

## Supplementary information

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## 1. Definition of deaths due to drug poisoning

The Office for National Statistics definition of deaths due to drug poisoning from 2001 onwards are included where one of the ICD-10 codes shown in Table 1 is the underlying cause of death. ICD-9 codes are also included, for the years 1993 to 2000.<sup>1</sup>

Table 1: International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10) codes used to define deaths related to drug poisoning

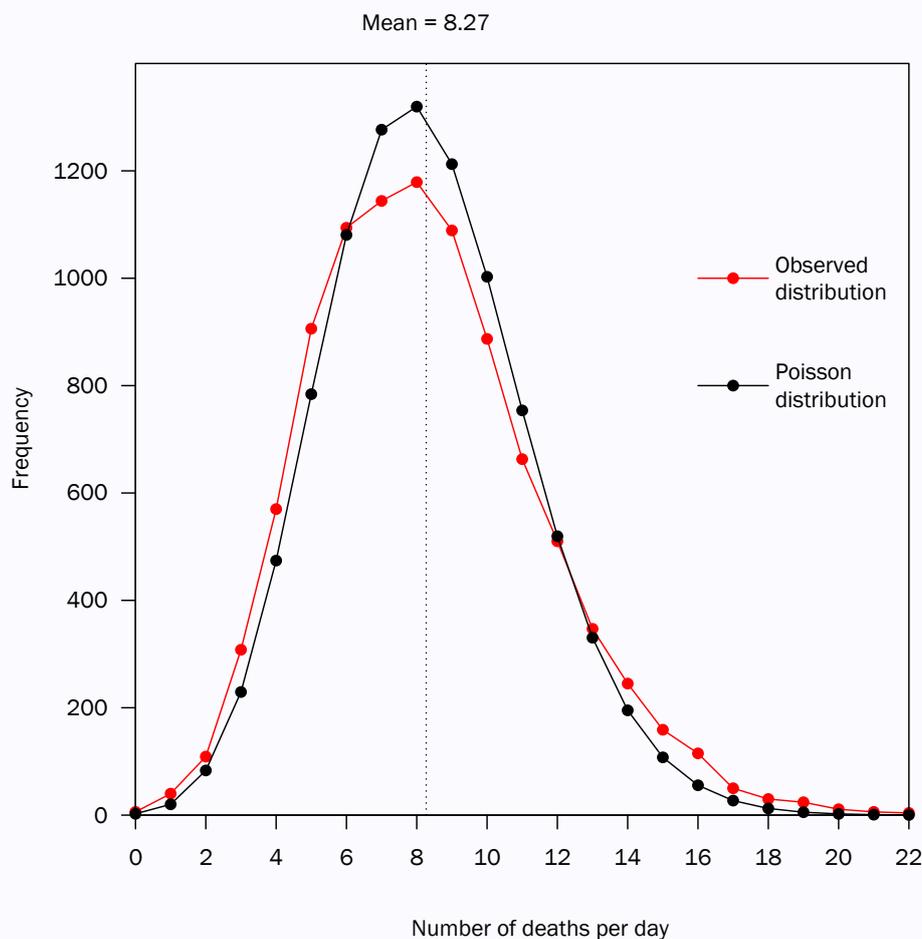
Description	ICD-9 Codes	ICD-10 Codes
Mental and behavioural disorders due to drug use (excluding alcohol and tobacco)	292, 304, 305.2-9	F11-16, F18-19
Accidental poisoning by drugs, medicaments and biological substances	E850-8	X40-44
Intentional self-poisoning by drugs, medicaments and biological substances	E950.0-5	X60-64
Assault by drugs, medicaments and biological substances	E962.0	X85
Poisoning by drugs, medicaments and biological substances, undetermined intent	E980.0-5	Y10-14

## 2. Tests for overdispersion and autocorrelation

### Overdispersion

We compared the distribution of daily drug-related deaths over the full period in the study (1993-2018) to a Poisson distribution for the same number of deaths (Figure 1). This is a crude test of overdispersion and suggests that the variance is similar to the mean.

Figure 1: Observed distribution of drug-related deaths per day in England and Wales between 1993 and 2018, compared to a Poisson distribution for the same number of deaths (78,583)



We then fit Quasipoisson and negative binomial models using the same parameters as the Poisson model used in the main analysis. We compared the models using a likelihood ratio test (since the Poisson model is nested in the Quasipoisson and negative binomial models) and compared the coefficients (Table 2). We did not find evidence that the Quasipoisson model was a better fit than the Poisson model ( $p=1$ ), and the Quasipoisson dispersion parameter was 1.046. There was statistical evidence that the negative binomial model was a better fit than the Poisson model ( $p = 0.005$ ), and the negative binomial dispersion parameter was 201.8. Despite the statistical evidence of overdispersion, the degree of overdispersion was unimportant and the model results were almost identical, hence we used a Poisson model.

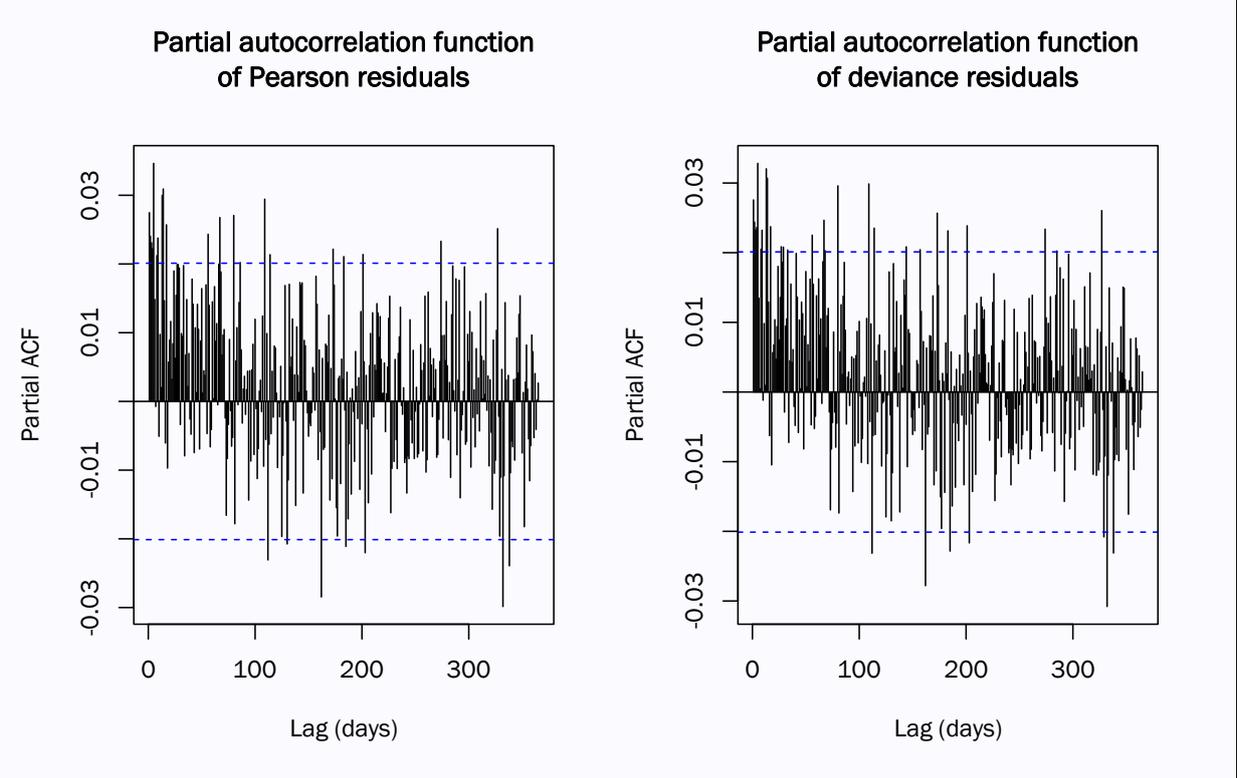
Table 2: Incidence rate ratios (95% CIs) from time series model; where the dependent variable is the count of drug-related deaths in England and Wales between 1993 and 2018

Variable	Level	Poisson model	Quasipoisson model	Negative binomial model
Day of year	First sine term	1.025 (1.015-1.035)	1.025 (1.014-1.035)	1.025 (1.014-1.035)
	First cosine term	0.997 (0.987-1.007)	0.997 (0.987-1.007)	0.997 (0.987-1.007)
	Second sine term	1.000 (0.990-1.010)	1.000 (0.989-1.010)	1.000 (0.990-1.010)
	Second cosine term	1.001 (0.991-1.011)	1.001 (0.991-1.012)	1.001 (0.991-1.012)
	Third sine term	1.000 (0.989-1.010)	1.000 (0.989-1.010)	1.000 (0.989-1.010)
	Third cosine term	1.006 (0.996-1.016)	1.006 (0.995-1.016)	1.006 (0.995-1.016)
Holiday	Not holiday (ref)	1	1	1
	Christmas	1.002 (0.948-1.059)	1.002 (0.947-1.060)	1.002 (0.947-1.060)
	New Year	1.239 (1.134-1.351)	1.239 (1.132-1.354)	1.239 (1.132-1.354)
	Other holiday	0.970 (0.927-1.013)	0.970 (0.926-1.014)	0.969 (0.926-1.014)
Long term trend	Days (linear)	0.904 (0.888-0.920)	0.904 (0.888-0.920)	0.904 (0.888-0.920)
	Days ^ 2 (quadratic)	1.149 (1.117-1.181)	1.149 (1.117-1.181)	1.148 (1.116-1.181)
	Days ^ 3 (cubic)	1.125 (1.115-1.135)	1.125 (1.115-1.135)	1.125 (1.115-1.135)
	Days ^ 4	0.968 (0.959-0.978)	0.968 (0.958-0.979)	0.969 (0.959-0.979)
Weekday	Monday	1	1	1
	Tuesday	0.983 (0.958-1.010)	0.983 (0.957-1.011)	0.983 (0.957-1.011)
	Wednesday	1.022 (0.995-1.049)	1.022 (0.994-1.050)	1.022 (0.994-1.050)
	Thursday	0.987 (0.961-1.014)	0.987 (0.960-1.014)	0.987 (0.960-1.014)
	Friday	1.016 (0.990-1.044)	1.016 (0.989-1.044)	1.016 (0.989-1.044)
	Saturday	1.048 (1.021-1.076)	1.048 (1.021-1.077)	1.048 (1.021-1.077)
	Sunday	0.997 (0.971-1.024)	0.997 (0.971-1.025)	0.997 (0.971-1.025)
Week of month	First (ref)	1	1	1
	Other	0.990 (0.973-1.007)	0.990 (0.972-1.008)	0.990 (0.972-1.008)
	Last	0.990 (0.970-1.011)	0.990 (0.969-1.012)	0.990 (0.969-1.012)

## Autocorrelation

We tested for the presence of autocorrelation by plotting the correlation between model residuals and lagged differences, adjusting for intermediate differences (ie. the partial autocorrelation function), using the R function `tseries::pacf`. This is shown in Figure 2. The figure suggests minimal autocorrelation, ie. the assumption that drug-related deaths occur randomly over time conditional on the independent variables appears reasonable.

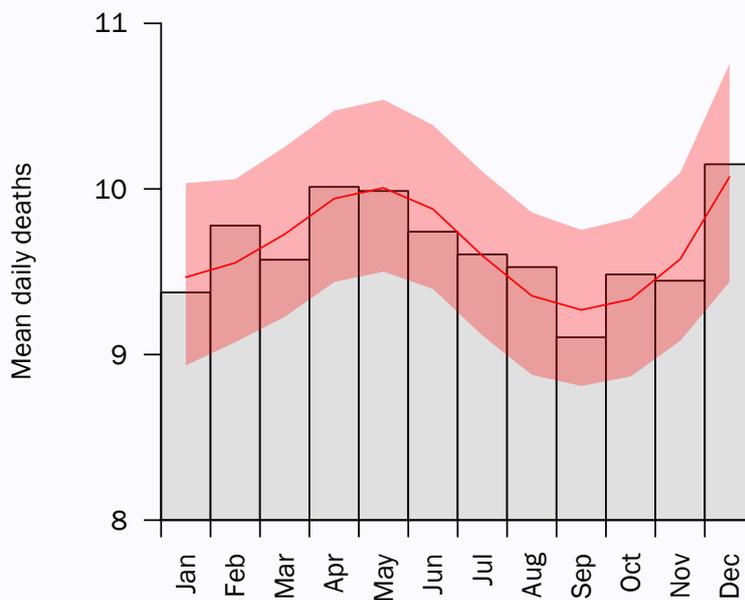
Figure 2: Partial autocorrelation functions, testing for autocorrelation in Poisson analysis



### 3. Comparison between observed counts of deaths per months and predicted trend using harmonic terms

In our time series model, we used harmonic terms (three pairs of sine and cosine terms) on the proportion of the year elapsed (eg. where 17 February 2016 is coded as  $48/366 = 0.1311$ , as this is the 48th day of the year and calendar year 2016 had 366 days). To visualise the this approach, we compared the observed mean daily deaths in each calendar month from 2011-2018 with the mean predicted by the model (Figure 3).

Figure 3: Mean daily deaths in each calendar month from 2011-2018, compared to the mean predicted by a Poisson model using harmonic terms (red band shows 95% confidence interval)



## 4. Detailed results stratified by time period

Table 3: Summary of cyclical variation in drug-related deaths in England and Wales, by time period

Time period	Variable	Peak	Low	Evidence of Variation*	Peak-to-low ratio (95% CI)	Attributable deaths (95% CI)
1993-2001	Season	2 April	20 October	None ( $p=0.259$ )	1.09 (1.05-1.13)	109 (55-174)
	Week of month	Other	Last	None ( $p=0.886$ )	1.02 (1.00-1.05)	32 (4-91)
	Weekday	Saturday	Sunday	Weak ( $p=0.010$ )	1.09 (1.05-1.13)	135 (68-215)
	Public holiday	New Year	Other public holiday	None ( $p=0.061$ )	1.28 (1.09-1.50)	191 (9-406)
2002-2010	Season	1 May	22 July	None ( $p=0.443$ )	1.08 (1.04-1.13)	97 (46-161)
	Week of month	First	Last	None ( $p=0.112$ )	1.04 (1.01-1.08)	51 (11-108)
	Weekday	Saturday	Tuesday	Moderate ( $p=0.002$ )	1.11 (1.06-1.16)	123 (65-198)
	Public holiday	New Year	Christmas	Weak ( $p=0.043$ )	1.31 (1.10-1.54)	124 (5-312)
2011-2018	Season	4 May	30 September	Strong ( $p<0.001$ )	1.13 (1.09-1.18)	296 (196-412)
	Week of month	Last	Other	None ( $p=0.173$ )	1.03 (1.01-1.06)	51 (14-102)
	Weekday	Saturday	Tuesday	Weak ( $p=0.023$ )	1.08 (1.05-1.12)	178 (91-286)
	Public holiday	New Year	Other public holiday	Weak ( $p=0.013$ )	1.31 (1.13-1.52)	104 (9-435)

\* Classified as strong where  $p \leq 0.001$ ; moderate where  $p \leq 0.01$ ; weak where  $p \leq 0.05$ ; and none where  $p > 0.05$ .

Figure 4: Daily drug-related deaths in England and Wales by calendar month. Error bars show 95% confidence intervals.

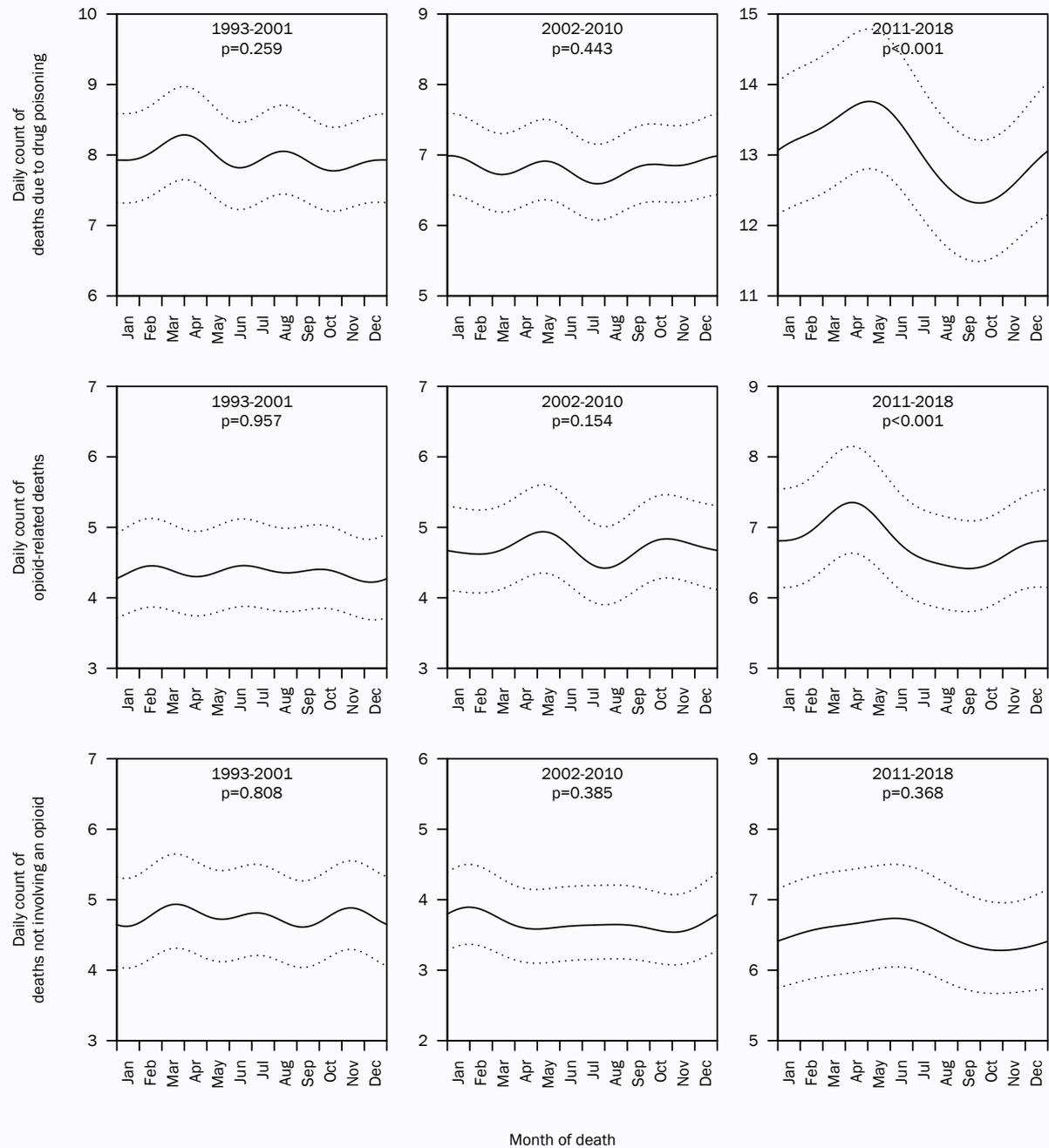


Figure 5: Daily drug-related deaths in England and Wales by week-of-month. Error bars show 95% confidence intervals.

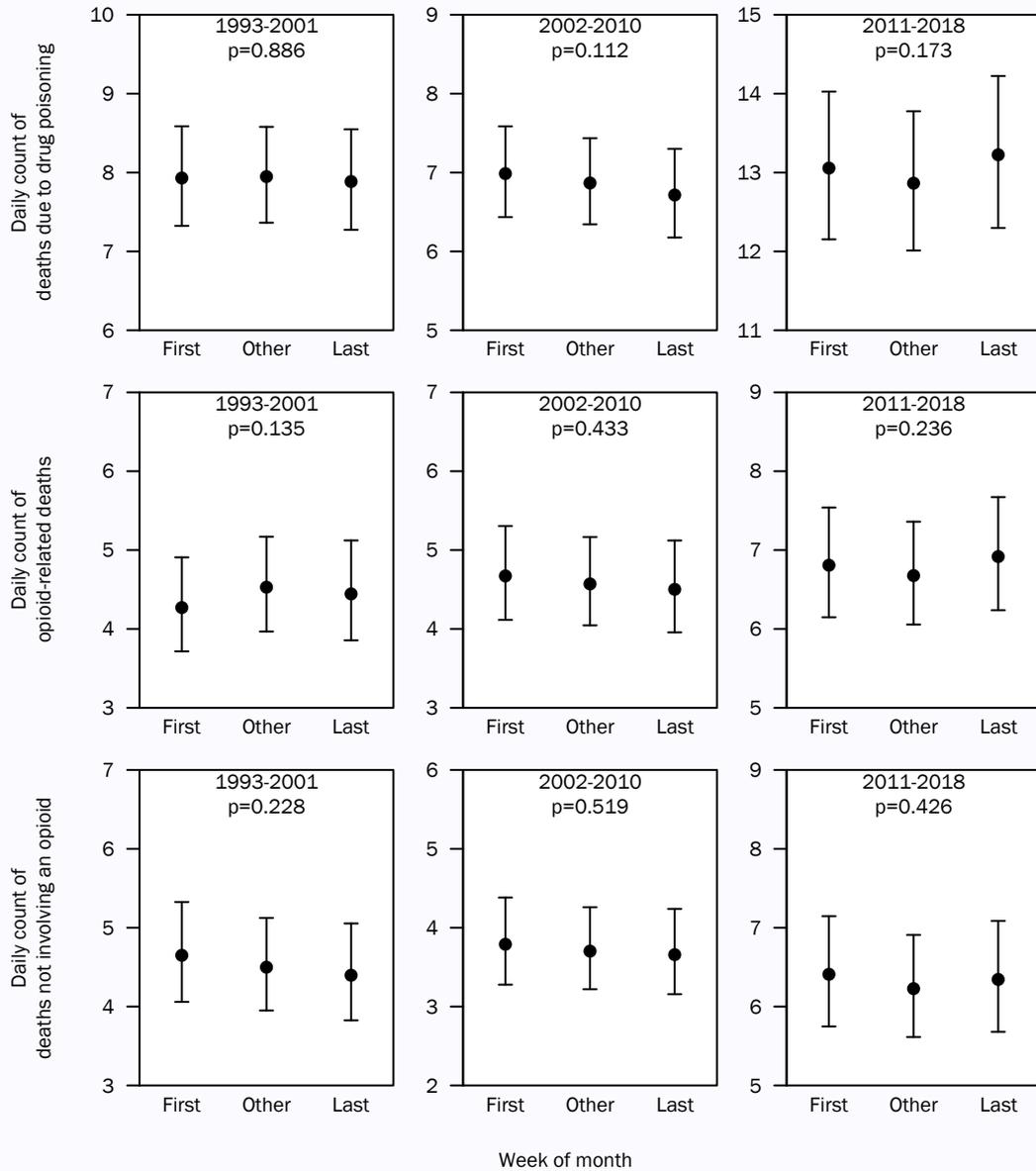


Figure 6: Daily drug-related deaths in England and Wales by weekday. Error bars show 95% confidence intervals.

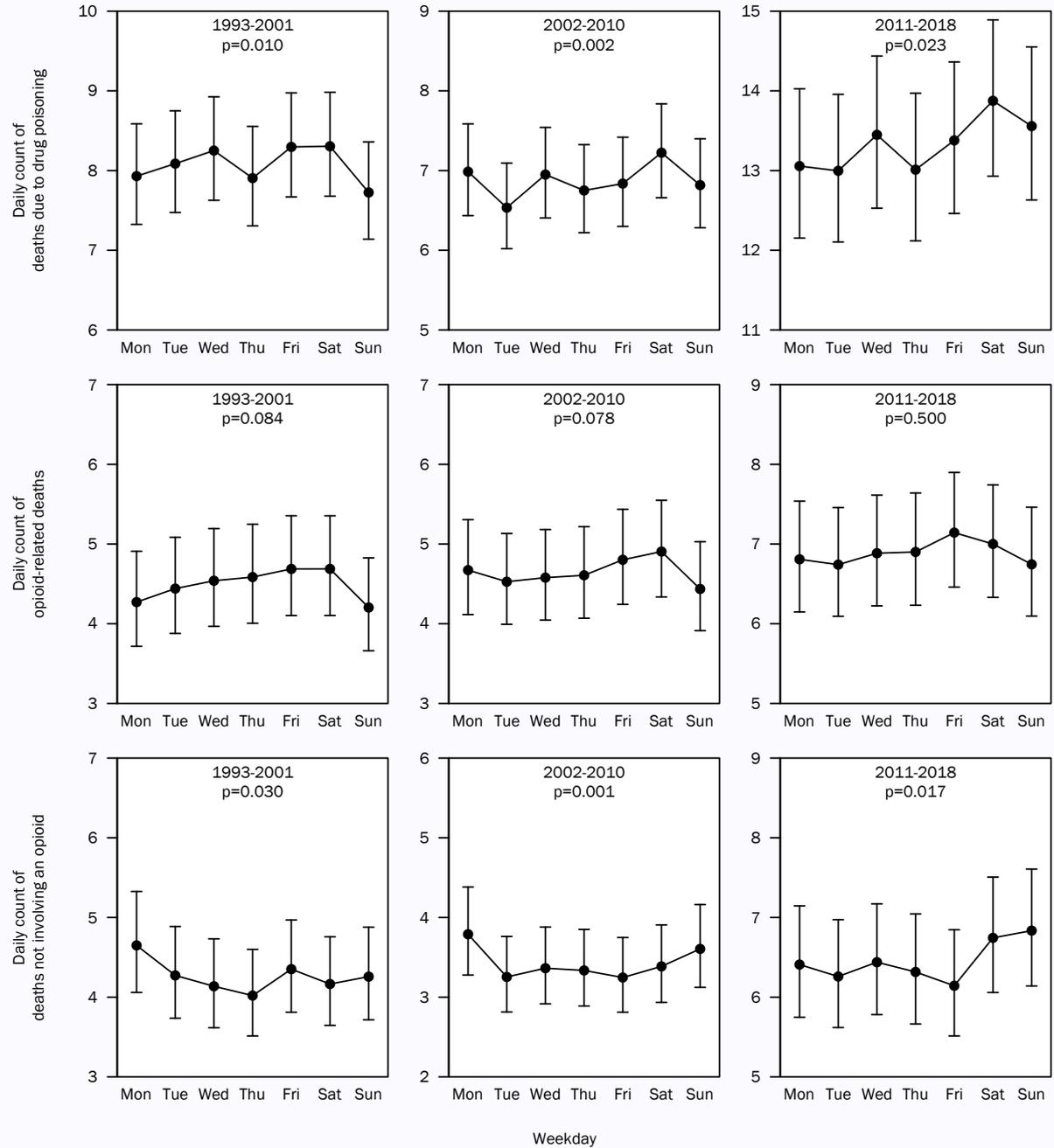
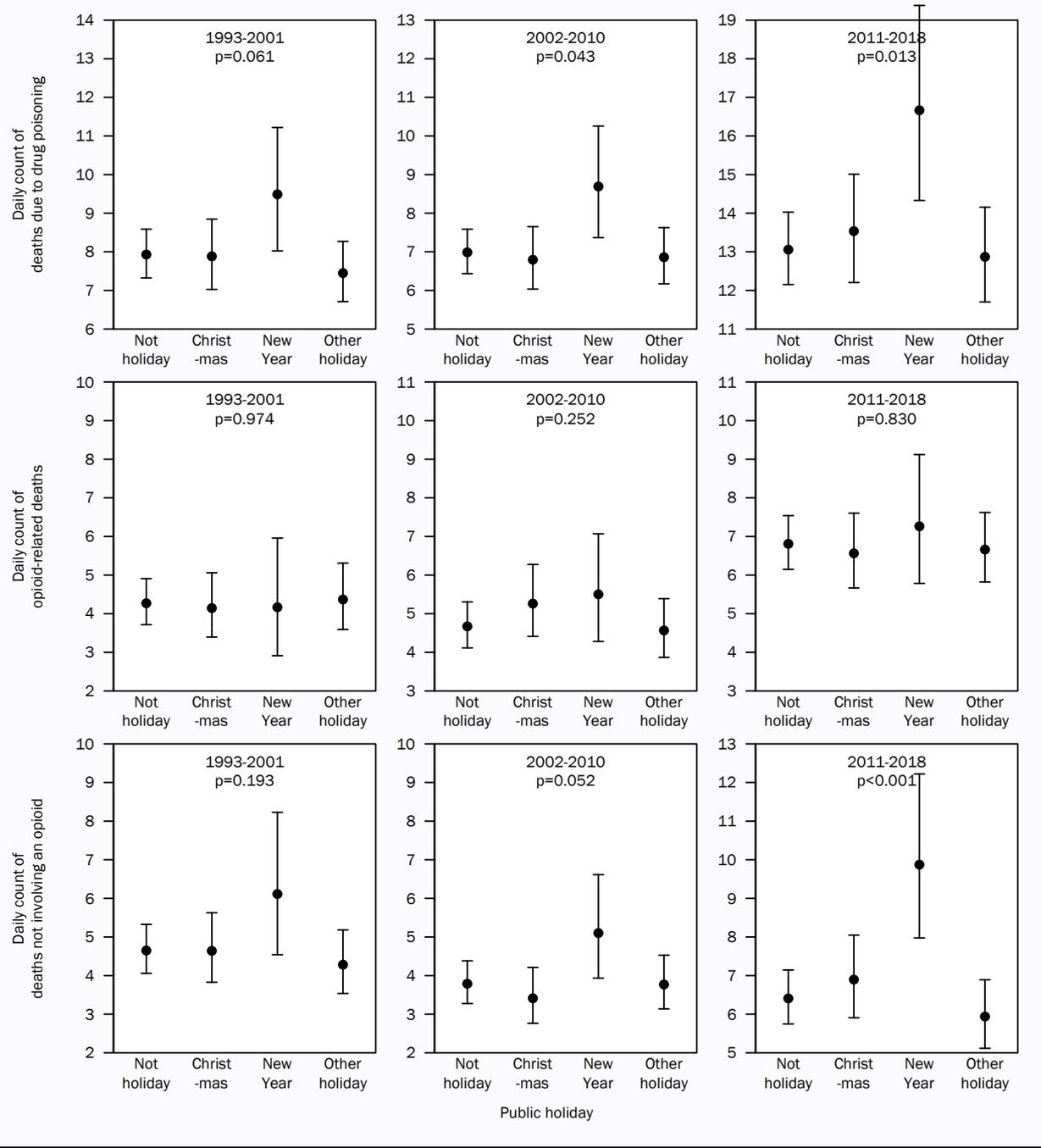


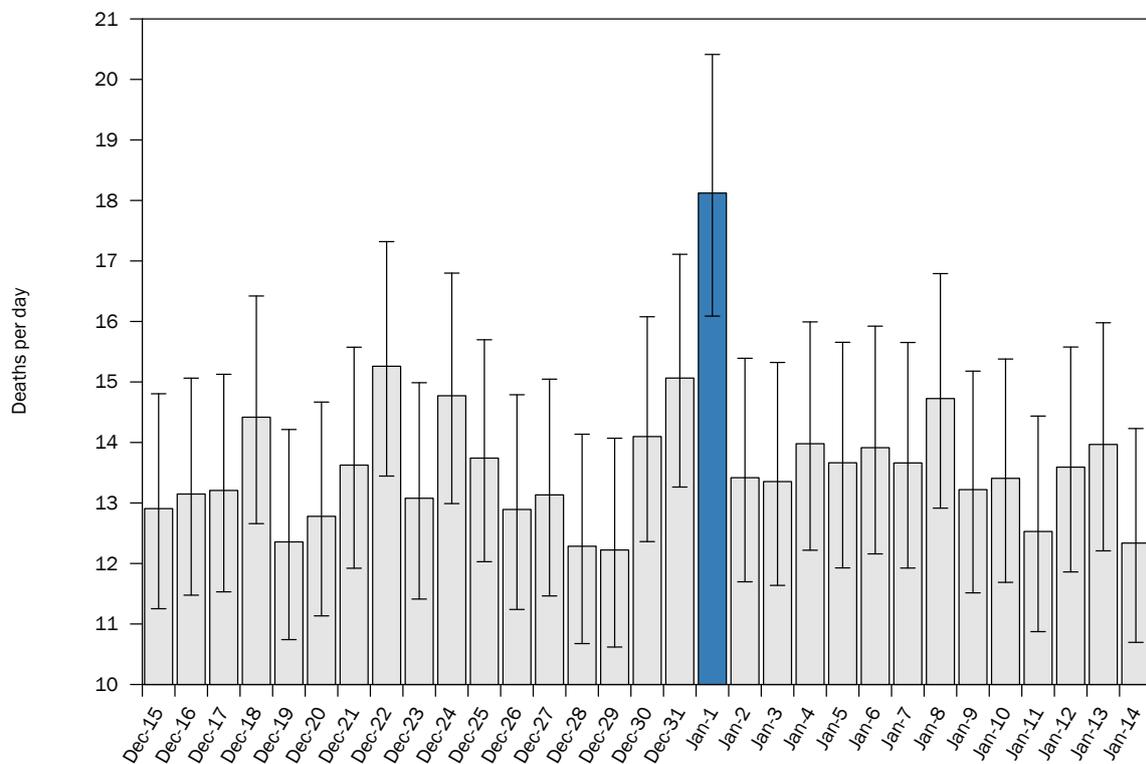
Figure 7: Daily drug-related deaths in England and Wales by public holiday. Error bars show 95% confidence intervals.



## 5. Estimated daily deaths between 15 December and 15 January

We planned to report the count of drug-related deaths by Christmas, public holidays and New Year. In our analysis plan, New Year was defined as 31 December and 1 January. We observed a substantially increased risk of death at New Year. In exploratory analysis after observing this result, we estimated the number of deaths on each day of the year. We did this by classifying each day in our dataset by the calendar month and day (ie. a variable with 365 levels of “1 January”, “2 January” etc.). We then fit a Poisson regression model with a dependent variable of the count of deaths, and independent variables of the month/day and polynomial terms for time (days since 1 January 1993), as in the main analysis. We then predicted the number of deaths for each month/day when the long-term trend was set to 31 December 2018. The results for 15th December – 15th January are shown in Figure 8.

Figure 8: Predicted deaths by day between 15th December and 15th January. Error bars show 95% confidence intervals.



## 6. Drug-related deaths in England and Wales, by selected substances

Table 4 shows the number of deaths due to drug poisoning in England and Wales, and the number with selected substances mentioned on the death certificate.<sup>2</sup> Values in the 'drug poisoning' column correspond to data used in the present study. Other columns are subsets of this value, but are not mutually exclusive because multiple drugs may contribute to a one death.

Table 4: Deaths in England and Wales by date of occurrence and presence of selected substances on the death certificate

Year	All drug poisoning	Any opiate	Antidepressant	Benzodiazepines	Paracetamol	Novel psychoactive substances	Amphetamine	Antipsychotic	Zopiclone / Zolpidem	Ecstasy / MDMA	Cannabis
2020*	4586	2170	571	507	208	194	180	167	130	70	30
2019*	4664	2280	489	436	227	110	193	132	150	86	39
2018	4586	2288	482	427	238	167	208	148	147	86	26
2017	4045	2094	526	410	211	96	181	125	138	84	22
2016	3972	2126	498	437	241	91	163	128	116	62	31
2015	3748	2057	445	367	192	128	149	95	84	52	22
2014	3307	1773	447	356	184	87	148	112	101	58	23
2013	3116	1676	498	343	215	71	145	115	87	43	18
2012	2734	1368	453	291	213	76	116	108	86	40	11
2011	2690	1420	449	308	177	43	81	97	87	26	12
2010	2572	1391	367	295	204	25	59	103	59	11	11
2009	2962	1684	418	308	229	23	49	87	76	4	15
2008	2867	1532	385	249	277	26	98	88	55	42	21
2007	2918	1587	380	234	249	17	106	89	51	53	18
2006	2703	1357	363	196	282	10	93	82	36	49	15
2005	2744	1311	375	164	403	5	101	91	55	49	19
2004	2815	1250	431	222	472	4	92	87	50	53	17
2003	2655	1062	456	226	494	3	74	62	50	39	12
2002	2861	1301	423	258	481	4	101	61	47	59	17
2001	3040	1440	427	240	567	6	91	64	39	63	15
2000	3118	1502	465	220	566	2	63	79	35	40	11
1999	3092	1360	513	255	577	1	83	64	29	28	8
1998	3036	1217	528	254	633	2	73	57	14	17	6
1997	2928	1048	545	256	677	1	54	59	15	13	13
1996	2786	1045	546	234	576	0	51	50	11	18	12
1995	2625	812	493	265	630	2	52	57	10	13	18
1994	2427	690	481	282	544	0	47	56	7	28	18
1993	2253	521	461	282	533	0	36	52	2	8	14

\* 2019 and 2020 are not included in the present study because counts of deaths by date of occurrence are not reliable in recent years.

## 7. References for supplementary information

- 1 Office for National Statistics. Deaths related to drug poisoning in England and Wales QMI. 2018.  
<https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/methodologies/deathsrelatedtodrugpoisoninginenglandandwalesqmi> (accessed July 22, 2020).
- 2 Office for National Statistics. Deaths related to drug poisoning by date of occurrence, England and Wales. 2022.  
<https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathsrelatedtodrugpoisoningbydateofoccurrence> (accessed Sept 2, 2022).