

# Prescribers be aware of fatal risks of methadone and clozapine

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New Zealand prescribers should be aware of the high risk of death associated with two prescription medicines, methadone and clozapine, University of Otago researchers warn.

In the largest review of medicine-related deaths in the National Coronial Information System between 1 January 2008 to 31 December 2013, Dr. John Fountain and his colleagues from the Dunedin School of Medicine and Best Practice Advocacy Centre identified methadone as the medicine with the highest prescription fatality rate in New Zealand, while clozapine was responsible for the most deaths of any antipsychotic drug.

Methadone is an opioid used for the treatment of morphine, heroin addiction and chronic pain, while clozapine is an antipsychotic drug used to treat schizophrenia.

Clomipramine, dothiepin and doxepin were identified as the most dangerous antidepressants, while zopiclone carried a similar fatal risk to benzodiazepines.

Over the six years, the researchers found 703 medicine-related deaths with opioids, antidepressants, antipsychotics and hypnotic anxiolytics causing most fatalities. Deaths were intentional in 252 cases (40 percent), unintentional in 284 (45 percent) and unknown in 91 (15 percent). Most deaths (78 percent) occurred in the community and mostly among 40 to 50-year-olds.

The leading medicines involved in intentional deaths were zopiclone, codeine and morphine. Unintentional deaths were most commonly attributed to methadone, morphine and clozapine.

Dr. Fountain explains that when prescribing or administering a medicine, it is important for the clinician to consider both the potential for harm as well as the anticipated benefit to the patient.

"For example, one person in every 175 patients using clozapine died from its [toxic effects](#) and careful consideration of the balance between

the potential for benefit and potential for harm is required when prescribing this therapy.

"It is therefore important to identify and quantify medicine-related harms so that informed decisions may be made regarding the frequency and severity of possible adverse outcomes when considering the risks and benefits to patients.

Analyzing the coronial data, the researchers focused on the fatal [toxicity](#) index (FTI), a measure for assessing the relative risks of death due to the medicines prescribed in a population. They used three different methodologies and [methadone](#) and [clozapine](#) were prominent in all three. Antidepressants clomipramine, dothiepin and doxepin consistently returned the highest fatal toxicity indexes in their group.

Dr. Fountain says fatal toxicity indices can recognize [prescription medicines](#) associated with higher rates of [death](#) when compared to similar drugs.

"Medicine-related deaths may be reduced if prescribers use pharmaceuticals with lower fatal toxicity indices.

"Certain medicines were found to have much higher fatal toxicity indices than other pharmaceuticals used to treat the same medical condition."

The paper, "Fatal Toxicity Indices for Medicine-Related Deaths in New Zealand, 2008-2013," has just been published in international medical journal *Drug Safety*.

**More information:** John S. Fountain et al. Fatal Toxicity Indices for Medicine-Related Deaths in New Zealand, 2008–2013, *Drug Safety* (2019). [DOI: 10.1007/s40264-019-00885-4](https://doi.org/10.1007/s40264-019-00885-4)

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