**Fatalities and polysubstance use among prescription opioid abuse cases using the RADARS System Poison Center program**

### Key points

- In more than half (61%) of the 140 intentional abuse deaths involving RADARS System tracked opioids since 1st quarter of 2006, more than one substance was mentioned.

- Among fatal intentional abuse cases where more than one substance was mentioned, the opioid classes tracked by the RADARS System most commonly mentioned were hydrocodone, methadone, and oxycodone. The most common non-opioid substances mentioned were benzodiazepines, alcohol, and cocaine.

- The case fatality rate among abuse cases who ingested more than one substance with a RADARS System tracked opioid was 42% higher those who ingested only one substance.

- After adjusting for population growth, the number of abuse cases reporting polysubstance use has increased by 10% annually since 2006.

### Background

Recent research demonstrates that prescription opioid overdose deaths are rising\(^1\)\(^2\) and that polysubstance use may be associated with deaths related to prescription opioids. One study reported that the majority of methadone overdose deaths in western Virginia were attributed to polysubstance use\(^3\). In Massachusetts, another study found that use of cocaine was observed in more than half of fatalities associated with illegal fentanyl use\(^4\). The purpose of this report is to estimate the increased risk of death attributed to polysubstance use among poison center calls classified as abuse. In addition, this report examines which substances are most commonly mentioned among fatal abuse cases where a RADARS System tracked opioid class was used. Trends in polysubstance abuse since 2006 are also examined and compared to trends in single substance opioid abuse.
Methods

The current study utilized data from the RADARS System Poison Center Program. The Poison Center program obtains data from participating poison centers, representing 44 states and covering 89% percent of the 2010 US population. The outcomes of interest were the number of confirmed intentional exposures classified as abuse mentioning at least one RADARS System tracked opioid and the percentage of these cases that were fatal. Cases with a medical outcome of “death, indirect” were excluded from the analysis because these calls did not originate with a call to a participating poison center. Cases from Oklahoma were excluded due to the inclusion of fatal cases not initiated by calls to poison centers. Opioid classes tracked by the RADARS System include: oxycodone, fentanyl, hydrocodone, hydromorphone, morphine, oxymorphone, methadone, buprenorphine, tramadol, and tapentadol. The current study utilized data from the 1st quarter of 2006 through the 3rd quarter of 2011. Cases were grouped into one of two mutually exclusive categories:

1) mention of one prescription opioid tracked by the RADARS System, and

2) mention of one or more substances with opioid tracked by the RADARS System

Poisson regression was used to estimate the relative risk of fatality among polysubstance use cases classified as abuse compared to the risk of fatality among single opioid use cases. Poisson regression was used to compare the trends over time in polysubstance abuse and single opioid abuse population rates. Linear interpolation was used to account for population growth over time. Based on the population change from 2000 to 2010 in the US Census, population was assumed to grow by 0.97% annually.

Results

Table 1 displays the number and percent of all abuse cases by polysubstance use group and outcome from the 1st quarter of 2006 through the 3rd quarter of 2011 from poison centers participating in the RADARS System Poison Center program. A RADARS System tracked opioid was mentioned without any other substances in 47% of cases classified as abuse, but only in 39% of the fatal cases. In contrast, at least one other substance was mentioned in addition to a RADARS System tracked opioid in 53% of cases classified as abuse and in 61% of fatal cases.

<table>
<thead>
<tr>
<th>Group</th>
<th>% of all not fatal cases (n=28,773)</th>
<th>% of all fatalities (n=140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>One RADARS System tracked opioid</td>
<td>47.2% (n=13,583)</td>
<td>38.6% (n=54)</td>
</tr>
<tr>
<td>One or more substances with opioid tracked by the RADARS System</td>
<td>52.8% (n=15,190)</td>
<td>61.4% (n=86)</td>
</tr>
</tbody>
</table>
Figure 1 displays the case fatality rate by polysubstance use classification. Poisson regression results indicate that the case fatality rate was 1.42 times greater (95% CI: 1.01-2.00, p=0.042) among abuse cases where more than one substance was mentioned versus those reporting use of only a RADARS System tracked opioid.

Table 2 displays the three most common substances used among fatal abuse cases where more than one substance was mentioned. The most common drug classes mentioned with another substance that resulted in death were hydrocodone, methadone, and oxycodone. The most common substances other than prescription opioids were benzodiazepines, alcohol, and cocaine.

<table>
<thead>
<tr>
<th>RADARS System tracked opioids</th>
<th>Other substances</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug class</strong></td>
<td><strong>% of cases</strong></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>34.9%</td>
</tr>
<tr>
<td>Methadone</td>
<td>33.7%</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>25.6%</td>
</tr>
</tbody>
</table>
Figure 2 displays the intentional abuse rates by polysubstance mention category by year/quarter. After adjusting for population growth, the polysubstance abuse population rate is estimated to have increased by 10% (95% CI: 9-11%, p<0.001) annually since 2006. The increase in the population rate of intentional abuse cases mentioning a single RADARS System tracked opioid has increased 8% (95% CI: 7-9%, p<0.001). Based on the observed trend, the estimated polysubstance use intentional abuse rate per 100,000 population was 18% (95% CI: 13-23% p<0.001) greater than the single substance intentional abuse population rate in the 3rd quarter of 2011.

Conclusions

The current report indicates that among Poison Center intentional abuse cases, the case fatality rate was about 42 percent higher among those cases where other substances were mentioned with a RADARS System tracked opioid compared to those who mentioned only one substance. Among fatal polysubstance abuse cases reported to Poison Centers participating in the RADARS System program, the most frequently reported prescription opioids were hydrocodone, methadone, and oxycodone. The most frequently mentioned non-opioid co-ingested substances were benzodiazepines, alcohol, and cocaine. Since the 1st quarter of 2006, the polysubstance abuse rate has shown a 10% annual increase and this is greater than abuse rates of only one prescription opioid.
The PC program data are limited in that cases are the results of calls to poison centers and may not reflect the entire population of abusers. In addition, mentions may not reflect confirmed exposures to additional substances. However, the strength of the data is that they represent a national surveillance program that follows up cases after initial contact through poison centers.

Future studies are needed to examine trends in specific substances ingested with prescription opioids and intervention programs targeted to instruct youth and those that abuse prescription opioids about the dangers of abusing prescription opioids with other substances.
