

## Pharmacokinetics

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## What Is Pharmacokinetics (PK)?

Pharmacokinetics, also known as PK, is the study of how medications behave in the body and move through it. PK is used to figure out how much of a drug gets into your bloodstream and how long it stays there.

Scientists study PK to determine the best dose for an HIV drug. The dose must be high enough to keep HIV from reproducing, but not so high that it causes many [side effects](#).

## How Is PK Studied?

The following PK values are important:

- Maximum concentration (C<sub>max</sub>): This is the highest level a drug reaches in the blood. When a drug is given, it reaches its peak (highest) level in the blood pretty quickly. The drug level then decreases as the body breaks down the drug and removes it from the blood.
- Minimum concentration (C<sub>min</sub>): This is the lowest level that a drug reaches in the blood. The lowest drug level, right before the next dose, is called the "trough" level.
- Area Under the Curve (AUC): This is the total amount of one dose of a drug to which someone is exposed. Because of the body's reaction to a drug, or a combination of drugs, this amount may not be the same as what is listed on the medication label for one dose. The "curve" is a graph that shows the drug level in the blood over time, as well as the total amount of drug exposure.
- Half-life (t<sub>1/2</sub>): A drug's half-life is the amount of time required for half of the drug to be removed from the bloodstream. For example, if the dose of a drug is 100 milligrams (mg), and the half-life is eight hours, 50 mg will be left in the blood after eight hours.
- Inhibitory Quotient (IQ): The IQ of a drug shows how much drug is necessary to control the virus effectively. The IQ is different for each drug.

**Health care providers who are aware of the pharmacokinetics of drugs and their interactions will make sure you get the right doses.** The PK values are used to figure out the correct dose – both the amount of drug and the timing (once a day, twice a day, etc.). In order for an HIV drug to work, it must have a high enough minimum concentration (C<sub>min</sub>) and total exposure (AUC) to be effective against HIV.

PK values are also used to help avoid toxic (poisonous) [side effects](#). If the maximum concentration (C<sub>max</sub>) gets too high, the drug can cause unwanted side effects. The goal of HIV treatment is to get the most benefit from the drug with the fewest side effects.

Last but not least, the half-life of the drug must be long enough to allow for a reasonable dosing schedule. Several drugs have a long enough half-life that they only need to be taken once a day.

## Drug Interactions and Drug Boosting

Liver proteins called enzymes help the body to process drugs by breaking them down. But enzymes are also affected by the drugs.

This has proven to be very useful in HIV therapy. Here is an example: Norvir (ritonavir) is a protease inhibitor (PI) that makes some enzymes work more slowly. This keeps other drugs in the body longer. So, if Norvir is given with another PI, like Reyataz (atazanavir), it "boosts" Reyataz by preventing it from being broken down too quickly by the liver. Boosting with Norvir increases both the minimum concentration (C<sub>min</sub>) and total exposure (AUC) of Reyataz. As a result, Reyataz can be given once a day with a little Norvir. The boosted regimen makes Reyataz more effective. There are many [protease inhibitors](#), and most of them are boosted with Norvir. Another "booster" drug is Tybost (cobicistat).

Health care providers who are aware of the pharmacokinetics of drugs and their [interactions](#) will make sure you get the right doses. That is why it is so important to tell your provider about all medications and [supplements](#) you are taking, including herbs, prescription drugs, over-the-counter medications, and street drugs. You can ask your health care provider to check whether any of your drugs interact with

each other or with anything else you take.

## Do Men and Women Process Drugs Differently?

There are some PK differences in men and women. At the same doses, some women have higher levels of certain drugs in their bloodstreams and experience more [side effects](#) than men. Despite these differences, women seem to benefit as much from HIV therapy as men.

Although differences between men and women have been seen in studies, no authority has recommended changing the dose of HIV drugs for women.

These PK differences may be related to hormonal changes during a woman's period, differences between the cells of men and women, or differences in weight or body composition (amount of fat versus lean muscle) between men and women.

Standard doses of drugs are usually based on research in men. This means women, who generally weigh less than men, may have higher amounts of the drug in their bodies than would be needed for the drug to be effective. Although differences between men and women have been seen in studies, no authority has recommended changing the dose of HIV drugs for women. However, because [pregnancy](#) can change how the body processes drugs, doses of some HIV drugs may change during pregnancy.

**If you are experiencing side effects, ask your health care provider for help. Do not change your dose or stop your drugs without speaking to your provider.**

Other factors can also affect PK, including:

- Genetic differences in how the body processes drugs
- Food
- [Tobacco](#) and [alcohol](#) use
- [Drug, vitamin, or supplement interactions](#)
- Race/ethnicity
- Hepatitis or other [liver problems](#)
- Kidney function

## Pharmacokinetic Testing

Because of PK differences, new tests are being developed to figure out if people are getting the right amount of a drug.

Therapeutic Drug Monitoring (TDM): TDM is designed to measure your specific drug levels. Basically, it measures the minimum concentration (Cmin) by drawing blood or collecting urine or hair samples before you take your morning medications. This test can help your health care provider decide if doses of your HIV drugs should be changed. TDM is expensive and is most often used in research studies. It may or may not be available through your health care provider. The US Department of Health and Human Services currently does not recommend its use for managing regular HIV treatment in adults.

## How to Make PK Work for You

The timing of medication doses has been carefully calculated to keep the drug in your bloodstream at levels that will control HIV. When you do not take a dose on time, the level of drug in your blood may become too low to be effective.

When this happens, HIV has a chance to make more copies of itself, which causes your [viral load](#) to go up. Having too little of an HIV drug in your blood also makes it easier for HIV to become [resistant](#) to the drug you are taking. If your virus becomes resistant to a drug, the drug will stop working for you. As a result, your viral load could go up, your [CD4 cells](#) could go down, and you might need to change drug treatments. The best way to avoid this is to take your HIV drugs exactly as they are prescribed (also called [adherence](#)). This keeps the drug level in your blood high enough to fight the virus effectively.

## Additional Resources

Select the links below for additional material related to pharmacokinetics.

- [Therapeutic Drug Monitoring \(Testing.com\)](#)
- [Pharmacokinetics and Pharmacodynamics: A Primer for HIV Prevention Advocates \(A...](#)
- [Antiretroviral Drug Levels in Hair Strongly Predict Viral Suppression \(aidsmap\)](#)
- [The ABCs of Pharmacokinetics \(Positively Aware, via TheBody.com\)](#)
- [Pharmacokinetics \(Association for Diagnostics & Laboratory Medicine, video\)](#)



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