A Manufactured Tragedy: The Origins and Deep Ripples of the Opioid Epidemic

Carolina Arteaga
University of Toronto

Victoria Barone
UCLA

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Motivation: The Opioid Epidemic

Overdose deaths involving opioids have increased dramatically in the US

- Since 1999, more than 250,000 have died due to poisoning from prescription opioids (CDC).
- The epidemic has also been accompanied by:
  - Increase in disability claims.
  - Worsening of birth outcomes.
  - Record numbers of children living in foster care.

Motivation: What caused the epidemic & what were the effects?

- Deteriorating socioeconomic conditions could have caused the increase in demand for opioids and the subsequent negative outcomes.
- Supply-side factors, such as the dramatic increase in opioid access, changes in physician prescribing attitudes, and the aggressive marketing of prescription opioids.
- The variation in the level of prescription opioids across geographies and over time is not random.
  - Incidence of pain.
  - Access to healthcare, number of physicians per capita.

This paper

Empirical approach

- Propose a novel instrumental variable based on Purdue Pharma's marketing strategy.
  - Recently unsealed court records from state litigation against Purdue Pharma.
- Exploit variation in the promotion of prescription opioids initially targeted to the cancer market.

1. Identify the **role of supply-side** forces on the origins of the epidemic.
2. Estimate the **causal effect** of the opioid epidemic on a host of important variables.
   - Drug-related mortality and all-cause mortality.
   - Disability & SNAP.
   - Birth outcomes & fertility.

This paper: Results

Purdue's initial marketing had large effects on the distribution of prescription opioids:

- Commuting zones with the highest cancer incidence at the time of the launch of OxyContin received 1.96 doses more of opioids per capita.
- 64% of the average change from 1999 to 2018.

Moving from the 25th to the 75th percentile in the distribution of prescription opioids:

- Increases deaths from prescription opioids by 89% and deaths from all opioids by 39% .
  - This corresponds to over 200,000 deaths.
  - We do not find evidence that the opioid crisis caused other deaths of despair.
- Increases claims from SNAP (57%) & disability (SSI 47% & SSDI 76%).
- Decreases pregnancy duration (0.24 weeks), birth weight (0.7%), and health at birth but has no effect on infant mortality.
- Increase in fertility rates (9%), driven by unmarried and young mothers.

Contribution to the Literature

1. Origins of the Opioid Epidemic
   - Demand: Case and Deaton (2015, 2017)
   - Supply: Alpert et al. (2019); Powell et al. (2020); Fernandez and Zejcirovic (2019); Finklestein et al. (2019); Currie and Schnell (2018); Eichmeyer and Zhang (2020); Miloucheva (2021)

   New evidence linking OxyContin's marketing to the rise in supply & mortality from opioids.

2. Effects of the Opioid Epidemic
   - Drug Mortality: Powell et al. (2015); Evans et al. (2018); Alpert et al. (2018); Eichmeyer and Zhang (2020), among others.
   - Disability: Park and Powell (2020); Dave et al. (2020).
   - Maternal, birth and children's outcomes: Caudillo and Villareal (2021); Lynch et al. (2018); Wolf et al. (2018); Ziedan and Kaestner (2020); Buckles et al. (2020).

   Direct causal evidence on a comprehensive group of outcomes.

Agenda

1. Context: The Opioid Epidemic
2. OxyContin & The Marketing of Prescription Opioids
3. Data
4. Empirical Strategy
5. Results
6. Policy Implications & Conclusions

Context: The Opioid Epidemic I

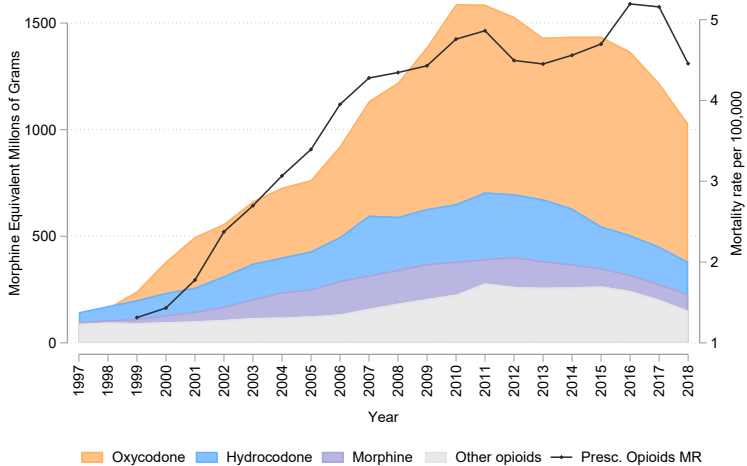
- "Opioids" refers to a class of a large number of drugs, both natural and synthetic.
  - Natural: heroine and morphine.
  - Synthetic: oxycodone and hydrocodone.
  - All pharmacologically similar.
- Opioids are highly addictive, with rapid progression to physiological dependence with tolerance and withdrawal.
- Physical dependence can occur even at prescribed doses & within a short period of time (Hah et al., 2017; Sharma et al., 2017).
  - Withdrawal symptoms include generalized pain, chills, cramps, diarrhea, dilated pupils, restlessness, anxiety, nausea, vomiting, insomnia, and intense cravings.

Context: The Opioid Epidemic II

- Prescription opioids are mostly used to treat moderate to severe pain.
- Opioid prescriptions peaked at 81.3 prescriptions per 100 persons in 2012 (CDC).
- In 2017, 35% of adults used opioid painkillers (NSDUH-2017).
- Between 4 and 5% of adults in the US misuse prescription opioids.
- Legitimate prescriptions of opioids have been linked to:
  - Long-term opioid dependency from a prescription in the ER (Barnett et al., 2017).
  - Increased probability of opioid overdose by a family member (Khan et al., 2019).
  - Heroin and other illegal drug use (APA, 2017).

Who uses and abuses opioids?

Rapid growth of oxycodone prescriptions and prescription opioid deaths



Notes: Authors' computation. Data on oxycodone, hydrocodone, morphine and other prescription opioids come from ARCOS and is expressed in morphine-equivalent doses. Deaths from prescription opioids are constructed from NVSS data.

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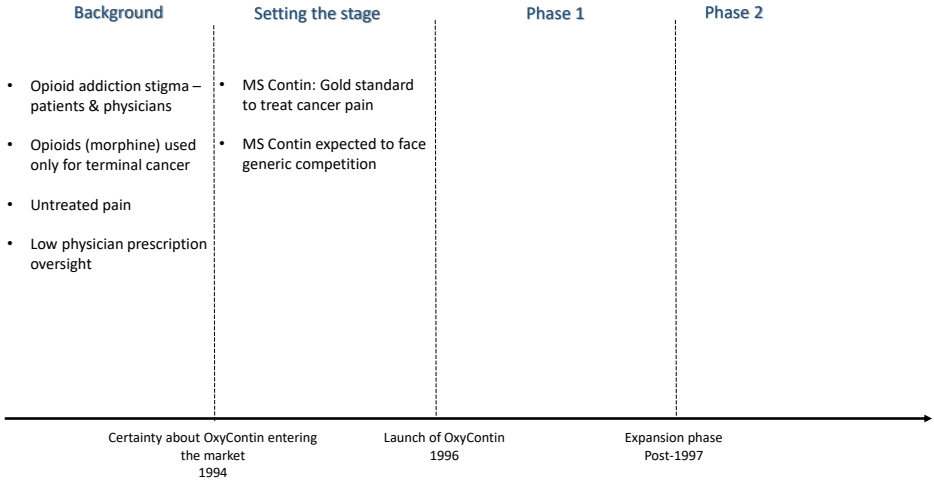
The opioid crisis & the success of OxyContin

OxyContin

Prescription opioid pain reliever from Purdue Pharma. Active ingredient: oxycodone.

- Technological innovation
  - Single-agent opioid: No ceiling allows for high opioid concentration.
  - Extended-release formulation: Relieves pain for up to 12 hours.
  - Mostly prescribed in 20 mg and 40 mg tablets.
- Sales and marketing strategy
  - Sales representatives making around 100k a year, and up to 250k.
  - Pushed a message of low addiction rate of opioids and of an epidemic of untreated pain.

Unsealed Court Records: Kentucky vs Purdue: The Marketing of Prescription Opioids



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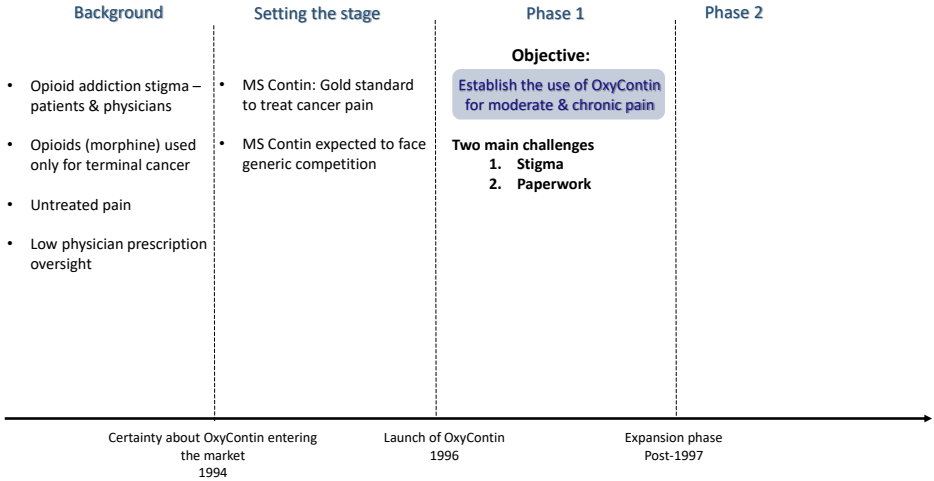

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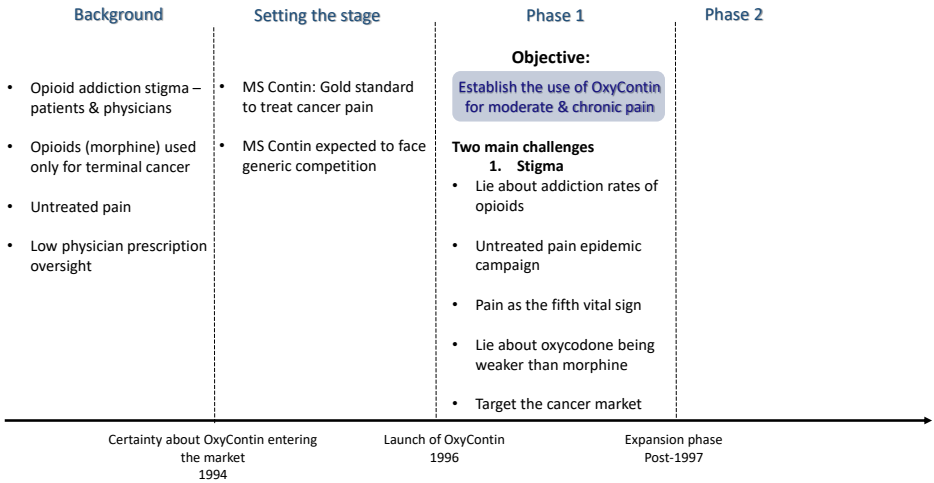

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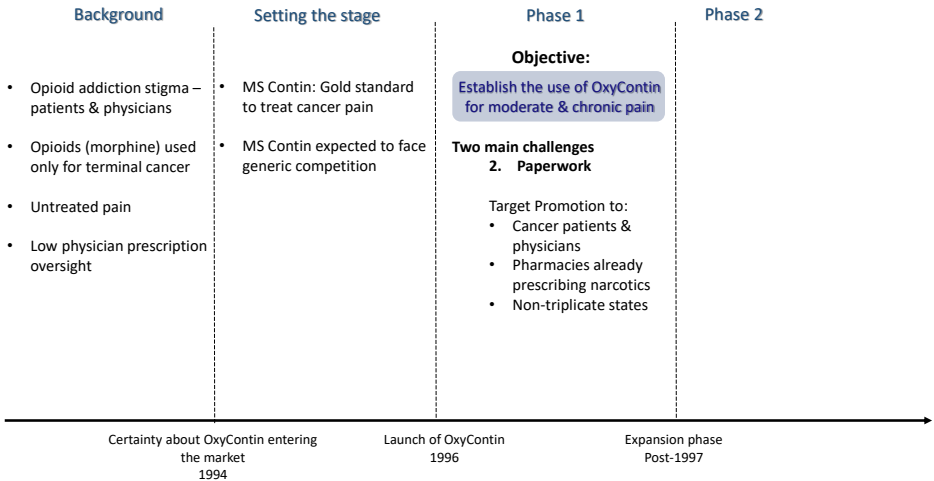

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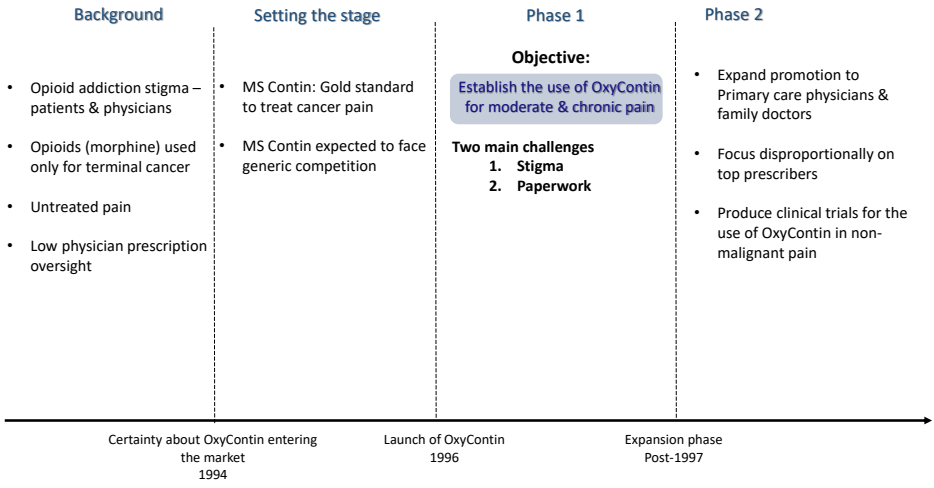
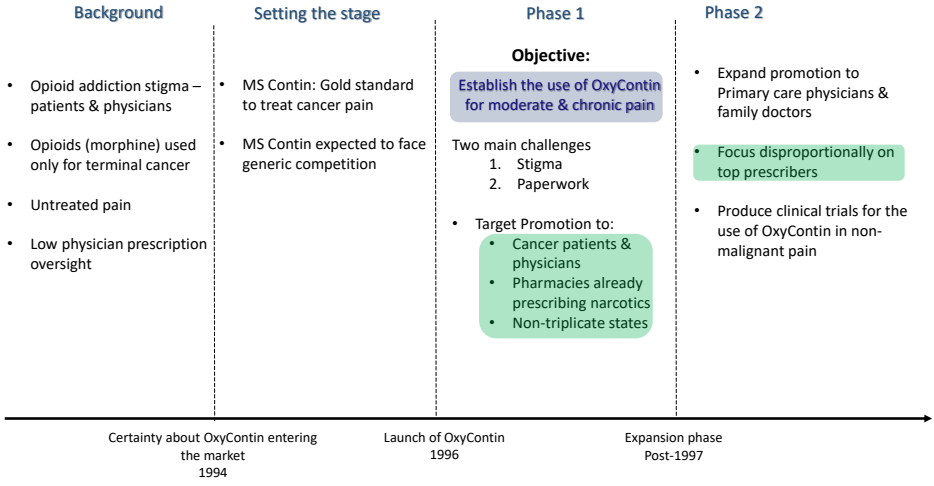


Unsealed Court Records: Kentucky vs Purdue: Our Identification Strategy



Unsealed Court Records: Kentucky vs Purdue

- *"OxyContin Tablets will be targeted at the cancer pain Market."*
  OxyContin Team Meeting, April 1994.
- *"OxyContin primary market positioning will be for cancer pain."*
  OxyContin Launch Team Meeting, March 1995.
- *"At the time of launch, OxyContin will be marketed for cancer pain."* OxyContin Launch Plan, September 1996.
- *"The use of OxyContin in Cancer Patients, initiated by their Oncologists and then referred back to FPs/GPs/IMs, will result in a comfort that will enable the expansion of use in chronic non-malignant pain patients also seen by the family practice specialists."* OxyContin Launch Plan, September 1996.

Unsealed Court Records: Kentucky vs Purdue

Marketing considerations for this decision:

- OxyContin Focus Group (1995)

"There is not the same level of enthusiasm toward this drug for use in non-cancer pain as we identified in cancer pain."

Logistic considerations for this decision:

- Cancer patients already have access to pharmacies that prescribe Schedule II drugs
  - By the time of the launch of OxyContin, only 40% of pharmacies had the paperwork to sell Schedule II drugs.

"Pharmacists are generally reluctant to stock Class II opioids."

"Initial targets will be the 25,000 stores who stock MS Contin."

Identification: Cancer & Opioid Prescriptions

- Areas with higher cancer incidence received disproportionate marketing of opioids.
- Purdue's later strategy to target high prescribers created a path dependency.
- This allows for the identification of
  1. The role of supply in the crisis.
  2. The causal effect of the opioid epidemic on a broad range of outcomes.

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Data

- ARCOS: transactions of controlled substances by active ingredient (e.g. oxycodone).
  - Wide variation among commuting zones Opioids prescription map
- National Vital Statistics System with geographic identifiers.
  - Prescription-opioids and all-opioids (includes heroin and synthetic opioids) mortality rate.
  - Measure of cancer incidence: cancer mortality rate. Cancer mortality map
  - Birth and maternal outcomes.
- Social Security Administration Reports: SSI and SSDI beneficiaries counts.
- Food and Nutrition Service Reports: beneficiaries counts of SNAP.
- Our final dataset: 11,800 observations, 590 commuting zones (+25,000 population).

Descriptive Statistics

	Mean	Median	SD	Min	Max
Opioid Prescriptions: Doses per capita					
All Opioids	6.42	5.48	4.32	0.00	57.65
Oxycodone	3.15	2.52	2.60	0.00	51.31
Cancer Mortality per 1,000					
Cancer mortality rate 1994-1996	2.53	2.53	0.58	0.12	6.24
Cancer mortality rate	2.48	2.49	0.55	0.59	4.75
Outcome measures					
Prescription opioids	0.04	0.03	0.05	0.00	1.06
Any opioids	0.07	0.05	0.07	0.00	1.22
Share SSI	0.04	0.03	0.02	0.00	0.30
Share SSDI	0.05	0.04	0.02	0.01	0.16
Share SNAP	0.12	0.11	0.07	0.00	1.20
Infant MR (per 1,000 births)	6.86	6.54	2.87	0.00	30.61
Birth weight	3,274.25	3276.53	79.47	2,930.28	3,569.76
Fertility rate	0.08	0.08	0.01	0.04	0.19

Descriptive stats - All variables | Opioids prescription map | Cancer mortality map | Opioids mortality map

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Empirical Strategy: IV

(i) Does cancer MR in the mid-1990s predict growth in the supply of prescription opioids?
Relevance

(ii) What determines cancer MR in the mid-1990s, and is it related to our outcome variables?
Exogeneity & Exclusion

(iii) Is cancer MR in the mid-1990s predictive of future mortality from opioids?
Reduce form

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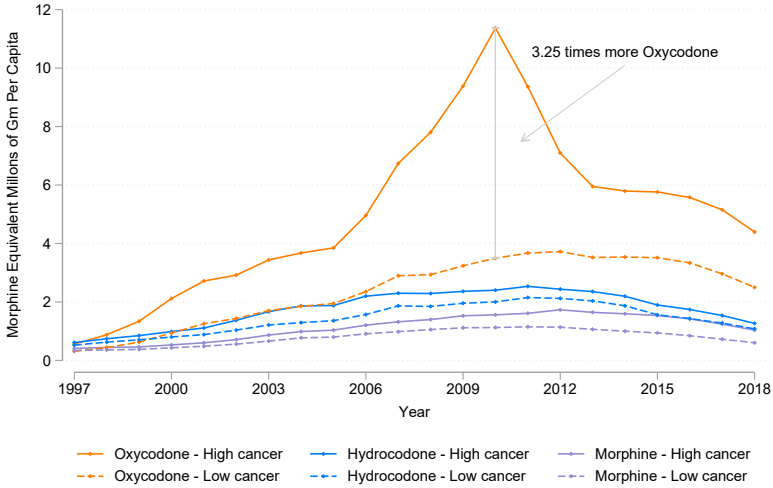
In high-cancer czones oxycodone supply increased 3 times more than in low-cancer czones



Notes: This figure shows the evolution of oxycodone, hydrocodone, and morphine in the forth quartile (solid lines) and first quartile (dashed lines) of the cancer mortality rate distribution before the launch of OxyContin. Oxycodone and hydrocodone are measured in morphine-equivalent mg.

All prescription opioids With cancer trends

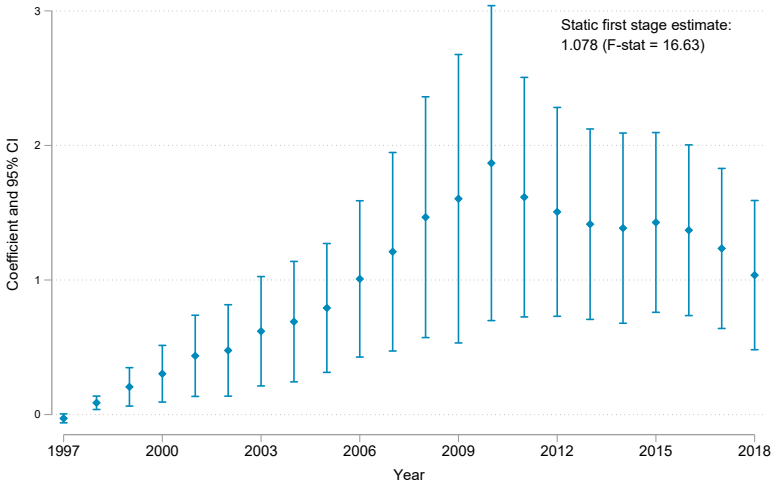
Positive and strong relationship between 94-96 cancer MR and the change in opioids

Dependent variable: Prescription opioids per capita					
	(1)	(2)	(3)	(4)	(5)
Cancer MR 94-96	0.960***	1.091***	1.061***	1.132***	1.078***
se	[0.210]	[0.222]	[0.231]	[0.258]	[0.264]
t-stat	4.571	4.914	4.593	4.388	4.083
Effective F-stat	20.894	24.147	21.096	19.254	16.630
Effect size (%)	56.92	64.69	62.91	67.12	63.92
Controls	No	No	No	Yes	Yes
FE	No	State Year	State × Year	State Year	State × Year
Observations	11,800	11,800	11,800	11,800	11,800
Clusters	590	590	590	590	590
Adjusted R^2	0.019	0.524	0.559	0.533	0.564

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years, share of Black, White, and Hispanic population, and share of female population. Effect size is computed as the predicted changes in doses of prescription opioids per capita from an increase in cancer mortality that would change a commuting zone in the 5th percentile of the cancer distribution to the 95th percentile. Standard errors are clustered at the CZ level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Placebo checks | Shift-share specification | Add population size controls | Leave out | Alternative measure of opioid supply | Sample restrictions - size | Sample restrictions - time

Positive and statistically significant relationship every year since 1998



Notes: This figure shows estimates of the coefficients of the dynamic first stage. We regress prescription opioids' distribution on a set of year-dummy variables interacted with our instrument—cancer mortality in 1994-1996.

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Reduce form

What determines mid-nineties Cancer mortality?

Dependent variable: Cancer MR 94-96	(1)		(2)
Sh. of population over 66	11.13***	Adult MR excluding cancer	0.0439**
	[1.895]		[0.0179]
Sh. of population 18-65	-0.664	Income per capita	-0.00000857
	[1.361]		0.118
Sh. of population under 1	2.156	Share with some college	0.518*
	[9.066]		[0.274]
Share Black	0.127	Share with high school or less	0.124
	[0.241]		[0.191]
Share Hispanic	-1.215***	Share working in manufacturing	-0.199
	[0.303]		[0.133]
Share female	-1.48	Labor Force Participation	0.528
	[1.565]		[0.399]
Prescription Opioids MR	1.093	Employment rate	-1.984*
	[1.078]		[1.118]
Infant Mortality rate	-0.00288	Share SNAP	0.484
	[0.00337]		[0.383]
Fertility rate	0.311	Share SSDI	1.856
	[0.426]		[1.929]
Observations	590	R^2	0.847

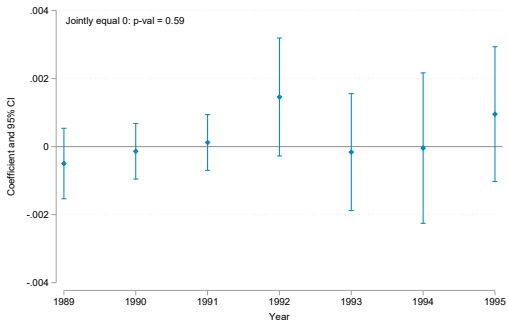
Higher cancer MR areas are not on a differential trend for education, income, or health.

Independent variable: Cancer MR 89-90			
Dependent variables:		*Dependent variables:*	
Income per capita	19.42	Labor force participation	-0.00153*
	[62.24]		[0.000821]
Share with some college	0.0063	Employment rate	-0.000781
	[0.00386]		[0.000489]
Share with high school or less	0.00257	Share SNAP	-0.000529
	[0.00420]		[0.000840]
Share working in manufacturing	0.0063	Share SSDI	-0.000523
	[0.00386]		[0.000890]
Prescription opioids MR	-0.000795	Share SSI	0.000151
	[0.000580]		[0.000345]
Any opioids MR	-0.00101	Total crime rate	44.5
	[0.000671]		[28.63]
IMR	-0.0989	Fertility rate	-0.641
	[0.154]		[0.490]

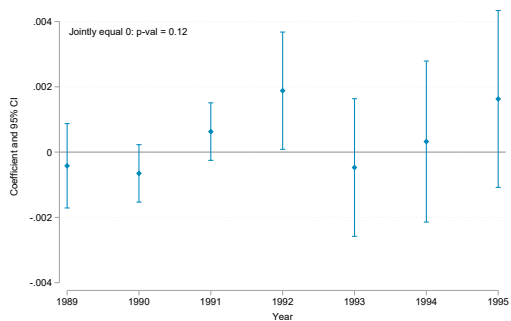
Notes: Each coefficient corresponds to a separate regression in which the dependent variable is measured as the change with respect to 1989-1990. For prescription opioids, any opioids, labor market variables, crime, SNAP, and IMR, we run a panel regression; for other variables, where yearly data are not available, we run one cross-sectional regression. All regressions include control variables. In panel-level regressions, standard errors are clustered at the commuting-zone level; in cross-sectional regressions, standard errors are robust to heteroskedasticity. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Lagged cancer mortality does not lead to a differential trend in the pre-period

(a) Prescription Opioid Mortality



(b) All Opioid Mortality



Notes: This figure shows the dynamic reduced-form relationship between outcomes of interest and our instrument in a out-of-sample period. That is, we replicate our dynamic reduced-form analysis in the pre-OxyContin period. We regress each outcome on a set of year-dummy variables interacted with the out-of-sample instrument—cancer mortality in 1989 - 1990.

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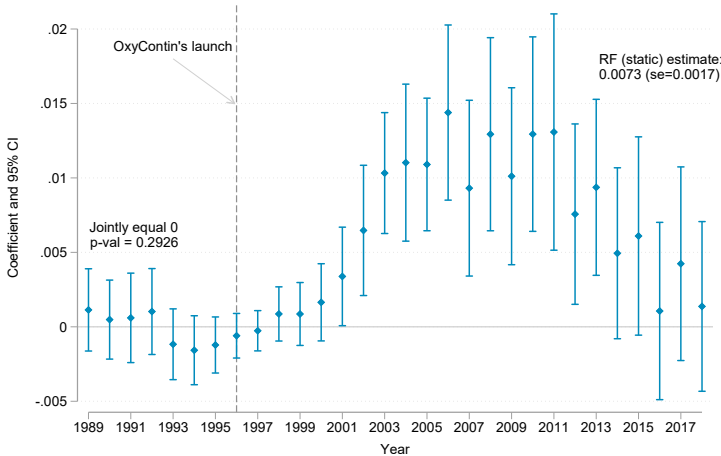
Empirical Strategy: Pre-trends and Effects

To estimate any pre-trends and obtain reduced-form results we run:

$$\Delta\ y_{ct} = \alpha_0 + \sum_{t=1989}^{2018} \phi_t\ CancerMR_{ct_0} 1(Year_t) + \alpha\ \Delta\ X_{ct} + \gamma_{st} + \upsilon_{ct} \tag{1}$$

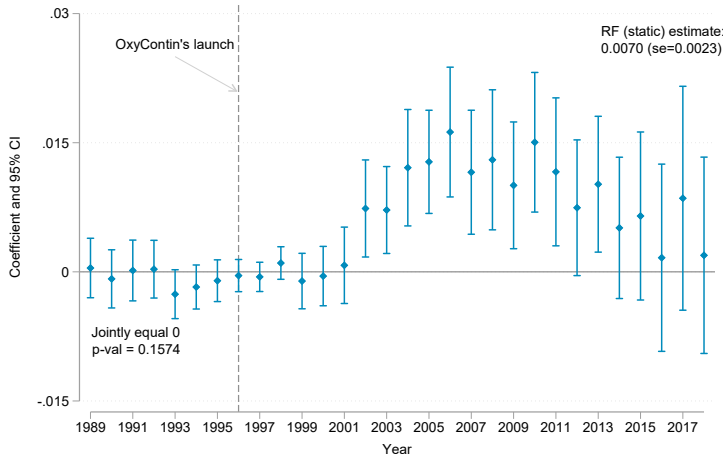
- Δ: long-change operator, i.e., $\Delta W_{ct} \equiv W_{ct} - W_{ct_0}$.
- $CancerMR_{ct_0}$: cancer mortality rate in commuting zone c in 1994-1996 (t_0).
- y_{ct}: outcomes of interest, e.g., a measure of opioid-related mortality.
- $\Delta\ X_{ct}$: time-varying control variables (expressed in long-changes).
- γ_{st} and λ_{st}: state times year fixed effects.

Higher cancer MR areas were not on a differential trend for opioid-related mortality but exhibit a large increase in deaths after the introduction of OxyContin



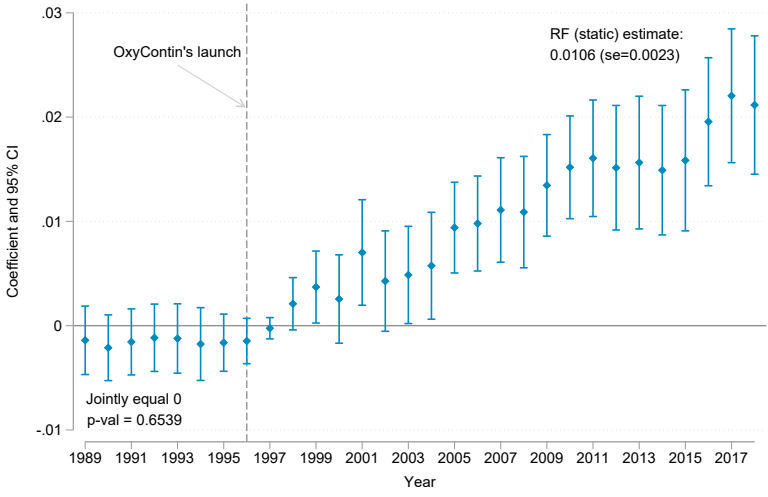
Raw Data

Same story for all opioid deaths: No pre-trends and large effects after the introduction of OxyContin



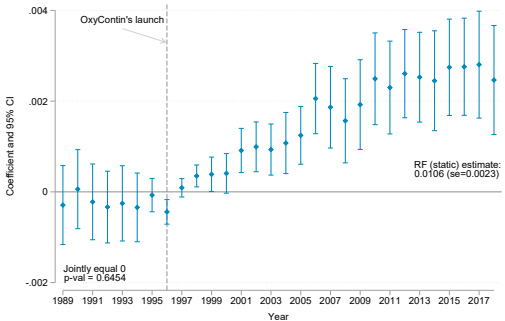
SNAP: No relationship before, strong effect after

Figure: Reduced Form - SNAP

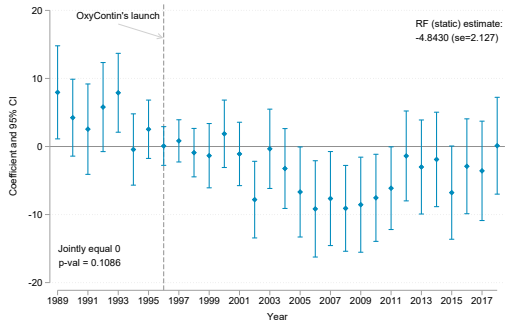


Again, no pre-trends but strong effects on Fertility and some worsening of birth-weight

(a) Fertility-unmarried women



(b) Birth-weight



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

Empirical Strategy: IV

- We estimate the causal effect of the supply of prescription opioids via the following equation:

$$\text{First Stage:} \quad \Delta \ \textit{Presc. Opioids}_{ct} = \alpha_0 + \phi \ \textit{CancerMR}_{ct_0} + \alpha \ \Delta \ X_{ct} + \gamma_{st} + \upsilon_{ct}$$

$$\text{Second Stage:} \quad \Delta \ y_{ct} = \tau_0 + \beta \ \Delta \widehat{\textit{Presc. Opioids}}_{ct} + \tau \ \Delta \ X_{ct} + \lambda_{st} + \varepsilon_{ct}$$

- Δ: long-change operator, i.e., $\Delta W_{ct} \equiv W_{ct} - W_{ct_0}$.
- $\textit{Presc. Opioids}_{ct}$: doses of opioids per capita shipped to commuting zone c in year t.
- $\textit{CancerMR}_{ct_0}$: cancer mortality rate in commuting zone c in 1994-1996 (t_0).
- y_{ct}: outcomes of interest, e.g., a measure of opioid-related mortality.
- $\Delta \ X_{ct}$: time-varying control variables (expressed in long-changes).
- γ_{st} and λ_{st}: state times year fixed effects.

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Results

(i) Direct effects: Opioid-related mortality

(ii) Other mortality outcomes

(iii) Social assistance benefits

(iv) Birth and maternal outcomes

Results

(i) Direct effects: Opioid-related mortality

(ii) Other mortality outcomes

(iii) Social assistance benefits

(iv) Birth and maternal outcomes

A 25th to 75th movement in the distribution of opioids increases prescription opioid mortality by 89%

Dependent var:	Prescription opioids MR		All opioids MR	
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00374***	0.00679***	0.00419***	0.00646***
	[0.00117]	[0.00200]	[0.00139]	[0.00231]
tF 0.05 se		(0.00281)		(0.00324)
AR p-value		0.0000		0.0019
Effect size (%)	49.47	88.63	25.73	39.30
Model	OLS	IV	OLS	IV
Adjusted R^2	0.4304		0.5368	
Effective F-stat		16.63		16.63
Cragg-Donald Wald F-stat		358.58		358.58

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level. Using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Sample restriction - size | Sample restriction - time | Shift-share IV | IV vs OLS | Reduced form - graph | Reduced form - results

A 25th to 75th movement in the distribution of opioids increases all opioid mortality by 39%

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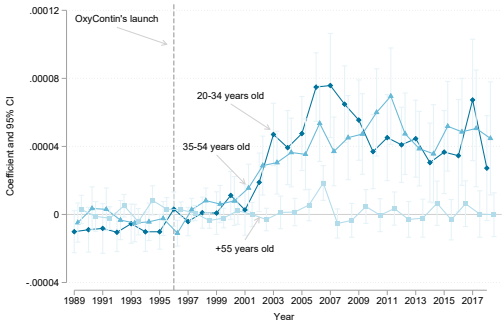
Effect size (%)	49.47	88.63	25.73	39.30
Model	OLS	IV	OLS	IV
Adjusted R^2	0.4304		0.5368	
Effective F-stat		16.63		16.63
Cragg-Donald Wald F-stat		358.58		358.58

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level. Using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

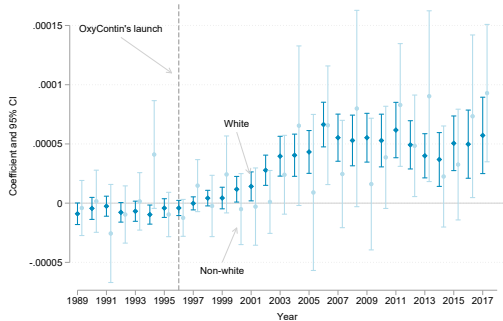
Sample restriction - size | Sample restriction - time | Shift-share IV | Reduced form - graph | Reduced form results

Excess mortality is all from young & middle age adults, and stronger for whites

(a) By age group



(b) By race



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

No effects for those 55+ also shows that effects are not driven by underlying health trends.

Results

(i) Direct effects: Opioid-related mortality

(ii) Other mortality outcomes

(iii) Social assistance benefits

(iv) Birth and maternal outcomes

No effects on all-cause mortality from the increase in prescription opioids

Dependent var:	All-cause Mortality	Deaths of Despair		
		All	Alcoholic liver dis. & cirrhosis	Suicide
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.0286	0.0127*	0.00552*	-0.00582
	[0.0469]	[0.00715]	[0.00292]	[0.00378]
tF 0.05 se	(0.06580)	(0.01003)	(0.00410)	(0.00530)
AR p-value	0.5319	0.0542	0.0351	0.1065
Effect size (%)	4.94	17.13	23.34	-19.80

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level. Using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Reduced form - graph Reduced form - results

Small increase in overall deaths from despair & deaths from alcoholic liver diseases and cirrhosis

Dependent var:	All-cause Mortality	Deaths of Despair		
		All	Alcoholic liver dis. & cirrhosis	Suicide
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.0286	0.0127*	0.00552*	-0.00582
	[0.0469]	[0.00715]	[0.00292]	[0.00378]
tF 0.05 se	(0.06580)	(0.01003)	(0.00410)	(0.00530)
AR p-value	0.5319	0.0542	0.0351	0.1065
Effect size (%)	4.94	17.13	23.34	-19.80

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level. Using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Reduced form - graph Reduced form - results

Results

(i) Direct effects: Opioid-related mortality

(ii) Other mortality outcomes

(iii) Social assistance benefits

(iv) Birth and maternal outcomes

The supply of prescription opioids deteriorated socioeconomic conditions

Dependent var:	SSDI	SSI	SNAP
	(1)	(2)	(3)
Prescription opioids pc	0.00574***	0.00311**	0.00982***
	[0.00132]	[0.00144]	[0.00299]
tF 0.05 se	(0.00185)	(0.00202)	(0.00420)
AR p-value	0.0000	0.0114	0.0000
Effect size (%)	76.39	46.88	56.58

Notes: All regressions include state times year fixed effects. Each regression is run over a sample of 11,800 observations with 590 clusters. Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the respective dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Social assistance outcomes - graphs | Social assistance outcomes by time | Social assistance outcomes - Shift-share IV

Results

(i) Direct effects: Opioid-related mortality

(ii) Other mortality outcomes

(iii) Social assistance benefits

(vi) Birth and maternal outcomes

No effects on infant mortality rate

Dependent var:	Infant	Birth weight		Preterm	APGAR score	
	mortality	median	share low	births	All	Infant fatalities
	(1)	(2)	(3)	(4)	(5)	(6)
Prescription opioids pc	-0.0232	-4.490**	0.000905	0.00141	-0.0169*	0.282*
	[0.140]	[2.143]	[0.000640]	[0.000937]	[0.00994]	[0.153]
tF 0.05 se	(0.19643)	(3.00676)	(0.00090)	(0.00131)	(0.01395)	(0.21467)
AR p-value	0.8678	0.0163	0.1272	0.1126	0.0674	0.0383
Effect size (%)	-1.83	-0.69	5.58	5.85	-0.91	25.17

Notes: All regressions include state times year fixed effects. Each regression is run over a sample of 11,800 observations with 590 clusters. Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the respective dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Infants' outcomes - graphs | Infants' outcomes by time | Infants' outcomes - Shift-share IV

Deterioration of infant health at birth: Reduction in birth weight and APGAR score

Dependent var:	Infant	Birth weight		Preterm	APGAR score	
	mortality	median	share low	births	All	Infant fatalities
	(1)	(2)	(3)	(4)	(5)	(6)
Prescription opioids pc	-0.0232	-4.490**	0.000905	0.00141	-0.0169*	0.282*
	[0.140]	[2.143]	[0.000640]	[0.000937]	[0.00994]	[0.153]
tF 0.05 se	(0.19643)	(3.00676)	(0.00090)	(0.00131)	(0.01395)	(0.21467)
AR p-value	0.8678	0.0163	0.1272	0.1126	0.0674	0.0383
Effect size (%)	-1.83	-0.69	5.58	5.85	-0.91	25.17

Notes: All regressions include state times year fixed effects. Each regression is run over a sample of 11,800 observations with 590 clusters. Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the respective dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Infants' outcomes - graphs | Infants' outcomes by time | Infants' outcomes - Shift-share IV

Median length of pregnancy decreases by 0.24 weeks

Dependent var:	Gestation	Fertility rate
	(1)	(2)
Prescription opioids pc	-0.0489***	0.00153***
	[0.0186]	[0.000566]
tF 0.05 se	(0.02610)	(0.00079)
AR p-value	0.0011	0.0010
Effect size (%)	-0.62	9.41

Notes: All regressions include state times year fixed effects. Each regression is run over a sample of 11,800 observations with 590 clusters. Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the respective dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

A 25th-to-75th-percentile increase in opioids increases fertility by 9%

Dependent var:	Gestation	Fertility rate	
		All births	Non-marital births
	(1)	(2)	(3)
Prescription opioids pc	-0.0489***	0.00153***	0.00166***
	[0.0186]	[0.000566]	[0.000475]
tF 0.05 se	(0.02610)	(0.00079)	(0.00056)
AR p-value	0.0011	0.0010	0.0000
Effect size (%)	-0.62	9.41	29.19

Notes: All regressions include state times year fixed effects. Each regression is run over a sample of 11,800 observations with 590 clusters. Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the respective dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Fertility rate by time | Fertility rate - Shift-share IV | Fertility rate by age

Agenda

1. Context: The Opioid Epidemic
2. OxyContin & The Marketing of Prescription Opioids
3. Data
4. Empirical Strategy
5. **Results**
   - **Robustness Checks**
6. Policy Implications & Conclusions

Placebo test: Alternative measures of mortality in 1994-1996 do not predict prescription opioid supply

Dependent variable: Prescription opioids per capita						
	(1)	(2)	(3)	(4)	(5)	(6)
CVD MR 94 96	0.372			-2.023**		
	[0.611]			[0.822]		
Accidental MR 94 96		1.067			-1.639	
		[1.411]			[1.406]	
Homicides MR 94 96			0.214			-0.474
			[3.379]			[3.173]
Cancer MR 94 96				1.381***	1.015***	0.923***
				[0.347]	[0.245]	[0.233]
Adjusted R^2	0.55	0.549	0.549	0.565	0.561	0.562

Notes: CVD stands for cerebrovascular diseases. Columns 1-3 report first-stage regression with alternative instrument. Columns 4-6 add our baseline instrument. All regressions include state times year fixed effects and a set of control variables Standard errors are clustered at the CZ level. All regressions are run on panel at the CZ level with 11,800 observations and 590 clusters. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Back - first-stage results

Robustness checks

- First stage
  - Results from implementing a shift-share research design are quantitatively indistinguishable.
    Opioids mortality | Social assistance outcomes | Infants' outcomes | Fertility rate
  - Is the FS capturing demographic variation along the age distribution? No. Results
  - Alternative choices of instruments: FS that is as strong as in our baseline. Results
  - Results are not driven by a particular state, neither by triplicate status. Results

- Oxycodone shipments as an alternative measure of opioid supply. Results
- Drug-induce deaths as an alternative measure of opioid-related deaths. Drug-induce results
- Alternative sample restrictions on the size of a commuting zone.
  First stage | Pres. opioids | All opioids | Other outcomes

Agenda

1. Context: The Opioid Epidemic
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3. Data
4. Empirical Strategy
5. Results
6. **Policy Implications & Conclusions**

Policy Implications & Conclusions

- We document that the marketing and promotion by pharmaceuticals ignited the opioid epidemic.
- Increasing the supply of prescription opioids:
  - Increased mortality from opioids.
  - Increased the demand for SNAP, SSDI; & SSI.
  - Deteriorated birth outcomes.
  - Increased fertility.

Policy Implications & Conclusions

- Our results have direct policy implications regarding the desirability of promotional efforts by pharmaceutical companies that target physicians, pharmacies, and patients

- We document the devastating and far-reaching consequences of aggressive and deceitful marketing:
  - Monitor/limit/disclose promotional efforts by pharmaceuticals.
  - Provide age-and diagnosis-specific drug risk profiles.
  - Drug-abuse reporting systems.

Thank you

Comments/questions are welcome

Appendix

Where are opioids mostly prescribed?

- No relationship with economic or employment conditions (Ruhm, 2018; Currie et al., 2019; Currie et al., 2020),
- Places with more physicians per capita, higher levels of income and education, lower Medicare spending per capita, and higher scores on a healthcare quality index have higher opioids abuse rates (Finkelstein et al., 2019).
- Medicare Part D: 10% increase in opioid medical supply leads to a 7.1% increase in opioid-related deaths (Powell et al., 2020)
- Opioids are also disproportionally prescribed to whites (Pletcher et al., 2008).

Context: Who uses and abuses pain medications?

	Use of pain killers	Misuse of painkillers		Use of pain killers	Misuse of painkillers
Female	0.0537***	-0.000906	Health insurance	0.0559***	-0.0101***
	[12.33]	[-0.51]		[7.38]	[-3.25]
18 to 25 years	0.0402***	0.00318	Unemployed	0.0239**	0.0196***
	[2.96]	[0.57]		[2.29]	[4.56]
26-34 years	0.0822***	-0.00215	White	0.0473***	0.00902***
	[6.06]	[-0.39]		[10.17]	[4.73]
35 and older	0.124***	-0.0188***	Use alcohol & tobacco	0.224***	0.225***
	[9.92]	[-3.65]		[18.91]	[46.27]
Some college or more	-0.00049	0.000999	Use of hard drugs	0.0888***	0.0203***
	[-0.10]	[0.50]		[17.21]	[9.58]
Income below 40k	0.0480***	0.00418**	Observations	47310	47310
	[9.87]	[2.10]	R^2	0.028	0.057
			Mean Dep. Var	30%	4.80%

NSDUH 2017. Omitted age category 15-17.

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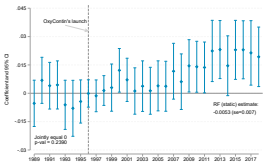
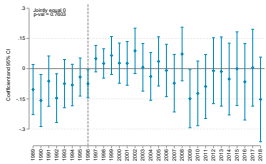
Higher cancer MR areas were not on a differential trend for our outcomes

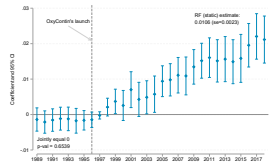
(a) Deaths of Despair



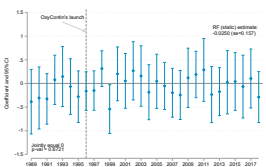
(b) All-non-cancer Mortality



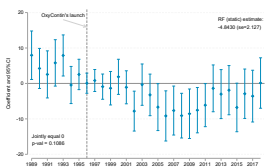
(c) SNAP



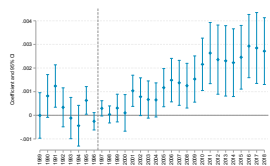
(d) Infant Mortality Rate



(e) Birth Weight



(f) Fertility Rate



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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Descriptive Statistics

	Mean	Median	SD	Min	Max
Opioid Prescriptions: Doses per capita					
All Opioids	6.42	5.48	4.32	0.00	57.65
Oxycodone	3.15	2.52	2.60	0.00	51.31
Hydrocodone	1.93	1.55	1.50	0.00	16.66
Morphine	0.94	0.77	0.69	0.00	10.67
Cancer Mortality per 1,000					
Cancer mortality rate 1994-1996	2.53	2.53	0.58	0.12	6.24
Cancer mortality rate	2.48	2.49	0.55	0.59	4.75
Outcome measures					
Prescription opioids	0.04	0.03	0.05	0.00	1.06
Any opioids	0.07	0.05	0.07	0.00	1.22
Deaths of despair	0.37	0.34	0.15	0.02	1.96
Deaths of despair - alcohol only	0.12	0.11	0.06	0.00	0.63
Deaths of despair - suicide only	0.15	0.14	0.06	0.00	0.48
All cause mortality	9.87	9.93	2.06	2.79	20.92
Share SSI	0.04	0.03	0.02	0.00	0.30
Share SSDI	0.05	0.04	0.02	0.01	0.16
Share SNAP	0.12	0.11	0.07	0.00	1.20
Infant MR (per 1,000 births)	6.86	6.54	2.87	0.00	30.61
Birth weight	3,274.25	3,276.53	79.47	2,930.28	3,569.76
Share low birth weight	0.08	0.08	0.02	0.02	0.20
Share preterm	0.12	0.12	0.03	0.05	0.62
APGAR score - all infants	8.82	8.84	0.19	5.00	10.00
APGAR score - dead infants	5.62	6.00	2.28	0.00	10.00
Median gestation	38.95	39.00	0.24	35.00	40.00
Fertility rate	0.08	0.08	0.01	0.04	0.19

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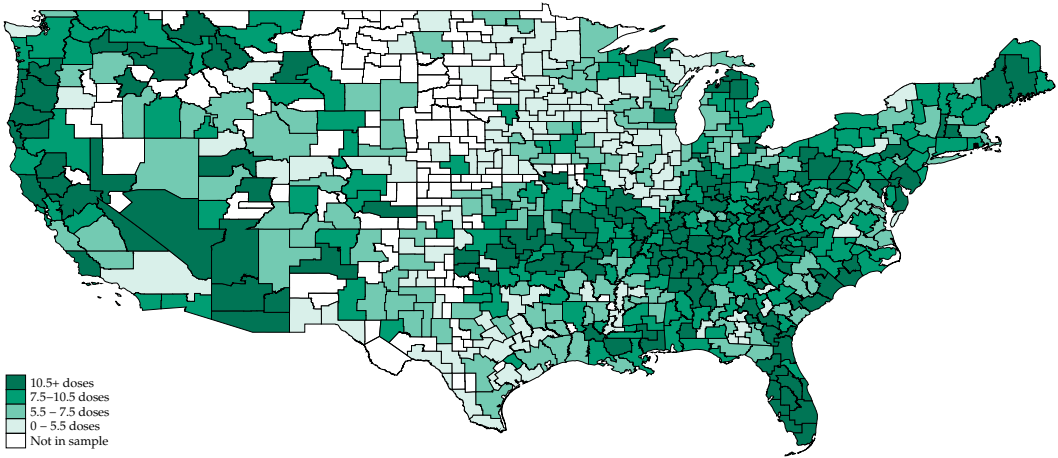
MAPS

Prescription Opioid Distribution in 2010



Notes: This map shows the distribution of prescription opioids in 2010. Lighter shades indicate commuting zones with a lower supply and darker shades indicate commuting zones with a higher supply. Each group corresponds to one quartile of the prescription opioid distribution; i.e., each color accumulates 25% of the mass of this distribution.

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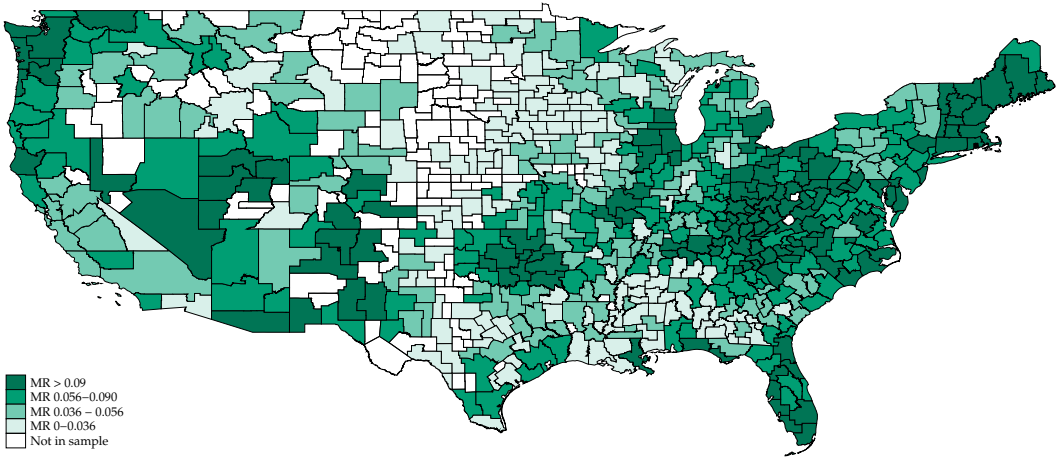
Any Opioid Mortality Rate 1999 - 2018



Notes: This map shows the distribution of opioid mortality for the period 1999 - 2018. Lighter shades indicate commuting zones with lower opioid mortality, while darker shades indicate commuting zones with higher opioid mortality. Each group corresponds to one quartile of the opioid mortality distribution; i.e., each color accumulates 25% of the mass of this distribution.

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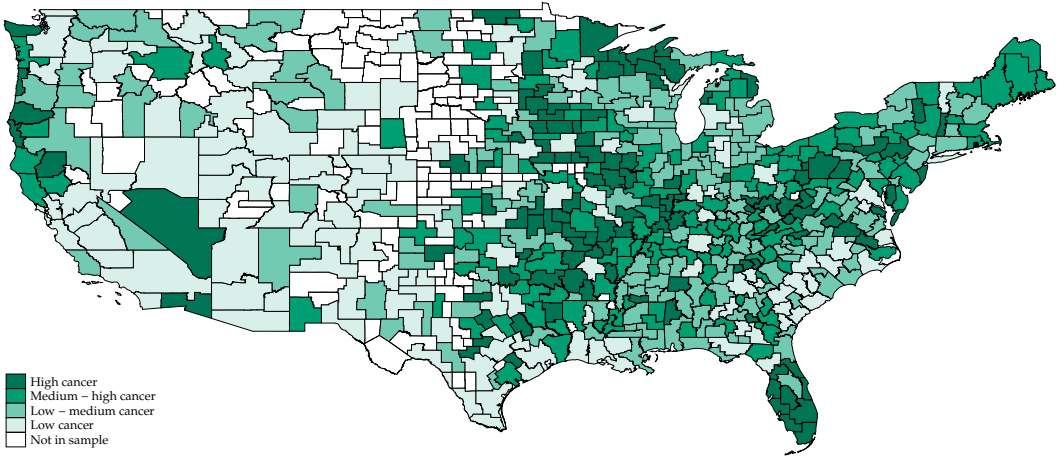
Distribution of Cancer Mortality 1994 & 1996



Notes: This map shows the cancer mortality rate at commuting-zone level in 1994 - 1996. Lighter shades indicate commuting zones with lower cancer prevalence, while darker shades indicate commuting zones with higher cancer prevalence. Each group corresponds to one quartile of the cancer mortality distribution; i.e., each color accumulates 25% of the mass of this distribution.

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Additional Tables

Determinants of opioids distribution in 2000

Dependent variable: Prescription opioids per capita					
	(1)		(2)		(3)
Demographics (in shares)		*Social assistance*		*Crime (in rates)*	
White	3.526***	SSDI	48.45***	Overall	-0.0000622
	[0.961]		[9.821]		[0.0000752]
Hispanic	-3.323***	SSI	5.740	Violent	0.00160***
	[0.807]		[8.944]		[0.000614]
Female	6.709	SNAP	-1.914	*Health outcomes*	
	[9.973]		[3.848]	Cancer mortality rate	-0.164
Aged 18-65	21.67***				[0.330]
	[4.348]	*Economic characteristics*		Infant mortality rate	-0.0117
Aged +66	6.211	Ln income	2.517***		[0.0199]
	[7.665]		[0.922]	Birth weight	0.000336
Infants	-100.8*	Sh. below poverty line	0.0521		[0.00127]
	[56.42]		[0.0625]	Share preterm births	2.330
Labor market		Sh. employed in manufacturing	-0.0374***		[4.796]
Employment rate	-16.18***		[0.0105]	Gestation	-0.200
	[6.031]	Sh. w/ some college education	0.00938		[0.396]
Labor force participation	-1.805		[0.0135]	Fertility rate	52.51***
	[2.493]				[14.07]

Notes: This table presents estimated coefficients from a cross-section regression of prescription opioid distribution per capita on demographic characteristics, labor market outcomes, measures of social assistance demand, crime outcomes, economic characteristics, and health outcomes at commuting-zone level. Standard errors are robust to heteroskedasticity. *$p<0.10$, **$p<0.05$, *** $p<0.01$.

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Estimates of the first-stage with alternative controls for population size

Dependent variable: Prescription opioids per capita					
	(1)	(2)	(3)	(4)	(5)
Cancer MR 94-96	1.078***	1.635***	1.072***	1.046***	1.608***
se	[0.264]	[0.483]	[0.276]	[0.266]	[0.490]
t-stat	4.08	3.39	3.88	3.94	3.28
Effective F-stat	16.63	11.49	15.05	15.52	10.76
Share pop +65 yo	No	Yes	No	No	Yes
Total pop +65 yo	No	No	Yes	No	No
Total population	No	No	No	Yes	Yes
Observations	11,800	11,800	11,800	11,800	11,800
Clusters	590	590	590	590	590
Adj. R^2	0.56	0.57	0.56	0.57	0.57

Notes: All specifications include as control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at the CZ level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Back Robustness summary

Estimates of the first stage under alternative sample restrictions

Dependent variable:	Prescription opioids per capita			
	(1)	(2)	(3)	(4)
Cancer MR 94-96	1.078***	1.191***	1.055***	1.018***
t-stat	4.083	4.79	3.55	3.54
Observations	11,800	12,820	10,8880	9,620
Clusters	590	641	544	481
Adjusted R^2	0.564	0.467	0.568	0.608
Sample	25,000+	15,000+	40,000+	55,000+

Notes: Our preferred specification restricts the sample to commuting zones with population higher than 25,000 residents and is presented in column (1). All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Estimates of the first stage using oxycodone as dependent variable

Dependent var:	Presc. Opioids pc (1)	Oxycodone pc (2)	Presc. Opioids pc (3)
Cancer MR 94-96	1.078***	0.605***	0.00417***
se	[0.264]	[0.186]	[0.000997]
t-stat	4.083	3.253	4.183
Effective F-stat	16.63	10.580	17.47
Effect size (%)	63.92	38.00	
Model	FS	FS	FS - Shift share IV
Observations	11,800	11,800	11,800
Clusters	590	590	590

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years, share of Black, White, and Hispanic population, and share of female population. Effect size is computed as the predicted changes in doses of prescription opioids per capita from an increase in cancer mortality that would change a commuting zone in the 5th percentile of the cancer distribution to the 95th percentile. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Estimates of the first stage using a shift-share instrument

Dependent var:	Presc. Opioids pc (1)	Oxycodone pc (2)	Presc. Opioids pc (3)
Cancer MR 94-96	1.078***	0.605***	0.00417***
se	[0.264]	[0.186]	[0.000997]
t-stat	4.083	3.253	4.183
Effective F-stat	16.63	10.580	17.47
Effect size (%)	63.92	38.00	
Model	FS	FS	FS - Shift share IV
Observations	11,800	11,800	11,800
Clusters	590	590	590

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years, share of Black, White, and Hispanic population, and share of female population. Effect size is computed as the predicted changes in doses of prescription opioids per capita from an increase in cancer mortality that would change a commuting zone in the 5th percentile of the cancer distribution to the 95th percentile. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Estimates of the first stage under alternative sample periods

Dependent variable:	Prescription Opioids pc			
	(1)	(2)	(3)	(4)
Cancer MR 94-96	1.078***	0.916***	1.047***	1.474***
se	[0.264]	[0.258]	[0.277]	[0.330]
t-stat	4.08	3.55	3.78	4.46
Observations	11,800	7,080	8,850	5,310
Adjusted R^2	0.564	0.565	0.582	0.425
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together, and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level . * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Marketing of prescription opioids had a positive effect on opioid-related mortality

Dependent var:	Prescription opioids	All opioids
	(1)	(2)
Cancer MR 94-96	0.00732***	0.00697***
	[0.00167]	[0.00229]
Model	RF	RF
Observations	11,800	11,800
Clusters	590	590
Adj R^2	0.3908	0.5144

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Effects on prescription opioid mortality for different sample restrictions

Dependent variable:	Prescription opioids mortality rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00679***	0.00355***	0.00684***	0.00826***
t-stat	3.35	2.65	2.96	3.08
Observations	11,800	12,820	10,880	9,620
Clusters	590	641	544	481
Sample	25,000+	15,000+	40,000+	55,000+

Notes: Our preferred specification restricts the sample to commuting zones with population higher than 25,000 residents and is presented in column (1). All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Effects on prescription opioid mortality for different time periods

Dependent variable:	Prescription opioid mortality rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00679***	0.00785***	0.00769***	0.00533***
	[0.00200]	[0.00259]	[0.00230]	[0.00169]
Observations	11,800	7,080	8,850	5,310
Effective F-stat	16.63	12.62	14.25	19.90
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together; and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Effects on prescription opioid mortality baseline IV and shift-share IV design

Dependent var:	Prescription opiod mortality rate		All opioids mortality rate	
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00679***	0.00644***	0.00646***	0.00635***
	[0.00200]	[0.00188]	[0.00231]	[0.00219]
Model	IV	Shift-share IV	IV	Shift-share IV

Notes: Columns (1) and (3) reproduce the main results and columns (2) and (4) present estimates from IV regressions using the shift-share instrument. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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OLS estimates suffer from a negative bias (OLS $<$ IV)

Prescription opioids: OLS (0.00374) $<$ IV (0.00679)

- The correlation between opioid supply and opioid deaths underestimates the role of the supply of pres. opioids in the $\uparrow$ mortality.
- Commuting zones that receive $+$ opioids are positively selected on observable chars:
  - Better access to healthcare
  - Larger number of physicians
  - Consistent with Finkelstein et al. (2018) findings.

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Effects on all opioids mortality for different sample restrictions

Dependent variable:	All opioids mortality rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00646***	0.00152	0.00697**	0.00885***
t-stat	2.77	0.89	2.56	2.69
Observations	11,800	12,820	10,880	9,620
Clusters	590	641	544	481
Sample	25,000+	15,000+	40,000+	55,000+

Notes: Our preferred specification restricts the sample to commuting zones with population higher than 25,000 residents is presented in column (1). All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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All-cause mortality: Reduced form results

Dependent var:	All-cause Mortality	Deaths of Despair		
		All	Alcoholic liver dis. & cirrhosis	Suicide
	(1)	(2)	(3)	(4)
Cancer MR 94-96	0.0309 [0.0515]	0.0137* [0.00751]	0.00596** [0.00302]	-0.00628 [0.00402]
Model	RF	RF	RF	RF
Observatoins	11,800	11,800	11,800	11,800
Clusters	590	590	590	590

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level. Using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Deaths of Despair: Reduced form results

Dependent var:	All-cause Mortality	Deaths of Despair: All	Deaths of Despair: Alcoholic liver dis. & cirrhosis	Deaths of Despair: Suicide
	(1)	(2)	(3)	(4)
Cancer MR 94-96	0.0309	0.0137*	0.00596**	-0.00628
	[0.0515]	[0.00751]	[0.00302]	[0.00402]
Model	RF	RF	RF	RF
Observatoins	11,800	11,800	11,800	11,800
Clusters	590	590	590	590

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level. Using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Effects on all opioids mortality for different time periods

Dependent variable:	All opioids mortality rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00646***	0.00677***	0.00672***	0.00562**
	[0.00231]	[0.00256]	[0.00232]	[0.00237]
Observations	11,800	7,080	8,850	5,310
Effective F-stat	16.63	12.62	14.25	19.90
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together; and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Effects on all opioids mortality baseline IV and shift-share IV design

Dependent var:	Presc. opiods mortality rate		All opioids mortality rate	
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00679***	0.00644***	0.00646***	0.00635***
	[0.00200]	[0.00188]	[0.00231]	[0.00219]
Model	IV	Shift-share IV	IV	Shift-share IV

Notes: Columns (1) and (3) reproduce the main results and columns (2) and (4) present estimates from IV regressions using the shift-share instrument. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Social assistance outcomes by time - SSDI

Dependent var:	SSDI			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00574***	0.00584***	0.00605***	0.00718***
	[0.00132]	[0.00144]	[0.00141]	[0.00135]
Observations	11,800	7,080	8,850	5,310
Effective F	16.63	15.22	17.06	25.7
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together; and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Social assistance outcomes by time - SSI

Dependent var:	SSI			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00311**	0.00226*	0.00248*	0.00320*
	[0.00144]	[0.00133]	[0.00141]	[0.00174]
Observations	11,800	7,080	8,850	5,310
Effective F	16.63	15.22	17.06	25.7
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together; and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Social assistance outcomes by time - SNAP

Dependent var:	SNAP			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00982***	0.00455*	0.00487**	0.00680***
	[0.00299]	[0.00250]	[0.00219]	[0.00205]
Observations	11,800	7,080	8,850	5,310
Effective F	16.63	15.22	17.06	25.7
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together; and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Social assistance outcomes using a shift-share IV

Dependent var:	SSDI		SSI		SNAP	
	(1)	(2)	(3)	(4)	(5)	(6)
Pres. opioids pc	0.00574***	0.00553***	0.00311**	0.00319**	0.00982***	0.00927***
	[0.00132]	[0.00127]	[0.00144]	[0.00158]	[0.00299]	[0.00277]
Effective F	16.63	17.47	16.63	17.47	16.63	17.47
Model	IV	Shift-share IV	IV	Shift-share IV	IV	Shift-share IV

Notes: Columns (1), (3), and (5) reproduce the main results and columns (2), (4), and (6) present estimates from IV regressions using the shift-share instrument. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Infant outcomes' by time - Infant mortality rate

Dependent var:	Infant mortality rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	-0.0232	0.0458	0.0512	0.0846
	[0.140]	[0.185]	[0.160]	[0.113]
Observations	11,800	7,080	8,850	5,310
Effective F	16.63	15.22	17.06	25.7
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together; and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Infant outcomes' by time - Birth weight

Dependent var:	Birth weight			
	(1)	(2)	(3)	(4)
Prescription opioids pc	-4.490**	-5.989**	-5.093**	-2.915*
	[2.143]	[2.811]	[2.316]	[1.623]
Observations	11,800	7,080	8,850	5,310
Effective F	16.63	15.22	17.06	25.7
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018, column (2) presents estimates for the first wave of the opioid epidemic, column (3) presents estimates for the first and second waves pooled together, and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Birth and maternal outcomes using a shift-share IV

Dependent var:	Infant mortality rate		Birth weight		Fertility rate	
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. opioids pc	-0.0232	-0.0218	-4.490**	-4.344**	0.00153***	0.00149***
	[0.140]	[0.120]	[2.143]	[1.964]	[0.000566]	[0.000548]
Effective F	16.63	17.47	16.63	17.47	16.63	17.47
Model	IV	Shift-share IV	IV	Shift-share IV	IV	Shift-share IV

Notes: Columns (1), (3), and (5) reproduce the main results and columns (2), (4), and (6) present estimates from IV regressions using the shift-share instrument. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Fertility rate by time

Dependent var:	Fertility rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00153***	0.00210***	0.00233***	0.00350***
	[0.000566]	[0.000696]	[0.000674]	[0.000778]
Observations	11,800	7,080	8,850	5,310
Effective F	16.63	15.22	17.06	25.7
Sample	1999-2018	1999-2010	1999-2013	2010-2018

Notes: Column (1) reproduces the main results for 1999-2018; column (2) presents estimates for the first wave of the opioid epidemic; column (3) presents estimates for the first and second waves pooled together; and column (4) presents estimates for the after-OxyContin reformulation period. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Birth and maternal outcomes using a shift-share IV

Dependent var:	Infant mortality rate		Birth weight		Fertility rate	
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. opioids pc	-0.0232	-0.0218	-4.490**	-4.344**	0.00153***	0.00149***
	[0.140]	[0.120]	[2.143]	[1.964]	[0.000566]	[0.000548]
Effective F	16.63	17.47	16.63	17.47	16.63	17.47
Model	IV	Shift-share IV	IV	Shift-share IV	IV	Shift-share IV

Notes: Columns (1), (3), and (5) reproduce the main results and columns (2), (4), and (6) present estimates from IV regressions using the shift-share instrument. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Effects on fertility rate by age

Age group:	10-19	20-24	25-29	30-34	35-39	40-44
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. Opioids pc	-0.00038	-0.00107	0.00327***	0.0000223	-0.00123**	-0.0000851**
	[-1.40]	[-0.96]	[2.83]	[0.05]	[-2.47]	[-2.08]
Effective F-stat	16.63	16.63	16.63	16.63	16.63	16.63
Observations	11,800	11,800	11,800	11,800	11,800	11,800
Clusters	590	590	590	590	590	590

Notes: This table presents results of the effect of the prescription opioid supply on the fertility rate of women age 10 to 44 years by age group. Standard errors in square brackets are clustered at the CZ level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Drug induced mortality

Dependent var:	Prescription opioids MR	All opioids MR	Drug-induced MR
	(1)	(2)	(3)
Prescription opioids pc	0.00679***	0.00646***	0.0112***
	[0.00200]	[0.00139]	[0.00369]
tF 0.05 se	-0.00281	-0.00324	-0.00518
AR p-value	0.0000	0.0019	0.0001
Effect size (%)	88.63	39.3	50.71

Notes: The drug-induced deaths category includes deaths from poisoning and medical conditions caused by use of legal or illegal drugs, as well as deaths from poisoning due to medically prescribed and other drugs. This category has the advantage that comparisons across years are less affected by changes in the ICD classification. All regressions include state times year fixed effects. Each regression is run over a sample of 11,800 observations with 590 clusters. Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the respective dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at commuting-zone level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Robustness summary

Direct Effects on Opioid Mortality by Age and Race

Dependent var:	Prescription opioids			All Opioids		
	Less than 50 yo	More than 50 yo	White	Less than 50 yo	More than 50 yo	White
	(1)	(2)	(3)	(4)	(5)	(6)
Prescription opioids pc	0.0155***	0.00184	0.00528***	0.0185***	-0.000391	0.0168***
	[0.00435]	[0.00133]	[0.00201]	[0.00530]	[0.00193]	[0.00486]
tF 0.05 se	(0.0061)	(0.0019)	(0.0028)	(0.0074)	(0.0027)	(0.0067)
t-stat using tF 0.05 se	2.5396	0.9860	1.8439	2.4878	-0.1125	2.4945
Effect size (%)	58.81	15.08	60.31	31.04	-1.25	64.28
Model	IV	IV	IV	IV	IV	IV
Observations	11,800	11,800	11,800	11,800	11,800	11,800
Clusters	590	590	590	590	590	590
Effective F-stat	16.63	16.63	16.63	16.63	16.63	16.63
Cragg-Donald Wald F-stat	358.58	358.58	358.58	358.58	358.58	358.58

Notes: Control variables are contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Effect size indicates the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level. Using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$. tF 0.05 se, t-stat using tF0.05 se, and the *AR p-value* correspond to weak-instrument-robust inference procedures.

Opioid-related deaths by time

Dependent variable:	Prescription Opioids Mortality Rate			
	(1)	(2)	(3)	(4)
Presc. Opioids pc	0.00679***	0.00785***	0.00769***	0.00533***
	[0.00200]	[0.00259]	[0.00230]	[0.00169]
Observations	11,800	7,080	8,850	5,310
Sample	**All**	**1999-2010**	**1999-2013**	**2010-2018**
Dependent variable:	Any Opioid Mortality Rate			
	(1)	(2)	(3)	(4)
Presc. Opioids pc	0.00646***	0.00677***	0.00672***	0.00562**
	[0.00231]	[0.00256]	[0.00232]	[0.00237]
Observations	11,800	7,080	8,850	5,310
Sample	**All**	**1999-2010**	**1999-2013**	**2010-2018**

Notes: This table presents results from a regression of the opioid mortality measure on all prescription opioids distribution per capita, instrumenting the latter by the cancer incidence in the commuting zone in 1994-1996. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at the CZ level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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Other outcome measures by time

	SNAP			SSDI		
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. Opioids pc	0.00455*	0.00487**	0.00680***	0.00584***	0.00605***	0.00718***
	[0.00250]	[0.00219]	[0.00205]	[0.00144]	[0.00141]	[0.00135]
Effective F	15.22	17.06	25.70	15.22	17.06	25.70
Sample	**1999-2010**	**1999-2013**	**2010-2018**	**1999-2010**	**1999-2013**	**2010-2018**

	SSI			IMR		
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. Opioids pc	0.00226*	0.00248*	0.00320*	0.0458	0.0512	0.0846
	[0.00133]	[0.00141]	[0.00174]	[0.185]	[0.160]	[0.113]
Effective F	15.22	17.06	25.70	15.22	17.06	25.70
Sample	**1999-2010**	**1999-2013**	**2010-2018**	**1999-2010**	**1999-2013**	**2010-2018**

	Birth weight			Fertility		
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. Opioids pc	-5.989**	-5.093**	-2.915*	0.00210***	0.00233***	0.00350***
	[2.811]	[2.316]	[1.623]	[0.000696]	[0.000674]	[0.000778]
Effective F	15.22	17.06	25.70	15.22	17.06	25.70
Sample	**1999-2010**	**1999-2013**	**2010-2018**	**1999-2010**	**1999-2013**	**2010-2018**

Notes: This table presents results from a regression of the opioid mortality measure on all prescription opioids distribution per capita, instrumenting the latter by the cancer incidence in the commuting zone in 1994-1996. All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at the CZ level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

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First Stage: Alternative choices of instrument

Dependent variable: Prescription opioids per capita	(1)	(2)	(3)	(4)	(5)	(6)
Age-adjusted Cancer MR 94-96	0.743***					
	[0.194]					
Cancer MR 1994		1.044***				
		[0.245]				
Cancer MR 1995			0.962***			
			[0.240]			
Cancer MR 1996				0.738***		
				[0.199]		
Cancer MR 94-96 (weighted)					1.865***	
					[0.408]	
Above-65-years-old Cancer MR 94-96						0.210**
						[0.0988]
Observations	11,800	11,800	11,800	11,800	11,800	11,800
Clusters	590	590	590	590	590	590

Notes: All regressions include state times year fixed effects and a set of control variables: Labor force participation, contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at the CZ level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Robustness summary

Alternative Measure of Opioid Supply

Dependent var:	Oxycodone pc (1)	Presc. opioids MR (2)	All opioids MR (3)
Cancer MR 94-96	0.605***		
	[0.186]		
Oxycodone pc		0.0121***	0.0115***
		[0.00412]	[0.00436]
tF 0.05 se		(0.00578)	(0.00612)
t-stat using tF 0.05 se		2.0932	1.8799
Effect size (%)	38.00	91.50	40.37
Model	FS	IV	IV
Observations	11,800	11,800	11,800
Clusters	590	590	590

Notes: All regressions include state times year fixed effects and a set of control variables. This table reproduces the main analysis using Oxycodone shipments as the measure of opioid supply. Effect size in column (1) is computed as the predicted changes in doses of oxycodone and prescription opioids per capita from an increase in cancer mortality that would change a commuting zone in the 5th percentile of the cancer distribution to the 95th percentile. Effect sizes in columns (2) and (3) indicate the percent change in the dependent variable relative to its mean when doses of prescription opioids per capita increase from the 25th to the 75th percentile. Standard errors in square brackets are clustered at the CZ level; using these standard errors, we report * $p<0.10$, ** $p<0.05$, *** $p<0.01$. tF 0.05 se, and t-stat using tF0.05 se correspond to weak-instrument-robust inference procedures.

Robustness summary

Estimates of the first stage under alternative sample restrictions

Dependent variable:	Prescription opioids per capita			
	(1)	(2)	(3)	(4)
Cancer MR 94-96	1.078***	1.191***	1.055***	1.018***
t-stat	4.083	4.79	3.55	3.54
Observations	11,800	12,820	10,8880	9,620
Clusters	590	641	544	481
Adjusted R^2	0.564	0.467	0.568	0.608
Sample	25,000+	15,000+	40,000+	55,000+

Notes: Our preferred specification restricts the sample to commuting zones with population higher than 25,000 residents and is presented in column (1). All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Robustness summary

Effects on prescription opioid mortality for different sample restrictions

Dependent variable:	Prescription opioids mortality rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00679***	0.00355***	0.00684***	0.00826***
t-stat	3.35	2.65	2.96	3.08
Observations	11,800	12,820	10,880	9,620
Clusters	590	641	544	481
Sample	25,000+	15,000+	40,000+	55,000+

Notes: Our preferred specification restricts the sample to commuting zones with population higher than 25,000 residents and is presented in column (1). All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Robustness summary

Effects on all opioids mortality for different sample restrictions

Dependent variable:	All opioids mortality rate			
	(1)	(2)	(3)	(4)
Prescription opioids pc	0.00646***	0.00152	0.00697**	0.00885***
t-stat	2.77	0.89	2.56	2.69
Observations	11,800	12,820	10,880	9,620
Clusters	590	641	544	481
Sample	25,000+	15,000+	40,000+	55,000+

Notes: Our preferred specification restricts the sample to commuting zones with population higher than 25,000 residents is presented in column (1). All regressions include state times year fixed effects and a set of control variables: contemporaneous cancer mortality rate, share of population under 1 year old, share of population between 18 and 65, share of population over 66 years old, share of Black, White, and Hispanic population, and share of female population. Standard errors are clustered at commuting-zone level. * $p<0.10$, ** $p<0.05$, *** $p<0.01$.

Robustness summary

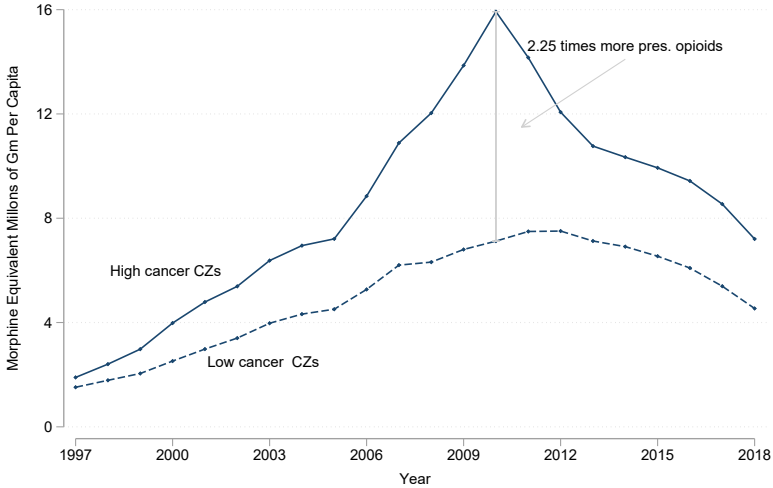
Effects on other outcome variables for different sample restrictions

Dependent var:	SSDI			SSI		
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. Opioids pc	0.00504***	0.00586***	0.00652***	0.00204**	0.00339**	0.00438*
	[0.00106]	[0.00155]	[0.00173]	[0.000851]	[0.00169]	[0.00239]
Sample	**15,000+**	**40,000+**	**55,000+**	**15,000+**	**40,000+**	**55,000+**
	SNAP			IMR		
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. Opioids pc	0.00941***	0.00997***	0.00919***	0.175	-0.0297	0.0604
	[0.00248]	[0.00336]	[0.00307]	[0.130]	[0.142]	[0.150]
Sample	**15,000+**	**40,000+**	**55,000+**	**15,000+**	**40,000+**	**55,000+**
	Birth weight			Fertility		
	(1)	(2)	(3)	(4)	(5)	(6)
Presc. Opioids pc	-4.896***	-3.770*	-6.480**	0.00108***	0.00156**	0.00160**
	[1.852]	[2.240]	[2.624]	[0.000404]	[0.000632]	[0.000706]
Sample	**15,000+**	**40,000+**	**55,000+**	**15,000+**	**40,000+**	**55,000+**

Robustness summary

Additional Figures

All prescription opioids supply by 1994-1996 cancer prevalence



Notes: This figure shows the evolution of prescription opioids in the forth quartile (solid lines) and first quartile (dashed lines) of the cancer mortality rate distribution before the launch of OxyContin. Prescription opioids are measured in morphine-equivalent mg.

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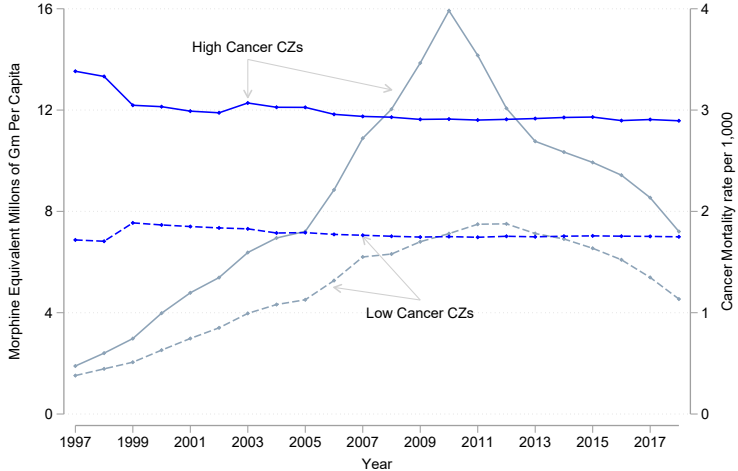
All prescription opioids supply and cancer mortality by 1994-1996 cancer prevalence



Notes: The left-hand axis shows the evolution of oxycodone in the fourth quartile (solid lines) and first quartile (dashed lines) of the cancer mortality rate distribution before the launch of OxyContin. The right-hand axis shows the evolution of cancer mortality in the top and bottom quartiles of the cancer mortality distribution before the launch of OxyContin. Oxycodone is measured in morphine-equivalent mg.

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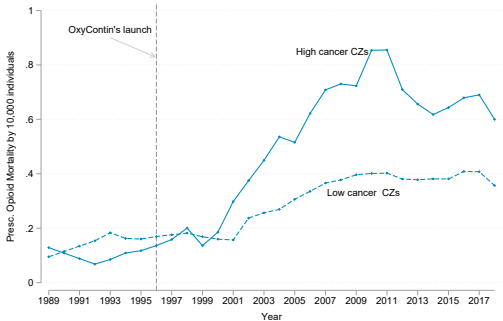
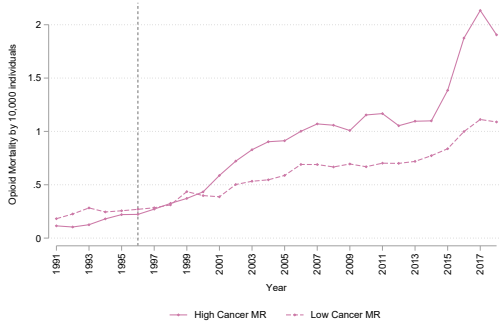
Opioid Mortality Rate by 1994-1996 Cancer Prevalence

(a) Prescription Opioids Mortality



(b) All Opioid Mortality



Notes: This figure shows the evolution of prescription opioid mortality (panel a) and the evolution of all opioid mortality (panel b) by 1994-1996 cancer prevalence. The high-cancer mortality rate corresponds to the group of commuting zones in the fourth quartile of cancer mortality in 1994-1996 and low cancer corresponds to the first quartile. The vertical line at 1996 indicates the year OxyContin was launched.

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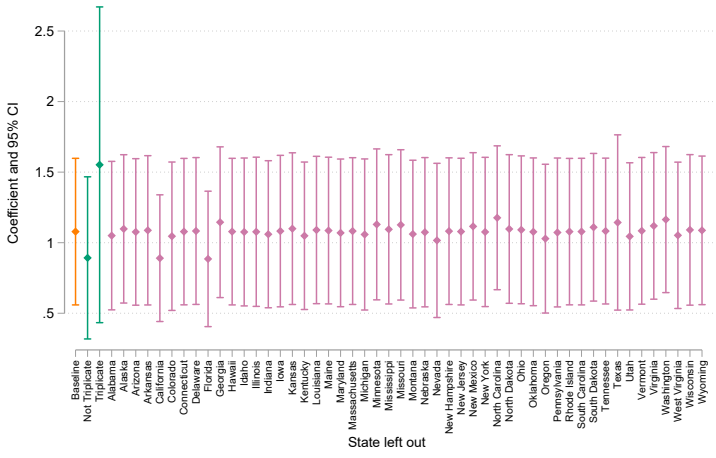
Estimates of the first stage: Leave out one state at a time



Notes: This graph reports the estimated coefficient of the first stage (ϕ) and the corresponding 95% confidence interval. The first coefficient and confidence interval replicate the result when all states are included in the sample. Each of the subsequent coefficients are computed by excluding all commuting zones in the state indicated on the horizontal axis.

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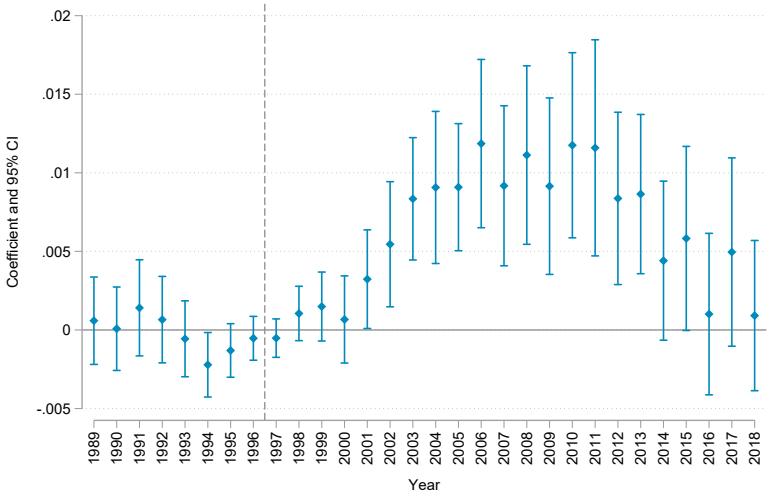
Dynamic reduced-form results: Prescription Opioids



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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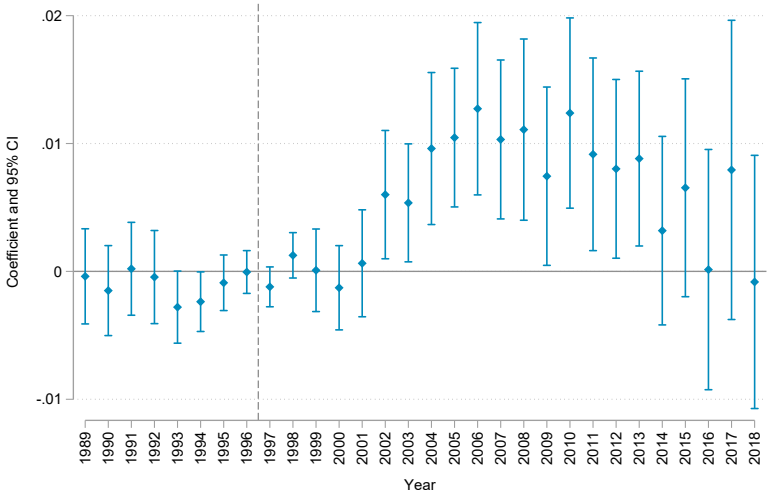
Dynamic reduced-form results: All Opioids



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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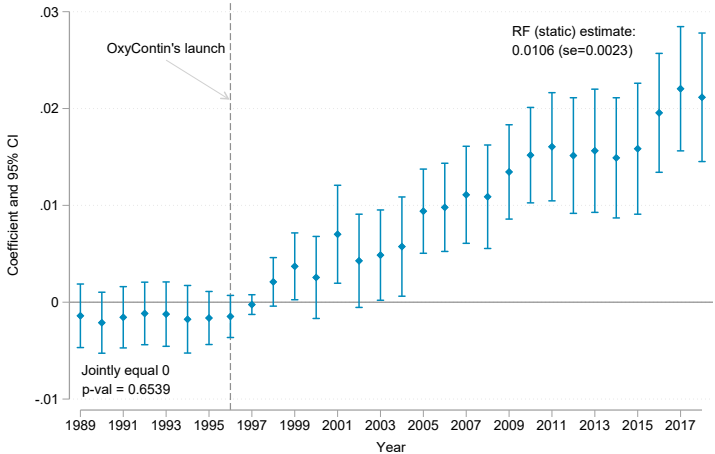
Dynamic reduced-form results: SNAP



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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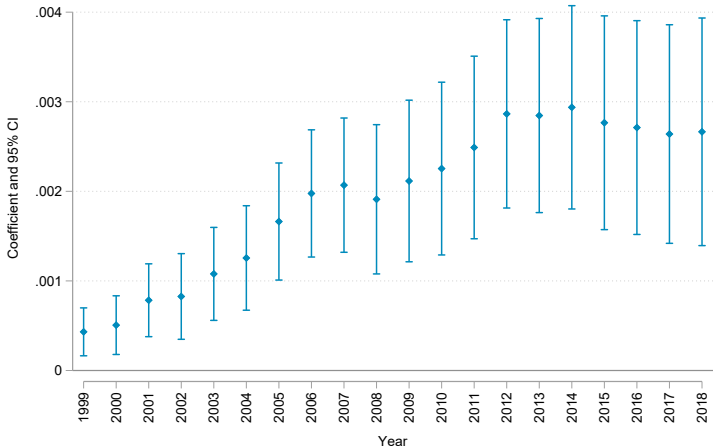
Dynamic reduced-form results: SSI



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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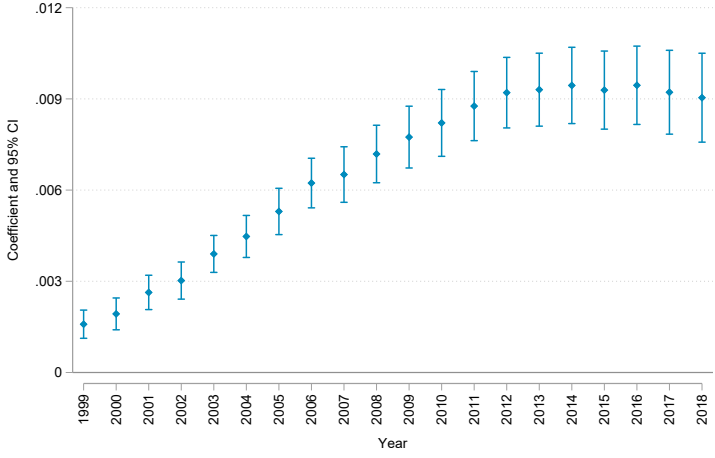
Dynamic reduced-form results: SSDI



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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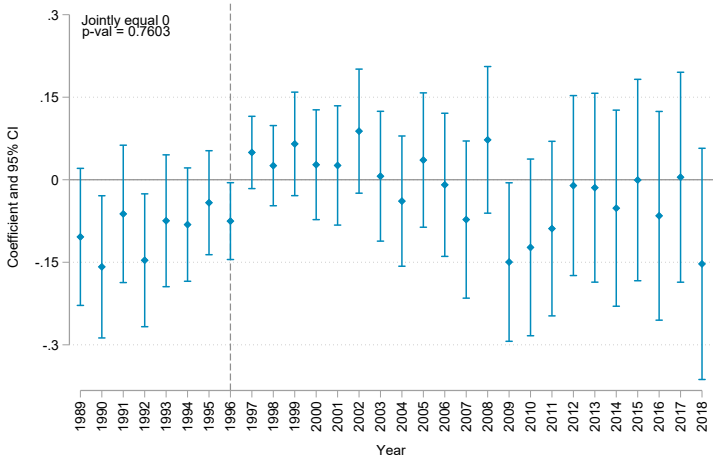
Dynamic reduced-form results: All-cause mortality



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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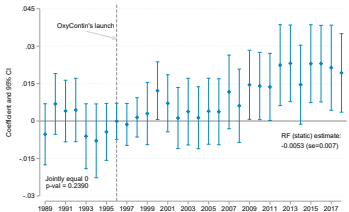
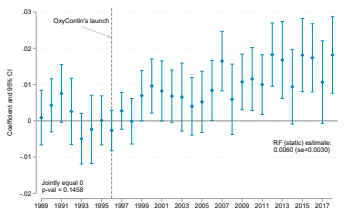
Dynamic reduced-form results: Deaths of Despair

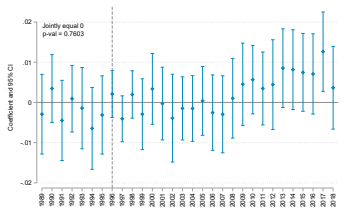
(a) All



(b) Alcohol liver des. & cirrhosis



(c) Suicides



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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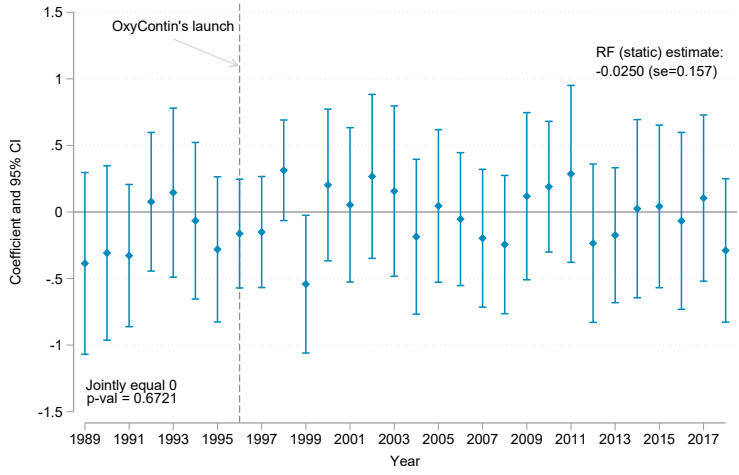
Dynamic reduced-form results: Infant Mortality Rate



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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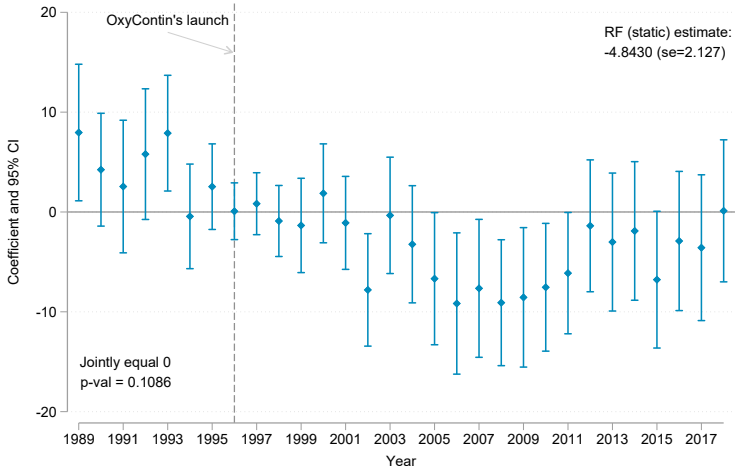
Dynamic Reduced-form: Birth weight



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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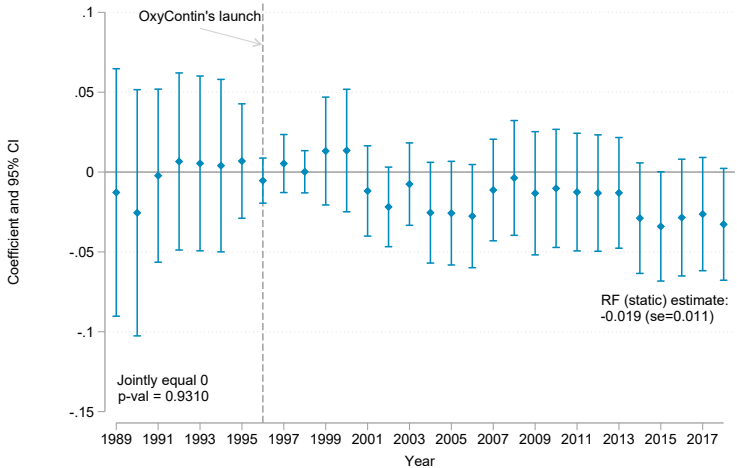
Dynamic Reduced-form: APGAR Score



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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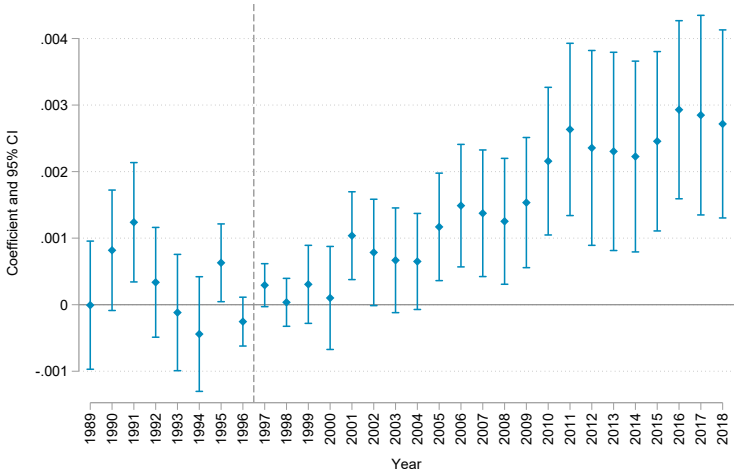
Dynamic Reduced-form: Fertility Rate



Notes: This figure shows the dynamic reduced-form relation between outcomes of interest and our instrument—cancer mortality in 1994 - 1996.

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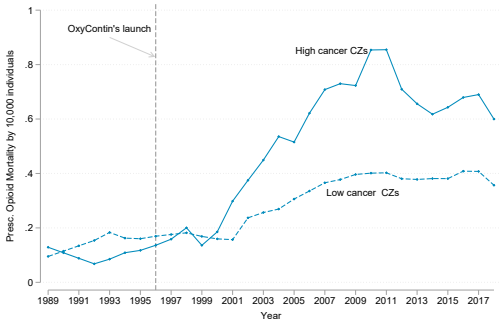
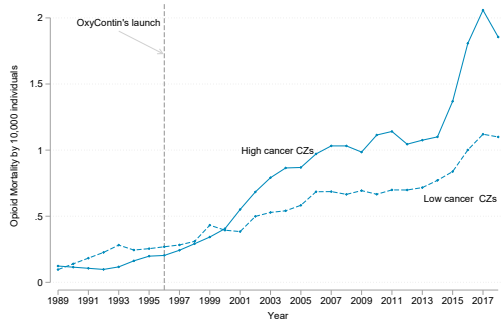
Raw data: No difference before the introduction of OxyContin, strong divergence after

(a) Prescription Opioids



(b) Any Opioids



Notes: This figure shows the evolution of prescription opioid mortality (panel a) and the evolution of all opioid mortality (panel b) by 1994-1996 cancer prevalence. The high-cancer mortality rate corresponds to the group of commuting zones in the fourth quartile of cancer mortality in 1994-1996 and low cancer corresponds to the first quartile. Prescription opioid mortality captures deaths whose underlying cause is substances usually found in prescription painkillers such as hydrocodone, methadone, morphine, and oxycodone, among others.

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