

[STD Update] FYI 1-19: Short or medium term PrEP is safer than Aspirin, Antibody infusion successfully combats HIV in early trials, Trials underway to evaluate solithromycin for gonorrhoea, 3 papers, more.

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### California Stories

*HIV-positive patients lost to follow-up successfully identified and re-engaged with care by programme in LA County*

*New institute focuses on HIV cure research*

### National Stories

*Short- or Medium-Term PrEP Is Safer Than Aspirin*

*Antibody Infusion Successfully Combats HIV in Early Trial*

*Legal barriers to adolescent participation in HIV, STI research need to be removed*

*Trials underway to evaluate solithromycin for gonorrhoea, NASH*

*Two cases of PrEP failure on solo tenofovir pose significant research questions*

### Scientific Papers/Conference Abstracts

*Economic Burden of HIV Antiretroviral Therapy Adverse Events in the United States*

*A Clinical Home for Preexposure Prophylaxis: Diverse Health Care Providers Perspectives on the "Purview Paradox"*

*Prevalence of transmitted HIV drug resistance among recently infected persons in San Diego, California 1996-2013.*

### Resources, Webinars, & Announcements

*HIVresource: A Guide to Clinical Research in the San Francisco Bay Area*

*New HealthCare.gov Page on Transgender Health Care Coverage*

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## California Stories

### **HIV-positive patients lost to follow-up successfully identified and re-engaged with care by programme in LA County**

Michael Carter, [aidsmap.com](http://aidsmap.com) | 1.11

A programme in Los Angeles County successfully re-engaged and retained patients who dropped out of HIV care, investigators report in the online edition of the Journal of Acquired Immune Deficiency Syndromes. Called the Navigation Program, it was a collaboration between health department staff and community organisations.

Public health databases were used to identify patients who were lost to follow-up. Best practices from programmes to trace hard-to-reach patients and a modified version of the CDC Antiretroviral Treatment Access Study (ARTAS) were employed to re-engage patients with care. Over 1000 patients lost to follow-up were identified, of which 36% were receiving care elsewhere and 29% could not be located. Of the

remainder, 78 people (8%) were successfully enrolled in the programme, most of whom re-engaged with care and remained in care.

Estimates of the proportion of HIV-positive patients in the US enrolled in long-term care range between 37% and 55%. Failure to engage with care is associated with poorer health outcomes and a higher risk of onward HIV transmission. A recent study attributed almost two-thirds of new HIV infections in the US to persons not engaged in care.

Interventions to support engagement with and retention in care are therefore urgently needed. The Patient Navigator model was developed for the care of cancer patients, but is potentially a tool to support patients with HIV. Investigators therefore designed a study to evaluate its utility and efficacy when applied to HIV-infected individuals lost to HIV care in Los Angeles County.

The programme involved seven HIV clinics, academic institutions and community support organisations. Six patient "Navigators" were hired. All had a college degree, experience of HIV case management, and most were bilingual in English and Spanish.

The Navigators worked closely with clinic staff to identify patients lost to follow-up.

A modified intervention designed by the CDC (ARTAS) to engage patients newly diagnosed with HIV care formed the basis for the study programme.

Patients were identified as lost to follow-up if they had no care visit for between six and twelve months and a viral load greater than 200 copies/ml; or no care visit for more than twelve months; or newly diagnosed and were never linked with care; or had recently been released from jail or an institution and had no regular HIV care provider.

The intervention had four components. These focused on building a relationship, needs assessment, linking to resources and enhancing strengths, and addressing reasons for disengagement.

Recruitment took place between 2012 and 2014. During this period 1139 individuals who did not establish contact with care or who dropped out of care were identified.

Of these patients, over a third (36%) has established care with another provider, 29% could not be contacted, 8% returned to the clinic independently, 7% no longer lived in the study area, 6% had died, 3% were in prison or a mental health institution.

A total of 78 individuals (7%) were located and enrolled in the Navigation Program. Most (78%) were male, 42% were aged 40 to 49 years, 50% self-identified as gay, 57% had no health insurance and almost two-thirds had an annual income below \$10,000.

Participants had been infected with HIV for an average of ten years, mean viral load was approximately 57,000 copies/ml and 51% had an undetectable viral load. A third of patients were taking HIV therapy at enrolment and 81% had taken antiretrovirals at some point.

Many of the patients had unmet needs at the time of enrollment. Over a third had unmet HIV-related medical needs, 35% required assistance with food and other basic necessities, 42% required pharmacy/medication services, 43% were in need of benefits support and 60% required dental care.

On average, patients participated in five intervention visits lasting approximately eleven hours. However, 46% needed only 1-3 intervention visits, suggesting that for many patients, "less resource-intensive interventions may be sufficient to re-engage many lost HIV clinic patients."

Participants received an average of five referrals. The most common were for mental health (24%), housing/transport (19%) and financial/employment (19%).

Over two-thirds (68%) of patients enrolled in the programme were linked to care within three months, 85% within six months and 94% within twelve months. The majority (82%) of these individuals were retained in care (defined as attending second appointments three to twelve months after linkage). The proportion of patients with viral suppression increased from 51% at enrollment to 63% at the second follow-up appointment ( $p < 0.01$ ).

The authors stress the importance of combining surveillance data with efforts to re-engage people in care. Navigators had access to surveillance data that allowed them to trace the address and clinic records of people missing from care, which showed that just over half were either in care elsewhere, in prison, resident outside LA County or dead. This allowed a more targeted approach to those who could be located, of whom just over half agreed to take part in the intervention study.

Nevertheless the study found that 29% of people had disappeared and could not be located either through clinic records or through at least three attempts to contact them through their last known address, including home visits, and scanning of people-finder databases, homeless shelters, jails and parks.

"The use of this combined approach is an effective model for identifying and re-engaging HIV-infected persons who are not receiving adequate HIV medical care," conclude the authors. "The combined approach presented here has widespread utility towards achievement of National HIV/AIDS Strategy goals to improve linkage, re-engagement, retention, viral load suppression and to reduce forward HIV transmission."

**Reference:**

Wohl AR et al. The Navigation Program: an intervention to re-engage lost patients at 7 HIV clinics in Los Angeles County, 2012-2014. *J Acquir Immune Defic Syndr*. Online edition, doi: 10.1097/QAI.0000000000000871 (2015).

**View the story online:** [Click here](#)

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## **New institute focuses on HIV cure research**

Liz Highleyman, The Bay Area Reporter | 1.14

UCSF researchers recently gave an overview of their latest work launching a new Institute for HIV Cure Research, funded by a \$20 million grant from amfAR, the Foundation for AIDS Research. Cure studies will also be a key theme of the Conference on Retroviruses and Opportunistic Infections and accompanying Community Cure Research Workshop coming up in February.

"We recognize that realistically we're not talking about delivering a cure to everyone who needs it by 2020," amfAR CEO Kevin Frost said at the HIV Cure Summit last month on World AIDS Day. "We believe a cure is evolutionary – we want to build the foundations and understand the science of what it takes."

UCSF was chosen to host the new institute, which will be headquartered at the Mission Bay medical campus, in a national competition. Frost stressed that the \$20 million allocated for the first five years is "a floor, not a ceiling."

"The San Francisco area has a higher concentration of scientific thought leaders in HIV than anywhere else in the world," said Rowena Johnston, amfAR vice president and director of research. "The Bay Area has consistently led the way in developing and implementing scientific advances in HIV prevention and treatment, and the potential for this team of researchers to develop a cure is unparalleled."

"San Francisco has a long and storied history of response to the HIV epidemic," added UCSF Center for AIDS Research director Dr. Paul Volberding, who will also head the new institute. "This will bring together a broad team of leading scientists who believe a cure is possible, and that it will happen here. We're ready to end this epidemic."

### **Scientific foundations**

Effective combination antiretroviral therapy, which debuted in the mid-1990s, has made HIV a chronic manageable disease for most people with access to treatment – in many cases using once-daily single-tablet regimens. But the drugs are not a cure, and if they are stopped the virus soon comes back. Even during treatment inactive HIV genetic material remains hidden in the body, and this low-level virus can cause inflammation that contributes to conditions such as cardiovascular disease and cancer.

"I don't talk to any patient who wouldn't rather be cured than take one pill once a day," Volberding said at the summit.

The past couple of years have seen some setbacks in the cure field, including the return of HIV in the "Mississippi baby," a child infected before birth who started antiretrovirals very early and was thought by many to be cured.

This leaves only one person – former San Francisco resident Timothy Brown, known as the Berlin Patient – who appears to have been truly cured of HIV. Brown has no detectable HIV in his blood or tissues more than eight years after receiving bone marrow transplants from a donor with a natural mutation that makes T-cells resistant to infection.

Researchers have tried various approaches to curing HIV, including very early antiretroviral treatment, mimicking Brown's cure by protecting cells from infection, flushing the virus out of hiding and destroying it – a strategy known as "shock and kill" – and strengthening the natural immune response against the virus.

Many researchers now speak of a "functional cure" or remission, rather than completely eliminating HIV from the body, and most experts think a combination of approaches will be necessary.

"Let's get to a place where we don't have to take medications every day, where we don't have to experience the side effects of the medications, and where we can get our immune systems to a state

where we're not at a risk of early aging," said longtime AIDS survivor and advocate Matt Sharp, speaking on a KQED program announcing the new institute. "But overall, of course, I'd like to see HIV completely eradicated from my body."

The HIV Cure Summit featured an overview by Johnston, followed by the researchers who will lead the four teams comprising the new institute.

"HIV is like a lawn," Johnston explained. "You can mow it and keep it under control, but that doesn't get at the roots."

Warner Greene, Ph.D., director of UCSF's Gladstone Institute of Virology and Immunology, will head an effort to study how so-called reservoirs of hidden HIV are established and persist in the body.

"Our strategy will be to exploit the innate immune system to help flush the virus out of hiding and ultimately to eliminate its ability to bounce back when drug treatment ends," said Greene, who is investigating how molecules known as TLR agonists set off immune activation, including activation of the T-cells that harbor latent HIV. "We may not be able to get every last virus, but maybe we can get to a low enough level that the immune system can control it."

Dr. Mike McCune and his team aim to figure out precisely where HIV hides within specific tissues in the body – including how viral reservoirs differ between men and women – while a group overseen by Satish Pillai, Ph.D., will work on better ways to measure hidden virus that is capable of replicating.

Finally, UCSF Professor Dr. Steven Deeks and his team will study how TLR agonists affect HIV reservoirs in the tissues of patients on antiretroviral treatment.

"With the support of the community in San Francisco, I think we have a responsibility to take these [ideas] quickly into the clinic, to quickly identify approaches that we can safely bring into human trials," Deeks said. "We're doing this differently than the traditional academic approach. We want to make an impact, so we're using a bit of an industry approach to move things into the clinic within the next four or five years."

Deeks predicted that the "next big game changer" will be long-acting injectable antiretrovirals that last one or two months. "This will have a huge impact on people who cannot take pills on a daily basis," he said, "but it will not be a substitute for a cure."

### **More cure research at CROI**

This year's CROI meeting will take place February 22-25 in Boston. The Community Cure Research Workshop on February 21, co-sponsored by the AIDS Treatment Activists Coalition; European AIDS Treatment Group; AVAC, a global HIV prevention advocacy group; Treatment Action Group; and Project Inform, will feature an overview for advocates of recent advances in the field and community strategy sessions to discuss how to promote cure research.

**View the story online:** [Click here](#)

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## National Stories

### Short- or Medium-Term PrEP Is Safer Than Aspirin

As reported by POZ.com | 1.12

Truvada (tenofovir/emtricitabine) as pre-exposure prophylaxis (PrEP) against HIV has comparable safety to aspirin, at least for the short- and medium-term. Publishing their findings in *Open Forum Infectious Diseases*, researchers compared safety data from the five major PrEP studies to data from two major aspirin safety studies, looking at the relative numbers needed to harm (NNH, or the numbers of individuals needed to take the drug to yield a specific safety outcome in one of them) between PrEP and aspirin.

Among men who have sex with men (MSM) and transgender women taking PrEP, the NNH was 114 for nausea and 96 for unintentional weight loss. Among heterosexuals, PrEP's NNH was 68 for moderate decreased absolute neutrophil count (infection-fighting white blood cells). Participants in the PrEP trials reported no serious irreversible health problems and no hospitalizations or deaths associated with Truvada.

PrEP was associated with a mild decrease in creatinine clearance, which is an indicator of kidney function, as well as a small decrease in bone mineral density. Both of these changes reversed after individuals stopped taking Truvada. The drug has not been associated with any bone fractures, pregnancy problems or permanent kidney failure.

For aspirin, the NNH was 909 for major gastrointestinal bleeding, 123 for any gastrointestinal bleeding and 15 for any bleeding problems in men. For women, aspirin's NNH for easy bruising was 10.

The researchers concluded that PrEP has a favorable safety profile compared to aspirin. Studies are still needed, however, to assess the long-term safety of PrEP.

To read the study abstract, [click here](#).

**View the story online:** [Click here](#)

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### Antibody Infusion Successfully Combats HIV in Early Trial

As reported by POZ.com | 1.11

An infusion of an HIV antibody called [VRC01](#) suppressed the virus in people not taking antiretrovirals (ARVs) and was safe or well tolerated. Publishing their findings in *Science Translational Medicine*, researchers conducted a Phase I trial of 23 HIV-positive participants, 15 of whom were on ARVs and eight of whom were not.

Those taking HIV treatment received two infusions of the antibody, spaced 28 days apart. The participants not on ARVs received one antibody infusion.

The infusions did not reduce the amount of virus in blood cells. It did reduce viral load by more than 10-fold in six of the eight individuals not taking ARVs. The two people in this group with the lowest viral loads at the study's outset saw their viral load drop to extremely low levels for about three weeks, which

coincided with the amount of time that the antibody remained at therapeutic levels in their bodies. The other four people who saw a decline in viral load experienced a substantial reduction, but not to undetectable levels. The remaining two people who did not experience a substantial viral load reduction turned out to have a predominant strain of HIV that was resistant to VRC01.

Among those taking ARVs, the antibody did not appear to have any effect.

The researchers will continue to study the antibody as a treatment and prevention for HIV.

To read the study abstract, [click here](#).

To read a press release about the study, [click here](#).

**View the story online:** [Click here](#)

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## **Legal barriers to adolescent participation in HIV, STI research need to be removed**

Jeff Falk, Medical Xpress | 1.11

Parental permission for adolescent participation in research on HIV pre-exposure prophylaxis and other sexually transmitted infections (STIs) is not required ethically and may undermine public health interests, according to a new paper by law and public health experts at Rice University's Baker Institute for Public Policy and Baylor College of Medicine.

The paper summarizes legal, ethical and policy considerations related to adolescents' participation in HIV- and STI-prevention research in the United States and explores strategies for facilitating adolescents' access. It was co-authored by Quianta Moore, a scholar in health policy at the Baker Institute and adjunct assistant professor in Baylor's Department of Pediatrics; Mary Paul, associate professor in Baylor's Department of Pediatrics-Retrovirology; Amy McGuire, the Leon Jaworski Professor of Biomedical Ethics and director of Baylor's Center for Medical Ethics and Health Policy; and Mary Majumder, associate professor in the Center for Medical Ethics and Health Policy.

The paper was published in the January issue of the American Journal of Public Health.

The second-largest percentage (26 percent) of new HIV infections in the U.S. occurs among people aged 13 to 24 years, and most of those new infections occur in gay and bisexual young men (72 percent), according to the Centers for Disease Control and Prevention. These rates of infection make high-risk adolescents an important target population for primary prevention. Used in conjunction with safer sex practices, pre-exposure prophylaxis has demonstrated effectiveness in preventing transmission in high-risk groups, such as men who have sex with men. In the context of HIV, pre-exposure prophylaxis is defined as the use of antiretroviral medications in HIV-negative individuals to prevent HIV transmission.

Whether adolescents can participate in clinical trials of pharmacologic therapies for HIV prevention, such as pre-exposure prophylaxis, without parental permission hinges on state minor-consent laws. Very few of these laws explicitly authorize adolescents to consent to preventive services for HIV and other sexually transmitted infections. The unclear state laws may lead to research cessation, according to the authors.

To address legal barriers, the authors propose two strategies:

"First, in states with existing minor-consent provisions for STI treatment that do not expressly include prevention, we urge public-health advocates and officials to partner with state legislators to promote amendments to minor-consent statutes that would explicitly authorize minors to consent to preventive care related to STIs, including HIV," the authors wrote. "There is little reason to believe that legislators craft treatment-focused state laws to exclude prevention.

Their second strategy is to urge institutional review boards to adopt an open stance toward claims that the word "treatment" in state minor-consent laws should be interpreted to encompass prevention. If there is no clear evidence of a legislative intent to exclude prevention from treatment, "we believe that institutional review boards act reasonably and responsibly in concluding that treatment includes prevention in states with laws that authorize adolescents to consent to STI treatment, including HIV, but do not explicitly authorize minors to consent to preventive services," the researchers wrote. They recommended consultation with legal counsel to ensure proper interpretation of state law.

The authors suggest it would be helpful if the Food and Drug Administration's Office of Human Research Protections provided guidance to foster greater consistency in institutional review board determinations within states that allow minors to consent to treating HIV and other STIs but do not explicitly address prevention.

**View the story online:** [Click here](#)

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## **Trials underway to evaluate solithromycin for gonorrhea, NASH**

As reported by Healio Infectious Disease News | 1.12

Solithromycin, a next-generation macrolide with activity against various strains of bacteria, will be assessed in two clinical trials as a potential drug candidate for urogenital gonorrhea and nonalcoholic steatohepatitis, according to a pair of press releases.

Previously, solithromycin (Cempra) was investigated among in vitro and in vivo studies and has shown "potent activity" against *Streptococcus pneumoniae*, and extended activity against CA-MRSA, streptococci, *Haemophilus*, enterococci and *Mycobacterium avium*, according to a release. In addition, data presented at IDWeek 2015 showed a 5-day regimen of oral solithromycin was noninferior to a 7-day regimen of moxifloxacin for the treatment of community-acquired bacterial pneumonia and performed as well as or better than moxifloxacin in the subgroup of patients who had identified *Mycoplasma pneumoniae* infection.

Solithromycin as a single oral dose agent against urogenital gonorrhea

Cempra recently launched a phase 3 trial, Solitaire-U, that will examine the safety and efficacy of solithromycin in patients with urogenital gonorrhea. To date, 250 patients, mostly men, from the U.S. and Australia have been enrolled in the trial. Through an agreement with the National Institute of Allergy and Infectious Diseases, Cempra will enroll 60 additional women and adolescents with confirmed gonorrhea. Researchers will randomly assign patients to 1,000 mg solithromycin or the standard-of-care, 500 mg ceftriaxone administered intramuscularly and 1,000 mg oral azithromycin.

“There is a tremendous need for an effective, single-dose, oral treatment such as solithromycin that can provide coverage for both gonococcus and chlamydia for the entire population at risk for these infections,” Prabhavathi Fernandes, PhD, president and CEO of Cempra, said in a press release. “We are pleased that the NIAID will be expanding this study to enroll the additional patient populations that could eventually be included for the label indication, should solithromycin be approved for the treatment of urogenital gonorrhea. This potential use could be an attractive secondary market, in addition to the primary indication we are seeking for the treatment of community-acquired bacterial pneumonia.”

Annual surveillance data from the CDC revealed large increases in nationally notifiable STD rates within the United States, with a record number of chlamydia cases reported in 2014. Reported gonorrhea cases (n = 350,062) resulted in a 5.1% rate increase to 110.7 cases per 100,000 population. In addition, the percentage of *Neisseria gonorrhoeae* isolates with reduced azithromycin susceptibility increased by 2.5%.

According to another press release, solithromycin is 8 to 16 times more potent than azithromycin and has activity against azithromycin-resistant strains.

“Solithromycin’s activity against resistant strains is driven by its ability to interact with three sites on the bacterial ribosome, compared to one for current macrolides,” the release said. “The binding to three ribosomal sites is expected to limit resistance development.”

If approved, solithromycin could offer a convenient oral treatment for patients with gonorrhea, the release said.

Immunomodulatory, anti-NASH activity observed with solithromycin

The safety of solithromycin also will be evaluated in patients with nonalcoholic steatohepatitis (NASH) without cirrhosis during a phase 2 trial, according to a press release.

Inflammation plays an important role in the progression of NASH, and the immunomodulatory and anti-NASH activity that has been observed with solithromycin in a murine diabetic NASH model may benefit patients, the release said.

“The commencement of this clinical trial represents an important potential step in furthering our understanding of solithromycin’s mechanism of action beyond antibacterial effects,” Fernandes said in the release. “There is a great need to develop medicines that target the hepatic inflammation caused by NASH and an effective immunomodulatory treatment may reduce disease progression.”

Up to 15 patients aged 18 to 70 years will be enrolled in the trial by the end of this year, according to the release. The patients will receive two 200-mg capsules of solithromycin daily for 13 weeks. Along with assessing safety and tolerability, other primary endpoints include a change in liver histology via the Nonalcoholic Fatty Liver Disease Activity Score, fibrosis measurement, ballooning degeneration and markers of liver inflammation.

**View the story online:** [Click here](#)

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## Two cases of PrEP failure on solo tenofovir pose significant research questions

Gus Cairns, [aidsmap.com](http://aidsmap.com) | 1.14

A report originally presented to the 2015 BHIVA conference last year details two cases where therapeutic levels of solo tenofovir unequivocally failed to prevent HIV infection in gay men. In one case, despite the tenofovir apparently suppressing the man's HIV viral load in his blood plasma, it failed to prevent HIV infecting the cells of his immune system.

The cases raise a number of questions: whether the levels of tenofovir required to prevent infection need to be higher than those used for treatment; whether hepatitis B co-infection may have made HIV infection more likely; whether the men would have been infected if they had been taking tenofovir + emtricitabine (Truvada); and if not, what are the exact contributions to prevention of the two drugs.

The men were not taking tenofovir specifically as pre-exposure prophylaxis (PrEP) but instead were taking it as treatment for chronic hepatitis B infection. One had had persistent hepatitis B infection for six years and had been on tenofovir for four years; the other had had hepatitis B for seven years and had taken tenofovir for three years.

In the case of the first patient (patient A), the date of HIV infection can be pinpointed almost exactly as he tested HIV-antibody positive only twelve days after a confirmatory HIV western blot antibody test found him HIV negative. Although this is an unusually short time in which to develop HIV antibodies, it is not unknown. It was estimated that the most likely date for his actual exposure to HIV, based on his report of condomless receptive anal sex with a casual male partner, was one day after his HIV-negative test result. Six days later, he reported mild flu-like symptoms suggestive of HIV seroconversion illness and was tested again.

The second patient (patient B) had not had a recent negative HIV test but was hospitalised with a severe flu-like illness with fatigue and muscle pain, suggestive of HIV seroconversion. Based on his first positive HIV test, where he was HIV antibody-negative but p24-positive, and also on his account of condomless receptive anal sex, it was estimated that his likely time of infection was about two weeks previous to the test.

Both men appeared to have excellent adherence to tenofovir based on pill counts. More to the point, tenofovir drug levels were taken on the day they tested HIV positive. Patient A had last taken tenofovir 24 hours before his drug level test and was therefore at the 'trough' or lowest blood level one would expect. His level of tenofovir was about 75 nanograms per millilitre of blood (ng/ml), meaning that he had lower trough levels than about 80% of patients, but still well within the therapeutic level to treat both hepatitis B and HIV. Patient B had taken tenofovir seven hours before his HIV test result and had a blood level of 230 ng/ml, or higher than 75% of the average patients, seven hours after a dose. Both results indicate that their absorption of tenofovir was normal.

Both patients had CD4 cells counts of 550-600 cells/mm<sup>3</sup> – notably lower than typical CD4 counts seen in HIV-negative people – and while patient A had a relatively normal CD4:CD8 ratio of 1.16, patient B had the 'inverted' ratio typically seen in people with HIV – 0.49. [HIV-negative people typically have more CD4 than CD8 cells: in people with HIV this ratio is usually inverted immediately after acute infection and stays that way without treatment.] Either way, these figures show that despite the tenofovir, both patients had suffered significant immune damage during acute HIV infection – as usually happens.

The biggest difference between the two patients was that in patient A the tenofovir, despite not preventing HIV infection, did seem to be suppressing his HIV viral load in the blood. Although testing HIV-positive and having HIV integrated into his cell (see below) at no point did he have a viral load over 50 copies/ml. This 'blunting' of the HIV viral load has been seen before in cases of PrEP failure, notably in the animal studies that established its efficacy. This means his HIV could not be tested to see if it had acquired, or already had, drug resistance to tenofovir. This patient was switched to Eviplera (rilpivirine/tenofovir/emtricitabine) as soon as he tested HIV positive.

Patient B had a viral load of just over 100,000 copies/ml – not especially high for acute or recent infection. Despite having HIV actively reproducing in the presence of high tenofovir levels, he had no drug resistance mutations, illustrating, as other studies have done, that resistance to tenofovir only rarely develops in cases where people with HIV take PrEP. However to forestall resistance, patient B was put on to an intensified three-class antiretroviral regimen of Truvada (tenofovir/emtricitabine), boosted darunavir and raltegravir, which resulted in successful suppression of his viral load.

Both patients had significant intracellular HIV infection, and HIV integrated into the genetic material of their immune cells – 587 copies per million CD4 cells in the age of patient A and 1432 copies in patient B. This indicates quite enough integrated HIV for an ongoing, productive infection in both patients and indeed transcribed RNA, evidence that cells were actively producing new HIV viral particles, was found in both patients, though at one-tenth the level in patients A as patient B.

These cases may be the first ones where it can be shown without doubt that a daily dose of tenofovir has failed to prevent HIV infection. In one of the largest randomised studies of PrEP, Partners PrEP, there were six cases of HIV infection (Donnell) in people who, at the visit they were diagnosed with HIV, had tenofovir levels consistent with daily dosing (two of these were also taking emtricitabine). However in all cases but one, the participants could have caught HIV at any time in the previous three months since their last visit, so may not have been taking PrEP at the actual time they were infected. In one case, the participant had a level of tenofovir consistent with daily dosing one month before being diagnosed with HIV and at the visit she was diagnosed: this is the only previous case where the failure of PrEP to protect against infection despite what should have been protective levels looks like the most likely interpretation of the data.

The researchers comment that their cases show that "tenofovir monotherapy PrEP in men who have sex with men has limited efficacy data and that HIV acquisition can occur in the presence of tenofovir drug levels within the therapeutic range required to treat HIV." They point out that it has never really been established whether the level of tenofovir (or any other single drug) sufficient to treat HIV is sufficient to prevent it. They also hypothesise that hepatitis B infection could increase susceptibility to HIV, even where it appears largely suppressed virologically. It may also cast further doubt over the use of solo tenofovir as PrEP in any patient, and should spur further research into even more protective PrEP regimens, and may add to nervousness about recommending some intermittent PrEP regimens.

Nonetheless, as the researchers note, the overwhelming majority of cases of so-called 'PrEP failure' are due to people not actually taking PrEP: the fact that these two cases have been reported underlines that HIV infection in situations where it looks like people have been taking PrEP consistently is extremely rare.

## References

Fox J et al. *Tenofovir disoproxil fumarate fails to prevent HIV acquisition or the establishment of a viral reservoir: two case reports*. Journal of Infectious Disease and Therapy, early online publication. DOI 10.1007/s40121-015-0102-x. [See abstract here](#). 2016.

Fox J et al. *Pre-exposure prophylaxis fails to prevent HIV-1 infection or the establishment of a significant viral reservoir*. 21<sup>st</sup> annual BHIVA conference, Brighton. Abstract P10. 2015. See <http://www.bhiva.org/documents/Conferences/2015Brighton/AbstractBook2015.pdf> for abstracts.

Donnell D et al. *HIV Protective Efficacy and Correlates of Tenofovir Blood Concentrations in a Clinical Trial of PrEP for HIV Prevention*. JAIDS 66(3): 340–348. 2014.

View the story online: [Click here](#)

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## Scientific Papers/Conference Abstracts

### Economic Burden of HIV Antiretroviral Therapy Adverse Events in the United States

Dekoven M, Makin C, Slaff S, et al. *JAPAC* 2016; 15(1):66-76

#### Objective:

To estimate health care costs associated with medical events identified as antiretroviral therapy (ART)-attributable adverse events (AEs).

#### Methods:

During September 2006 to June 2012, adults with  $\geq 1$  HIV International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis code (042/V08),  $\geq 1$  claim for ART prescription (March 2007-June 2011; index date), and continuous health plan enrollment for  $\geq 6$  months pre- and  $\geq 12$  months postindex were included (IMS' PharMetrics Plus Health Plan Claims Database). Patients with events of interest/ART claim during preindex period or with pregnancy/hepatitis C virus diagnosis/hepatitis B virus/cancer/tuberculosis during the study period were excluded. Postindex medical events were defined as first diagnosis code of event with ART claim  $\leq 60$  days prior to start of the event.

#### Results:

Differences in median total all-cause health care costs observed for diabetes/insulin resistance management (US\$14 547 median all-cause health care costs during time periods identified as diabetes/insulin resistance medical events versus US\$11 237 without diabetes/insulin resistance events;  $P = .0021$ ), lipid disorders (US\$12 825 versus US\$10 033;  $P = .0004$ ), and renal disorders (US\$1389 versus US\$0;  $P < .0001$ ).

#### Discussion/Conclusion:

Health care costs of ART AEs should be key consideration for payers/providers in HIV management.

View the paper online: [Abstract](#)

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## A Clinical Home for Preexposure Prophylaxis: Diverse Health Care Providers Perspectives on the "Purview Paradox"

Hoffman G, Collier JA, Mantell KL, et al. *JAPAC* 2016;15(1):59-65

### Background:

One barrier to wider preexposure prophylaxis (PrEP) availability is uncertainty about the most appropriate providers and practice settings for offering PrEP.

### Methods:

The authors conducted in-depth interviews with 30 clinicians—primary care and HIV specialists—in the New York City (NYC) region to explore issues related to PrEP rollout, including who should provide it and in what settings.

### Results:

A diverse group favored offering PrEP in non-HIV specialty settings in order to reach high-risk HIV-negative individuals. Yet, for each clinical skill or ancillary service deemed important for providing PrEP—knowledge of the medications, ability to assess and counsel around sexual risk behavior, and ability to provide support for retention and medication adherence—participants were divided in whether they thought primary care providers/practices could achieve it. Five participants strongly favored providing PrEP in HIV care practices.

### Conclusion:

Although there may be multiple "homes" for PrEP, implementation research is needed to identify the most effective delivery approaches.

View the paper online: [Abstract](#)

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## Prevalence of transmitted HIV drug resistance among recently infected persons in San Diego, California 1996-2013.

Panichsillapakit T, Smith DM, Wertheim JO, et al. *JAIDS* 2016; [Epub ahead of print]

### BACKGROUND:

Transmitted drug resistance (TDR) remains an important concern when initiating antiretroviral therapy (ART). Here, we describe the prevalence and phylogenetic relationships of TDR among ART-naive, HIV-1 infected individuals in San Diego from 1996 to 2013.

### METHODS:

Data were analyzed from 496 participants of the San Diego Primary Infection Cohort who underwent genotypic resistance testing before initiating therapy. Mutations associated with drug resistance were identified according to the WHO-2009 surveillance list. Network and phylogenetic analyses of the HIV-1 pol sequences were used to evaluate the relationships of TDR within the context of the entire cohort.

### RESULTS:

The overall prevalence of TDR was 13.5% (67/496), with an increasing trend over the study period ( $P = 0.005$ ). TDR was predominantly toward nonnucleoside reverse transcriptase inhibitors (NNRTIs) [8.5% (42/496)], also increasing over the study period ( $P = 0.005$ ). By contrast, TDR to protease inhibitors and

nucleos(t)ide reverse transcriptase inhibitors were 4.4% (22/496) and 3.8% (19/496), respectively, and did not vary with time. TDR prevalence did not differ by age, gender, race/ethnicity, or risk factors. Using phylogenetic analysis, we identified 52 transmission clusters, including 8 with at least 2 individuals sharing the same mutation, accounting for 23.8% (16/67) of the individuals with TDR.

#### **CONCLUSIONS:**

Between 1996 and 2013, the prevalence of TDR significantly increased among recently infected ART-naive individuals in San Diego. Around one-fourth of TDR occurred within clusters of recently infected individuals. These findings highlight the importance of baseline resistance testing to guide selection of ART and for public health monitoring.

**View the paper online:** [Abstract](#)

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## **Resources, Webinars, & Announcements**

### **HIVresource: A Guide to Clinical Research in the San Francisco Bay Area**

A new issue of HIVresource is available online.

In the winter 2016 edition of HIVresource, read about a \$20 million grant awarded to University of California San Francisco researchers to investigate an HIV cure, find out about the next Positive Living for Us Seminar (PLUS) held at the new San Francisco AIDS Foundation health and wellness center, called Strut, and learn how to get involved in a community service and social group for gay, bisexual and transgender men.

[In this issue of HIVresource](#), you will also find a list of more than 50 clinical trials that offer HIV or hepatitis C treatment and care. HIVresource is a free publication produced by San Francisco AIDS Foundation.

Please feel free to share HIVresource.

Very best,  
Emily Newman, Editor

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### **New HealthCare.gov Page on Transgender Health Care Coverage**

The Department of Health and Human Services added a new page on [HealthCare.gov for transgender health care](#). The purpose of this page is to provide information for transgender consumers to consider when applying for and using their health care coverage. **January 31, 2016** is the last day of open enrollment for 2016.

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