Changes to the daily pattern of methadone-related deaths in England and Wales, 1993–2003

O. W. Morgan1,2, H. Johnson2, C. Rooney2, V. Seagroatt3, C. Griffiths2

1Department of Primary Care and Social Medicine, Imperial College London, London W6 8RP, UK
2Mortality Statistics Branch, Office for National Statistics, London SW1V 2QQ, UK
3Unit of Health-Care Epidemiology, Department of Public Health, University of Oxford, Oxford OX3 7LF, UK

Address correspondence to Oliver Morgan, E-mail: omorgan@bigfoot.com

ABSTRACT

Previous studies suggest that fatal poisoning deaths involving methadone occur more frequently on the weekends. We assessed changes in the daily pattern of mortality because of methadone poisoning following a review of drug misuse services in 1996 and publication of revised clinical guidelines in 1999. We also compared this to the daily pattern of deaths involving heroin/morphine. The Office for National Statistics provided data on all deaths in England and Wales between 1993 and 2003 for which methadone and heroin/morphine were mentioned on the coroner’s certificate of death registration after inquest, with or without alcohol or other drugs. There were 3098 deaths involving methadone. The death rate increased up to 1997 and then declined. Initially, there was a marked excess of deaths occurring on Saturdays. The rate of decline was greatest for deaths occurring on Saturdays. As a result, the Saturday peak disappeared (P = 0.006). There were 6328 deaths involving heroin/morphine. No change in the daily pattern of heroin/morphine deaths was observed during the study period. Although the marked change in the epidemiology of methadone deaths coincided with recommendations for service redevelopment and clinical management of methadone treatment, the contribution of improved prescribing practice or treatment services is unclear.

Keywords drug misuse, epidemiology, public health

Introduction

The risk of premature mortality among heroin users is between 6 and 20 times that in the general population.1 In England and Wales, heroin users have access to free drug treatment either from their general practitioner (GP) or from specialist drug treatment services, although waiting times for these services vary considerably across different areas. Oral methadone accounts for almost 90% of all pharmacological treatment for heroin addiction in the UK.2,3 The number of prescriptions for methadone in England increased almost 3-fold between 1993 and 2003. The benefits of oral methadone therapy include reductions in the risk of fatal overdose,4 use of illicit drugs,5 high-risk injecting behaviour5,6 and mortality.6 However, methadone taken in overdose can be fatal,7 and a particular concern is the diversion of methadone for sale to individuals who are not part of a managed methadone treatment programme.8

Since its introduction in the 1970s, the provision of methadone treatment in the UK has differed from that in other countries.9 Notable features of the so-called ‘British system’ are that patients are not supervised when they take their methadone but rather are provided methadone to take at home,10 there is a lot of variation in how methadone is prescribed, with many patients receiving a week’s worth of methadone on a single prescription10 and the ability for any medical practitioner to prescribe methadone without a specialist licence.9 There have been concerns that under the ‘British system’, multiple doses of methadone were frequently prescribed to cover weekends, leading some commentators to describe it as a risk factor for opiate-related deaths.8

Consequently, the Department of Health for England formed a Task Force to review the effectiveness of treatment services for drug misusers. The Task Force published its findings in 1996,11 followed by the publication of revised clinical guidelines in 1999.12 A number of specific recommendations were made to improve both the effectiveness
and the safety of methadone prescribing. These included supervised consumption of methadone during the first 3 months of treatment, daily dispensing until treatment stability is achieved, avoiding the prescribing of take-home doses, closer liaison between prescribers and pharmacists and preferential use of oral methadone syrup.

Under previous arrangements for methadone treatment, a greater proportion of methadone-related deaths occurred on Saturdays. In this article, we evaluate whether the 1996 report and 1999 guidelines have reduced the Saturday peak of methadone deaths, and if any reduction is observed, whether this has contributed to (i) an overall decline in methadone deaths or (ii) a redistribution of deaths to other days.

**Methods**

**Data sources**
The Office for National Statistics (ONS) has been maintaining a dedicated database of drug-poisoning deaths in England and Wales since 1993. Drug-poisoning deaths are extracted from the national death database using specific International Classification of Diseases codes for the underlying cause of death as described elsewhere. In addition to information supplied in the cause of death section of the coroner’s death certificate, the database also contains textual information supplied voluntarily in confidence by coroners to ONS about circumstances of the death, which may include more detailed information about the drugs involved. Deaths from methadone were defined where methadone was mentioned either in the death certificate or in the confidential information, with or without alcohol or other drugs.

To consider whether any observed changes in the daily pattern were unique to deaths involving methadone, we used data on deaths involving heroin as a comparison. These were defined in a similar way, except that because heroin (diamorphine) is metabolized to morphine, toxicological investigation is unable to distinguish between the two drugs and we therefore combined deaths for heroin and morphine. However, morphine is not widely used outside the clinical setting, and most of these deaths are likely to involve heroin. We have published a detailed analysis of deaths involving heroin elsewhere.

A sensitivity analysis excluding deaths with mentions of other drugs or where heroin/morphine and methadone were both mentioned on the death certificate had no discernible effect on the results. We therefore included all deaths with mentions of other drugs or heroin/morphine and methadone together. A previous study reported that drug-poisoning deaths with a verdict of suicide were more likely to occur on Mondays. However, because there were relatively few methadone or heroin/morphine deaths with a verdict of suicide, excluding these deaths from our analysis made little difference. We therefore included these deaths in the analysis.

**Analysis**

We calculated directly age-standardized mortality rates using the European Standard Population as the reference population. To assess the annual rate of change in methadone-poisoning deaths for each day of the week, we used Poisson regression to estimate the annual rate ratio. We calculated the proportion of deaths occurring on each day of the week for two time periods: before the introduction of the guidelines (1993–98) and afterwards (1999–2003). To assess the impact of the guidelines, we tested the difference between the proportions of methadone-poisoning deaths occurring on Saturdays for these two periods (using a chi-squared test). We performed a similar analysis for heroin/morphine-poisoning deaths, which were not subject to the guidelines.

**Results**

Between 1993 and 2003, there were 3098 deaths involving methadone and 6328 deaths involving heroin/morphine. Between 1993 and 1997, directly age-standardized mortality rates among males were similar for both the drugs, increasing from about five to 15 per million (Fig. 1). From 1997 to 2000, age-standardized rates for heroin/morphine continued to increase to more than six times that of 1993, subsequently declining to 20 deaths per million population in 2003. For methadone, age-standardized rates among males decreased from 1997 to 2003 to below 1993 levels. Among females,
age-standardized rates were lower than those for males throughout the study period. Rates were similar for methadone and heroin/morphine until 1999, after which rates for heroin/morphine increased, whereas rates for methadone remained stable.

The number of methadone deaths by day of the week is shown in Fig. 2. The total number of deaths increased from 1993 to 1997 (Fig. 2a). The increase occurred on every day of the week (Fig. 2b). The day with the fastest rate of increase was Monday (annual rate ratio = 1.34, 95% CI = 1.19–1.50). From 1997 until 2001, there was a sustained period of decline, during which the number of methadone deaths fell to below 1993 levels (Fig. 2a). There followed a brief increase in 2002 until falling further in 2003 (Fig. 2a). During the period of decline from 1997 to 2001, the number of deaths decreased on every day of the week (Fig. 2b). The fastest rate of decrease was on Saturday, and the annual number of deaths fell steeply after 1998 (annual rate ratio = 0.70, 95% CI = 0.61–0.80). During the whole study period, the variability in the number of deaths between days of the week reduced: the variance of the number of deaths decreased from 192.3 during 1993–98 to 63.1 during 1999–2003 ($F = 9.29$, df = 5 and 4, $P < 0.05$).

From 1993 to 1998, the proportion of methadone deaths on Saturday was higher than the proportion of deaths on other days of the week (Fig. 3). During this period, the Saturday peak was observed for all age groups, although it was most pronounced among 15- to 24- and 25- to 34-year olds (data not shown). From 1999 to 2003, the faster decline in the number of Saturday deaths (Fig. 2b) resulted in a smaller proportion of deaths occurring on Saturday (Fig. 3). Between the two time periods, the proportion of deaths occurring on Saturday decreased from 19.5 to 15.5% ($\chi^2 = 7.6574$, df = 1, $P = 0.006$) (Table 1). The pattern of heroin/morphine deaths by day of week differed from that for methadone; it was lowest for Sunday and Monday, intermediate on Tuesday and

![Fig. 2](https://academic.oup.com/jpubhealth/article-abstract/28/4/318/1622744)
Discussion

Main finding of this study

The increase in methadone deaths on every day of the week between 1993 and 1997 was followed by a decline in the number of deaths. The rate of decline was greatest for deaths occurring on Saturdays. As a result, the Saturday peak disappeared. The decline in methadone deaths coincided with the publication of a report on drug treatment services in 1996 and revised clinical guidelines in 1999. By contrast, the daily pattern of deaths from heroin/morphine was consistent throughout the study period.

What is already known on this topic

Abuse of methadone by non-tolerant individuals has previously been implicated in fatal methadone poisoning.17,18 As drug users in treatment are the main source of diverted methadone, the 1996 review of drug treatment services11 and the revised 1999 clinical guidelines12 recommended that take-home methadone prescriptions should be avoided. Instead, methadone should be prescribed as an oral preparation for daily supervised consumption. Several studies have assessed whether the published recommendations resulted in changes to prescribing practice. A study of methadone prescribing in the Thames region (covering London) found little change in prescribing practice 1 year after the 1996 review was published, with ~56% of prescriptions issued for daily dispensing.10 In another study of methadone prescribing, prescriptions for methadone tablets fell from 9.8 to 4.0% and for ampoules of injectable methadone from 8.7 to 3.9% between 1996 and 2001.19 The authors concluded that the guidelines had resulted in a gradual sustained change in prescribing practice at the national level, which appears to be supported by our finding that there was a period of transition from 1997 to 2001 during which methadone deaths decreased gradually. However, a more recent survey of 1415 GPs in England and Wales in 2001 found that nearly half of all prescriptions for methadone are issued as take-home prescriptions.3

What this study adds

Assessing the impact of service redevelopment and national-level guidelines aimed at public health improvement depends on the analysis of surveillance data. The large increase in methadone prescriptions and concurrent decline in methadone-related poisoning deaths and the disappearance of the Saturday peak point to improvements in drug treatment. However, attributing the observed decline in methadone-related deaths to such interventions is difficult, and it is uncertain whether changes in prescribing practice were the principal driver for this. An alternative explanation for our findings may be improved retention on methadone treatment because of better access via GPs. Retention in drug treatment is shown to improve several outcomes including reduced mortality.20 Furthermore, because the risk of fatal accidental methadone poisoning is up to seven times higher for patients

Table 1

Deaths from methadone and heroin/morphine overdose on Sunday to Friday compared to Saturday, England and Wales

<table>
<thead>
<tr>
<th></th>
<th>Number of deaths</th>
<th>% on Saturday</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sunday to Friday</td>
<td>Saturday</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>1993–98</td>
<td>1578</td>
<td>382</td>
</tr>
<tr>
<td></td>
<td>1999–2003</td>
<td>958</td>
<td>176</td>
</tr>
<tr>
<td>Heroin/morphine</td>
<td>1993–98</td>
<td>2020</td>
<td>353</td>
</tr>
<tr>
<td></td>
<td>1999–2003</td>
<td>3314</td>
<td>636</td>
</tr>
</tbody>
</table>

Fig. 3 Proportion of deaths from methadone and heroin/morphine overdose by days of the week, England and Wales, 1993–2003.
during the first 2 weeks of methadone treatment compared with heroin addicts not in treatment, reducing the start-stop cycle is important to reduce methadone-poisoning deaths. Increased psychosocial interventions and keyworker support also contribute to improved outcomes of methadone treatment and have been promoted as part of the new National Drug Treatment Agency commissioning framework.

Limitations of this study
Although the ONS database is the most comprehensive source of data on fatal drug poisoning for England and Wales, it may not capture all deaths attributable to methadone. About 10% of all drug-poisoning deaths in the ONS database do not mention any specific substance. Toxicological investigations are not standardized, and coroners are not required to provide details of all toxicological examinations on the death certificate. Where multiple substances are detected, it may not be possible to identify which substance was the principal cause of poisoning, and hence, mentions of methadone on the death certificate may be incidental. A study of 352 deaths in Scotland where methadone was detected suggested that methadone was not a contributing factor in 23% of deaths. However, a recent study of coronial records in London suggests that although the total number of poisoning deaths is probably not underestimated by the ONS surveillance system, coroners do not consistently document the presence of methadone among deaths where methadone was present (M. Hickman, unpublished data). Nevertheless, there is no evidence to suggest that the likelihood of coroners’ reporting methadone or heroin/morphine deaths has changed since 1993 or that their recording practice would vary by day of the week on which the death occurred. Moreover, no guidelines or recommendations about the investigation of poisoning deaths have been published that may have changed their recording within the ONS system.

Conclusion
The epidemiology of fatal methadone poisoning has changed noticeably since 1997, with fewer deaths and the disappearance of the Saturday peak. These changes coincided with a substantial review of drug misuse services and publication of revised clinical guidelines aimed at reducing diversion of methadone. There is little evidence from other studies that prescribing practices have driven these changes. Further work is needed to assess the contribution of non-prescribing factors to the changing epidemiology of fatal methadone poisoning.

Acknowledgements
We thank Sue Davies at the Office for National Statistics, Dr Matthew Hickman at the University of Bristol and Professor Azeem Majeed at Imperial College London for comments on the article. O.W.M. is funded by the National Health Service London Deanery of Postgraduate Dental and Medical Education.

References


