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US regional and demographic differences in prescription opioid and heroin-related overdose hospitalizations

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ABSTRACT

Background: US opioid overdose death rates have increased between 2000 and 2014. While, the increase in prescription opioid use has been linked to the increase in heroin use, there are reasons to view this relationship as a partial explanation for the recent increase in heroin-related harms. This study documents the differences in trends in prescription opioid overdose-related (POD) and heroin overdose-related (HOD) hospitalizations.

Methods: Data come from the National Inpatient Sample (NIS) for the years 2000 through 2014. POD and HOD hospitalizations were abstracted from ICD-9 codes. Rates of POD and HOD by census region and census division were constructed along with separate rates for age and race. Regression analysis analyzing trends across region were estimated along with graphs for documenting differences in POD and HOD rates.

Results: POD hospitalization rates were highest in the South and lowest in the Northeast. HOD hospitalization rates were highest in the Northeast region and grew the fastest in the Midwest. There was statistically significant heterogeneity in HOD trends but not POD trends across the four regions between 2000 and 2014. Between 2012 and 2014 POD rates decreased in eight of the nine census divisions, with only New England showing an increase. HOD hospitalization rates increased in all nine census divisions between 2012 and 2014. Both POD and HOD rates show different demographic patterns across the nine census divisions.

Conclusion: Comparing POD and HOD hospitalization trends reveals significant disparities in geographic as well as demographic distributions. These epidemics are evolving and the simple opioid-to-heroin transition story is both supported and challenged by this paper. The opioid pill, heroin and fentanyl crises are intertwined yet increasingly have drivers and outcomes that support examining them as distinct. Addressing these complex and interrelated epidemics will require innovative public health research and interventions which need to consider local and regional contexts.

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Introduction

It is well documented that drug overdose death rates have increased dramatically between 2000 and 2014 in the US and that opioid drugs are the largest contributor to these deaths (Hedegaard, Warner, & Minino, 2017; Rudd, Seth, David, & Scholl, 2016). However, overdose deaths represent the tip of the iceberg of harm associated with licit and illicit opioid (e.g. medical and non-medical prescription opioids and heroin) drug use. The increase in opioid overdoses could be attributable to several mechanisms that can broadly be distilled to one of two main causes: (1) increased number of users or (2) increased danger of use.

The widespread availability of prescription opioids (PO) is well documented and has resulted in increase in both their medical and non-medical use (Compton, Jones, & Baldwin, 2016; Dart et al., 2015). Prevalence estimates from nationally representative population studies suggest that PO use increased between 1999 and 2012 but has been flat since then (Frenk, Porter, & Paulozzi, 2015). However, these trends mask a divergence between non-medical prescription opioid (NMPO) use which peaked in 2010 and has since declined and rates of PO medical use which have not declined from their peak (Dart et al., 2015; Frenk et al., 2015).

More recently the number of heroin users in the US has increased. Between the 2002 and 2013 past year heroin use has increased from 1.6 per 1000 persons to 2.6 per 1000 (Jones, Logan,

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Gladden, & Bohm, 2015; Martins, Sarvet, & Santaella-Tenorio, 2017). While the increase in heroin use disorder has been spread evenly across the 4 census regions, it has been concentrated in white non-Hispanic males under the age of 44 (Martins et al., 2017).

This reduction in the use of NMPO and corresponding increase in heroin use have led to a hypothesis that the opioid and heroin epidemics are intertwined (Unick, Rosenblum, Mars, & Ciccarone, 2013). Many investigators have linked the increase in prescription opioid use to the increase in heroin use (Banerjee et al., 2016; Cerda, Santaella, Marshall, Kim, & Martins, 2015; Cicero, Ellis, & Harney, 2015; Cicero, Ellis, Surratt, & Kurtz, 2014; Dart et al., 2015; Jones, 2013; Unick et al., 2013). There are several reasons to believe that there is a causal relationship between PO availability and use and the recent rise in heroin use. First, from the perspective of a person highly dependent on opioids, PO and heroin are substitutable, i.e., both can stave off withdrawal symptoms and produce the desired psychoactive effects. While many users have preferences for one type of opioid or another based on route of administration, desired effects, etc., availability and cost will also have an effect on which drugs users buy and consume. For example, the recent change in high-dose extended-release oxycodone (brand name *OxyContin*) to an abuse deterrent formulation may have reduced non-medical use of this drug by increasing its price and decreasing its availability relative to heroin (Cicero et al., 2014). A second reason to suspect that NMPO use set the stage for the recent increase in heroin use is research which reports young heroin users initially developing dependence on opioids with PO but switching to heroin due to its greater availability and lower cost (Mars, Bourgois, Karandinos, Montero, & Ciccarone, 2014). These studies suggest that PO use has been a recent gateway for initiation of heroin use (Cicero et al., 2014; Compton et al., 2016; Grau et al., 2007; Mars et al., 2014). The implication of these findings is that the reduction in access or relative desirability of PO for non-medical use has led to an increase in the number of individuals using heroin and thus responsible for the increase in heroin-related harm.

However, there are reasons to view the causal relationship between PO availability and use and heroin use as only a partial explanation for the recent increase in heroin use and subsequent harms. First, drug use gateway arguments in general have been widely discredited and should be viewed with caution (Kleinig, 2015). Second, there is reason to believe that other factors are affecting rates of drug overdoses for both prescription opioids and heroin. Survey data suggest that the number of individuals using prescription opioids plateaued between 2003 and 2006 but that the number of prescriptions and the morphine equivalence of those prescriptions continued to increase (Cicero et al., 2014; Frenk et al., 2015). Logically, these data suggest that use intensified for those that were prescribed opioids and perhaps even for those whom obtained PO through diverted supply. Escalating dosage of PO per user and the corresponding higher levels of opioid dependency is a potential explanation for the increasing harms seen after transition to heroin.

There are also reasons to believe that the heroin supply is changing and maybe becoming more dangerous. Recent reports on overdose due to synthetic opioids highlights the role of illicitly manufactured fentanyl and fentanyl analogs in the adulteration of the heroin supply (Gladden, Martinez, & Seth, 2016). Fentanyl's potency, 30–40 times that of heroin (author DC's calculation), and fluctuations in potency are implicated in heroin-related overdose (Ciccarone, Mars, & Ondocsin, 2017; Lucyk & Nelson, 2017; Somerville et al., 2017). Furthermore, there is evidence that the macro heroin supply is changing with the introduction of a new source-form of heroin coming from Mexico; with unknown risk implications for individuals and user populations (Ciccarone, 2017; Ciccarone et al., 2017; Unick, Rosenblum, Mars, & Ciccarone, 2014).

Furthermore, evidence from ecological data suggest that there is a positive synergy between prescription opioid-related harm and heroin-related harms rather than a substitution. Prior work has found that increases in POD hospitalizations are associated with subsequent year increases in HOD hospitalization and that the converse is true as well (Unick et al., 2013). This suggests that rather than a substitution of heroin for prescription opioids, increases in observable drug related harm happen concurrently, which is consistent with several hypotheses other than a simple pills-to-heroin transition story.

The purpose of this study is to document differences in the distribution of and trends in POD and HOD hospitalizations. POD and HOD hospitalizations make up a limited but unique contribution to the literature on opioid-related harms. Overdoses that result in hospitalization encompass a wider range of overdose severity, and so capture events that may be missed in death data. Hospitalizations also are well documented and available for long time frames, allowing a more detailed assessment of the demographic and medical factors associated with the overdose event (Reardon, Harmon, Schult, Staton, & Waller, 2016). Biases in the coding of hospital data are likely to be different than those affecting death data and so present an opportunity to triangulate with excising literature on POD and HOD deaths. We will look at the rates of POD and HOD at the Census Region and Division geographic levels and examine variation in the distribution of the demographics of overdose related hospitalization. The goal of this paper is to provide a map of POD and HOD hospitalizations to identify deviation from the simple pills-to-heroin transition story. This map can then serve as a guide for future studies seeking to identify more detailed and specific causal mechanisms behind the recent increase in HOD and heterogeneity in POD to inform surveillance and prevention efforts.

Methods

Data come from the National Inpatient Sample (NIS), an approximately 20% stratified national sample of United States Hospitalizations (Houchens, Ross, Elixhauser, & Jiang, 2014). The 2000 through 2014 NIS were used to estimate the number of POD and HOD. Because of design changes to the NIS we used the trends weights file for the 2000–2011 data as recommended by HCUP (Healthcare Cost and Utilization Project (HCUP), 2015). The 2000 through 2011 NIS sampling strategy used Census Regions, the 2012 through 2014 NIS used Census Divisions. For the initial analysis of the 2000 through 2014 POD and HOD trends we use the hospital region as the geographic unit but switch to the hospital division for the 2012 through 2014 analysis.

Cases of POD and HOD were coded using ICD-9 codes included in the billing records reported by participating states to the NIS. An admission was considered a POD or HOD if one of the two following conditions was met: any diagnosis of 965.00, 965.01, 965.02 or 965.09, or an E code of E850.0, E850.1, or E8502. Recent research suggests that use of any diagnoses is more sensitive without a loss of specificity compared with primary diagnoses (Slavova, Bunn, & Talbert, 2014). Overdoses were split into HOD and POD. HOD were restricted to diagnoses coded as 965.01 or an E code of E850.0. POD were restricted to diagnoses coded as 965.00, 965.02 or 965.09, or an E code of E850.1 or E8502.

The goal of this analysis is primarily descriptive and designed to characterize changing geographic and demographic patterns of hospital admissions for POD and HOD. Both Stata 14.2 and SAS 9.2 were used in data coding and analysis(SAS Institute Inc., 2013; StataCorp, 2015). Proc Surveyfreq was used to estimate the number of admissions adjusting the estimates for the sampling design using weights, strata and sampling units. The use of weights and complex sample design characteristics allows for

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