

DRUG & ALCOHOL FINDINGS *Research analysis*

This entry is our analysis of a study considered particularly relevant to improving outcomes from drug or alcohol interventions in the UK. The original study was not published by Findings; click [Title](#) to order a copy. Free reprints may be available from the authors – click [prepared e-mail](#). [Links](#) to other documents. [Hover over](#) for notes. [Click to](#) highlight passage referred to. Unfold extra text The Summary conveys the findings and views expressed in the study. Below is a commentary from Drug and Alcohol Findings.

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▶ **Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal.**

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Annals of Internal Medicine: 2013, 158, p. 1–9.

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The first simulation of the cost-effectiveness of supplying naloxone kits to heroin users to enable them to prevent overdose deaths estimates that in the US context these programmes would be well within the range considered a cost-effective health intervention. Findings are likely to broadly apply to the UK, one weak link being whether drug users given the kits actually carry them around.

SUMMARY Naloxone is a safe and effective antidote to **opioid** overdose. At first administered by medical personnel, since the late 1990s laypersons who might witness an opioid overdose have been provided naloxone and trained in its use. Naloxone 'kits' for laypersons are usually wallet-sized packets containing two doses of naloxone ready for injection and other items, including syringes, brochures, simple rescue-breathing masks, and brief educational materials about overdose risks and management.

Naloxone distribution programmes seem to reduce both community-level overdose death rates and the likelihood of any individual overdose progressing to death. These programmes may be highly cost-effective because the medication is inexpensive and its use may result in a life saved, but phenomena such as the recurrent nature of overdose complicate these calculations. Based on existing findings, the featured analysis was the first to simulate the expected outcomes and cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal, compared to usual procedures in the absence of a naloxone programme.

Costs were estimated not just for the programme but also associated costs for US society as a whole. These costs were set against resultant changes in the years of life (adjusted for the quality of those years – quality-adjusted life-years or QALYs) to be expected for the entire population of heroin users in the programme's target area. If on average the programme saved one quality-adjusted life-year at a cost of less than \$50,000 more than usual care, it would meet conventional US criteria for qualifying as cost-effective health intervention.

Based on the available data, among the assumptions made by the core analysis was that naloxone was distributed to a fifth of the heroin users in the programme's area, that typically heroin was used for 15 years, that experiencing an overdose makes users 10% more likely to stop using, that each year about 1 in 8 heroin users overdose, and that as a result 1 in a 100 die.

Without a naloxone programme, assumptions were made about the chances of an overdose being witnessed and if it was, that emergency medical services would be called, and as a result the chance that the incident would end in death. With a programme, the analysts combined the proportion of heroin users to whom naloxone was distributed with the likelihood that one would witness the overdose, and that they would administer naloxone, resulting over a year in a 13.6% or roughly 1 in 7 chance of a prescribed dose of naloxone being administered. The same reduction in risk of death was assumed if either naloxone was administered or emergency services called, and a yet lower risk if both happened.

Costs for replacement kits were incurred after each overdose in which naloxone was administered and biannually among active heroin users to account for product expiration. When emergency medical care was simulated to have been called, these costs too were included. A supplementary analysis accounted for the concern that heroin users who survive overdose will impose large health-care and criminal justice costs. The core assumptions were varied to test the degree to which naloxone's cost-effectiveness varied in a wide range of feasible scenarios.

Main findings

It was estimated that if naloxone were distributed to a fifth of heroin users in the programme's target area, over the entire heroin-using careers of all the users 6.5% of overdose deaths would be prevented. The preventive impact would increase proportionately the more heroin users were supplied naloxone. At the 20% distribution level, one overdose death would be prevented for every 164 naloxone kits distributed. An alternative methodology produced similar estimates, with 6.1% of overdose deaths prevented and one death prevented per 227 kits. Whatever feasible assumptions were made, naloxone distribution reduced the rate of overdose death among active users and across all active and former heroin users in the simulated samples.

Additionally, over the entire simulation period naloxone programmes were forecast to result in a 1.7% increase in the proportion of users who stop using heroin. Though lives would be saved because fewer overdoses progress to a fatality, due to the survival of high-risk heroin users naloxone distribution would result in a 1.3% increase in overdose incidents. Under core assumptions and in all feasible scenarios, each quality-adjusted life-year gained by a naloxone programme

Key points
From summary and commentary

The first simulation of the cost-effectiveness of supplying naloxone kits to heroin users to enable them to prevent overdose deaths has endorsed them as a cost-effective health intervention.

Though constructed for a US context, the results are so robust under widely varying assumptions that the study's implications are likely to apply broadly to the UK.

However, in the UK one study has found that very few users given naloxone kits carry them around, reducing the programme's potential to save lives.

Under core assumptions and in all realistic scenarios, each quality-adjusted life year gained by a naloxone programme cost society much less than the extra \$50,000 below which a health intervention is conventionally considered a cost-effective use of resources. Core assumptions yielded an extra cost to society of \$421 per quality-adjusted life year gained. When naloxone administration was assumed to reduce calls on emergency medical services, naloxone programmes not only saved lives, but also imposed lower costs on society than the usual-care comparator.

The degree of cost-effectiveness varied under different assumptions about how much the programme cost and how effectively lay-administered naloxone saved lives, but was relatively unaffected by how widely naloxone was distributed, rates of overdose and other drug-related deaths, rates of abstinence and relapse, assumed quality of life, or the cost of medical services. Even in a worst-case scenario (maximised cost of naloxone; minimised chances of an overdose being witnessed, of naloxone being used, and of it preventing death), each extra quality-adjusted year of life gained cost society an extra \$14,000. Under opposing assumptions, the programme resulted in lower costs for society per quality-adjusted year of life saved.

An alternative methodology gave similar results – based on core assumptions, an extra cost to society of \$438 per quality-adjusted life year gained. Taking into account extra health and criminal justice costs due to the survival of heroin users who would otherwise have died earlier, the equivalent figure rose to \$2429, still well within the range considered a cost-effective use of health resources.

The authors' conclusions

This simulation study indicates that in the US context, distributing naloxone to heroin users would reduce mortality and be cost-effective even under markedly conservative assumptions about use levels, effectiveness, and cost. Estimates are uncertain due to the absence of randomised trials, but there are few or no scenarios in which naloxone would not be expected to gain quality-adjusted years of life at associated costs well within the range for cost-effective health-care interventions. Data from areas which have implemented naloxone programmes suggest that in practice the benefits may be far greater than those forecast.

The model's predictions in respect of repeat overdoses may be thought to have implications for targeting naloxone programmes. Repeat overdoses emerged as responsible for 61% of overdose deaths in the first 10 years of a heroin use career and 85% over an entire career. The implication is that active heroin users who survive late into their use careers are likely either to have experienced no overdoses, or several; few will have experienced just one. This pattern blunts the benefits of naloxone distribution because those who survive an overdose are likely to overdose again. Targeting naloxone at heroin users who have overdosed at least once (for example, individuals recruited from emergency departments) may reduce intervention costs, but benefits would be offset by failure to prevent early death among the youngest users and, possibly, by failure to reach those more likely to carry naloxone because of their attention to health. Ultimately, naloxone distribution is likely to have similar cost-effectiveness regardless of the age of the target population or how long they had been using heroin.

Drug users face substantial stigma and are often considered to be of low value to society. To address this, one scenario considered the survival of heroin users to impose net costs on society due to health service usage and crime. Even under such assumptions, distributing naloxone remained cost-effective.

Despite effectiveness and cost-effectiveness at preventing overdose deaths, the predictions were that the absolute number of averted deaths would be small. Studies of actual programmes may find it difficult to identify and attribute these small changes to naloxone, despite there being real benefits.

FINDINGS COMMENTARY Though constructed for a US context, the results of this analysis are so robust under widely varying circumstances, and the margins so great before cost-effectiveness became questionable, that its implications are likely to apply broadly to the UK. Notably, cost-effectiveness was largely unaffected by differences in how widely an area distributed naloxone, the cost of medical services, or in rates of overdose, other drug-related deaths, abstinence or relapse.

In line with the featured analysis, experts convened by the World Health Organization [have judged](#) the "risk-benefit profile to be strongly in favour of naloxone distribution", and strongly recommended naloxone provision and associated training for people likely to witness an [opioid](#) overdose.

Naloxone is, however, far from a total solution. WHO's experts cautioned that naloxone "does not address the underlying causes of opioid overdose"; further reducing the number of deaths would also entail monitoring and curbing inappropriate opioid prescribing and over-the-counter sales, and extending treatment for opioid dependence. Wider initiatives of this kind were among those recommended by Public Health England in its [guidelines](#) on preventing drug-related deaths and by the US authorities in their [Opioid overdose toolkit](#).

An Effectiveness Bank [hot topic](#) has assessed the evidence for naloxone programmes and the UK practice and policy context. Yet to be incorporated in that entry are [findings](#) on Scotland's national naloxone programme, which implied that it was likely to have resulted in a 36% reduction in the proportion of all opioid-related deaths accounted for by the four weeks after release from prison. The effect was to gain a quality-adjusted year of life for from £560 to £16,900, both well within the range considered a cost-effective use of resources in Britain. In contrast, the programme had little apparent effect on deaths after discharge from hospital, perhaps because effects were too small to register, and/or because the risks of this transition are less well known than those associated with leaving prison. Uncertainty over pinning down any impacts to the naloxone programme may have been an illustration of the difficulty [alluded to](#) by the authors of the featured analysis, despite the probability of there having been real benefits.

One variable which emerged as a critical factor in Scotland was not separately accounted for in the featured analysis – the proportion of drug users given a naloxone kit who actually carry it with them. Unless they do, outside the home they cannot respond to overdose by administering naloxone. On the basis of a [US study](#), the featured analysis assumed that if an overdose was witnessed by a drug user who had been trained in overdose management and given a naloxone kit, 8 in 10 times they would administer naloxone. But in Scotland in 2013–14, just 5% of needle exchange attendees prescribed a kit in the past year [were carrying it](#) with them when interviewed at the needle exchange. It means that if on that day they had been present at an overdose outside their home, only 1 in 20 would have been in a position to use the kit, and probably fewer would actually have done so. Though disappointing, the low carriage rate might have been related to the bulkiness of the naloxone kits used in Scotland and the fact that many of the exchanges were run by a service which also provided maintenance prescribing, possibly raising concerns in patients that carriage would be interpreted as a sign of continuing illegal drug use. Failure to carry naloxone with you is of less concern to the degree to which overdoses tend to happen in the home. [In 2014 in Scotland](#) over two-thirds of drug-related overdose deaths involved drugs taken at home and nearly two-thirds also occurred in the home.

Last revised 18 December 2016. First uploaded 12 December 2016.

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