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► **To cite this version:**

Caroline Petit. Could we safely reduce the frequency of treatments for HIV-positive people?. 2017. hal-03140947

HAL Id: hal-03140947

<https://hal.science/hal-03140947v1>

Submitted on 14 Feb 2021

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Fermer

THE CONVERSATION

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Could we safely reduce the frequency of treatments for HIV-positive people?

30 novembre 2017, 22:07 CET • Mis à jour le 8 janvier 2018, 16:08 CET



Pillbox (illustration only). Shutterstock

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**Langues**

- English
- Français

Most HIV-positive people under treatment take a daily dose of antiviral drugs for life. However, a major trial is currently underway in France that may confirm that patients could safely omit several days of treatment a week without risk to their health. Some 300 patients have already switched to a treatment mode called “Intermittent in short cycles”, taking their medication four days a week instead of the seven currently specified. The small protocol began several years ago and the patients are doing well.

A larger trial is currently underway, and if the initial findings are confirmed, it could have significant benefits around the globe. At the end of 2016, 37 million people were living with HIV, with 1.6 million new infections that year alone. The vast majority of those living with HIV are in lower-income countries, particularly in Sub-Saharan Africa. Globally, only 21 million of those infected have access to antiretroviral therapy. If only four days of treatment are necessary for many patients, however, the same supply of antiretroviral drugs would go much further – and in particular, out into the developing world.

In September 2017, the French Agency for Research on HIV/AIDS, ANRS, launched a large clinical

trial called Quatuor (Quartet in English) of the four-day-a week protocol. It involves 640 volunteers recruited from 63 public hospitals in France and the Caribbean. Dr. Pierre de Truchis, at Raymond Poincaré Hospital in Garches (Hauts-de-Seine), is the principal investigator.

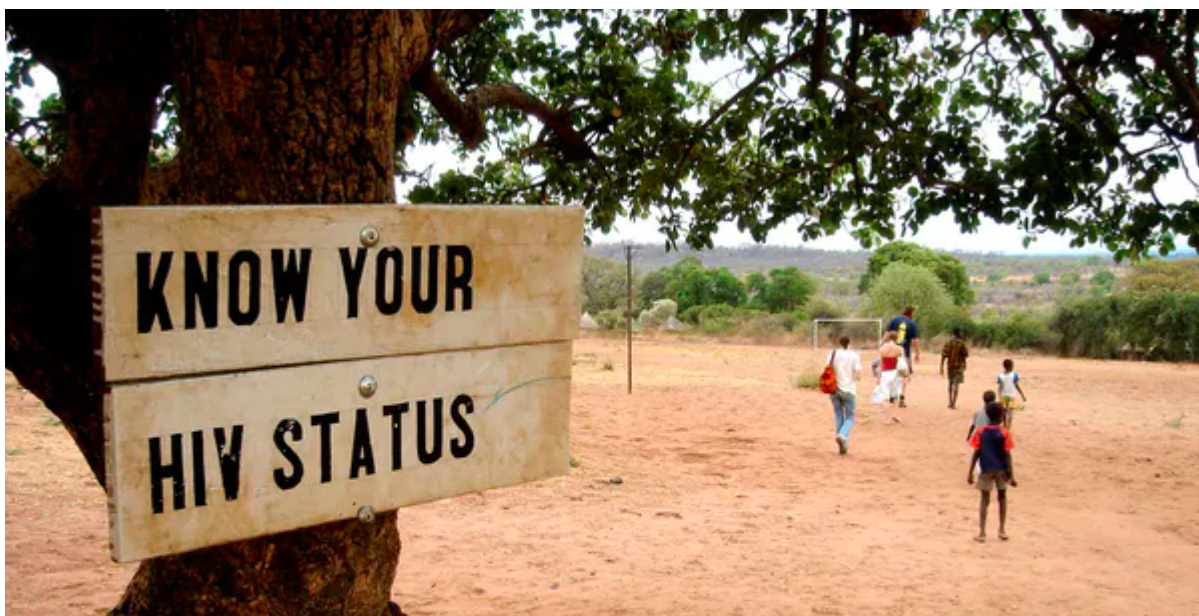
Four-days-a-week treatment, in the making for 15 years

We now have 15 years of experience concerning the safety of maintenance medicine treatments alleviated with short breaks. The primary experiment started in 2003 as part of a protocol called ICCARRE, which stands for “intermittent in close cycles, antiretrovirals remain effective”. Led by Dr. Jacques Leibowitch of the Raymond Poincaré Hospital, a group of 48 patients went from seven to five days of treatment per week, and then to four. Their viral load remained below detection level, and the results were considered sufficiently robust by the international scientific community that they were published in 2010 by the *FASEB Journal*. Similar observations on 94 patients led to a second publication in 2015.

In 2009, Assistance Publique-Hôpitaux de Paris (AP-HP) and Versailles Saint-Quentin University jointly filed for two international patents, one for “maintenance therapies under any standard triple combination” taken four days a week or less, the other for the use to that purpose of innovative quadruple combination therapies.

A first nationwide clinical trial

Convinced by the first results of the ICCARRE protocol, in 2014 ANRS launched its first clinical trial called 4D (four days) over two years at 17 medical centres in France. More applications to participate in the trial were received than could be accepted, indicated Professor Christian Perronne, the trial’s principal investigator. The results, presented at the 2016 International AIDS Conference in Durban, South Africa and published in the *Journal of Antimicrobial Chemotherapy*, indicate that 96 of the 100 patients who scrupulously followed the “four consecutive days out of seven” pattern were 100% successful. Early in the fourth week of the study three patients had a newly detectable viral load, which became undetectable upon the return to daily treatment. One patient left the study.





Sign in Simonga village, Zambia (2005). Jon Rawlinson/Flickr, CC BY

The results were sufficiently encouraging that the ANRS continued with the Quatuor test. To allow a comparison, it includes a “control” group consisting of patients who continue to take their treatment seven days a week for 48 weeks. This methodology meets the requirements of health authorities for the level of evidence to accumulate before a change in prescribing recommendations.

Experience has shown that daily treatments with anti-retroviral drugs can have substantial negative side effects, including nausea, diarrhoea and fatigue. Some patients consequently take their medication less consistently than they should – a problem that arises in many chronic diseases. Reducing the treatment frequency could reduce the negative side effects, and thus improve patients’ well-being. Indeed, a four-days-a-week regime is the equivalent of five treatment-free months every year the individual patient, a significant reduction.

Where do we go from here?

The full results of the Quatuor trial will be available at the earliest in 2019, at which time it may be possible in France to officially recommend the four-days-a-week treatment. Internationally, the results of the study will not necessarily be followed, even in the United States. Yet this is the country that in 2001 first opened the path to intermittence treatments, which was then followed by Dr. Leibowitch.

It’s worth asking why, more than 15 years later, the reduction of treatment still remains at the experimental level. In France, a number of HIV/AIDS associations have not yet fully grasped this issue. Instead, they have focused on preventive treatments, including as pre-exposure prophylaxis (PrEP). Under the impetus of artist Richard Cross, some of Dr. Leibowitch’s patients have created an association, The Friends of ICCARRE that aims to promote the possibility of a lightened treatment program.

Désolé

Cette vidéo n'existe pas.

While the Quatuor trial is still underway, some AIDS clinicians in France have already begun to lighten their patients' prescriptions. Such a possibility is consistent with Article 8 of the French Code of Medical Ethics and was confirmed in May 2017 by the National Council for AIDS and Hepatitis (CNS). The organisations remained cautious, however: Any such change requires a rigorous medical follow-up, with close biological examinations of the patient.

The continuing dominance of the daily treatment regime may be explained by resistance to change – which is not unique to physicians – and by the difficulty of questioning established rules within the medical community. Other factors can play a role as well, including the caution of patients and physicians, as well as doctors' fear of lawsuits.

Another factor is the influence of the pharmaceutical industry. After all, four days of treatment rather than seven represents 42 percent reduction in medication. If expanded throughout France, such a treatment program would result in a savings of some 500 million euros each year (based on 100,000 patients on treatment, with an average monthly cost per patient of 1,000 euros). Beyond reducing costs nationally, reduced treatment frequency could also increase the availability of antiretroviral treatments to those currently not being treated, particularly in the developing world.

An additional trial, called “big ICCARRE”, also led by Dr. Leibowitch, is exploring the possibility of that HIV treatment can safely be reduced to three, two or even one day per week, while maintaining a controlled viral load in patients. The objective is to find the medical dosage that is both necessary and sufficient for each patient, and is in accordance with the phrase often attributed to Hippocrates, “First do no harm”.

La version originale de cet article a été publiée en français.



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