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# Fatal opioid poisoning: a counterfactual model to estimate the preventive effect of treatment for opioid use disorder in England

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## ABSTRACT

**Aim** A counterfactual model was used to estimate the number of fatal opioid-related poisonings prevented by public treatment services for opioid use disorder (OUD) in England between April 2008 and March 2011. **Methods** Patient OUD treatment episode data recorded by the English National Drug Treatment Monitoring System were linked to data on opioid deaths recorded by the Office for National Statistics. The source population was the official estimate of non-medical opioid users (aged 15–64 years; approximately 260 000 each year). The target population was all individuals (aged 15–64 years) treated for OUD in the study period ($n = 220\,665$). The outcome measure was fatal opioid-related poisoning (opioid death). The opioid death rate [per 100 person-years (PY)] and mortality rate ratios (MRR) were computed for study year, age group (15–24, 25–34, 35–64 years) and for three treatment-related states: time spent 'prior to treatment', 'during treatment' and 'after treatment'. **Results** Between April 2008 and March 2011, there were 3731 opioid deaths in the study: 741 during treatment (0.20 per 100 PY; referent category); 2722 prior to treatment [0.77 per 100 PY; MRR = 3.76, 95% confidence interval (CI) = 3.18–4.44]; and 268 after treatment (0.41 per 100 PY; MRR = 1.99, 95% CI = 1.64–2.41). By counterfactual estimation, national OUD treatment services prevented an average of 880 opioid deaths each year (95% CI = 702–1084). **Conclusions** Between April 2008 and March 2011, a counterfactual model shows that the English public treatment system for opioid use disorder prevented an average of 880 deaths each year from opioid-related poisoning. Counterfactual models of mortality prevention can be used for outcome and performance monitoring of substance use disorder treatment systems.

**Keywords** Counterfactual model, fatal opioid poisoning, opioid use disorder, treatment.

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## INTRODUCTION

The non-medical use of opioid drugs (particularly illicit heroin) is associated with premature death in many countries (22–54 drug-related deaths per million population aged 15–64 in 2011 [1]). One per cent of the illicit opioid-using population dies each year, a rate 10 times higher than the general population [2,3]. Their most common cause of death is acute opioid-related poisoning following accidental overdose inducing respiratory depression, hypoventilation and hypoxia [4]. Opioids are also frequently mentioned in mortality records which describe violence, road traffic accidents and long-term health conditions [5].

The opioid medications methadone and buprenorphine are front-line, randomized controlled trial-supported therapies for the treatment of opioid addiction [6]. Opioid addiction is diagnosed as opioid dependence or opioid use disorder by two conceptually identical systems (World Health Organization, ICD-10 [7] and American Psychiatric Association, DSM-5 [8], respectively; OUD herein). In most countries, methadone and buprenorphine treatment for OUD are provided by specialist community, primary care and hospital providers. In-patient withdrawal management services and drug-free residential rehabilitation are also available.

In addition to case management, national clinical guidelines recommend additional psychosocial interventions to

address cognitive and behavioural symptoms of OUD and comorbid psychiatric disorders (e.g. National Institute for Health and Care Excellence for the UK [9]). Some OUD patients receive psychosocial interventions without an opioid medication. Taken together, longitudinal cohort studies have demonstrated the effectiveness of these services in public treatment systems [10–13].

During screening and case formulation, clinicians assess a patient's drug overdose history and deliver appropriate interventions to reduce risk. It is difficult to determine the specific effectiveness of this element of OUD programmes in health services evaluation studies, but patient self-reports suggest that treatment reduces the risk of overdose [14,15]. Epidemiological studies which link patient and public mortality records show that the rate of fatal opioid-related poisoning (opioid death herein) is reduced substantially during treatment, but then increases during the first few weeks after leaving [16–20].

Treatment policy and service commissioning would benefit from regular evaluation of the preventive effect of treatment on opioid mortality, but database linkage studies are conducted infrequently. In this report, we present a counterfactual model to estimate the preventive effect of OUD treatment on opioid death. Framing questions about events using counterfactual conditional logic has deep roots in the philosophy of causation [21,22], and has been used for health-care modelling studies (e.g. cancer [23]; tobacco smoking [24]). To our knowledge, counterfactual estimation has not been used to estimate the effectiveness of OUD treatment.

A counterfactual statement takes the general form: 'if X had not happened, then Y would have happened'. To give a simple example: a traveller changes their mind and decides to avoid boarding a train that crashes subsequently. On the assumption that their presence on board has no influence on the train's risk of crashing, then if the decision to change travel plans (X) had not happened, the traveller would have been in the accident (Y).

Our focus concerns a target outcome (Y; 'opioid death') and an event (X; treatment for OUD). For an individual who is at risk of an opioid death and is considering entering treatment, we can ask the question: 'If this person is not treated will they die?'. Ethical principles for research preclude an experimental design to test this question, and the problem with non-experimental designs is that it is not possible to evaluate Y with and without X in the same study participant. Although causal effects cannot be determined at the individual level, non-experimental studies are able to use aggregation in the population to estimate what Rubin calls the average causal effect [21].

Accordingly, the aim of this study was to estimate the preventive effect of OUD treatment in England on opioid death. We asked the following counterfactual question: 'how many opioid misusers would have an opioid death if they were not treated, and how does this compare to the actual rate?'. This report presents the results of our analysis.

## METHOD

### Design and outcome

This was a counterfactual model of opioid death prevented by treatment for OUD in England. The outcome measure was fatal opioid-related poisoning recorded by the Office for National Statistics (ONS [25]) using codes from the World Health Organization (WHO)'s International Statistical Classification of Diseases and Related Health Problems (ICD-10 [7]) and with reference to the coroner's inquest report and/or certificate. The number of opioid deaths fluctuates, so the present study covered a 3-year period.

Following the approach taken by ONS, case definition was met where death was attributed to: 'Mental and behavioural disorders due to drug use' (ICD-10 codes: F11-F16, F18, F19) and an opioid was mentioned on the death certificate; or to any of the following: 'Accidental poisoning by drugs, medicaments and biological substances' (X40–X44); 'Intentional self-poisoning by drugs, medicaments and biological substances' (X60-X64); 'Assault by drugs, medicaments and biological substances' (X85); and 'Poisoning by drugs, medicaments and biological substances, undetermined intent' (Y10–Y14), where any controlled drug[1] and an opioid was mentioned (and potentially referring to the same drug, such as heroin).

### Source and target population

The source population was the national estimate of illicit opioid users in England (aged 15–64 years) for April 2008–March 2011. A university research group calculates this estimate for the April–March financial year using capture–recapture and multiple indicator estimation techniques at the level of the local treatment system. The group then tabulates the estimate at the national level by three age-bands: 15–24, 25–34 and 35–64 years [26].

The target population for the study was all patients (15–64 years) who received treatment for OUD from a specialist clinic or primary care team in the National Health Service (NHS) or a non-governmental organization between April 2008 and March 2011. Patient data were reported to the English National Drug Treatment Monitoring System (NDTMS). NDTMS includes almost all specialist treatment services in the country and provides national

[1]For this definition, ONS does not include compound analgesics based on paracetamol or ibuprofen, which contain relatively small amounts of opioids (e.g. dextropropoxyphene in co-proxamol, dihydrocodeine in co-drydamol and codeine in co-codamol).

outcome monitoring and performance benchmarking for each local treatment system (for an operational description see Marsden *et al.* [13]).

The target population comprised patients who received a single episode of OUD treatment as well as those who had two or more episodes, either concurrently or consecutively. It included those who commenced treatment in the study period and those who were already enrolled in April 2008. Variables for the study obtained from service provider reports to NDTMS were as follows: date of admission and discharge for each treatment episode; reasons for leaving treatment; and reports of patients who died (see procedure below for descriptions).

### Procedure

At the level of clinical service delivery, each patient gave their informed consent for their data to be used for aggregated analysis. Aggregated and encrypted NDTMS data are not subject to research ethical clearances, but approval for data sharing was secured from the ONS Microdata Release Panel.[2] With this agreement in hand, we obtained an extract from the ONS poisoning database, which included demographic information and the date of all opioid deaths in England (15–64 years; 2008–11).

At this point, it is helpful to illustrate the way in which opioids are mentioned in coronial reports and death certificates: across the study period there were 3731 opioid deaths (see Table 1), of which 406 (11%) certificates did not specify the exact opioid. For the remaining 3325 deaths, 1968 certificates (59%) specified heroin/morphine and 1112 certificates specified methadone (33%).[3] For the remaining cases, codeine and dihydrocodeine were mentioned in 242 and 243 death certificates, respectively. In 2010, there was a notable decline in the proportion in which heroin was specified (49%), and an increase in the proportion in which methadone was specified (41%) compared to the first 2 years of the study. We took all opioid deaths to be from the source population.

Estimates for the counterfactual model were generated in three steps, as follows:

**1** Database linkage

The NDTMS and poisoning databases were linked using a protocol developed by Pierce *et al.* [20]. Patient information (initials, date of birth and gender) was used to search for a probabilistic match to a death recorded in the poisonings database. Local government region of residence[4] was also used to capture patients who moved to another area within the same region after leaving treatment and then died.

While developing the Pierce protocol, author T.M. assessed the matching algorithm using an NHS data set for the UK population (in which unique identifying information was additionally available) and observed that the level of false positive matching for all-cause mortality did not exceed 10%. For the present study, this rate is likely to be much lower because opioid deaths are relatively rare in the general population and largely confined to the illicit opioid-using population.

Nine separate analyses were conducted, one for each combination of the 15–24, 25–34 and 35–64 age bands and for each April–March financial year (2008, 2009, 2010). Within each analysis, all members of the source population were assumed initially to be at risk of an opioid death on each day of each year [thereby contributing 1 person-year (PY) of risk exposure]. As these analyses were mutually exclusive, they were aggregated by age and year.

Where a match was found, the risk period was truncated to the date of death on the poisonings database. In the event that a patient died in treatment (i.e. their treatment episode was terminated due to their death) but no match could be found in the poisonings database, the risk period was truncated to the date of discharge from treatment as a proxy because the date of death was unknown. Non-matched decedents reported to NDTMS were assumed to have died from a different cause. We recognized that there would be similar decedents in the untreated population, but there was no means of accounting for this in the data.

**2** Time prior to, during and after treatment

Within each analysis, the number of days each individual spent in three treatment-related states was calculated, as follows:

- prior to treatment (i.e. the individual had not yet been admitted to treatment in the risk period);
- during treatment; and
- after treatment (i.e. the time following treatment and between any subsequent episodes).

Subtraction of the target population from the source population each year gave an estimate of the number of opioid users not treated. As these individuals never entered treatment, they were assigned to the prior to treatment state throughout their risk period.

**3** Assigning decedents to treatment state

Each death was assigned to a treatment-related state by comparing the date of death from the poisonings database with the date of discharge recorded on NDTMS. The assignment rules were as follows:

- if not treated, the decedent was assigned to the prior to treatment state;

[2]The study was based on encrypted data on which ethics committees do not require informed consent. All patient data reported to NDTMS are based on local informed consent procedures.

[3]2842 cases (85%) mentioned either heroin/morphine or methadone.

[4]Local government region, accessed on 01.03.15 at:https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/7448/1622442.pdf.

**Table 1** Number of opioid users (95% confidence interval), total person-years of follow-up (PY) and number in treatment by number of opioid deaths in each treatment state (England: 2008–11; 15–64 years).

| | | | | *Opioid deaths by treatment state* | | | |
|---|---|---|---|---|---|---|---|
| *Year* [a] | *Number of opioid users (source population)* | *Total person-years (PY)* [b] | *Number in treatment* | *Prior to treatment* | *During treatment* | *After treatment* | *All* |
| 2008 | 262 428 (257 518–269 996) | 261 488 (256 578–269 056) | 160 972 | 934 | 235 | 93 | 1262 |
| 2009 | 264 073 (256 681–270 611) | 262 986 (255 594–269 525) | 165 214 | 1007 | 257 | 107 | 1371 |
| 2010 | 261 793 (255 405–268 699) | 260 827 (254 438–267 732) | 165 402 | 781 | 249 | 68 | 1098 |
| Total | – | 785 301 (766 610–806 313) | 220 665 | 2722 | 741 | 268 | 3731 |

Totals in all tables may not sum due to rounding. [a]Financial year (April–March 2008–09; 2009–10; 2010–11). [b]Each person is subject to 1 PY for each year eligible, or their risk period is truncated to the date of their death.

- if the date of death indicated they had died during treatment, the decedent was assigned to the during treatment state; or
- if the date of death was after discharge, the decedent was assigned to the after treatment state.

We decided to add a conservative clause to these assignment rules as follows: if it was reported that a patient had either died while in treatment, or had left treatment without notice or advice and the poisonings database indicated that they had died within 14 days of discharge, the death was assigned to the during treatment state.

In England, a medical prescriber's instruction for methadone and buprenorphine can be authorized for a maximum of 14 days.[5] Therefore, the patient was assumed to have been assigned a discharge date with the last face-to-face contact and to still be in receipt of an opioid prescription when they died (as per NDTMS definitions[6]).

### Statistical analysis

The statistical analysis plan was based on the assumption that the risk of opioid death did not differ among those admitted to treatment in the study period and those not treated, so that comparisons could be made between individuals in the same age group in different treatment states. The analysis (two-sided hypothesis testing with alpha at 5%) was performed in SPSS (version 21) in three steps:

**1** Number and opioid death rate in each treatment state

The time each individual spent in the three treatment-related states was aggregated across the 3 years and tabulated by age band. The number of opioid deaths was expressed as an unadjusted rate per 100 PY for each state and as a time-specific mortality rate ratio (MRR).[7] Ninety-five per cent confidence intervals (CI) were computed by the Wilson score interval method [27]. The size of the source population used a CI computed as part of the derivation of the original local estimate [26]. As this would create uncertainty in the calculation of the volume of person-time (specifically for the prior to treatment state given that OUD treatment numbers are known), a conservative approach was followed to anchor the lower bound of each mortality rate for the prior to treatment state on the upper bound of the source population.[8]

For each MRR, CIs were computed by contrasting the upper and lower bound on the opioid death rates in each treatment-related state. Each lower bound was computed as the ratio of the lower bound of the given rate to the upper bound of the during treatment rate (as referent; and vice versa). We judged that this approach was justified because of the greater uncertainty about person-time in the prior to treatment state.

**2** Prior to treatment death rate applied to the source population

The counterfactual mortality estimate was calculated by applying the death rates in the prior to treatment state to the whole source population within each age group. This modelled a scenario in which no member of the source population received any treatment across the three years. CIs were applied to these estimates, taking into account the uncertainty in the size of the source population.[9]

**3** Estimation of the number of fatal opioid poisonings prevented by treatment

The observed numbers of opioid deaths were subtracted from the counterfactual estimate to give an estimated number of excess opioid deaths in the counterfactual scenario within each age group. The estimates were divided by three to give annual averages.

[5]See http://www.nhsbsa.nhs.uk/PrescriptionServices/Documents/PPDImpact/imPACTjul2006.pdf

[6]See http://www.nta.nhs.uk/uploads/adultdrugtreatmentbusinessdefinitionv11.03.pdf, p.14—'If a client's discharge was unplanned then the date of last face to face contact with the treatment provider should be used'.

[7]The MRR is the ratio of the opioid death rate per 100 PYs (during treatment rate as referent).

[8]And *vice versa* for the upper bounds, which were anchored to the lower bounds of the source population.

[9]In order to derive the lower bound of the counterfactual estimate, the lower bound of the confidence interval limit of the prior to treatment death rate was applied to the upper bound of the size of the source population (from which it is ultimately derived), and vice versa.

*Sensitivity analysis*

The time individuals from the target population spent in the after treatment state was variable, but our decision rule truncated this time at the end of each year. Using our classification rules, the scenario in which a patient left treatment in the latter part of a year and then died in the early part of the following year would be classified as a death in the prior to treatment state, despite the patient having recently received treatment.

A sensitivity check was therefore used to determine whether the variable follow-up time inflated the mortality rate in the prior to treatment state relative to the after treatment state. All estimates were re-calculated with treatment leavers initially assigned a uniform 365-days follow-up period in the after treatment state, including where this crossed into the next financial year. Individuals already in this state at April 2008 were included and all individuals were followed-up to March 2011.

In the event of a re-admission to treatment or an opioid death within the follow-up period, we truncated the time spent in the after treatment state. With the indication of either event, any time identified within the follow-up period and within the next financial year was deleted from the prior to treatment state. Where neither event occurred, there remained a risk that time in the follow-up period within the next financial year would be double-counted in the prior to treatment state. However, retaining this time was conservative for the counterfactual calculation, as the opioid death rate in any such time was zero.

## RESULTS

### Opioid deaths and treatment status

Between 2008 and 2011 there was an estimated annual population of approximately 260 000 users of non-medical opioids (aged 15–64 years) in England. NDTMS recorded an annual population of approximately 160 000 individuals treated for OUD during 2008 and 2011 (220 665 individuals in total). The treatment interventions received by this national cohort were as follows: opioid medication-assisted treatment (43%), opioid medication and psychosocial intervention (38%), psychosocial intervention only (10%), in-patient withdrawal management (5%) and drug-free residential rehabilitation (3%). A small minority (3%) were triaged to receive a structured intervention but did not receive or commence treatment during the study.

Among the 3731 opioid deaths during the study (Table 1), 62 deaths were re-assigned to the during treatment state from the after treatment state (by conservative clause). For the analysis, 2722 (72.9%) of these deaths occurred prior to treatment, 741 (19.9%) during treatment and 268 (7.2%) after treatment. Treatment service providers reported a further 2386 deaths which were not opioid-related.

The total risk exposure time across the study was estimated to be 785 301 PY (Table 2), with 491 317 PY directly observable due to the individual either being in treatment for OUD or dying from opioid-related poisoning in one of the study years. The remainder was inferred using the estimated source population.

Table 3 displays the unadjusted opioid death rates per 100 PY. The rate was highest among the 35–64 age group and lowest in the 15–24 age group. Across all age groups, there was a significantly higher rate in the prior to treatment state, followed by the after treatment state, and the lowest rate during treatment.

Figure 1 shows the associated MRR by treatment status and age group and reveals significantly high MRRs in the prior to treatment state across all age groups. This was also observed in the after treatment state, apart from in the 15–24 age group where there was no significant difference.

### Counterfactual number of opioid deaths

Table 4 displays the total number of opioid deaths (6372) that we estimate would have occurred in the 3-year study period in the absence of any OUD treatment (95% CI = 5837–6982).

Under this counterfactual scenario, there would have been 880 excess opioid deaths (95% CI = 702–1084) each year during the study period. There was a gradient of risk by age, with the majority of the estimated additional deaths in the 35–64 age group (72.6%, based on the point estimate), and the smallest number were among the 15–24 age group (2.8%).

### Sensitivity analysis

The sensitivity analysis added 54 114 PY to the after treatment state, while 22 692 PY were correspondingly deducted from the prior to treatment state using the assignment rules. Some 154 opioid deaths assigned previously to the prior to treatment were re-assigned to the after treatment state. As a result, there was a modest reduction in the after treatment rate (0.35; 95% CI = 0.32–0.39), but the prior to treatment rate was comparable (0.77; 95% CI = 0.70–0.85). The estimated excess deaths in the counterfactual scenario was similar to the main analysis (annual average of 901 fewer deaths; 95% CI = 711–1120).

## DISCUSSION

Consistent with previous studies of mortality risk among opioid users [19,20], the risk of opioid death was approximately halved during treatment compared to after leaving

**Table 2** Time at risk (person-years, PY) for opioid users (95% confidence interval) by treatment state and mortality status (England: 2008–11; 15–64 years).

| *Status* | *PY 2008* | *PY 2009* | *PY 2010* | *PY 2008 to 2011* |
|---|---|---|---|---|
| Prior to treatment (all) | 123 241 (118 331–130 809) | 118 718 (111 326–125 256) | 113 372 (106 983–120 277) | 355 331 (336 640–376 342) |
| Prior to treatment (then treated) [a] | 22 253 | 20 382 | 17 396 | 60 031 |
| Prior to treatment (then died)[b] | 467 | 484 | 365 | 1315 |
| Prior to treatment (unobserved)[c] | 100 522 (95 612–108 090) | 97 852 (90 460–104 390) | 95 610 (89 222–102 516) | 293 984 (275 293–314 996) |
| During treatment | 115 220 | 122 990 | 125 613 | 363 823 |
| After treatment | 23 027 | 21 279 | 21 842 | 66 147 |
| Observed total[d] | 160 966 | 165 135 | 165 216 | 491 317 |
| Total | 261 488 (256 578–269 056) | 262 986 (255 594–269 525) | 260 827 (254 438–267 732) | 785 301 (766 610–806 313) |

[a]Risk time for individuals who had not yet been in treatment in the year but were admitted later in that year. [b]Risk time for unmatched opioid deaths ($n = 2722$). [c]Risk time for members of the source population who were not observed in the National Drug Treatment Monitoring System (NDTMS) or the poisonings database. [d]Total risk time for all those observable in NDTMS and poisonings database.

treatment. To our knowledge, there has not been a comparable assessment of risk prior to treatment in previous studies, although an international study has explored risk of overdose while on treatment waiting-lists [17]. With approximately 350 000 PY of time attributable to the prior to treatment state, we estimate that the risk was four times greater prior to treatment than during treatment. The sensitivity analysis indicated that the prior to treatment mortality rate calculated in the main analysis (which underpins this estimate) was not inflated by the variable follow-up time in the after treatment state.

The finding of significantly increased risk in the prior to treatment and after treatment categories was maintained across age groups (with the exception of those aged 15–24 years in the after treatment state). The present data do not shed light as to why the prior to treatment risk was double that of risk after treatment. However, a continued benefit of treatment in terms of abstinence, reduced drug use and reduced overdose risk behaviour would seem the probable and welcome explanation [14].

This is one of the largest studies of opioid deaths conducted to date, covering 220 665 people accessing treatment for OUD and spending 363 823 PY in treatment. Previous research has used samples, and a key strength of the present study is that it was conducted using the entire treatment population. Several study limitations are also acknowledged. First, having only annual estimates, we assumed that all members of the source population were at risk on all days each year: this approach is conservative, but it represents a crude simplification of the natural flow of opioid initiation and cessation in the population. Secondly, we assumed that all opioid deaths related to members of the source population. There will have been some opioid deaths in which the victim was not a member of the source population (e.g. where death occurred very shortly after commencing illicit heroin use), as well as some deaths involving codeine or dihydrocodeine as prescribed for pain control.

The counterfactual model does not take into account any impact of the availability of opioid medication-assisted treatment in contributing indirectly to opioid deaths among those not receiving this intervention. Research in Norway has shown that a large proportion of methadone-related deaths occur outside treatment and these will include cases of diversion of opioid medication [28,29]. In the 3 years studied here, there were 661 deaths outside treatment (in the prior to treatment or after treatment state) in which methadone was mentioned on the death certificate (59% of all deaths where methadone was mentioned). It is not possible from the available data to determine how many deaths are attributable to diversion of methadone, although in 342 of these cases no other drug was indicated.

Previous research has highlighted increased periods of risk in an opioid user's life, such as prison release [30] and, of particular relevance here, admission and exit from

**Table 3** Unadjusted opioid mortality rate (95% confidence interval) by age band and treatment state (England: 2008–11).

| | *Treatment state* | | |
|---|---|---|---|
| *Estimates by age group* | *Prior to treatment* | *During treatment* | *After treatment* |
| 15–24 years | | | |
| PY of follow-up | 70 637 (67 641–77 380)[a] | 24 083 | 7674 |
| Number of opioid deaths | 254 | 24 | 14 |
| Deaths per 100 PY | 0.36 (0.29–0.42)[b] | 0.10 (0.06–0.15) | 0.18 (0.10–0.31) |
| 25–34 years | | | |
| PY of follow-up | 137 374 (129 973–144 156) | 148 214 | 29 805 |
| Number of opioid deaths | 768 | 232 | 116 |
| Deaths per 100 PY | 0.56 (0.50–0.63) | 0.16 (0.14–0.18) | 0.39 (0.32–0.47) |
| 35–64 years | | | |
| PY of follow-up | 147 320 (139 025–154 806) | 191 526 | 28 669 |
| Number of opioid deaths | 1700 | 485 | 138 |
| Deaths per 100 PY | 1.15 (1.05–1.28) | 0.25 (0.23–0.28) | 0.48 (0.40–0.57) |
| All (15–64 years) | | | |
| PY of follow-up | 355 331 (336 640–376 342) | 363 823 | 66 147 |
| Number of opioid deaths | 2722 | 741 | 268 |
| Deaths per 100 PY | 0.77 (0.70–0.84) | 0.20 (0.19–0.22) | 0.41 (0.36–0.46) |

[a]Prior to treatment person-years (PY) are computed using CIs from the source population and subject to an estimated range. [b]Prior to treatment opioid death rates are subject to broader CIs, taking into account CIs from the source population.

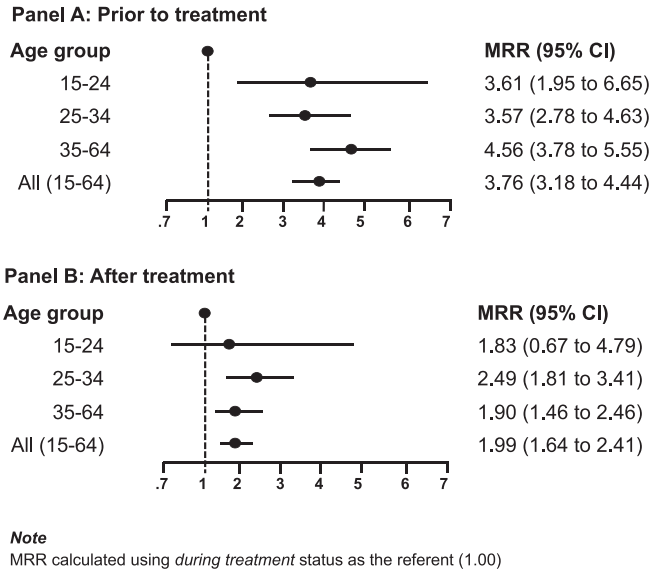


**Figure 1** Mortality rate ratios (MRR) by treatment state and age

**Table 4** Counterfactual estimate of the number of opioid deaths (95% confidence interval) prevented by treatment by age group (England: 2008–11).

| *Age group* | *Person-years* | *Counterfactual opioid death rate*[a] | *Counterfactual number of opioid deaths*[b] | *Observed number of opioid deaths* | *Mean number of deaths prevented by treatment annually* |
|---|---|---|---|---|---|
| 15–24 | 102 393 (99 398–109 137) | 0.36 (0.29–0.42) | 368 (316–422) | 292 | 25 (8–43) |
| 25–34 | 315 393 (307 992–322 175) | 0.56 (0.50–0.63) | 1763 (1597–1953) | 1116 | 216 (160–279) |
| 35–64 | 367 515 (359 220–375 001) | 1.15 (1.05–1.28) | 4241 (3925–4606) | 2323 | 639 (534–761) |
| All | 785 301 (766 610–806 313) | – | 6372 (5837–6982) | 3731 | 880 (702–1084) |

[a]Counterfactual opioid death rate is per 100 person-years (PY) and is the prior to treatment mortality rate reported in Table 3. [b]The counterfactual number of deaths calculated by applying the counterfactual opioid death rate to the total PY.

treatment [18–20]. Periods of elevated risk are not explored in the present study, and accordingly overall estimates may mask complex interactions. The counterfactual scenario modelled here in the absence of treatment does not take into account the possibility of elevated risk arising from treatment exit. The model, therefore, should not be taken as a prediction of what would occur in the event of sudden cessation of treatment.

## CONCLUSION

Our analysis highlights an important and under-recognized outcome from the English OUD treatment system, which we consider to be of public health significance. Bringing together estimates of source population prevalence, treatment provision and opioid deaths suggested that, on average, there would have been 880 excess deaths from opioid-related poisoning annually if there had been no OUD treatment.

The data sources used were all accessible and, with data-sharing agreements secured, we can calculate the preventive clinical and economic effect of treatment on a periodic basis alongside other routinely monitored measures of outcome (such as opioid abstinence, cessation of illicit injecting and reductions in drug use at national and local levels [31–33]).

A counterfactual model can be undertaken where there is an estimate of the source and target population and a mortality register recording opioid deaths. Wider use of counterfactual models could facilitate international comparisons of OUD and other treatments for substance use disorders.

### Declaration of interests

S.D. is employed at the National Drug and Alcohol Research Centre at the University of New South Wales, which is supported by funding from the Australian Government. J. M. works in an integrated university [Institute of Psychiatry, Psychology and Neuroscience (IoPPN), King's College London] and National Health Service Academic Health Sciences Centre (King's Health Partners) and declares the following financial relationships in the past 5 years: addition treatment-related research grant support from the English Department of Health, Institute for Health Research (Health Technology Assessment), and the Biomedical Research Centre for Mental Health (South London and Maudsley NHS Foundation Trust and IOPPN); part-time employment as Senior Academic Adviser for the Alcohol, Drugs and Tobacco Division, Health and Wellbeing Directorate, Public Health England; educational grant funding at King's College London via Reckitt Benckiser Pharmaceuticals (RBP) to Action on Addiction for a study of psychological interventions in opioid dependence (2010–16); consultation to RBP (2011) and Merck Serono (2013); and honorarium as co-chair of the Improving Outcomes in Treatment of Opioid Dependence conference (2015) via educational grant funding from RBP (Indivior PLC) to PCM Scientific. He holds no stocks in any company. T. M. declares the following financial relationships: co-investigator on research funded by the Alcohol, Drugs and Tobacco Division, Health and Wellbeing Directorate, Public Health England. He is a member of the organizing committee for, and chairs, conferences supported by unrestricted educational grants from Reckitt Benckiser, Lundbeck, Martindale Pharma and Britannia Pharmaceuticals Ltd, for which he receives no personal remuneration. M.W., R.B., B.E., J.K. and V.M. are employees of the Alcohol, Drugs and Tobacco Division, Health and Wellbeing Directorate, Public Health England and declare no additional conflicts of interest.

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