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Cost-Effectiveness of Take-Home Naloxone for the Prevention of Overdose Fatalities among Heroin Users in the United Kingdom

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ABSTRACT

Background: Heroin overdose is a major cause of premature death. Naloxone is an opioid antagonist that is effective for the reversal of heroin overdose in emergency situations and can be used by nonmedical responders. **Objective:** Our aim was to assess the cost-effectiveness of distributing naloxone to adults at risk of heroin overdose for use by nonmedical responders compared with no naloxone distribution in a European healthcare setting (United Kingdom). **Methods:** A Markov model with an integrated decision tree was developed based on an existing model, using UK data where available. We evaluated an intramuscular naloxone distribution reaching 30% of heroin users. Costs and effects were evaluated over a lifetime and discounted at 3.5%. The results were assessed using deterministic and probabilistic sensitivity analyses. **Results:** The model estimated that distribution of intramuscular naloxone, would decrease overdose deaths by around 6.6%. In a population of 200,000 heroin users this equates to the prevention of 2,500 premature deaths at an incremental cost per quality-adjusted life year (QALY) gained of £899. The sensitivity analyses confirmed the robustness of the results. **Conclusions:** Our evaluation suggests that the distribution of take-home naloxone decreased overdose deaths by around 6.6% and was cost-effective with an incremental cost per QALY gained well below a £20,000 willingness-to-pay threshold set by UK decision-makers. The model code has been made available to aid future research. Further study is warranted on the impact of different formulations of naloxone on cost-effectiveness and the impact take-home naloxone has on the wider society.

Keywords: cost-effectiveness, death, drug overdose, economic model, heroin addiction, naloxone, preventative measures, quality-adjusted life-years.

Introduction

Heroin use carries a high risk of respiratory depression and overdose death, which accounts for substantial mortality in Europe, and has recently increased in some regions in Europe [1,2]. Naloxone, an opioid antagonist, has been shown to decrease overdose-related mortality when used by nonmedical responders in emergency situations, in combination with training and education [3–6]. European drug agencies [7] and the World Health Organization [8] recommend that take-home naloxone be more widely available. Prefilled formulations of naloxone for intramuscular administration have been the predominant form used in take-home naloxone programs across Europe [7,9]; an intranasal form has, however, been used in recent programs in Norway and Denmark (prefilled syringe with nasal adaptor kit) [10,11].

To date, no studies have assessed the cost-effective of take-home naloxone in Europe. Two studies in the United States [12,13], one of which was later adapted to Russia [14], modeled the costs and benefits of distributing intramuscular naloxone to heroin users for use by nonmedical responders. In both cases, naloxone was considered to be robustly cost-effective. Given the recent rise of drug-related mortality in some countries across Europe and the call for the increase in availability of take-home naloxone programs, it will be critical for decision makers to understand the pharmacoeconomic implications of implementing new programs or expanding existing ones.

There is a need for an economic assessment of take-home naloxone in the European setting from a public health system perspective. The main objective of this study was to replicate the US economic model developed by Coffin and Sullivan [12] and adapt it to the United Kingdom to assess the cost-effectiveness of distributing naloxone to adults at risk of heroin overdose for use by nonmedical responders (i.e., heroin users, family, friends, and carers). We chose the United Kingdom because of its high and increasing

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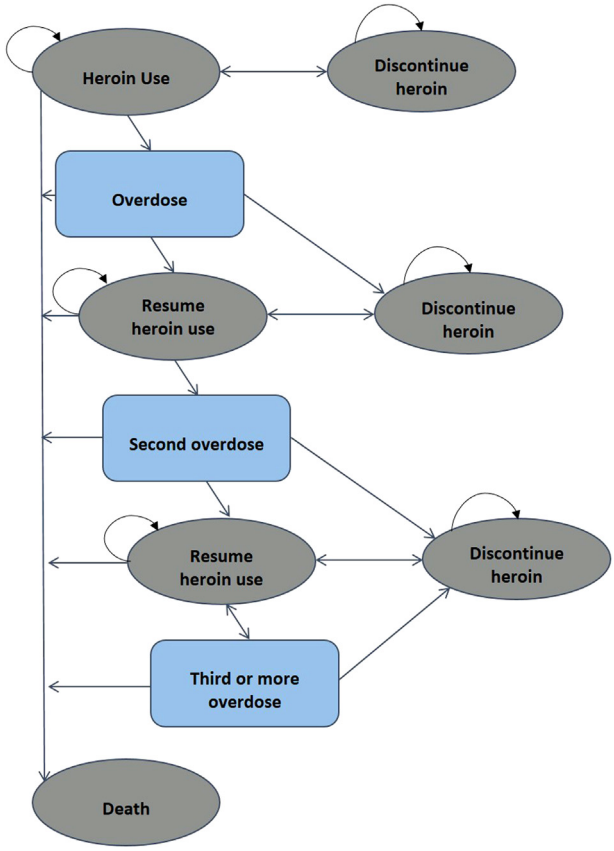

Fig. 1 – Markov model of heroin use, discontinuation overdose, and death. Adapted from Coffin and Sullivan [12].

heroin-related mortality rate [1,15], the introduction of new government regulations in 2015 making naloxone exempt from prescription-only medicine requirements [16], and policy imperatives aimed at widening use [17]. Because current health economic models in the area are not widely available, a secondary objective of this study was to make a version of our model publicly available in R language, version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria) [18]. This version is available as a supplementary file with an associated "readme" instruction file. It allows researchers to investigate further the costs and benefits of interventions aimed at reducing overdose deaths and also aids health care decision makers with resource allocation decisions by presenting fully transparent and adaptable calculations.

Methods

Model Structure

A Markov model [19] with an integrated decision tree was developed to estimate the costs and outcomes of distributing take-home naloxone to adults at risk of heroin overdose. The model was a replication of the Coffin and Sullivan model [12] and adaptations were made to both structure and content to make it relevant for the UK health care system. The model had a lifetime horizon (default value set at 64 years), a health care perspective, 1-year cycles and it included standard background mortality [20].

The Markov model tracked heroin users through four health states (Fig. 1). Heroin users were to enter the model in "heroin use" and could discontinue heroin use, resume heroin use, or die for other reasons (all-cause death). Heroin users could also have an overdose (fatal or nonfatal), which was modeled separately using a decision tree (Fig. 2). The decision tree produces three cycles of overdose, with the final cycle for the third and all subsequent overdose events. The decision tree models the potential pathway of a patient through an overdose event for intramuscular naloxone distribution versus no naloxone distribution. An overdose could be witnessed or not witnessed, and of those witnessed, naloxone may or may not be administered when available. Furthermore, in overdoses that are witnessed, an ambulance may or may not be called. At the terminus of each arm, the patient may either live or die. The probabilities at each stage differ depending on whether the overdose is witnessed, naloxone is available, naloxone is used, and whether an ambulance is called.

First, a replication of the Coffin and Sullivan model was developed using the same structure and parameter inputs for all clinical and cost variables as published in the original article [12]. The accuracy of the model was assessed by comparing the clinical and cost-effectiveness outcomes with those provided by Coffin and Sullivan (personal communication, June, 2016). We were confident that we had replicated the original model as closely as possible with differences in incremental costs, quality-adjusted life-years (QALYs) and cost-effectiveness ratio being no more than $5, 0.01, and $23, respectively. This variance resulted from rounding effects and uncertainty regarding inputs not reported or referenced in the Coffin and Sullivan article, for example, standard background mortality rates.

Second, the replicated model was adapted to the UK health care system, which included structure and content changes. A targeted literature review was conducted to identify UK-specific input parameters, when available. Key terms were used to search MEDLINE and online search engines (search terms included heroin, opioid, drug-related mortality, overdose, and naloxone). No date limit was applied to the searches. The baseline model was adjusted to begin at 22 years, which reflects the average age of onset of heroin use in Europe [21], and age-specific background mortality for the United Kingdom was used [22]. The input parameters and ranges are presented in Table 1, with detailed rationale for parameter selection given in Appendix Table 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2018.07.014. The model was built in Microsoft Excel 2016 and subsequently reproduced in R version 3.3.2 [18] and validated against the Excel version.

Markov Model Transitions

Annual transition probabilities outlined in the Coffin and Sullivan model were based on epidemiological evidence derived from North America, Australia, and Europe [12]. It was assumed that these estimates were relevant for the United Kingdom. The estimates are based on evidence demonstrating that 50% of users relapse over 5 years resulting in a medium duration of heroin use of 15 years, 33% to 70% of users overdose over a lifetime, and the principal risk factor for overdose is previous overdose and therefore risk increases with each overdose [12].

Decision-Tree Parameters

Decision-tree input parameters were adapted to align with the availability and structure of UK health care services and were sourced from UK studies when available. The proportion of heroin users reached by the naloxone take-home program was assumed to be 30%. This was based on the target coverage for the Scottish naloxone take-home program aiming to reach one-third of injecting heroin users [23]. The proportion of witnessed overdoses was assumed to be 85%, on the basis of a UK study demonstrating that 85% of heroin users in treatment had a