SSRI medication for depression does more harm than good, according to Danish researchers. A leading Norwegian psychiatrist questions their research methods.

“We conclude that these pills don’t benefit the patient. Quite simply, the group receiving selective serotonin reuptake inhibitors (SSRIs) seems to be worse off than patients receiving the placebo.”

Janus Christian Jakobsen shared his research team’s conclusion with forskning.no. Jakobsen led the recently published major review of research on SSRI antidepressants at the University of Copenhagen.

Jakobsen and his Danish research colleagues have pooled results from 131 studies on SSRIs to conduct their meta-analysis.

“If you look at the number of patients who experience an increased risk of dying, committing suicide, going to hospital or otherwise come to serious harm, it appears that SSRIs increase the risk of these severe adverse events,” says Jakobsen.

Not impressed

Norwegian psychiatrist Ulrik Fredrik Malt, considered an authority in the field by other psychiatrists that forskning.no consults with, carefully studied the Danish research review.

He is far from impressed.

Malt believes the researchers’ analysis offers little new information, because they do not discuss a number of error sources and limitations in the underlying studies. He also finds a personal bias in the researchers’ interpretation.

All the previous studies of antidepressant medications reviewed by the Danish researchers were randomized and controlled, which is considered the gold standard in scientific studies that look at the effect of a treatment.

However, Malt finds that the research does not meet professional standards, because “it doesn’t matter how many studies and patients are included in a meta-analysis if you choose to interpret them in a personal way and present this as an indisputable truth.”

He adds, “The authors found that antidepressants were better than a placebo. There’s actually less than a one in a million chance that this wouldn’t be the case. To interpret this that antidepressants do not have any clear effect is – to put it mildly – very strange.”

The Danish researchers also failed to properly analyse the studies, according to Malt.

“They combine study conclusions as if all the studies had the same treatment length, and they don’t
differentiate between high- and low-quality studies,” he says.

The result, he believes, is that the assumptions that underlie their analysis simply do not measure up scientifically.

**SSRIs can be useful**

2.7 percent of patients receiving SSRIs experienced serious side effects, according to the meta-analysis. The same applied to 2.1 percent of those who received a placebo. That reflects a difference of nine patients for every 1,000 patients treated, says Malt.

He acknowledges that SSRIs are associated with a few more adverse events than the placebo.

“But I think the actual numbers – that is, how many real people are affected – are very low. The great majority of patients don’t have truly troublesome SSRI side effects that they can’t get help for,” Malt says.

The important thing is to be aware of the adverse events and intervene early when they do arise, he adds.

Jakobsen, for his part, says it sounds like Malt is belittling the study results because of the small percent difference between patients who received an SSRI versus a placebo.

**Personal interpretations**

Malt believes Jakobsen has found exactly what other researchers have in previous meta-analyses of SSRIs. But in coming to a different conclusion, it is the Danish researchers’ personal interpretation of the findings that differs from previous analyses.

“Moreover, when they discuss their findings, their bias favours claims and interpretations made by others who are critical of SSRI. Contrary to what the authors argue, they don’t cite publications that oppose such interpretations, like the Swedish medical authorities,” says Malt.

In his opinion, this is not proper scientific practice.

Jakobsen is of a different opinion on this. He says that he has not systematically excluded research that goes against the researchers’ own interpretation.

“What we found is not the same as previous meta-analyses. Our primary finding is that SSRIs increase the risk of serious adverse effects. This has never been shown before,” says Jakobsen.

The Danish researcher says that they are the first to have thoroughly evaluated the quality of all studies ever done on SSRIs.

“If our critic read us carefully, he would discover that we carefully describe that almost all studies conclude that SSRIs work and should be used,” Jakobsen says, “but the effect of the medicine is so small that a patient would not notice the difference between it and the placebo.”

For this reason they conclude that SSRI pills do not work better than a placebo.

**Mixed reviews in Denmark**

The Danish study has also generated great interest – as well as considerable academic debate – in Denmark.
Jakobsen told forskning.no that he has had almost non-stop interviews with the media in the weeks since the study was released.

Poul Videbech, professor of psychiatry at the University of Copenhagen and a senior consultant for Mental Health Services – Capital Region of Denmark, has also looked closely at the new study. "It’s a fine study. It’s really well put together. Studies like this drive science forward. The result tells me that we need to be even more thorough and more aware of the relationship between the medicine’s effects and side effects," he says to the Danish science news site, videnskab.dk.

However, he stresses that in his view the study has several methodological problems that the researchers should have mentioned in their article. For example, when testing a patient using the Hamilton rating scale for depression, the side effects of the medicine can skew the score.

The Hamilton scale includes questions about sexual disorders, for instance, but the medication itself can cause sexual disorders, so the side effects end up counting as a depressive symptom.

As Videbech explains, this means that you’re measuring a bad effect on a false basis. “You can’t blame the authors for this, but it points to some built-in method weaknesses in the underlying studies they used. Therefore, you have to be careful with your conclusions," he says.

Doesn’t help everyone

Malt believes the Danish meta-analysis simply found out something we already know: SSRI medications do not help everyone.

“Of course we know that this medicine doesn’t work for some patients. Current research is attempting to find biological characteristics of the patient. We’re hoping that this research will be able to tell us who will benefit from SSRIs and who won’t,” he says.

Malt thinks it is unfortunate that the Danish researchers are presenting their findings so categorically, when their foundation is so flimsy.

“The consequence of Jakobsen and his colleagues being so bombastic may first of all be that patients who could benefit from the drug, say no to it. Second, it may result in some patients interrupting their treatment, with potentially negative consequences,” he says.

Jakobsen says that no one should stop taking their SSRI medication without consulting their doctor.

“We don’t know what might happen when patients abruptly stop using these pills after being on them for a long time. It may be dangerous. The pills have a strong effect on serotonin, which is a critical substance in the brain. The nervous system seems to have difficulty coming off SSRI medication,” says Jakobsen.

No really good alternative

Poul Videbech researches treatment of depression and also treats depressed patients. He can see that for some patients the medication works really well, while others experience no effect or even get worse from side effects.

The challenge in treating depression, he says, is that many interventions often have a questionable effect.

That is why Videbech believes he and other researchers must work extra hard to find alternative methods of
treatment.

“Until we come up with those alternatives, we have to use the treatment options that exist,” he says.

Read the Norwegian version of this article at forskning.no [6]

6.3 per cent of Norway’s population used an antidepressant in 2016. Now Danish scientists are calling out a warning about their overuse and serious side effects. They believe the pharmaceutical industry’s profit motives have pushed a positive picture of what are popularly known as "happy pills." (Photo: Shutterstock/NTB scanpix) [7]


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