

Title:	Intentional Exposures to Prescription Opioids in Rural Areas of the United States	
Authors:	Lavery SA, Le Lait MC, Bucher Bartelson B, Poppish L, Green JL, Dart RC	
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Abstract:

Background: Intentional exposures (IEs) to opioids in the US are rising. Studies suggest that abuse is highest in rural areas. This study examines the association between the proportion of individuals residing in rural areas and rates of IEs by 3-digit ZIP code (3DZ) level. We hypothesized that, across 3DZs, there will be a positive association between the percent of individuals residing in rural areas and rates of IEs.

Methods: Data on IE (suspected suicide, misuse, abuse, intentional unknown, withdrawal) cases from the RADARS® System Poison Center program were used. Case mentions of buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, tapentadol, and tramadol in 2012 were summed by 3DZ. Melissa® Data using US Census definitions were used to calculate the proportion of the population in each 3DZ code living in rural areas, classified as all regions not included in urban areas. For this analysis 3 rates were calculated: Unique recipient of dispensed drug (URDD), a measure of retail availability, was used in 2 of the rates. For each 3DZ, the number of IEs adjusted for population (pop rate), URDD adjusted for population (URDD per pop rate), and IEs adjusted for URDD (URDD rate) were determined using negative binomial regression. The proportion of the population residing in rural areas was used as a covariate. The models were also used to estimate the rates and 95% confidence intervals in areas that are 10% rural, 50% rural, and 100% rural.

<u>Results</u>: As the proportion of a 3DZ that is rural increases, the pop rate shows a highly significant increase (p-value=0.0004), the URDD per pop rate also has a highly significant increase (p-value<0.0001), and the increase in URDD rate was non-significant (pvalue = 0.84). For every 10% increase in the rural percentage of a 3DZ, the pop rate increases by 2.96%, the URDD per pop increases by 3.32%, and the URDD rate increases by 0.17%.

Conclusion: Results indicate that rural regions have a significantly higher rate of IEs involving opioid analgesics. Results also suggest there is a higher rate of prescriptions dispensed to individuals in rural areas. However, the number of opioid IEs and number of individuals receiving opioid prescriptions are increasing at approximately the same rate as the percent rural increases. The URDD rate is relatively constant across all rural percentage levels even though the pop rate and URDD per pop rates are increasing as the percent rural increases.

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% Rural	Pop rate (95% CI)	URDD per pop rate (95% CI)	URDD rate (95% CI)
10	3.53 (3.34, 3.73)	13.54 (13.01, 14.10)	0.28 (0.27, 0.30)
50	3.97 (3.77, 4.18)	15.43 (14.90, 15.99)	0.28 (0.27, 0.30)
100	4.59 (4.08, 5.16)	18.17 (16.73, 19.73)	0.29 (0.25, 0.32)