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napwha national association of people with HIV australia

2022 CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTION

10 May 2022

The Conference on Retroviruses and Opportunistic Infections (CROI) provides a forum for scientists and clinical investigators to present, discuss, and critique their investigations into the epidemiology and biology of human retroviruses and associated diseases.

The CROI conference is held annually in a different city in the USA. In 2022, the conference was held from the 12 to 16 of February.

AFAO and the National Association of People with HIV Australia (NAPWHA) summarised the following stories from NAM AIDSMap to highlight key themes in the conference and their application to the Australian context. One theme of particular interest was the summary of reports on HIV and ageing available here. Other areas of interest are outlined below.

PREVENTION

Heterosexual contact in the United Kingdom now accounts for more new HIV notifications than gay and bisexual men

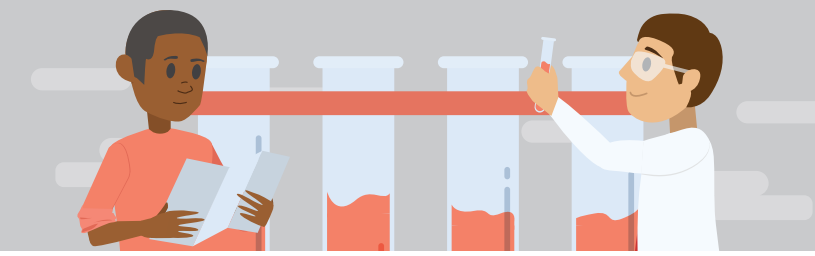
HIV incidence in the United Kingdom among gay and bisexual men continues to fall and now accounts for fewer cases than those reporting heterosexual contact. If the 75% decline in HIV transmissions continues at this rate, new HIV cases in gay and bisexual men will be considered a rarity by 2040. The model presented by Dr Valentina Cambiano and colleagues demonstrates how a suite of prevention measures has led to the decline, including an increase in HIV testing, antiretroviral therapy (ART) and preexposure prophylaxis (PrEP). The study also used counterfactual scenarios to demonstrate the contribution of each prevention method. In one scenario demonstrating the significance of condoms, there would have been a two-fold increase in new HIV cases if the proportion of people on ART and PrEP were both at today's levels, but condom use remained at 10%, the level seen among gay and bisexual men in 1980.

Generic branded PrEP in the United States can be cost-saving and avert new HIV infections among young gay and bisexual men

Greater access to cheap and generic-branded PrEP could reduce HIV transmission among young gay and bisexual men in the United States, according to Alyssa Amick from Massachusetts General Hospital. Challenges with PrEP adherence and subsequent retention in HIV-related care have occurred due to cost-related issues associated with branded prescriptions. This study compared the cost of branded PrEP with generic PrEP, both of which could be provided at a lesser price than ART and HIV-related clinical care. Over a ten-year period, generic PrEP is half the cost of branded PrEP, which has the potential to avert infections by 15% due to higher uptake and consequently save healthcare costs related to treatment. Generic versions of PrEP provide the same protection as branded PrEP, as they contain the same active ingredients.

Prevention policy impact

Like Australia, the United Kingdom has reported a drop in the proportion of gay and bisexual men reporting consistent condom use with non-regular partners. However, HIV-self testing is comparatively more accessible in the United Kingdom, with several organisations providing free kits that can be ordered online. The percentage of people with HIV aware of their status is similar, but nearly all are on ART, suggesting a strong linkage to care in the United Kingdom. Likewise, PrEP is available for free from NHS sexual health clinics, regardless of visa status. A separate opinion piece highlights the importance of regular testing for a broader group of people – irrespective of their gender or sexuality. In Australia, heterosexual contact accounted for 24% of HIV cases in 2020, and this figure has been steadily increasing as the proportion of cases among gay and bisexual men continues to decline.



Equitable access to PrEP, regardless of visa status, is critical if Australia is to virtually eliminate HIV transmission. Through the Pharmaceutical Benefits Scheme (PBS), the Australian Government subsidises the price of the lowest-priced brand – meaning community members can access several generic versions of PrEP in Australia

Injectable PrEP: the HPTN083 trial

A four-year trial of long-acting injectable PrEP shows encouraging results

Cabotegravir, as long-acting injectable PrEP, is delivered every two months by a healthcare professional through two injections into each buttock. An update on the HPTN083 trial shows that Cabotegravir has superior efficacy to daily oral PrEP in gay and bisexual men and transgender women. The placebo-controlled blind study directed participants to take either active injections and fake pills or fake injections and active pills. They were eventually told which PrEP they were taking and invited to continue their regimen. Participants receiving injectable PrEP as Cabotegravir had just a third as many HIV infections as those taking daily oral PrEP. Overall, there were 66% fewer infections among participants taking injectable PrEP than oral PrEP when comparing the placebo-controlled blind study and the open-label phase. Adherence was slightly slower in the open-ended phase of the trial for both forms of PrEP.

PCR testing can help identify rare breakthrough cases sooner than antibody tests

Another study found PCR testing could help identify rare breakthrough cases where HIV is acquired even when someone is taking PrEP. While PrEP, when taken correctly, minimises the risk of HIV transmission, taking injectable PrEP during seroconversion can limit future treatment options because PrEP slows down replication of the virus and the production of antibodies, allowing more time for the development of mutations that are resistant to integrase inhibitors.

There were seven unexplained cases of HIV transmission where the participants had sufficient PrEP coverage in the HPTN083 trial, even though injectable Cabotegravir was shown to be 66% more effective than daily oral PrEP. Retrospective testing was conducted among these participants, using PCR assays capable of detecting HIV before the appearance of antibodies. The retrospective PCR testing detected HIV between three and 20 weeks earlier than the HIV rapid antibody tests used for the purpose of testing participants in the trial, which also found that injectable Cabotegravir helped participants reach an undetectable viral load after their first PCR test. It is unclear whether these people acquired HIV due to pre-existing drug resistance from their sexual partners or whether resistance was transient through their drug levels.

Given the unexplained cases of HIV transmission in HPTN083, this finding raises the question of whether people who commence using Cabotegravir as long-acting injectable PrEP should be tested for HIV with a PCR test at baseline. This, it seems, would not be necessary for individuals transitioning from oral PrEP to injectable PrEP as the risk of commencing the use of injectable PrEP with undiagnosed HIV would be negligible.

TREATMENT

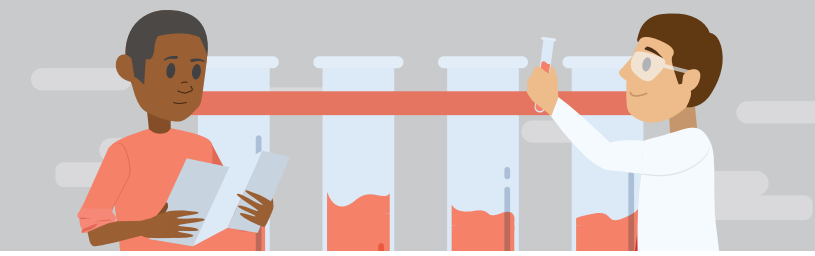
Injectable treatment: the CALIBRATE and CAPELLA trials

Injectable Lenacapavir as HIV treatment could prove effective for first-line treatment

Lenacapavir is a long-acting HIV therapy that has shown promising results for sustaining viral suppression, both in people newly diagnosed with HIV and those who have demonstrated multidrug resistance. Unlike existing classes of HIV treatment, Lenacapavir works by inhibiting HIV at multiple stages of its lifecycle.

The second phase results of the CALIBRATE trial – a study evaluating Lenacapavir as a component of first-line treatment in combination with other ART medication were presented at CROI 2022. Those who reached viral suppression at 28 weeks simplified their ART regime while they continued taking Lenacapavir either through a daily pill or a second subcutaneous injection. One control group received 12 months of standard therapy using the *Biktarvy* once-daily pill regimen (bictegravir/tenofovir alafenamide/emtricitabine). After 54 weeks, between 85 and 90% of people in the groups receiving Lenacapavir had an undetectable viral load under 50 copies/mL, slightly less (92%) than those in the control group taking Biktarvy as first-line treatment.

If approved, Lenacapavir would become the first drug administered twice yearly. This outcome would transform how HIV clinical care is delivered and reduce the demand for care from people who would otherwise need care associated with suboptimal treatment adherence and, consequently, compromised immunity. The impact would be particularly acute for people who struggle to take daily ART and those in outer metropolitan and rural areas, where access to specialist HIV physicians and culturally appropriate care is limited.



Lenacapavir also shows encouraging results for drug-resistant HIV

The phase two/three CAPELLA trial demonstrated that Lenacapavir injected every six months in combination with other ART regimens achieves a high rate of virological suppression and helps increase CD4 count in people who were previously unable to achieve viral suppression through alternative treatments. After 52 weeks, 83% of participants achieved an undetectable viral load while taking Lenacapavir.

While Lenacapavir is not currently approved by any regulatory body, findings from both studies support ongoing research into the drug for HIV treatment. It is anticipated that twice-yearly subcutaneous injections, when made available, could enhance adherence in some groups with sub-optimal adherence to HIV treatment. Likewise, the CAPELLA trial suggests Lenacapavir could be used by people who have experienced prior resistance to existing ART treatment.

Injectable treatment policy impact

Ensuring novel HIV treatment receives priority evaluation for TGA registration and PBS subsidisation is a critical objective in *Agenda 2025* to enhance treatment options for people with HIV. While these trials support continued research, additional consideration is needed to assess for whom injectable treatment would benefit in contrast to daily ART. For example, injectable treatment requires a lead-in period of oral treatment before switching to injections. At this stage, adherence to injections from a healthcare worker becomes essential to sustain an undetectable viral load – meaning injections may not be suitable for those facing barriers to healthcare access. On the other hand, injectable treatment could benefit people who travel to countries where ART is challenging to access or carrying a personal supply is prohibited.

Cabotegravir, in combination with Rilpivirine, has now been registered on the Australian Register for Therapeutic Goods for use as treatment and listed on the PBS. While trials exhibit efficacy, community members are advised to determine their suitability for this therapy in consultation with their treating physician.

Other treatment news

Stem cell transplant in New York woman may have cleared her from HIV

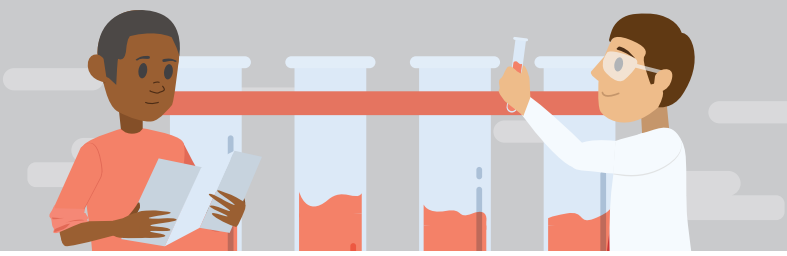
A transplant of HIV-resistant stem cells to treat leukaemia has resulted in one woman showing no detectable HIV more than a year since stopping ART. While both her leukaemia and HIV are in remission, further monitoring will determine whether she has been cleared of the virus. If so, the 'New York patient' would become the third person free of HIV over the long-term due to stem cell transportation – joining the 'Berlin' and 'London' patients following similar procedures in 2006 and 2016, respectively. Researchers have signalled these procedures present significant risks and are not feasible curative options for most people with HIV.

In all three cases, the patients received stem cell transplantations from donors with a rare genetic double mutation that allowed them to develop a 'new' HIV-resistant immune system following chemotherapy and radiotherapy. As the woman is of mixed race, the chances of finding a donor with similar genetics and the rare genetic double mutation CCR5-delta-32 was extraordinarily slim, as the mutation is prevalent in just 1% of northern Europeans. However, core blood taken from the umbilical cord is more forgiving than adult stem cells and does not require as close a genetic match – meaning the mutation in the umbilical cord could be combined with adult stem cells from another donor with similar genetics.

The procedure performed at the Weill Cornell Medical Center was well tolerated by the patient, essentially providing a new HIV-resistant immune system, according to Professor Yvonne Bryson. ART was continued for three years following the procedure. After sero-reverting and becoming HIV antibody negative, ART was paused and closely monitored – with HIV not detected 14 months after ceasing ART. According to Professor Sharon Lewin, president-elect of the International AIDS Society, the procedure 'confirms that a cure for HIV is possible and further strengthens using gene therapy as a viable strategy for an HIV cure.'

Australia meets global hepatitis targets for people with HIV due to broad access to antiviral medication

Direct-acting antivirals for hepatitis C could have a 'treatment as prevention' type effect for people with HIV co-infection, but only when universal access to these drugs is guaranteed for those who need them, according to Dr Daniela van Santen of the Burnet Institute. The broad availability of this medication has led to a 50% reduction in new cases of hepatitis among people with HIV, as demonstrated by a study of six high-income settings. Data was collected from over 100,000 people in Australia, France, Spain, Switzerland, and the Netherlands – finding an overall decline in hepatitis C that exceeded the World Health Organisation interim target of a 30% reduction by the year 2020 and equalled the absolute target of five cases for 100,000 people.



A more significant reduction was seen in Australia and the Netherlands, both countries with higher hepatitis C incidence among people with HIV before direct-acting antivirals became available. While only 0.4% of the participants in this trial were injecting drug users, these data indicate that direct-acting antivirals could be used to prevent onward transmission of hepatitis C. Further monitoring is required to determine if these results will be sustained over time.

TESTING

Risk of anal cancer in people with HIV reduced through early screening and swift commencement of treatment

Results from the ANCHOR study have demonstrated that early screening and testing for anal cancer can substantially lower the cancer risk in people with HIV. These findings support the inclusion of regular screening as a part of HIV clinical care for people with HIV over the age of 35, according to lead investigator Professor Joel Palefsky of the University of California San Francisco.

Anal cancer is caused by the human papillomavirus (HPV), one of the most common sexually transmitted infections. While anal cancer is uncommon in the broader population, the incidence is much higher among people with HIV, especially gay and bisexual men, older individuals, women with cervical cancer, and others with compromised immunity. Of the screened participants who had abnormal cells known to progress to invasive cancer, more than 80% were on ART with an undetectable viral load and a healthy CD4 count. Half of the cohort were allocated to an immediate treatment arm, while the other half were actively monitored. The trial was discontinued ahead of schedule after the results showed that the quick removal of abnormal cells has clear benefits for people with HIV.

Twenty-one people in the active monitoring arm were diagnosed with invasive cancer, compared to nine people in the immediate treatment arm. This represents a 57% risk reduction – and the participants in the monitoring arm were recommended for cancer treatment. It is expected that further updates on this study and its implications will be provided at the Australasian Conference on HIV and Sexual Health later in the year.