



Mortality Involving Prescription Drugs

16 May, 2019

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Disclosure

Work presented here was funded by the Opioid Analgesic REMS Programs Companies.

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Outline

1. Overview of CDC Drug Mentions with Involvement (DMI) Database
2. Opioid and Benzodiazepine Mortality Rates
3. Polysubstance Overdose Prevalence
4. Specificity as a Limitation of DMI
5. Conclusion

Drugs Mentioned with Involvement (DMI) Database

- Created from National Vital Statistics System – Mortality linked to death certificates
- Cause of death and injury text searched for drug mentions
 - Rules-based search algorithm
 - Misspellings (“OCYCODONE”) & product names (“OXYCONTIN”) are mapped to individual molecules (“OXYCODONE”)
 - Non-specific key terms are present (e.g. “OPIUM”)
 - Terms were built from DAWN (2012) and updated via manual adjudication
- Transposition to case level can assess mortality rates and polysubstance prevalence

Trinidad JP, Warner M, Bastian BA, et al. Using literal text from the death certificate to enhance mortality statistics: Characterizing drug involvement in deaths. National Vital Statistics Reports; Vol 65 No 9. Hyattsville, MD: National Center for Health Statistics. 2016.



Study Design and Setting

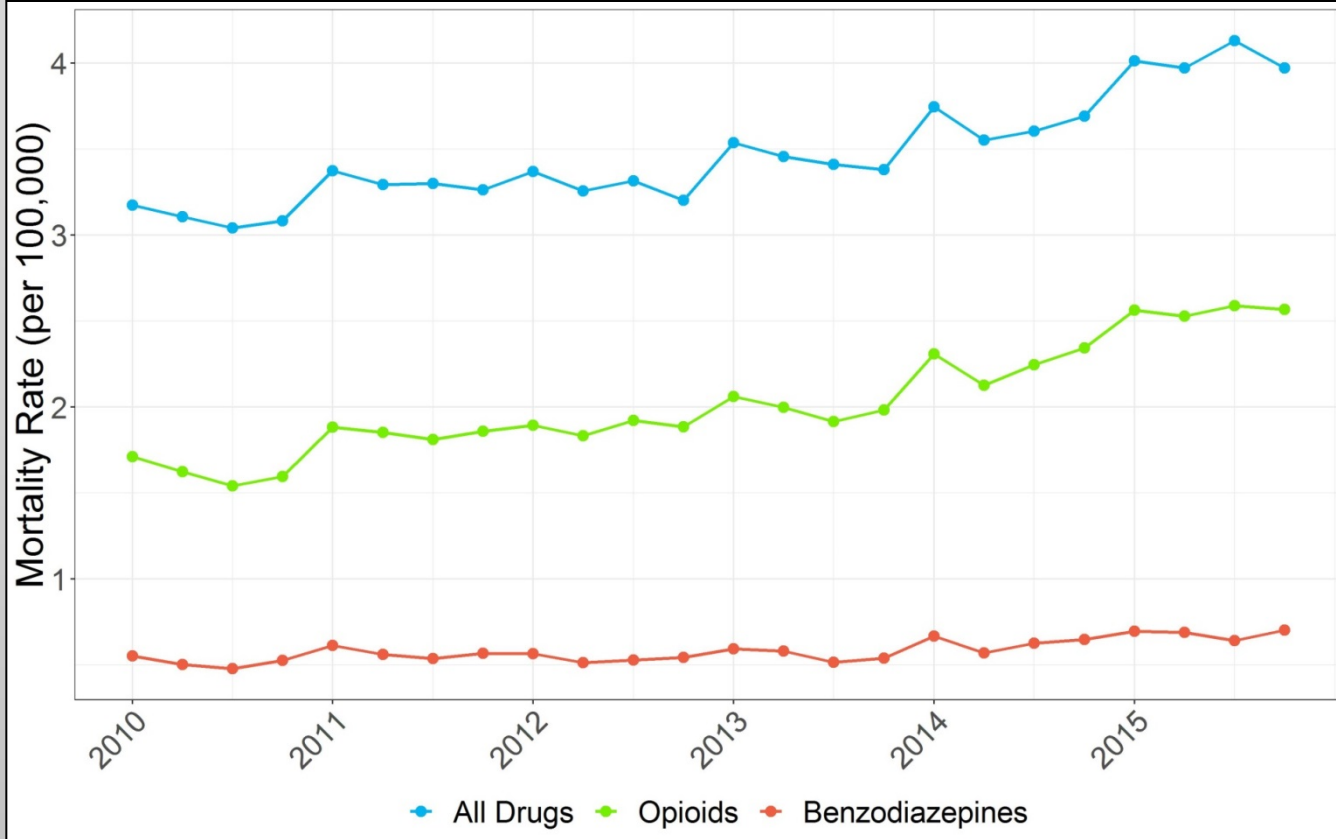
- Mortality data from 2010 to 2015
- Decedents from entire US with drug overdose codes
- Drug groups
 - All drugs
 - Opioids in aggregate and individually
 - Heroin, fentanyl, other prescription opioids
 - Benzodiazepines in aggregate
- Denominator data
 - US Census
 - IQVIA's US-based Longitudinal Patient Data

Decedent Demographics

- Demographics are generally similar across drug classes (2010-2015)
- Slightly higher proportion of female decedents with benzodiazepine involvement
- Slightly higher proportion of white decedents with benzodiazepine involvement

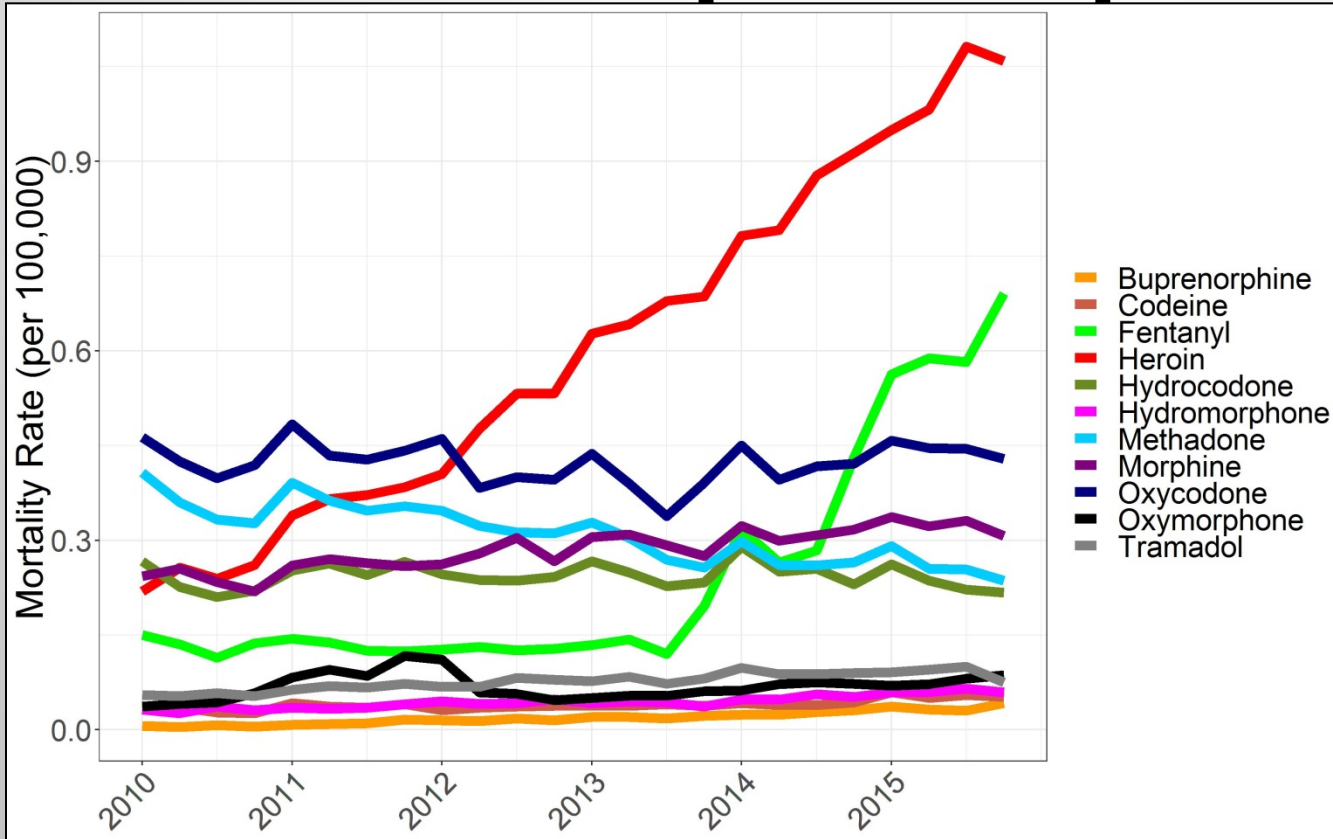
Characteristic	Statistic	All Drug Overdose Deaths N = 264,612	Opioid Overdose Deaths N = 154,822	Benzodiazepine Overdose Deaths N = 44,437
Age in Years	Median (IQR)	44 (32, 53)	42 (31, 52)	43 (32, 52)
Sex	Female (N, %)	102,938 (38.9%)	55,661 (36.0%)	19,032 (42.8%)
	Male (N, %)	161,674 (61.1%)	99,161 (64.0%)	25,405 (57.2%)
Race	Asian or Pacific Islander (N, %)	2,735 (1.0%)	1,055 (0.7%)	348 (0.8%)
	Black (N, %)	23,885 (9.0%)	11,742 (7.6%)	1,859 (4.2%)
	Native American or Alaskan Native (N, %)	3,160 (1.2%)	1,850 (1.2%)	422 (0.9%)
	White (N, %)	234,832 (88.7%)	140,175 (90.5%)	41,808 (94.1%)

Drug Class Population Rates



- Steady rise in mortality for all drugs, opioids, and benzodiazepines
- Opioid rates approximately half the rate for all drugs

Individual Opioid Population Rates



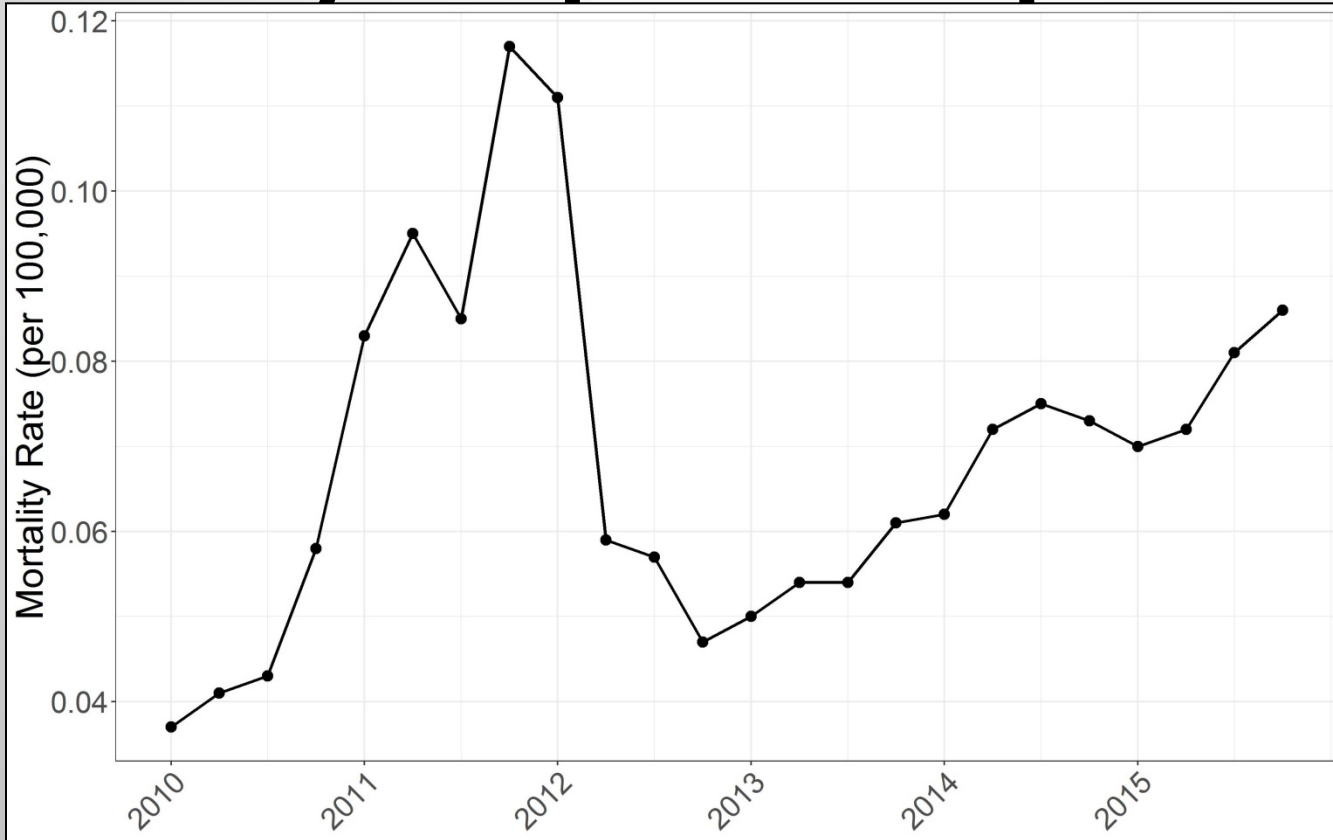
- Major contributors since 2013 are fentanyl (likely illicit) and heroin

Individual Opioid Population Rates

Drug Group	Trend	3-Year Linear Slope (Rate Change per Year)
Fentanyl	Rapidly Increasing	0.217
Heroin	Rapidly Increasing	0.177
Oxycodone	Increasing	0.020
Oxymorphone	Increasing	0.012
Morphine	Increasing	0.010
Hydromorphone	Increasing	0.009
Buprenorphine	Increasing	0.007
Codeine	Increasing	0.007
Tramadol	Increasing	0.004
Hydrocodone	Decreasing	-0.011
Methadone	Decreasing	-0.021

- Crude past 3-year trends are increasing for most APIs

Oxymorphone Population Rates

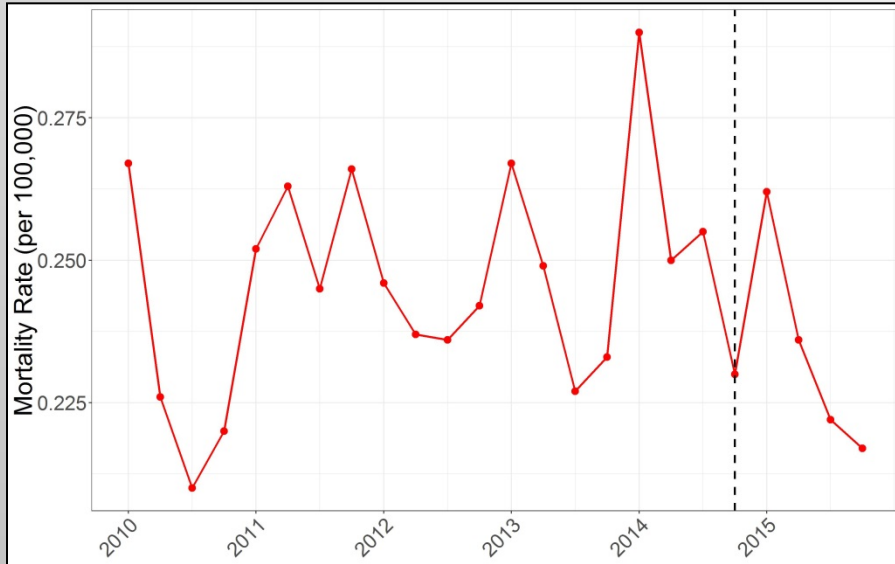


- Large drop in mortality after reformulation in 2012
- Increasing rates since 2012 and approaching peak levels

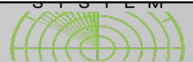
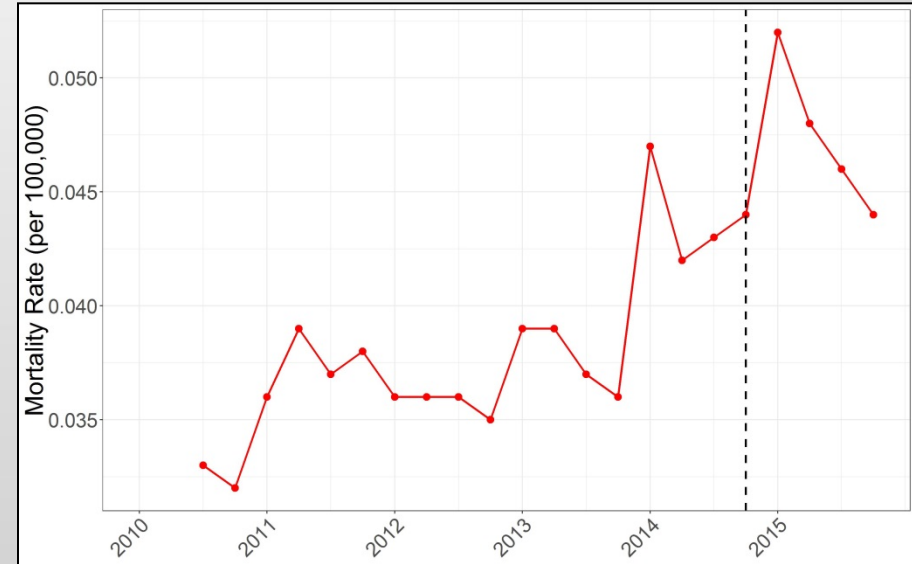
Hydrocodone Rates

- Adjustment by dispensing does not change trends for any API except hydrocodone
- Rescheduling (black dashed line), might indicate turning point

Adjustment by Population



Adjustment by Units Dispensed



Polysubstance Mortality – Any Drug

Drug Group	Total Deaths	Deaths with >1 Specific Substance
Codeine	3,018	2,882 (95.5%)
Hydromorphone	3,375	2,948 (87.3%)
Hydrocodone	18,569	15,887 (85.6%)
Buprenorphine	1,453	1,226 (84.4%)
Oxymorphone	5,224	4,293 (82.2%)
Tramadol	5,816	4,655 (80.0%)
Oxycodone	32,222	25,702 (79.8%)
Morphine	21,759	16,180 (74.4%)
Fentanyl	18,911	12,589 (66.6%)
Methadone	23,615	15,471 (65.5%)
Heroin	46,259	27,781 (60.1%)

- A majority of deaths involved more than 1 specific substance
- APIs with combination products (unsurprisingly) have high proportions
- Oxymorphone and hydromorphone are also high

Polysubstance Mortality – Any Opioid

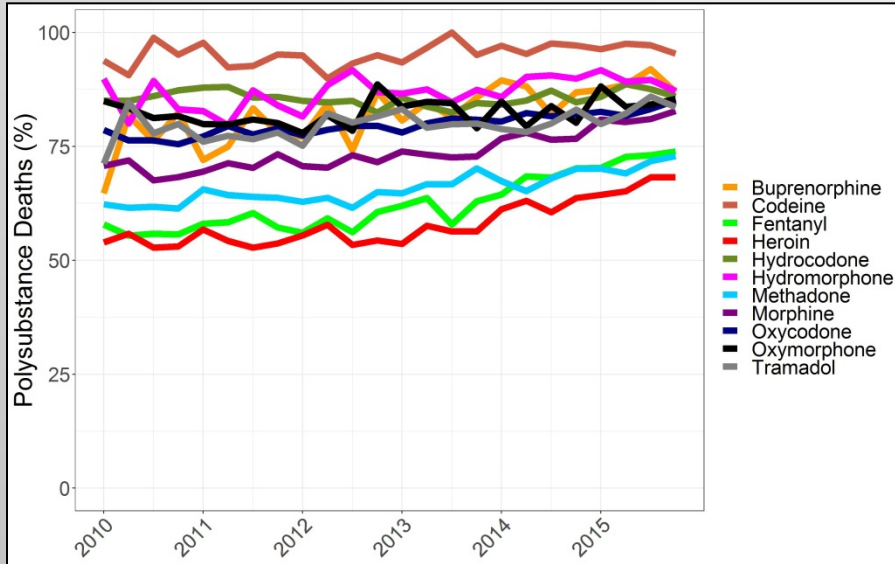
Drug Group	Total Deaths	Deaths with >1 Specific Opioid
Codeine	3,018	2,448 (81.1%)
Hydromorphone	3,375	2,160 (64.0%)
Oxymorphone	5,224	3,083 (59.0%)
Hydrocodone	18,569	9,003 (48.5%)
Tramadol	5,816	2,807 (48.3%)
Morphine	21,759	10,202 (46.9%)
Fentanyl	18,911	8,238 (43.6%)
Oxycodone	32,222	13,587 (42.2%)
Buprenorphine	1,453	509 (35.0%)
Methadone	23,615	7,183 (30.4%)
Heroin	46,259	10,473 (22.6%)

- Poly-opioid mortality is also frequent
- Morphine in metabolism pathway for heroin and codeine

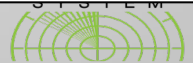
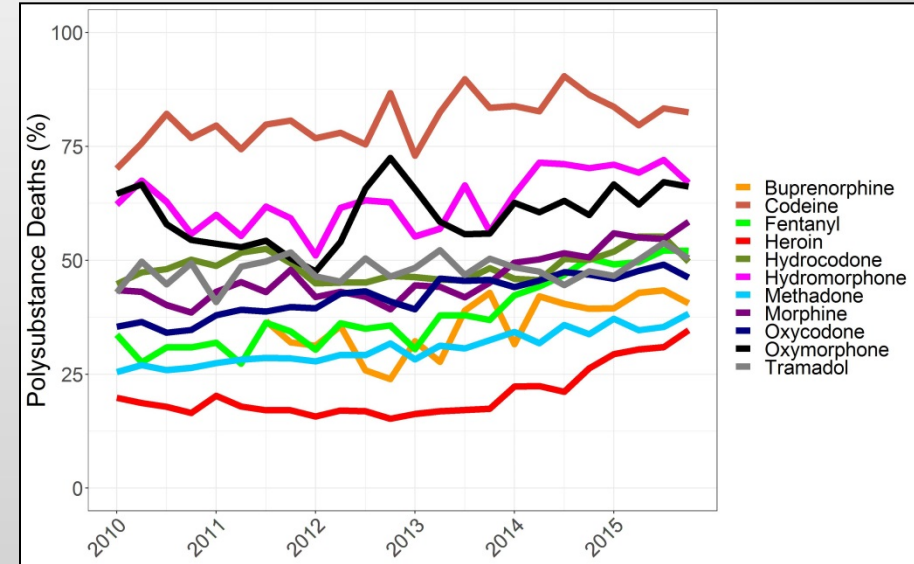
Polysubstance Mortality

- Prevalence of multi-opioid deaths is increasing for most APIs

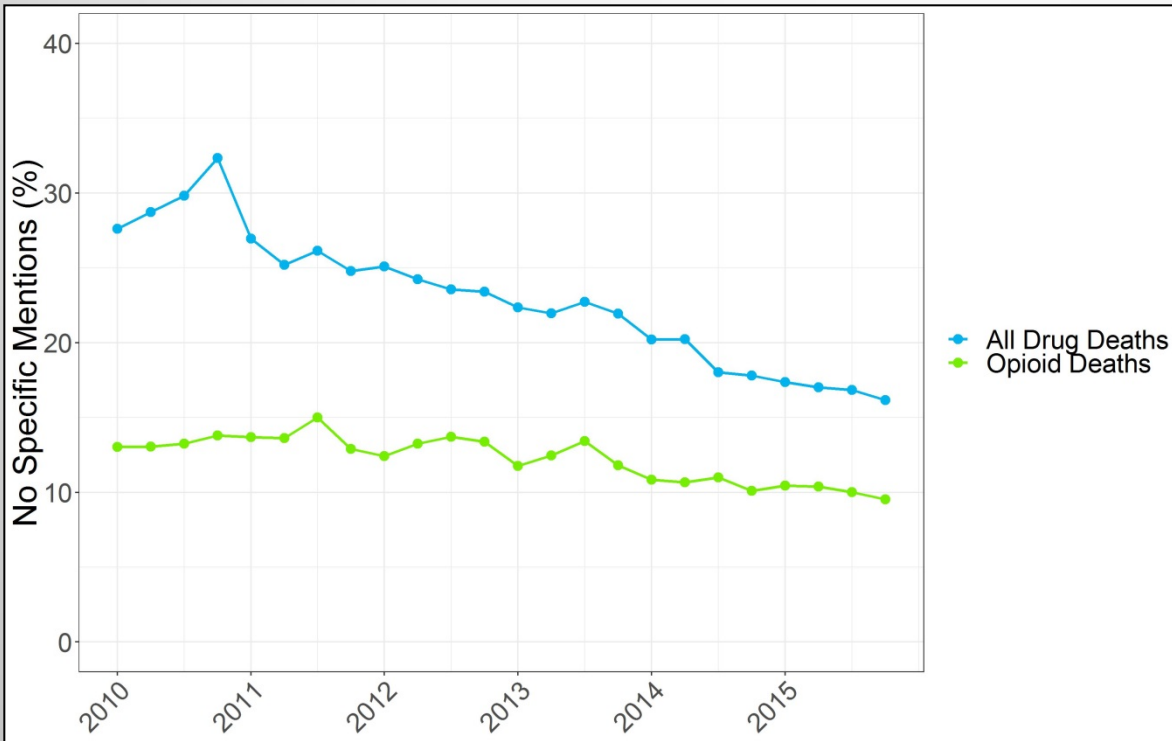
>1 Specific Substance



>1 Specific Opioid

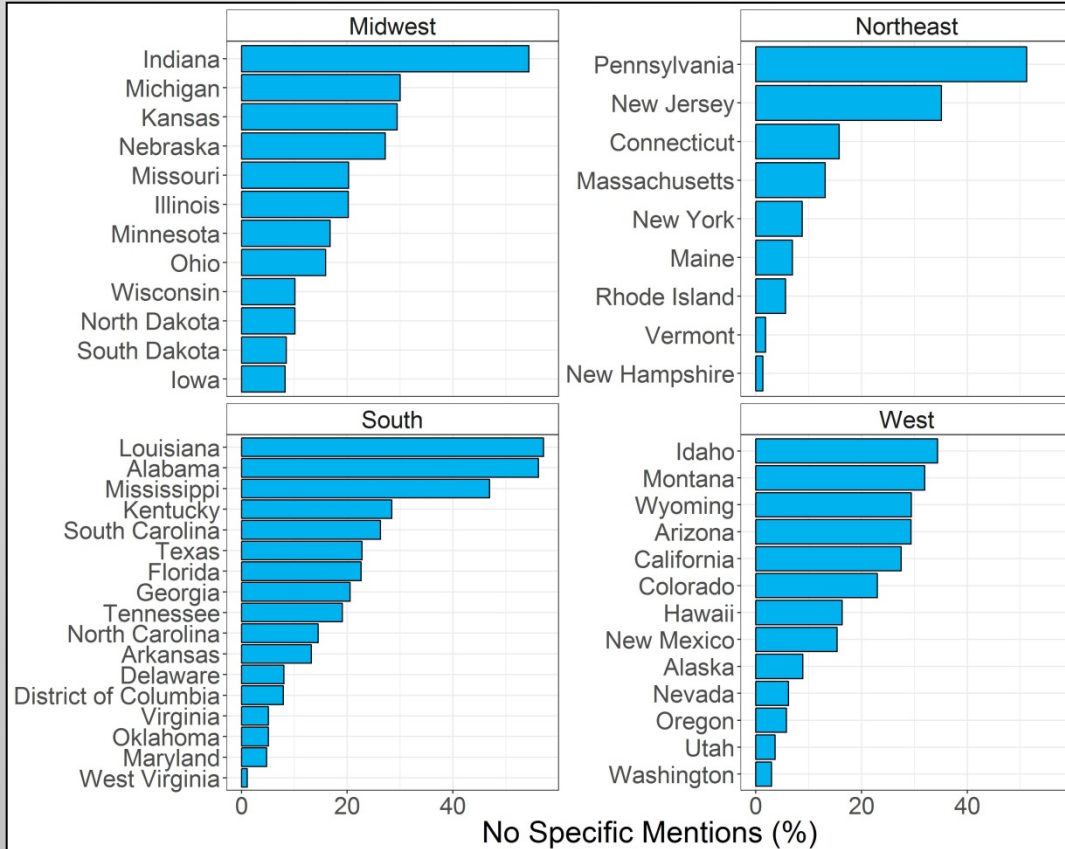


Detection as a Limitation



- A key limitation of mortality data is the standards for detection of specific drugs
- Over time, the proportion of certificates with no specific mentions has fallen

Detection as a Limitation



- Substantial state-by-state variability in certificates without specific mentions

Detection as a Limitation

- Options:
 - Do nothing and accept limitation
 - Sensitivity to exclude states with low reporting specificity
 - When modeling rates, include specificity as covariate

Other Limitations

- Suppression
 - Small states (e.g. Vermont)
 - Low volume drugs (e.g. buprenorphine)
- Toxicology results
 - Heroin vs morphine
 - Codeine vs morphine
 - Standard panel screens vary
- Text analysis
 - Certificate must mention a drug (e.g. “OVERDOSE” not classified)
 - Relies on detail provided by medical examiners and coroners

Conclusions

- Rates of mortality involving opioids are increasing for most APIs
- Scale of increase varies widely
 - Rapid increases recently with heroin and fentanyl
- Polysubstance mortality is majority of deaths
- Poly-opioid mortality could be increasing
- Heterogeneity in reporting is a limitation