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Contents

I SEXUALLY TRANSMITTED INFECTIONS

A. Post-exposure doxycycline helps reduce the risk for some sexually transmitted infections

Over the past decade there has been a resurgence of common sexually transmitted infections (STIs), including bacterial STIs such as syphilis, gonorrhea and chlamydia.

These STIs can cause serious complications, as follows:

- syphilis – the germs that cause this STI can attack nerves in the eyes (causing blindness) and ears (causing loss of hearing). Syphilis can also injure the heart, brain, kidneys and liver.
- gonorrhea – this STI can cause pain and discomfort. It can also cause infertility. Over the past 50 years, gonorrhea-causing germs have acquired the ability to resist different antibiotics and there are fewer treatment options today.
- chlamydia – this STI can cause pelvic inflammatory disease and infertility in women. Complications from chlamydia are less common in men, though it can cause inflammation in the testicles and prostate.

Researchers in San Francisco and Seattle conducted a study with the antibiotic doxycycline to assess if it could reduce the risk of syphilis, gonorrhea and chlamydia when taken after sexual exposure. Participants were mostly gay, bisexual and other men who have sex with men (gbMSM); a small proportion of participants (less than 5%) were transgender women.

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555 Richmond Street West, Suite 505
Box 1104
Toronto, Ontario M5V 3B1 Canada
www.catie.ca
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At the start of the study, 501 participants were screened for STIs and provided treatment if needed. Once in the study, participants were randomly assigned to either take 200 mg doxycycline (doxy-PEP) within 72 hours of condomless sex or no doxycycline. Participants visited study clinics every three months for STI screening and to answer surveys about sexual behaviour, adherence and reports of side effects. Researchers monitored participants for at least one year.

Overall, doxy-PEP reduced the risk of syphilis, gonorrhea and chlamydia by two-thirds. This was statistically significant. Doxy-PEP was highly effective at reducing the risk of STIs whether or not participants had HIV.

Adherence to doxy-PEP was high (around 86%), suggesting a highly motivated group of participants.

Study details

Researchers reported results on 501 participants who were randomized in a 2:1 ratio to one of two groups:

- Doxy-PEP group – these people were given bottles of delayed-release tablets of 200 mg doxycycline and told to take one within 72 hours of condomless sex.
- Standard care group – these people were not given doxy-PEP

As mentioned previously, all participants visited study clinics every three months. If they needed to, they could visit the study clinics more frequently.

Researchers recruited 174 HIV-positive people and 327 HIV-negative people. The HIV-negative people were taking pre-exposure prophylaxis (PrEP) to reduce their risk for acquiring HIV.

The average profile of participants upon study entry was as follows:

- age – 38 years
- 96% cisgender men; 4% transgender women or gender-diverse people
- major ethno-racial groups: White – 67%; multiple races – 15%; Asian – 11%; Black – 7%
- STIs in the past six months: gonorrhea – 30%; chlamydia – 12%; syphilis – 4%
- number of sexual partners in the past three months – nine
- engaged in transactional sex at any time in the past – 29%
- commonly used drugs in the past three months: marijuana – 48%; poppers – 45%; ecstasy, GHB or ketamine – 32%; opioids – 3%; stimulants (meth, cocaine or crack) – 30%

HIV-related characteristics
Among participants with HIV at the start of the study, more than 99% were taking HIV treatment (ART) and 95% of ART users had a suppressed viral load (less than 50 copies/mL). Their average CD4+ count was 700 cells/mm^3.

In nine HIV-positive people, their viral load at the start of the study was detectable (an average of 1,354 copies/mL).

The study was done from August 2020 through May 2022.

Results – overall STI diagnoses

Overall, the use of doxy-PEP reduced the risk of developing bacterial STIs (syphilis, gonorrhea or chlamydia) by 66%.

People taking HIV PrEP
Among HIV-negative people taking PrEP, an STI was diagnosed in 11% of clinic visits in people who were also taking doxy-PEP vs. 32% who did not receive doxy-PEP.

People with HIV
Among HIV-positive people, an STI was diagnosed in 12% of clinic visits in people who were taking doxy-PEP vs. 31% who did not receive doxy-PEP.

Results – specific STIs

Gonorrhea
Among HIV-negative people taking PrEP, gonorrhea was diagnosed in 9% of people who took doxy-PEP vs. 20% of people who did not receive doxy-PEP.

Among people with HIV, gonorrhea was diagnosed in 9% of people who took doxy-PEP vs. 20% of people who did not receive doxy-PEP.

Chlamydia
Among HIV-negative people taking PrEP, chlamydia was diagnosed in 1% of people who took doxy-PEP vs. 12% of people who did not receive doxy-PEP.

Among people with HIV, chlamydia was diagnosed in 4% of people who took doxy-PEP vs. 15% of people who did not receive doxy-PEP.

Syphilis
Among HIV-negative people taking PrEP, syphilis was diagnosed in 0.4% of people who took doxy-PEP vs. 3% of people who did not receive it.

Among people with HIV, syphilis was diagnosed in 1% of people who were taking doxy-PEP vs. 2% of people who did not receive it.

Safety

In general, doxy-PEP was well tolerated. Only 2% of people who were given doxycycline-PEP stopped taking it because of side effects or other reasons. This is not surprising, as doxycycline has been in use as a treatment for different bacterial infections for decades and has a good track record.

According to the researchers, the following adverse events were probably caused by use of doxycycline:

- 2 people had temporarily increased levels of liver enzymes in their blood
- 3 people had temporary severe diarrhea
- 2 people had temporary severe headaches

There was a modest degree of weight loss in people who took doxy-PEP (0.8 kg) and there was a very modest degree of weight loss among people not taking the antibiotic (0.2 kg).

When surveyed, nearly 90% of participants agreed that doxy-PEP was acceptable or very acceptable for them.

Resistance

As with the use of any antibiotic, there are concerns that bacteria, particularly STIs, may develop the ability to resist the effects of antibiotics. Researchers performed analyses of swabs taken from participants at different times in the study. However, antibiotic resistance was not common and the researchers did not think that it was a significant issue.

Gonorrhea resistance
For many reasons, researchers were only able to get a limited number of gonorrhea-causing bacteria for analysis (from 17% of participants). At the start of the study, doxycycline resistance was found in four out of 15 samples (27%). During the study, the distribution of gonorrhea that was resistant to doxycycline was as follows:

- people taking doxy-PEP – 38% (5 out of 13 samples)
- people not taking doxy-PEP – 12% (2 out of 16 samples)

Staph aureus
Another bacterium of interest is Staphylococcus aureus (S. aureus). It lives on the skin and some mucosal surfaces (such as inside the nose). The skin and lining of the nose act as barriers preventing the bacteria from getting inside the body. As this bacterium rarely gets inside the body, the immune system does not have experience dealing with it and can become overwhelmed when S. aureus gets inside because of cuts or breaks in the skin. Once inside the body, S. aureus can spread to tissues and, via the blood, to vital organs such as the heart and lungs, where it can cause serious and sometimes deadly infection.

At the start of the study, S. aureus was found in swabs of the nasal cavity in 45% of all participants and it was resistant to doxycycline in 12% of participants.

After 12 months of the study, 28% of participants taking doxy-PEP had S. aureus in their nasal samples vs. 47% in participants not taking doxy-PEP.

The researchers stated that, overall, resistant S. aureus was found in 5% of people taking doxy-PEP and in 4% of people not taking the antibiotic.

Bear in mind

The use of doxy-PEP in this study, which consisted of highly motivated gbMSM and transgender women participants, was very effective at minimizing the onset of chlamydia, gonorrhea and syphilis. As a result, doctors will be interested in prescribing this antibiotic for some, perhaps many, of their sexually active gbMSM patients who can adhere to doxy-PEP.

Some public health departments in California have recommended the use of doxy-PEP for gbMSM. However, at the time we went to publication, Public Health England and the British Association

for Sexual Health and HIV do not recommend its use for fear of creating more and widespread strains of bacteria resistant to doxycycline (and related antibiotics).

As mentioned earlier, there are fewer treatment options for gonorrhea due to the development of resistance. Long-term monitoring for the possibility of gonorrhea (and other bacteria) becoming resistant to doxycycline needs to be done, particularly in populations of gbMSM. This is important, as some laboratory experiments suggest that bacteria that become resistant to doxycycline may also somehow acquire the ability to resist unrelated antibiotics such as ceftriaxone.

The long-term effect of doxycycline on bacteria that naturally live in the gut and are necessary for human health also needs to be studied.

The present study was focused on highly motivated gbMSM and 19 transgender women (or gender diverse people). Studies of doxy-PEP need to be designed for other populations at high risk of STIs.

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II HIV

A. Large study confirms near-normal life expectancy for many people on HIV treatment

Prior to the availability of effective HIV treatment (ART) people with HIV had a relatively shortened lifespan, with most expected to live for around 10 years after infection. However, beginning in 1996, effective HIV treatment became available in Canada and other high-income countries. By suppressing HIV to very low levels, ART significantly reduces the ability of this virus to damage the immune system. Also, ART greatly reduces HIV-related excess inflammation and activation of the immune system. All of these effects allow the immune system to make repairs and largely rebuild itself. As a result, in the vast majority of ART users, the immune system becomes stronger with higher CD4+ cell counts and the risk of dying from AIDS-related complications greatly diminishes.

In the first decade that ART was available, there were some downsides, such as the following:

- ART had many side effects
- there were food and water restrictions for some medications
- regimens required taking a large number of pills – two or even three times daily

As a result, some people interrupted ART and others may have had poor adherence. Such interruptions to therapy allowed the virus to re-surge and inflammation to increase, which could have degraded survival.

Since that era, treatments have become simplified and they are much safer and more powerful. Many people who initiate ART in the current era are prescribed an entire regimen in a pill, just once daily. Leading drugs that anchor such regimens include the following:

- bictegravir – in Biktarvy
- dolutegravir – sold as Tivicay and co-formulated with other drugs and sold in pills called Dovato, Juluca, and Triumeq
- doravirine – sold as Pifeltro and co-formulated with other drugs in a pill called Delstrigo

In the past several years, a regimen of two HIV drugs became available (sold as Cabenuva) that can be injected once a month or every two months, greatly simplifying adherence requirements.

Another change from the early ART era is that around 2015, based on data from clinical trials, treatment guidelines greatly encouraged the initiation of ART as soon as a diagnosis of HIV was made.

Due to these improvements in HIV treatment—better treatments and earlier initiation of ART—it is important to review changes in life expectancy in people with HIV in the current era.

A team of researchers in Europe and North America, including southern Alberta, merged information from 20 databases and reviewed and compared changes in life expectancy in 206,891 people who initiated ART between 1996 and 2014 or between 2015 and 2019.

The researchers found that between 1996 and 2019 about 3% of people died. They also found that among people with high CD4+ cell counts who started ART prior to 2015 and who survived to 2015 or who started ART after 2015, "life expectancy was only a few years lower than in [people without HIV]." However, among people who had low CD4+ cell counts when they initiated ART (regardless of the time period), prospects for survival were generally poorer.

In general, men had reduced life expectancy compared to women. People who injected drugs had reduced life expectancy compared to people who did not inject drugs.

Overall, the present study confirms earlier research that found that ART has long-term benefits, greatly narrowing the survival gap between people with and without HIV. The study was a snapshot of some immunological and virological data and linked the data to records about survival from medical databases.

To ensure that more people with HIV reach the life expectancy of HIV-negative people, the researchers emphasize the importance of "early [HIV] diagnosis and sustained treatment of HIV." However, more attention needs to be paid to the broader needs of people with HIV, including reducing the risk for and managing comorbidities (such as heart, liver, lung and kidney disease, cancer prevention and treatment) as well as support for mental health. In addition, access to harm reduction services for people who inject drugs and support for reducing alcohol consumption and smoking are also needed.

Results

In general, people who initiated ART in the earlier part of the study, particularly the years 1996 to 1999, had a greater risk of death. Beginning in 2015, when recommendations to start ART were extended to all people with HIV (regardless of CD4+ cell count or duration of infection), researchers found that the risk of death fell compared to the early ART era (1996 to 1999).

People who initiated ART prior to 2015 had a higher risk of death. The factors that were linked to an increased risk of death included having less than 500 CD4+ cells/mm^3, having a high viral load, a diagnosis of an AIDS-related infection or cancer, and chronic hepatitis C virus (HCV) infection.

Life expectancy

To estimate life expectancy, researchers divided people into two groups:

- those who initiated ART before 2015
- those who initiated ART in 2015 or later

They then divided people based on their CD4+ cell count at the time they entered the study and their sex assigned at birth.

Overall, people who initiated ART prior to 2015 had reduced life expectancy compared to people who initiated ART in 2015 or later. The CD4+ counts were also important. In general, people who began ART with low CD4+ counts had reduced life expectancy compared to people who began ART with higher CD4+ counts.

In people without HIV, women tend to have a longer life expectancy than men. This was also the case among women with HIV in this study.

The researchers found that people who acquired HIV as a result of sharing equipment for drug use had shorter life expectancy than people who acquired it in other ways. Also, people who had

AIDS when they entered the study had shorter life expectancy than people who did not have AIDS.

Life expectancy among women

ART – overall impact on survival

Among women who began ART before 2015 and who were 40 years of age, researchers estimated that they would live for 36 more years—for a total of 76 years.

Among women who began ART in 2015 or later at 40 years old, life expectancy would be about 39 more years—for a total of 79 years.

Note that the above figures are overall estimates. Researchers found that CD4+ cell counts at the time that ART was initiated could have a huge impact on life expectancy, as shown by the following:

Starting ART at low or high CD4+ cell counts prior to 2015

Among women who started ART before 2015 and who had low CD4+ cell counts (less than 50 cells/mm^3), their remaining life expectancy at age 40 would be 19.4 years, for a total survival of 59.4 years. Women who initiated ART at higher CD4+ cell counts could expect longer life expectancy, reaching as high as 40.2 additional years if they began treatment at age 40 (for a total of 80.2 years of life expectancy). This higher figure was found in women who initiated ART when their CD4+ counts were 500 cells/mm^3 or greater.

Starting ART at low or high CD4+ cell counts after 2015

Among women who initiated ART at age 40 after 2015 with less than 50 CD4+ cells/mm^3, life expectancy was 25 additional years, for a total of 65 years. However, among women who initiated ART with a CD4+ count of 500 or more cells/mm^3 at age 40, life expectancy was projected to reach an additional 40 years, for a total of 80 years.

Among women without HIV, life expectancy at age 40 after 2015 was estimated to be an additional 45.8 years, for a total of nearly 86 years.

Life expectancy among men

ART – overall impact on survival

Among men who began ART before 2015 and who were aged 40, researchers estimated that they would live for 34.5 more years—for a total of 74.5 years.

Among men who began ART in 2015 or later and who were aged 40, researchers estimated that they would live for 37 more years—for a total of 77 years.

However, results could be different depending on the CD4+ count when ART was initiated, with people who started ART at higher CD4+ counts having a longer life expectancy.

Starting ART at low or high CD4+ cell counts prior to 2015

Among men who began ART prior to 2015 and who had very low CD4+ counts (less than 50 cells/mm^3), their remaining life expectancy at age 40 would be 18.2 years, for a total of 58.2 years. Life expectancy increased when ART was initiated at higher CD4+ cell counts in this period. For instance, among men who started ART when they had 500 or more CD4+ cells, life expectancy at age 40 would be an additional 38 years, for a total of 78 years.

Starting ART at low or high CD4+ cell counts in 2015 or later

Among men who were aged 40 and who started ART in 2015 or later with less than 50 CD4+ cells/mm^3, researchers estimated that they had an additional 23.7 years of life expectancy, for a total of 63.7 years. However, among men who initiated treatment in this period with a CD4+ cell count of 500 or more cells/mm^3, life expectancy at age 40 was projected to reach an additional 39.2 years, for a total of 79.2 years.

Among HIV-negative men, life expectancy at age 40 after 2015 was estimated to be an additional 40.7 years, for a total of 80.7 years.

Life expectancy – considering age and gender

Women

The researchers estimated that overall life expectancy at age 20 among women who began ART prior to 2015 was 72 years. Among women who began ART at age 20 in 2015 or later, life expectancy was estimated to be 77 years.

Men

The researchers estimated that overall life expectancy at age 20 among men who began ART prior to 2015 was 71 years. Among men who began ART at age 20 in 2015 or later, life expectancy was projected to be 75 years.

Bear in mind

The study's findings are estimates and some people may live for longer or shorter periods depending on personal circumstances. As studies continue to monitor life expectancy over longer periods, estimates of life expectancy will become more precise.

Part of the reason that people were more likely to die in the early ART era (1996 to 1999) was that they were exposed to more toxic drugs (which made adherence difficult) and were likely sicker than people in the latter period of the study. Despite this, the researchers stressed that two factors—age and CD4+ count around the time they began ART—were "the factors most strongly associated with [the risk of death] from 2015 onward."

Thus, a young adult who is infected today and who is diagnosed and initiates ART shortly thereafter should live well into their senior years, all other things being equal.

Inequalities

Not every ART user will have such a rosy future. In people without HIV, life expectancy can be affected by socio-economic issues, which were not measured in the study. Also, people in this study who injected drugs had significantly reduced survival compared to people who did not inject drugs.

Other studies of people with HIV in the U.S. have found that people who inject drugs have reduced survival compared to people who don't inject drugs. The same study also found that Black men have reduced survival compared to White men. The present study did not analyse data by race/ethnicity.

Life expectancy and beyond

The present study underscores efforts to improve life expectancy among people with HIV. The researchers call for continued efforts on early diagnosis of HIV and sustained treatment. This means that more opportunities need to be made for HIV testing and swift referral to care. There also needs to be a focus on supporting the mental health needs of people with HIV, as mental health issues can affect adherence to ART. Some people who use drugs, alcohol and tobacco also need harm reduction services. However, there are other issues that can also affect health, such as coinfection with hepatitis B and C viruses and monitoring for cancer.

In addition to life expectancy, efforts (and funding) are needed to help clinics focus on improving quality of life for people with HIV. This can include more widespread use of modern, tolerable and effective therapy. However, studies are needed to understand the issues that affect quality of life and to craft interventions to maintain or improve it.

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B. Australian researchers find treatment as prevention (TasP) works in men who have sex with men

HIV treatment (ART) has at least two important benefits. At the level of the individual, when used as directed, ART eventually suppresses the amount of HIV in the blood of the vast majority of people to very low levels that are below the threshold of detection of routinely used tests. Such very low levels are commonly called "undetectable." This suppression of HIV reduces inflammation and HIV-related injury to the body. Over time, the immune system is able to rebuild itself to the point where the risk of AIDS-related infections and cancers becomes extremely rare. The power of ART is so tremendous that research increasingly finds that many ART users will have near-normal life expectancy.

ART and a suppressed viral load also have a big impact on the sexual transmission of HIV. Nearly a decade ago, well-designed clinical trials were initiated in couples where one partner was HIV positive and the other was HIV negative. After the partner with HIV initiated ART and achieved and maintained a suppressed viral load, both partners underwent regular HIV testing and engaged in condomless intercourse. Researchers found no cases of new HIV infection from partners whose viral load was suppressed. This finding occurred in gay, bisexual and other men who have sex with men (gbMSM) as well as in heterosexual people.

Based on these results, the phrase "U=U" was developed. This phrase is shorthand for undetectable equals untransmittable. U=U is an important part of HIV prevention campaigns and efforts to reduce the stigma that has followed HIV for decades.

Stopping the spread over a large area or population

Researchers are interested in deploying interventions at the level of a city, country or region to help reduce the spread of HIV. In particular, a key part of HIV prevention campaigns is enhancing the availability of HIV testing followed by swift referral of newly diagnosed people into care so that they can be offered treatment. Once in care and on treatment, the vast majority of patients ultimately achieve and maintain an undetectable viral load. This use of treatment (and undetectable viral load) to help prevent HIV is called Treatment as Prevention (TasP).

An Australian study

Researchers in Australia conducted a large study of TasP in more than 100,000 participants—all were gbMSM. There were 90,304 HIV-negative men and 11,468 HIV-positive men. The study took place between January 2010 and December 2019 in two large Australian states—New South Wales and Victoria.

Over the course of the study, the percentage of men with HIV who had a suppressed viral load increased from 69% to 88%. During that time, the rate of new HIV infections fell almost threefold. The researchers estimated that for every 1% increase in the proportion of people with HIV suppression, there was a 6% decrease in HIV infections.

HIV pre-exposure prophylaxis (PrEP) was introduced in Australia in 2016. That year, researchers estimated that about 18% of gbMSM (who were HIV negative) were using it. By 2019, researchers estimated that 36% of gbMSM were using PrEP. However, they noted that the effect of TasP was seen before PrEP became available. The results from Australia are very encouraging. For comprehensive HIV prevention, the researchers recommend deploying both TasP and PrEP.

Study details

Researchers collected de-identified information from sexual health clinics, doctors' offices, community-based HIV testing sites, hospital clinics and other places that provided services for people with and at risk for HIV.

According to the researchers, they focused on cisgender men because although the clinics had information as to whether a person was transgender, they did not have further information available for the study on whether they were transgender men or transgender women.

Most of the men were of European ancestry and many had been previously diagnosed with rectal sexually transmitted infections.

Although the researchers included more than 90,000 HIV-negative men in the study, they focused their analysis on 59,234 men who were initially HIV-negative and had two or more subsequent HIV test results available during the 10 years of the study.

Results

A total of 1,201 new cases of HIV occurred during the study (about 2% of the 59,234 initially HIV-negative men). However, the rate of new HIV infections fell overall by 66% over a decade.

The decrease in new HIV infections among some age groups was as follows:

- 30 to 39 years old – a decrease of 89%
- 16 to 29 years old – a decrease of 63%
- 40 and older – a decrease of 49%

Over the study period, as mentioned previously, the proportion of men who were virally suppressed with ART increased significantly. There was a statistical association between the increase in men on ART with viral suppression and a decreased risk of other men acquiring HIV.

The researchers found that there was a broad increase of ART initiation and viral suppression across the age groups in the study.

Bear in mind

New South Wales and Victoria are the two most populous states in Australia, with gbMSM concentrated in urban areas. During the study, there was an increased use of ART and viral suppression, and this was associated with a significantly reduced spread of HIV. The decrease in new HIV infections occurred prior to the introduction of PrEP in Australia.

After PrEP was introduced in 2016, new HIV infections continued to fall, suggesting that both TasP and PrEP complement each other's prevention effects.

However, researchers found that between 2017 and 2019 the rate of decline in new HIV infections became and stayed stable. The researchers stated that this stabilization in infection rates may have occurred because TasP and PrEP had reached a saturation point among some gbMSM. They added that a previous study had found that gbMSM who were migrants to Australia had lower rates of HIV diagnosis, treatment and viral suppression.

Back to Australia. It is possible that TasP and PrEP had not sufficiently been used by gbMSM who had immigrated to Australia. Therefore, the researchers added that in order to achieve the full potential of TasP and PrEP in Australia, better access among migrant gbMSM is needed.

A related finding has been seen in the Netherlands. In that country, a recent study has found that young gbMSM born outside of Western Europe are at heightened risk for HIV compared to young gbMSM born in Western Europe.

The researchers noted that another study found that the use of condoms "declined substantially" between 2010 and 2019 among gbMSM in New South Wales and Victoria.

Another point worth considering is that during the study there were initiatives outside of the study that likely enhanced the impact of TasP. The researchers stated that governments, clinics and community-based organizations "worked to remove ART prescribing restrictions, enabled community pharmacy dispensing, reduced patient treatment costs, and educated those at risk of HIV about the individual and prevention benefits of early and sustained treatment. Furthermore, there have been a range of HIV testing initiatives [focusing] on gbMSM…"

The Australian study was not a randomized controlled trial, so its findings are not definitive. However, its results are strongly encouraging and align with the science of HIV treatment's effects on transmission potential and PrEP in a well-resourced setting.

The findings from Australia are likely transferrable to other high-income countries that also have a concentrated epidemic of HIV among gbMSM. However, for TasP to be successful in other countries with populations of gbMSM at risk of HIV, a similar increase (as happened in Australia) in the availability of HIV testing, care and access to treatment and PrEP must occur over the long term.

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C. Safety and effectiveness of dolutegravir + 3TC in people with HIV aged 65 and older

Thanks to the tremendous benefits of HIV treatment (ART), researchers are finding that more people with HIV who are on ART are living into their senior years. Projections from large studies suggest that many ART users will have a near-normal life expectancy.

As more people with HIV grow older thanks to ART, more research is needed with older people. This research is vital because the metabolism of older people is slower than in younger people and older people tend to have other health conditions—high blood pressure, diabetes, high cholesterol—that require treatment. The drugs used to treat these other health conditions may interact with HIV treatment.

A team of researchers at the University of Bologna in Italy has reviewed medical records of 72 people with HIV whose average age was 69. Participants had been living with HIV for many years and were taking ART regimens that consisted of three or four drugs. These regimens suppressed their HIV to an undetectable level. All participants were switched to a combination of two anti-HIV drugs: dolutegravir + 3TC (sold in a pill called Dovato). Researchers then collected laboratory and clinical data for one year afterward.

In general, researchers found that the combination was well tolerated and when side effects did occur, they were mild and temporary. Three people developed virological failure—in all cases less than 2,000 copies/mL. Analysis of their blood samples did not reveal HIV that was resistant to dolutegravir or 3TC. Doctors reported that all three people did not take their pills as directed. However, they were given alternative regimens and subsequently re-suppressed HIV. The remaining participants all maintained a suppressed viral load (in this case, less than 20 copies/mL).

The present study was not a randomized clinical trial. However, the results are likely similar to what occurs in the everyday world of an HIV clinic (outside of the setting of a clinical trial). The results of the Italian study, though relatively small, are encouraging. A larger analysis from an observational study also in Italy and data from randomized clinical trials involving people over the age of 50 are summarized at the end of this report. Their results are all in alignment.

Study details

The average profile of participants upon study entry was as follows:

- 82% men and 18% women
- age – 69 years
- lowest-ever CD4+ count – 184 cells/mm^3
- current CD4+ count – 503 cells/mm^3
- time since HIV diagnosis – 22 years
- duration of ART regimen prior to switching to dolutegravir + 3TC – 7 years
- viral load – prior to switching to dolutegravir + 3TC, all participants had a suppressed viral load (which the researchers defined as less than 20 copies/mL due to the assay in use at the study centre)
- comorbidities – nearly 90% of participants had other health conditions, including high blood pressure, osteoporosis, type 2 diabetes, heart disease
- weight – on average, participants weighed 68 kg and their body mass index (BMI) was 23 kg/m^2

Common reasons for switching to dolutegravir + 3TC included the following:

- avoiding interactions between ART and medicines used to treat comorbidities
- wanting to simplify ART
- reducing side effects from the current regimen

Note that participants were not supposed to have any of the following:

- a history of virological failure
- resistance testing that revealed the presence of HIV that was resistant to dolutegravir or 3TC
- hepatitis B virus (HBV) coinfection
- a diagnosis of alcohol or substance use disorder
- kidney injury
- liver injury

Prior to switching to dolutegravir + 3TC, drugs that participants took as part of their HIV treatment that were causing problems included the following:

- elvitegravir + cobicistat (in Genvoya and Stribild)

- efavirenz (in Atripla and generic formulations)
- darunavir + cobicistat (in Prezcobix)
- rilpivirine (Edurant and in Odefsey); rilpivirine is also found in another pill called Juluca (dolutegravir + rilpivirine) but participants were not taking this

Some of the side effects from their previous ART regimens that participants developed included the following:

- high levels of cholesterol and triglycerides in the blood
- unspecified gastrointestinal symptoms
- a significant increase in weight

Results

Viral suppression

All participants had an undetectable viral load (less than 20 copies/mL) just prior to switching regimens. Subsequently, all but three participants maintained viral suppression.

Three participants developed a persistently detectable viral load between 600 to 1,800 copies/mL. Resistance testing revealed that none of the three people developed HIV that was resistant to dolutegravir or 3TC. Upon questioning, the three people disclosed that they had not been adherent to ART; the reasons for non-adherence were not disclosed by the research team. Although participants in the study were not supposed to have a history of virological failure, researchers stated that two of these three people disclosed past episodes of virological failure with previous regimens.

Two of these three people were then given their previous regimen: in one case this was darunavir + cobicistat and two nucleoside analogues; in the other case, the treatment was Odefsey. The third participant was given Triumeq (a pill containing dolutegravir + 3TC and abacavir). All three people subsequently re-suppressed their HIV.

Side effects

According to the researchers, none of the participants developed serious side effects. However, three people discontinued dolutegravir + 3TC because of problems sleeping (two people) and headache (one person).

Other people reported the following adverse events, but these were graded as mild to moderate and resolved within a couple of weeks:

- sleeping problems – 11%
- diarrhea – 10%
- nausea and loss of appetite – 6%
- headache – 6%
- depression – 4%

Lipids and weight

Researchers reported that at the 12th month of the study, concentrations of fatty substances in the blood—total cholesterol, LDL cholesterol and triglycerides—all fell significantly. There was no change to HDL cholesterol.

There was a slight and non-significant increase in weight and BMI by the 12th month of the study. Weight increased by 0.67 kg and BMI increased by one-third of a point (0.31 kg/m^2).

Drug interactions

Researchers reported that the risk of drug interactions decreased "considerably" after participants switched to dolutegravir + 3TC. In 12 people, it was possible that an interaction between metformin (a drug used to help control blood sugar levels) and dolutegravir occurred during the study; however, the researchers are not certain about this. In general, published reports suggest that if such an interaction occurs, it can be dealt with by prescribing a lower dose of metformin.

Bear in mind

The present study was not a randomized clinical trial. However, it does provide useful information on some older people who used dolutegravir + 3TC.

A larger Italian study, also observational in design, which was published two years ago analysed data from 822 people whose average age was 70 years. Participants were taking the following integrase inhibitors:

- a dolutegravir-based regimen – 483 people
- a raltegravir-based (Isentress) regimen – 243 people
- Genvoya – 96 people

Rates of discontinuation were lowest for dolutegravir-based regimens and no cases of virological failure occurred.

The manufacturer of Dovato, ViiV Healthcare, has collected data from four randomized controlled trials and re-analysed these studies to assess the effects of dolutegravir + 3TC (or other combinations of dolutegravir) in people aged 50 and older. ViiV focused on 242 people with HIV who were virologically suppressed. According to ViiV, people aged 50 and older had high and similar rates of viral suppression as younger people. Rates of side effects in older people were similar to those seen in younger people. A total of 14 people aged 65 and older were given dolutegravir + 3TC in two of the trials (code-named Tango and Salsa); rates of virological suppression and side effects were similar to those seen in younger people.

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505-555 Richmond Street W
Box 1104
Toronto, Ontario
M5V 3B1
Canada