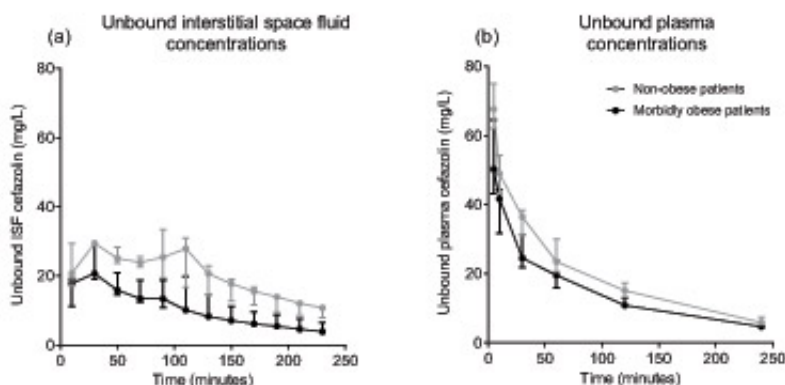


# Extreme obesity calls for individualized medication

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Cefazolin concentrations versus time after a 2 g dose in morbidly obese patients (grey) and non-obese patients (black) in (a) subcutaneous tissue (ISF fluid) and (b) plasma. Credit: Figure reprinted from Brill et al, *J Antimicrob Chemother.* 2014 Mar;69(3):715-23.

Doctors and pharmacists often do not take obesity into account when prescribing medication. For this, more insight into the influence of obesity on the distribution and elimination of drugs is of the utmost importance. This is emphasized by Catherijne Knibbe in the most recent issue of the *Annual Review of Pharmacology and Toxicology*

## Effect of drugs unpredictable

People who suffer from extreme [obesity](#) have as a rule undergone

physical changes that can impact the uptake, distribution and elimination of drugs. These changes require individualized dosing, advises Catherijne Knibbe, Leiden Professor of Individualized Drug Treatment. Her publication appeared on 6 January in the prestigious journal Annual Review of Pharmacology and Toxicology.

## Physiological changes

Obesity leads to an enlarged heart, wider blood vessels and a larger blood volume. This in turn leads to effects such as an increase in bloodflow through the liver, as a result of which the elimination rate of certain drugs may increase. In addition, altered body composition in obese people may also lead to a highly different distribution of the [drug](#) throughout the body.

## Customised drug dose

Knibbe warns: 'Obese patients are often prescribed a standard drug dose, or doctors and pharmacists tend to automatically assume that these people need a higher dose. However, that is not necessarily the case. Moreover, a higher dose can also be harmful. For example, [obese people](#) are more likely to suffer from sleep apnoea: they do not breathe well when they sleep. We have to think carefully before giving these patients a higher dose of sedatives or morphine.'

## Research in obese patients

To optimally treat [obese patients](#), research is required to gain insight into how drugs are distributed and eliminated from the body. This is what Knibbe, a clinical pharmacologist, does at the St. Antonius Hospital in Nieuwegein, Utrecht, where she works. After administering the usual dose, blood samples are taken from the patient. These samples provide

information on the uptake, distribution and breakdown of active substances in the body. The optimal dose in obese patients can be derived from these studies.

## **Distribution of antibiotics into the tissues**

For some drugs, such as antibiotics, we should also look at the distribution into the tissues, because that is where the drug is supposed to work. As an example, Knibbe mentions a study she conducted with the drug cefazolin, an antibiotic that is prescribed to prevent wound infections. The standard dose is 2 grams, which was administered to patients without overweight and to obese patients.

The concentration of the drug in the blood did not differ significantly between the two groups (Figure). However, in the skin, where wound infections might in fact occur, the concentration of the drug was more than 30 percent lower in obese patients than in non-obese patients. 'This means that a standard dose of this drug may potentially be less effective in these patients.'

## **Obesity on the rise**

Obesity is an increasing problem, warns Knibbe. Everywhere in the world, including in developing countries, a growing number of patients are suffering from obesity. In addition, those people who are obese are becoming even heavier.

**More information:** Knibbe, C.A. et.al "Drug Disposition in Obesity: Toward Evidence-Based Dosing. Drug Disposition in Obesity: Toward Evidence-Based Dosing, Annual Review of Pharmacology and Toxicology," Volume 55. [www.ncbi.nlm.nih.gov/pubmed/25340929](http://www.ncbi.nlm.nih.gov/pubmed/25340929)

Provided by Leiden University

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