RADARS® SYSTEM

Researched Abuse, Diversion and Addiction-Related Surveillance System

QUARTERLY Technical REPORT

Second Quarter, 2020

Use of Self-Report Data Results in Differential Misclassification and Results in Biased Estimates of Differences in Use between Specific Opioid Analgesic Products

Key Findings

- Misclassification is different between specific opioid analgesic products making comparisons between products biased
- Agreement between use utilization estimates based on self-report responses and tracking of prescriptions dispensed at retail pharmacies was weak (intraclass correlation coefficient=0.32) for select opioid analgesic drug groups, even with product images to aid in recall
- Utilization estimates based on self-report showed brand name products tended to be inflated whereas generic products tended to be underestimated relative to estimates obtained from dispensing at retail pharmacies
- The magnitude of difference between self-reported use and unique recipients of dispensed drug (URDD) estimates may help in quantifying bias due to self-report in surveys

Introduction

The assessment of non-medical use (NMU) of prescription products requires precision in the identification of specific prescription medications. Identification of specific medications is relatively straightforward when identifying information about product can be obtained; for example, if the imprint code on a tablet is available, the shape or color of a pill, or details from the packaging. However, many assessments of misuse and abuse rely on participant recall on self-report questionnaires. While self-report questionnaires are recognized as an essential tool to obtain information on abuse in the general population and high-risk samples, misclassification of specific products is frequently acknowledged as a limitation [1-3].

Efforts to reduce misclassification have focused on inclusion of product images to aid in recall [4,5]. However, the benefits of this approach remain unclear as results are not compared to a reference standard. Furthermore, no studies have quantified the degree to which products may be over- or underestimated. This is an important gap in understanding differences in misuse of specific products as any misclassification results in biased estimates. If the magnitude of these biases varies by drug product (differential misclassification) then comparisons between these drug groups are either over- or underestimated. For this reason, understanding whether product images result in more accurate estimates and if magnitude and direction of misclassification across drug groups is essential.

Several surveys assess NMU of specific opioid analgesic products. While endorsement patterns of NMU can be compared to dispensing rates, the assumption underlying this comparison is that the distribution of misuse and abuse is proportional to dispensing. This assumption cannot be directly tested which limits the interpretability of the findings. The National Survey on Drug and Health (NSDUH) is the only survey that provides general population estimates of past-year use of specific products. These estimates include individuals who take medications as prescribed and those who non-medically use opioids. This allows for comparisons to estimates of the number of

individuals filling prescriptions. IQVIA™ (Danbury, CT) US-based Longitudinal Patient Data provides projections of unique recipients of dispensed drug (URDD), or the number of individuals who fill prescriptions at retail pharmacies. Because product specific data is recorded when the drug is dispensed, product specific misclassification is thought to very low.

The aim of this study was to assess agreement between self-reported utilization estimates obtained with the assistance of including product images (captured by the NSDUH) and compare a reference standard, URDD for specific products estimated based on prescriptions dispensed at retail pharmacies. The second aim was to quantify the degree of misclassification of specific opioids by comparing past-year utilization estimates to estimates obtained from tracking prescriptions dispensed at retail pharmacies.

Methods

Data Sources

Data from two sources were used to assess these aims. Annual average past year use estimates of select products from the 2016 and 2017 NSDUH launches were obtained using https://rdas.samhsa.gov. This study provides self-reported estimates for specific products where participants are provided images to assist in recall. The NSDUH is a frequent reference for abuse of illegal and legal drugs, estimates of misuse of specific products is susceptible to misclassification, as noted in the 2016 Public Use Codebook [6]:

> Self-reports capture information on the use or misuse of prescription drugs that contain a given active ingredient. However, these self-reports are not necessarily accurate for identifying the exact drugs that respondents took, especially when respondents identify certain drugs by their brand names (e.g., if a respondent actually took the generic drug alprazolam but reported use or misuse of the brand name tranquilizer Xanax® because of name recognition).

Annual average of IQVIA™ US-based Longitudinal Patient Data provides projections of URDD in the retail channel in 2016 and 2017. This data source provides information on specific products dispensed at retail pharmacies. URDD is the estimated number of unique individuals filling a prescription for specific products at retail pharmacies.

Statistical Analysis

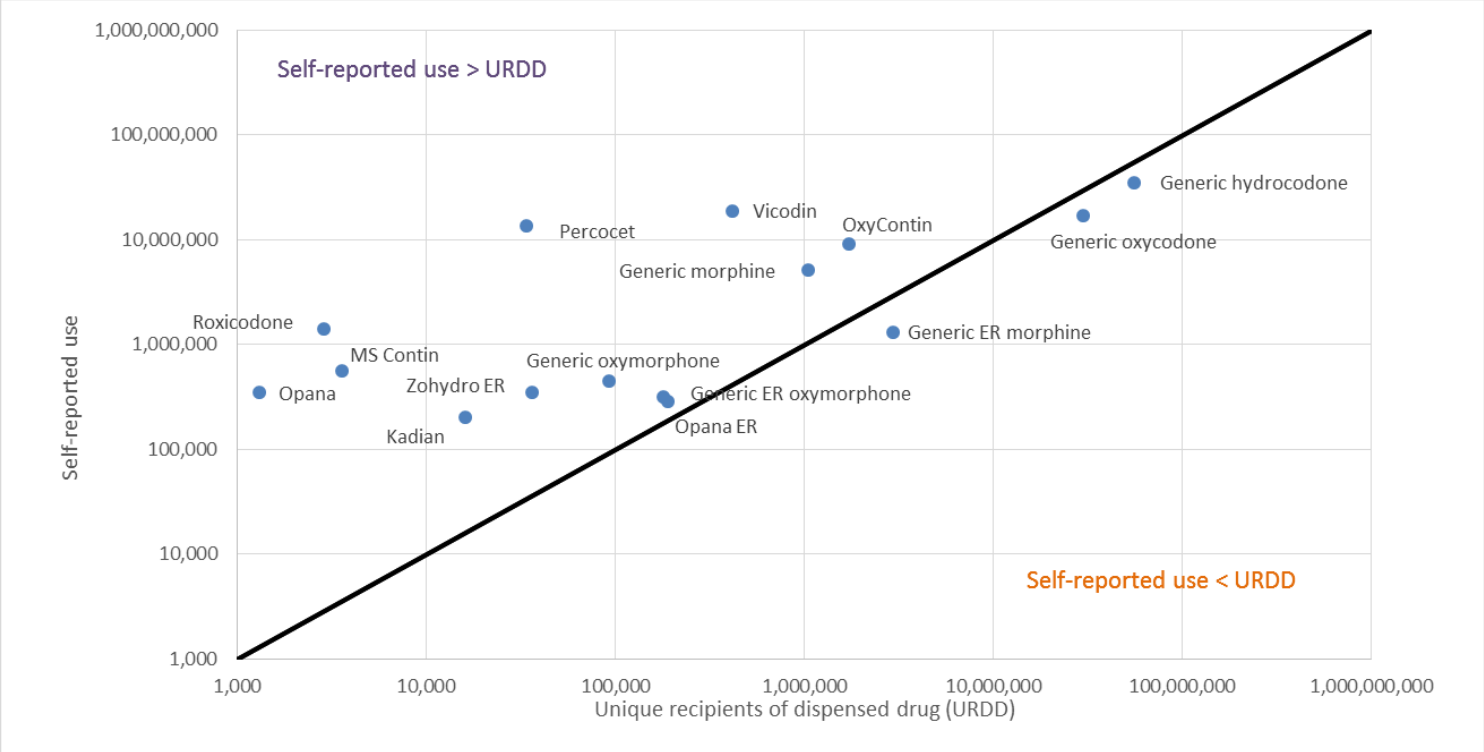
To estimate agreement between self-reported use versus observed product distribution, we compared the natural log of NSDUH past year use estimates to the natural log of URDD estimates from IQVIA. URDD represents the number of unique individuals who filled a prescription for a particular opioid product within a given quarter. We compared values from ten drug groups asked on the NSDUH drug screener questionnaire. These included OxyContin, generic oxycodone (images are of generic equivalents of Percocet and Roxicodone), Vicodin, Zohydro ER, generic hydrocodone (images are of generic equivalents of Vicodin), generic morphine (images are of generic immediate-release morphine products), generic ER morphine (images are of generic equivalents of MS Contin, Avinza, or Kadian), Opana, Opana ER, and generic ER oxymorphone (images are of are generic equivalents of Opana ER). Agreement was assessed using the intraclass correlation coefficient (ICC), a standard statistic to assess agreement between two raters. With the presence of agreement between to measures, values can range from 0 to 1. Values under 0.50 are indicative of poor agreement, 0.5 to 0.75 moderate agreement, and scores higher than 0.75 good to excellent agreement [7].

We also estimated the degree of bias due to self-report and how the magnitude of bias affects drug group comparisons. We use OxyContin as an example because the brand name is widely recognized due to extensive product marketing and the focus of several studies examining misclassification of specific products.

Results

Comparisons of self-reported use to URDD suggest a tendency for self-reported use estimates for branded products to be overestimated (Figure 1). The diagonal line represents perfect agreement between self-reported use and URDD. For drug groups above the line, self-reported values are inflated and for drug groups below the line, self-reported values are underestimated. Self-reported use values for Opana, Roxicodone, Vicodin, Zohydro ER, and OxyContin are all higher for self-reported misuse. Across drug groups, the ICC was 0.32, suggesting poor agreement.

Figure 1. Scatterplot of average annual URDD and average annual self-reported use estimates for select opioid analgesic products, 2016 through 2017, log scale



The ratio of the average annual self-reported use values and URDD values from 2016 and 2017 are presented below for each drug group displayed in the figure (Table 1). The number of individuals who used generic oxycodone and generic ER morphine in the past year was under-reported by more than 40% relative to the URDD for these products. It is noteworthy that these estimates held after removing individuals who reported misuse of the product, so the discrepancies cannot be fully explained by differences in product acquisition.

This ratio, referred to as the reporting bias statistic allows for an estimation of the degree to which the way an item is worded on a survey affects between drug group comparisons. If we take the reporting bias statistic for Zohydro ER (9.73) and divide this value by the bias estimate from another group, e.g. generic hydrocodone (0.64) we can assess the bias in rate comparisons. By relying on self-reported use data, the rate of Zohydro ER versus generic hydrocodone would be inflated 15-fold (9.73/0.64). The rate of OxyContin use versus generic oxycodone would be inflated 9-fold (5.20/0.57).

Table 1. Estimated bias in self-reported estimates of use for select drug groups, 2016 and 2017

Drug Class	Drug Product	Past Year Used (in thousands)	Unique Recipient of Dispensed Drug (in thousands)	Reporting bias (Self-report use/ URDD)	Reporting bias (Self-report use excluding Misuse/ URDD)
Hydrocodone	Vicodin	18,933	420	45.11	37.72
	Zohydro ER	351	36	9.73	8.62
	Generic hydrocodone	35,476	55,650	0.64	0.57
Oxycodone	OxyContin	9,039	1,737	5.20	4.35
	Percocet	13,500	34	397.03	337.00
	Roxicodone	1,415	3	489.22	302.52
	Generic oxycodone	16,990	29,988	0.57	0.50
Morphine	Kadian	201	16	12.54	11.60
	MS Contin	568	4	159.39	133.29
	Generic morphine	5,092	1,047	4.87	4.53
	Generic ER morphine	1,307	2,945	0.44	0.37
Oxymorphone	Opana	349	1	267.14	134.72
	Opana ER	314	179	1.75	1.18
	Generic oxymorphone	454	93	4.89	3.31
	Generic ER oxymorphone	284	191	1.49	1.14

Conclusions

Self-report surveys are vulnerable to misclassification biases. These biases are still present after providing images to aid respondents in recall. The magnitude of the misclassification varies by active pharmaceutical ingredient and by specific product. Comparing utilization rates between products without correcting for misclassification may result in biased estimates of relative differences between drug groups. Comparing utilization assessed by self-report to dispensing observed from retail pharmacies may provide insight into direction and magnitude of misclassification for individual products.

This analysis has notable limitations. Images provided on the NSDUH are not a comprehensive list of all available products; therefore individuals may not see a product that they used. URDD data are captured by quarter, three-digit ZIP code, product, and product dosage. Because individuals may fill prescriptions for different strengths of the same product or may fill prescriptions for products over multiple quarters, URDD values are overestimates of the number of individuals who filled a prescription for a product within a given year and these overestimates may differ across products. Finally, this analysis assesses misclassification among all recipients of prescription opioids. The degree of misclassification may differ by individual characteristics within the sample. For example, individuals who misuse prescription opioids may be more (or less) likely to accurately identify specific products.

Potential methods to assess and address differential misclassification are important when comparing prescription products. Continued efforts to adjust for product specific misclassification are needed. Estimating utilization through self-report should be considered when comparing drug groups where differential misclassification is suspected.

Suggested Citation

Severtson SG, Bau E, Iwanicki JL, Dart RC (2020): Use of self-report data results in differential misclassification and results in biased estimates of differences between specific opioid analgesic products. RADARS® System Technical Report, 2020-Q2.

References

[1]Jones CM, Muhuri PK, Lurie PG. Trends in the Nonmedical Use of OxyContin, United States, 2006 to 2013. Clin J Pain. 2017;33(5):452–461. doi:10.1097/AJP.0000000000000426

[2]Cicero TJ, Ellis MS, Kasper ZA. A tale of 2 ADFs: differences in the effectiveness of abuse-deterrent formulations of oxymorphone and oxycodone extended-release drugs. Pain. 2016;157(6):1232–1238. doi:10.1097/j.pain.0000000000000511

[3]Vosburg SK, Beaumont J, Dailey-Govoni ST, Butler SF, Green JL. Evaluation of Abuse and Route of Administration of Extended-Release Tapentadol Among Treatment-Seeking Individuals, as Captured by the Addiction Severity Index–Multimedia Version (ASI-MV), Pain Medicine, Volume 21, Issue 9, September 2020, Pages 1891–1901, https://doi.org/10.1093/pm/pnz250

[4]Biondo G, Chilcoat HD. Discrepancies in prevalence estimates in two national surveys for nonmedical use of a specific opioid product versus any prescription pain reliever Drug Alcohol Depend., 134 (2014), pp. 396-400

[5]Smith M, Rosenblum A, Parrino M, Fong C, Colucci S. Validity of self-reported misuse of prescription opioid analgesics. Subst Use Misuse. 2010;45(10):1509–1524. doi:10.3109/10826081003682107

[6]Center for Behavioral Health Statistics and Quality. (2018). 2016 National Survey on Drug Use and Health Public Use File Codebook. Substance Abuse and Mental Health Services Administration, Rockville, MD. Retrieved from https://datafiles.samhsa.gov/

[7]Koo TK, Li MY. “A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research.” Journal of chiropractic medicine vol. 15,2 (2016): 155-63. doi:10.1016/j.jcm.2016.02.012