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Review Article

Acceptability and feasibility of naloxone prescribing in primary care settings: A systematic review

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ABSTRACT

Naloxone access through established healthcare settings is critical to responding to the opioid crisis. We conducted a systematic review to assess the acceptability and feasibility of prescribing naloxone to patients in primary care. We queried PubMed, EmBase and CINAHL for US-based, peer-reviewed, full-length, original articles relating to acceptability or feasibility of prescribing naloxone in primary care. Searches yielded 270 unduplicated articles; one analyst reviewed all titles and abstracts. Two analysts independently reviewed eligible articles for study design, study outcome, and acceptability and/or feasibility. Analyses were compared and a third reviewer consulted if discrepancies emerged. Seventeen articles were included. Providers' willingness to prescribe naloxone appeared to increase over time. Most studies provided prescribers in-person naloxone trainings, including how to write a prescription and indications for prescribing. Most studies implemented universal prescribing, whereby anyone prescribed long-term opioids or otherwise at risk for overdose was eligible for naloxone. Patient education was largely provided by prescribers and most studies provided take-home educational materials. Providers reported concerns around naloxone prescribing including lack of knowledge around prescribing and educating patients. Providers also reported benefits such as improving difficult conversations around opioids and resetting the culture around opioids and overdose. Current literature supports the acceptability and feasibility of naloxone prescribing in primary care. Provision of naloxone through primary care may help normalize such medication safety interventions, support larger opioid stewardship efforts, and expand access to patients not served by a community distribution program

1. Background

The United States is amidst a drug overdose epidemic of unprecedented proportion. In 2016, there were an estimated 64,000 drug overdose fatalities, the majority of which involved opioids (National Institute on Drug Abuse, 2017). Naloxone, the short-acting opioid antagonist used to reverse the effects of opioid overdose, has been distributed to people who inject drugs through community based organizations and syringe exchanges for nearly two decades. In this context, naloxone is typically prescribed via a standing order, enabling non-physicians to furnish naloxone to individuals at risk for experiencing or witnessing an opioid overdose. Naloxone distribution programs have proven to be widely successful: people who use drugs can be trained to respond to overdoses effectively (Green et al., 2008; Mcauley et al., 2010) and between 1996 and 2014, organizations across the US distributed over 152,000 naloxone kits to laypersons and received reports of over 26,000 overdose reversals (Wheeler et al., 2015). Furthermore, naloxone is associated with a reduction in heroin use among naloxone recipients (Seal et al., 2005) and a population-level reduction in overdose mortality (Walley et al., 2013; Bird et al., 2016; Paone et al., 2010; Maxwell et al., 2006; Bennett et al., 2011; Enteen et al., 2010; Hart, 2011; Hart, 2004). Every US state has some legislation supporting naloxone access (Policy Surveillance Project, 2017).

The demographics of individuals at risk for opioid overdose has expanded since 2000 to include people who use prescription opioids who may not utilize community based services or syringe exchanges and thus may not have easy access to naloxone through standard means of distribution. Furthermore, syringe exchanges and harm reduction services may be difficult to access for individuals living in non-metropolitan areas. Thus, expanding naloxone availability through diverse mechanisms is considered an important component of overdose prevention, with primary care access a potentially valuable intervention. In fact, the Centers for Disease Control and Prevention now recommends that naloxone be co-prescribed to patients receiving opioids for chronic pain with risk factors such as receipt of > 50 morphine milligram equivalents, concurrent benzodiazepine use, or a history of substance

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use disorder (Dowell et al., 2016). Despite this federal endorsement, naloxone prescribing is still a relatively nascent intervention in primary care. This systematic review aims to assess the acceptability and feasibility of prescribing naloxone to patients in primary care settings.

2. Methods

2.1. Search methodology

This review was conducted following PRISMA guidelines and was registered in PROSPERO prior to initiation. We queried PubMed, EmBase and CINAHL using the following Medical Subject Heading (MeSH) terms: (naloxone) AND (primary health care OR primary care nursing OR primary care physician). A complete list of database search terms can be found in Appendix 1. Database searches were conducted in October 2017, yielding 270 unduplicated articles. In addition to formal database searches, we hand searched citations from the eligible articles and consulted experts in the field to identify articles not found through our initial searches, adding one additional article to our results. Search results were exported to a reference manager, Mendeley Ltd., and then into Microsoft Excel (2013) for analysis. A PRISMA diagram illustrates the article selection process (Fig. 1).

2.2. Inclusion criteria

Articles were included in our analysis if they discussed the acceptability or feasibility of prescribing naloxone to patients in a primary care setting. The search was limited to US-only peer-reviewed, full-length articles that were written in English and based on original research. There was no restriction on publication date. Articles could include patient, provider or medical staff perspectives, could be evaluation or feasibility studies, and could use either qualitative or quantitative analytic methods. Articles were excluded if they focused on prescribing naloxone outside of a primary care setting (e.g. standing order or prescribing through an emergency department).

2.3. Article selection and review

One analyst (EB) reviewed the titles of all queried articles. Articles that clearly did not pertain to the topic of this systematic review were excluded immediately (e.g. articles referring to the co-formulation of buprenorphine/naloxone). We eliminated 218 articles based on title review. One reviewer (EB) then independently reviewed the remaining 52 abstracts for inclusion. If eligibility was unclear, the reviewer consulted a second reviewer (PC) for a final decision. After title and abstract review, 20 articles met inclusion criteria.

Two analysts (EB and RB) then independently read the full-text of the eligible articles and recorded general information such as date, location, study design, study sample, research question, and primary study outcomes. Additionally, reviewers also collected data relating to either the acceptability or feasibility of naloxone prescribing, depending on the study's primary purpose. Three articles were excluded during this phase; two did not meet inclusion criteria upon reading the complete text and one did not have full-text availability. We conducted a quality assessment of the eligible articles, however due to a high degree of heterogeneity in study design and inconsistencies in study metrics, we did not include the assessment in our results.

2.4. Analysis

To assess acceptability, we evaluated the articles for providers' awareness and willingness to prescribe naloxone, attitudes, and anticipated barriers/concerns. To assess feasibility, we evaluated the articles for descriptions of programmatic implementation (e.g. training

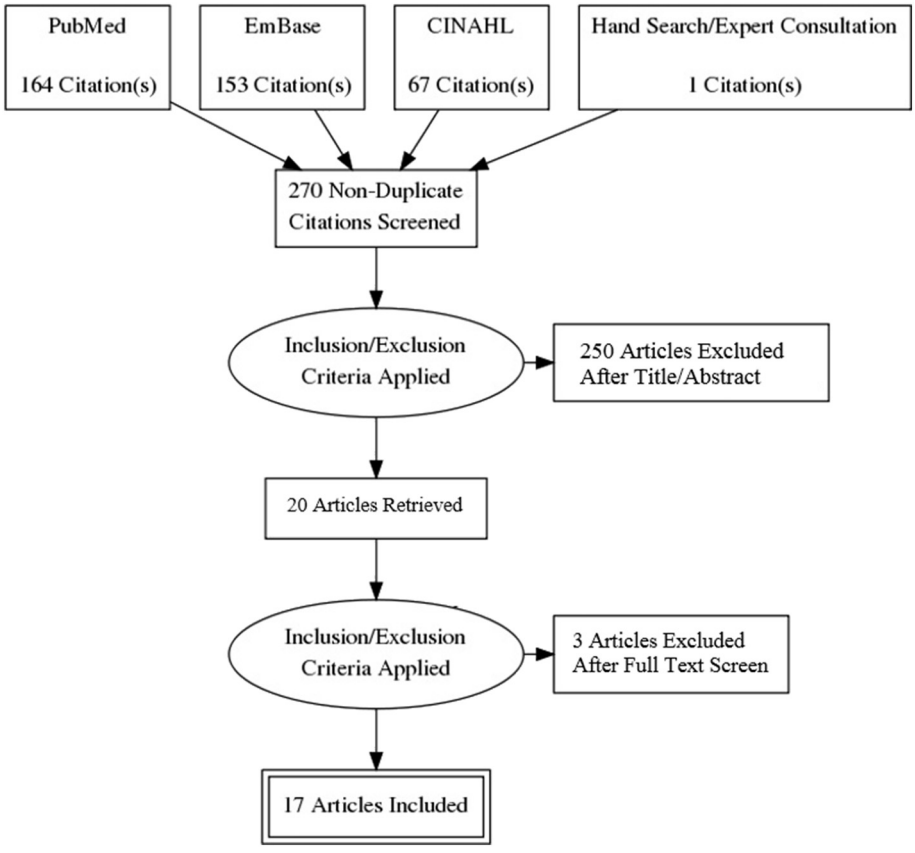

Fig. 1. PRISMA study selection flow diagram.