

Virtual children help prevent withdrawal syndrome in real children

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When children wean off from heavy medication, they often experience withdrawal symptoms. The severity of these symptoms is often difficult to predict. Pharmacologist Bas Goulooze developed a computer model to determine the best weaning strategy for each child. His research has now been published in the *Journal of the American Association of Pharmaceutical Scientists*.

"It is highly undesirable that severely ill [children](#) also have to deal with [withdrawal](#) symptoms," Goulooze says. "We are talking about a treatment with heavy painkillers. The children really need these medicines, so that is something we can't change. But what we can do, is see if we can reduce medication after treatment in a smarter way."

Research in children is difficult

This is difficult to investigate in children, explains Goulooze. There are a lot of ethical objections. Traditional research is therefore nearly impossible.

For this reason, doctors reduce medication according to experience and adjust their plan if children start experiencing [withdrawal symptoms](#) (see box). However, it is difficult to draw general lessons from this.

Goulooze: "Every child is different. And medication use differs too, such as the type of medication, the amount and the duration."

How is it currently done?

Weaning strategy varies depending on the type of medication and the duration of the treatment. Often doctors work with a fixed percentage. For example, they reduce the [medication](#) by 10 percent every day. If signs of withdrawal syndrome appear, doctors pause the weaning or increase the dosage again.

Model creates order in clinical chaos

It would be better if doctors could act proactively to prevent withdrawal syndrome, thought Goulooze. That's why he created a [mathematical model](#) that he filled with information from earlier studies conducted at the Sophia Children's Hospital in Rotterdam: "How long was a child

treated with which drug, and what was the weaning strategy? How old is the child, and how much did he or she suffer from withdrawal syndrome? Our model creates order in the clinical chaos. By comparing all the information collected, we can understand and predict why some children suffer a lot from withdrawal and others don't."

Virtual children to test ideas

With the model, Goulooze can also create virtual children. "This allows us to experiment and test all kinds of scenarios without real children being affected," he explains. "This allows us to focus on finding the most promising ideas for real patients."

Weaning off sometimes has to be done in smaller steps

Goulooze discovered that it is important to take into account the amount of medicine that children receive each day. "With a higher dose, you need to reduce more slowly and not by the standard 10 percent a day. This is actually quite logical: if you are used to a lot of medicine, it also takes more time to slowly wean off again."

According to Goulooze's model, for the painkiller fentanyl specifically, the risk of withdrawal syndrome might be lower when weaning with smaller dose reductions every 12 hours, instead of weaning with bigger steps every 48 hours. "According to doctors, this drug has a higher risk of withdrawal syndrome than other painkillers. So, it's interesting to see our model indeed shows that we need to reduce it more gradually. A great example of how our virtual children can help the real kids."

Cum laude for relevant research

Goulooze now works at LAP&P, a pharmaceutical consultancy. "We help companies develop new drugs," he explains. "I use the same techniques and models, but now to predict the effects of new drugs." He obtained his Ph.D. cum laude. Besides, he was nominated for the C.J. Kok Jury Prize. His supervisor Elke Krekels especially praises the clinical relevance of his research. "It is a challenging and difficult subject, but Bas did not shy away from it. His new model has made an important contribution to the field."

The cum-laude designation came as a surprise to Goulooze. "The assessment of my dissertation did take a bit longer than expected, but I thought that was due to corona. Getting a Ph.D. alone is special, this title is an extra crowning achievement."

Provided by Leiden University

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