HIV Treatment Interruptions

Staying on HIV treatment is a long-term commitment. For most, once treatment is started people must continue on it indefinitely, being careful to take all of the medications exactly as prescribed. This, however, is easier said than done.

Generally speaking, treatment interruptions are not recommended. Clinical studies generally show that doing so often makes HIV more difficult to manage and more dangerous to your health over time. HIV levels can become detectable, CD4 counts can decrease and may not recover to pre-interruption levels, and disease progression may occur.

However, interruptions may be necessary because life can sometimes get in the way of taking HIV meds: surgeries, new illnesses, loss of health care, accidents, extended travel, etc. Here, we look at this topic in two ways: reasons to stop meds for the very short-term and reasons to stop meds for longer periods of time.

At a minimum, do not attempt to stop and restart your HIV meds on your own. Seek direct support from your provider on the best way to do this. If necessary, your medical provider can contact the experts at UCSF’s Clinician Consultation Center (800-933-3413) for guidance.

Are treatment interruptions ever necessary?

According to most experts as well as the HIV treatment guidelines published by the U.S. Department for Health and Human Services and the International AIDS Society-USA, once treatment is started it should be continued indefinitely. However, certain situations can arise that may require a person to temporarily stop therapy. These include:

- Severe toxicities. Sometimes a severe side effect occurs that requires HIV treatment to be stopped, such as a life-threatening allergic reaction (although rare).
- Other illnesses. New conditions may arise that make it difficult or impossible for people to swallow or absorb oral medications, such as severe morning sickness, painful thrush, pancreatitis or gastroenteritis.

- Some surgical procedures require that nothing be taken by mouth (such as liquids, food or pills)
12 hours beforehand. Surgery may also not allow someone to swallow meds for a time afterwards, especially oral or neck surgery.

- **Interrupted drug access.** People can lose track of getting refills on time. A loss of health coverage can also occur or a person may not be able to afford their meds.
- **Travel restrictions.** Some governments prohibit HIV-positive people from entering their countries. Travelers have also had their HIV meds lost in transit or taken by customs agents. Therefore, stopping treatment may be unavoidable for some people who must travel to certain parts of the world. (The website, [hivtravel.org](http://hivtravel.org), provides a global database of HIV-specific travel and residence restrictions.)
- **Clinical studies.** As researchers continue looking at ways to cure HIV, people living with HIV who participate in these studies may be asked to temporarily stop their meds. A vaccine, other meds or procedures may be given while off treatment to see how the virus and immune system responds, which are essential steps for this research.

### Short-term interruptions

The following situations may occur when a person is taking HIV medications. **NOTE:** Those who also have chronic [hepatitis B](https://www.cdc.gov/hepatitis/B basic/index.htm) must be careful in these cases. Four commonly used NRTIs (emtricitabine, lamivudine, tenofovir disoproxil fumarate, tenofovir alafenamide) are also active against hepatitis B. Therefore, abruptly stopping any of these may cause sudden, serious damage to the liver. Liver enzymes should be closely monitored during this time.

- **“Drug holidays”.** Sometimes people want to take a few days off from their meds every now and then. Doing this once may not cause long-term problems. However, the more often this happens, the more chances HIV has to become resistant.
- **Unplanned interruptions.** If a person develops a severe or life-threatening condition or can no longer take pills by mouth, it is best to stop all HIV drugs at the same time to ensure the person’s safety in light of their immediate medical need. The meds should be restarted altogether when the person is able to resume.
- **Planned interruptions (up to 2 weeks)** when drugs have similar half-lives. If the HIV meds do not
need to be taken with food, the regimen could be taken with a sip of water if it’s allowed (for example, before surgery). Otherwise, all drugs should be stopped at the same time and restarted altogether as soon as possible. If the HIV meds must be taken with food, then they should be stopped at the same time and restarted altogether as soon as possible.

- Planned interruptions (up to 2 weeks) when drugs don’t have similar half-lives. In this case, if all drugs are stopped then HIV has a chance to become resistant to the drug that has a longer half-life (for example, efavirenz) because it lingers in the blood on its own for a longer period. Two options are possible: 1) stop the longer half-life drug 2 to 4 weeks before the other drugs are stopped, or 2) stop the drug but replace it with a boosted protease inhibitor for 4 weeks, and then stop all the HIV meds at the same time. However, there isn’t consensus on the best timing when stopping meds in this situation.

- During pregnancy. There are several reasons for stopping HIV meds while pregnant: acute illness, surgery, severe drug toxicity, untreatable vomiting and patient choice. If the HIV regimen must be stopped, all drugs should be stopped at the same time and restarted as soon as possible. An added risk while off meds is the increased risk of transmission to the fetus.

Long-term interruptions
Beyond the acute situations described above, longer-term “structured” treatment interruptions have been explored in clinical studies for various reasons. This includes reducing overall treatment cost, giving a break to having to take daily meds, and possibly reducing the risk of long-term side effects. They have also been studied as a way to boost the immune system and to help people who have tried and failed many HIV drugs to respond better to “salvage” regimens. The following are some of these clinical studies.

Immune system boost
One approach included trying to boost the activity of HIV-specific CD4 cells. In very early infection, these cells are quickly overcome by the substantial early activity of HIV. When HIV treatment is started, viral load is greatly reduced, and these CD4 cells no longer attempt to mount the necessary immune response against HIV. Research has tried to exploit this feature of the immune system by trying to spark HIV-specific CD4 cell activity to control HIV reproduction on its own, perhaps without HIV medications.
This theory has been tested in people who began treatment within a few months after they were infected with HIV, during what is called “primary HIV infection.” The immune systems of these individuals may be better equipped to successfully control HIV during treatment interruptions. While some studies showed short-term benefits associated with these interruptions, almost everyone eventually saw their viral loads increase and CD4 counts decrease.

Researchers have also concluded that treatment interruptions are not an effective way to boost the immune systems in people with “chronic HIV infection,” or those who have had HIV for at least a year. There are conflicting results of the benefits in people with chronic infection.

Treatment failure

A growing number of people living with HIV have been on multiple HIV regimens and are unable to stay undetectable. These individuals may be faced with having to use a “salvage” regimen, or a combination of HIV drugs that are active against HIV as much as possible but aren’t fully suppressive.

Researchers have theorized that temporarily stopping therapy might help their virus switch to a strain that is more sensitive rather than resistant to the drugs, much like it was before treatment was started in the first place. In turn, this might increase the chance of reducing viral load—perhaps keeping it undetectable—when starting a salvage regimen.

Unfortunately, clinical studies of this type did not produce encouraging results and are not recommended, especially for those with low CD4 counts. Even though salvage regimens may not be able to keep viral loads undetectable, they can still protect the immune system and help ward off new illnesses until newer drugs come to market.

Good viral load and CD4 cell responses to treatment

Most people who take HIV meds see their viral loads decrease and CD4 counts increase, often to similar levels seen in HIV-negative people. In turn, researchers have looked at treating HIV like other chronic diseases: starting therapy when the immune system shows signs of damage or when there are symptoms of disease, stopping it when a person’s health improves, and then restarting treatment when the CD4 count falls again.

Several clinical studies have looked at this approach. The most notable, called SMART, compared a group of people who stayed on treatment to a group who stopped their meds when their CD4 counts went above 350 and then restarted when they fell below 250, over and over. However, the planned 9-year study was stopped after 14 months due to very worrisome results. Early data showed that those who had treatment interruptions had an increased risk of disease progression, other complications (heart attacks, stroke, organ damage, etc.) and death. Similar results were seen in the TRIVACAN study.

In contrast, other studies have looked at using fixed time frames to schedule treatment
interruptions. For example, one looked at 5 days on/2 days off while others looked at one week on/one week off, one month on/one month off or even longer periods of time. Others have looked at increasing the length of time of multiple interruptions over time. Although a few participants appeared to benefit in the short-term in some of these studies, collectively the data shows that those who took treatment interruptions experienced more side effects, declining CD4 counts, detectable viral loads, opportunistic infections, and new resistance, among other complications.

In the end, as often happens with studies that are designed to give a “final answer” to a major question, the results from these studies raise even more questions than answers. For now, the message for people who want to take a break from their HIV meds remains the same: treatment interruptions are risky and should not be attempted without a careful evaluation of the possible risks and benefits, and certainly not without the guidance of an HIV expert or within a clinical study. Perhaps, the future of easing a person’s pill burden is through long-acting HIV medications, such as those currently in clinical study.

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