THE TOX LAB

Podcast Transcript

Episode 11: The Rise of Street Benzodiazepines

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TRANSCRIPT

Hi everyone, welcome back to The Tox Lab. I'm Rebecca.

I'm Rob.

This week on The Tox Lab, we're going to be looking at the rising trend of street benzodiazepines, in particular the rise of novel benzodiazepines that have never been approved for therapeutic use.

Before we jump into this week's paper, I wanted to talk a bit about benzodiazepines more generally, because we have mentioned them a few times on this podcast.

So what are they?

Benzodiazepines, or benzos, are a group of drugs that act on the central nervous system and generally make you feel calm, relaxed, sleepy, or sedated. Medically, they are used for things like anxiety, insomnia, and sometimes muscle spasms.

How do they work? If you imagine your brain as a huge network of neurons sending messages in every direction, one of the neurotransmitters involved in slowing things down is GABA, gamma-aminobutyric acid.

Its job is basically to put the brakes on neuronal signalling. Benzodiazepines boost those brakes. They bind to the GABA-A receptor, not at the main GABA binding site itself, but at a different site that makes the receptor more responsive to GABA.

So they effectively turn up the strength of the brain's inhibitory system. That enhanced GABA effect helps quieten the mind, reduce anxiety, relax muscles, and make people drowsy.

And that is why they can be very effective in the short term, for panic attacks, acute anxiety, stress, insomnia, things like that.

But there is a downside. Over time, people can become dependent on that effect. If you then stop taking the drug, you can experience rebound anxiety and insomnia.

And in more severe cases, withdrawal can cause seizures. Benzodiazepine withdrawal has been fatal, so this is not something trivial.

So Rebecca, why don't you introduce this week's study?

The paper we're looking at this week is titled Impact of street benzodiazepines on drug-related deaths in England, Wales and Northern Ireland.

In this paper, the authors looked at drug-related deaths in England, Wales, and Northern Ireland where benzodiazepines had been detected. To do this, they used NPSUM data.

NPSUM stands for the National Programme on Substance Use Mortality. It collates coroner-reported data on drug-related deaths dating back to the late 1990s across England, Wales, and Northern Ireland, although it does not cover every single coroner jurisdiction.

And in this context, a drug-related death basically means a death where drugs are thought to have contributed.

Using that dataset, the authors looked at the types of benzodiazepines detected and whether they were prescribed benzodiazepines or so-called street benzos.

For the purposes of the paper, street benzodiazepines were defined as benzodiazepines not available via NHS prescription. Some of these have been licensed in other countries, for example etizolam in some parts of Asia, but are not licensed in the UK. Others, like bromazolam, are essentially research chemicals that were never intended for human use.

Many of these street benzos may be more potent than diazepam, and some have shorter durations of action, which can encourage repeat dosing.

The authors looked at deaths in which benzodiazepines were detected between 1999 and 2021, including cases reported to the NPSUM database up to 1 November 2022. Because of delays in inquests and reporting, the 2021 data may not have been entirely complete.

They identified 14,837 deaths with 16,208 benzodiazepine detections in total. Annual deaths involving benzodiazepines had more than doubled over the previous decade, rising from 556 in 2010 to 1,245 in 2020.

The dataset also allowed them to look at GP and hospital records to see whether individuals had been prescribed benzodiazepines at the time of death.

Quite a large chunk of the benzodiazepines detected, around 62 percent, were thought to have come from an illicit source. Diazepam was the most commonly detected prescribed-type benzodiazepine that had been obtained without a prescription, accounting for about 77 percent of those detections.

So even when licensed benzodiazepines were being detected, a lot of that did not necessarily represent legitimate prescribed use. There was a lot of diversion and illicit access.

What about the street benzos specifically?

Street benzodiazepines contributed to a relatively small proportion of all benzodiazepine-related deaths overall, around 8.5 percent, but their detection increased dramatically over time.

Between 2015 and 2020, street benzodiazepine detections increased by roughly 1,200 percent, which is a huge rise.

And because this paper only really captures data up to 2021, our own practical experience suggests that trend probably continued afterwards.

Definitely. We certainly see a lot more bromazolam and related compounds now than we used to.

Another interesting point was that the types of street benzodiazepines changed over time. The authors identified 18 street benzos in total, and eight of those were first detected between 2019 and 2021.

So not only are street benzos increasing, but the diversity of the market is increasing too.

They also looked at demographic patterns. Street benzos were more likely to be detected in males and in younger age groups. Interestingly, though, the average age of people in whom street benzos were detected increased over time, from about 34 years in 2011 to 39 years in 2021.

That may simply reflect the ageing drug-using population more broadly, which is something we see with a lot of drug-related death data.

Let's step back for a second. A lot of these street benzos are designer compounds, aren't they? Chemically similar to known benzodiazepines, but modified to try to stay ahead of legislation.

Yes. They are structurally related to therapeutic benzodiazepines but chemically altered. Some are very potent. Some have shorter half-lives than diazepam. But not all of them are short-acting. For example, flubromazolam can actually have a very prolonged effect.

We had a case years ago where someone thought they had bought diazepam and it turned out to be flubromazolam. They were essentially unconscious, or at least very significantly impaired, for days.

And that is really the problem, isn't it? These drugs are often not what people think they are. They are not produced to pharmaceutical standards, so the dose can be unpredictable, the compound can be different from what was advertised, and the duration of action may be very different from what the user expects.

The paper also brought in other data, didn't it, from seizures and testing services?

Yes. The authors included data from TICTAC, a drug identification service that works with samples from events such as music festivals, and also data from WEDINOS, which is the Welsh Emerging Drugs and Identification of Novel Substances service.

WEDINOS allows people to send in pills or powders for testing, and the results are published online as part of a harm reduction approach.

The TICTAC data in this paper covered benzodiazepines collected from 22 music festivals in England and Wales between 2017 and 2021, although obviously there was effectively no festival data for 2020 because of the COVID-19 pandemic.

They reported 461 benzodiazepine detections involving 14 different benzos. Diazepam was the most common at around 42 percent, followed by alprazolam, better known as Xanax, at about 30 percent, and etizolam at about 20 percent.

The WEDINOS data covered 3,554 submissions between 2017 and 2021, with 23 different benzodiazepines detected. Again, diazepam was the most common, followed by etizolam, alprazolam, flubromazolam, and bromazolam.

So overall, the seizure and testing-service data broadly matched the trends seen in the post-mortem data: benzodiazepine detections overall were increasing, and there was a growing range of novel and street benzos appearing in later years.

Exactly.

So what are the implications of all of this?

From a post-mortem toxicology point of view, the rise in different types of novel benzodiazepines makes things more complicated. We have to stay up to date with which compounds are out there so we can actually detect them analytically.

And once we do detect them, interpretation is difficult. For many of these novel compounds we do not have much robust data on potency, half-life, active metabolites, or what typical post-mortem concentrations even mean.

Another important point is that in drug-related deaths, benzodiazepines are often not the only drugs present. They are commonly found alongside opioids, alcohol, or other sedatives.

So although benzos can contribute significantly to harm, including fatal harm, a lot of the deaths in this kind of dataset reflect polydrug use rather than isolated benzodiazepine toxicity.

That is true, but there are also harms outside the death data. Benzodiazepines can absolutely cause dependence, severe withdrawal, impaired functioning, blackouts, accidents, and hospital admissions. If the market shifts from something relatively predictable like diazepam to a mix of 20 or more unpredictable compounds, that creates harms beyond what mortality data alone can show.

And one of the really striking things when you look at the WEDINOS data is the purchase intent. People often think they are buying diazepam or Xanax, but the testing results show they are often getting something else entirely.

We should probably briefly explain the Xanax point. Alprazolam is not prescribed on the NHS in the same way diazepam is, but it is a well-known pharmaceutical product in other countries, especially the United States.

So when people think they are buying Xanax, they may well believe they are getting a real, pharmaceutical, standardised product, when in fact they may be getting flualprazolam, bromazolam, or something else entirely.

And even if it is the compound they expect, it may be very inconsistently dosed because it is not being manufactured to proper pharmaceutical standards.

The paper also discusses possible reasons for the rise in illicit benzodiazepine use. One possibility is that prescribing of traditional benzodiazepines has reduced, so people who want them are increasingly sourcing them illicitly.

There is also the broader issue of anxiety, self-medication, and poor access to mental health services. It is not difficult to imagine people turning to illicit benzodiazepines when they are struggling and cannot get timely help elsewhere.

The study also looked a bit at regional patterns, didn't it?

Yes. Northern Ireland stood out as having relatively high rates in some of the analyses, and there were also links with deprivation. That suggests some socioeconomic component, although this paper cannot really explain the causal mechanism.

So Rob, what trends have you seen personally in benzodiazepines?

My experience is definitely consistent with this paper. There has been a clear rise in newer benzodiazepines over the last few years, and we have seen cases with significant harm.

I remember one case where someone thought they had bought diazepam, but it turned out to be clonazolam. That is the only time I have personally seen clonazolam in a real case, and the person ended up in hospital for a significant period.

There was also a run of cases involving flubromazolam where several people were admitted after a particularly potent batch of tablets appeared locally over one weekend.

So there is a very real harm from these compounds, particularly because people cannot accurately dose them and often do not even know what they are taking.

Why do benzodiazepines seem to carry less stigma than some other illicit drugs?

Possibly because they are associated with pharmaceuticals. People may think of them as medicines and therefore somehow safer or more legitimate, even when they are not coming from a pharmacy at all.

You also hear them referred to casually in pop culture, music, and social media, which probably adds to that normalisation.

What harm reduction strategies are there if people do choose to use illicitly sourced benzodiazepines?

WEDINOS is a very good place to start. It is a genuinely useful harm reduction service, because at least it gives people some chance of finding out what they actually have.

If you are not aware of WEDINOS, it is worth looking at what they do.

Prediction time: what do you think the next few years are going to look like?

I think we are going to keep seeing more street benzos and more different types of street benzos. As legislation changes and specific compounds are controlled, other analogues will likely appear in their place.

We have seen that already with compounds like bromazolam, and I suspect that pattern will continue.

I think we are going to wrap it up there. I hope you have enjoyed listening.

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We would love to hear from you there as well. If you have recommendations for topics you would like us to cover, feel free to send us a message.

Hope you have all had a wonderful week, and we will see you next time. Bye.