ORIGINAL ARTICLE

Opioid-related clinical outcomes and associated healthcare costs following abuse/misuse of oxycodone formulations: A HEOR analysis from real-world data

Jody L. Green, PhD; Taryn Dailey-Govoni, MPH; Suzanne K. Vosburg, PhD

ARTICLE INFO

Keywords:
pain management
opioid therapy
healthcare outcomes
real-world data
health economics and outcomes research

DOI:10.5055/jom.0878

ABSTRACT

Objective: *The United States (US) opioid epidemic is a continued burden on the healthcare system and on the lives of individuals affected by the consequences of opioid abuse/misuse. The objective of this study was to use real-world data from intentional abuse/misuse exposures managed by US poison centers to compare clinical outcomes and quantify healthcare costs among three study cohorts: exposures that involved Xtampza ER®, other oxycodone extended-release (ER), and oxycodone immediate-release (IR).*

Study design: *A real-world, observational study.*

Main outcome measures: *Descriptive statistics were used to describe patient and exposure characteristics. Drug utilization-adjusted rates of intentional abuse/misuse and clinical outcomes were used to determine relative risk. Healthcare cost estimates were calculated by extrapolating average charge per opioid-related disorder emergency department (ED) visit and per inpatient stay based upon case disposition rates, adjusted for population and drug utilization.*

Results: *Compared to Xtampza ER, exposures that involved other oxycodone ER were 7.4 times more likely to be intentional abuse/misuse, 25.9 times more likely to result in major effect or death, 9.7 times more likely to require a visit to the ED, and 14.3 times more likely to result in hospital admission. Similar results were found for oxycodone IR when compared to Xtampza ER.*

Conclusions: *This study is the first of its kind to synthesize clinical outcomes with opioid-related healthcare costs, suggesting that even when Xtampza ER is abused/misused, the rates of major effect/death, ED visits, and hospital admissions were significantly lower than those for other oxycodone-containing medications, resulting in relatively low downstream opioid-related healthcare costs.*

OBJECTIVES/INTRODUCTION

The United States (US) opioid epidemic is a continued burden on the healthcare system and on the lives of individuals affected by the consequences of opioid abuse/misuse. The economic toll of the opioid crisis in the US was estimated at nearly USD 1.5 trillion in 2020.[1] According to the most recent report by the Society of Actuaries, healthcare costs associated with opioid overdose, misuse, and dependence were estimated at USD 60.4 billion in 2018 and expected to exceed USD 65 million in 2019.[2] Despite countless initiatives to curb opioid abuse, the annual rate of emergency department (ED) visits for nonfatal opioid overdoses per 100,000 persons has increased from 45.4 in 2018 to 62.4 in 2022.[3] In 2021, opioids were involved in 80,411 (75.4 percent) drug overdose deaths in the US, with 88 percent of these involving synthetic opioids such as fentanyl and fentanyl analogs (a 22 percent increase from 2020).[4]

While deaths involving synthetic opioids are on the rise, deaths involving natural and semisynthetic opioids such as oxycodone and hydrocodone have not significantly changed since 2010.[4] Deaths involving natural and semisynthetic opioids tripled from 2001 to 2010 and have plateaued through 2021. This drug class includes the majority of prescription opioid medications used to treat pain. The sustained flattening of the death rate trajectory suggests significant progress in reducing abuse in this drug grouping. The updated Centers for Disease Control and Prevention clinical practice guidelines for prescribing opioids encourages providers to focus on patient-centric pain management (with opioids and other therapies), with consideration of opioid-related risks.[5] Several examples of risk mitigation strategies are listed in the guidelines, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring programs, and use of abuse-deterrent formulations (ADFs). ADFs are opioid medications designated by the US Food and Drug Administration (FDA) as products that may meaningfully deter abuse, even if they do not fully prevent abuse.[6] ADF opioid medications include technology expected to make manipulation of an opioid more difficult or reduce the potent effects of manipulation, particularly from use via nonoral routes (such as snorting or injecting), which are associated with higher risk of life-threatening events/death.[7] Several studies have illustrated the effectiveness of ADFs, demonstrating reduction in abuse, therapeutic errors, and accidental exposures reported to US poison centers,[8-10] reduction in prevalence and frequency of overall abuse and abuse via nonoral routes in adults evaluated for substance use,[10-12] and reduction in drug diversion.[9] A study of real-world managed care populations determined that broad formulary coverage of ADF opioids was associated with 15-25 percent reduction in opioid abuse or overdose-related hospitalizations in the ADF opioid coverage group compared to those without ADF opioid coverage.[13]

As of 2013 in the US, all oxycodone extended-release (ER) formulations are required to have abuse-deterrent properties[14]; however, not all oxycodone ER products are formulated with the same ADF technology. The comparative effectiveness against abuse (especially via nonoral routes) and the reduction in the severity of clinical outcomes between the different formulations of oxycodone ER medications have been studied. Xtampza ER (an oxycodone ER capsule that may be taken by swallowing whole or by sprinkling the capsule contents on soft foods, into a cup, or through a gastrostomy or nasogastric feeding tube) had significantly lower rates of nonmedical use (NMU) than solid dosage forms of other oxycodone ER products and oxycodone immediate-release (IR) products, as well as significantly lower rates of nonoral NMU than oxycodone IR products among a population of individuals assessed for substance use treatment.[12] Xtampza ER abuse, misuse, diversion, and tampering were lower compared to other prescription opioid analgesics in poison center cases, substance use treatment centers, and drug diversion units.[10] In a study of commercial and Medicare claims, total healthcare costs in patients switched from oxycodone IR to Xtampza ER were significantly lower than costs in patients switched from oxycodone IR to OxyContin (USD 22,630 versus USD 28,386 [p = 0.005], respectively).[15]

While total healthcare costs have been compared between oxycodone ER products, costs specific to opioid-related ED visits and hospital admissions have yet to be enumerated. The objective of this study was to (1) compare the abuse/misuse rates captured by the National Poison Data System (NPDS) between Xtampza ER, other ER oxycodone (ADF group excluding Xtampza ER), and IR oxycodone, adjusted for population and drug utilization; (2) compare the medical outcome severity and level of healthcare required, eg, ED visit and hospital admission, to manage NPDS abuse/misuse cases that involved Xtampza ER versus other oxycodone medications; and (3) compare extrapolated cost estimates associated with ED visits and hospital admissions associated with Xtampza ER NPDS abuse/misuse cases to other oxycodone medications.

METHODS

This is a health economics and outcomes research (HEOR) study using real-world data from four data sources.

NPDS (America's Poison Centers [APC]) is a national repository of exposures reported to and managed by US poison centers.[16] While the primary role of a poison center is medical management, patient reports are recorded in a standardized, electronic form and uploaded to the NPDS in near real-time. Exposures in patients aged 12 years and older with exposure dates from January 1, 2019 through

December 31, 2022 were used to estimate rates of abuse/misuse, severity of medical outcome, treated/evaluated and released disposition, and hospital admissions. For purposes of this study, combined outcomes were created based on the exposure reason of abuse/misuse (intentional abuse/intentional misuse/intentional unknown), medical outcome (major effect/death), and healthcare facility (HCF) level of care (hospital admission to noncritical care/to critical care/to psychiatric).[17]

IQVIA's National Prescription Audit™ (*NPA*) data use algorithms to project the number of dosage units dispensed, ie, number of tablets or capsules, during a given time frame and within a given geographic area. Estimated dosage units dispensed, ie, tablets and capsules, were used to calculate drug utilization adjusted rates for each study group for the study period of January 1, 2019 through December 31, 2022.

Healthcare Cost and Utilization Project (HCUP) is a family of healthcare databases and related software tools and products developed through a federal–state–industry partnership and sponsored by the Agency for Healthcare Research and Quality (AHRQ). The most recent data from the 2020 Nationwide Emergency Department Sample provided the average hospital charge per opioid-related disorder ED visit, and data from the 2020 National (Nationwide) Inpatient Sample provided the average hospital charge per opioid-related inpatient hospital stay. These cost estimates were used to extrapolate and compare ED visit and hospital admission costs between study groups. HCUP and AHRQ Use Guidelines were followed.

US Census Bureau's American Community Survey data were applied to the extrapolated healthcare costs to adjust for population. The most recent national population estimates from 2021 for those aged 12 years and older were applied to match the NPDS data age range.

The primary product of interest was Xtampza ER, an oxycodone ER ADF medication. Comparator opioids include other oral solid dosage formulations of oxycodone ER products (excluding Xtampza ER) and oxycodone IR products (Table 1). Descriptive statistics were used to summarize patient demographics (age and gender), exposure reason for intentional abuse/misuse, and the proportion of intentional abuse/misuse exposures involving one versus multiple study groups. Rates of intentional abuse/misuse and clinical outcomes (major effect/death, evaluated/treated/released, and hospital admission) were calculated per 100,000 dosage units dispensed. Relative risk was calculated by dividing the rate of the event occurring in the comparator group by the rate of the event occurring in the reference group (Xtampza ER). A relative risk of 1.0 indicates identical rates among the two groups and a value greater than 1.0 indicates an increased risk in the comparator group. Statistical significance is indicated when the 95 percent confidence interval (CI) does not include 1.0.

Healthcare cost estimates were calculated by extrapolating the 2020 HCUP average hospital charge per opioid-related disorder ED visit (USD 3,795 ± 95 percent CI 365) and average hospital charges per inpatient stay per opioid-related disorder (USD 20,706 ± 95 percent CI 1,222) based upon

Table 1. Study groups and drug utilization

Group	Description	Total dosage units dispensed* (2019-2022)	Percentage of all oxycodone dosage units dispensed (2019-2022)
Xtampza ER (product of interest)	Includes Xtampza ER	128,680,031	1.2
Other oxycodone ER (comparator)	Includes oral solid dosage forms of oxycodone ER products, excluding Xtampza ER	364,541,517	3.4
Oxycodone IR (comparator)	Includes oral solid dosage forms of all oxycodone IR products, both single ingredient and combination products	10,295,942,944	95.4

*Data include estimated dosage units dispensed within all US states as well as those dispensed by mail order.
ER: extended-release; IR: immediate-release.

NPDS rates of evaluated/treated/released and hospital admission (2019-2022), adjusted for population (US Census data) and drug utilization (dosage units dispensed).

RESULTS

A total of 301 exposures to Xtampza ER, 2,159 to other oxycodone ER, and 17,694 to oxycodone IR were reported to NPDS during the study period (Table 2). All but one abuse/misuse exposure to Xtampza ER involved substances from only one study group; one exposure involved Xtampza ER and oxycodone IR. Similar to Xtampza ER, the majority (>90 percent) of intentional abuse/misuse exposures to the comparator opioids were exposures involving only one study group.

Compared to Xtampza ER (34.4 percent), exposures to the comparator opioids occurred more frequently among individuals aged 39 years or younger (other oxycodone ER, 57.5 percent; oxycodone IR, 64.3 percent) (Table 3). The mean age of those reporting exposure to Xtampza ER (49.4 years) was greater than the mean age for other oxycodone ER (37.5 years) and oxycodone IR (35.1 years). While females accounted for 53.1 percent of Xtampza ER exposures, males accounted for most exposures to other oxycodone ER (63.9 percent) and oxycodone IR (61.4 percent).

The relative risk analysis adjusted for drug utilization resulted in significantly higher risk of all outcomes for other oxycodone ER and oxycodone IR compared to Xtampza ER (Figure 1). Intentional abuse/misuse was 7.4 (95 percent CI 5.2-10.5) times more likely for other oxycodone ER and 2.0 (95 percent CI 1.4-2.9) times more likely for oxycodone IR. Intentional abuse/misuse exposures resulting in major effect or death were 25.9 (95 percent CI 8.3-80.9) times more likely for other oxycodone ER and 7.2 (95 percent CI 2.3-22.4) times more likely for oxycodone IR. Intentional abuse/misuse exposures resulting in ED visits were 9.7 (95 percent CI 5.3-17.6) times more likely for other oxycodone ER and 2.8 (95 percent CI 1.5-5.0) times more likely for oxycodone IR. Intentional abuse/misuse exposures resulting in hospital admission were 14.3 (95 percent CI 5.9-34.8) times more likely for other oxycodone ER and 4.0 (95 percent CI 1.7-9.6) times more likely for oxycodone IR.

When considering rates of HCF level of treated/evaluated and released per 100,000 US population per 100,000,000 (100 m) dosage units dispensed, the extrapolated cost of ED visits involving intentional abuse/misuse of Xtampza ER was USD 1,135.36 (USD 1,026.17-1,244.56), which was markedly lower than the extrapolated costs associated with other oxycodone ER (USD 10,966.63, USD 9,911.86-12,021.39) and oxycodone IR (USD 3,143.71,

Table 2. All NPDS exposures, intentional abuse/misuse exposures, single study group intentional abuse/misuse exposures, and multiple study group intentional abuse/misuse exposures by study group reported to NPDS (January 1, 2019 through December 31, 2022)

	All NPDS exposures	Intentional abuse/misuse exposures		Cases with substances in only one study group*		Cases with substances in more than one study group	
	n	n	Percentage of any exposure	n	Percentage of intentional abuse/misuse exposures	n	Percentage of intentional abuse/misuse exposures
Xtampza ER	301	32	10.6	31	96.9	1	3.1
Other oxycodone ER	2,159	668	30.9	656	98.2	12	1.8
Oxycodone IR	17,694	5,149	29.1	5,125	99.5	24	0.5

*For Xtampza ER, cases with substances in only one study group are those that involve Xtampza ER but do not involve other oxycodone ER or oxycodone IR products. For other oxycodone ER, cases with substances in only one study group are those that involve at least one other oxycodone ER but do not involve Xtampza ER or oxycodone IR. For oxycodone IR, cases with substances in only one study group are those that involve at least one oxycodone IR but do not involve Xtampza ER or other oxycodone ER.
NPDS: National Poison Data System; ER: extended-release; IR: immediate-release.

Table 3. Patient demographics of intentional abuse/misuse exposures by study group reported to NPDS (January 1, 2019 through December 31, 2022)

		Xtampza ER (N = 32)		Other oxycodone ER (N = 668)		Oxycodone IR (N = 5,149)	
	Response	**n**	**Percent**	**n**	**Percent**	**n**	**Percent**
Age	12 to ≤19 years	0	0.0	88	13.2	957	18.6
	20 to ≤39 years	11	34.4	296	44.3	2,354	45.7
	40 to ≤59 years	10	31.3	183	27.4	1,090	21.2
	60+ years	11	34.4	72	10.8	584	11.3
	Unknown adult (20+ years)	0	0.0	29	4.3	164	3.2
	Total N*	32		634		4,949	
	Mean (years)	49.4		37.5		35.1	
	Standard deviation (years)	15.5		16.9		16.8	
	Median (years)	55		34		30	
	Range (years)	24-72		12-94		12-100	
Gender	Male	15	46.9	427	63.9	3,162	61.4
	Female	17	53.1	240	35.9	1,981	38.5
	Unknown/no response	0	0.0	1	0.1	6	0.1

*Some exposures do not list a specific age but instead provide an age category, eg, "20s," "unknown adult." Age statistics (mean, standard deviation, median, and range) include only exposures with a specific age (in years) reported.
NPDS: National Poison Data System; ER: extended-release; IR: immediate-release.

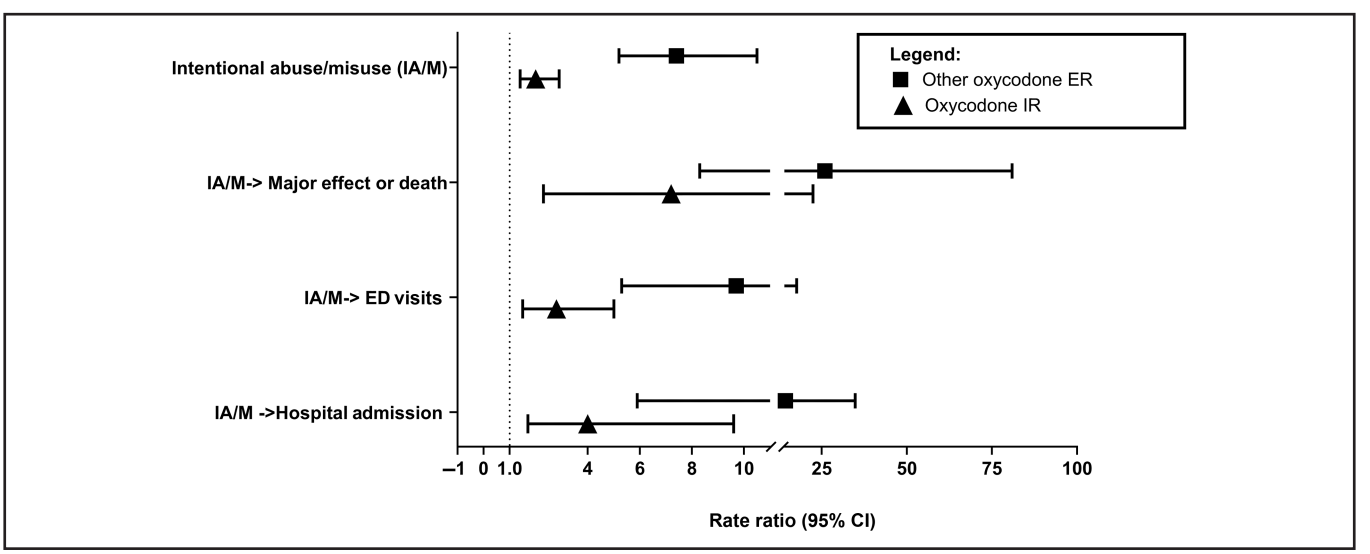

Figure 1. Relative risk of intentional abuse/misuse, major effect/death, ED visit, and hospital admission by study group (2019-2022). ER: extended-release; IR: immediate-release; ED: emergency department; CI: confidence interval.

USD 2,841.35-3,446.07). When adjusted per 100,000 US population per 100 m dosage units dispensed, the extrapolated cost of hospital admission involving intentional abuse/misuse of Xtampza ER was USD 2,815.77 (USD 2,649.59-2,981.94), which was markedly lower than the extrapolated costs associated with other oxycodone ER (USD 40,354.04, USD 37,972.47-42,735.60) and oxycodone IR (USD 11,191.00, USD 10,530.54-11,851.46) (Figure 2).

DISCUSSION

This study supports previous post-market reports of lower abuse/misuse rates of Xtampza ER compared to other oxycodone-containing medications, even when adjusted for the variation in drug utilization between the study groups. Similar trends have been observed across different populations—eg, exposures managed by poison centers, individuals assessed for substance use treatment, and medical/pharmacy claims data—and study outcomes—eg, intentional abuse/misuse, severity of medical outcome, and level of HCF required to manage an intentional abuse/misuse event—when comparing Xtampza ER to other opioid medications.

This study also provides a novel HEOR evaluation using real-world data on clinical outcomes and healthcare costs associated with abuse/misuse of Xtampza ER compared to other opioid medications. Rates of serious clinical outcomes resulting from abuse/misuse exposure (adjusted for dosage units dispensed) were greater for other oxycodone ER and oxycodone IR compared to Xtampza ER. Specifically, major effect (life-threatening)/death was 25.9 times higher for other oxycodone ER and 7.2 times higher for oxycodone IR, HCF level of treated/evaluated and released (ED visit) was 9.7 times higher for other oxycodone ER and 2.8 times higher for oxycodone IR, and hospital admission was 14.3 times higher for other oxycodone ER and 4.0 times higher for oxycodone IR.

In addition to the human toll, these outcomes translate to exponentially higher healthcare costs. The incremental costs of ED visits for the comparator groups were from USD 2,009 to 9,832 higher per 100,000 persons per 100 m dosage units dispensed and the incremental costs for hospital admissions were from USD 8,375 to 37,538 higher per 100,000 persons per 100 m dosage units dispensed.

Despite real-world evidence of the effectiveness of ADF opioid medications at reducing abuse and associated outcomes, there has been a slow uptake of utilization of these products, which account for only 5-6 percent of opioid medications dispensed.[18] From 2015 to 2019, utilization of ADF products decreased by 51 percent. However, not all ADFs exhibited the same prescribing pattern. While OxyContin utilization decreased during that time period, utilization of Xtampza ER actually increased. In our study, Xtampza ER is compared to other oxycodone ER (including OxyContin), all of which are required by FDA to have ADF properties. Compared to Xtampza ER, NPDS exposures of other oxycodone ER were 7.4 times more likely to involve abuse/misuse,

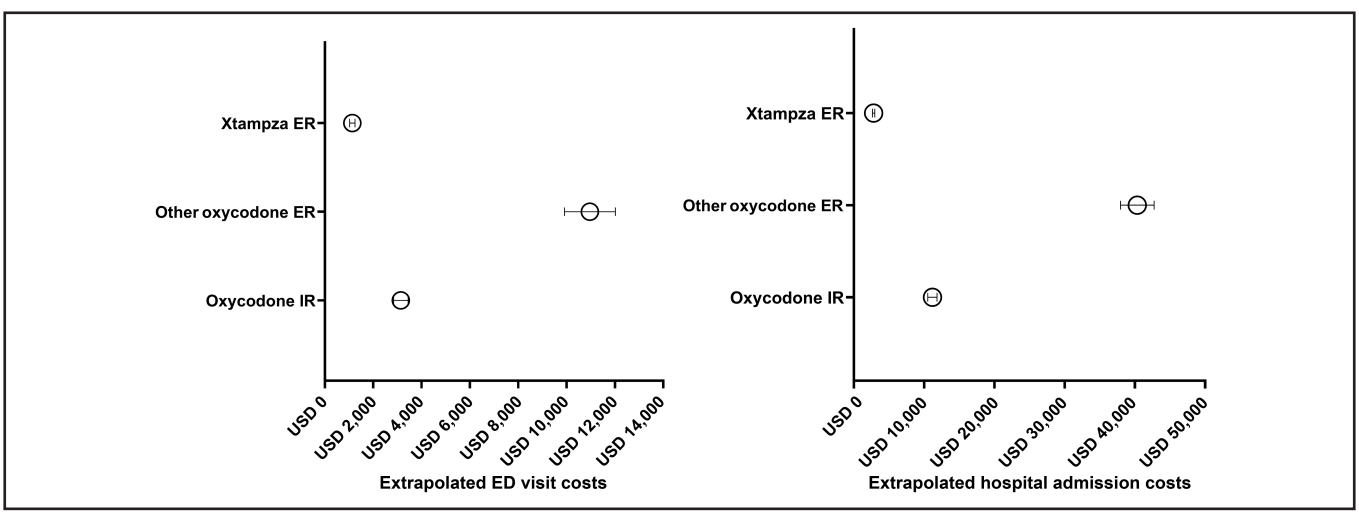

Figure 2. Extrapolated costs (95 percent confidence interval) of intentional abuse/misuse exposures resulting in ED visits and hospital admission per 100,000 US population per 100 million dosage units dispensed (2019-2022). ER: extended-release; IR: immediate-release; ED: emergency department.

25.9 times more likely to result in major effect or death, 9.7 times more likely to result in ED visit, and 14.3 times more likely to result in hospital admission. The difference in extrapolated costs between ED visit and hospital admission was substantial and would be expected to far exceed any incremental costs for branded ADF medications. These data suggest that not all ADF opioids will exhibit the same effectiveness in deterring abuse or the related costs of ED visits and hospital admissions, which may be due to the variations in technology. Additional studies that expand upon the relative cost effectiveness of specific ADF medications for overall healthcare costs (including the differential costs of the medications) are warranted.

Limitations

As with all observational studies, this study has limitations. NPDS data are not intended to capture all abuse/misuse exposures; hence, there is underreporting for rates and estimated healthcare costs. There was minimal overlap between study groups (0.5-3.1 percent); however, due to the small sample size for Xtampza ER, these cases were included in all relevant groups and were not expected to change study findings. The interpretation of the results should focus on the relative differences (relative risk) between study groups rather than absolute rates. NPDS relies on self-reported data, as do most real-world data sources. Specific products are not verified; however, healthcare professionals managing cases recorded in NPDS are trained to obtain as much information as possible to accurately identify and code products, and there are no data that suggest any differential reporting bias. HCUP estimates are generalized and not product specific. Variability in healthcare costs for a specific ED visit or hospital admission would be expected based upon the severity of the opioid-related event, which is not accounted for in this model. Interpretation of the healthcare cost estimates should focus on the relative differences between study groups rather than absolute costs.

CONCLUSIONS

This study is the first of its kind to synthesize clinical outcomes captured in NPDS with opioid-related healthcare costs, suggesting that even when Xtampza ER is abused/misused, the rates of major effect/death, ED visits, and hospital admissions were significantly lower than those for other oxycodone-containing medications, resulting in relatively low downstream opioid-related healthcare costs.

ACKNOWLEDGMENTS

This research was supported by Collegium Pharmaceutical, Inc. While the sponsor provided research support and reviewed the manuscript, all content of this article, data collection, analysis, and ultimate data interpretation were made by the authors without the sponsor's influence.

This research was approved by WCG IRB on February 6, 2023.

Jody L. Green, PhD, Uprise Health/Inflexxion, Irvine, California. ORCID: https://orcid.org/0000-0003-1776-6400.

Taryn Dailey-Govoni, MPH, Uprise Health/Inflexxion, Irvine, California. ORCID: https://orcid.org/0000-0002-2942-4267.

Suzanne K. Vosburg, PhD, Uprise Health/Inflexxion, Irvine, California. ORCID: https://orcid.org/0000-0002-1794-7116.

REFERENCES

1. Joint Economic Committee Democrats: The economic toll of the opioid crisis reached nearly $1.5 trillion in 2020. 2022. Available at *https://www.jec.senate.gov/public/_cache/files/67bced7f-4232-40ea-9263-f033d280c567/jec-cost-of-opioids-issue-brief.pdf*. Accessed July 10, 2024.

2. Davenport S, Weaver A, Caverly M: Economic impact of non-medical opioid use in the United States, annual estimates and projections for 2015 through 2019. Society of Actuaries. 2019. Available at *https://www.soa.org/globalassets/assets/files/resources/research-report/2019/econ-impact-non-medical-opioid-use.pdf*. Accessed July 10, 2024.

3. Centers for Disease Control and Prevention: *Drug Overdose Surveillance and Epidemiology (DOSE) System: Nonfatal Overdose Emergency Department and Inpatient Hospitalization Discharge Data*. Atlanta, GA: US Department of Health and Human Services/CDC, 2023. Available at *https://www.cdc.gov/overdose-prevention/data-research/facts-stats/dose-dashboard-nonfatal-discharge-data.html?CDC_AAref_Val=https://www.cdc.gov/drugoverdose/nonfatal/dose/discharge/dashboard/index.html*. Accessed July 10, 2024.

4. Spencer MR, Miniño AM, Warner M: Drug overdose deaths in the United States, 2001–2021. In *NCHS Data Brief No. 457*. Hyattsville, MD: National Center for Health Statistics, 2022. DOI: 10.15620/cdc:122556. Accessed July 10, 2024.

5. Dowell D, Ragan KR, Jones CM, et al.: CDC clinical practice guideline for prescribing opioids for pain—United States, 2022. *MMWR Recomm Rep*. 2022; 71(RR-3): 1-95. DOI: 10.15585/MMWR.RR7103A1.

6. United States Food and Drug Administration CDER: Abuse deterrent opioids—Evaluation and labeling, guidance for industry. 2015. Available at *https://www.fda.gov/downloads/Drugs/Guidances/UCM334743.pdf*. Accessed November 16, 2023.

7. Green JL, Bucher Bartelson B, Le Lait MC, et al.: Medical outcomes associated with prescription opioid abuse via oral and non-oral routes of administration. *Drug Alcohol Depend.* 2017; 175: 140-145. DOI: 10.1016/j.drugalcdep.2017.01.039.

8. Coplan P, Kale H, Sandstrom L, et al.: Changes in oxycodone and heroin exposures in the national poison data system after introduction of extended-release oxycodone with abuse-deterrent characteristics. *Pharmacoepidemiol Drug Saf.* 2013; 22(12): 1274-1282.

9. Severtson S, Bartelson B, Davis J, et al.: Reduced abuse, therapeutic errors, and diversion following reformulation of extended-release oxycodone in 2010. *J Pain.* 2013; 14(10): 1122-1130.

10. Severtson SG, Kreider SED, Amioka EC, et al.: Postmarketing analysis of misuse, abuse, and diversion of Xtampza ER. *Pain Med.* 2020; 21(12): 3660-3668. DOI: 10.1093/pm/pnaa272.

11. Butler S, Cassidy T, Chilcoat H, et al.: Abuse rates and routes of administration of reformulated extended-release oxycodone: Initial findings from a sentinel surveillance sample of individuals assessed for substance abuse treatment. *J Pain.* 2013; 14(4): 351-358.

12. Green JL, Robbins RS, Dailey-Govoni T, et al.: Nonmedical use of Xtampza® ER and other oxycodone medications in adults evaluated for substance abuse treatment: Real-world data from the addiction severity Index-Multimedia version (ASI-MV®). *J Pain Res.* 2021; 14: 1773-1783. DOI: 10.2147/JPR.S304805.

13. Petrilla A, Marrett E, Shen X, et al.: Association between formulary coverage and use of abuse-deterrent prescription opioids, risk for abuse or overdose, and associated healthcare resource utilization. *Am Health Drug Benefits.* 2020; 13(1): 21-31.

14. Department of Health and Human Services, Food and Drug Administration: Determination that the oxycontin (oxycodone hydrochloride) drug products covered by the new drug application 20-553 were withdrawn from sale for reasons of safety or effectiveness. *Fed Regist.* 2013; 78(75): 23273-23275.

15. Olatoke O, Zah V, Stanicic F, et al.: A US retrospective claims analysis comparing healthcare costs of patients transitioning from immediate-release oxycodone to two different formulations of extended-release oxycodone: Xtampza ER or OxyContin. *Clinicoecon Outcomes Res.* 2022; 14: 119-128. DOI: 10.2147/CEOR.S340290.

16. American Poison Centers: Available at *https://www.aapcc.org/national-poison-data-system*. Accessed November 16, 2023.

17. Gummin DD, Mowry JB, Beuhler MC, et al.: 2021 annual report of the national poison data system© (NPDS) from America's Poison Centers: 39th annual report. *Clin Toxicol.* 2022; 60(12): 1381-1643. DOI: 10.1080/15563650.2022.2132768.

18. US Food and Drug Administration: FDA analysis of long-term trends in prescription opioid analgesic products: Quantity, sales, and price trends. 2018. Available at *www.fda.gov/media/111695/download*. Accessed November 28, 2023.