Association between drug poisoning deaths and season, week, weekday, and public holidays: protocol for a time series analysis of daily counts in England and Wales, 1993-2018

Version 1: 12 August 2022

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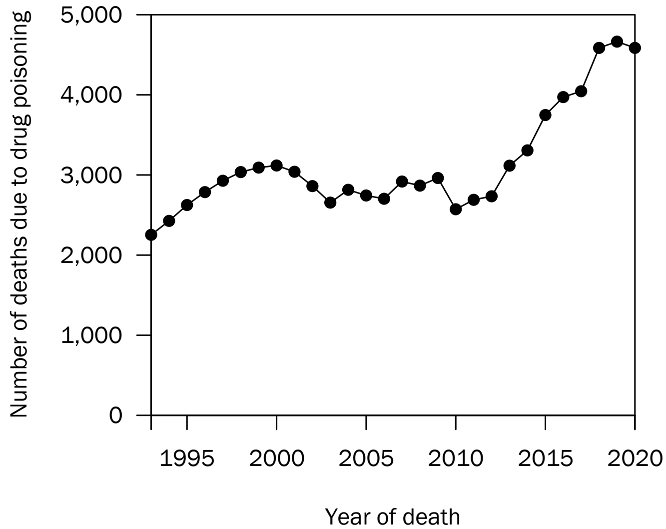
Summary

The number of deaths due to drug poisoning in England and Wales is increasing rapidly. Annual data shows that deaths plateaued in the decade before 2011 and then sharply increased. To improve our understanding of this problem and identify potential opportunities to prioritise harm reduction and addiction treatment services, we will investigate within-year and cyclical variation in deaths. This is a protocol for a time series analysis to assess whether risk of drug-related varies by season, by week of the month, by day of the week, and at public holidays. These trends have not been widely studied. The results could contribute to our understanding of environmental drivers of death due to drug poisoning, and to the planning of public health and clinical services that aim to prevent drug-related deaths.

Background

The number of deaths due to drug poisoning in England and Wales has increased by approximately 80% over the past decade, from 2,572 in 2010 to 4,586 in 2020.[1] For several years before 2010, the number of deaths was approximately constant at roughly 3,000 per year (Table 1). Epidemiologists and policymakers have tried to identify the causes of this rapid increase and identify modifiable risk factors. Potential causes include an ageing cohort of people who use drugs, though this theory is not supported by evidence showing that the age-specific risk of death has increased;[2] a reduction in the availability of methadone and other treatments for opioid dependence; and an increase in poly-drug use.

Figure 1: Annual number of deaths due to drug poisoning in England and Wales, by date of occurrence



Source: Office for National Statistics[1]

The risk of many causes of death varies within years, including by season, day, or even hour. For example, many respiratory viruses such as influenza and respiratory syncytial virus are extremely seasonal and peak in winter months;[3] deaths related to car crashes are more likely at the weekend,[4] and deaths from heart attacks are more likely in the morning.[5] These trends might be driven by planetary (e.g. climate), physiological (e.g. circadian rhythms) or social (e.g. changes in alcohol consumption) processes.

There has been relatively little research on shorter-term or cyclical trends in deaths due to drug poisoning. There may be demand-side drivers, such as drug use to cope with stress at holidays or during periods of monthly financial pressures, and there may also be supply-side drivers, such as regular changes in the availability, quality and potency of drugs.[6,7] These temporal risks could be important part of the 'risk environment'[8] for drug-related deaths, and an understanding of these risks could contribute to the planning of public health and clinical services that aim to prevent drug-related deaths.

Several prior studies (mostly in North America) have examined temporal patterns in deaths due to drug poisoning, with varied findings:

- **The first week of the month.** A study of death certificates in the US between 1973 and 1988 found that drug-related deaths occurred 7% more often in the first week of the month compared to the preceding week.[9] The authors attributed this in part to stressful events such as bill payments and evictions being more common at the start of the month; and to payments for many benefits being at the beginning of the month. Similarly, a study of overdose deaths in Rhode Island, USA, from 2014 to 2016 found there were 17% more deaths in the first week of the month relative to the preceding week.[10] Some studies have shown that drug-related deaths are more likely shortly after benefits payments (known as the 'cheque effect'),[11] which may contribute to this monthly pattern. However, a literature review of variations in drug use across calendar months found that drug use is typically higher at the beginning of the month; but this did not differ by receipt of benefits payments,[12] which may suggest that the 'start of the month effect' is not fully explained by the 'cheque effect'.
- **Cold weather and winter months.** A case-crossover study of drug-related deaths in New England, US, between 2014 and 2017 found that deaths were associated with cold weather. Relative to 11C, a temperature of 0C was associated with a 1.3x (95% CI 1.1-1.5) the odds of death over the following 7 days.[13] The authors proposed several mechanisms, including: (1) opioid use and cold temperatures may act synergistically to depress respiratory function; and (2) cold temperatures may alter patterns of

drug use (e.g. people might be more likely to use indoors and alone where there is less likely to be a bystander capable of responding). Similarly, a study modelling overdose death trends in British Columbia, Canada, determined that the rate of death was 14% higher in the winter than summer.[14] In contrast, a study of drug-related deaths in New York City from 1990 to 2006 found cocaine-related deaths were more likely during warmer months, while drug-related deaths not involving cocaine appeared to have no association with temperature.[15] Studies of suicide by intentional drug overdose in the US[16] and the UK[17] find that deaths were lowest around Christmas and higher in summer (but peak on 1 January) – though these studies focuses on deaths deemed to be intentional, which are the minority of deaths due to drug poisoning.

- **Weekday.** A study of deaths due to drug poisoning in England and Wales between 1993 and 2002 found that deaths were more likely to occur on Saturdays, with approximately 1.3x more deaths on Saturdays than Mondays (the day with the lowest rate).[17] The authors did not propose potential reasons for this pattern.

There is therefore a gap in our understanding of how the rate of drug-related deaths varies across the year. To date, the Office for National Statistics (ONS) in the UK has only published annual data on this subject. The ONS is now planning to publish a dataset showing the number of daily deaths since 1993. We plan to use this data to investigate patterns of drug-related deaths by season, weekday, time of month, and other special occasion. Our hypotheses are that deaths due to drug poisoning are:

- Higher in the first week of the month than the last week.
- Higher on Saturday than other days of the week.
- Lower at Christmas than other times, reflecting the pattern in drug-related suicides.
- Higher in winter than summer, following evidence from the US that drug-related deaths are highest in winter and cold weather.

Methods

Data source

The data source will be the count of deaths due to drug poisoning in England and Wales by day, from 1 January 1993 to 31 December 2018, and the subset of deaths in which an opioid was involved (example shown in Table 1). The data is only available until 2018 because there is sometimes a substantial lag in the official registration of deaths. This means that time trends in very recent years are unreliable. The data will be published by the UK Office for National Statistics. At the time of writing this analysis plan, the dataset is not available.

In addition, we will use a list of public holidays in England and Wales from 1993-2018 from the Nager.Date project (https://date.nager.at/PublicHoliday/Country/GB; data are also available here: https://github.com/danlewer/drd-time-trends/tree/main/public-holidays).

Table 1: Example of the dataset (this table does not include real data)

Date	Number of deaths due to drug poisoning in England and Wales	Number of deaths due to drug poisoning in England and Wales where an opioid was involved
1 Jan 1993	4	2
2 Jan 1993	6	4
3 Jan 1993	10	5
4 Jan 1993	1	0
Etc …		

Analysis

The analysis will follow six steps:

1. Classification of dates according to four variables:
    a. Calendar month: January to December
    b. Week of the month: first 7 days, last 7 days, other times
    c. Weekday: Monday to Sunday
    d. Public holidays and special occasions. This will be classified as (i) Christmas, defined as 24-30 December; (ii) New Year, defined as 31 December-1 January; (iii) other public holidays using the Nager.Date dataset (see above); (iv) other times.
2. Using a Poisson model to estimate the association between these risk periods and the number of deaths due to drug poisoning, using polynomial terms for time to account for the long-term trend. Based on previously observed annual data, we will use quadratic terms up to time^4. 'Time' will be measured as the number of days since 1 January 1993. A chart of this time trend based on annual data is show in Figure 2. The R syntax for this regression model will be:

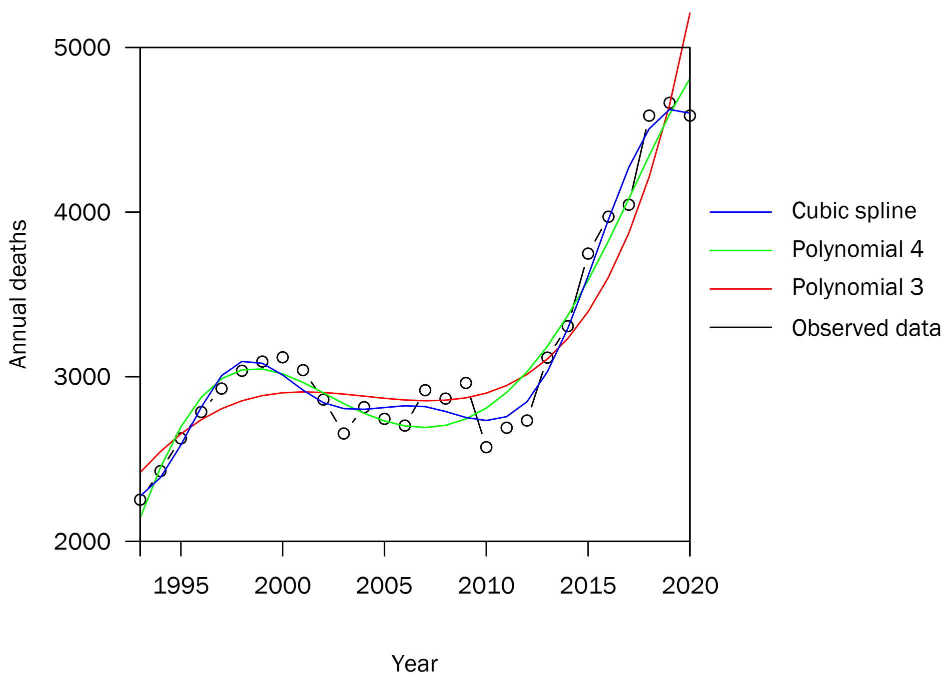
```
glm(deaths ~ poly(time, 4) + month + weekOfMonth + weekday + holiday, family =
'poisson')
```

3. Using the model to predicting and graphically representing the number of daily deaths for each variable listed in step 1, when the other variables are at their baseline values. Baseline values will be arbitrarily set at time = 31 December 2018; month = January; weekday = Monday; week = last week of month; public holiday = 'other times' (ie. not a public holiday).
4. Estimating the 'peak-to-low' ratio for each variable listed in step 1. This will be based on calculating the ratio between the highest and lowest predicted value (for example if we predict a maximum of 14 daily deaths on Saturdays and a minimum of 10 daily deaths on Mondays, the peak-to-low ratio would be 1.4), and estimating confidence intervals using a Monte-Carlo method. The Monte-Carlo method is based on simulating multiple datasets in which the number of deaths each day is sampled from a Poisson distribution with a mean of the observed deaths, and a distribution of peak-to-low ratios is derived from these datasets.
5. Repeating steps 1-4 for the subset of deaths involving opioids.
6. As a secondary analysis, repeating steps 1-5 for data stratified into three time periods (1993-2001; 2002-2010; 2011-2018), to test whether the associations with weekday, month, and holiday changed during the study period. These three periods are roughly equal-duration, but also correspond to (i) an

earlier increase in drug-related deaths in the 1990s; (ii) a plateau in the 2000's; (ii) the recent rapid increase.

We have simulated a dataset and written code for these analyses here: https://github.com/danlewer/drd-time-trends/blob/main/simulate_results.R

Figure 2: Time trend in annual deaths due to drug poisoning in England and Wales, showing that polynomial terms can provide a reasonable estimate of long-term changes



"Polynomial 3" means polynomial terms up to time^3, using the R formula syntax poly(time, 3). "Polynomial 4" means polynomial terms up to time^4, using the R formula syntax poly(time, 4). Cubic splines were fitted using the 'splines' package and the syntax bs(time, knots = c(1995, 2000, 2005, 2010, 2015)).

Ethics and approvals

All data used in this study will be publicly available and no ethical consideration or other approvals will be needed.

Potential impact on policy and practice

The results from this study could inform:

- Opening hours for harm reduction services, including services such as community pharmacies that provide opioid substitution therapy, and overdose prevention centres / drug consumption rooms (though overdose prevention centres are not currently commissioned in the UK).
- Prioritization of naloxone training for first responders (eg. those working at weekends)
- Further research into the risk environment – such as studies into the contribution of service availability, family support, and social events.

Limitations

- The analysis will not provide insight into long-term trends in drug-related deaths (beyond the trend that has already been observed in annual data).
- The study will use aggregate data (the daily count of deaths) and will not use information about the individuals who died. This means we cannot study potential mechanisms related to individual behaviours such as drug use or engagement with harm reduction services, which may vary over time (though the results may lead to hypotheses for further research about these factors).
- Death may be recorded on a different day to the overdose. Usually this would only be one day difference (for example if someone uses drugs late in the evening and then dies early the next morning) but may be longer if someone was treated in hospital and received supportive care, but ultimately died. We expect this occurs in a minority of cases, as 85% of deaths due to drug poisoning happen in the community with no hospital care.[18]
- The data will not be stratified by demographic characteristics such as age, sex, and deprivation. It is possible that time trends will differ according to these characteristics. For example, an increase in deaths at the weekend may be stronger for younger people who are more likely to go to parties. Stratifying the data by characteristics that are captured on death certificates is technically possible but may raise issues with confidentiality.
- The data will not be stratified by intention (ie. whether the death was considered to be a suicide or not). Temporal patterns in suicides may be different to patterns in unintentional deaths. According to ICD-10 codes, less than 10% of opioid-related deaths are considered intentional;[18] and other evidence suggests that most fatal drug overdoses are accidental (with other methods more commonly used in suicides, such as hanging).

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