Post-mortem Toxicology Reports on Deaths Associated with Prescribed Benzodiazepines and Z-drugs: A Statistical Analysis from 2011-2015 in England

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INTRODUCTION

Benzodiazepines (BZPs) and Z-drugs are two commonly prescribed sedative-hypnotics that are indicated for short-term relief in severe anxiety, insomnia, and behavioural disturbance (1).

The most prescribed BZPs include diazepam, lorazepam, and clonazepam. Z-drugs include zopiclone, zolpidem, and zaleplon (2,3). While two distinct drug classes, they are often grouped together due to sharing similar mechanisms of action on the $GABA_A$ receptor (herein referred to as BZPs/Z-drugs). While efficacious when used short-term, long-term use or overdose of either of these sedative-hypnotics can cause dependence, addiction, cognitive disturbance and decline, coma, and death (2).

There has been an increase in public and professional concern over the high rates of prescribing of sedative-hypnotics and the sequelae of long-term, inappropriate administration. Public Health England published data showing 2.4 million UK patients received a prescription of either BZPs or Z-drugs in 2019 (3).

AIMS

Primary aim was to gain a snapshot of the impact of BZP/Z-drug prescriptions in drug-related deaths.

Objectives:

- Quantify the percentage of prescribed BZPs/Z-drugs in BZP/Z-drug-related deaths
- Quantify the percentage of BZPs/Z-drugs in the total number of drug-related deaths where the contributing drug had been prescribed.
- Calculate the percentage change in prescribed BZPs/Z-drugs involved in drug-related deaths over the time period.

METHODS

Ethical approval was not required for this research.

The National Programme on Substance Abuse Deaths (NPSAD) receives coroner reports on drug-related deaths in the UK.

For a death related to BZPs/Z-drugs to be counted, it must have occurred in England 2011-2015 and met one of the following inclusion criteria:

- Presence of one or more BZPs and/or Z-drugs that coroners solely implicated in the death.
- Presence of one or more BZPs and/or Z-drugs at post-mortem.
- Prescence of one or more BZPs and/or Z-drugs in combination with other drugs all implicated in the death and/or detected at post-mortem.

Coroner inquests also provide details on demographics, cause of death, and their prescribed medications, which were all reported on by NPSAD.

Statistical analysis was performed with GraphPad Prism 9.

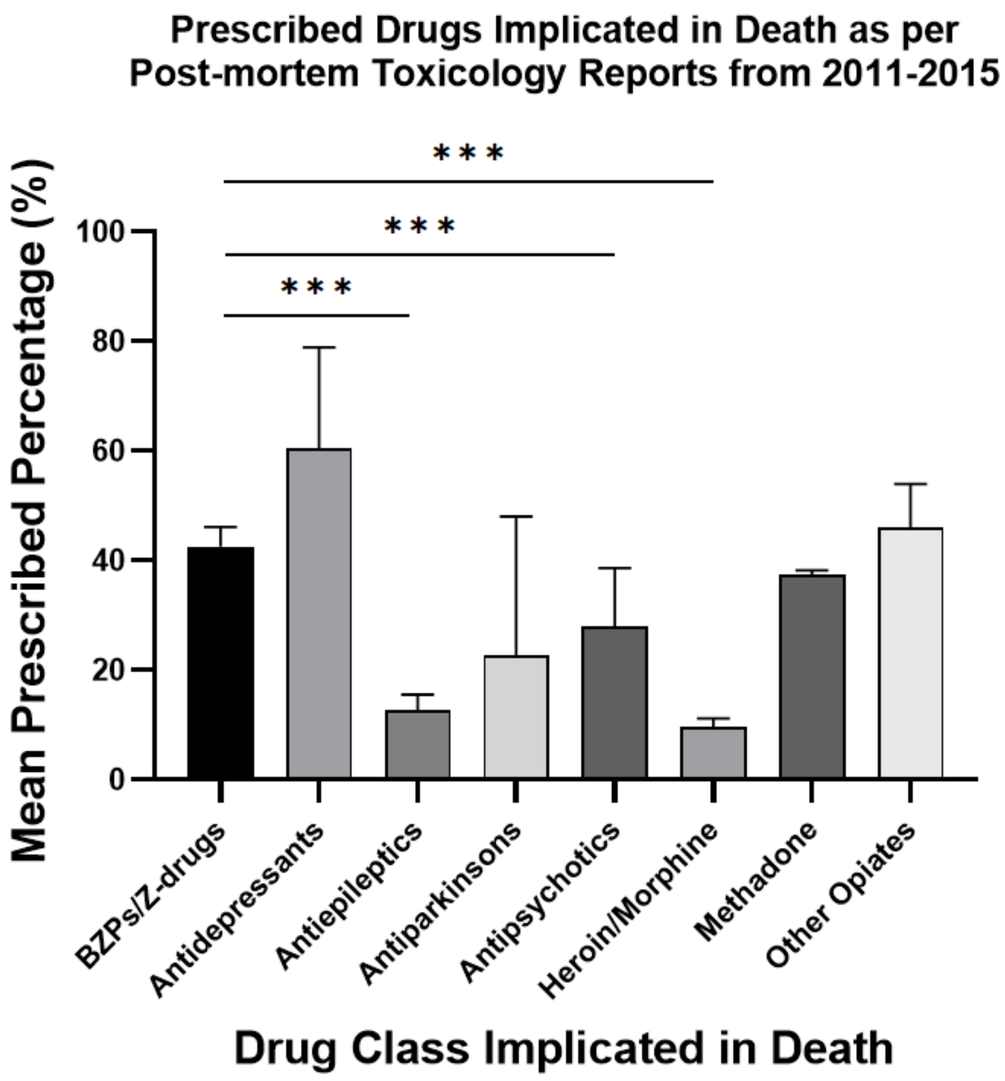

Figure 1: Bar chart depicting the mean proportion of prescribed drugs coroners implicated in drug-related deaths per drug class. ***$p < 0.05$ showing significant difference between classes.

RESULTS

From 2011 to 2015, BZP/Z-drug-related deaths have increased by 34.2%.

On average, BZPs/Z-drugs that were implicated alone or in combination with another drug in the death were prescribed by a doctor 42.5% of the time.

BZPs/Z-drugs alone were implicated in 28.2% of cases where they were prescribed by a doctor.

Over the same time period, the percentage of total drug-related deaths caused by BZPs/Z-drugs (both prescribed and non-prescribed) has decreased by 11%.

From 2013 to 2015, accidental BZP/Z-drug deaths rose significantly by 37.7%.

When adjusting for suicide, BZPs/Z-drugs were implicated in the greatest number of accidental deaths from prescribed drugs, in front of “other opiates” and “methadone”. However, this was not the case where BZPs/Z-drugs were the sole cause of death.

One-way ANOVA revealed the mean number of deaths due to prescribed BZPs/Z-drugs was significantly higher than three other drug classes that had also been prescribed [$F(7,18) = 6.455$, $p < 0.001$)]. Post-hoc analysis confirmed significance (Fig. 1).

CONCLUSIONS

The results support public health concerns. Prescriptions constitute a large percentage of total BZP/Z-drug-related deaths, despite BZPs remaining an accessible street drug. The biggest anomaly was in 2014, where 47.1% of BZPs/Z-drugs found to be the sole cause of death were prescribed by a doctor.

Overall, drug-related deaths are increasing, but the percentage of total deaths where BZPs/Z-drugs are implicated is decreasing. This points to a growing epidemic of drug misuse, and not necessarily an improvement in BZP/Z-drug prescribing practices, as BZPs/Z-drugs deaths are not decreasing.

Prescribed BZPs/Z-drugs and opiates had the greatest prevalence in accidental drug deaths. This suggests a lack of stewardship from healthcare professionals in stopping unnecessary prescriptions.

In conclusion, incautious BZP/Z-drug prescriptions significantly contributed to patient deaths. The most common cause of death was accidental and in combination with other drugs, alluding to overdose or drug interactions from not stopping repeat prescriptions. This is evidenced with 5% of BZP prescriptions lasting 12 months or more (3). Greater emphasis should be placed nationally on limiting unnecessary long-term BZP/Z-drug prescriptions to prevent accidental death.

References:

1. Joint Formulary Committee. Hypnotics and anxiolytics [Internet]. British National Formulary. National Institute for Health and Care Excellence. Available at: https://bnf.nice.org.uk/treatment-summaries/hypnotics-and-anxiolytics (Accessed: January 20, 2023)
2. Crowe SF, Stranks EK. The Residual Medium and Long-term Cognitive Effects of Benzodiazepine Use: An Updated Meta-analysis. Arch Clin Neuropsychol. 2018 Nov 1;33(7):901–11.
3. Taylor S, Annand F, Burkinshaw P, et al. Dependence and withdrawal associated with some prescribed medicines. Public Health England. 2019.