


## Letter to the Editor

# Etizolam and Irish drug poisoning deaths

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While the majority of drug poisoning deaths across Europe involve opioids, benzodiazepines are implicated in many deaths, and are frequently present in deaths involving opioids (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2023). Benzodiazepines have been associated with morbidity and implicated in drug poisoning deaths since the 1980s, both in Ireland (Health Research Board, 2023a) and in Scotland (National Records of Scotland 2023). In the past number of years, Scotland has recorded some of the highest rates of drug poisoning deaths in the UK and in Europe (McAuley et al., 2022). The benzodiazepines involved are not always prescription benzodiazepines; indeed, one driver behind the increase of drug poisoning deaths in Scotland was the emergence of etizolam, a benzodiazepine-type new psychoactive substance (NPS) (McAuley et al., 2022). Initially produced and prescribed in Japan in the 1980s, etizolam has also been legally prescribed in India and Italy, but for years, etizolam was neither scheduled nor controlled in most other countries (Cornett et al. 2018).

Phenazepam was the first major NPS benzodiazepine that emerged, but when it was regulated in 2012, etizolam emerged (Home Office UK, 2011). Etizolam is five times more potent than diazepam (Nielsen S and McAuley A, 2020). Non-controlled and new benzodiazepine derivatives have continued to be available in European countries, contributing to what has become known as a 'street benzos' market (EMCDDA, 2023). This led to costs being driven down and increased availability, resulting in a considerable increase in benzodiazepine use, associated with drug poisoning deaths (EMCDDA, 2023).

Historically, drug poisoning deaths in Ireland have broadly followed the same trends as Scotland (albeit with lower absolute numbers). However, in recent years, Ireland has not mirrored the trend of record numbers of drug poisoning deaths seen in Scotland. In 2020, Scotland reported 1,339 deaths due to drug misuse (National Records of Scotland, 2021), while Ireland reported 409 drug poisoning deaths (Health Research Board, 2023a). A number of factors may explain this disparity, including different patterns of use, provision of public health measures such as opioid agonist treatment and naloxone, engagement with services, as well as the introduction of NPS onto the drug market.

One possible reason for the divergence between Scotland's and Ireland's mortality rates, is that the number of deaths where etizolam was implicated remains relatively low in Ireland, as 2020 data from the Irish National Drug-Related Deaths Index (NDRDI)

show (Figure 1) (Health Research Board, 2023a). While etizolam is the most common NPS drug implicated in poisoning deaths in Ireland, the numbers remain low, ranging from 7 in 2015 to 16 in 2020. However, in 2021, almost 60% of drug misuse deaths involved etizolam in Scotland (National Records of Scotland 2023). This difference can possibly be explained by the fact that, the prescribed benzodiazepines, diazepam and alprazolam, contribute to a greater number of deaths in Ireland (from prescriptions, diversion or indeed illegal laboratories). Also noteworthy, is that in Ireland in 2021, the most commonly seized benzodiazepine was alprazolam, followed by diazepam, and a small amount delorazepam (Health Research Board 2023b). Seizures of etizolam in 2021 were low, although more seizures were recorded in 2020. Similar to Scotland, most deaths in Ireland involving etizolam also involve other drugs (NDRDI 2023, unpublished data).

The number of Irish poisoning deaths where a prescribable benzodiazepine was implicated has risen over the past number of years, while the Scottish number has decreased (Figure 1).

McAuley et al. (2022) point to the policy change in Scotland during the mid-2000s, when after decades of increasing prescribing of benzodiazepines (and diversion to street markets), concerns about the level of dependence in Scotland led to a reduction in prescribing. This policy change coincided with the emergence of the NPS drug market, which moved to fill the gap for benzodiazepine-type drugs in Scotland. McAuley and colleagues state that, while the aim of the change was well meaning,

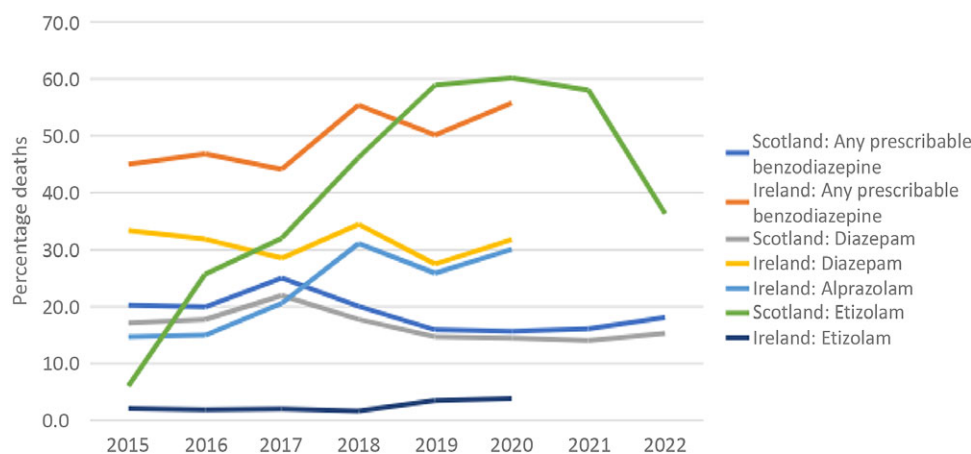
*an unintended consequence of the move toward more limited benzodiazepine prescribing in Scotland has undoubtedly been its role in driving people who use illicit supplies from diverted prescriptions to a more dangerous array of street benzos, thus increasing the risk environment for those at-risk of overdose (p. 5).*

In Ireland, there has been no similar policy change in relation to prescribing benzodiazepines, although, in 2017, there was a change to the Misuse of Drugs Regulations whereby individuals have to have a prescription to carry benzodiazepines, along with a tightening of prescription writing (Misuse of Drugs Regulations, 2017). These do not appear to have had an impact on the role of benzodiazepines in poisoning deaths (Figure 1). However, the impact of the legislation on prescribing patterns for benzodiazepines is difficult to determine, as although there has been a slight decrease in the amount of benzodiazepines prescribed between 2017 and 2020 for those entitled to medical cards, there is no information for private prescriptions (Cadogan et al., 2021).

Scotland has tried to tackle the problem of increasing deaths by increasing rehabilitation beds and expanding access to Medication Assisted Treatment, advocating for supervised injecting centres,

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**Cite this article:** Keenan E, Kelleher C, Lyons S, and Sweeney N. Etizolam and Irish drug poisoning deaths. *Irish Journal of Psychological Medicine* <https://doi.org/10.1017/ipm.2024.38>



**Figure 1.** Prescribable benzodiazepines as a percentage of drug misuse deaths (Scotland 2015 to 2022) and poisoning deaths (Ireland 2015 to 2020) in comparison to etizolam. Sources: National Drug-Related Deaths Index unpublished data (2023) and National Records of Scotland (2023).

increasing naloxone availability, increasing toxicology testing and speedy distribution of information to stakeholders, which appears to have had some effect (McAuley et al. 2022). There was a significant decrease in etizolam-related deaths in 2022 (National Records of Scotland 2023) but it is not yet clear if this will be sustained, as with the control of etizolam internationally, bromazolam, another NPS, has increased in use (Public Health Scotland 2023).

In conclusion, regulation of benzodiazepines is challenging because as soon as one drug is regulated, another NPS can emerge. Important considerations with regard to changing prescription practices are demand, supply, and cost. The persistence of benzodiazepines involved in drug poisoning deaths must be considered, particularly in light of the emergence of synthetic opioids. A recent article has highlighted nitazenes appearing in the UK market contaminating benzodiazepines (Holland et al., 2024). Ireland needs to be vigilant and establish effective early warning systems to be prepared for this emerging trend (Griffiths et al., 2023).

Clearly, the role of benzodiazepines in poisoning deaths in Ireland needs to be addressed. However, any significant change to prescribing practices for benzodiazepines in Ireland must consider the Scottish experience and any change should include intensive and evidence-based wrap around psychosocial supports for those who currently use non-prescribed benzodiazepines.

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