

OTHER ORIGINAL PAPERS

Association between availability of heroin and methadone and fatal poisoning in England and Wales 1993–2004

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Background The UK heroin market is the biggest in Europe and ~70% of heroin deaths are due to fatal poisoning. Methadone treatment for heroin addiction in the UK, the 'British system', is unique as it is largely provided by General Practitioners.

Methods The Office for National Statistics provided data on deaths, the Home Office provided law enforcement data on drug seizures and the Department of Health data on prescriptions. For methadone treatment we calculated the death rate per 1000 patient years. We used Spearman's rank correlation to assess the association between illicit drug seizures for heroin and methadone and deaths.

Results Between 1993 and 2004 there were 7072 deaths involving heroin/morphine (86% males) and 3298 deaths involving methadone (83% male). From 1993–1997, directly age-standardized mortality rates for males were similar for both drugs, increasing from ~5 to 15 per million. Mortality rates for heroin continued to increase until 2000, subsequently decreasing from 30 to 20 per million by 2003, and rising again to 24 per million in 2004. In contrast, mortality rates for methadone decreased between 1997 and 2004 to just above 1993 levels. Among females the mortality rate for both drugs was lower than for males throughout the study period, remaining relatively stable. Methadone deaths per 1000 patient years remained similar between 1993 and 1997, after which they fell by three quarters. For both heroin/morphine and methadone, deaths were strongly associated with seizures (Spearman's coefficient for males: heroin, $P = 0.95$, $P < 0.001$ and methadone, $P = 0.83$, $P = 0.0013$).

Conclusions Our study suggests the 'British System' can deliver substantial expansion of treatment without increased mortality risk. The fall in heroin/morphine deaths since 2000 may also be an indication of success of increasing methadone treatment. Data on mortality risk is needed to determine whether increased methadone treatment has reduced drug-related deaths.

Keywords substance abuse, Intravenous/epidemiology, substance abuse, Intravenous/mortality, methadone, heroin

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There are over 13 million injectors and heroin users world-wide.¹ The United Kingdom (UK) is the largest consumer of heroin in Europe²: ~270 000 individuals use heroin, of which ~150 000 are regular injectors.^{3,4} The mortality rate for individuals who regularly use illicit opiates is more than 13 times the age and sex-matched general population^{5,6} and in the UK, almost 70% of deaths among opiate misusers are

due to fatal poisoning, which is higher than many other countries.^{5,7}

Methadone is the main treatment for heroin dependence, and has been shown to reduce mortality and morbidity, crime, use of other drugs, injecting drug use and HIV infection, while also improving social functioning and quality of life.^{1,8,9} However, methadone can be fatal in overdose, and may be toxic at treatment levels when taken with other central nervous system depressants such as benzodiazepines and alcohol.¹⁰ Diversion and abuse of methadone is an ongoing public concern and is frequently implicated in fatal methadone poisoning.¹¹

Some countries such as the USA deliver methadone treatment through centralized specialist drug treatment centres. In contrast, the 'British system' encourages widespread universal access to methadone maintenance treatment (MMT) provided through General Practitioners (family doctors), without a requirement for special licence or training; specialist drug treatment centres are reserved for the most problematic cases. Unlike other countries, any doctor in Britain is able to prescribe methadone (oral, injectable, or tablets) without a special licence.^{12,13} Access to MMT at the primary care level is increasingly being adopted by several countries, including the USA,¹⁴ Canada,¹⁵ Australia,¹⁶ and 10 European Member States² to increase treatment coverage.

There are, however, concerns that the 'British system' leads to lax prescribing, which increases diversion of methadone, and in turn, results in more drug-related deaths.^{13,17} Studies in Manchester and Scotland reported that in over half of all poisoning deaths involving methadone, methadone was obtained illegally.^{18,19} To reduce diversion, current guidance encourages supervised methadone consumption (by community pharmacists) and preferential use of oral methadone.²⁰

In this paper we describe trends in fatal poisoning involving heroin and methadone in England and Wales and assess the association with drug availability. We also assess the impact of the current clinical guidelines on prescribing and diversion of methadone.

Methods

Mortality data

The Office for National Statistics maintains a dedicated database of drug poisoning deaths in England and Wales since 1993. Drug poisoning deaths are extracted from the national deaths database using specific International Classification of Diseases codes for the underlying cause of death (Table 1). In addition to data 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.²¹

Deaths involving methadone were defined where methadone was mentioned on the coroner's death certificate, with or without alcohol and other drugs. Deaths involving heroin (including morphine) were defined in a similar way. We conducted a sensitivity analysis excluding deaths where heroin/morphine and methadone were mentioned together ($n = 568$). This made no discernable difference to the results and so these

Table 1 ICD-9 and ICD-10 codes for drug poisoning deaths

Description	ICD-9	ICD-10
Mental and behavioural disorders due to drug use (excluding alcohol and tobacco)	292, 304 305.2-9	F11-F16, F18-F19
Accidental poisoning by drugs, medicaments and biological substances	E850-E858	X40-X44
Intentional self-poisoning by drugs, medicaments, and biological substances	E950.0-E950.5	X60-X64
Poisoning by drugs, medicaments and biological substances, undetermined intent	E980.0-E980.5	Y10-Y14
Assault by drugs, medicaments, and biological substances	E962.0	X85

deaths were included both with deaths involving heroin/morphine and deaths involving methadone.

Methadone prescriptions

The Department of Health supplied data on prescriptions for methadone in England from 1993 to 2004. National data on prescriptions include all drugs prescribed by GPs in England and dispensed in the community in the United Kingdom. This does not include prescriptions that are written in hospitals or clinics and dispensed in the community, prescriptions dispensed in hospitals or private prescriptions. In England 98% of prescriptions for methadone are dispensed in the community.¹² Prescriptions for oral methadone are all recorded under British National Formulary (BNF) chapter 4.10 *Drugs used in Substance Dependence*, whereas prescriptions for other methadone preparations (tablets, injectable ampoules, reefer, and linctus) are all recorded under BNF 4.7.2 *Opioid analgesics* or BNF 3.9.1 *Cough suppressants*. Because neither the dosage and indication for the prescription nor the characteristics of the patient (e.g. age and sex) are recorded, it is not possible to distinguish prescriptions used for methadone maintenance. We therefore included all prescriptions for methadone. A subset of methadone prescriptions are issued using form FP10(MDA), which is specifically designed to enable instalment prescriptions for drug addicts (repeat daily doses supervised by a community pharmacist for up to 14 days). Data were available for prescriptions for oral methadone issued on form FP10(MDA) by financial year (April to April) from 2000/1 to 2004/5.

Drug seizures

Drug seizures by law enforcement agencies in England and Wales from 1994 to 2004 were provided by the Home Office.²² Data include seizures made by the police, HM Revenue & Customs and the National Crime Squad. Data about seizures by HM Revenue & Customs before 2000 are not complete. However, HM Revenue & Customs make only ~5% of seizures and these mostly include drugs other than heroin or methadone.

Analysis

We calculated directly age-standardized mortality rates using the European Standard Population as the reference population. Trends in the proportion of different methadone preparations and quantity of oral methadone per prescription were assessed using linear regression. To assess how much methadone was prescribed on an instalment basis, we calculated the proportion of the total quantity of methadone issued using form FP10(MDA). Data were not available about the number of individuals receiving MMT for the whole time period. We therefore calculated MMT patient years by dividing the total quantity of oral methadone prescribed each year by an estimated yearly individual dose. We estimated the individual daily methadone dose as 40 mg (14 570 mg per year), which is the average dose reported by recent studies of methadone prescribing in the UK.^{23,24} We calculated the death rate per 1000 MMT patients years in England for males and females combined. We used Spearman's rank correlation coefficient to measure the association between age-standardized rates of poisoning mortality and seizures. Statistical analysis was done using STATA 8.2.

Results

Between 1993 and 2004 there were 7072 deaths involving heroin/morphine (86% males). The median age for males was 31 years (interquartile range IQR, 25–37) and for females 32 years (IQR, 25–41). About half (52%) of deaths involving heroin/morphine received a coroners' verdict of drug abuse/dependence, 36% accidental, 12% suicide (open and intentional combined) and <1% homicide (often cases in which the person who supplied the heroin was prosecuted for manslaughter²¹). Methadone was mentioned in 3298 poisoning deaths, of which 83% were male with a median age of 30 years (IQR, 24–36). The median age for females was 31 years (IQR, 24–38). Forty-one percent were assigned a coroners' verdict of drug abuse/dependence, 47% accidental, 12% suicide and <1% homicide.

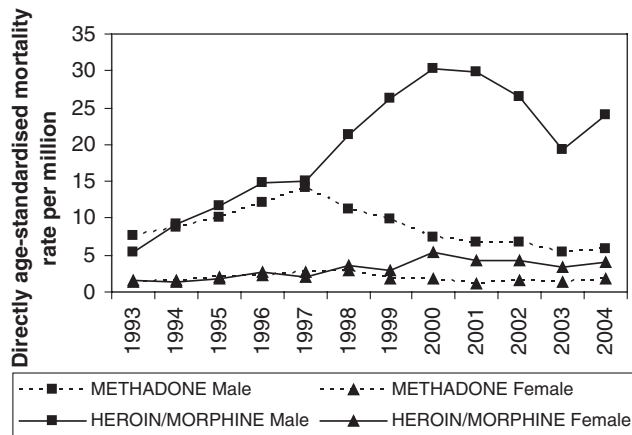


Figure 1 Directly age-standardized mortality rates for heroin and methadone poisoning, England and Wales, 1993–2004.

From 1993 to 1997, directly age-standardized mortality rates for males were similar for both drugs, increasing from ~5 to 15 per million (Figure 1). From 1997 to 2000, age-standardized rates for heroin/morphine increased to six times that of 1993, subsequently declining to 20 deaths per million in 2003 and rising again to 24 deaths per million in 2004. For methadone, age-standardized rates among males decreased between 1997 and 2004 to just above 1993 levels. Among females, age-standardized rates for heroin/morphine and methadone were lower than for males throughout the study period. Rates were similar for heroin/morphine and methadone until 1999, after which rates for heroin/morphine increased slightly, while rates for methadone remained stable.

Age-specific rates for heroin/morphine deaths (Table 2) were highest for males 25–34 years old, followed by 15–24 and 35–44 year olds. Mortality rates among females were highest for 15–24 and 25–34 year olds. Similarly, for methadone deaths, the highest rates for both males and females were among 15–24 and 25–34 year olds.

The proportion of deaths where other drugs were mentioned was similar throughout the study period. Twenty-seven percent of deaths involving heroin/morphine and 44% of deaths involving methadone mentioned other drugs. Heroin/morphine and methadone were both mentioned in 568 deaths (8% of heroin deaths and 17% of methadone deaths). The proportion of deaths mentioning both heroin/morphine and methadone was similar throughout the study period. Alcohol was mentioned for 28% of deaths involving heroin/morphine and 26% of deaths involving methadone (Table 3). Benzodiazepines were mentioned in a tenth of deaths involving heroin/morphine and a fifth of deaths involving methadone. The proportion of deaths where other classes of drug were mentioned was similar, except for antidepressants, which were proportionately twice as common among deaths involving methadone.

Prescriptions for methadone more than doubled from 735 100 in 1993 to 1 810 000 in 2004. The quantity of oral methadone issued on each prescription increased throughout

Table 2 Age-specific mortality rates for heroin/morphine and methadone, England and Wales, 1993–2004

Age group	Males		Females	
	Deaths	Rate per million	Deaths	Rate per million
Heroin/morphine				
15–24	1238	31.6	242	6.3
25–34	2856	61.8	327	7.0
35–44	1472	33.2	215	4.8
45–54	401	10.0	91	2.2
55+	122	1.7	106	1.2
Methadone				
15–24	751	19.2	138	3.6
25–34	1135	24.6	218	4.7
35–44	629	14.2	142	3.2
45–54	196	4.9	45	1.1
55+	20	0.3	6	0.1

Table 3 Number of deaths involving heroin/morphine and methadone with mentions of other drugs, England and Wales, 1993–2004

	Heroin/morphine (N = 7072)		Methadone (N = 3298)	
	n	%	n	%
Alcohol	1949	27.6	853	25.9
Benzodiazepines	759	10.7	675	20.5
Methadone	568	8.0	—	—
Heroin/morphine	—	—	568	17.2
Cocaine	325	4.6	110	3.3
Antidepressants	186	2.6	149	4.5
Dihydrocodeine (without paracetamol)	168	2.4	97	2.9
Amphetamines	149	2.1	86	2.6
Paracetamol including compounds*	70	1.0	26	0.8
Codeine (without paracetamol)	58	0.8	29	0.9
Barbiturates	8	0.1	5	0.2

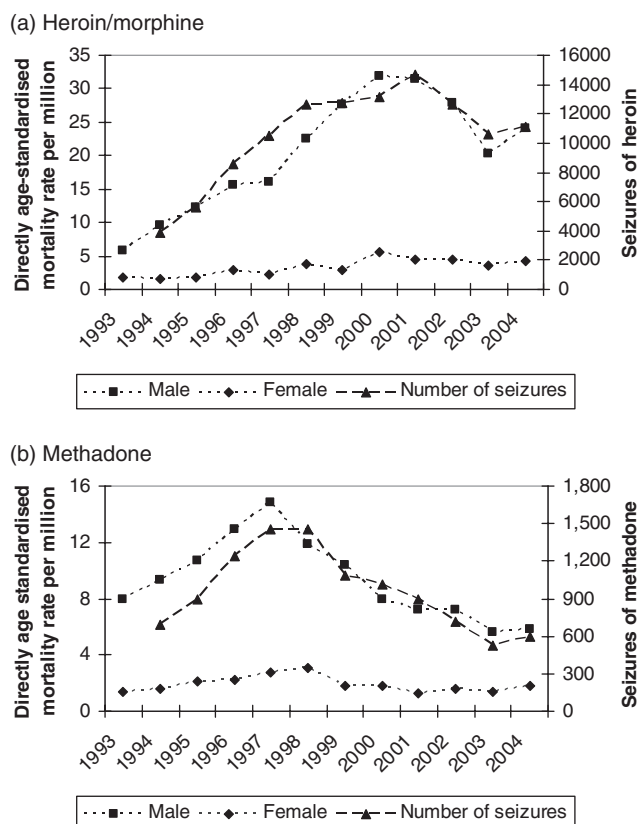
*Includes dextropropoxyphene.

Deaths where more than one substance was involved will be counted twice.

Table 4 Prescriptions for methadone, estimated treatment years for methadone maintenance and death rates, England, 1993–2004

Year	Methadone (England)			Deaths per 1000 patient years
	Quantity of oral methadone (kg)	Estimated treatment years	Number of deaths	
1993	253.8	17 419	226	13.0
1994	295.3	20 270	258	12.7
1995	347.7	23 867	287	12.0
1996	400.4	27 484	342	12.4
1997	448.6	30 789	391	12.7
1998	461.6	31 685	352	11.1
1999	480.2	32 958	286	8.7
2000	509.0	34 934	226	6.5
2001	549.9	37 743	199	5.3
2002	626.2	42 979	205	4.8
2003	764.8	52 488	167	3.2
2004	923.8	63 407	194	3.1

the study period from 421 mg in 1993 to 536 mg in 2004 (data not shown). As a proportion of all methadone prescriptions, oral suspension increased from 79% in 1993 to 93% in 2004. Between 2000/1 and 2004/5 the proportion of oral methadone prescribed in instalments increased from 74.9 to 80.8%. The annual quantity of methadone prescribed in tablet form rose from 30 kg in 1993 to 50 kg in 1996, subsequently declining to 1993 levels in 2004. There was a similar pattern for injectable methadone, which increased from 38 kg in 1993 to 52 kg in 1997, declining to 30 kg in 2004. There was a more than 3-fold increase in MMT patient treatment years (Table 4). The death

**Figure 2** Directly age-standardized mortality rates for heroin/morphine and methadone in England and Wales and police seizure of heroin in the United Kingdom, 1993–2004 (a) Heroin/morphine. (b) Methadone.

rate per 1000 patient years was relatively stable from 1993 to 1997, but fell by three quarters between 1997 and 2004 (Table 4).

From 1994 to 2001, the number of heroin seizures in England and Wales increased year on year from 3840 to 14 630, declining to 10 570 in 2003 and rising again to 11 070 in 2004 (Figure 2a). There was a strong statistical association between the directly age-standardized rate for fatal heroin/morphine poisoning and heroin seizures for males ($n = 11$, Spearman's $\rho = 0.95$, $P < 0.001$) and females ($n = 11$, Spearman's $\rho = 0.86$, $P = 0.0006$). Similarly, age-standardized rates for fatal methadone poisoning were statistically associated with methadone seizures for males ($n = 11$, Spearman's $\rho = 0.83$, $P = 0.0013$) and females ($n = 11$, Spearman's $\rho = 0.74$, $P = 0.0092$) (Figure 2b).

Discussion

During the 1990s there were marked changes in the epidemiology of fatal poisoning involving heroin/morphine and methadone in England and Wales. Between 1993 and 1997 the quantity of methadone prescribed in England almost doubled. During the same period methadone deaths per 1000 patient years remained similar, although the number of

deaths increased in line with the number of heroin/morphine related deaths. However, after 1997 the annual quantity of methadone prescribed continued to increase while the rate of methadone deaths per 1000 patient years fell by three quarters, with a corresponding fall in the number of deaths of 10% per year. The number of methadone and heroin seizures was strongly correlated with the age-standardized death rates of methadone and heroin respectively, suggesting that both indicators may be related to trends in availability/consumption. Furthermore, our results suggest that the 'British System' can deliver substantial expansion of treatment without increasing mortality risk from diversion. Heroin/morphine deaths, however, continued to rise from 1997 to 2000 by 2-fold, but recently declined.

Strengths and limitations

The ONS Drug Poisoning Mortality Database is a uniquely rich source of drug poisoning mortality data. At a national level, it systematically includes and codes textual information from the coroner's death certificate that can be used to identify specific drugs beyond the level of detail given by using ICD codes alone. However, not all deaths attributable to heroin/morphine or methadone may be captured.²¹ In England and Wales, post-mortem toxicological investigations are not standardized and coroners report inconsistently, sometimes only mentioning drugs they consider to have directly caused the death (unpublished data, Matthew Hickman 2005). About 10% of deaths in the ONS database have no specific substance mentioned.²¹ Where multiple substances are mentioned it may not be possible to identify which substance was the principle cause of poisoning. This may have led to misclassification of deaths. We found that 27% of heroin/morphine deaths mentioned other drugs, which is less than a questionnaire survey of coroners that found 46% of heroin/morphine deaths involve other drugs.²⁵ This may be because coroners have selected heroin poisoning as the most likely cause of death and not written other substances on the death certificate. However, the proportion of methadone deaths where other drugs were mentioned (44%) is consistent with other UK studies.^{18,19,26}

Interpretation of results

Estimating availability of heroin within an illicit market is difficult, however drug seizures have previously been used as an indicator of drug availability.^{2,27} Heroin availability is influenced by a number of factors such as supply from source countries, changes in trafficking routes, expansion of drug markets in other countries and law enforcement activities.²⁸ In Western Europe, price has decreased steadily from about USD\$140/g in 1990 to about USD\$40/g in 2002,²⁸ which may in part explain some of the large increase in heroin availability and fatal poisoning between 1997 and 2000. The fall in heroin seizures in England and Wales in 2001 coincided with the almost total cessation of opium cultivation in Afghanistan in 2000–2001, which was enforced by the Taliban before being overthrown in 2001. However, a recent analysis suggests that the heroin market in Western Europe was relatively unaffected due to release of pre-2001 stockpiles.²⁸

The finding that trends in fatal heroin poisoning closely track heroin seizures lends support for the thesis that seizure data may be indicators of drug availability (rather than simply changes in policing strategy) and be related to underlying trends in the prevalence of heroin use and/or heroin consumption. Firstly, increasing and decreasing heroin availability may have affected the number of heroin users or average heroin consumption, and hence the number of deaths from heroin poisoning. This occurred recently in Australia, with a sudden fall in heroin availability during 2001 accompanied by fewer fatal and non-fatal heroin poisonings,^{29,30} but is unlikely in the UK as no equivalent shortage was documented. Alternatively, both heroin seizures and deaths may reflect changes in the size and age of the underlying population of heroin users (i.e. reflecting demand); or the fall in heroin deaths (and seizures) following 2001 could be due to treatment availability increasing at a faster rate than heroin users leading to a reduced population risk and heroin consumption. Owing to the ecological nature of our study we were unable to distinguish which of these two explanations is most plausible. This would require knowledge of mortality risk among heroin users over time.

Similarly, a reduction in seizures of illicit methadone may suggest that less methadone is being diverted. Drug users in treatment are the primary source of diverted methadone and are mainly motivated by dissatisfaction with the dose or formulation of their methadone prescription.³¹ Higher doses of methadone (>60 mg) achieve maximum treatment benefit³² and are thus likely to minimize diversion. However, other studies have found that prescriptions for methadone in general practice are consistently sub-optimal, at ~40 mg.^{23,24} Reduced supply of illicit methadone may alternatively be due to reduced market demand. Some drug users purchase illicit methadone for self-medication because they are reluctant to visit their doctor or have difficulties accessing services.³¹ Greater availability of prescribed methadone may have reduced demand for illicit methadone, and our finding of a 3-fold increase in MMT patient years supports this hypothesis. However, a recent review by the National Audit Office found that although there have been improvements in the provision of drug treatment services, there remain problems with access to services in some parts of England and Wales.³³

We found some evidence that methadone prescribing has changed in line with Department of Health guidance.^{20,34} Prescriptions for tablets and injectable methadone declined, with the decline coinciding with the publication of the Department of Health's review of drug services in 1996. Prescribing of oral methadone increased and the proportion of methadone prescribed in instalments rose from 75% in 2001/2 to 81% in 2004/5. However, our findings conflict with that of Strang *et al.*²⁴ whose survey of about 2000 general practitioners in 2001 found that only 43% of methadone prescriptions were for instalment. The short time series available about instalment prescribing makes it difficult to assess its effect on fatal methadone poisoning. We were unable to assess changes in prescribing practice by private doctors, who although they account for only 5% of all

methadone prescribing, are more likely to prescribe larger doses and more injectable methadone.³⁵

Conclusion

Availability of illicit heroin and methadone is a key determinant of fatal poisoning involving these drugs. Expansion of methadone treatment does not appear to be associated with more poisoning deaths. Changes in methadone prescribing were in line with clinical guidelines introduced in 1996 and 1999 and may have contributed to reduced diversion. Increased methadone prescribing is also consistent with greater accessibility to methadone treatment, which is a key feature of the 'British System'. Knowledge of mortality risk is required to assess whether the fall in heroin-related deaths can also be attributed to the success of increased methadone treatment leading to a reduction in consumption

and mortality risk, or to changes in the underlying population of drug users.

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Conflict of interest: None declared.

KEY MESSAGES

- Age-standardized mortality rate for heroin/morphine increased from 5 to 30 per million between 1993 and 2000, subsequently declining to 24 deaths per million in 2004.
- Age-standardized mortality rates involving methadone were similar to heroin until 1997, after which they decreased to just over 1993 levels in 2004.
- During this period the number of methadone prescriptions more than doubled and the death rate per 1000 patient years fell by three quarters.
- The age-standardized rate for heroin/morphine deaths and methadone were strongly associated with law enforcement seizures of these drugs.

References

- 1 Aceijas C, Stimson GV, Hickman M, Rhodes T. Global overview of injecting drug use and HIV infection among injecting drug users. *Aids* 2004;**18**:2295–303.
- 2 European Monitoring Centre for Drugs and Drug Addiction. The State of the Drugs Problem in Europe. Annual Report 2005. Available at: <http://europa.eu.int>.
- 3 De Angelis D, Hickman M, Yang S. Estimating long-term trends in the incidence and prevalence of opiate use/injecting drug use and the number of former users: back-calculation methods and opiate overdose deaths. *Am J Epidemiol* 2004;**160**:994–1004.
- 4 Fischer B, Rehm J, Kirst M *et al*. Heroin-assisted treatment as a response to the public health problem of opiate dependence. *Eur J Public Health* 2002;**12**:228–34.
- 5 Hulse GK, English DR, Milne E, Holman CD. The quantification of mortality resulting from the regular use of illicit opiates. *Addiction* 1999;**94**:221–29.
- 6 Bargagli AM, Hickman M, Davoli M *et al*. Drug-related mortality and its impact on adult mortality in eight European countries. *Eur J Public Health* 2005;**16**:198–202.
- 7 Gossop M, Stewart D, Treacy S, Marsden J. A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. *Addiction* 2002;**97**:39–47.
- 8 Ward J, Hall W, Mattick RP. Role of maintenance treatment in opioid dependence. *Lancet* 1999;**353**:221–26.
- 9 Gossop M. Treatment outcomes: what we know and what we need to know: National Treatment Agency for Substance Misuse, 2005.
- 10 Caplehorn JR, Drummer OH. Methadone dose and post-mortem blood concentration. *Drug Alcohol Rev* 2002;**21**:329–33.
- 11 Corkery JM, Schifano F, Ghodse AH, Oyefeso A. The effects of methadone and its role in fatalities. *Hum Psychopharmacol* 2004;**19**:565–76.
- 12 Strang J, Sheridan J, Barber N. Prescribing injectable and oral methadone to opiate addicts: results from the 1995 national postal survey of community pharmacies in England and Wales. *BMJ* 1996;**313**:270–72.
- 13 Gabbay MB, Carnwath T, Ford C, Zador DA. Reducing deaths among drug misusers. *BMJ* 2001;**322**:749–50.
- 14 Fiellin DA, O'Connor PG. Clinical practice. Office-based treatment of opioid-dependent patients. *N Engl J Med* 2002;**347**:817–23.

- ¹⁵ Strike CJ, Urbanoski K, Fischer B, Marsh DC, Millson M. Policy changes and the methadone maintenance treatment system for opioid dependence in Ontario, 1996 to 2001. *J Addict Dis* 2005;**24**:39–51.
- ¹⁶ Ritter A, Di Natale R. The relationship between take-away methadone policies and methadone diversion. *Drug Alcohol Rev* 2005;**24**:347–52.
- ¹⁷ Neeleman J, Farrell M. Fatal methadone and heroin overdoses: time trends in England and Wales. *J Epidemiol Community Health* 1997;**51**:435–37.
- ¹⁸ Cairns A, Roberts IS, Benbow EW. Characteristics of fatal methadone overdose in Manchester, 1985–94. *BMJ* 1996;**313**:264–65.
- ¹⁹ Seymour A, Black M, Jay J, Cooper G, Weir C, Oliver J. The role of methadone in drug-related deaths in the west of Scotland. *Addiction* 2003;**98**:995–1002.
- ²⁰ Department of Health, Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland. *Drug Misuse and Dependence—Guidelines on Clinical Management*. London: The Stationery Office, 1999.
- ²¹ Christophersen O, Rooney C, Kelly S. Drug-related mortality: methods and trends. *Popul Trends* 1998;Autumn:29–37.
- ²² Mwenda L, Ahmad M, Kumari K. Findings 265. Seizures of drugs in England and Wales, 2003. Home Office, 2005.
- ²³ Strang J, Sheridan J. Effect of government recommendations on methadone prescribing in South East England: comparison of 1995 and 1997 surveys. *BMJ* 1998;**317**:1489–90.
- ²⁴ Strang J, Sheridan J, Hunt C, Kerr B, Gerada C, Pringle M. The prescribing of methadone and other opioids to addicts: national survey of GPs in England and Wales. *Br J Gen Pract* 2005;**55**:444–51.
- ²⁵ Ghodse AH, Corkery JM, Schifano F, Oyefeso A, Bannister D, Annan J. National Programme on Substance Abuse Deaths (np-SAD)—Annual Report 2005. St George's, University of London, 2005.
- ²⁶ Milroy CM, Forrest AR. Methadone deaths: a toxicological analysis. *J Clin Pathol* 2000;**53**:277–81.
- ²⁷ United Nations Office on Drugs and Crime. *World Drugs Report 2005*. New York: United Nations, 2005.
- ²⁸ Gibson A, Degenhardt L, Day C, McKetin R. Recent trends in heroin supply to markets in Australia, the United States and Western Europe. *Int J Drugs Policy* 2005;**16**:293–99.
- ²⁹ Roxburgh A, Degenhardt L, Breen C. Changes in patterns of drug use among injecting drug users following changes in the availability of heroin in New South Wales, Australia. *Drug Alcohol Rev* 2004;**23**:287–94.
- ³⁰ Degenhardt L, Day C, Gilmour S, Hall W. Patterns of illicit drug use in NSW, Australia following a reduction in heroin supply. *Int J Drugs Policy* 2005;**16**:300–07.
- ³¹ Fountain J, Strang J, Gossop M, Farrell M, Griffiths P. Diversion of prescribed drugs by drug users in treatment: analysis of the UK market and new data from London. *Addiction* 2000;**95**:393–406.
- ³² Faggiano F, Vigna-Taglianti F, Versino E, Lemma P. Methadone maintenance at different dosages for opioid dependence. *Cochrane Database Syst Rev* 2003;CD002208.
- ³³ National Audit Office. Changing habits. The commissioning and management of community drug treatment services for adults. Audit Commission, 2002.
- ³⁴ The Task Force to Review Services for Drug Misusers. Report of an Independent Review of Drug Treatment Services in England. Department of Health, 1996.
- ³⁵ Strang J, Sheridan J. Methadone prescribing to opiate addicts by private doctors: comparison with NHS practice in south east England. *Addiction* 2001;**96**:567–76.