infusion ended, an event better supervised during the normal working day.

We do not agree that all patients with methadone overdose should be admitted empirically for 72 hours or that pulse oximetry should be performed continuously for this time. This would result in unnecessarily protracted admissions and inappropriate use of monitoring equipment. Pulse oximetry will not detect hypoventilation in a patient being given supplemental oxygen.⁵ After an initial bolus, the early introduction of a naloxone infusion titrated to the clinical response is appropriate management; this can be stopped after 12-24 hours with the patient kept under close clinical scrutiny for several hours thereafter, particular attention being paid to the conscious level and respiratory rate and depth. Any deterioration in these variables necessitates resumption of the naloxone infusion with an initial bolus as required.

In summary, in this case flumazenil was inappropriately given and the use of naloxone can best be described as too little, with the infusion being given too late and stopped too soon, apparently without adequate clinical supervision. The clinical toxicology results are interesting, but only in relation to the postmortem discussion. The lessons in this case are not those advanced by the authors.

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- 1 Hendra TJ, Gerrish SP, Forrest ARW. Fatal methadone overdose. *BMJ* 1996;313:481-2. (24 August.)
- 2 Association of the British Pharmaceutical Industry. Anaxate (flumazenil). *ABPI data sheet compendium 1995-6*. London: ABPI, 1995:1419-20.
- 3 Haverkos GP, DiSalvo RP, Imhoff TE. Fatal seizures after flumazenil administration in a patient with mixed overdose. *Ann Pharmacother* 1994;28:1347-9.
- 4 BMA and Royal Pharmaceutical Society of Great Britain. Emergency treatment of poisoning—analgesics (opioid). *British national formulary: number 31 (March 1996)*. London: BMA and RPSGB, 1996:22.
- 5 Hutton P, Clutton-Brock T. The benefits and pitfalls of pulse oximetry. *BMJ* 1993;307:457-8.

Patient may have injected methadone while in hospital

EDITOR,—The case of fatal methadone overdose reported by T J Hendra and colleagues relied for its diagnosis on the ability of hot chocolate to release a large load of methadone from the patient's gut, where it had been stored for some hours.¹ Such an event is possible, but the authors do not convincingly show it to have been the cause of death.

An alternative suggestion for the role of the hot chocolate is that the patient used the request for it to distract a nurse while obtaining a needle and syringe. He could then have injected a dose of methadone intravenously before retiring to bed. This would explain the high serum concentration and the absence of methadone in his gut as well as the timing of his death. Although the patient was in hospital at the time, it is not unknown for inpatients to obtain supplies of illicit drugs. In addition, any injection site would be likely to be overlooked in a patient with multiple venepuncture sites from his time in the intensive care unit.

The authors' conclusion that patients presenting with methadone overdose need to be carefully monitored is justified, but the availability of the means to inject drugs must also be considered.

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Close observation in intensive care unit is required when naloxone infusion ends

EDITOR,—T J Hendra and colleagues report the death of a young man from methadone toxicity.¹ This case provides an important lesson that the authors have missed. The patient, who had a potentially fatal serum methadone concentration, was discharged from an intensive care unit to a general medical ward while receiving treatment with naloxone by intravenous infusion. The infusion stopped at 3 30 am, and 30 minutes later he was sleeping, but no report of his neurological status is given, and he may have been comatose at that time. The authors report no further assessment of the patient until he was found dead 2 hours 55 minutes later.

Naloxone's elimination half life may be as short as 30 minutes, and recurrence of coma after treatment is stopped is well recognised. This is especially likely when long acting opioids are involved. Patients requiring a naloxone infusion should be managed in an intensive care unit and closely observed for recurrence of toxicity after the infusion stops. The likely sequence of events in this case is that the naloxone infusion ended while the patient was in a darkened general medical ward in the middle of the night and he then lapsed into a coma induced by methadone, had an unwitnessed respiratory arrest, and died.

The shortfall in resources for intensive care in Britain is well known internationally.² If the crisis has reached such proportions that simple lifesaving measures such as naloxone infusions cannot be managed in intensive care units then explicit instructions must be given to ward nursing staff for close observation and formal neurological assessment of patients when naloxone infusions end. This is particularly so if the infusion is to stop in the middle of the night, when casual observation of deterioration is least likely. If these measures are not taken this tragic incident will be repeated. In the hospital where I work all deaths in hospital of patients who have been treated in the intensive care unit are reviewed at a monthly meeting attended by the intensive care specialists and a representative of the hospital's quality assurance programme. Had this death occurred in my hospital it would have been classified as preventable, and the management of the patient after the naloxone infusion finished would have been considered substandard.

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- 1 Hendra TJ, Gerrish SP, Forrest ARW. Fatal methadone overdose. *BMJ* 1996;313:481-2. (24 August.)
- 2 Ryan DW. Providing intensive care. *BMJ* 1996;312:654.

Authors' reply

EDITOR,—We agree with Emyr W Benbow and colleagues' suggestion that tissue redistribution may partly explain the postmortem increase in blood methadone concentration seen in our patient. In another recent case one of us (ARWF) found that a postmortem blood sample contained 71 µg methadone/l, whereas a sample obtained shortly before death contained 38 µg/l. One potential mechanism for the possible increase in blood methadone concentrations associated with food intake is that food increases mesenteric and portal blood flow, causing release of methadone from the liver. Whatever the explanation, the implication of Benbow and colleagues' letter is that, as we proposed, methadone overdose requires prolonged monitoring in hospital.

We accept N Nichol and colleagues' point about the use of flumazenil but do not agree with

their comments about naloxone in this patient. The initial doses of naloxone were small but sufficient to produce the desired effect; the infusion was titrated against the clinical response, with the dose given being sufficiently small to make the late occurrence of further problems unexpected and indicative of another mechanism. We agree that pulse oximetry will not detect hypoventilation in the absence of hypoxia but believe that it has a place in the inpatient management of this problem.

The point by Aidan J Byrne about surreptitious use of drugs on the ward is well made, particularly when a patient's condition unexpectedly deteriorates, though in this instance no syringes or other paraphernalia of drug misuse were found in the patient's possession after his death.

Simon Finfer's statement that all patients requiring a naloxone infusion should be managed in an intensive care unit may not be sustainable in many hospitals owing to competing clinical demands and limited resources. In retrospect, stopping the naloxone infusion in the middle of the night without monitoring the patient by pulse oximetry was not optimal management—which was the point of our report.

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Methadone treatment

Methadone treatment is not the only option

EDITOR,—The recent editorial and three papers about methadone raise many points of interest and controversy.¹⁻⁴ The editorial's message—that methadone works, and so we should get on and use it—conceals not only the issue of deaths in drug users² but also several other issues: drug users in prison, social inequalities and poverty relating to drug users, the spread of HIV from drug users to the heterosexual population, the fact that drug users are a national pool of infection with hepatitis B and C viruses, and many other issues that decades of experience in North America, Australia, and the rest of Europe have shown do not disappear with methadone treatment. More worrying still, the problems that politicians have recently experienced over comparatively uncontroversial drug issues make one wonder what has happened to politics and politicians in the past 20 years that makes it so much less possible than it was in the 1960s to consider radical solutions to these issues.

The arguments about the efficiency of methadone in the well resourced American system are well rehearsed; in contrast, the various European systems have a shorter history and have developed along the more comprehensive harm minimisation approach. The contrast between Europe and North America was evident at the recent AIDS conference in Vancouver, where it became apparent that the United States still has major problems in implementing strategies such as needle exchange that have been accepted in Europe for 10 years.

Although methadone is undoubtedly the pharmacological mainstay, it is not a panacea. Other options tried have been injectable methadone, injectable heroin, and shorter acting drugs such as buprenorphine. Our experience with dihydrocodeine over 15 years has been that this is a safe alternative for the many drug users who do not wish to give up the use of a short acting drug.⁵ Unlike buprenorphine, dihydrocodeine is

not injected and is a good alternative to injectable methadone. In detoxification it seems much easier to reduce.

Rather than suggesting that the treatment of drug use should be a single strand management package—the use of oral methadone in a restricted and supervised manner—it would be useful to point out the many complex issues relating to drug dependence, which require exploration and constant innovation, evaluation, and modification of policies.

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- 1 Sorensen JL. Methadone treatment for opiate addicts. *BMJ* 1996;313:245-6. (3 August.)
- 2 Cairns A, Roberts ISD, Benbow EW. Characteristics of fatal methadone overdose in Manchester 1985-94. *BMJ* 1996;313:264-5. (3 August.)
- 3 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;313:270-2. (3 August.)
- 4 Sheridan J, Strang J, Barber N, Glanz A. Role of community pharmacies in relation to HIV prevention and drug misuse: findings from the 1995 national survey in England and Wales. *BMJ* 1996;313:272-4. (3 August.)
- 5 Robertson JR. Dihydrocodeine—a second strand of treatment for drug misusers. *Drug Alcohol Rev* 1996;15:199-201.

Only half of patients store methadone in safe place

EDITOR,—The value of oral methadone maintenance programmes in opiate dependence has now been established,¹ but supplies of methadone given to patients to take home pose risks of overdose to adults and children who inadvertently drink the linctus.^{2,3} Altogether 36% of prescriptions for methadone are reportedly dispensed in weekly instalments,⁴ yet no information is available on the adequacy of the storage of take home supplies. We report on the domestic storage arrangements of 87 patients who were dependent on opiates and receiving prescribed take home supplies of methadone.

Forty patients had current parental responsibility for at least one child under the age of 12. Current parental responsibility was commoner among the women (16/27 (59%)) than the men (24/60 (40%)) ($\chi^2 = 2.06$, $P < 0.05$). Methadone supplies were stored in a wide variety of locations: in a cupboard or wardrobe (32 patients), fridge (7), or drawer (6) or by the bed (12). We considered 43 to be storing their methadone safely. Safe storage was commoner among those with children at home (75% v 28%, $P < 0.001$; table 1). Nevertheless, 18 reported leaving methadone lying around the home, including five with current parental responsibility. Women were more likely to store their methadone safely (17/27 (63%) v 26/60 (43%)),

although, among those with parental responsibility, three quarters of both men and women stored their methadone safely.

Greater precautions were taken in storing illicit drugs: of the 68 still using illicit drugs, 51 stored them safely. As with methadone, safe storage was commoner among those with current parental responsibility (90% v 63%, $P < 0.05$; table 1). For the 51 patients with needles and syringes at home safe storage was commoner among those with current parental responsibility (83% v 32%, $P < 0.001$). Sixty four patients had seen posters in drug agencies warning of the dangers of methadone to children. Only 25, however, were aware of someone having discussed with them the dangers of methadone to children, although this was twice as likely among patients with parental responsibility than without (43% v 17%, $P < 0.05$; table 1).

Widespread reliance on weekly take home supplies of methadone⁴ increases the risks of inadvertent overdose by children and others. A substantial minority of patients do not take adequate safeguards over the security of drugs in the home. The greater precautions taken with illicit drugs may indicate a failure to appreciate the equivalent risk of overdose associated with prescribed supplies. The lack of attention to this important issue is disturbing. Counselling on this danger should become routine when take home supplies of methadone are prescribed.

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- 1 Farrell M, Ward J, Des Jarlais DC, Gossop M, Stimson GV, Hall W, *et al*. Methadone maintenance programmes: review of new data with special reference to impact on HIV transmission. *BMJ* 1994;309:997-1001.
- 2 Cairns A, Roberts I, Benbow E. Characteristics of fatal methadone overdose in Manchester 1985-94. *BMJ* 1996;313:264-5. (3 August.)
- 3 Binchy J, Molyneux E, Manning J. Accidental ingestion of methadone by children in Merseyside. *BMJ* 1994;308:1335-6.
- 4 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;313:270-2. (3 August.)

Methadone concentrations taken as indicating deaths due to overdose need to be reviewed

EDITOR,—We are concerned that recent reports of death from methadone overdose may be greatly exaggerated owing to the use of inappropriately low serum methadone concentrations in attributing cause of death.^{1,2}

Alison Cairns and colleagues do not specify what was considered to be a fatal serum methadone concentration in the 90 cases reported from Manchester,¹ but a recent study from Sheffield of deaths due to methadone reported an average concentration of 560 $\mu\text{g/l}$.² Pathologists generally regard a serum methadone concentration of over 400 $\mu\text{g/l}$ as sufficient to cause death in those who have tolerance to opiates (A Cairns, personal communication). This is at odds with recommendations for monitoring patients receiving methadone maintenance, whose serum concentrations should be kept within a range of 150-600 $\mu\text{g/l}$ or above a minimum of 400 $\mu\text{g/l}$.⁴

Furthermore, methadone seems to have a high safety margin in those receiving maintenance treatment. We were recently contacted by a pharmacist who had mistakenly made up methadone mixture to a strength of 10 mg/ml instead of 1 mg/ml and dispensed 10 times the normal daily dose of methadone to three of our patients. The pharmacist delayed informing us of his mistake until all three had failed to appear for their next dispensing the following day. We immediately visited the patients at their homes and were relieved to find them alive. Two were used to taking their methadone twice daily and had not felt the need to take their second dose. One had swallowed all of her 50 ml daily dose, thereby taking 500 mg of methadone, a 10-fold overdose. Although all three felt grossly intoxicated, none had felt the need for treatment.

There is an urgent need to review the criteria by which pathologists attribute cause of death to methadone overdose. Inflated statistics on deaths due to methadone will only impede the development of effective services, which should be available to all people dependent on opiates.⁵

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- 2 Clark JC, Milroy CM, Forrest ARW. Deaths from methadone use. *J Clin Forensic Med* 1995;2:143-4.
- 3 Dole VP. Implications of methadone maintenance for theories of narcotic addiction. *JAMA* 1988;260:3025-9.
- 4 Loimer N, Schmid R, Grunberger J, Jagge R, Linzmayer L, Presslich O. Psychophysiological reactions in methadone maintenance patients do not correlate with methadone plasma levels. *Psychopharmacology* 1991;103:538-40.
- 5 Sorensen JL. Methadone treatment for opiate addicts. *BMJ* 1996;313:245-6. (3 August.)

Treatment in general practice can be successful

EDITOR,—We are not surprised that John Strang and colleagues found that prescribing of injectable methadone was widespread and was prevalent in non-specialist settings.¹ At our practice we receive many requests from drug users to prescribe injectable methadone as well as other replacement drugs at higher doses than those recommended by the specialist service protocols or, indeed, the prescribing guidelines suggested by the Department of Health. This position is partly forced on us by the limited prescribing practices of the local specialist services, which often seem unwilling to support or take on the care of drug users whose needs are complex and fall outside the accepted criteria for those who are perhaps best managed in general practice.

We have often taken on such drug users, because from a public health and client centred perspective the options of continued and increased harm, both through continued consumption of drugs obtained on the black market and through the use of private prescribers, is

Table 1—Storage of methadone by patients with and without children at home. Figures are numbers (percentages) except where stated otherwise

	No children at home (n = 47)	Children at home (n = 40)	Significance
Clinical practice:			
Daily dose (mg)	67	67	$t = 0.02$, NS
Daily pick up was usual arrangement	29 (62)	24 (60)	$\chi^2 = 0.003$, NS
Childproof caps used	47 (100)	36 (90)	$\chi^2 = 2.91$, $P < 0.05$
Aware of danger through posters	36 (77)	28 (70)	$\chi^2 = 0.20$, NS
Aware of danger through discussion	8 (17)	17 (43)	$\chi^2 = 5.6$, $P < 0.05$
Safe storage at home of:			
Methadone	3/47 (28)	30/40 (75)	$\chi^2 = 19.4$, $P < 0.001$
Illicit drugs	24/38 (63)	27/30 (90)	$\chi^2 = 6.4$, $P < 0.05$
Needles and syringes	9/28 (32)	19/23 (83)	$\chi^2 = 13.0$, $P < 0.001$