Value for money in reducing opioid-related deaths

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During the past decade, overlapping epidemics of opioid overdose deaths have occurred in the USA. A steep increase in overdose deaths caused by pharmaceutical opioids during the past 15 years[1] has been followed more recently by a new epidemic of heroin overdose deaths.[2] Opioid overdose deaths have been a major contributor to the reversal in life expectancy of middle-aged white people in the USA,[3] and opioids cause the greatest loss of life from fatal drug overdoses worldwide.[4] Opioid overdose deaths can be prevented by engaging opioid-dependent people in methadone or buprenorphine substitution treatment, and distributing the opioid antagonist naloxone to enable bystanders to reverse opioid overdoses.[2]

In a study reported in *The Lancet Public Health*, Jennifer Uyei and colleagues[5] used economic modelling to identify the most efficient ways of reducing mortality from injected opioids in the USA. They probabilistically modelled the cost-effectiveness of current practice in Connecticut—namely, distributing naloxone via syringe service programmes. They also modelled the cost-effectiveness of combining naloxone distribution with linkage to addiction treatment and adding an HIV prevention measure—namely, antiretroviral drugs for pre-exposure prophylaxis (PrEP) against HIV infection. The investigators developed a decision analytic Markov model to simulate the effects of these combinations of interventions on opioid overdoses, HIV incidence, overdose-related deaths, and HIV-related deaths. They compared the modelled effects of each strategy with no additional intervention (syringe service programme only) and considered the cost-effectiveness of all feasible combinations of the strategies. They also did sensitivity analyses to assess the effects on estimated cost-effectiveness of the uncertainty about the values of key parameters in their modelling (eg, baseline prevalence of HIV infection, uptake in the at-risk population, and likely degree of compliance).

The investigators' findings support those of a previous modelling study in demonstrating that it is cost-effective for syringe service programmes to distribute naloxone to opioid users so that bystanders and peers can reverse opioid overdoses.[6] The small incremental cost-effectiveness ratio (ICER) for distributing naloxone via syringe service programmes (US$323 per quality-adjusted life year) reflects the modest cost of naloxone, its effectiveness in reversing opioid overdoses, the strong interest among opioid injectors in using naloxone, and the minimal risks of doing so.[7] For these reasons, naloxone distribution to high-risk opioid injectors has already been implemented in parts of the USA[8] and Scotland.[9]

Uyei and colleagues' analysis also suggested that the combination of naloxone distribution plus linking syringe service programme attendees into methadone treatment is cost saving. This finding is consistent with a substantial body of evidence that opioid substitution treatment reduces illicit heroin use and opioid overdose mortality[10] and is a highly cost-effective intervention.[11] The sensitivity analyses suggest that we can have reasonable confidence in the public health benefits and cost-effectiveness of combining naloxone distribution with linkage to methadone treatment. The combination was no longer cost saving if the risk of relapse to drug use was higher than in the base model, but the combination remained highly cost-effective.

The cost-effectiveness of adding PrEP to naloxone distribution and linkage to methadone treatment alone or in combination was less certain. The best case estimate was that the ICER for this combined intervention was just under $100 000, a commonly used threshold for funding health-care interventions in the USA. The sensitivity analyses suggested substantial uncertainty about this estimate because the ICER remained below the $100 000 threshold in only a third of simulated cases. The $100 000 threshold may be acceptable for the USA, which has a high prevalence of HIV infection in injecting drug users (because of failure to implement syringe service programmes early in the HIV epidemic). However, the total cost of distributing PrEP to injecting opioid users would be substantial, even for the USA. This caveat raises the question of whether it would be more efficient to expand access to opioid substitution treatment (including buprenorphine), which is still difficult to access in many parts of the USA.

Uyei and colleagues' analyses should provide an important stimulus to more sophisticated modelling of policies to reduce opioid overdose deaths in the USA. Such modelling will require more epidemiological research and clinical trials to reduce uncertainties about

the likely uptake, compliance with, and effectiveness of different combinations of interventions. In the meantime, these findings support decisions by many public health authorities in the USA to distribute naloxone to high-risk opioid users.[8] They also strengthen the case for expanding access to and engaging more opioid-dependent people in addiction treatment. Public health interventions to reduce opioid-related deaths should be accompanied by prospective investigations to assess the extent to which the modelled public health benefits and cost-effectiveness findings are realised when these interventions are scaled up on a population level.

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