



## Introduction




**50.2M**

- 50.2 million adults in the United States suffer from chronic pain.<sup>1</sup>
- Use of opioids as treatment for chronic pain has resulted in significant morbidity and mortality.<sup>2</sup>



**74.8%**

- 74.8% of all deaths due to drug overdose involved an opioid.<sup>3</sup>
- Efforts have focused on reducing opioid use to mitigate these effects, and less on use of opioids with other harmful drugs, such as benzodiazepines, skeletal muscle relaxants, or gabapentin.



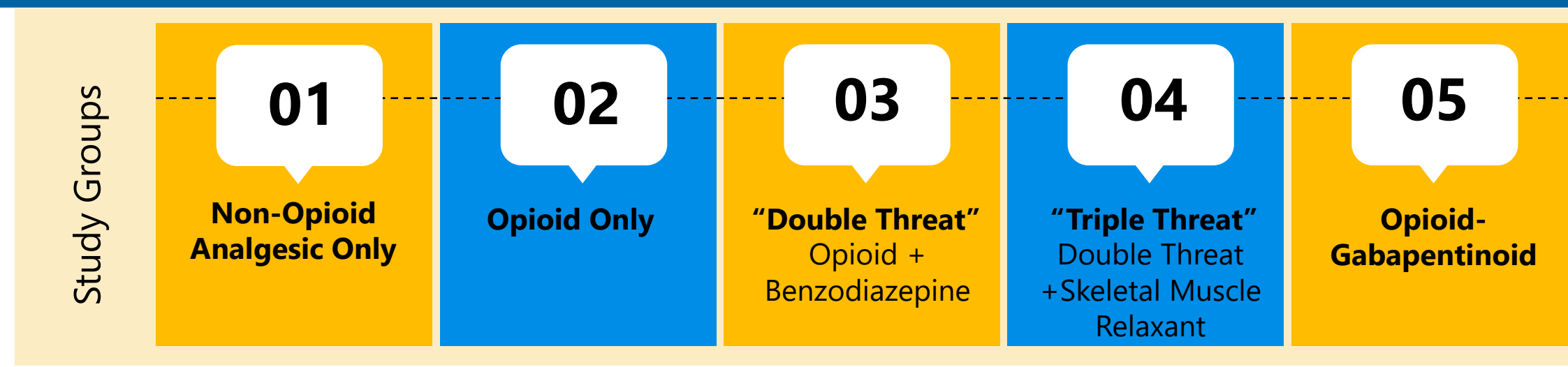
**29.0%**

- For example, 29.0% of those who die from opioid overdose have evidence of concurrent benzodiazepine use.<sup>4</sup>
- Patients using opioids, benzodiazepines, and skeletal muscle relaxants are **nine times more likely** to use the Emergency Department than those who do not.<sup>5</sup>
- It is largely **unknown** how trends in use of these combinations has shifted over time and how they vary in medical expenditure and resource utilization

## Objectives


- To evaluate differences in healthcare expenditure and resource utilization among non-opioid analgesic, opioid-only, opioid + benzodiazepine ("double threat"), opioid + benzodiazepine + skeletal muscle relaxant ("triple threat"), and opioid-gabapentinoid ("opioid-gaba") users from 2009-2019 among adults in the US
- To evaluate changes in healthcare expenditure and resource utilization over time between non-opioid analgesic, opioid-only, double threat, triple threat, and opioid-gaba users from 2009-2019 among adults in the US

## Methods



- Medical Expenditure Panel Survey (MEPS) data were pooled from 2009-2019 to generate five study groups that were defined based on medications reported by adult (age > 18 years) participants during distinct survey periods per year (three periods/year).
- Study outcomes were evaluated comparing each distinct study group compared to the non-opioid analgesic group using the pooled data.

## Primary Outcomes



**Total Medical Expenditure**  
Adjusted using Personal Consumption Expenditure Health (PCE-H) index


- Study groups were compared to the non-opioid analgesic group using a series of survey weighted two-part models; results reported as average marginal effects (\$)
- For study groups where no participants had total expenditure of \$0, survey weighted generalized linear models with a gamma log link function were used.



**Resource Utilization**  
Split into distinct categories: inpatient discharges, emergency department visits, outpatient visits, office-based visits, prescription medicines purchased

Two-part models were performed using STATA's twopm package. All other analyses were performed using R (Boston, MA) with a significance level of 0.05. All models were adjusted for covariates.

## Secondary Outcomes



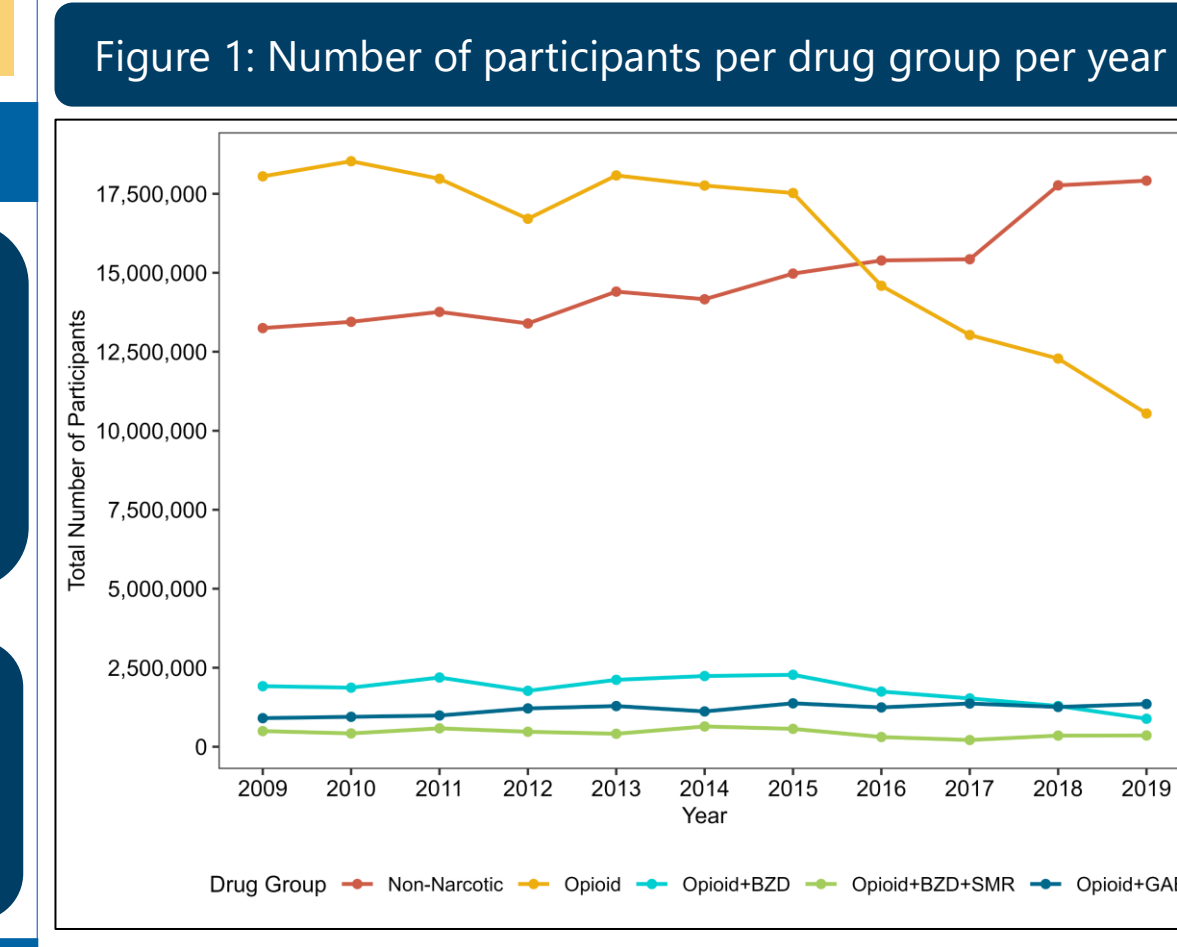
**Medical Expenditure Categories**  
Inpatient expenditure, ED expenditure, outpatient expenditure, office-based expenditure, prescription medicine expenditure

- Study groups were also compared to non-opioid analgesic users according to individual expenditure categories using the same methods for total medical expenditure



**Average Yearly Changes from 2009-2019**  
For all study outcomes

## Results



In total, 370,738 participants were pooled, representing a weighted **376.6 million lives**:

- Non-Opioid Only** N = 18,214 (4.9%) unweighted
  - Mostly middle aged (45-64 years): 37.4%, male (55.3%), white (75.2%), non-Hispanic (86.4%), married (53.0%), with high income (37.8%) and private insurance (62.4%)
- Opioid Only** N = 16,796 (4.5%) unweighted
  - Mostly middle aged (mean age: 50 yrs.), white (82.0%), non-Hispanic (10.3%), high income (40.1%), and had private insurance (72.0%)
  - Similar demographic distribution to non-opioid analgesic users
- Double Threat** N = 1,742 (0.47%) unweighted
- Triple Threat** N = 439 (0.12%) unweighted
- Opioid-Gaba** N = 1,230 (0.33%) unweighted
  - Similar distribution to double/triple threat users, but mostly older adults (age 65+: 46.6% vs. 31.0% non-narcotic) and a higher comorbidity burden (mean Charlson comorbidity index score: 3.2 vs. 2.0 non-narcotic)

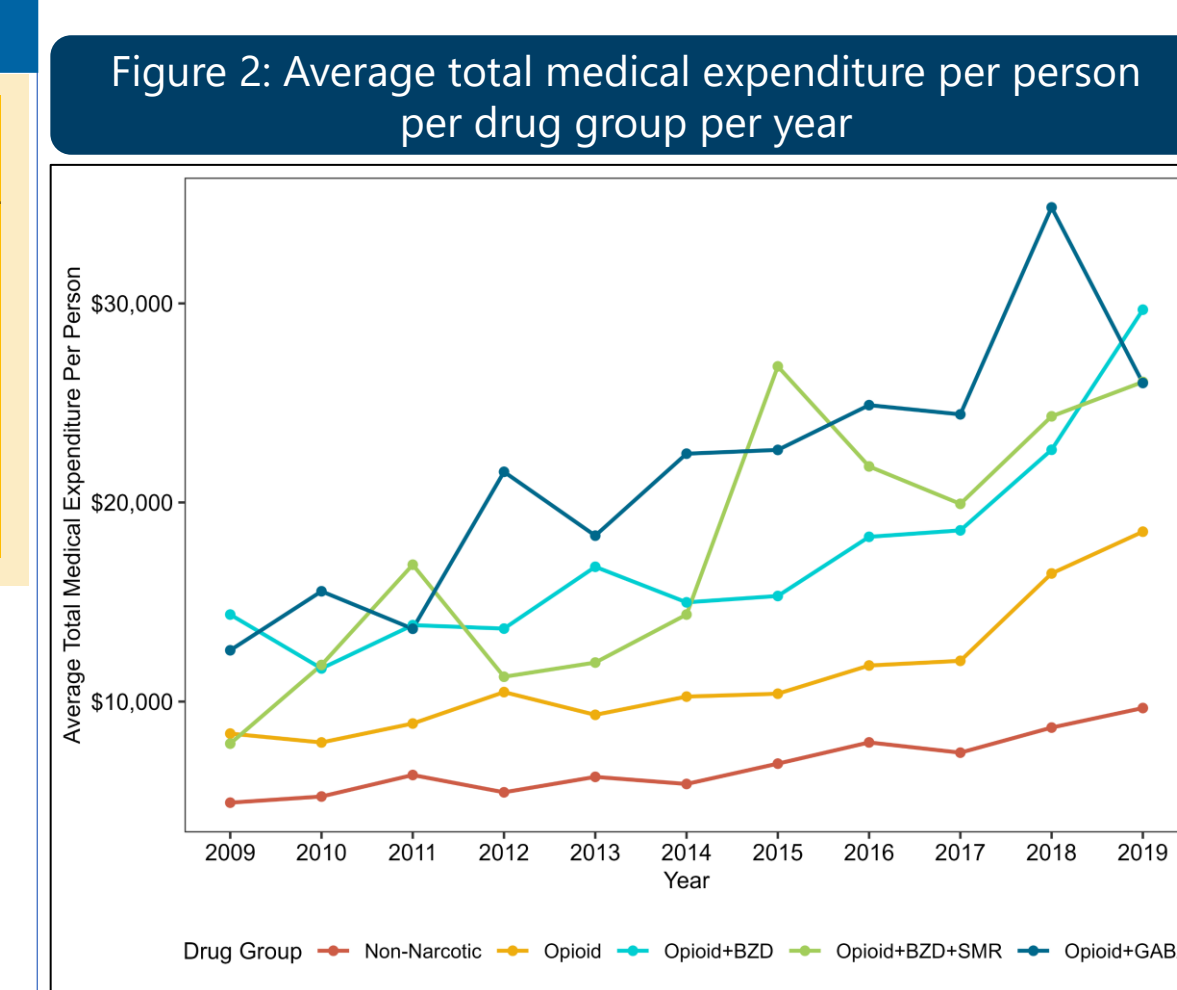


Table 1: Estimated Average Marginal Effects (\$) of Healthcare Expenditures and Incidence Rate Ratios of Resource Utilization Categories of Drug Groups compared to Non-Narcotic Only Users, 2009-2019

	Outcome	Opioid-Only	Double Threat	Triple Threat	Opioid-Gaba
Expenditures	Total Medical Expenditure	+5,228**	+8,789**	+9,878**	+11,684**
	Inpatient Expenditure	+1,918**	+2,594**	+2,665**	+3,897**
	Outpatient Expenditure	+950**	+699**	+518**	+687**
	Office-Based Visit Expenditure	+741**	+1,429**	+1,485**	+1,849**
	ED Expenditure	+253**	+322**	+397**	+258**
Resource Utilization	Prescription Drug Expenditure	+117**	+2,560**	+3,270**	+3,334**
	Number of Inpatient Discharges	2.02**	2.69**	2.39**	2.93**
	Number of Outpatient Visits	1.56**	1.80**	1.65**	2.02**
	Number of Office-Based Visits	1.24**	1.92**	2.12**	2.01**
	Number of ED Visits	1.68**	1.97**	1.97**	1.75**
	Number of Prescription Medications	0.94**	1.87**	2.74**	1.92**

**From 2009 to 2019, compared to the Non-Opioid Analgesic Only Group...**

- +\$1,237\*\*** Opioid-Gaba users had the highest yearly average increase in total medical expenditure
- +0.030\*\*** Opioid-GABA users had the highest yearly increase in number of inpatient discharges and outpatient visits (+0.17\*\*)
- +0.042\*\*** Triple threat users had the highest average yearly increase in number of ED visits
- +0.22\*\*** Opioid-only users had the highest average yearly increase in number of office-based visits
- +0.042\*\*** Triple threat users had the highest average yearly increase in number of ED visits
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No groups had a significant change in average yearly number of prescription medicines compared to non-narcotic analgesics only users.

Interaction term regression coefficients reported. \*\*p<0.05

## Conclusions

- Based on our findings, three major conclusions can be made:
- Compared to non-analgesic users, the number of opioid users has gone down over time, but group expenditures have increased. This may have been driven by an increase in outpatient and office-based visits, suggesting more recent emphasis on outpatient case and management for opioid users due to various policies and scrutiny on the opioid epidemic
  - Double and triple threat users demonstrated very high rates of inpatient and ED use and expenditure compared to non-opioid only users in addition to office-based visit use. Based on demographic characteristics, these patients may be older with lower socioeconomic status and have multiple comorbidities. We hypothesize these patients may be experiencing higher rates of adverse events due to compounded drug effects. Policies should focus on centralizing the management of these patients.
  - Of the groups, opioid-gaba users had the highest total medical expenditure compared to non-opioid users with exceedingly high inpatient use and prescription medication use. We hypothesize this drug combination has been gaining traction over time to supplant opioid use for chronic pain. However, the compounded effects of both drugs may also be associated with the rise in inpatient and ED use observed

In conclusion, while use opioids alone appears to be resulting in more favorable resource use for patients, combinations of opioids and other drugs with a risk of compounded adverse drug events continue to persist and lead to an increase in expenditure and resource utilization. Future policies should focus on the importance on continuous evaluation of the safety of these drug combinations in the outpatient setting.

## References

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