being cancelled. Eventually, when I insisted on an appointment and was seen, they told me I'd have to have immediate surgery and radio- and chemotherapy.

"I phoned one of the HIV consultants who in turn got me to talk to a cancer specialist at another hospital who said 'Don't be ridiculous, we can manage this'." David didn't have to have surgery.

Conversely, he says, he's sometimes had to insist on medical intervention. "I've had skin cancer before and a few years ago I was getting a one-sided headache and a feeling I had persistent sunburn. I took it to the on-call registrar at my HIV clinic and she said 'Yes, it's basal cell carcinoma [the most common form of skin cancer], and we'll see you in two months'. I said 'If this is cancer, get it out of me now!'"

The key, he says, is "always to get a second opinion". He doesn't mean by this to set doctors against each other – unless necessary – but, for instance, to get checked out regularly by your GP too.

“I see my GP practice every three months or so ... GPs will do things HIV clinics don't.”

David, 67

Use your GP

"I see my GP practice every three months or so. You can nominate which doctor you want to see. GPs will do things that HIV clinics don't – such as automatically check your blood pressure."

Mike Youle agrees with this. "I took a long time to engage with GPs, but HIV clinics won't be able to do everything for older HIV patients."

He also thinks all HIV clinics should be setting up age clinics, along the lines of London's Chelsea and Westminster Hospital, which already runs a specialist age and HIV clinic.

David says: "There should be a standard set of good-practice guidelines on what to do for older HIV patients, with a user-friendly version for patients. And there should be a special appointment at the HIV clinic when someone is 50, and maybe every five to ten years thereafter, to do a comprehensive 'MOT' and check for anything likely to cause trouble."

To be really comprehensive, a health MOT would also need to include psychological and cognitive tests. David thinks the psychological and socioeconomic situation of many older people with HIV is crucial to their health.

Depression, anxiety and ageing

Studies show that there is an association between high cholesterol and Alzheimer's disease,¹⁴ and that diabetes and Alzheimer's may be caused by similar metabolic disturbances, to which HIV may add its own kind of impairment. But David feels a lot of ill-health has social and psychological causes. "There are a lot of isolated, mildly depressed older people out there – especially men – who don't look after themselves and for whom life has little to offer."

There's even research that shows that depression and anxiety may have a direct effect on genes that control ageing – and levels of depression in older people with HIV are scandalously high.

Recently, a study in San Diego, California, compared old with young and HIV positive with negative, in a group of 179 locals.¹⁵ It got them to complete separate questionnaires on how easy they found it to deal with tasks of daily life, and assessed their overall emotional quality of life and their burden of diseases common in older people.

It found that daily functioning was worse in people with HIV, especially older people, and that HIV had a stronger effect on ability to carry out daily tasks than age. But the only factor in the HIV-positive over-50s that predicted poorer functioning in every domain, especially compared with HIV-

positive under-40s, was major depressive disorder, sometimes called 'clinical depression'.

That means depression strong enough to stop you getting out of bed. The prevalence of current major depression in the HIV-negative participants, regardless of age, was 2.3%. In HIV-positive people over 50 it was ten times as common – 24.5%.

This is of particular concern because it does not reflect the experience of most people as they age. Older people are generally happier people. In 2010, a study in New York asked nearly 350,000 18- to 85-year olds how stressed, angry, worried, sad or happy they were.¹⁶ The peak age for being happy was 70, and the peak age for overall wellbeing was 85; perhaps the only reason it wasn't older is because that's where the survey stopped. Other research shows that the patterns holds true for western and eastern Europe, Latin America and Asia.¹⁷

There is also research – among HIV-negative people – that indicates a direct link between emotional upset and length of life.¹⁸ Not because it makes people smoke or drink or kill themselves, but because stress directly harms genetic material that protects us against the effects of ageing.

Given levels of depression as high as those seen in the San Diego study, it could mean that a large portion of the reduced life expectancy seen in people with HIV can be directly laid at the door of isolation, stigma, shame and worry. And the key to a longer life might be to make friends, stay proud, fight stigma and stay calm.

A sense of belonging

Mike Youle says: "It's a cultural thing, operating at several levels. One is that older people feel on the shelf generally: the best thing you can do for them is offer the chance to work. Secondly, there's not been a place for retired men to go to. The Women's Royal Voluntary Service is now actually doing some work with older single men and how to engage them... Thirdly, there's never been any model for how you age gracefully as a gay man, not even in the pre-HIV days."

One thing he'd like to see, he says, "is one of the best things I think the Terrence Higgins Trust ever did – buddying. This time, not for people with AIDS, but for older people with HIV."

One recipe: friends, dancing and good food

John might be an example to follow. The 70-year-old retired lecturer in earth sciences has regrets, in particular the loss of his beloved partner of 25 years, Nick, who died of AIDS in 1993, and that he has not found another to be with in later life.

“Staying positive and surrounding yourself with people who like you is the key, and especially retaining an interest in helping others ... [E]very time you take an interest in someone else it prolongs your own life.”

John, 70

In other ways, however, his life is very full. "I love London and would not want to move out of it, even though most of my friends have," he says. But he maintains a group of friends, gay and straight, men and women, and visits one nearly every weekend.

He also has his weekly exercise workout. "Every Thursday I go to Heaven gay disco in London and dance for a couple of hours. It keeps me fit and I'm surrounded by 20 year-olds who are nice and friendly; I have been with younger people most of my working life and I'm sure this helps me keep a youthful outlook." Having said that, realising dancing didn't exercise his upper body, he's just bought a set of dumbbells.

He is very concerned about his diet, not in a faddish way, though he does worry about the constantly changing dietary advice. "But I do always cook myself a proper meal in the evening and will have a large glass of single malt Scotch whisky – never more – to speed me along while I'm doing it."

Like David, he believes in the value of getting second opinions and questioning medical decisions. He has reason to: he has multi-class drug resistance and lipodystrophy, and had lactic acidosis that nearly killed him, partly because doctors attributed all the acute symptoms he was suffering from to one drug, nevirapine, when in fact most were caused by another, ddI. John's health picked up when he decided to follow his original "wonderful" HIV doctor to his new clinic.

"Doctors, and especially GPs, don't pick things up," he says. "You have to push things in front of them". Like David, he sees a GP practice where there are two nominated doctors he chooses to see.

Also like David, he's had more problems with inexperienced staff. "I went [to my HIV clinic] and my regular doctor wasn't there. I saw a registrar who said 'Your results are fine', implying I could leave, but when I asked what my viral load actually was, it was 220. I said 'Excuse me, it's supposed to be under 50!' and demanded another test. This was in fact the first sign of my drugs failing, as subsequent tests showed higher viral loads. I'm now on a new regimen which I'm pleased to say is working well."

He keeps himself mentally alert, saying "I read *The Economist* rather than sit there doing Sudoku.

"I think staying positive and surrounding yourself with people who like you is the key," he concludes, "and especially retaining an interest in helping others. Some older people get very self-absorbed. I think every time you take an interest in someone else, it prolongs your own life. Ask not what they can do for older people like you, but what an older person like you can do for them." 

“How are we going to have a baby? I’m positive and you’re not”

Joanna Moss of the African Health Policy Network (AHPN) looks at conception and fertility guidelines and services for people living with HIV in the UK.

With effective HIV treatment and a managed delivery, the risk of mother-to-child transmission of HIV is very low. In the UK, the risk of mother-to-child transmission for women who have been diagnosed and who receive the right advice and treatment, is below 1%, with transmission rates for babies of women on combination therapy and a viral load of less than 50 copies/ml at 0.1%.¹ So for many people with HIV, having a healthy, HIV-negative child is an achievable goal.

Currently, advice on how a heterosexual couple of differing HIV status (often called ‘serodiscordant’) should go about conceiving if they wish to have a child is changing rapidly. In the last two years, significant research findings have changed opinions on conception methods considered safe for people living with HIV and their HIV-negative partners. In particular, there has been considerable debate about the risk of HIV transmission through unprotected sex. This is because of new evidence for the efficacy of HIV treatment

as prevention (when a person living with HIV takes effective HIV treatment and their viral load is suppressed to an undetectable level, this reduces infectiousness), and of pre-exposure prophylaxis (PrEP; the use of anti-HIV drugs prior to exposure to HIV to prevent infection). These prevention methods – individually or in combination – should significantly increase options for conception methods for some serodiscordant couples.

The UK’s National Institute for Health and Clinical Excellence (NICE) covers conception services for people living with HIV in its national fertility guidelines.^{2,3}

This article looks at the guidelines for conception and fertility services for people living with HIV in the UK, examines experiences of using conception services, and considers whether recommendations are struggling to keep up with new research.

HIV and pregnancy in the UK

Each year from 2005 to 2010, between 1100 and 1300 children were born in the UK to women with HIV.⁴ This means that, since





2005, thousands of women with HIV have successfully conceived and nearly all had babies born without HIV, thanks to effective HIV treatment and care. Many of these women have sought advice or assistance on the safest way to conceive.

In 2009, HIV prevalence was estimated at 0.28% amongst women giving birth in the UK. The majority of pregnancies in women with HIV are in sub-Saharan Africans (with 2.19% HIV prevalence amongst sub-Saharan African mothers giving birth in London, and 3.41% prevalence elsewhere in England in 2009). African people comprise the second-largest group affected by HIV in the UK, accounting for more than half of heterosexual transmission. There is also significantly greater HIV prevalence amongst women born in Central America and the Caribbean (0.78% in 2009).⁶

The *Plus One* study,⁷ published in 2011, investigated the experiences of African people in different-status relationships living in the UK. Their experiences of conception and fertility services inform this article, as well as giving this article its title.

Fertility and HIV infection

Before discussing conception guidelines, it is useful to be aware of ongoing discussions about reduction in fertility as a result of HIV infection or treatment.

Multiple studies have documented reductions in fertility among women with HIV in comparison to HIV-negative women, because of reduced ovarian reserves (the capacity of the ovary to produce eggs capable of fertilisation) or damaged fallopian tubes,^{8,9} which make it harder to conceive. Preliminary results from a study at the University of Milan suggest that antiretroviral therapy might be associated with higher sperm DNA fragmentation in men with HIV.¹⁰ Higher sperm DNA fragmentation increases the chance of miscarriage, reduced-term pregnancy and foetal abnormalities.

Theories vary on the extent to which fertility is affected. However, it is sensible to consider this possibility when seeking conception advice, particularly if your age also means your fertility is likely to be reduced (fertility starts to decline from the age of 30 in women, and drops sharply at 35¹¹).

Current conception guidelines

Guidelines currently in use in the UK tend to consider three scenarios to determine the safest method of conception:¹²

1. Couples where both have HIV.
2. A serodiscordant couple where the woman is HIV positive and the man HIV negative.

3. A serodiscordant couple where the man is HIV positive and the woman HIV negative.

Since the mid 1990s, treatments for all three scenarios have been relatively well established in the UK and these were formalised in NICE's 2004 fertility guidelines. (An update to these guidelines is currently in progress and is due to be published later in 2012.)

For couples where the woman is HIV positive and the man is HIV negative, self-insemination, using the man's semen and a needleless syringe, is recommended as the best way to conceive, with no risk of HIV transmission.

For a couple where the man is HIV positive and the woman HIV negative, the development of sperm washing technology enabled safer conception. Sperm washing separates the sperm (which is required for conception) from the seminal fluids (which are not required and may contain HIV). The couple are then helped to conceive using the 'washed' sperm by the most appropriate artificial insemination technique for that couple, which depends on their fertility. These techniques include intra-uterine insemination (IUI), where the washed sperm is placed directly into the uterus (womb) of the female partner (done around the time she is ovulating and most likely to become pregnant) and *in vitro* fertilisation (IVF, where the eggs are inseminated with washed sperm in a laboratory). Sperm washing is not risk free, though studies have shown that the risk is minimal.

For couples where both the man and the woman have HIV, unprotected sex may carry a risk of drug-resistant HIV being passed on. The current guidelines therefore suggest that safer conception should involve testing each partner's HIV for drug-resistant mutations. If neither partner has drug resistance, or they have the same type of resistance, they could conceive naturally by unprotected sexual intercourse. If one partner has resistant virus, or both do, with different resistant viruses, the recommendations are the same as for a couple who had different HIV status and, to avoid possible superinfection, conception using sperm washing is recommended.

Real-world experiences

Quotes from the Plus One study illustrate some of the criticisms of methods of assisted conception for people living with HIV. These include the idea that assisted conception is not 'natural', with a number of people wishing to conceive through unprotected intercourse instead:

"I would be very happy to have it, um, natural, natural sex with her and make sure get impregnated. I don't want to go for the sperm wash."

Male, positive

Occasionally related to this was an expression of shame or regret at having had discussions about, or having had, unprotected serodiscordant intercourse. This shows that risk of transmission is not always enough to prevent unprotected intercourse if a couple wants to conceive. For example:

"We did it once without a condom and then I told him 'no we can't carry on doing it without'."

Female, positive

Others commented on practical reasons why they felt that available assisted conception techniques are not acceptable. A number talked about the prohibitive cost of sperm washing:

"It's too expensive to wash them, it's too expensive."

Female, negative

And others about the embarrassment or sadness of having to plan a pregnancy with clinicians:

"I must discuss it with my doctors. [...] It makes me feel bad sometimes. [...] But now I have to discuss with this and discuss with this, everyone has to be aware that if I want to get pregnant. No it's not funny."

Female, positive

The study was designed to give insight into individual experience rather than providing a sample size large enough to make generalisations. There were also a handful of positive experiences from participants who had successfully conceived using the assisted reproduction technologies discussed in the previous section.

Treatment as prevention

Options for preventing HIV transmission have changed radically in the last two years. In 2011 and 2012, research demonstrating the efficacy of HIV treatment as prevention¹³ and the potential effectiveness of pre-exposure prophylaxis (PrEP) was published. Both findings are beginning to have, and will continue to have, a significant impact on the recommended routes for safer conception for people living with HIV.

Reading the quotations from *Plus One*, from couples desperate to conceive, it is easy to understand why there has

been so much excitement about new recommendations for less invasive, less expensive, but still safer conception, and why it is important that they are implemented quickly.

"I have been told that I might have sex with her without a condom if I want babies, some sort of the risk of her being infected is very low. [...] people they talk like that but it is, I have heard about that [...] But is it true anyway that statement?"

Male, positive

Uncertainty about whether or not it is safe to conceive by unprotected intercourse (as expressed in the quote above) is not surprising, given how recent the news on the effectiveness of treatment as prevention is.

To summarise, a pivotal study (referred to as HPTN 052) involving over 1700 couples, showed that there was a 96% reduction in transmission between heterosexual discordant couples if the partner with HIV was taking antiretroviral therapy (ART).¹⁴ This confirms that the risk of sexual HIV transmission is very low when someone with HIV is taking effective HIV treatment and meets certain criteria. This concept is often referred to as 'treatment as prevention' or TasP.

HPTN 052 confirmed what a lot of doctors had suspected for some time: if a person with HIV is taking treatment, the likelihood of their transmitting HIV is reduced to such an extent that in many cases a serodiscordant couple and their doctor may regard this as sufficient protection from HIV. In the light of these findings, a significant revision of fertility guidelines was warranted.

NICE's draft revised fertility guidelines are due to be published in a final version in autumn 2012. They are likely to include a new recommendation for heterosexual couples wanting to conceive. NICE says that, in certain circumstances, using treatment to prevent transmission during unprotected sex is as safe as sperm washing, to enable conception between an HIV-positive man and an HIV-negative woman. Providing the following conditions are met, serodiscordant unprotected sex is considered a safe method of conception:

- Unprotected intercourse is limited to the time of ovulation.
- The man is on highly active antiretroviral therapy (HAART) and is adhering to his treatment regimen.
- The man has a plasma viral load of less than 50 copies/ml (an 'undetectable' viral load).
- Neither partner has any other sexually transmitted infections.¹⁵

If any conditions are not met, or if a couple believes the risk of unprotected intercourse is unacceptable, NICE still recommends considering sperm washing. You will need to discuss whether or not this might be a suitable option for you with your partner and your doctor.

It is thought that some clinicians, who have independently reviewed the evidence, have been recommending this approach for some time.

NICE does not mention this situation specifically, but it might be assumed that in couples where both partners are living with HIV, but have infection with different strains, they might also follow this guidance for safer conception, providing all the conditions are met.

At the moment, NICE is not planning to change its advice for women with HIV whose partner is HIV negative.

In contrast, the Greater Manchester Sexual Health Network also reviewed its advice in 2012 and came to the opposite conclusion. Its advice for couples wishing to conceive by unprotected intercourse is:

"UPSI [unprotected sexual intercourse] is not recommended either in this protocol or in national BHIVA guidelines; [the] only recommended option is sperm washing due to risk of transmission."

At the moment, different clinicians and guidelines are saying different things about the safety and risk of unprotected intercourse, in combination with treatment as prevention, for conception. Once NICE publishes its guidelines, it is likely that local guidelines, such as those from Manchester, will be revised again. Until then, the contradictory advice available from different sources is likely to be confusing. To make sure you get the best advice, it's best to start discussions with your doctor early. They, and other staff at your HIV clinic, will be able to talk through your particular situation and what options may be open to you. They can also talk to you about preparations you can make for pregnancy, such making sure you are in the best possible health.

Pre-exposure prophylaxis (PrEP)

PrEP is the term used to describe the use of antiretroviral treatment by HIV-negative people to prevent HIV infection. An HIV-negative person might take PrEP for a short time while they are at high risk of infection. It is not the same as post-exposure prophylaxis (PEP), which aims to prevent HIV infection taking hold after someone has been exposed to it.

Clinical trials on daily oral PrEP have been

running since 2005. There have been mixed results as to PrEP's efficacy, but the study most relevant to serodiscordant couples, the Partners PrEP study,¹⁶ found that if the HIV-negative partner took tenofovir/FTC (*Truvada*), their likelihood of HIV infection was reduced by 75%. Lower efficacy rates in some other trials, however, led the World Health Organization (WHO) to state¹⁷ that, although trials of daily oral PrEP have shown evidence of effectiveness, "it remains unclear how PrEP may best be implemented and scaled up in settings where its use might be most beneficial".

Their recommendation is that, in cases where additional prevention choices are needed and early treatment for the HIV-positive partner is for one reason or another not taken, PrEP "may be considered as a possible additional intervention for the uninfected partner".¹⁸

The Centers for Disease Control and Prevention (CDC) in the United States (US) has released interim guidance to license the use of PrEP for heterosexual, serodiscordant couples. The guidance sets out the need for healthcare providers to discuss available information about potential risks and benefits of beginning or continuing PrEP with women considering pregnancy, so that they can make an informed decision.¹⁹

Although there has been lots of discussion about whether PrEP could help couples in the UK who want to conceive, NICE's draft guidelines suggest clinicians inform couples that "there is insufficient evidence to recommend that HIV-negative women use pre-exposure prophylaxis". The Greater Manchester Sexual Health Network guidelines state that the network is not making a recommendation at the moment, "though individual clinicians and patients may wish to discuss this issue further as evidence becomes available".

There is anecdotal evidence that some serodiscordant couples are seeking PrEP for extra reassurance, in addition to HIV treatment and/or other measures, while they try to conceive. It is likely to be a confusing issue in the UK until a clear guideline makes a recommendation. In the meantime, there is incorrect and potentially dangerous advice about this on the internet. Always talk to your HIV doctor before making decisions about the best course of action.

In the next few months, there will be crucial developments in conception recommendations. If NICE's guidelines are published in their current form, other fertility guidelines are likely to align themselves and recommend the same conception options, including unprotected

sexual intercourse in certain circumstances. Ideally, this agreement should be reached quickly so that clinicians can give up-to-date and consistent advice.

It is possible that you might be told different things by different doctors at different times, particularly because opinions about the safest way to conceive are likely to keep changing as new research is published. The wider range of options also means clinicians have the responsibility of explaining the benefits and risks of each possible method of conception to each couple.

While more conception options mean more choice, there are also new risks. Unprotected sexual intercourse is not always the safest way to conceive and the draft NICE guidelines do not recommend it for everyone. If you want to conceive, you must still discuss the best option for you with your HIV doctor and - if it becomes relevant - with staff at a fertility clinic.

Sometimes, your options will be determined by other factors as well, such as your general health and your fertility, or that of your partner. Starting discussions early with your healthcare team about having a baby will give you the best possible chance of having a healthy, HIV-negative baby.

Availability and regulation of sperm washing

During research for this article, it became apparent that, for people who still want sperm washing as additional assurance against HIV transmission, information about the availability and regulation of sperm washing in the UK is not always clear. This is useful to be aware of when finding or recommending a clinic.

The Human Fertilisation and Embryology Authority (HFEA) is the independent regulator of fertility services. The HFEA licenses semen preparation and sperm washing is monitored in that category.²⁰

The HFEA also provides a database of licensed treatment centres, which they encourage new patients to use to find fertility services. The database shows that although 42 clinics in the UK say that they provide sperm washing, actually, sperm washing for people with HIV is only available at a small number of clinics, notably at Chelsea and Westminster Hospital and King's College Hospital in London, and the Hewitt Centre for Reproductive Medicine at Liverpool Women's Hospital. Prospective calls to some of the other clinics listed confirmed that there is no referral procedure for people with HIV to these services.

If you want to access sperm washing, ask your HIV doctor where you would be able to get this treatment. **can**

The bottom line in clinical care

The new BHIVA standards



Gus Cairns summarises this important new document.

The British HIV Association (BHIVA) is issuing a new set of standards for the care of people living with HIV.¹

The final version will be launched in time for World AIDS Day 2012. Here we're reviewing the draft version which is, at the time of writing, up for public consultation – which means there may be changes in the final published version.

The new standards represent a radical departure from the previous set, issued in 2007, which were primarily concerned with how HIV care in England and Wales should be structured. The new standards place less emphasis on *where* people with HIV should get care, and more on *what care* they should receive.

BHIVA comments in the supporting text accompanying the consultation draft: "In the ensuing five years there have been significant changes in the field of HIV as well as in the commissioning and financial environment. Changes to the structure of the NHS mean that people living with HIV may access many different health services and organisations delivering health care.

"The [2012] standards [should] appropriately reflect the current health care needs of people with HIV and are relevant to all health services that may provide their care."

Why standards?

BHIVA issued the original clinical standards because it was recognised that while they had been issuing clinical guidelines on what treatment patients people with HIV should receive since the 1990s, (with the latest

version issued this March and published in July), many other factors, aside from which medicines were used, go into the success or failure of treatment and care.

The 2007 standards³ sought to establish a minimum level of expertise, resources and support for different levels of patient need, recommending three different levels of HIV care – primary care (largely about testing and sexually transmitted infections), HIV clinics with outpatient care, and HIV centres with inpatient beds – with properly managed clinical networks.

The landscape for HIV treatment has changed considerably since then, and so has the NHS. The health of a person with HIV will be the responsibility of an increasing variety of providers, for a number of reasons:

- The success of HIV treatments and their standardisation (see *The generic generation*, page 4);
- The drive for wider HIV testing and stronger links with primary care in order to facilitate it;
- The split between national commissioning for HIV treatment and local authority management of HIV testing and STI care;
- The increasing proportion of people with HIV who will need old-age care (see *A healthy old age with HIV*, page 8);
- The fact that sexual health and HIV testing services in England could be run by commercial providers.

BHIVA has recognised that standards specifying *what* should be provided are probably more urgently needed than ones that specify *how*.

At the launch of the new draft standards, Professor Jane Anderson, Chair of BHIVA, said: "We are at a crucial clinical and political juncture. Systemic [NHS] reforms coming into effect in April 2013 bring a risk of fragmentation of a highly effective and cohesive area of medicine, which would be a major setback in the UK response to HIV.

"To secure the current high quality outcomes for HIV care, reduce new infections and reverse the current health inequalities associated with HIV, many different elements need to come together as a cohesive, well planned and executed programme that is both locally responsive and nationally appropriate."

The new standards comprise "a specific, concrete set of statements about the care that an adult living with HIV in the UK should expect to receive".

The new standards

There are 12 separate standards. An introduction emphasises that, like the previous standards, they are about "the ways in which people with HIV should be able to access appropriate services" – although they add that, this time, they explicitly include the undiagnosed.

It again emphasises the importance of networks of clinical services: "No HIV provider...should deliver services in isolation. HIV care should be planned and delivered through networks." However, it adds, "there is no single model for network design," abandoning the three-step model of the previous document.

This lack of one-size-fits-all care means that communication between healthcare providers and with the patient becomes even more important. Here the new standards make a recommendation that may be controversial – which is that, from now on, HIV clinics start tagging the records of their patients with their unique NHS identity number (the one that appears on the NHS card you get when you register with a new GP). Until now, data on the use of HIV-specific services have been submitted by clinics and GPs to the Health Protection Agency and are only shared as anonymous data with commissioners.

“As the delivery of healthcare becomes increasingly shared across a number of NHS clinical areas and providers,” the standards say, “so the effective linking up and flow of information becomes ever more important.”

The 12 standards themselves are each laid out in three sections: a rationale, a set of ‘quality statements’ – that is, minimum standards that should be achieved – and outcomes that could be measured to see if those standards are being achieved. They concern:

1 HIV testing. This standard mainly reiterates the call of the 2008 BHIVA testing standards⁴ to provide HIV testing in a variety of different settings and for all GP registrants in areas where more than one in 500 adults has HIV.

2 Access to and retention in treatment. This reiterates the previous standard that anyone with an HIV diagnosis should be seen by an HIV specialist within two weeks, and within 24 hours if they have symptoms suggestive of AIDS or acute HIV infection. It adds that clinics should have arrangements for tracing people registered with them who disappear from care, and should be able to offer an alternative doctor if a patient is unhappy with theirs. Although they say that “unmet financial and social care needs are common in people with HIV” and that clinics need close links with social, legal, benefit, voluntary sector and peer support agencies, they don’t suggest an auditable standard for the quality of a clinic’s links with such agencies.

3 Provision of outpatient care, including for complex co-morbidities. ‘Complex co-morbidities’ means anything from viral hepatitis through cardiovascular disease to psychiatric illness. This standard emphasises the importance, for patients’ safety above all else, of good communication between the HIV clinic and patients’ GPs and any other specialists. Its auditable outcomes include targets for screening for HIV drug resistance, viral hepatitis, blood pressure, smoking

history, kidney function and cardiovascular risk. It also stipulates that there should be at least annual contact between a patient’s HIV clinic and their GP and that surveys of patient satisfaction should be carried out at least every three years.

4 Safe antiretroviral prescribing. This section concerns adherence support, doctors’ competence to prescribe ARVs, mechanisms to check with GPs to guard against drug interactions, and sets, among others, a target of 80% for the proportion of patients who have disclosed their HIV status to their GP. It also explicitly states that “HIV services should collaborate with commissioners to develop strategies to maintain cost-effective prescribing.”

5 Inpatient care. This points out that most deaths due to HIV disease these days are due to people presenting very late with AIDS and specifies maximum admission times, infection control measures, and expected qualifications for HIV physicians involved in inpatient care for acutely ill people.

6 Psychological care. Pointing out that studies show strong links between adverse life events (including diagnosis and starting treatment), emotional turmoil, and downturns in adherence and physical health, this standard recommends routine and event-triggered screening for depression, anxiety, brain impairment, drug and drink problems and stress levels. It refers to last year’s Standards for psychological support⁵, published jointly by BHIVA, the British Psychological Society (BPS) and the Medical Foundation for AIDS & Sexual Health (MedFASH), for other delivery standards in this area.

7 Sexual health and secondary HIV prevention. This says that sexual health assessment should be offered within four weeks of diagnosis and annually thereafter, with more frequent syphilis screening in gay men, by a practitioner with specific knowledge of HIV transmission risk and sexual behaviour and behaviour change. It also says that people diagnosed with HIV should be helped with the screening for HIV of any children they have and with partner notification. It specifies risk-reduction counselling within four weeks of diagnosis and appropriate referral to further support if necessary. It recommends that post-exposure prophylaxis (PEP) be made available to HIV-negative notified partners, but makes no recommendation for pre-exposure prophylaxis (PrEP).

8 Reproductive health. In line with the soon-to-published 2012 NICE guidelines on fertility treatment,⁶ this standard does not mention sperm

washing as a recommended measure for couples seeking to have children when the father has HIV, saying instead that “timed unprotected sexual intercourse for men...on successful ARV therapy” is as safe. In cases where the woman has HIV, it recommends self-insemination. It says that people with HIV should have the same access to fertility and conception services as anyone else (see *How are we going to have a baby?* on page 12).

9 Self-management. This section says that people living with HIV should have access to services that promote self-management of HIV. It primarily emphasises the benefits of one-to-one and group peer support and peer support schemes by appropriately skilled peer workers with HIV, both in person, on the phone and online. It does, however, also highlight the valuable part occupational therapists and physiotherapists may play in helping people feel more able to manage their daily lives and suggests ongoing auditing of patients’ wellbeing to assess the success of self-management promotion.

10 Service user engagement. This standard takes much of its text from the “Patient involvement in decision making” section of the 2012 BHIVA treatment guidelines. It says that people with HIV “should be as actively involved in decisions relating to their own treatment and care as they wish” and should have opportunities to be involved in the planning of HIV service delivery. It specifies that all formally constituted boards should have a community representative on them and that “HIV services must be able to demonstrate that they have an active patient group or patient representative either locally or regionally within a network arrangement.”

11 Competencies. This sets out the minimum training and experience needed for practitioners at different levels of HIV care.

12 Data, audit and research. This brings together recommendations in the other standards for information flow, auditing practice and research and recommends maximum times for the sending of surveillance data. It reiterates the recommendation that “All NHS services involved in the care of people with HIV should ask and encourage them to consent to the use of their NHS number for data linking.”

The final version of the standards will be launched on 29 November this year. We will report any significant changes to the consultation draft on aidsmap.com. 

News in brief

As well as our news reporting, the news pages on our website include selected stories from other sources. Here we highlight stories from the last quarter – visit www.aidsmap.com/news for the full news reports and references to the original sources.

FUNDING

Funding cut for HIV phonelines

The Department of Health has stopped funding the HIV phone helplines operated by Terrence Higgins Trust (THT Direct) and the Black Health Agency (BHA), and contraception advice lines run by fpa and Brook. Funds will now go to a national Sexual Health Line at 0800 567 123 – the former National AIDS Helpline number – run by the private company Serco. The BHA's I Do it Right phone line closed at the end of September. THT Direct (0808 802 1221) will continue but will no longer run at weekends. Its new hours are 10am to 8pm, Monday to Friday.

➔ www.aidsmap.com/page/2533765

TREATMENT

Double doses don't mar adherence

An Italian study has found that people's adherence to their antiretroviral therapy (ART) was not affected by how many pills

they had to take or even whether they were prescribed one or two doses a day. The study of 2114 patients in Milan found that 79% reported taking all their ART doses and that this was independent of pill burden or dose frequency. The continued importance of adherence was underlined, however, by finding that average adherence was 95% in those with an undetectable viral load and 88% in people with detectable HIV.

➔ www.aidsmap.com/page/2530789

EPIDEMIOLOGY

Africans get more UK HIV than thought

Over 40% of sub-Saharan Africans recently diagnosed with HIV in Britain may have become infected here rather than in Africa, new figures from the Health Protection Agency (HPA) suggest. The HPA's previous estimates were based on people's own views on where they got HIV, and reported that in the 2004-10 period, about 10% of black African people were infected over here. But when they used CD4 cell count to estimate the time of infection, the HPA found that

31% had probably already arrived in the UK before becoming HIV positive and that this proportion increased to 43% in 2010.

➔ www.aidsmap.com/page/2524386

PREVENTION

Condoms only protect if used properly

A US study has found that using condoms in heterosexual sex prevents 60% of infections by the common sexually transmitted infections (STIs) gonorrhoea, chlamydia and trichomonas. However, consistent condom use wasn't good enough: only people who reported no breakage or slippage in condoms were protected. The proportion of people who caught at least one of the STIs in a year was 8.5% in people with inconsistent or no condom use, 6.7% in people who used them consistently, and 3.35% in people who used them consistently *and* correctly. In the group who used condoms consistently but said they slipped or broke sometimes, STI incidence was as high as in inconsistent users.

➔ www.aidsmap.com/page/2522036

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News picks from
 other sources

TREATMENT

New injectable drug shows promise

A new integrase inhibitor called S/GSK1265744 is active against a broad range of HIV strains that have developed resistance to this class, the 52nd ICAAC in San Francisco was told last month. This third-generation integrase inhibitor can also be formulated as an injectable drug with a single jab lasting a month or more. A trial is now underway combining the new drug with the injectable formulation of the NNRTI drug rilpivirine, which also lasts a month. Meanwhile, a study comparing the second-generation integrase inhibitor dolutegravir with efavirenz found that 88% of patients on dolutegravir-based ART had undetectable viral loads after 48 weeks, compared with 81% on *Atripla* (efavirenz/tenofovir/FTC).

➔ www.aidsmap.com/page/2279476

TREATMENT

Women's adherence drops after giving birth

A meta-analysis of 51 studies involving 20,000 women from the US and Africa has found that their average adherence to ART dropped to levels likely to be ineffective after

they gave birth. At 76% (i.e. one-in-four doses missed), adherence was not very high during pregnancy, but it dropped to 53% once the women had become mothers. In this case, frequency of ART dosage and pill burden did impact on adherence, as did poverty, alcohol or drug use, but the strongest predictor of poor adherence was postnatal depression.

➔ www.aidsmap.com/page/2521871

MENTAL HEALTH

HIV treatment cuts depression

When people start HIV treatment, their risk of common non-AIDS-related illnesses such as depression, anxiety, liver disease, cancers, kidney disease, heart attacks and strokes also declines, Spanish researchers have found. In the study, of 5185 people diagnosed between 2004 and 2010, the incidence of AIDS-related and non-AIDS-related illnesses was about the same – 2.5 to 3% a year – but most AIDS cases were overwhelmingly concentrated in the first three months after diagnosis. Starting treatment reduced the annual incidence of non-AIDS-related illness by 29% over the study period. Notably, there were bigger falls in the incidence of mental health problems including depression (which formed 20% of all non-AIDS diagnoses) and kidney disease.

➔ www.aidsmap.com/page/2531806

NS AIDS aids *Salmonella*

New Scientist | 30 September 2012
Salmonella may be evolving by using people with HIV as a low-immunity environment in which to develop, UK researchers found. A new, more virulent form, invasive non-typhoidal *Salmonella*, is linked to the spread of HIV around Africa.

➔ <http://bit.ly/St4BHX>

VS Condoms aren't enough, says Canada

The Vancouver Sun | 5 October 2012
 Using a condom or having an undetectable viral load alone are not enough to protect you from the law if you have sex without disclosing your HIV status, the Canadian Supreme Court has ruled. *Both* conditions must have been complied with.

➔ <http://bit.ly/R56ORP>

USN No treatment boon for poor US blacks

US News | 8 October 2012

The death rate in poorly educated black people with HIV in the US has not declined since before the introduction of HIV therapy, a US study has found. In contrast, deaths have fallen tenfold in US whites and well-educated black people since 1993.

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"How are we going to have a baby? I'm positive and you're not" [p.12]

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The bottom line in clinical care - the new BHIVA standards [p.16]

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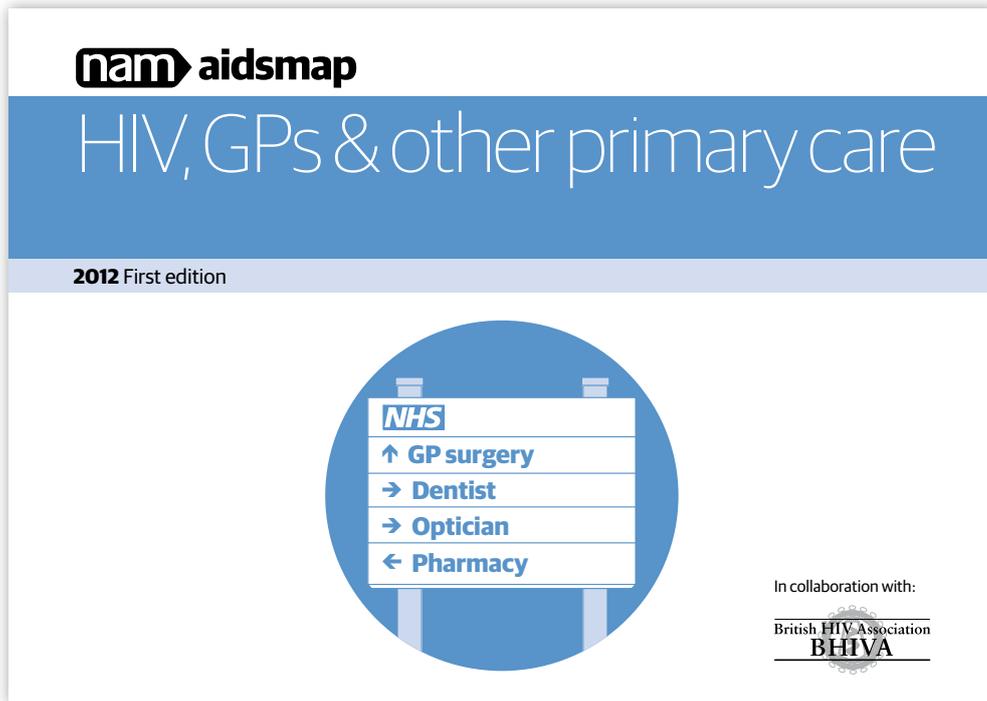
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