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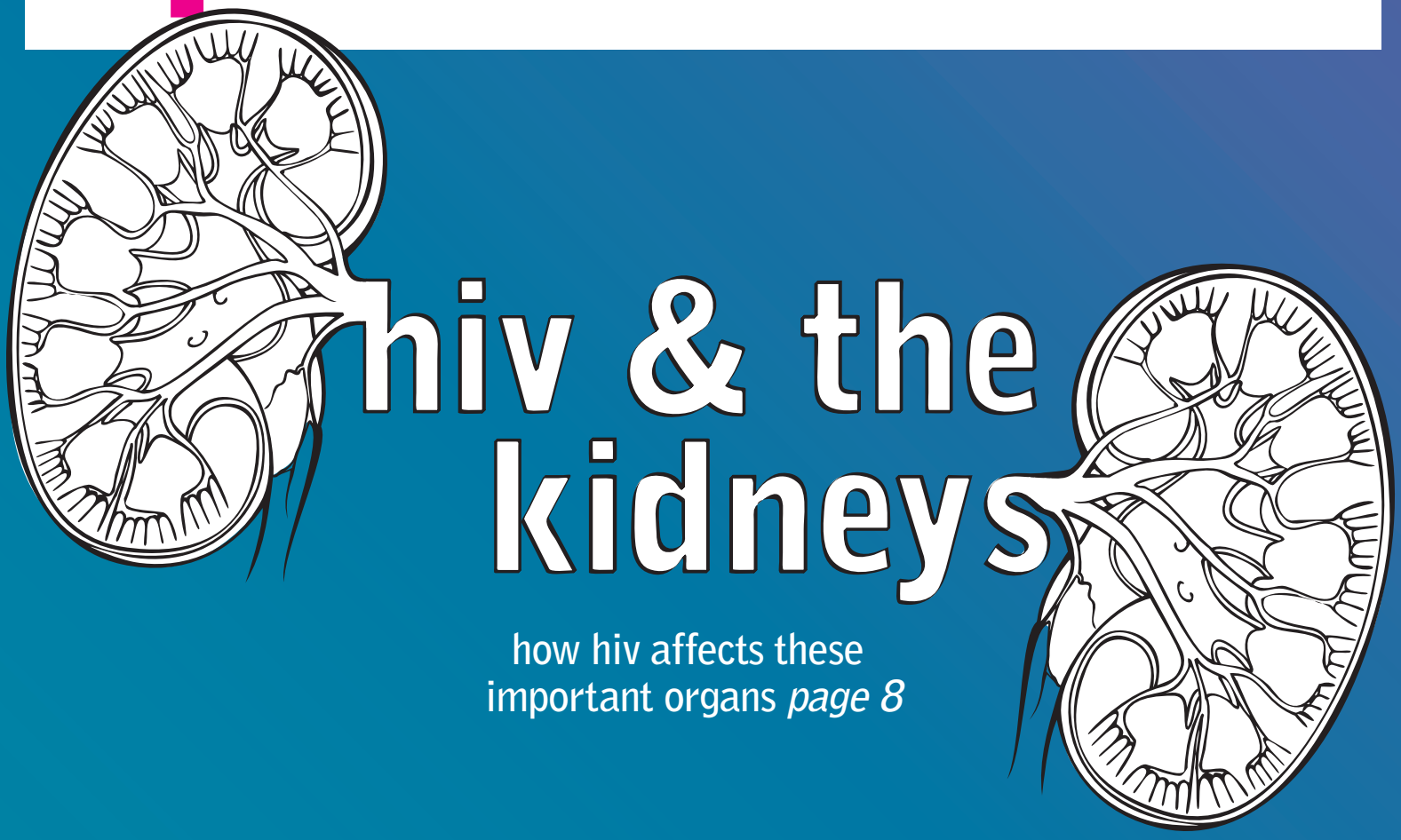
hiv treatment update



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Craig's incredible bike ride

Two issues ago we introduced you to our intrepid fundraiser, Craig, who was about to embark on a cycle ride from London to Vienna to raise money for NAM.

Craig's 2200-mile route took him through six countries - and not only that, it took him over the Pyrenees, French Alps, Dolomites and Austrian Alps, resulting in some physically gruelling terrain.

The weather wasn't always kind to Craig and he found himself cycling through wind, rain and snow, but he battled on and arrived triumphantly in Vienna after 21 days.

Craig says the highlights of his trip were cycling through stunning scenery with beautiful ravines, rivers, mountains and breathtaking sunsets along the Drau River.

"*I have to say it's been an amazing experience and it's going to take me a while to register it all, especially climbing the Stelvio. The Stelvio is something I've wanted to do since I heard of it 4 years ago and it didn't disappoint.*

Thanks to everyone who has donated so far, I couldn't have got through it without all those messages of support to spur me on. Thank you"

You can see some of Craig's amazing photographs here and there are more on our website at www.aidsmap.com/page/1448335. To read his blog from the journey, or to donate, visit his fundraising page at www.justgiving.com/vienna. So far Craig has raised an incredible £1865 through the justgiving page, but there's still time to increase that total!

Fundraising for NAM

If Craig's efforts have inspired you, there are lots of ways you can support our work. It could be that you're thinking of taking part in a sporting event, or you could ask people to donate in support of you kicking a bad habit. Maybe you can see yourself arranging an event or you could draw on the talents of your friends, family or colleagues.

We really value individual donations and every donation helps us to continue creating high-quality information resources, both in print and online. Some of our supporters make a regular donation, some send a donation now and then, and others remember us in their will.

You can also help us by spreading the word about NAM's resources, by passing on resources and sharing weblinks. We want our resources to reach as many people who need them as possible – and from a fundraising perspective, you might also inspire someone else to make a donation!

To find out more about fundraising for NAM, or make a donation, visit our website at www.aidsmap.com/donate. If you are planning to fundraise on our behalf then we would love to hear about it – contact us at info@nam.org.uk or on 020 7840 0050.

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about NAM
NAM is a charity that exists to support the fight against HIV and AIDS with independent, accurate, up-to-date and accessible information for affected communities, and those working to support them.

For more information, and details of our other publications and services, please contact us, or visit our website, **www.aidsmap.com**.

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upfront

What you think about *HTU* now and for the future

Many thanks to all of you who responded to our readers' survey this year. It was included in the July edition of *HTU* and was also available online. We've received lots of useful feedback, comments and suggestions.

This year we were particularly interested to hear how you get your information on HIV-related topics, how you prefer to get it, and what you value (and dislike) about different methods of information provision.

We're aware of the need not to be complacent about *HTU* in its current format. We wanted to explore, amongst other things, how a change such as a move to an electronic version of *HTU* would be received. That's for two reasons.

One, as you might expect in the current environment of economic restraint, is cost. It's cheaper to produce and distribute an electronic document and it would free up resources to use elsewhere.

But the other reason is that technology is moving fast and many of you are moving with it. Some of the newer options for receiving information, such as mobile phone applications, may actually work better for some of you.

In this survey, you told us clearly that you like the print version of *HTU* – and many of you will be relieved to hear that we're not proposing to change *HTU* from a print publication to one that is only available electronically at present.

But you were also clear in many cases that this is a preference, rather than a necessity: 78.5% of respondents use the internet daily and another 15.4% at least once a week; 88.9% have access to the internet at home, with 30.2% able to go online via a mobile phone. And 77.5% of you felt very comfortable (58.1%) or comfortable (19.4%) with using the internet to receive information about HIV.

We won't forget that online information and electronic communications don't work for everyone, but the survey results suggest that we could make *HTU* content available in new ways you might welcome. We've starting this process already by, for example, including feature articles from *HTU* as part of our news pages on aidsmap.com.

Perhaps most importantly, your survey responses suggest that *HTU* is still an important source of information for you. We asked what you particularly valued:

> *"The expertise. I would not believe everything I read except from this source.*
>
> *The tone and level of technical terminology are pitched perfectly to enable in-depth engagement with a topic without getting out of your depth with scientific jargon.*
>
> *Its impartiality and objectivity."*

Just over a quarter of respondents felt they had learnt something vitally important from *HTU*, and 65% something useful. You particularly valued information on new and changing treatments, side-effects, adherence, hepatitis C co-infection, mother-to-baby transmission, ageing and healthy living.

Just under 80% of respondents felt better equipped to take decisions regarding their treatment and care; 61.8% were more likely to discuss their health and treatment with their healthcare team; and 66.9% felt more confident in doing so. 43.6% of people responding had made a change to their treatment, or taken another decision, based on information from *HTU*.

Thank you again for letting us know your views, and for letting us know we're still meeting your needs. We welcome feedback on any of NAM's resources at any time, so if you have comments or suggestions, do be in touch.

> *"I like to be kept informed and this publication does that very effectively, in one place, in an easy to read and digestible format."*

You can ring us on 020 7840 0050, email us at info@nam.org.uk, write to us at NAM, Lincoln House, 1 Brixton Road, London, SW9 6DE, or use our 'Contact us' page at www.aidsmap.com/contact.

New HIV information resource for African communities in south London

The SAFER Partnership delivers primary HIV prevention programmes with African communities in the south London boroughs of Lambeth, Southwark and Lewisham. The partnership comprises seven organisations with expertise in HIV and other health issues for African people: LEAT, Naz Project London, African Cultural Promotions, Africa Advocacy Foundation, Ethnic Health Foundation, North Brixton Islamic Cultural Centre and SHAKA Services.

This month, SAFER will launch its new website. This will be a source of clear information for anybody who has questions about HIV or HIV services for people of African origin. The website will raise awareness of HIV, its modes of transmission and, importantly, how to live well and stay healthy if you are HIV-positive. It will also provide up-to-date information on the services from the partnership and other organisations.

For more information on SAFER, please contact SAFER Co-ordinator Krystle Lai on 07960 281 229 or email krystle@leat.org.uk.

www.saferpartnership.org.uk

Policies on safer sex and needle exchange in UK prisons seem to have stalled. With a high and increasing prevalence of hepatitis C in our jails, and HIV figures last researched properly in 1997, guest writer *Chris O'Connor* asks whether the UK could do a lot better.

Health care and prevention of HIV and hepatitis C in prisons is euphemistically described as 'challenging'. To understand the challenges of devising policies to prevent blood-borne viruses in a prison, one needs to look not only at health policies devised by agencies outside the prison walls, but also the experience of those inside, whether living with or treating these conditions.

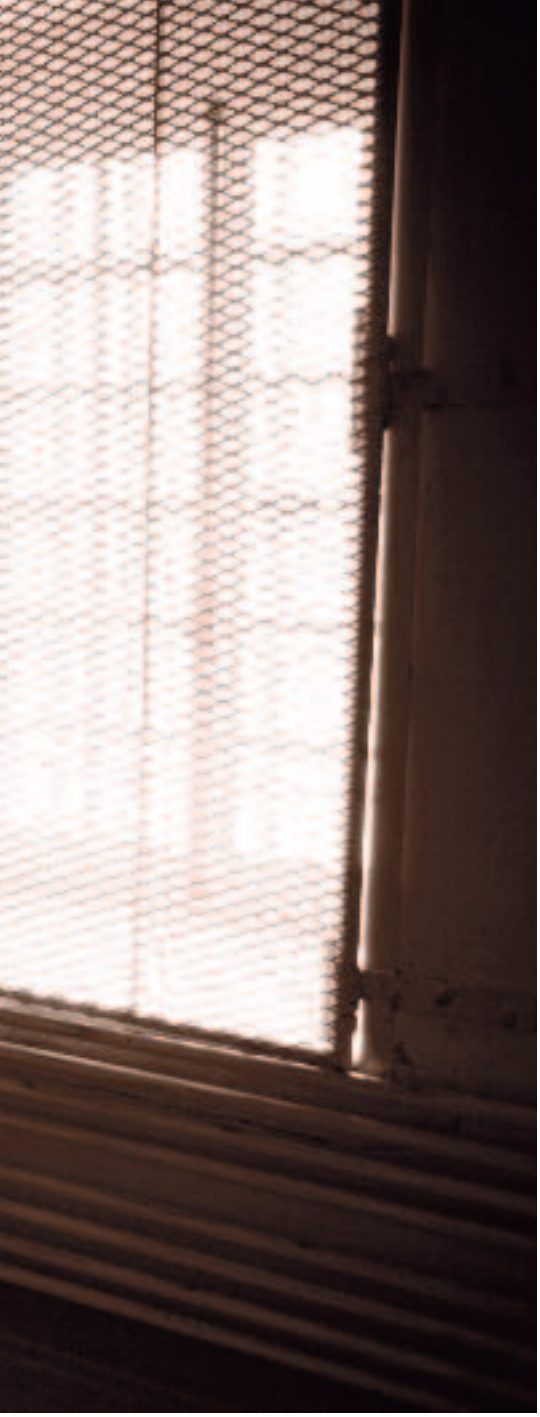
Even when the outside powers have proposed measures such as a needle exchange, inside prison walls, the answer has been no. Security issues; a growing, transient population; fears around stigma and confidentiality; these are just some of the unique challenges of caring for incarcerated people – and that's without worrying about drug injection and sex between men.

Surveillance out of whack

A new report by the Health Protection Agency (HPA), published this September,[1] says: "There still remains a significant number of people passing through the prison estate without being tested for blood-borne viruses, and this situation needs to change."

In particular, they say that current surveillance systems, necessary to develop HIV and hepatitis C services, are "inadequate".

Yusef Azad, Director of Policy at the National AIDS Trust (NAT), agrees: "There is a significant and worrying gap



in the data which is essential to close if we are to get a proper understanding of how many prisoners remain undiagnosed, or at risk of infection. NAT has been calling for a new anonymous survey of blood-borne viruses in prisons for several years.''

Now there has been movement. The 2010 HPA report includes – for the first time since 1997/98 – unlinked anonymous surveillance figures for prisoners with hepatitis C and HIV. But they tell a complex story.

The last time there was a specific survey of HIV prevalence in prisoners was back in 1997. In this survey, from a sample of 3942 prisoners drawn from eight of the UK's 130 or so prisons, 7% tested positive for hepatitis C and 0.4% for HIV.[2]

The 2010 data set consisted of results from prisoners who were tested for hepatitis C (but not HIV) as part of their routine health care. This covered the period 2005 to 2008 and included 39 prisons (30% of the prison estate). Of the 10,723 tested for hepatitis C antibodies, 24% tested positive.

This apparently large increase may be due to the fact that these were prisoners assessed specifically for healthcare problems and may also be partly due to different prisons being included: in the big prisons in north-west England, hepatitis C prevalence is known to be above average. But it also appears partly real.

To assess HIV prevalence, the HPA looked at its existing SOPHID (Survey of Prevalent HIV Infections) database of people accessing HIV treatment and care services. It states that: ''In 2008 171 prisoners were reported to be resident in English prisons at the time of reporting, and an additional 82 individuals were reported as resident in prison prior to 2008''. What this latter figures means is ''some of these may be in prison and some are not: we don't know''.

With the UK prison population numbering some 85,000, the lower SOPHID figure would imply that HIV prevalence in prison was 0.2% – exactly the same prevalence as in the UK general adult population aged 15 to 59. Even if you include the 82 'possibles', it's still only 0.3%: lower than in 1997, against a background where the general adult population HIV prevalence has more than doubled.

The HPA says that these HIV figures are ''likely to underestimate the true figure, with under-reporting particularly affecting prisoners with shorter custodial sentences''. Their rough estimate is that there are about 300 to 500 people with HIV in prison – about 0.5% or double the general-population prevalence. This means that the number of people accessing HIV care in prisons is lower than the number who actually have the virus.

The HPA adds that injecting drug use (IDU) risk is likely to be substantially under-reported too, with the 19% of prisoners identified as injecting drug users likely to underestimate the true total.

Who takes responsibility?

Prison health in England used to be run by Her Majesty's Prison Service itself, but in 2000 responsibility was moved to the Department of Health, and in 2006 budgets and administration were transferred to primary care trusts (PCTs), like every part of the NHS. Scotland, with its own legal and prisons system, is undergoing the same process. In Wales, health care is funded by the National Assembly and commissioned by local health boards, and in Northern Ireland it is the responsibility of one regional health and social care trust. The commissioning of prison health care by PCTs has led to contracts that split into a variety of services and a patchwork of providers.

A prison healthcare worker who preferred to remain anonymous told *HTU*: ''PCTs don't know how to run a prison healthcare unit, and so they farm it out as quick as they can.''

In late 2009, Secure Healthcare, a not-for-profit organisation which had the contract for Wandsworth Prison, went bankrupt, forcing NHS managers to step in to ensure care for 1600 prisoners. The collapse of Secure came only three months after it signed a three-year contract extension with Wandsworth PCT.[3]

Although Secure had made some service improvements, Anne Owers, the Chief Inspector of Prisons, visited Wandsworth in June 2009 and noted ''staff vacancies... no immunisation clinic... too many external appointments cancelled or missed''.[4]

A concern for contractors in this area is indemnity. As a contractor, Secure was not governed by NHS indemnity and had to provide its own expensive clinical negligence insurance.

Staff from the HIV charity Positively UK (formerly Positively Women) visit three women's prisons on a regular basis; the organisation has a long history of supporting women at HMP Holloway. They also face uncertainty over their future role. Their current access agreement at Holloway is with the Royal Free Hospital, which has not been

shortlisted for the new healthcare contract there: it is believed the prison authorities wanted a GP-led polyclinic instead. The Independent Monitoring Board's annual report on HMP Holloway for 2009 states that: "the Board regrets the fact that [Islington] PCT does not appear to have a full understanding of the complexities of prison healthcare."[5]

Opportunity unlocked

Despite these changes, the move to NHS governance has largely been seen as a positive step. Dr Wassim Malas is a GP who was formerly a doctor at a large prison with health care run under Home Office guidance and, more recently, at a privately operated prison where health care came under the NHS umbrella.

"There was a huge difference between the two," he says. "Previously, the priority was the running of the prison and getting people to court. If a prisoner had an appointment with an HIV consultant, and there was no staff to escort him, he missed that appointment." It could be weeks, if not months, before the prisoner obtained another consultation and they might experience an equally long gap in HIV medication.

"People in prisons are now a lot more aware and they try harder to ensure a prisoner sees [their] consultant," adds Dr Malas. "Previously a prisoner had no voice; the stigma around HIV and hepatitis C was so strong that they couldn't kick up a fuss if they had no meds. Now, where I have worked, it is much more open, and prisoners are usually not afraid to say they are on medication."

Mark Wilson is a sexual health nurse specialist who works for the Terrence Higgins Trust. Dealing with a number of positive prisoners in HMPs Dartmoor, Exeter and Channings Wood in Devon, he says that the supply of antiretrovirals at the prisons where he works is generally not an issue. "If a prisoner is deemed okay to keep drugs in his cell then it is usually not a problem. ARVs are prescribed a month at a time because of the turnover of prisoners and to help with adherence issues. But difficulties can arise when a prisoner is deemed a threat to himself and cannot keep his own medication: supervised dosing every twelve hours can be a nightmare."

Prison can be a safe and even a good place to be diagnosed and treated. We have experience of women managing to turn their lives around after diagnosis, having established stability in prison. Sophie Strachan, Positively UK

Sophie Strachan, prison worker with Positively UK, comments: "Prison can be a safe and even a good place to be diagnosed and treated. We have experience of women managing to turn their lives around after diagnosis, having established stability in prison." She says she has seen at first hand the need for HIV-positive women to receive peer support. Having turned up at one prison to offer support to one prisoner, seven other HIV-positive women also wanted a visit – with two more requesting one next time.

Positively UK adds that a list of medical conditions specified in the British HIV Association (BHIVA)/British Association for Sexual Health and HIV (BASHH) testing guidelines should trigger a HIV test but they often don't. They support opt-out testing "providing prison staff and healthcare workers are trained and a positive diagnosis does not result in discrimination".[6]

Let's talk about sex

Sex between men in prison is an area shrouded in obscurity. It's not allowed, it does happen, but how often it does is unknown. There were two surveys investigating risk behaviour associated with blood-borne viruses in prison in the 1990s. The first showed that between 1.6 and 3.4% of adult male prisoners had sex with another man whilst in prison and the second one 4%, with little use of condoms.[7,8]

Anecdotally, sex is socially frowned upon by the prisoners. One nurse told *HTU*: "If a guy is having gay sex he leaves himself open to a punishment beating. I have had three guys admitting to having sex with a man since I have worked in prison, and they were all on the vulnerable prisoners unit (VPU).

"It is extremely rare on the main wing. On the VPU it is relatively common, say 20% of the guys in there, although the majority of it seems to be oral sex. A lot more research needs to be done."

A statement by a Department of Health spokesperson to *HTU* said: "Prison authorities owe a duty of care to protect all prisoners. Sexual activity between prisoners carries with it a known public health risk. Prison staff must therefore make condoms, dental dams and water-based lubricants available to any prisoner who requests them." The statement goes on to say that healthcare staff should assess risk, "…provide appropriate information and guidance on sexual health education and any necessary counselling".

It is prison service policy to prescribe condoms where appropriate. But in practice, condom distribution is difficult. Wassim Malas says: "Ten years ago I tried to issue a gay guy a condom. The nursing staff was up in arms and I had to write a prescription – his confidentiality was definitely compromised. Condoms would draw attention if you requested one. I never had a big box of condoms to dish out; sex between men in prison is dangerous."

To some in prison health care, condom provision provides more problems than solutions. One nurse told *HTU*: "Security in prison hates condoms; they are seen as being used for 'plugging' [smuggling drugs or mobile phones in through the anus]. I have only had two

to three requests for a condom since I worked in prison."

In 2009 there was a pilot condom-supply scheme at a male prison in the south of England. Support was raised from staff and health managers, staff concerns were identified and addressed in workshops, and condom distribution was gradually introduced across the prison. No untoward incidents were reported.

Confidentiality in prisons is a huge issue. Positively UK workers have to space their appointments so that prisoners do not meet en route, and many prisoners often cancel at the last moment through fear of being identified as HIV-positive.

Mark Wilson says: "The reality of life and health care in prison means staff have to be flexible in their approach ... and assertive in understanding the needs of the prison establishment and the prisoner. We have to work out effective compromises."

One HIV consultant working in prisons says: "Someone who is involved in risky behaviour, needles or sex, who comes to me looking for help, I respect his right to anonymity. What happens in health care stays in health care – or it should. But I have consulted with one prisoner about his HIV while he was surrounded by four prison officers – he needed to see me, but was classed as dangerous, and so his confidentiality was totally compromised."

Needle exchange pilot scheme stonewalled

Successful efforts to reduce blood-borne viruses among injecting drug users have included the use of needle exchange programmes. Within UK prisons, however, such a strategy has so far failed even to be assessed. The best that has been done so far is a Prison Service Instruction ordering prisons to provide disinfectant tablets.

No needle exchange provision or pilot projects have been planned in England, Wales or Northern Ireland. But when Scotland rolled out phase two of its Hepatitis C Action Plan in May 2008,[9] it included recommendations for a study into the pros and cons of needle exchange.

This has hit a wall. According to Ruth Parker, a Substance Misuse Manager at the Scottish Prison Service, "There continues to be a failure to negotiate with the Scottish Prison Officers Association to support the introduction of an in-prison needle and syringe exchange feasibility pilot." The SPOA says it is negotiating, but so far has refused to entertain the idea of needle exchange.

David Johnson of Scottish HIV charity Waverley Care says this pilot clean-needle scheme, at HMP Aberdeen, has been touted for many years. "There is a lot of opposition from prison staff: if they are not behind it, it will be difficult to implement."

He adds that, as part of the action plan, hepatitis C has become the focus of attention in prisons and HIV prevention could be left behind.

"After the 'Glenochil outbreak' in 1994, when 13 out of one group of prisoners became infected with HIV through sharing home-made injecting kit, HIV awareness was really raised in prisons – yet it now feels that HIV has slipped down the agenda," he says.

A 2010 report recommended a pilot scheme which would see a tattoo studio established in a long-stay prison to prevent hepatitis C transmission – but that has also met with a blank. The report suggested prison bosses should increase inmate education about tattooing and make clean materials available.[10]

A study in the International Journal of Drug Policy 2008, showed that 54% of Scotland's 8000 prisoners said they had a tattoo, including 18% who claimed to have had theirs done while in jail. The link between hepatitis C and tattooing is well-established.

As with needle exchange in prisons, the disconnect between evidence-based approaches to public health and what is deemed acceptable by staff and public continues. The Scottish Prison Officers Association warned in the local press: "It raises the issue of where do we stop if we do something like this. We've never been approached about this, but it wouldn't be appropriate. If we have these tattoo kits in, do we then bring in hairdressers from outside?"

Wider dimensions

Globally, "prisons and HIV are a public health challenge of crisis proportions", to quote Joanne Csete of the Canadian HIV/AIDS Legal Network,[11] at this year's International AIDS Conference in Vienna. She was speaking at one of several sessions around HIV and correctional systems. We do not have enough space here to discuss how prisons worldwide serve as amplifiers of TB, HIV and hepatitis infections.

Instead, an example of one country's good practice. Mercedes Gallizo Llamas is Secretary-General of the Spanish Prison Administration. She told the conference that in 1996 24% of inmates of Spanish jails were HIV-positive. By 2009, the proportion had fallen to 7%.

This was possible because, confronted with a huge public health threat, the Spanish authorities moved fast to curb it. Voluntary and confidential HIV tests were made available to all, and syringe exchange, health education, access to condoms and lubricant and methadone maintenance programmes were all introduced. As a result, the annual incidence of new HIV infections within prisons decreased from 0.6% in 2000 to 0.09% in 2008.

"We needed a change in the mentality of prison authorities and politicians," said Ms Llamas. "There was a fear of risk. We had to prove the risks were unfounded: the results spoke for themselves."[12]

Mark Wilson says that the view from the prison wing is similar. "Prison officers want to do the right thing: they just don't know what the right thing is." ■

Further reading

For more on prisons and many other issues, NAM has just published *Social and legal issues for people with HIV*, a 140-page practical guide on non-medical issues that can affect people with HIV.

To buy a copy, phone NAM at **020 7840 0050** or email **info@nam.org.uk**.

hiv & kid

It's becoming increasingly clear that, when it comes to HIV, amongst the most vulnerable organs in the body are those two little waste filters in the small of the back – our kidneys. Guest writer *Kelly Safreed-Harmon* investigates renal disease and what can be done about it.

Within the first few years of the AIDS epidemic, physicians recognised that one symptom of this devastating new syndrome was a collapse in kidney function. In 1986, an especially severe type of renal (kidney) failure was characterised as a distinct disease: HIV-associated nephropathy (HIVAN).

Research could not find effective treatments for HIVAN until combination antiretroviral (ARV) therapy came along. This rapidly halts the progression of HIVAN in most people. The kidney-related benefits of ARVs can be seen in a sharp decline in renal mortality in the first few years of the new treatment era.[1]

While the outlook has greatly improved, kidney disease remains a prominent challenge to the management of HIV. A survey of five cohorts of HIV-positive people in Europe, North America and China found between one in eleven and one in twenty people had moderate to severe kidney disease.[2]

This compares with one in fourteen to one in eighty in the general population under 50, according to which study you pick and how chronic kidney disease is defined.[3]

These findings are perhaps not surprising to anyone who has followed recent medical trends in relation to HIV, antiretroviral treatment, chronic disease and ageing. The longer we live with HIV, it seems, the more the range of HIV-related health issues keeps expanding. What is notable about renal health in the context of HIV is that it intersects in complex ways with other key aspects of managing the disease.

An overview of kidney function

The kidney is an organ that performs vital tasks related to the filtering of blood and the elimination of waste from the body. In a healthy kidney, about a million tiny structures called nephrons filter waste from substances that the body can still use. The waste travels to the bladder in the form of urine and the other substances re-enter the bloodstream. Proper kidney functioning is necessary for the body to maintain the optimal balance of these substances, which include sodium, phosphorus and potassium.

The kidneys also release hormones that regulate blood pressure, stimulate the creation of red blood cells and help the body absorb the calcium that is required to keep bones strong.

Many different kidney diseases can interfere with these processes. The term chronic kidney disease (CKD) does not refer to a specific type of disease, but rather to the sustained loss of kidney function that can result from various medical conditions. Similarly, the term end-stage renal disease (ESRD) is used to characterise the near-complete loss of kidney function, which quickly results in death without dialysis or a kidney transplant.

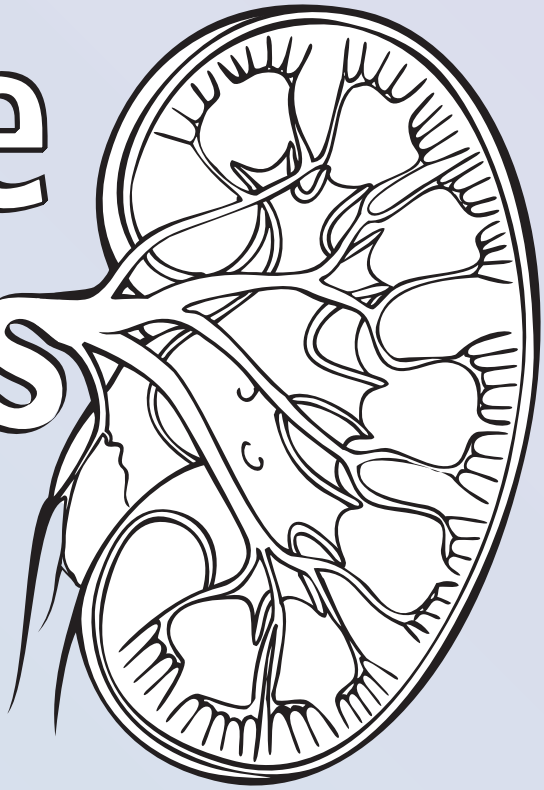
The two most important causes of kidney disease are diabetes and high blood pressure – both conditions that can often be successfully prevented or treated. In diabetes, excess glucose in the blood injures the nephrons, while high blood pressure damages the small blood vessels that surround the nephrons: in both cases this makes it harder for the kidneys to sort waste from substances that should be reabsorbed into the body.

How drugs used to manage HIV disease interact with the kidneys

As the kidneys perform their processing functions, they can be exposed to harmful levels of drugs. Some drugs are more likely than others to cause serious organ damage, and some people are more vulnerable than others to drug toxicities. While cases of kidney damage thought to be caused by several ARVs have been documented in the medical literature, only three of those drugs have been consistently associated with adverse kidney-related effects.

There is ample evidence that the protease inhibitor indinavir (*Crixivan*) causes kidney stones in a sizeable number of people – and this is one reason why this drug is very rarely used

& the dneys



now. (Waste products in the kidneys can sometimes form crystals and these can accumulate to form hard lumps called 'kidney stones'.)

Of more concern are case reports of kidney stones associated with the protease inhibitor atazanavir (*Reyataz*). They appear to occur much more rarely than with indinavir, but atazanavir is a frequently used drug. A French cohort study found that about one in 100 patients developed atazanavir-related kidney stones after an average of two years on the drug,[4] 30 cases were reported to the American Food and Drug Administration in the first three years of its use,[5] and one patient out of 121 in a trial comparing maraviroc with tenofovir/FTC, both combined with atazanavir, had to pull out due to kidney stones.[6]

The kidney stones associated with both these drugs, although painful, may be avoidable by drinking plenty of water, and resolve if the drugs are withdrawn.

The impact of tenofovir (*Viread* – also in *Truvada* and *Atripla*) on the kidneys remains a matter of greater concern. Since this drug's approval almost ten years ago, a number of studies have suggested that tenofovir may negatively affect renal functioning in subtle ways. In some people it damages the upper portion of the nephrons, resulting in symptoms similar to a condition called Fanconi's syndrome.

There is no clear consensus about the importance of the findings, but many clinicians take them seriously.

An Australian study published in early 2010 found that kidney functioning had failed to return to normal in almost half of 24 men with tenofovir-induced renal toxicity more than a year after discontinuing the drug.[7]

In the EuroSIDA cohort, a group of nearly 7000 patients, cumulative exposure to tenofovir or atazanavir was associated with a 16% and 21% increased risk, respectively, of chronic kidney disease, though the actual proportion of people who developed CKD for any reason was relatively low, at one case per 105 patients a year.[8]

On the other hand, a US group found no association between tenofovir use and decline in kidney function in a prospective cohort study involving 554 people,[9] and a recent meta-analysis of 17 studies involving 11,000 HIV-positive people concluded that from a statistical standpoint, taking tenofovir was indeed associated with higher risk of impaired kidney functioning, but that "the clinical magnitude of this effect was modest".[10]

What are we to make of the barrage of data about tenofovir and kidney toxicity? Dr John Connolly of University College London's Centre for Nephrology encourages HIV-positive people to look at the big picture.

"It's important to be pragmatic, because tenofovir is a very safe and very good drug overall," he says.

Connolly characterises tenofovir-induced renal toxicity as "a small problem for a significant minority of people", and notes that protocols for screening tenofovir users for renal damage are well established.

"If I were a patient, I would want to know that whoever is looking after me knows about this potential problem, and has procedures in place to detect it," he says. Patients at Connolly's HIV nephrology clinic provide blood and urine specimens for what he characterises as "simple" screening tests every four to six months.

Antiretroviral toxicity is not the only kidney-related HIV treatment concern. Because kidney damage impairs the body's ability to process drugs, dose reductions are required when prescribing certain antiretrovirals to people with CKD.

A number of drugs used to treat and prevent opportunistic infections are

known to be hard on the kidneys, some to the point of making them hard to use. These include amphotericin B, cidofovir, foscarnet, pentamidine and sulfadiazine and to a lesser extent cotrimoxazole (*Septrin*) and the herpes drug aciclovir.[11,12]

Certain non-prescription substances such as most of the over-the-counter pain relievers, herbal supplements (including yohimbe, a component of 'herbal Viagra') and recreational drugs are potentially more hazardous to HIV-positive people with existing kidney problems than they are to the general population.

How HIV directly damages the kidneys: HIV-associated nephropathy

HIV itself still has the potential to add considerably to the complexity of kidney disease. A number of HIV-specific kidney diseases have been identified, the most notable being HIV-associated nephropathy (HIVAN). Genetic factors make HIVAN predominantly a disease of people of African ancestry. Before the discovery of potent new antiretroviral regimens in the mid-1990s, HIVAN often led rapidly to end-stage renal disease and death.

ARVs have been found to greatly slow HIVAN-related kidney decline. ARV-naive people diagnosed with HIVAN are therefore advised to start taking HIV treatment, even if they do not show other signs of HIV disease progression.

A category of blood pressure medications known as angiotensin-converting enzyme (ACE) inhibitors may also benefit people with HIVAN, as may corticosteroids.[13]

Confirming widespread clinical observations, a US cohort study showed a significant drop in HIVAN incidence from 1995-97 to 1998-2001, and also determined that ART use reduced HIVAN risk by 60% in cohort members.[14] A more recent study looking at kidney biopsy results in 86 HIV-positive US residents with symptoms of renal impairment found that the most common cause was high blood pressure rather than HIVAN.[15] Nonetheless, HIVAN continues to contribute substantially to the burden of HIV-related kidney disease, especially in Africans and people of African descent.

If I were a patient, I would want to know that whoever is looking after me knows about this potential problem, and has procedures in place to detect it.
Dr John Connolly
University College London

Risk factors for HIVAN, besides African ancestry, include decreased CD4 cell count and family history of renal disease.[16]

How HIV indirectly damages the kidneys: diabetes and high blood pressure

As noted earlier, diabetes and high blood pressure are leading causes of kidney disease. Both conditions are also of growing concern to HIV-positive people in the current treatment era.

While it is important to bear in mind that genetic, lifestyle and environmental factors contribute much of the variation in diabetes incidence across different populations, studies of HIV-positive people taking ARVs have consistently called attention to this problem. One large multicentre study, for example, found that ARV use was associated with a fourfold increase in diabetes.[17] The drugs most strongly associated with diabetes are the 'first-generation' NRTI drugs (the 'nukes' or nucleoside reverse transcriptase inhibitors): AZT (zidovudine, *Retrovir*), ddI (didanosine, *Videx*) and especially d4T (stavudine, *Zerit*).[18]

HIV-positive people who developed high blood pressure in one German study, had far higher prevalence of elevated urine protein levels, signalling the presence of kidney disease, than those who did not.[19]

However, with blood pressure, findings are hard to interpret because the kidneys play a role in regulating blood pressure and so kidney disease not only can result from high blood pressure (hypertension), but can cause it too. Nonetheless, since high blood pressure is clearly an independent risk factor for kidney disease (and many other diseases), it makes sense to treat it.

HIV, ageing and the kidneys

With ART enabling such a large number of HIV-positive people in developed countries to achieve long-term viral suppression, health issues associated with ageing are becoming increasingly significant. Some diseases tend to manifest earlier in HIV-positive people than in their HIV-negative counterparts, for reasons that may relate to how both antiretroviral drugs and HIV itself affect the body over time.

A combination of factors may put people living with HIV at a higher risk of kidney disease as they grow older. First, kidney functioning declines in everyone from midlife onward, and older people in general are at higher risk of kidney disease and kidney failure. Second, the likelihood of developing diabetes and high blood pressure increases with age as well.

Kidney disease also has the potential to trigger or exacerbate certain other ageing-related health problems, and is strongly associated with cardiovascular disease.

Bone health is less widely discussed in relation to kidney disease, but the kidneys' contribution to maintaining bone mass has important implications for HIV-positive people. Both disease-related and ageing-related bone thinning are already a matter of concern for HIV-positive people (see *Skeleton key* in *HTU* 196, May 2010). Since kidney disease is associated with the loss of bone mass in the general population, it is logical to speculate that it may further accelerate bone thinning in some HIV-positive people as they grow older.

This is especially important for people susceptible to tenofovir-related kidney disease, as this features a loss of bone minerals and vitamin D.

HIV and end-stage renal disease

HIV-positive people with ESRD can potentially benefit from both dialysis and transplantation, the only two interventions that can avert the death of someone experiencing complete renal failure. Dialysis, which involves using medical technology to filter waste from the blood, is a standard component of the management of ESRD in HIV-positive people. And in recent years, kidney transplantation has become an increasingly viable option for HIV-positive people with good viral control.[20]

What are the symptoms of kidney disease and how is it diagnosed?

Chronic kidney disease (CKD) can progress for years without causing symptoms and, even when symptoms do occur, they may not be specific enough to lead to an immediate diagnosis. Because of this, many people with CKD are not diagnosed until considerable organ damage has occurred. The damage is often irreversible, but careful medical management and lifestyle changes can help some people avert or delay end-stage renal disease (ESRD).

When kidney function has declined greatly, people may experience a combination of the following:

- tiredness
- loss of appetite
- nausea and vomiting
- headaches
- a more frequent or less frequent need to urinate
- reduced urine flow
- drowsiness
- difficulty concentrating
- darkening of the skin
- muscle cramps
- itching and numbness
- swelling in the hands and feet
- puffiness around the eyes.

Other indications of kidney disease can be detected through medical tests. The most important ones for making the initial diagnosis of kidney disease look for two markers of impaired kidney functioning: protein in the urine and a level of creatinine, a waste product, in the blood. The kidneys are supposed to leave protein in the blood and filter out the waste products; damaged kidneys do the opposite.

On their own, measurements of urine protein levels and serum (blood) creatinine levels provide only a general picture of kidney functioning. Of greater significance is the estimated glomerular filtration rate (eGFR), which takes into account additional variables relating to age, sex and race. A person's eGFR is expressed in terms of millilitres filtered per minute (ml/min). Someone with healthy kidneys can be expected to have an eGFR of 90 ml/min or greater, and people with eGFRs of over 60 ml/min are unlikely to have symptoms.

Different stages of chronic kidney disease are defined in terms of eGFR and other markers of kidney damage. Stage five CKD, the least severe, is defined as a normal eGFR alongside some evidence of kidney damage such as protein in the urine. At stage one, the most severe stage, an eGFR value of less than 15 ml/min indicates kidney failure, at which point a person cannot be expected to survive for long without being given dialysis or a kidney transplant.

Protecting kidney functioning in the context of HIV infection

The renal health issues associated with HIV may seem vast, but the good news is that a complex strategy is not required for most people to act on this body of information. Perhaps the simplest measure HIV-positive people can take to protect their renal health is to follow screening guidelines. The European AIDS Clinical Society has issued guidelines that call for kidney functioning to be evaluated at the time of HIV diagnosis for everyone, and on an annual or twice-yearly basis after that for HIV-positive people at higher risk of kidney disease.[21]

Factors often considered to put people at higher risk include a low CD4 cell count; a high viral load; a diagnosis of diabetes, high blood pressure or hepatitis C; cigarette smoking; prior use of nephrotoxic drugs; a family history of kidney disease; and African ancestry.[22,23]

It is also advisable for HIV-positive people to consider what they can do about the risk factors that are modifiable. Key steps may already be on the self-care agenda, since there is a great deal of overlap among modifiable risk factors for kidney disease, diabetes, high blood pressure and other diseases associated with metabolic and cardiovascular functioning.

All of the following well-known health-promoting measures can reduce the risk of kidney disease:

- giving up smoking
- eating a healthy low-fat diet
- exercising regularly
- not using recreational drugs
- getting regular medical check-ups
- reducing high blood pressure levels
- for people with diabetes, keeping blood glucose under control.

news in brief

Cardiovascular disease

Risk factors for heart attacks in people with HIV

There's now significant evidence showing that people with HIV have an increased risk of cardiovascular disease (CVD). The reasons for this are debated, but are likely to be a mix of traditional risk factors (such as smoking and male gender), the effects of some anti-HIV drugs and infection with HIV itself.

US researchers have found more evidence that having a low CD4 cell count increases the risk of heart attack.[1] Their study of over 6000 patients between 1998 and 2008 found about 4% had a heart attack.

After traditional risk factors were taken into account, investigators found that a CD4 cell count below 200 substantially increased the risk of heart attack. There was some evidence that having a viral load above 100,000 copies/ml also increased risk.

The anti-HIV drug abacavir (*Ziagen*, also in *Kivexa* and *Trizivir*) has been associated with an increased risk of CVD and heart attack, as shown in the 2008 results of the D:A:D study.[2]

At first sight, the statistics were alarming, with those taking the drug apparently 90% more likely to have a heart attack than people in the general population. As a result, treatment with abacavir is not recommended for people with other risk factors for CVD.

Now, researchers have reassessed the heart attack risk associated with abacavir treatment, taking into account individual risk factors.[3]

They estimated that a 40-year-old man on abacavir, with no other risk factors for CVD, had a 1-in-1000 risk of a heart attack in the next five years. The risk increased with each traditional risk factor a patient had. These include lipid levels (such as cholesterol), blood pressure, age, smoking and previous history of CVD.

The researchers have developed an online tool for doctors and patients to calculate the impact of abacavir use on CVD risk, taking into account individual risk factors (see www.cphiv.dk/TOOLS/NNHforabacavir/tabid/436/Default.aspx).

Cancer

Are people with HIV developing cancer at a younger age?

Two studies came to different conclusions about the risks of people with advanced HIV disease developing so-called 'non-AIDS defining' cancers.

Since the 1980s it's been known that some types of cancer occur more frequently in people with HIV than in the general population. Some cancers, including Kaposi's sarcoma (KS) and non-Hodgkin's lymphoma, are considered to be AIDS-defining illnesses.

Thanks to effective HIV treatment, far fewer people have these AIDS-defining cancers than before.

But some research has shown that, even in the era of effective HIV therapy, people with HIV also have an increased risk of having other cancers.

Italian researchers reported that patients with AIDS are seven times more likely to die of a non-HIV-related cancer than people of the same age and sex in the general Italian population.[1]

Their study involved approximately 10,000 patients who developed an AIDS-defining illness between 1999 and 2006. A total of 3209 of these people died, with a non-AIDS-related cancer as the cause of death in 7% of patients. The most common cancers were those of the lung (58 cases), liver (28), Hodgkin's lymphoma (28) and of the head and neck (18).

The researchers noted that death rates associated with cancers caused by viral infections were especially high. The mortality rate from anal cancer – caused by certain strains of human papillomavirus (HPV) – was 240 times higher in people with HIV than in the general population, and 174 times higher for Hodgkin's lymphoma, caused by the Epstein-Barr virus. Deaths from liver cancer were eleven times higher in people with HIV, possibly due to HIV and hepatitis C co-infection.

The researchers feel the results "highlight the importance of monitoring the cancer burden on mortality of people with AIDS".

In contrast, a US study reported that people with AIDS are generally not developing non-HIV-related cancers at a younger age than people in the general population.[2]

Although people with AIDS who have cancers do tend to be younger than other people with cancers, the researchers say that this is simply because a smaller proportion of people with AIDS (with or without cancer) are over the age of 65, compared to the general population.

The study took into account differences in the age profiles of people with AIDS and the general population. After adjustment, there was no real difference in age of diagnosis for most cancers.

Nonetheless, they did find that people with AIDS developed anal cancer and lung cancer earlier than in the general population. These might be explained by differences in sexual behaviour and in rates of smoking.

The researchers do not believe that cancer is associated with premature

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ageing in people with HIV or that more intensive cancer screening is warranted for people with HIV.

HIV therapy

No benefit from adding drugs to already successful therapy

New research has shown that there's no benefit from adding an extra anti-HIV drug – one that crosses the blood-brain barrier – to a combination that is already suppressing viral load to undetectable levels.[1]

An undetectable viral load in the blood is now, with advances in HIV treatment, a realistic goal for many people with HIV. But ultra-sensitive viral load tests have shown that most people still have low levels of HIV in their blood. Moreover the virus may continue reproducing in other parts of the body, including cerebrospinal fluids. Even very low levels of HIV replication may be damaging, causing harmful inflammation and immune activation.

The researchers investigated whether adding an additional drug to successful regimens lowered residual viral load in cerebrospinal fluids and blood, and reduced immune activation and inflammation in the brain.

This small study involved ten patients and lasted eight weeks. All participants were taking HIV treatment, with an undetectable viral load for an average of 6.5 years. Most of the patients had evidence of inflammation in the brain.

Treatment was intensified by the addition of either maraviroc (*Celsentri*) or lopinavir/ritonavir (*Kaletra*), both of which have good penetration into the central nervous system, and then with T-20 (enfuvirtide, *Fuzeon*), which does not.

This intensified therapy did not reduce residual viral load any further, in either cerebrospinal fluids or blood. Also, it did not reduce inflammation or immune activation.

Anti-HIV drugs

Saquinavir side-effect warning

Some protease inhibitors have been associated with an irregular heartbeat. It's already known that this is the case with saquinavir/ritonavir.[1]

Now drug regulatory bodies in both the US and Europe have strengthened their warnings about heart rhythm disturbances caused by ritonavir-boosted saquinavir (*Invirase*).[2]

Although this side-effect is rare, it's now recommended that all patients should have an electrocardiogram (ECG) before they start treatment with saquinavir.

The US Food and Drug Administration recommends that anyone taking the drug should: "Seek immediate care if you experience an abnormal heart rate or rhythm or other symptoms including dizziness, light-headedness, fainting or heart palpitations."

European regulators have made specific recommendations about saquinavir doses for those starting HIV treatment for the first time. These state that the dose of saquinavir for the first week of treatment will be reduced from 1000mg twice daily to 500mg twice daily. This dosage adjustment is not necessary in patients who are switching from other antiretroviral drugs; the European Medicines Agency says the risk of an irregular heart beat is greatest in people who have never taken antiretroviral drugs before.

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do hiv drugs *really* mean you aren't infectious?

Gus Cairns looks at new research on this controversial subject.

The impact of HIV treatment on infectiousness has been a hotly debated topic in recent years. It's now nearly three years since several Swiss doctors upset the HIV prevention applecart by writing a paper that said that, under carefully stipulated conditions – viral load under 50 copies/ml for at least six months, no sexually transmitted infections, 100% adherence to HIV therapy – a person on antiretroviral drugs was essentially unable to transmit HIV sexually.[1]

Far from settling the issue, the 'Swiss statement' stirred up huge amounts of argument in the HIV prevention community. Everyone agrees people on successful HIV therapy are probably quite a lot less infectious than people not on treatment. But are they uninfectious enough to mean it's worth taking the risk of not using condoms? The past month has seen the publication of several new studies which, unfortunately, muddy the waters on this particular issue rather than clarify them.

The Swiss doctors based their findings on research involving heterosexual couples that showed there were no HIV transmissions when viral load was below a certain level. This is because HIV treatment reduces the amount of virus in body fluids, including genital fluids.

But there are concerns that even people who have an undetectable viral load in their blood may not always have an undetectable viral load in their genital fluids. A number of studies have shown this in men – and an even higher proportion in women.

Now researchers believe they have identified the main reasons why this can happen.[2]

Their study involved women starting HIV treatment. The researchers monitored viral load in blood, cervical fluids and vaginal secretions for six months.

Treatment reduced viral load in the blood and genital fluids. The researchers also found that the level of viral load in the blood tended to predict viral load in these genital fluids.

At the end of the study, after taking treatment for six months, 69 women had an undetectable viral load in their blood, but viral load was still detectable in the cervical fluids of 10% of these women and in the vaginal secretions of 32%.

So far, this is what other studies have found. But there's never really been an explanation as to why some women maintained a viral load in their genitals when they haven't got one in their veins. One theory was that it was to do with low-level, asymptomatic infection with sexually transmitted viruses like HSV-2 (herpes) and the genital wart virus HPV (human papillomavirus). Others thought it was just constitutional – some people were just, to use a delightful phrase coined by the researchers, "super-shedders" when it came to producing HIV.

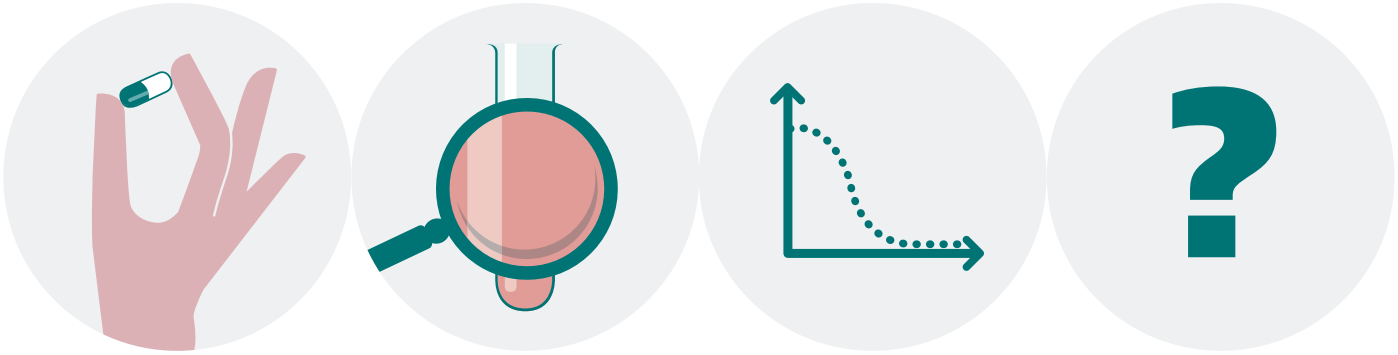
This study found a much simpler, and more easily fixed, explanation: the single most important factor associated with a detectable viral load in genital fluids was poor adherence to treatment. When we say 'poor', it was actually very good: on average, the women forgot only one in a hundred doses. Nonetheless, the women who didn't do quite so well on adherence were considerably more likely to have a detectable viral load in their genital fluids than ones whose adherence was perfect.

On the one hand, this means that when the Swiss statement specified 100% adherence to ensure non-infectiousness it really meant it, which may be a tall order for anyone. On the other hand, it does mean there may be a simple and relatively fixable explanation as to why some people are more infectious than others.

Real-world evidence

The evidence about the impact of treatment on the risk of HIV transmission largely comes from big randomised controlled studies. For instance, a study in Africa last year found that the chances of HIV being passed on between partners was reduced by 92% – better than the average reduction due to attempted consistent condom use – if the HIV-positive partner was on treatment.[3] That's a big treatment bonus.

People enrolled in these trials generally receive a lot of support and good medical care. Often this is at a higher level than is available from routine medical services.



However, 'real-world' evidence from the US and Canada has suggested that high rates of treatment within the community may be starting to help prevent new infections.

However, Chinese researchers also looked at this question recently, and found a result that was completely out of line with this.[4] Their research involved 1927 couples where one partner was HIV-positive and the other HIV-negative. These couples were monitored for approximately three years.

The transmission rate in couples where the HIV-positive partner was taking treatment was 5%, compared to a transmission rate of 3% in the other couples. That makes it look as if taking treatment was worse in terms of infectiousness than not taking it, but in statistical terms the 2% difference is within the margin of error, and it essentially means the risk was the same, regardless of treatment. Nonetheless, this is a drastically different result from the African study.

In an editorial that accompanied the study, Myron Cohen, a senior US HIV doctor, said the results of this study should cause those who support the wider use of HIV treatment as a way of controlling the spread of the virus to "pause".[5]

But why was the result so wildly out of line? In their own paper, the researchers note that people on treatment who did not switch their regimens were much more likely – nearly three times as likely – to transmit HIV than people who had switched their drug regimens.

Why might this be a clue? Well, the researchers did not provide any information on the viral load of the individuals who transmitted HIV to their partners, about whether they had drug resistance, or about measures to support adherence.

However, they also noted that a previous study of drug resistance in Henan province found that only one third of people with HIV were adherent to their treatment after six months of therapy, and that by this time (from an original figure of 14% with drug-resistant HIV), no less than 63% had drug resistance.[6]

We can't tell if the same situation applied in this study. But if adherence is poor and people in this region do have high rates of resistance, perhaps due to a lack of support or treatment education, then failing to switch therapies might mean they are much more likely to have drug-resistant HIV – which they then transmit to their partner – than they are if they move to a new therapy.

Until we get more information, we won't know if that's the explanation and, as Dr Cohen says, this gives us pause for thought. However, what this study may be showing us is simply that suboptimal treatment regimens and levels of support produce prevention failure as well as treatment failure.

HIV transmission risk in gay couples

Most of the evidence on the impact of treatment on infectiousness comes from heterosexuals.

But now researchers have attempted to calculate the HIV transmission risk in stable gay couples where one partner is HIV-negative and the other HIV-positive and taking treatment.[7]

Using condoms all the time provided the most protection against HIV. The researchers calculated that there was a 1% risk of transmission in these circumstances.

Having unprotected sex within six months of the most recent undetectable viral load, but using condoms at all other times, was associated with a 3% risk of transmission. Never using condoms was associated with a 22% risk of transmission.

The researchers say the key message is that consistent condom use is the best way of protecting one's partner. They also say that the most crucial time to use condoms is when more than three months have gone by since the last undetectable viral load result.

So there you are. HIV treatment *will* reduce your viral load if it's successful, and if that happens, you are probably less infectious. But what these studies seem to suggest collectively is that there are an awful lot of ifs and buts to add to that statement and it might not be time to throw away the condoms quite yet. ■

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- **Find out more about HIV treatment:**
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- **www.aidsmap.com**
  Visit our website for the latest news about HIV & AIDS, a fully searchable treatments database and a complete list of sexual health clinics in the UK.
- **THT Direct**
  Offers information and advice to anyone infected, affected or concerned about issues relating to HIV and sexual health.
  0845 1221 200
  Mon-Fri, 10am-10pm Sat-Sun, 12pm-6pm
- **i-Base Treatment Phoneline**
  An HIV treatment phoneline, where you can discuss your issues with a treatment advocate.
  0808 8006 013
  Mon-Wed, 12pm-4pm