Can a Single Opioid Prescription Make a Difference? Evidence from Physician Prescribing Variation in Emergency Departments

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Poll Question #1

What is your background?

- Researcher - Economics
- Researcher - Health Services
- Researcher - Other
- Clinician - Emergency Medicine
- Clinician - Other

The United States has an opioid epidemic

- The opioid epidemic has reached epic proportions
  - Every day over 130 Americans die from an opioid overdose
- Over 32 states have laws that impose limits on opioid prescribing (Chua et al. 2019)
- Disagreement among medical community; **trade-offs** in prescribing a patient opioids:
  - **Short-term benefit**: Pain is real and opioids are effective at managing acute pain
  - **Long-term cost**: Opioids can increase risk of misuse and addiction
- Quantifying the cost informs physicians and patients of the cost in a complex physician-patient agency relationship (Arrow 1963)

Research Questions

1. Can a single opioid prescription in an acute setting induce **long-term use and dependence**?

2. What are the **causal effects** on the entire **chain of downstream long-term outcomes**?
   - Opioid abuse and overdose, transition into illicit drugs, mortality
   - Attempted suicide, depression, accidental falls, homelessness

Preview of Research Design

- Veterans receiving opioid prescriptions in **emergency departments** (ED)
- **Quasi-random assignment** of patients to physicians in EDs
  - Patients arriving to the same ED, at the same time, for the same condition
  - Alleviates patient-physician selection (e.g., primary care settings)
- Physicians exhibit **large variation** in their **propensity to prescribe opioids**, even within the same hospital and treating the same conditions

Preview of Findings

A **single opioid prescription** in the ED to veterans:

- Increases probability of **long-term prescription opioid use** for over 24 months later
- Can lead to **opioid dependence** and increased patient demand via opioid-seeking behavior
- Increases probability of **opioid overdose** and **mortality**
- Suggestive evidence of **illicit opioid use**

Roadmap

1. Data and summary statistics
2. Research design and physician leniency instrument
3. Main results
    - Mechanism and Source of Opioids
4. Robustness and alternate specifications

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Poll Question #2

How much experience do you have with the Corporate Data Warehouse data?

- A lot
- Some
- None

Data

1. VHA Corporate Data Warehouse)

- VHA and community care (Fee Basis and PIT data)
- Ideal health setting:
  1. Large integrated system: observe history of patient care with little attrition
  2. Many physicians work exclusively at the VHA: observe entire prescribing history for a given physician

2. VHA-CMS Data

- Medicare and Medicaid claims linked to veterans (50% on Medicare, 10% on Medicaid)
- Medicare (Part A, B, and D): 2011-2016
- Medicaid: 2011-2014

3. Death Data

- Date of death: SSA Death Master File, Medicare Vital Status File, and internal VA records
- National Death Index (NDI) Plus: cause of death

Sample

- Veterans with an emergency visit between 2006-2016; keep the first visit:
  1. Non-terminal cancer/end-of-life hospice care
  2. Diagnosis condition that is prescribed an opioid at least sometimes ($\geq$ 10%)
  3. Not already a heavy opioid user (exclude top 15%)
  4. Treated by a provider with at least 200 ED cases that year
- N=1,958,209, attended by 5,313 providers at 120 EDs
- 26.1% are prescribed an opioid for that ED visit Distribution of Intensive Margin

Veterans are a vulnerable population

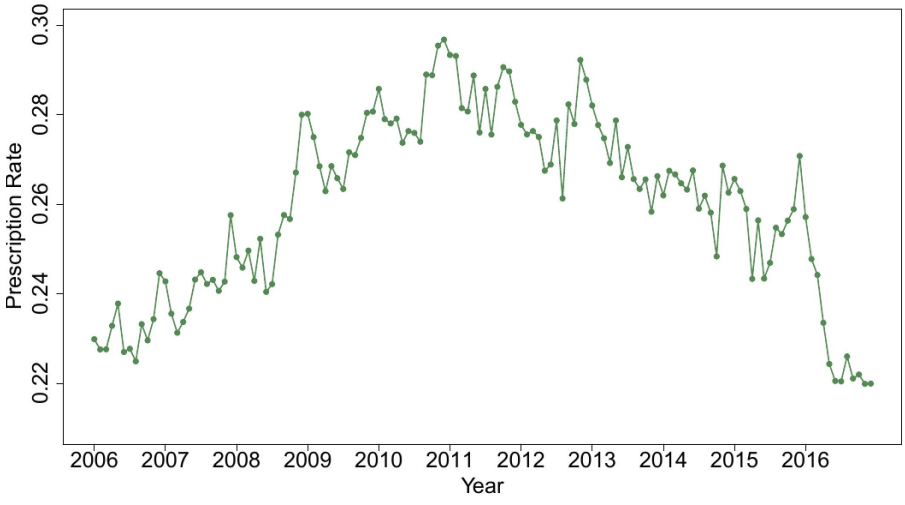
	Mean	p25	Median	p75
Age	56	45	58	67
Income	20,626	5,100	15,000	31,188
Male	0.89			
White	0.70			
Black	0.26			
Prescribed in ED	0.26			

Previous year medical episode:	Our Sample	Adult Americans	Opioid Use Disorder†
Depressive Disorder?	0.24	0.07	0.28
Post-traumatic stress disorder?	0.13	0.03	
Self-inflicted harm/suicide?	0.006	0.002	0.03
Opioid use?	0.27	0.19*	
Homeless (seeking help w/ shelter)?	0.08		

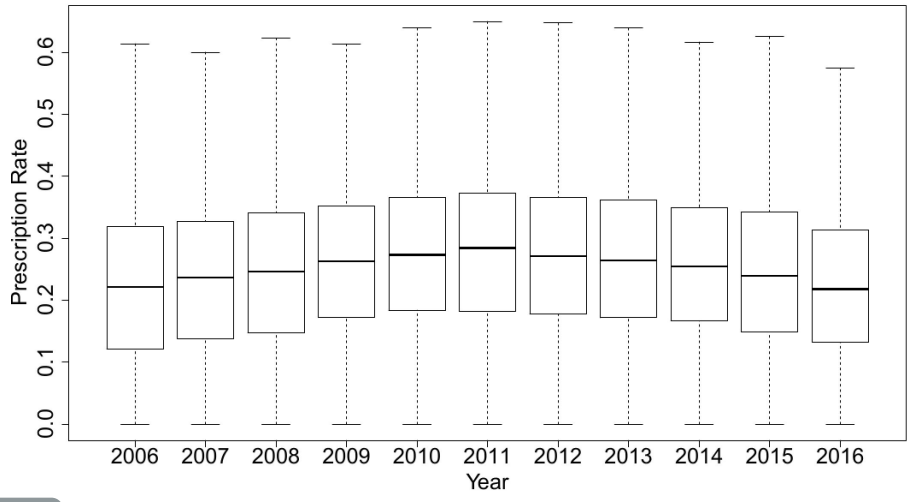
† National Survey of Drug Use and Health (NSDUH) 2018
*Privately insured Optum population *first time* visiting EDs

ED Diagnoses

Prescribing rates in VHA EDs for our baseline sample



Variation in physician prescribing is roughly stable over time



Leniency Measure

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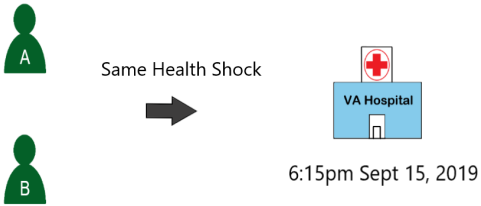
Assignment Process in EDs

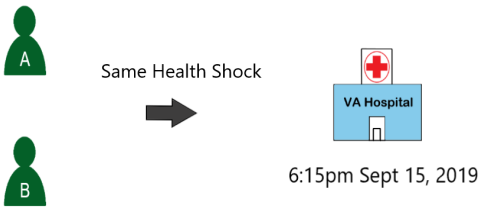
Assignment Process in EDs

Same Health Shock

Assignment Process in EDs



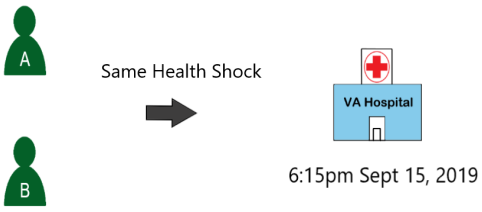
Assignment Process in EDs



Physician A

Physician B

Assignment Process in EDs

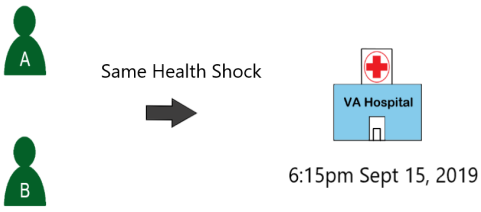


Physician A

Lenient:
Prescribes 30%

Physician B

Assignment Process in EDs



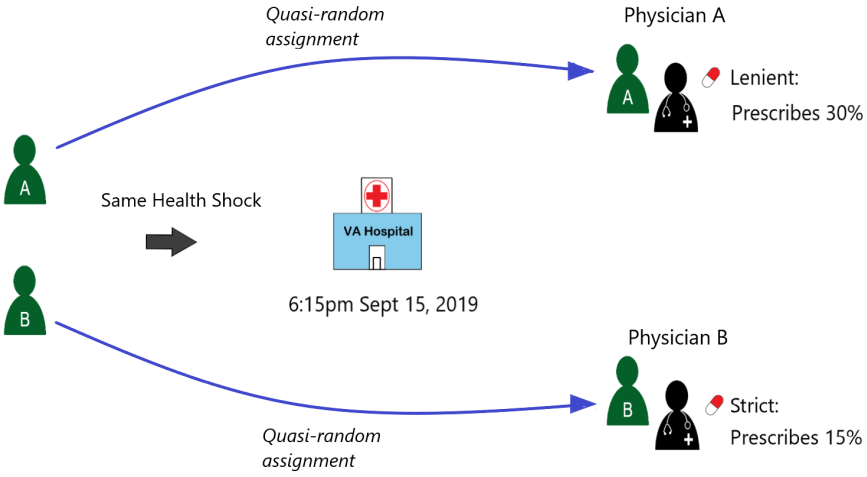
Physician A

Lenient:
Prescribes 30%

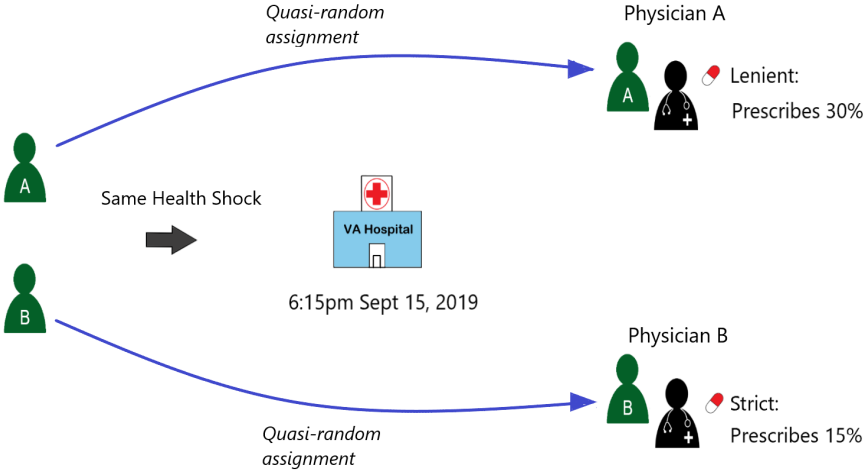
Physician B

Strict:
Prescribes 15%

Assignment Process in EDs



Assignment Process in EDs



Quasi-random assignment in EDs of patients to physicians (conditional on *hospital, arrival time, and diagnosis condition*), who vary in their **propensity to prescribe** opioids

Poll Question #3

How much experience do you have with instrumental variables, causal inference?

- A lot; fully familiar with the assumptions
- Some; perhaps vaguely familiar with the assumptions
- None

Measuring Physician's Propensity to Prescribe Opioids (IV)

- For each patient *i*, treated by provider *j*, in year *y*, what is their provider's underlying **propensity to prescribe opioids**, that year?

1. Using *all* 20M emergency encounters, residualize at the encounter level:

$$Prescribed = \underbrace{\alpha_{hym}}_{hosp \times year \times month} + \underbrace{\alpha_{hdt}}_{hosp \times dayofweek \times timeofday} + \theta X + \epsilon$$

X: Elixhauser comorbidity score, pain score, ED visit number, previous opioid use, diagnosis, and age bin fixed effects

2. Average across physician's other cases that year (**year-varying** "jackknife" IV):
   Compute mean residual of all encounters seen by physician *j* in year *y*, excluding patient *i*:

$$Leniency_{-i,jy} = \frac{1}{N_{-i,jy}} \sum_{i' \in \{\mathcal{J} \setminus i\}} \hat{\epsilon}_{i'}$$

First Stage: Large within-ED variation in prescribing tendency

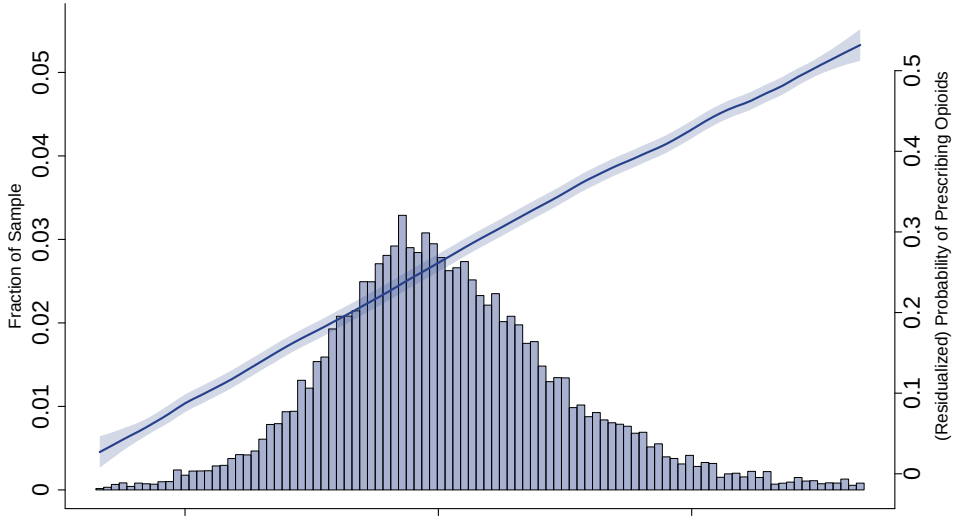


Table Format | Who are lenient docs?

Empirical Model

For veteran *i*'s "first" ED visit, we estimate the following model:

$$Y_{it} = \beta_1 Prescribed_i + \theta X_i + \epsilon_i$$

- Instrument $Prescribed_i$ with physician's opioid prescribing leniency, $Leniency_{iy}$
- Controls:
  - Hosp-year-month, hosp-day of week-time of day, diagnosis and age bin FEs
  - Elixhauser comorbidity score, ED pain score, gender, race, prior opioid use
- Outcomes Y_{it} will be at the year level relative to the ED encounter date
- β_1 identifies the **causal effect** of the single ED opioid on outcome Y under several identifying assumptions

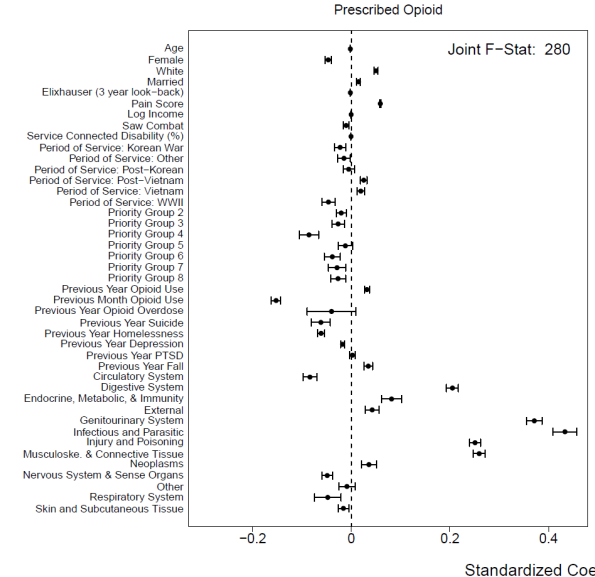
Identifying Assumptions

1. **Conditional Independence**: quasi-random assignment
   - Check for balance along observables

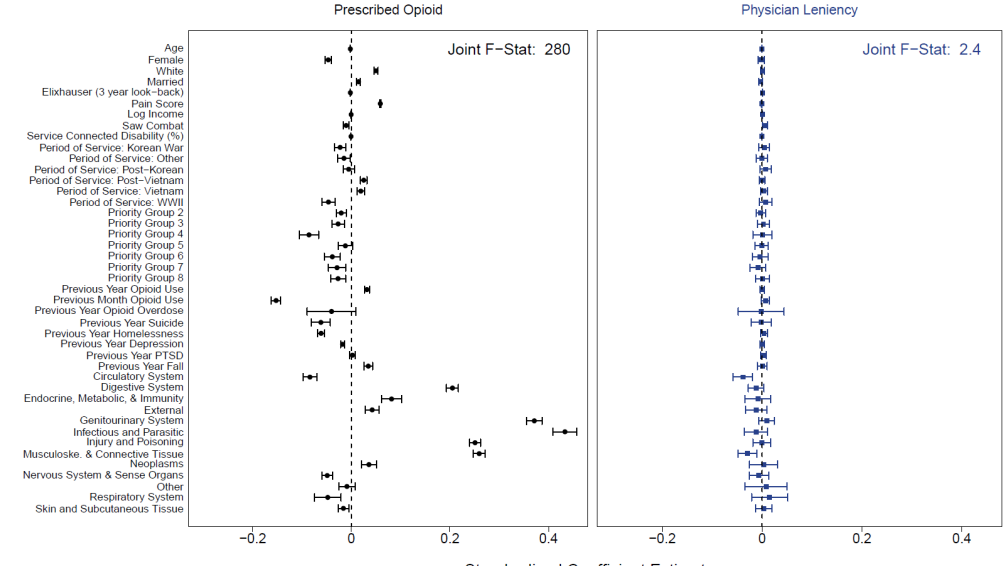
2. **Exclusion Restriction**: physician leniency affects patient outcomes only through ED opioid prescription
   - Model admission and procedures as endogenous decisions
   - Estimate physician quality (proxied by one month mortality) and control for it
   - Placebo checks using never-prescribed diagnoses

3. **Monotonicity**: if a patient is prescribed by a strict physician, they must also be prescribed by any physician who is more lenient
   - Subsample & reverse-sample first stage (Frandsen et al. (2019): "average monotonicity")
   - Diagnosis related group specific prescribing leniency

Patient observables and medical morbidities predict opioid prescription dummy



But are not correlated with physician leniency



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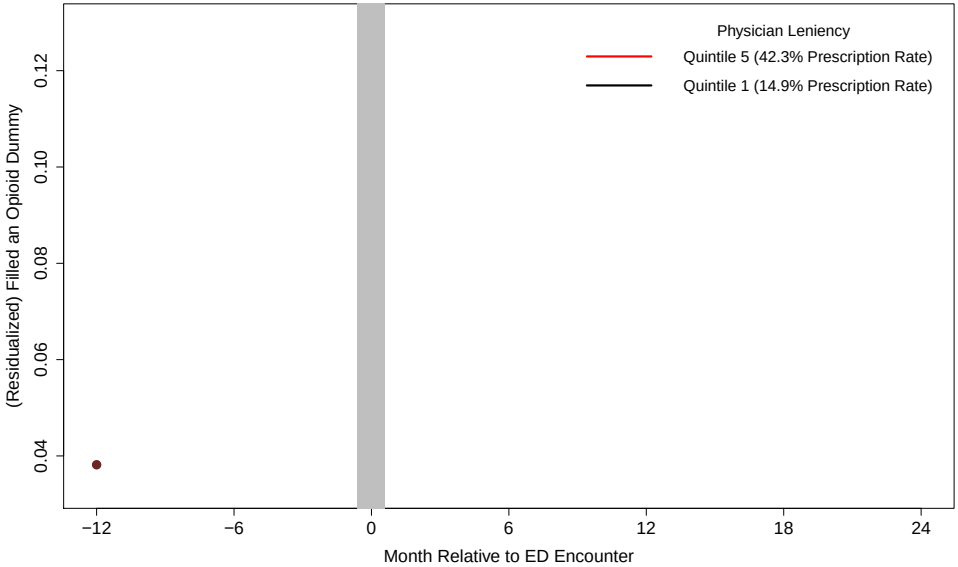
Reduced Form Event Study

- Look at *new* opioid prescriptions filled each month
- *Exclude* any prescriptions within 7 days of the emergency visit
- While subsequent prescriptions could be related to the ED visit condition, current practice guidelines caution against this

Reduced Form: Increased probability of opioid use persists for over 24 months



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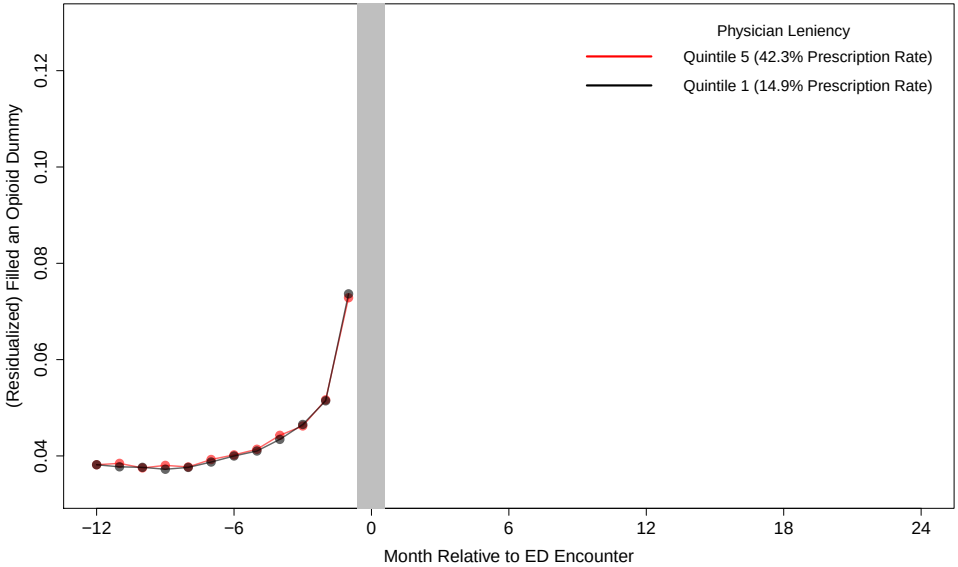

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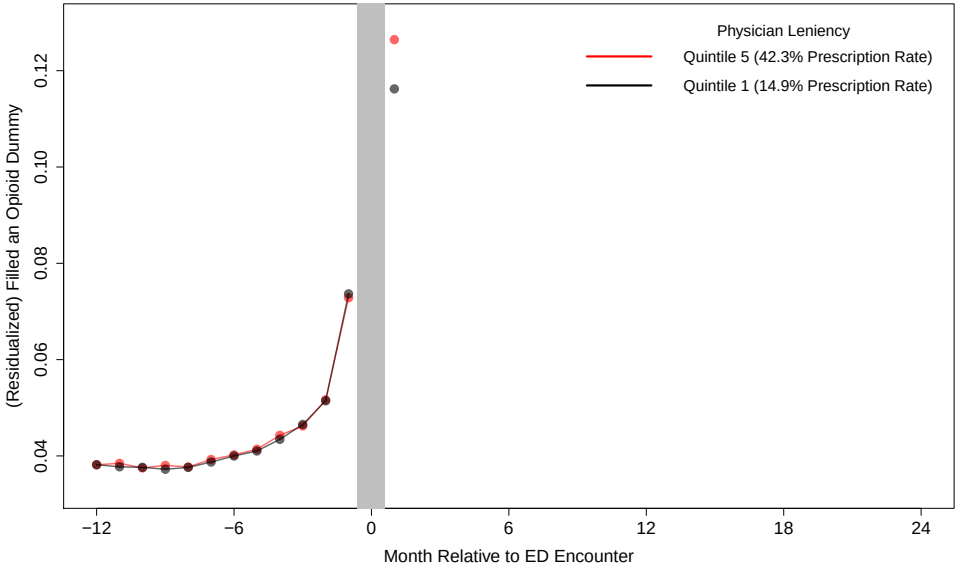

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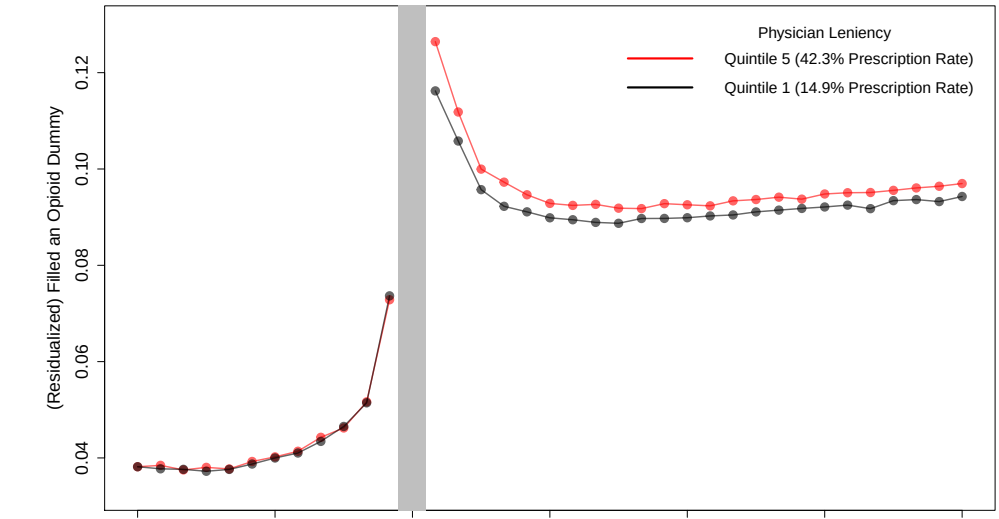
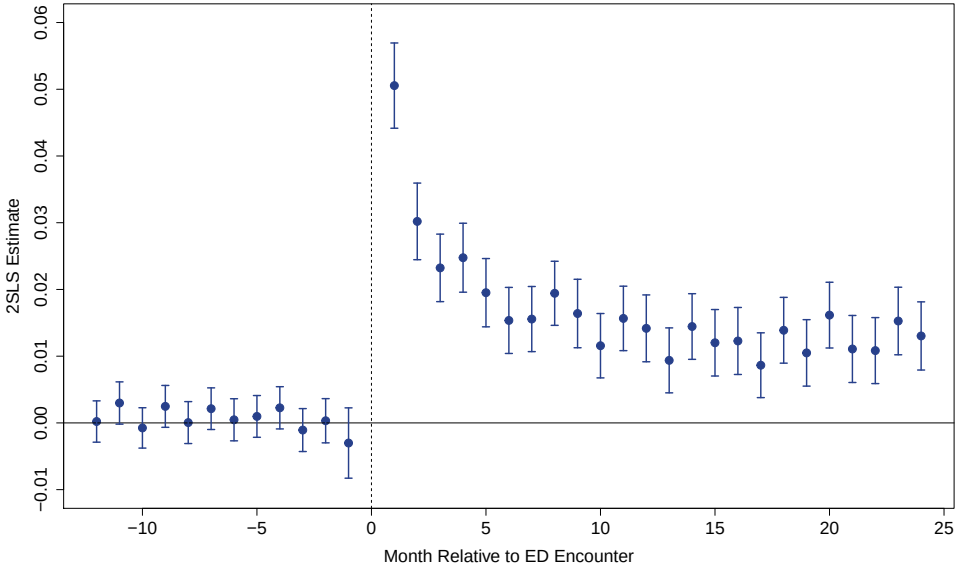


2SLS: Single ED opioid prescription increases probability of monthly opioid use by 1-1.5pp



Long-Term Opioid Use

Long-term use: 180 days supply (length) of opioids in the first 12 months (excluding initial 7 days)

	Mean	OLS	2SLS	N=
Dependent Variable:	(1)	(2)	(3)	(4)
Long-Term Use ($\times 100$)				
	5.8	2.63***	1.17***	1,879,150
		(0.061)	(0.202)	
Total Milligrams of Morphine				
Prior Year	214	−12.9***	3.6	1,958.209
		(0.66)	(3.01)	
Year 0-2	1573	600.1***	360.3***	1,825,450
		(14.4)	(45.6)	

- A single ED opioid prescription increases the probability of long-term use of legal prescription opioids by 1.2pp
- Without relying on pharmacy prescriptions: similar effect on positive urine drug screens
- Over 24 months, average *prescribed* veteran fills $\sim$ 500 additional mg of morphine (average ED prescription is 140mg)
- An *underestimate*: dual insurance coverage, black market, illicit heroin, etc.

Is this medically appropriate long-term use or abuse and misuse?

- Thus far: physician prescribes a drug, some patients continue taking it even 2 years later
- Is this medically appropriate (physician supply) or misuse (patient demand)?
- We construct four proxies for opioid-seeking behavior:

  1. Overlapping prescriptions: 25% overlap of days between two prescriptions
  2. Pharmacy shopping: fill opioids at $\geq$ 3 pharmacies over 90 day period
  3. Back pain and headaches: $\geq$ 5 encounters for back problems or headaches in one year
  4. Self-reported pain score

- 1 and 2 are standard in the opioid literature (Yang et al. 2015, Finkelstein et al. 2018), 3 is from conversation with VA researchers, and 4 is unverifiable, manipulable, and frequently measured

Increased patient demand via opioid-seeking behavior

2SLS Estimates	*Dependent variable* (×100)*:*			
	Overlapping Prescriptions	Pharmacy Shopping	5+ Back Pain & Headaches	Pain Score
Prior Year	0.20	0.06	0.30	0.03
	(0.14)	(0.04)	(0.20)	(0.02)
Year 1	1.9***	0.30***	0.55**	0.08***
	(0.20)	(0.07)	(0.27)	(0.02)
Mean Dep. Var (Year 1).	9.9	0.6	6.2	2.81
Observations	1,840,595	1,840,595	1,532,610	1,682,968

- Some of the long-term prescription opioid use is medically inappropriate and represents misuse, and some of the prescriptions are unnecessary

Opioid use disorder, overdose, and mortality

- Long-term use does not necessarily lead to severe adverse health outcomes
- Three severe and salient outcomes:
  1. *Opioid overdose mortality*
  2. *Opioid use disorder*: problematic pattern of opioid use leading to clinically significant impairment or distress
  3. *Opioid overdoses*

Dependent Variable: (×100)	Mean	OLS	2SLS	N=
Opioid Overdose Mortality	0.17	0.044***	0.075**	1,846,133
		(0.008)	(0.034)	
Opioid Use Disorder				
Prior Year	1.53	−0.487***	0.025	1,958,209
		(0.025)	(0.105)	
Year 0-3	3.16	0.006	0.325**	1,775,800
		(0.038)	(0.158)	
Opioid Overdose				
Prior Year	0.10	−0.016***	0.028	1,958,209
		(0.005)	(0.027)	
Year 0-3	0.50	0.019	0.035	1,775,800
		(0.014)	(0.061)	

Illicit Drug Use

Heroin is a cheaper and more effective substitute for prescription opioids (common chemical compound of morphine)

Proxies for illicit drug use:

1. **Intended heroin/fentanyl drug screens**: indicator for whether a physician orders a drug test (urine or blood) mentioning heroin or fentanyl
2. **Hepatitis C diagnosis**: bloodborne disease that is most commonly contracted via sharing needles; injection drug use is highest risk factor
    - a third of injection drug users are diagnosed with hepatitis C within one year of injection (Hagan et al. 2008)

Health and Non-Opioid Outcomes

3-Year Outcome	Mean	OLS	2SLS	N=
Dependent Variable ($\times 100$)	(1)	(2)	(3)	(4)
Intended Heroin/Fentanyl Drug Screen	0.70	0.113***	0.015	1,775,800
		(0.020)	(0.072)	
Hepatitis C Diagnosis	5.8	0.123***	0.270	1,775,800
		(0.046)	(0.207)	
Accidental Falls	6.9	0.065	0.420*	1,775,800
		(0.047)	(0.233)	
Depression	35.5	0.205**	0.558	1,775,800
		(0.094)	(0.450)	
Suicide Attempt/Self-Harm	1.38	−0.031	−0.030	1,775,800
		(0.023)	(0.107)	
Homeless	11.9	−0.802***	0.232	1,775,800
		(0.068)	(0.294)	
Residualization FE?	-	Yes	Yes	-
Baseline Controls?	-	Yes	Yes	-

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Mechanism and Sources of Opioid Supply

- Veterans who are opioid dependent, need a source of opioids
- But what happens if they don't have a steady source of legal opioids?
- Studies have shown that patients are more likely to resort to illicit opioids if their legal supply is restricted (Alpert et al. 2018, Evans et al. 2019, Meinhofer 2018)
- Investigate two settings where *legal* supply of prescription opioids are restricted:
  1. Primary care provider (PCP) who is a strict prescriber
  2. Post-2012 (Various VA initiatives -> 40% drop in total opioids dispensed)

Substitution Between Legal & Illicit Sources

	Dep. Var. (×100)			
Subsample:	Long-Term Use	Overdose	Overdose Death	Hep C
Lenient PCP	1.297***	0.085	−0.098	0.181
	(0.491)	(0.084)	(0.065)	(0.410)
Strict PCP	0.762***	0.193**	0.185***	0.315
	(0.381)	(0.075)	(0.059)	(0.394)
2006-2011	1.375***	0.056	0.113*	−0.109
	(0.312)	(0.056)	(0.061)	(0.334)
2012-2016	0.979***	0.087	0.032	0.687***
	(0.264)	(0.054)	(0.034)	(0.249)

- One potential explanation: veterans choose legitimate prescription opioids when readily available, otherwise they may resort to illicit and more dangerous black market opioid

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Robustness and Alternate Specifications

1. Conditional Independence:
   - Across-shift variation with team based leniency
2. Exclusion Restriction:
   - Model admission and intensity of care as endogenous decisions (Bhuller et al. 2018, Mueller-Smith 2015)
   - Estimate and control for physician quality
   - Placebo check with diagnoses that are never prescribed (Card et al. 2019)
3. Monotonicity:
   - Diagnosis group specific physician leniency

Robustness and Alternate Specifications

	2SLS Estimates				
	Main Baseline	Team Leniency	Endog. Admit & Procedures	Physician Quality	MDC IV
Dep. Var. ($\times 100$):	(1)	(2)	(3)	(4)	(5)
Long-Term Use	1.172***	1.313***	1.165***	1.104***	1.921***
	(0.202)	(0.305)	(0.202)	(0.203)	(0.258)
Opioid Use Disorder	0.325**	0.361	0.298*	0.329**	0.206
	(0.158)	(0.234)	(0.157)	(0.159)	(0.180)
Overdose	0.072*	0.099	0.070*	0.072*	0.130***
	(0.038)	(0.062)	(0.038)	(0.039)	(0.045)
Opioid Overdose Death	0.075**	0.104*	0.076**	0.076**	0.066
	(0.034)	(0.055)	(0.034)	(0.034)	(0.042)
Fall (Year 0-3)	0.420*	0.491	0.372	0.398*	0.551**
	(0.233)	(0.360)	(0.232)	(0.234)	(0.268)
Hepatitis C (Year 0-3)	0.270	0.011	0.257	0.240	0.444*
	(0.207)	(0.321)	(0.207)	(0.209)	(0.244)
Observations	1,775,800	1,775,800	1,775,800	1,739,337	982,679

Putting magnitudes into context of VHA Deaths

Some back of the envelope calculations:

5.8% of all veteran opioid overdose deaths were caused by an ED prescription

Calculation:

- 9,200 veterans died of an opioid overdose between 2006-2016
- 3,077 of them visited an ED and enter our baseline sample
- 39% of our sample are compliers
- 0.075/0.166 is the causal effect of an opioid on mortality

52 veteran opioid overdoses per year caused by ED prescription

Calculation:

- Each year, 178,000 new veterans (satisfying our sample restrictions) visit the ED
- 300 will eventually die from an opioid overdose
- Multiply by complier share and causal effect

Conclusion

- Leverage quasi-random assignment of veterans to physicians in EDs and find that even a single opioid prescription can have **lasting adverse effects** on opioid dependence and mortality
  - In a supplementary paper, we find veterans with a 10pp higher prescribing PCP have a 3.3pp higher probability in long-term opioid use and 1.7pp increase in major depressive diagnosis within 3 years
- This suggests that more **conservative opioid prescribing policies** can have large impacts on mitigating **new opioid abusers** (prescription or illicit)
- However, substitution between prescription and black market illicit opioids for the already **opioid-dependent**, suggest a **one-size-fits-all** policy will create **unintended consequences**
  - **Mandatory opioid monitoring** and screening to identify the opioid-dependent users
  - Better access to **medication-assisted treatment** (MAT) (e.g., buprenorphine)

Thank You!

Comments, questions, and suggestions are welcomed:
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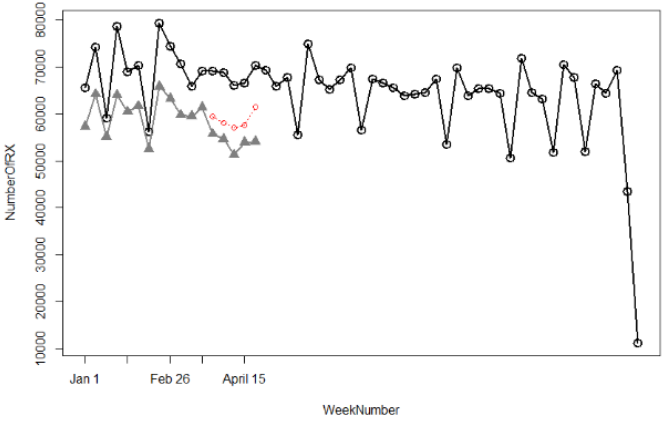
Opioid Epidemic During the COVID Pandemic

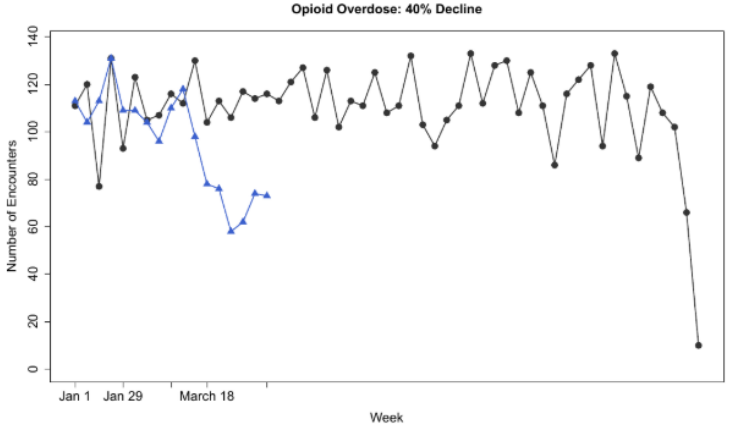
Supply of prescription opioids are down significantly

- 8.7% reduction in prescription opioids, mainly from surgery dental (25,500 fewer RX)
- Only 3.6% drop in total mg of morphine
- Concentrated in regions that have a larger pre-COVID opioids from surgery share

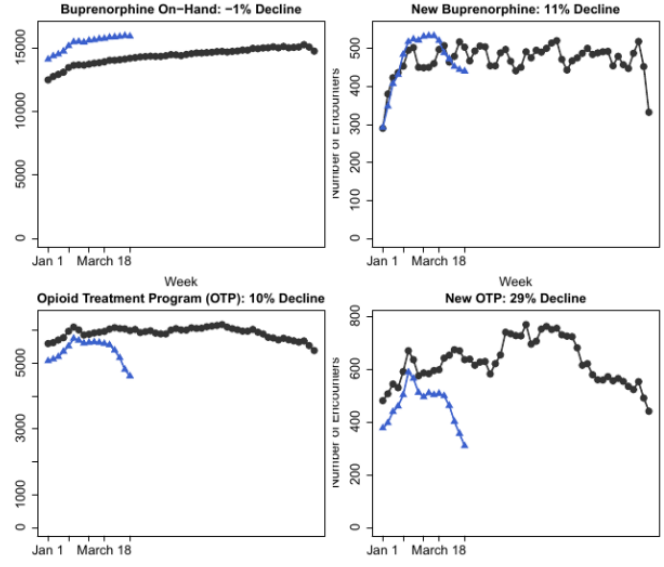


Opioid overdoses are “down”

- Opioid overdoses are “down” 40%
- Is this good or bad?



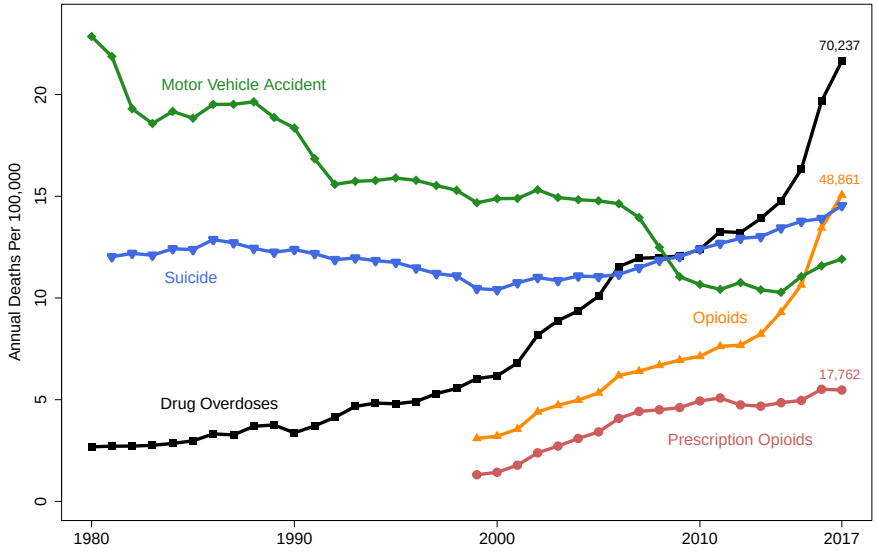
Substance abuse treatment is down



Takeaways

- Disruptions to legal prescription opioid and illicit heroin/fentanyl supply
- Unclear how this impacts those who are already dependent
- Fewer overdoses? Do we expect more to seek treatment now due to shelter-in-place?
- Need more time: cause of death data and for medical utilization to come back to “normal”

Annual Death Rates Per 100,000 Americans



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Comparison with Barnett, Olenski, and Jena (2017) and Barnett et al. (2019)

Two main differences:

1. **Patient outcomes**: Barnett et al. 2017 and 2019 study long-term prescription opioid use, along with opioid related hospitalizations as a secondary outcome. Our paper studies additional long-term outcomes including measures of abuse and dependence, opioid-seeking behavior, mortality, depression, attempted suicide, homelessness, and illicit drug use.
2. **Econometrically**: Both Barnett et al. 2017 and 2019 classify ED physicians as high and low "intensity" prescribers by calculating each physicians' raw opioid prescribing rate as the number of ED resulting in a prescription, divided by the total number of visits. They then classify physicians (grouping all years) as high (low) intensity prescribers if they fall in the top (bottom) quartile within their hospital. We use a residualization approach accounting for seasonality, shift, diagnosis, etc.

Long-Term Use Estimate: Incrementally Moving From Barnett et al. (2019) to Eichmeyer & Zhang

	Outcome: Long-Term Prescription Opioid Use	High Intensity (1)	Low Intensity (2)	High/Low Ratio (3)	Wald Estimate (4)
1.	**Barnett et al. (2019)**	1.39	1.26	1.10	0.903
2.	**Replicating Barnett et al. (2019)**	1.96	1.79	1.10	0.987
	Incremental changes to sample restriction and data definition:				
3.	+Extend long-term use defn. to opioid avail.	2.59	2.33	1.11	1.46
4.	+Exclude urgent care clinics	2.53	2.30	1.10	1.39
5.	+No prior enrollment/encounter restriction	2.70	2.38	1.14	2.01
6.	+No post-ED cancer restriction	2.74	2.44	1.12	1.84
7.	+Include admitted patients	2.97	2.68	1.11	2.00
8.	+Include prior users	5.36	5.17	1.04	1.32
9.	+Exclude rarely prescribed conditions	6.73	6.37	1.06	1.36
10.	+Add CMS prescriptions	7.63	7.17	1.06	1.97
11.	+Include all years (2006-2016)	6.05	5.36	1.13	2.75
12.	**Year-varying physician intensity**	6.01	5.60	1.07	1.75
	Incremental controls in leniency residualization:				
13.	+Hospital-Year-Month (seasonality)	5.87	5.67	1.04	1.08
14.	+Hospital-DayOfWeek-TimeOfDay (shift)	5.90	5.71	1.03	1.10
15.	+Diagnosis	5.90	5.70	1.04	1.20
16.	+Age, Elixhauser, pain score	5.90	5.69	1.04	1.25

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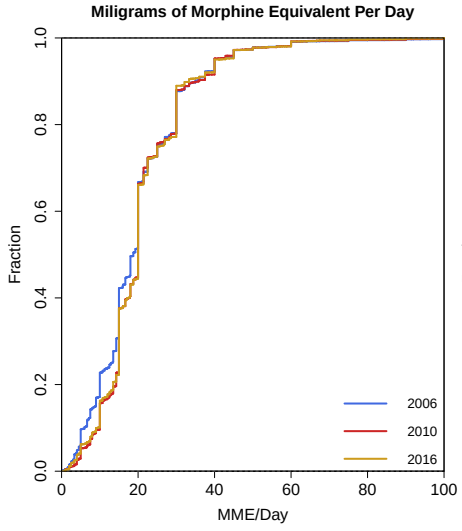
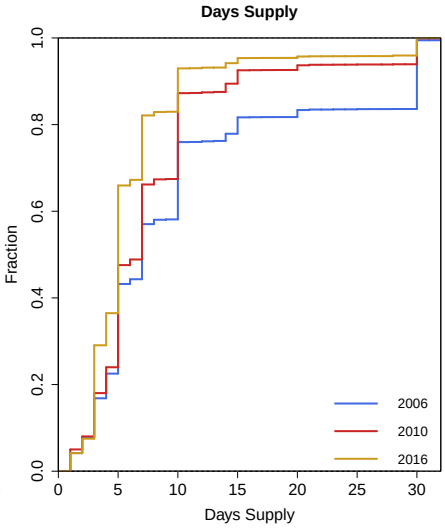
Empirical CDF of intensive margin of opioid prescriptions in ED





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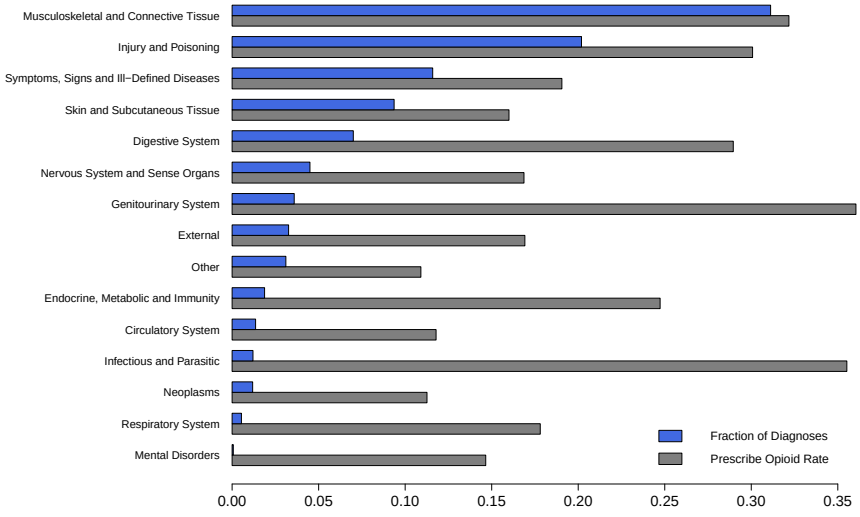
Diagnosis Categories in Emergency Departments



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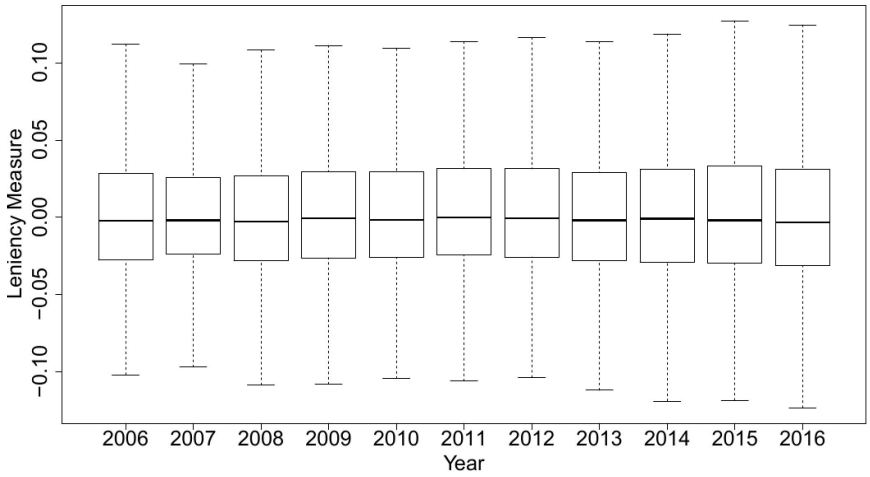
Annual Variation in Leniency Measure



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First Stage Table

	Dependent Variable: Prescribed in ED		
	(1)	(2)	(3)
Physician Leniency	1.691***	1.702***	1.710***
	(0.012)	(0.012)	(0.012)
Hospital, Seasonality, Shift FE?	Yes	Yes	Yes
Diagnosis and Elixhauser?	No	Yes	Yes
Patient Observables?	No	No	Yes
F-Stat	12	21	25
Observations:	1,958,209	1,958,209	1,958,209

Notes: Estimates of the first stage for the baseline sample described in the text. Hospital, seasonality, shift fixed effects include Hospital-Year-Month and Hospital-Day of week-Hour of day fixed effects. Elixhauser comorbidity is constructed with a 3-year look-back period, excluding the ED encounter. Patient observables include female, black, prior month opioid use, age bins, and log prior year total milligrams of morphine equivalent. Column 3 corresponds to the baseline controls. Robust standard errors are clustered at the physician level. * $p<0.1$; ** $p<0.05$; *** $p<0.01$

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Table 1: Average Characteristics of Physicians in the Top and Bottom Quartile of Leniency

	Lenient	Strict
Male	0.717	0.612
Age	47.4	46.1
Cases per year	929	789
Days worked per year	114	105
Patients per day	8.25	7.68

Notes: This table displays the simple mean of each variable for physician-years classified as lenient or strict. Lenient and strict are based on the top and bottom quartile of our leniency instrument measure each year. Only physician-years that treat at least 200 patients per year are included.

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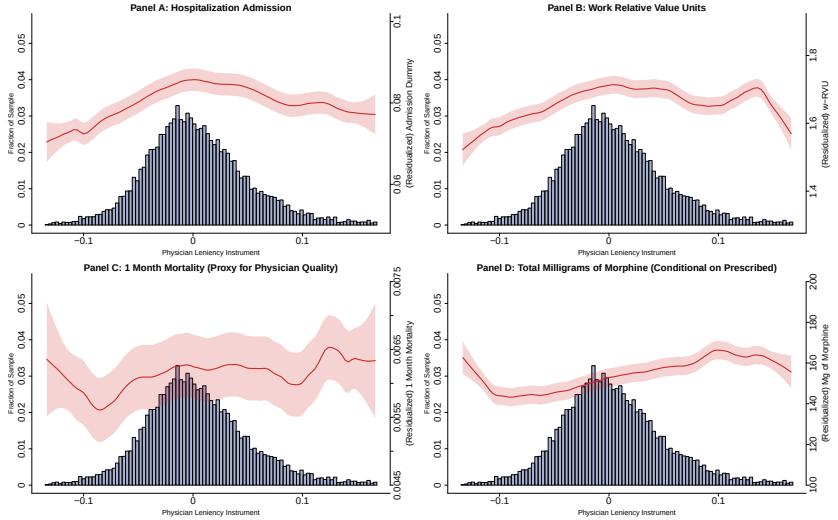
Who are lenient physicians? Cont.

Figure 1: First Stage of Baseline Physician Opioid-Prescribing Leniency Instrument on Other Dimensions of Physician Characteristics



Monotonicity

First Stage:	*Dependent variable:* Prescribed Opioid	
Subsample:	Baseline Leniency (1)	Reverse-Sample Leniency (2)
Male	1.696***	1.046***
	(0.012)	(0.014)
Female	1.758***	1.917***
	(0.027)	(0.035)
Black	1.836***	1.951***
	(0.02)	(0.028)
White	1.649***	1.378***
	(0.013)	(0.016)
Opioid-Naive	1.745***	1.524***
	(0.015)	(0.024)
Prior Users	1.584***	1.628***
	(0.016)	(0.024)
No Depression or PTSD	1.688***	1.608***
	(0.014)	(0.022)
Depression or PTSD	1.74***	1.839***
	(0.015)	(0.019)
Priority Groups 1-4	1.738***	1.851***
	(0.014)	(0.019)
Priority Groups 5-8	1.695***	1.733***
	(0.014)	(0.018)
Injury and Poisoning	1.714***	1.905***
	(0.028)	(0.039)
Musculoskeletal & Connective Tissue	2.267***	2.845***
	(0.023)	(0.043)
Digestive System	1.683***	1.807***
	(0.035)	(0.039)
Circulatory System	0.711***	0.746***
	(0.088)	(0.095)

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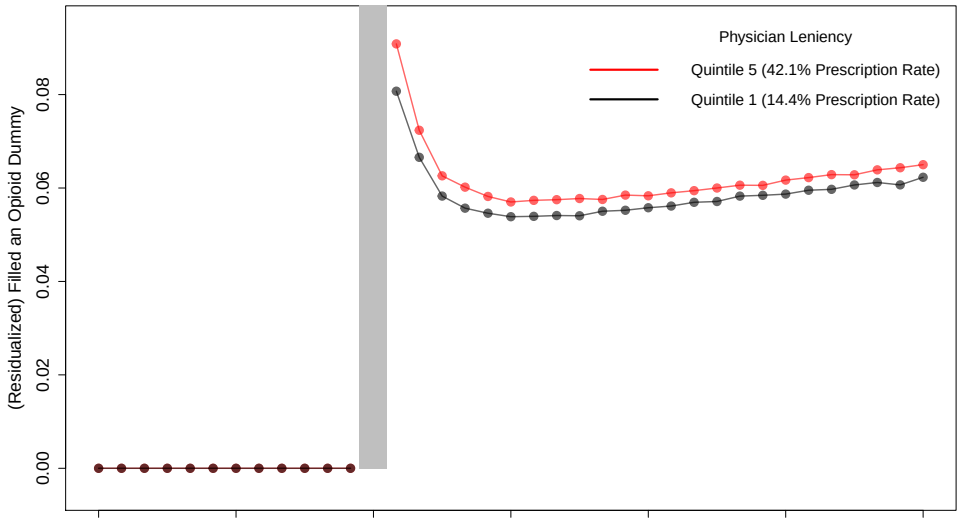
Sample: No observed opioids filled in the prior year



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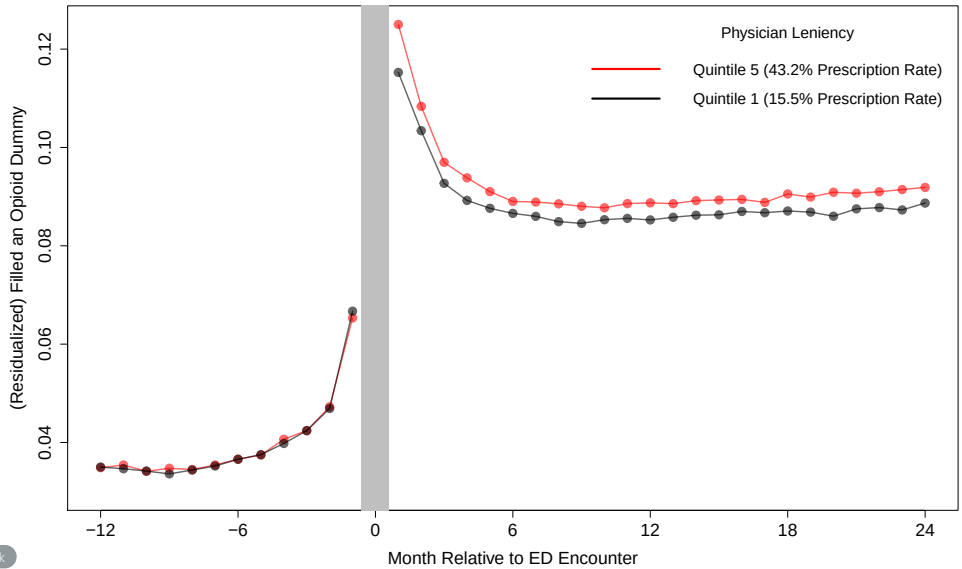
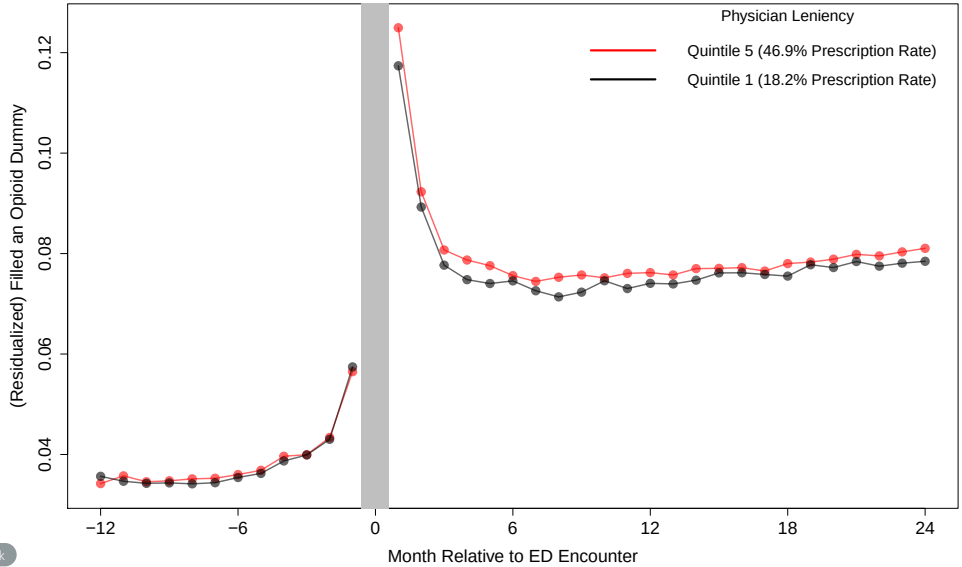
Sample: No ED visits in the prior year but did utilize some VHA care (NOT ED shopping)



Sample: ED Diagnosis of Injury and Poisoning



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Positive Urine Drug Screens

	Mean	OLS		2SLS		N=
Dependent Variable:	(1)	(2)	(3)	(4)	(5)	(6)
Positive Opioid Urine Drug Screen (×100)						
Year 2	25.6	4.37***	3.52***	1.94*	1.99**	273,115
		(0.21)	(0.21)	(1.03)	(1.00)	

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Complier Analysis

- We are identifying the LATE for those ptaients for whom their ED physician's leniency determined whether they received an opioid
- Can computer fraction and characteristics of compliers based on moments in the first stage (Abadie 2003; Dahl et al. 2014)
- 39% are compliers, 8% always-takers, and 53% never-takers
- Compared to the average ED patient, compliers are:
  - 1.8% more likely to be opioid-naive
  - 4.6% more likely to be between ages 40 and 60
  - 17% more likely to be diagnosed with musculoskeletal & connective tissue in the ED
  - 6.4% more likely to be above average risk of opioid overdose death (predicted with veteran demographics, prior medical morbidities, and opioid use)

Table 2: Heterogeneous Effects of a Single Opioid Prescription on Outcomes

	Heterogeneity Margin:							
	Opioid-Naïve?		PCP Leniency		Year		Gender	
	Naïve	Prior User	Lenient	Strict	2006-11	2012-16	Male	Female
Outcome:	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Long-Term Use	1.217***	1.328**	1.297***	0.762**	1.375***	0.979***	1.193***	1.050*
	(0.165)	(0.648)	(0.491)	(0.381)	(0.312)	(0.264)	(0.215)	(0.547)
p-value	0.964		0.445		0.414		0.791	
Opioid Use Disorder	0.150	0.943**	0.528*	0.247	0.450*	0.212	0.269	0.827**
	(0.169)	(0.374)	(0.320)	(0.280)	(0.232)	(0.222)	(0.171)	(0.364)
p-value	0.072		0.568		0.52		0.341	
Opioid Overdose Death	0.057	0.118	−0.098	0.185***	0.113*	0.032	0.069*	0.102
	(0.035)	(0.088)	(0.065)	(0.059)	(0.061)	(0.034)	(0.037)	(0.092)
p-value	0.811		0.011		0.362		0.828	
Hepatitis C	0.218	0.433	0.181	0.315	−0.109	0.687***	0.263	0.558
	(0.229)	(0.493)	(0.410)	(0.394)	(0.334)	(0.249)	(0.229)	(0.374)
p-value	0.732		0.839		0.097		0.712	
Observations	1,351,472	424,328	411,791	484,931	982,671	793,129	1,577,038	198,762

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Effect of Opioid on Outcomes by PCP Leniency for Opioid-Naïve Veterans

	Dependent variable (×100):								
	Long-Term Use	Overdose Year 0-1	Overdose Death	Fall Year 0-3	Depression Year 0-3	Suicide Year 0-3	Homeless Year 0-3	Hep C Year 0-3	N=
PCP Leniency									
Lenient	1.456***	−0.017	−0.063	0.657	2.781***	−0.265	1.429**	−0.122	307,656
	(0.426)	(0.088)	(0.077)	(0.553)	(1.001)	(0.259)	(0.647)	(0.492)	
Strict	1.276***	0.125	0.089	0.295	−0.438	0.141	0.917	0.583	376,295
	(0.335)	(0.077)	(0.062)	(0.506)	(0.996)	(0.222)	(0.668)	(0.454)	

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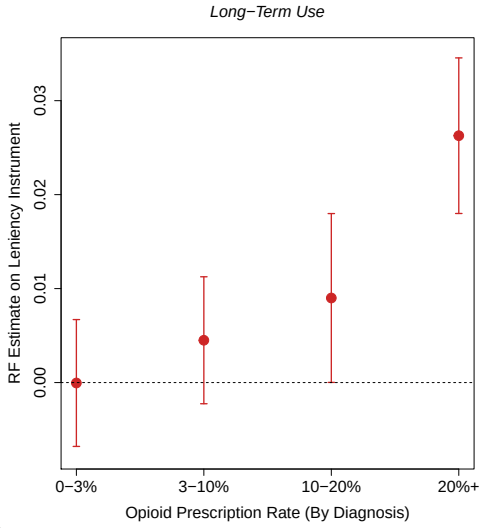
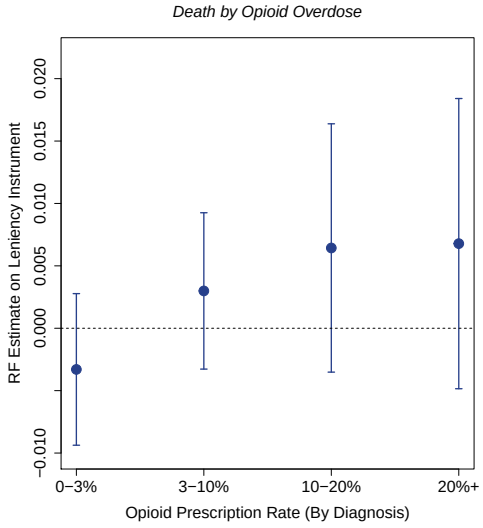
Exclusion: Prescribing leniency has no effect on diagnoses that are never prescribed





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ED Condition: Injuries and Poisonings

	Dependent variable (×100):								
	Long-Term Use	OUD Year 0-1	Overdose Year 0-1	Overdose Death	Fall Year 0-3	Depression Year 0-3	Suicide Year 0-3	Homeless Year 0-3	Hep C Year 0-3
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Prescribed	1.438***	0.149	0.179**	0.031	0.575	0.543	−0.209	−1.370**	0.788*
	(0.391)	(0.240)	(0.087)	(0.070)	(0.589)	(0.957)	(0.261)	(0.632)	(0.422)
N=	382,034	382,034	382,034	373,178	361,090	361,090	361,090	361,090	361,090

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Bounds on Black Market vs. Legal Market Mortality Rates

Goal: Conditional on being a long-term user (or have overdosed) in the unobserved black market, what is the probability you ultimately die from an opioid overdose, relative to the observed legal market?

Lower bound: Assume that unobserved black market mortality probability are at least as high as patients observed in the legal market

Upper bound:

- We can approximate long-term use and opioid overdose with presence of opioid substance use disorder (SUD). Then we can estimate:

$$\frac{\text{\# Overdose deaths for black market SUD patients}}{\text{\# black market SUD patients}} \Big/ \frac{\text{\# Overdose deaths for legal market SUD patients}}{\text{\# legal market SUD patients}}$$

- Assume all black market use is heroin use and legal market use is prescription opioids $\implies$ upper bound
- Assume heroin users only die from heroin and prescription users die from prescription $\implies$ upper bound
- Assume death/user counts are growing at constant rate, allowing us to estimate deaths with CDC death counts and SUD patients with NDSUH use estimates

$\implies$ 2017 estimates: $\frac{28{,}466}{652{,}000} \Big/ \frac{17{,}762}{1{,}458{,}000} = 3.58$

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