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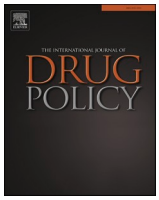

Research Paper

Changing dynamics of drug overdoses in the United Kingdom: An attempt to replicate the Jalal et al. findings of steady exponential growth

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ABSTRACT

Background: Jalal et al. discovered that between 1979 and 2020 total rates and counts of fatal drug overdoses in the United States exhibited exponential growth at a very steady rate even though deaths from individual drugs did not. That is a startling result because it means that the different drugs are in effect "taking turns", with one growing faster just as another drug's death rate growth ebbs. That raises the question of whether this steadiness in the all-drug death rates is in some sense just a coincidence peculiar to the United States or whether it might reflect some more general phenomenon and so manifest in other countries.
Methods: We fit the same model used by Jalal et al. to data on drug-related death rates for the countries of the United Kingdom.
Results: The main finding is largely a failure to replicate the United States result. Simple graphical display of the trends and a number of statistical measures show that the growth in the United Kingdom was not only slower than in the United States, it was also less steady, with the exception of Northern Ireland.
Conclusions: Steady exponential growth in the all-drugs mortality rate may be a phenomenon specific to certain contexts. It remains an open question whether the explanation of steady exponential growth in the United States and Northern Ireland relates to demand and supply mechanisms, to social and political conditions, or to coincidence.

Introduction

Jalal et al. published a series of provocative papers (2018, 2020, 2021) which observed that for 40 years the drug-related mortality rate and the number of drug overdose deaths in the United States grew at a steady exponential rate. That growth was striking not only because of its speed (about 7.4% per year, compounded) but also because of how steady that growth was in aggregate. Trajectories for specific drugs were not exponential, but somehow the sum across drugs was. "The U.S. drug overdose epidemic has been inexorably tracking along an exponential growth curve since at least 1979. Although there have been transient periods of minor acceleration or deceleration, the overall drug overdose mortality rate has regularly returned to the exponential growth curve" (Jalal et al., 2018, p. 1). A variety of commentators have debated the causes and implications, including wondering whether the steadiness in growth was more or less coincidence or whether it betrayed some underlying behavioral law (Borquez & Martin, 2022; Caulkins, 2022; Compton et al., 2022; Keyes & Cerdá, 2022; Reuter, 2022).

Here we replicate Jalal et al.'s analysis for the countries that comprise the United Kingdom separately and in aggregate. There are minor technical differences across countries, e.g., affecting exactly which deaths get counted in official statistics. However, Jalal et al.'s findings are so prominent that if they held also in other countries, those patterns should not be hidden by such minor variations.

In brief we find that in England and Wales, Scotland, and the U.K. as a whole the growth was sizable, sustained, and convex, but it did not constitute the sort of rigidly exponential growth associated with the U.S. epidemic trajectory. Steady exponential growth effectively describes the trend only in the smallest of the four U.K. countries: Northern Ireland. We estimate the annual growth in mortality rate in Northern Ireland at 10.6%; meaning that the death rates doubled approximately every 6 and a half years. Jalal et al. (2018) estimate the U.S. doubling time to be about 9 years. As in the U.S., in Northern Ireland that steady growth only manifests in aggregate, summing across drugs, and not when separately considering each individual drug type.

The paper is organized into three sections. The next section presents

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the methods and data. The second illustrates the main results for total mortality across all drugs and disaggregated by drug type. The third section discusses these empirical findings in light of the ongoing debate about the implications of Jalal et al.'s observations. The limitations we encountered in conducting our analyses are outlined in the supplementary material where we report also summary statistics on drug-related deaths in the U.K.

Methods

We fit the same model used by Jalal et al. (2018, 2020, 2021) to aggregated data on drug-related deaths per capita for the three reporting jurisdictions comprising the four countries of the U.K.: England and Wales (combined), Scotland, Northern Ireland. For each, we fit an exponential curve to the trends in the drug-related mortality rate per capita:

$$m_i = e^{\alpha+\beta \cdot year_i} \tag{1}$$

Expressing the mortality rate (m_i) as the number of deaths divided by population and taking logs yields:

$$\log\left(\frac{d_i}{pop_i}\right) = \alpha + \beta \cdot year_i \tag{2}$$

$$\log(d_i) - \log(pop_i) = \alpha + \beta \cdot year_i \tag{3}$$

$$\log(d_i) = \alpha + \beta \cdot year_i + \log(pop_i) \tag{4}$$

where d_i is the expected number of deaths in $year_i$, pop_i are the millions of inhabitants in the country in $year_i$, α is the intercept, and β is the average annual rate of growth in drug-related mortality.

Even if the model perfectly described the trend in expected deaths, the observed number of drug-related deaths would exhibit random variation. So we estimate β via Poisson and quasi-Poisson regressions using Generalized Linear Models (GLM) (Nelder & Wedderburn, 1972) as well as via Poisson regressions using generalized estimating equation (GEE) (Liang & Zeger, 1986). The offset $\log(\text{pop}_i)$ allows us to adjust estimates for population size while not estimating additional coefficients. Indeed, the coefficient of $\log(\text{pop}_i)$ is fixed at 1.

We also want a measure of the steadiness of growth, not just its magnitude. Jalal et al. observe that the R2 is high, but that is a weak test in this context. When the overall growth rate is high, even unsteady growth can be fit by an exponential curve in a way that produces a high R2. E.g., if we manufacture a hypothetical time series whose year-on-year growth alternates between years with 20% and years with 0% growth, then an exponential fit still yields an R2 of about 0.96 even though the growth is stair-stepped, not steady. Other common error measures include the mean absolute deviation or mean absolute percentage deviation, but neither of those captures well how surprising a given departure from the exponential curve would be if that exponential model were "true", so we take a different approach.

Overdose deaths are primarily individual events; events with multiple decedents account for a small share of deaths. And overdose deaths are not directly related the way that deaths from a contagious disease are, or deaths from natural disasters such as earthquakes. Therefore, it may be reasonable to model the randomness in the actual death count in any given year by a Poisson random variable (RV), and hence as having a variance equal to its mean (See Barnett, 1981; Leiter & Hamdan, 1973; Morse & Kimball, 1946 for other examples of this modeling approach.)

When the expected value of a Poisson RV is reasonably large, it can be approximated by a Normal RV, with standard deviation equal to the square root of its mean. Hence, we measure the distance of any given year's actual number of deaths from its expected value under an exponential model, by the (absolute value of) of its z-score, assuming the standard deviation equals the square root of that expected value. Two overall measures for the series then are the average absolute value of its z-score and the probability a normally distributed RV has a z-score at least as large (in absolute value).[1]

We report those values, as well as the Efron's (1978) R2 for GLM and the p-value for the deviance goodness of fit $\chi 2$ test for Poisson regression. We conduct our analysis also fitting a quasi-Poisson log-linear model and without approximating the Poisson RV by a Normal RV as robustness tests.

Finally, we run Bayesian posterior predictive tests (Rubin, 1984) for evaluating the fit of a model to observed data. The tests involve simulating new data sets from the posterior predictive distribution of the model and comparing the simulated data to the observed data. This process provides a direct assessment of the fit of the model to the data and can be used to evaluate the performance of different models (Gelman et al., 1996).

We performed our analysis in terms of rates per capita to facilitate comparisons across the four jurisdictions. However, since population exhibits slow and fairly stable exponential growth, our results provide indications on the nature of trends in fatal drug overdoses too. Indeed, because population grows exponentially with a reasonably steady rate, the number of overdose deaths will exhibit stable exponential growth if and only, if the mortality rate changes exponentially.

Data

We retrieved openly available data from the statistical offices of England and Wales, Scotland, Northern Ireland (Tab. SM1 in the Supplementary material).[2] The U.K. Office for National Statistics (ONS) provides annual death counts by sex and drug type and by age group and drug type for deaths that occurred in England and Wales from 1993 through 2019. The National Records of Scotland (NRS)'s website provides consistent death counts by drug type for the years 2000–2020. The Northern Ireland Statistics and Research Agency (NISRA) provides 2001–2020 data on death counts by drug-type and age group in Northern Ireland. We retrieved mid-year population estimates for the four countries from the ONS's website to calculate drug-related annual mortality rates.

As discussed in the supplementary material, these institutions adopt similar but not identical definitions of drug-related death. Notably the U.K. definitions for drug-relatedness are somewhat broader than those in Jalal et al. (2018, 2020) and are more similar to those used by Jalal and Burke (2021). However, in our judgment those differences between countries do not preclude summing them to produce a figure for the U.K. as a whole, as others have also done. For example, the NRS produce a figure of drug-related deaths in the U.K. starting from data provided by the ONS and the NISRA. Likewise, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) also combines data from England and Wales with data from Scotland and Northern Ireland to create figures for the U.K., which allow international comparisons with other European countries.

To elaborate, British statistics on deaths are compiled in accordance

[1] Formally, $z_i = \frac{d_i - \widehat{d_i}}{\sqrt{\widehat{d_i}}}$ where d_i are the observed drug-related deaths in $year_i$, and $\widehat{d_i}$ is the expected number of deaths estimated on the base of the fitted exponential curve. $z = |\frac{\sum_{i=1}^{I} z_i}{I}|$ is the average of the z-scores over the total number of years considered (I). The p-value associated with the average z-score (z) is calculated with a two-tailed test whose null hypothesis is that the number of expected deaths is equal to the number of observed drug-related deaths ($\widehat{d_i} = d_i$).

[2] England and Wales: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathsrelatedtodrugpoisoningbydateofoccurrence. Scotland: https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/deaths/drug-related-deaths-in-scotland/2020. Northern Ireland: https://www.nisra.gov.uk/statistics/cause-death/drug-related-deaths.

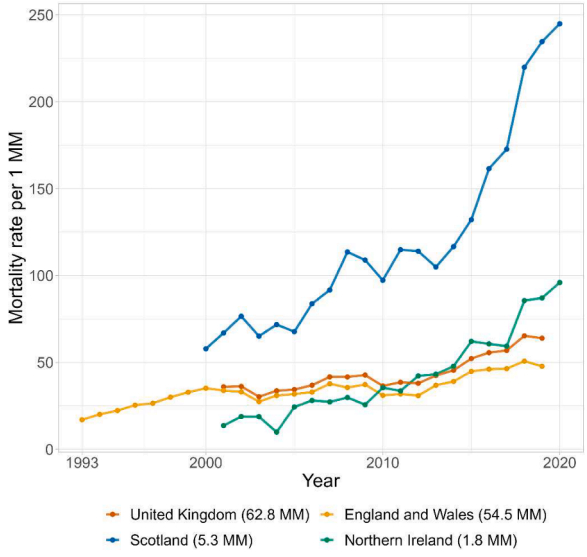

Fig. 1. Growth in the drug-related mortality rate in England and Wales (1993–2019), Scotland (2000–2020), Northern Ireland (2001–2020), and the United Kingdom as a whole (2001–2019).
Note: The data in parentheses report the average population size of the country over the considered period, expressed in millions.

with the WHO International Classification of Diseases, Ninth Revision (ICD-9) for the years 1993 to 2000 and Tenth Revision (ICD-10) from 2001 onwards, using information supplied when deaths are registered, which gives complete population coverage (ONS, 2021). Drug-related death refers to cases where the underlying cause of death is drug abuse or drug dependence or where any of the substances controlled under the U.K. Misuse of Drugs Act 1971 and its amendments are involved (NRS, 2021; ONS, 2021). With respect to ICD-10 Codes, drug-related death refers to categories F18 (except in Scotland); X40–X44; X60–X64; X85; and Y10–Y14 where 1) a specific drug listed under the U.K. Misuse of Drugs Act (1971) was known to be present in the body at the time of death, even if the pathologist did not consider the drug to have had any direct contribution to the death; and/or 2) the underlying cause is mental and behavioral disorders due to opioids, cannabinoids, sedatives or hypnotics, cocaine, other stimulants, including caffeine, hallucinogens, and multiple drug use and use of other psychoactive substances (NRS, 2021; ONS, 2021).

Results

Results for totals across drugs

Over the 19 years from 2001 to 2019, the drug-related mortality rate in the entire U.K. increased by 77.7% from 36.0 deaths per million inhabitants to 63.9 (Fig.1). The annual growth rate of the corresponding fitted exponential curve obtained with the Poisson model is 3.8% [$\widehat{\beta}$ = 0.038; 95% confidence interval (CI) = (0.036, 0.039)] (Table 1). That is rapid growth, but still about half what Jalal et al. (2018) observed in the U.S. (about 7.4%). The estimated growth in mortality rates is lower when considering data for England and Wales only (about 2.8% [$\widehat{\beta}$ = 0.027; 95% CI = (0.026; 0.029)]) but higher in both Scotland (7.4% [$\widehat{\beta}$ = 0.071; 95% CI = (0.068; 0.074)]) and Northern Ireland (10.6% per year [$\widehat{\beta}$ = 0.101; 95% CI = (0.091; 0.111)]). Since England and Wales (about 54.5 MM people during the considered period) account for roughly 90% of the U.K.'s population (about 62.8 MM people), the trends for England and Wales tend to mirror those for the U.K. as a whole.

What is striking about the Jalal et al. (2018, 2020, 2021) findings for

Table 1
Regression coefficients (Generalized linear model).

	United Kingdom				England and Wales			
Predictors	*Log-mean*	*Robust std. error*	*Conf. int (95%)*	*p-value*	*Log-mean*	*Robust std. error*	*Conf. int (95%)*	*p-value*
Intercept	−10.438	0.059	−10.458; −10.418	<0.001	−10.702	0.061	−10.722; −10.682	<0.001
Year - 2000	0.038	(0.055) 0.005	(−10.546; −10.332) 0.036; 0.039	(<0.001) <0.001		(0.054)	(−10.809; −10.597)	(<0.001)
Year - 1992		(0.004)	(0.029; 0.046)	(<0.001)	0.027	0.003	0.026; 0.029	<0.001
Observations	19				27	(0.003)	(0.021; 0.033)	(<0.001)
p-value χ^2 test	0.000				0.000			
	Scotland				Northern Ireland			
Predictors	*Log-mean*	*Robust std. error*	*Conf. int (95%)*	*p-value*	*Log-mean*	*Robust std. error*	*Conf. int (95%)*	*p-value*
Intercept	−9.904	0.066	−9.948; −9.860	<0.001	−11.289	0.091	−11.433; −11.149	<0.001
Year - 1999	0.071	(0.075) 0.005	(−10.052; −9.760) 0.068; 0.074	(<0.001) <0.001		(0.079)	(−11.447; −11.136)	(<0.001)
Year - 2000		(0.005)	(0.061; 0.081)	(<0.001)	0.101	0.006	0.091; 0.111	<0.001
Observations	21				20	(0.005)	(0.090; 0.111)	(<0.001)
p-value χ^2 test	0.000				0.185			

Note: Coefficients refer to Eq. (4). For each coefficient, robust standard errors, confidence intervals, and *p*-values reported in the first line refer to the fitting of a Poisson log-linear model for the log mortality rates; the values reported in brackets in the second line refer to the fitting of a quasi-Poisson log-linear model for the log mortality rates. The *p*-value χ^2 test are for the Poisson models.

Table 2
Regression coefficients (Generalized estimating equations).

	United Kingdom	England and Wales	Scotland	Northern Ireland
Intercept	−10.423 ***	−10.732 ***	−9.914 ***	−11.288 ***
	(0.000)	(0.000)	(0.000)	(0.000)
Year - 2000	0.037 ***			0.101 ***
	(0.000)			(0.000)
Year - 1992		0.029 ***		
		(0.000)		
Year - 1999			0.073 ***	
			(0.000)	
χ^2 test statistic	492.419	695.401	209.169	21.779
Degrees of freedom	17	25	19	18
p-value χ^2 test	0.000	0.000	0.000	0.242
Scale parameter: γ	25.917	25.756	9.960	1.089
Scale parameter: SE	0.000	0.000	0.000	0.000
Correlation parameter: α	0.446	0.497	0.467	−0.121
Correlation parameter: SE	0.000	0.000	0.000	0.000
Observations	19	27	21	20
Num. clusters	1	1	1	1

Note: Table2 presents the results of a Poisson generalized estimating equations (GEE) model fit to the observed data. The model examined the association between years and mortality rates while accounting for the autocorrelation structure of the data (AR1). The estimated coefficients, scale parameter, correlation parameter and results of the χ^2 test are presented in the table along with significance levels (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$) and adjusted standard errors in brackets.

the U.S. is not just that death rates increased so much, but also how steadily they grew. A number of measures show that the growth in the U.K. is not only slower than in the U.S., it is also less steady, with the exception of Northern Ireland. The first of these is the R2 of the exponential model's fit. Whereas Jalal et al.'s reported log linear R2 was 0.99, for the U.K. the Efron's R2 is 0.87. The values for the three component areas were 0.84 for England and Wales, 0.92 for Scotland, and 0.97 for Northern Ireland.

Perhaps of greater interest is the goodness-of-fit $\chi 2$ test from the Poisson regression. Results should be interpreted cautiously, given the relatively short length of the available time series but the test indicates that the exponential curve model is rejected for the U.K. as a whole, for England and Wales, and for Scotland (p-values = 0.000; see Table 1), but not for Northern Ireland (p-value = 0.185). The GEE models, which were fitted using the Poisson distribution with an autoregressive correlation structure (AR1), confirm these results. The p-values for U.K. as a whole, for England and Wales, and for Scotland models are <0.001, indicating strong evidence against the null hypothesis of no difference between the observed and expected rates. P-value for Northern Ireland is, instead, equal to 0.242 (Table 2).

A more visual measure is to observe the extent to which the actual trend in mortality rates did or did not fall within a confidence interval. To this purpose, we first used the 95% confidence interval surrounding the values that would be expected if a steady exponential growth model were correct and the number of overdoses could reasonably be modeled as following a normal distribution with a standard deviation equal to the square root of its mean. To some, that may seem too stringent a test (i.e., it may generate standard deviations that are too small), but it has the virtue of building in an adjustment for the size of the jurisdiction. Large

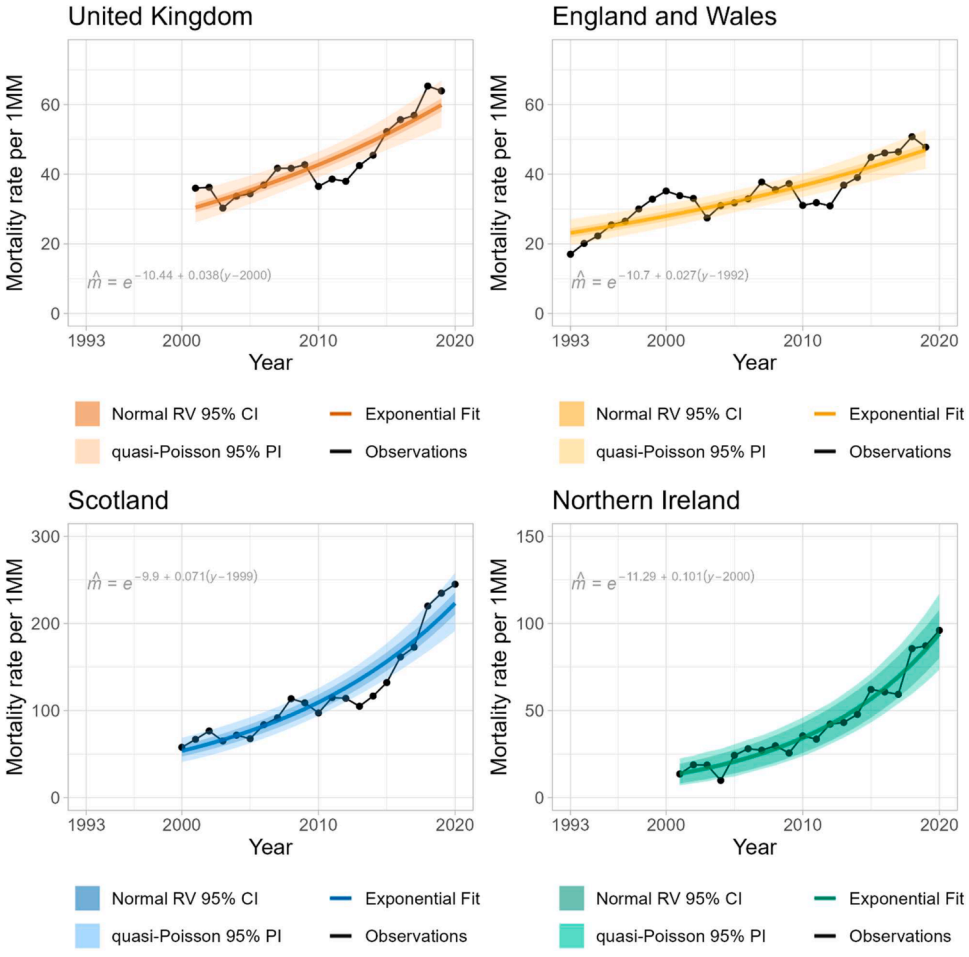

Fig. 2. Exponential fits to the growth of drug-related mortality rate in the United Kingdom, in England and Wales, in Scotland, in Northern Ireland.
Note: Fig. 2 represents fits of exponential growth models to the drug-related mortality-rate data for all drugs combined. Solid colored lines represent the best fitting exponential curves. The darkest shades of color (i.e., Normal RV 95% CI) represent the 2.5th and the 97.5th percentiles of the Normal approximations to the Poisson RVs with means taken from that best fitting curve and standard deviation equal to the square root of the mean. We have also computed the 95% confidence intervals with the Poisson RV's themselves, and they are visually indistinguishable from the ones produced by the Normal approximation of the Poisson RV. The lightest shades of color (i.e., quasi-Poisson 95% PI) represent the 95% prediction intervals for predictions from quasi-Poisson GLM log-linear models.

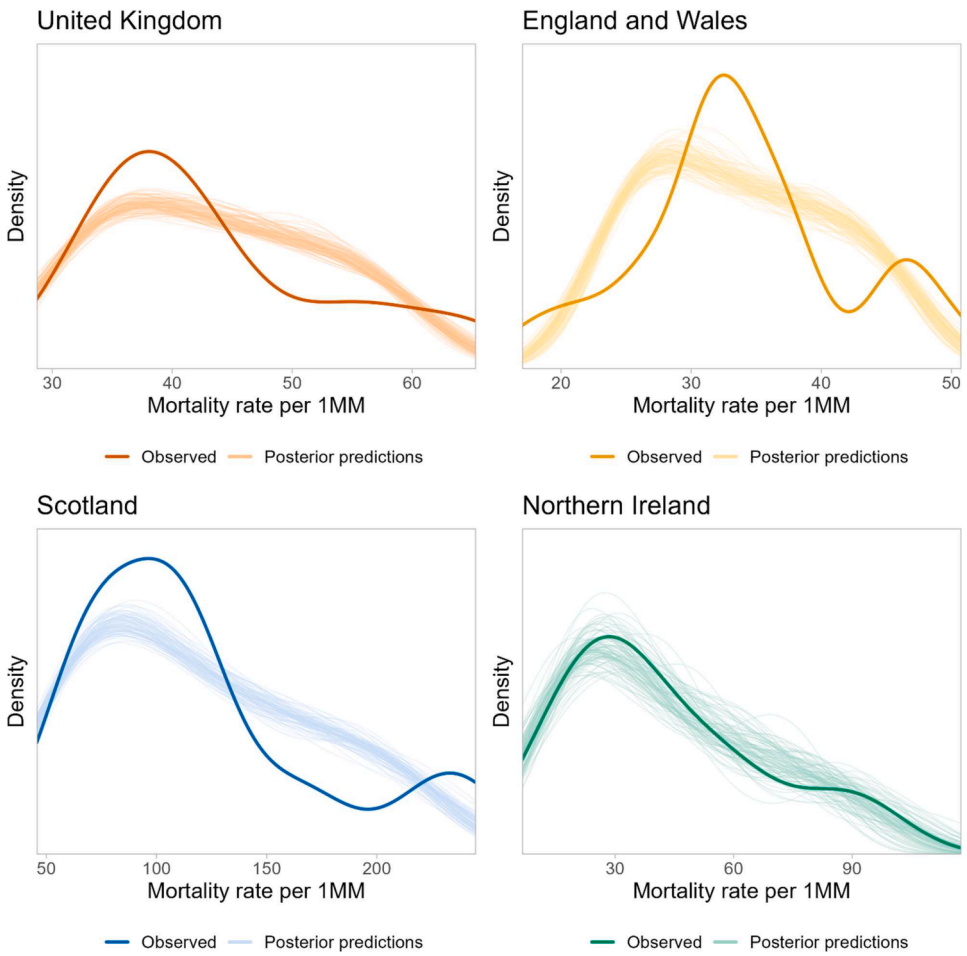

Fig. 3. Posterior predictive tests for the mortality rate in the United Kingdom, in England and Wales, in Scotland, in Northern Ireland.
Note: The posterior predictive tests compare the observed data (solid colored lines) with the posterior predictive distributions (shades of color), which are distributions of simulated data (1000 simulations) based on the quasi-Poisson models.

percentage fluctuations are less surprising in smaller jurisdictions (notably Northern Ireland, whose population is about 1.8 MM) than in larger ones (e.g., England and Wales or the U.K. as a whole). This is due to the fact that a smaller absolute number of cases can result in a larger percentage fluctuation, and the confidence intervals capture that idea.

In Fig. 2, the confidence intervals created with the Normal approximation of a Poisson random variable and represented by the darkest shades of color show that the U.K. mortality rate did not exhibit steady or monotonic growth over the years 2001–2019. In particular, drug-related mortality rate in the U.K. contracted from 2002 to 2003 and again from 2009 to 2010. The same was true to an even greater degree in England and Wales, where drug-related mortality rate decreased for three consecutive years from 2000 to 2003, again between 2009 and 2010, and between 2018 and 2019, with the majority of observations falling outside the 95% confidence interval.

By contrast, all Northern Irish observations except 2004 fall within the 95% confidence interval. That is in part because Northern Ireland's smaller population leads to a broader confidence interval in percentage terms, but visually the growth in Northern Ireland's mortality rate followed the exponential growth curve, just as Jalal et al. found for the U.S.

Once again Scotland falls in between. Roughly speaking, the broad sweep of the growth in Scotland's mortality rates can loosely be seen as following the exponential growth curve, but that appears to be because of averaging periods with lower growth (i.e., 2008–2013) and periods with higher growth (i.e., 2014–2018).

Our first robustness test confirms that the drug-related mortality rate in England and Wales, Scotland, and the U.K. did not grow steadily during the considered periods. Most observations fell outside from the 95% confidence intervals constructed directly from the Poisson distributions. The 95% prediction intervals of the quasi-Poisson models better capture the trends of each country (Fig. 2), as the majority of observations for all countries fall within the prediction intervals. Nevertheless, Scotland, the United Kingdom as a whole, and particularly England and Wales still have numerous observations that are not accounted for by the 95% prediction intervals for the predictions from quasi-Poisson GLM log-linear models. Almost all Northern Irish observations, instead, fall within the 95% confidence interval computed with the Poisson RVs themselves. Therefore, these additional analyses cautiously support that the drug-related mortality rate in Northern Ireland tends to follow an exponential curve.

As second robustness test we compute posterior predictive tests, which are a type of diagnostic tool used in Bayesian statistics to assess the fit of a statistical model to the data. The basic idea behind these tests is to simulate new data from the posterior predictive distribution of the model and compare it to the observed data. The comparison of the observed data with the posterior predictive distributions indicates that the Poisson model provides a good fit to the Northern Irish data. Contrarily, the posterior predictive tests show systematic discrepancies between the model and the data for the United Kingdom, England and Wales, and Scotland (Fig. 3).

Fig. 4 presents another simple visual display: it plots the year-on-year growth rates over time relative to the overall average annual growth rate. A country with perfectly steady growth would have all its bars with zero height. A country with irregular growth would have many large

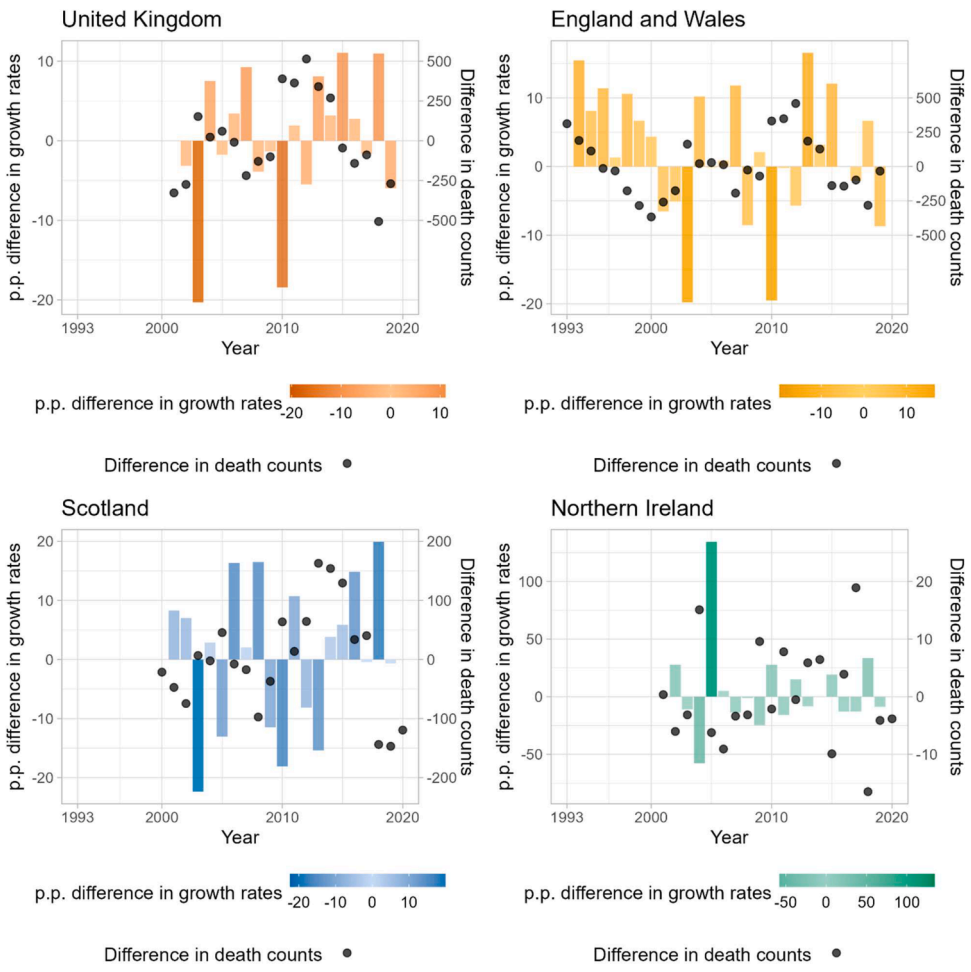

Fig. 4. Differences in growth rates between observed and fitted values.
Note: Fig. 4 displays the difference in annual growth rates of drug-related mortality rates predicted on the base of the fitted exponential curves and actual observations in the U.K., England and Wales, Scotland, Northern Ireland. Differences are expressed in percentage points and shown using colored bars. The dots represent the difference between observed and estimated counts of drug-related deaths in each country.

bars in both the positive and negative directions (indicating years with higher and lower growth than the long run average). Fig. 4 shows that all countries displayed quite unsteady growth with relatively large bars in both directions.

The visual depiction in Fig. 4 can be made more rigorous by measuring the bar heights in terms of z-scores; a given size gap between actual and expected death rates is more surprising (z-score larger in absolute value) for a populous jurisdiction like England and Wales or all of the U.K. than it would be for a less populous jurisdiction such as Northern Ireland. The average z-score is quite large for the U.K. as a whole (4.24) and England and Wales (4.03), intermediate but still large for Scotland (2.60) and smaller for Northern Ireland (0.84). The corresponding probabilities of exceeding such z-values are 0.000 for both the entire U.K. and England and Wales, 0.009 for Scotland and 0.402 for Northern Ireland.

Results for specific drugs

We replicated the analysis just discussed for each of the major drugs individually (Fig. 5). Table 3 summarizes the results, alongside those for the totals across drugs. The analysis shows that trends for individual drugs mostly did not exhibit steady exponential growth. Rather, many followed traditional drug epidemic curves, rising to a peak and then receding, as Jalal et al. (2018) previously observed for various specific drugs in the U.S.

Codeine is the only drug-type whose mortality rate tracked along an exponential curve for the U.K. overall (P(>z-score) = 0.305; p-value $\chi 2$ test 0.080) and for England and Wales (P(>z-score) = 0.460; p-value $\chi 2$ test 0.591). In Scotland none of the drug-specific mortality rates exhibited steady exponential growth.

It is hard to assess Northern Ireland drug-specific mortality rate growth because of the very low annual number of deaths per specific drug (Tab. SM1 in the Supplementary material), but steady growth does not appear to describe the major drugs such as heroin or cocaine. One cannot reject a steady exponential growth model for several other drugs, including: methadone, benzodiazepines, amphetamines, and other opiates, but even for them, the R2 describing the trends of these drugs are relatively low (i.e., Efron's R2 between 0.604 and 0.952). Therefore, in Northern Ireland—as Jalal et al. found for the U.S.—the steadiness in growth of overdoses overall comes not from summing drug-specific curves that grow steadily, but rather from the various drugs "taking turns" in terms of which is driving the growth in total deaths U.S.

Discussion and conclusion

Jalal et al. showed that over the last 40 years fatal overdoses in the U.S. have been rising very steadily by about 7.4% per year even though which specific drugs were contributing to increases have varied. In a mechanical sense, the only way the total could increase steadily when none of its components did so is for the various drug-specific

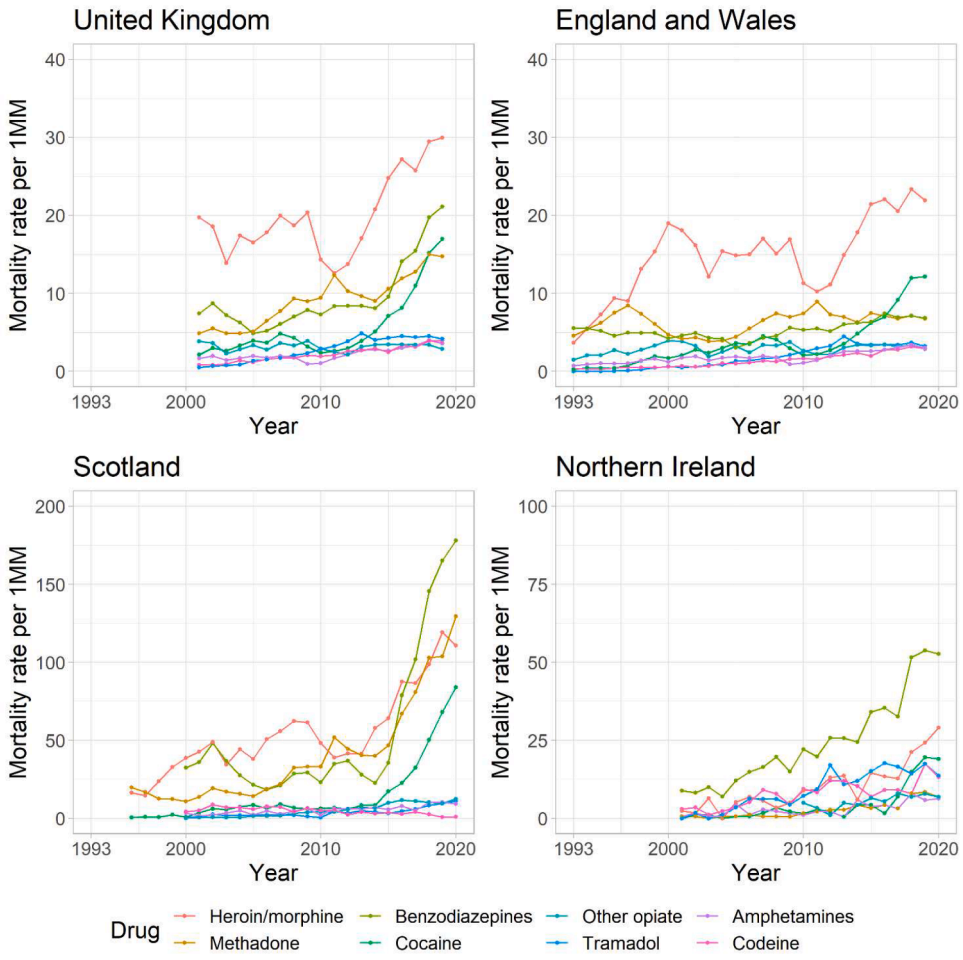

Fig. 5. Drug-related mortality rates by type of drug in the United Kingdom, England and Wales, Scotland, Northern Ireland.
Note: Fig. 5 represents mortality rates by drug type (the eight drug types most frequently involved in drug-related deaths).

components to "take turns", with deaths from a second drug starting sharp increase just as deaths from another drug plateaued. Jalal et al. did not offer or test theories as to what causal mechanisms might underly this peculiar regularity in the increase in aggregated fatal overdoses in the U.S. Did it perhaps reflect some fundamental as-of-yet-unspecified social driver, or was it, for lack of a better word, coincidence?

This journal hosted a forum debating the interpretation of Jalal et al.'s U.S. results, but before investing too much more effort trying to discern causal mechanisms it is worth asking whether the empirical regularity was peculiar to the U.S. or whether it also manifests elsewhere. Hence, we replicated Jalal et al.'s analyses with U.K. countries' data to assess to what extent Jalal et al.'s findings are specific to the U.S.

Our overall finding is a failure to replicate the Jalal et al. result. The exponential function describes the pattern in drug-related mortality rate in Northern Ireland only, but it does not in England and Wales, in Scotland, and in the U.K. as a whole. Departures from the exponential model for Scotland are not particularly pronounced, but in England and Wales, while growth in drug-related mortality rates was sizable, it does not follow an exponential trajectory.

Data availability confronted us with various issues that are described in the supplementary material. However, in our judgment they are not sufficient to account for such a large departure from steady exponential growth if that were in fact a good model of trends in drug-related mortality.

Random variation can obscure true trends, and the U.K. population is only about a fifth of U.S. population. That might raise concerns that steady growth only emerges for a large enough geographic area, such as all of Europe instead of the U.K. or its parts. However, the steady exponential growth model fits better for (relatively small) Northern Ireland than it does for England and Wales (whose population is more than 30 times bigger).

That the drug-related mortality rate did not grow steadily in England and Wales, Scotland, or the U.K. as whole suggests that if there are factors that cause the growth in deaths in the U.S. to be steady they may not be intrinsic human characteristics but rather should be searched for in the contextual features specific to those countries where increases are stable. On the other hand, the North Irish data suggest that exponential growth in rates of fatal overdoses may not be just American exceptionalism.

To be clear, the results here do not offer any explanation of what the causal drivers of steady growth in fatal drug overdoses might be. Whether the reasons behind steady exponential growth where it exists relate to demand or supply mechanisms, to social and political conditions, to coincidence, or to a combination of these factors remains an open question. Nevertheless, additional replication studies that investigate whether there is stable exponential growth in drug-related mortality rates in still other countries could complement efforts to identify such explanations.

Jalal et al. (2018, p. 5) themselves state that "the dynamics of the substance use epidemic are not fully captured in drug overdose mortality data alone. A more complete analysis would also describe the initiation, natural history, treatment, and progression of drug use." However, the more countries there are where summing deaths across drugs converts jumbled, irregular drug-specific death trends into steady patterns overall, the more it might make sense to study and understand trends in drug misuse in aggregate terms. Conversely, the more countries there

Table 3
Summary results of drug-specific analyses.

All drugs	Country			
	England and Wales	Scotland	Northern Ireland	United Kingdom
Growth rate	0.028	0.074	0.106	0.038
R^2	0.844	0.922	0.969	0.869
z-score	4.028	2.600	0.838	4.236
P(>z-score)	0.000	0.009	0.402	0.000
p-value χ^2 test	0.000	0.000	0.185	0.000
Heroin/morphine				
Growth rate	0.033	0.056	0.131	0.032
R^2	0.624	0.752	0.881	0.594
z-score	5.564	3.203	1.049	5.270
P(>z-score)	0.000	0.001	0.294	0.000
p-value χ^2 test	0.000	0.000	0.003	0.000
Methadone				
Growth rate	0.011	0.129	0.187	0.063
R^2	0.334	0.949	0.882	0.893
z-score	3.014	1.956	0.536	2.429
P(>z-score)	0.003	0.050	0.957	0.592
p-value χ^2 test	0.000	0.000	0.957	0.000
Benzodiazepines				
Growth rate	0.016	0.119	0.107	0.072
R^2	0.604	0.740	0.952	0.770
z-score	2.091	6.952	0.696	5.191
P(>z-score)	0.037	0.000	0.486	0.000
p-value χ^2 test	0.000	0.000	0.692	0.000
Cocaine				
Growth rate	0.111	0.212	0.254	0.121
R^2	0.864	0.896	0.867	0.804
z-score	4.071	3.651	1.092	5.630
P(>z-score)	0.000	0.000	0.275	0.000
p-value χ^2 test	0.000	0.000	0.002	0.000
Other opiate				
Growth rate	0.011	−0.059	0.092	−0.001
R^2	0.285	0.467	0.604	0.059
z-score	2.154	1.293	0.618	1.817
P(>z-score)	0.031	0.196	0.536	0.069
p-value χ^2 test	0.000	0.000	0.455	0.000
Tramadol				
Growth rate	0.121	0.157	0.121	0.105
R^2	0.775	0.872	0.728	0.805
z-score	2.737	1.143	1.142	2.439
P(>z-score)	0.006	0.253	0.253	0.015
p-value χ^2 test	−1.000	0.007	0.000	0.000
Amphetamines				
Growth rate	0.046	0.122	0.101	0.055
R^2	0.791	0.859	0.622	0.743
z-score	1.469	1.127	0.862	1.819
P(>z-score)	0.142	0.260	0.389	0.069
p-value χ^2 test	0.000	0.001	0.109	0.000
Codeine				
Growth rate	0.094	0.070	0.077	0.084
R^2	0.971	0.753	0.641	0.957
z-score	0.739	1.127	1.052	1.026
P(>z-score)	0.460	0.260	0.293	0.305
p-value χ^2 test	0.591	0.003	0.038	0.080

Note: Table 3 summarizes results of the fit of the exponential curve to the eight major drugs separately as well as for all drugs combined. For each drug and for each country it provides the growth-rate of the exponential fitted curve (Growth rate), the Efron's R^2 (R^2); the average z-score of the distance of any given year's mortality rate from its expected value under an exponential model (z-score); the probability a normally distributed random variable has a z-score at least as large (P(>z-score)); *p*-value of the deviance goodness of fit χ^2 test (*p*-value χ^2 test): the null hypothesis of the test is that the model is correctly specified.

are whose drug-specific trends do not aggregate into a simple pattern, the more it makes sense to study the patterns one drug at a time, e.g., paying attention to particulars about each drug's mode of administration and distinct target population. In the U.K. countries, the overall drug mortality rate—for the most part—does not exhibit steady exponential growth. This supports the traditional approach to drug policy and prescriptions, which emphasize the need to consider general social and population level dynamics to understand drug epidemics.

Author contributions

The present work is the joint product of the work of all the authors. Alberto Aziani: Conceptualization; methodology; formal analysis; writing. Jonathan P. Caulkins: Conceptualization; methodology; writing.

Declaration of Competing Interest

None to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2023.104146.

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