Assessment of prescription opioid intentional exposures across the rural-urban continuum in the United States using both population and drug availability rates

Marie-Claire Le Lait, Erin M. Martinez, Stevan G. Severtson, Sarah A. Lavery, Becki Bucher-Bartelson and Richard C. Dart

ABSTRACT

**Purpose** Prescription opioid abuse and misuse are a serious problem in the U.S. today. Several studies have shown that the epidemic disproportionately affects rural areas. This paper uses three different rates to gain a more complete picture of opioid abuse in rural areas.

**Methods** This study examines prescription opioid intentional exposures using opioid classes tracked in the RADARS® System Poison Center Program. Intentional exposure rates were calculated adjusting for population and unique recipients of dispensed drug (URDD). These rates were analyzed using time (quarter) and the proportion of a three-digit zip code residing in a rural area as covariates. Additionally, the URDD per population rate was calculated to examine the proportion of the population filling prescriptions for opioids.

**Results** After adjusting for population, intentional exposure cases significantly increased as the proportion of the population residing in a rural area increased. However, when adjusting for URDD, intentional exposure cases decreased with increasing rural population. The URDD per population increased as the proportion of people residing in a rural area increased.

**Conclusions** Using both population and URDD adjusted intentional exposure rates gives a more complete picture of opioid abuse in rural areas. Considering product availability can be used to develop opioid abuse prevention strategies and further the education of physicians serving rural areas about this epidemic. Copyright © 2014 John Wiley & Sons, Ltd.

INTRODUCTION

Prescription drug abuse and misuse are a substantial and growing epidemic in the United States. From 2010 to 2011, 4.5 million individuals 12 and older reported using prescription pain relievers nonmedically. Research indicates that the prescription opioid epidemic may disproportionately affect rural areas compared to urban and suburban ones.

This study assessed how rates of intentional opioid exposures reported to poison centers and the number of individuals filling prescriptions for opioids vary as the proportion of the population that resides in a rural area changes. This ecological study used a novel approach to examine prescription opioid abuse in rural areas. Three different rates were analyzed separately in order to gain a more complete picture of opioid abuse in rural areas: (i) intentional exposures adjusting for population, (ii) intentional exposures adjusting for drug availability, and (iii) drug availability adjusting for population.

METHODS

Data from the RADARS® System Poison Center (PC) Program from first quarter 2010 through fourth quarter 2012 were used. In 2012, 49 out of 57 poison centers in the U.S. and Puerto Rico participated in the program,
covering 90.8% of the country’s population. Cases involving specific drugs of interest from the participating centers were quality reviewed by trained personnel. Data are updated every 12 weeks, closely corresponding to calendar quarters. Opioid classes included in this study are buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, tapentadol, and tramadol. Intentional exposure cases are defined as suspected suicide, misuse, abuse, intentional unknown, and withdrawal. 7 Our sample of n = 110005 unique cases was 44.6% male, 55.1% female, and 0.3% unknown gender. The mean (standard deviation) age was 36.4 (15.05) years and ranged from 0 to 119 years.

Intentional exposure rates were calculated using two different denominators: drug availability and population. IMS Health8 estimates the unique recipients of dispensed drugs (URDD) in each three-digit ZIP code for each drug class by obtaining prescription drug distributions from about half the retail pharmacies in the US and making projections to the rest of the country. The population of each three-digit ZIP code was estimated in each calendar quarter by using linear extrapolation of the 2000 and 2010 US Censuses.

Demographic data from the 2000 and 2010 US censuses were used to calculate the proportion of a ZIP code’s population residing in a rural area every quarter. Definitions of urban, suburban, and rural are also taken from the US census.9 Data were collapsed by using the first three digits of the five-digit ZIP code. The percent of the population living in a rural area was calculated by dividing the rural population by the total population for the 2000 and 2010 censuses and then extrapolating these for each quarter in the analysis.

Population and URDD rates were calculated for each three-digit ZIP code and quarter. Only three-digit ZIP codes covered by the PC program each quarter were included in these calculations. The population rate is the number of intentional exposure cases per 100000 population, and the URDD rate is the number of intentional exposure cases per 1000 URDD. In order to address our goal of examining the availability of opioids per population based on the proportion of population residing in a rural area, we also examined the rate of URDD per 1000 population. This measure assesses URDD adjusting for the number of people residing in that area.

A generalized linear model using a negative binomial distribution was used for the URDD and population rate analyses. Separate regression models were fit for the population and URDD rates with percent rural and quarter (continuous) as covariates. Quarter was included to account for trends in intentional opioid exposures over time. A separate generalized linear model using the normal distribution was used to examine the relationship of URDD per population, percent rural, and quarter. An interaction term for percent rural and quarter initially was included in all three models but was dropped from each due to insignificance. A first-order autoregressive covariance structure was included for each ZIP code to account for correlation among quarters. The percent change in the rates for a 10% increase in the percentage of population residing in a rural area and per quarter was computed along with 95% confidence intervals. All analyses were generated using SAS® software version 9.3.

RESULTS

Results of all three models are displayed in Table 1. The proportion of a population residing in a rural area was positively associated with greater numbers of intentional exposures to prescription opioids after adjusting for differences in population (p < 0.001). Results indicated that, across quarters, a 10% absolute difference in the proportion of the population residing within rural areas was associated with a 3.64% increase in the expected number of intentional exposures to prescription opioids, adjusting for population. Results suggest that the population rate is not increasing over time (p = 0.139).

Using the URDD adjustment, both quarter and percentage of the population residing in a rural area were significantly associated with intentional exposure rates (p < 0.001). Across quarters, a 10% absolute difference in the proportion of the population residing within a rural area was associated with a 4.69% decrease in the expected number of intentional exposures to prescription opioids, adjusted for URDD. Holding the proportion of the population residing within a rural area constant, the URDD rate decreased

<table>
<thead>
<tr>
<th>Rate</th>
<th>Effect</th>
<th>Percent change (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population rate</td>
<td>Percent rural (10% increments)</td>
<td>3.64%(2.21,5.09)</td>
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<td>Quarter</td>
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<tr>
<td>URDD rate</td>
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<tr>
<td>Quarter</td>
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<tr>
<td>URDD per population rate</td>
<td>Percent rural (10% increments)</td>
<td>5.78(4.26,7.31)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Quarter</td>
<td>1.85(1.51,2.2)</td>
<td>&lt;.001</td>
<td></td>
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</table>
every quarter by 1.88%. This suggests that the number of individuals filling prescriptions was increasing at a faster rate over time than intentional exposures to prescription opioids.

In the URDD per population model, both quarter and percent of the population residing in a rural area were significantly associated with the URDD per population rate \((p < 0.001)\). Across quarters, a 10% absolute difference in the proportion of the population residing within a rural area was associated with an expected increase of 5.78 URDD per 1000 population. Holding the proportion of the population residing in a rural area constant, there was an expected increase of 1.85 URDD per 1000 population every quarter.

DISCUSSION

This study demonstrates the value of considering product availability when assessing prescription opioid abuse across the rural–urban continuum. Our results indicate that intentional exposure rates of prescription opioids increased when adjusted for population, but decreased when adjusting for URDD as the proportion of people residing in a rural area increased. This demonstrates the importance of examining both methods since investigating only the population or URDD rate may lead to incomplete conclusions. The population rate increase in our study is consistent with previous research showing that rural areas are affected disproportionately by the prescription opioid abuse epidemic.\(^1\)\(^–\)\(^4\) However, the decrease in URDD rate as the percent of the population residing in a rural area increases is a new finding.

In examining the number of unique individuals filling a prescription per population, we found that rural areas appear to have a greater proportion of population filling prescriptions for opioids relative to the urban and suburban areas.

The discrepancy in intentional exposure cases adjusted per population and per URDD requires further investigation. It may reflect inflated URDD values in rural areas due to physicians and/or pharmacies serving rural populations being targeted by individuals who divert prescription opioids or overprescribing of opioids by non-pain specialists. It is also possible that rural opioid prescription holders are less likely to abuse or misuse their medication since intentional exposures are increasing at a slower rate than unique recipients of dispensed drug.

This study does have limitations. It is important to note that results should be interpreted at the population level rather than at the individual level. Two major limitations of an ecologic analysis are the ecologic fallacy, which is the failure of the estimates to reflect associations among individuals, and the inability to control for potentially confounding covariates at the group level. Further, the RADARS System PC data is self-reported, so the actual number of intentional exposures in each ZIP code is likely underestimated and may differ by region. It is possible that our findings are due to under reporting of exposures in rural areas. However, we have found no research that addresses this issue. Another limitation is that the number of pills dispensed in each prescription may vary by the three-digit ZIP code. Future research could determine if variability in the number of pills in a prescription is significantly different in rural areas, leading to higher intentional exposure rates. Despite these limitations, this study demonstrates the importance of examining population rates, URDD rates, and URDD per population rates together in order to develop a more complete picture of the prescription drug abuse problem.

CONFLICT OF INTEREST

Rocky Mountain Poison & Drug Center is a governmental (Denver Health and Hospital Authority) facility that provides poison and drug information to various entities. No entity supported the research involved in this submission or the development of the information therein in any manner.

KEY POINTS

- Examination of prescription opioid intentional exposure rates, adjusting for population and drug availability (unique recipients of dispensed drug or URDD), along with rates of drug availability per population, can show a more complete picture of prescription opioid abuse and misuse in areas with varying proportions of the population residing in rural areas.
- Our results suggest that the number of individuals filling opioid prescriptions rises as the proportion of the population residing in rural areas increases, as does the number of intentional exposures. Drug availability is increasing faster than intentional exposures as the proportion of the population residing in rural areas increases.
- This information can be used to develop targeted opioid abuse prevention strategies and further the education of physicians in rural areas about this epidemic.
ETHICS STATEMENT

The Poison Center Program study protocol was reviewed and received approval from the Colorado Multiple Institutional Review Board. In addition, the study protocol was reviewed and approved by the IRB of each participating poison center.

ACKNOWLEDGEMENT

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AUTHOR CONTRIBUTIONS

Ms. Le Lait performed statistical analyses and literature review and wrote the manuscript. Ms. Martinez, Dr. Severtson, and Dr. Bucher-Bartelson contributed to the design, validation, and review of this study. Dr. Dart contributed to the review, and Ms. Lavery contributed to the topic and design. All authors approved the submission of the article.

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8. URDD Study: LifeLink, IMS Healthcare, a healthcare technology and information company, 2012.