Drivers of the Fatal Drug Epidemic

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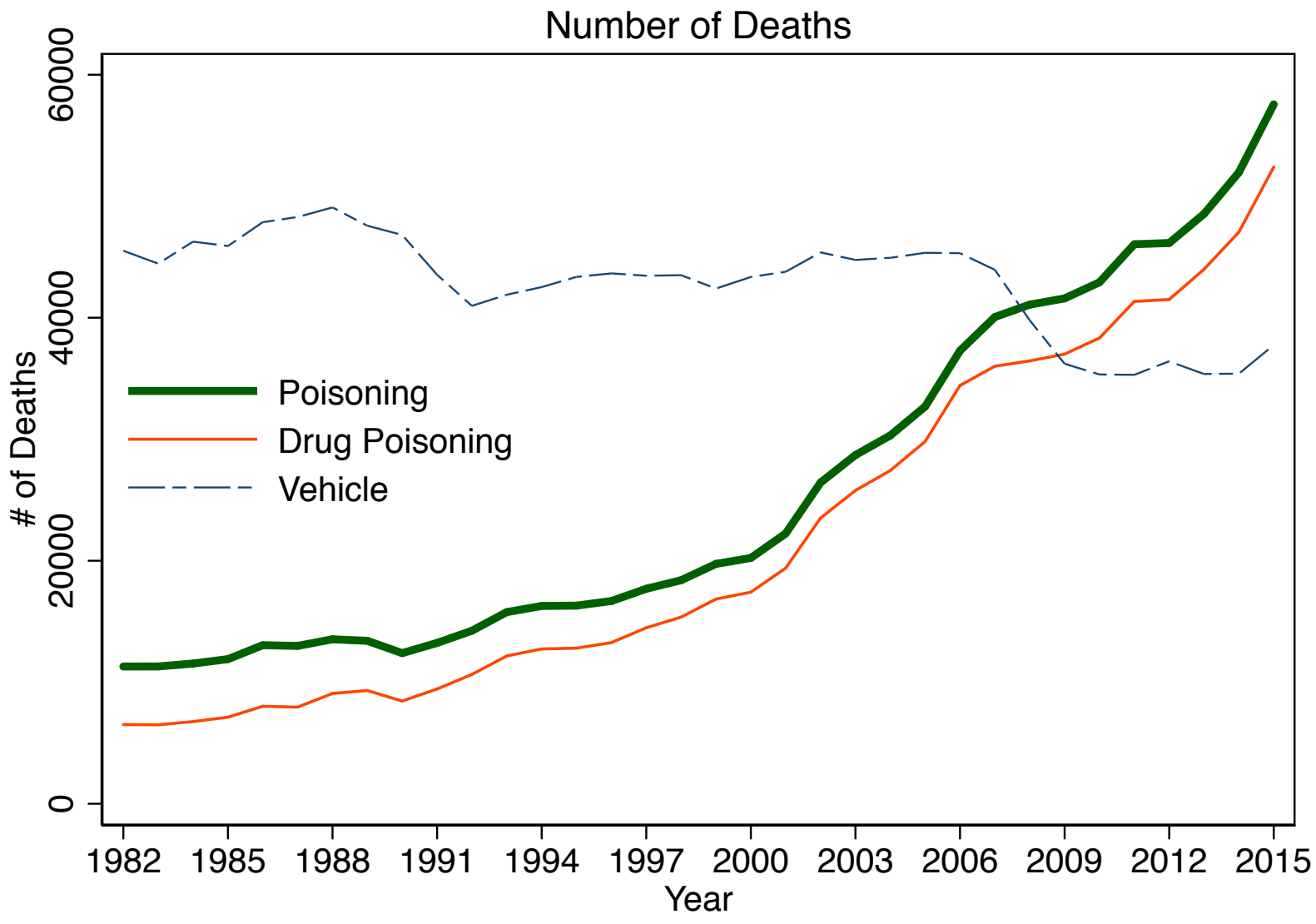
Why Study Fatal Overdoses?



Background

- Deaths from Overdoses
  - 1999: 16,849
  - 2016: 63,632
- Drugs Involved
  - Initially opioid analgesics (often with other drugs)
  - Rising role for heroin after 2006 (& particularly after 2009)
  - & Fentanyl after 2012

Background

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- Drugs Involved
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  - Rising role for heroin after 2006 (& particularly after 2009)
  - & Fentanyl after 2012
- Drug overdoses most important cause of declining life expectancy among mid-life whites
  - Case & Deaton (2015) emphasize 45-54 year olds
  - But effects are: concentrated among females
  - & found at younger ages
- Suicides & alcoholic liver disease also play a role

Prior Economic Research

- Transitory Economic Fluctuations: Arkes (2007), Ruhm (2015), Carpenter et al (2017), Hollingsworth et al. (2017)
- Medical Marijuana: Powell et al (2015), Chu (2015), Bradford & Bradford (2016), Ozluk (2017)
- Abuse-deterrent Drug Formulations: Alpert et al (2017), Evans et al (2017)
- Naloxone Availability: Rees et al (2017), Doleac & Mukherjee (2017)
- Medicare Part D: Powell et al (2015)
- Availability of Substance Abuse Treatment: Swensen (2015)
- Advertising: Anderson (2010)
- Physician Market Structure: Bradford (2017)
- State Drug Policies: Dowell et a (2016), Meinhofer (2016), Dave et al (2017), Buchmueller & Cary (2018)

- But specific policies or factors explain at most a small part of increase

"Deaths of Despair" (Case & Deaton)

- Seems consistent with overdose patterns
  - Big increases in Appalacia, Rust Belt
  - Largest growth for less educated
- But high rates in other areas as well (e.g. NH, MA) & relationships could be spurious ▸ Map

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- But high rates in other areas as well (e.g. NH, MA) & relationships could be spurious ▸ Map
- Poorly Defined
  - Result from long-run declines in economic & social conditions?
  - Why aren't larger effects seen for blacks, midlife individuals in other countries

This Project

- Δ in county economic conditions as explanation for Δ in drug death rates?
  - Explained Δ in death rates as % of total Δ
  - Potentially important "demand-side" factor
  - Also examine idrug, suicide & alcohol (DSA) mortality
  - Multiple proxies for underlying latent variable
  - Selection on Unobservables

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  - Potentially important "demand-side" factor
  - Also examine idrug, suicide & alcohol (DSA) mortality
  - Multiple proxies for underlying latent variable
  - Selection on Unobservables
- Alternative Hypothesis: changes in *drug environment* are of key importance (supply-side)
  - Some groups more vulnerable than others
  - Relative risk changes with "drug environment
  - "Effects" identified by changes in drug environment occurring over analysis period

Results So Far

- Economic conditions have limited explanatory power
  - Explain $< 1/10$ of 1999-2015 Δ in drug death rates (probably much less)
  - Virtually none of Δ in nondrug DSA death rates explained

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  - Explain $< 1/10$ of 1999-2015 Δ in drug death rates (probably much less)
  - Virtually none of Δ in nondrug DSA death rates explained
- Drug environment probably more important
  - Initial period (1999-2010)
    1. Prescription opioids dominate
    2. Relative mortality risk $\uparrow$ for women, older adults
  - Later period (2011-2015)
    1. Illicit opioids dominate
    2. Relative mortality risk $\uparrow$ for men, younger adults

Basic Approach: Economic Conditions Analysis

- County-level analysis
- Mortality data from Multiple Cause of Death (*MCOD*) Files
  - All Drugs: ICD-10 codes: X40-44, X60-64, X85, Y10-14, Y352
  - Opioid Analgesics: T-Code 40.2
  - Illicit Opioids: T-Code 40.1, 40.4
  - Nondrug Suicides: ICD-10 codes: X65-X84, Y87.0, *U03
  - Alcoholic Liver Disease: ICD-10 code: K70
  - Opioid involvement adjusted for incomplete reporting on death certificates

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- Population data from Surveillance Epidemiology End Results System (*SEER*)
- Many other data sources used
- Focus on mortality changes from 1999-2015
  - Subperiods used in some analyses
  - Also examine population subgroups

Model & Methods

$$M_{kt} = E_{kt} b + X_{kt} c_t \tag{1}$$

- M_{kt} = Mortality rate , county k, time t, $t = [0, 1]$
  - E= $\geq$1 proxy for Δ in economic conditions
  - X= additional covariates

$$\Delta M_k = M_{k1} - M_{k0} = \Delta E_k b + X_{k0} \Delta c + \Delta X_k c_1 \tag{2}$$

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Regression analog to (2)

$$\Delta M_k = \Delta E_k \beta + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \varepsilon_k \tag{3}$$

- $\hat{\beta}$ is of key interest
- Problem including ΔX_k if caused by ΔE_k
- So estimate models with actual & "instrumented" ΔX_k
- "Instrumented" changes, ΔX_k^I based on census division (rather than county) changes ▸ instrument

Methods (cont.)

$$\Delta M_k = \Delta E_k \beta + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \varepsilon_k$$

- ΔE_k, X_{k0}, ΔX standardized to $\mu = 0$, $\sigma = 1$
- Coefficients indicate "effect sizes" (of 1 sd Δ in regressor)

$$\%\ of\ \Delta M\ Explained\ = \frac{\hat{\beta}}{\sigma_M} \tag{4}$$

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- Observations weighted by 2015 county populations
- Standard errors
  - MP Estimates: Bootstrapped (1000 replications)
  - Other Covariates: robust, clustered by commuter zone

Multiple Proxy Estimates

$$\Delta M_k = \Delta E_k \beta + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \varepsilon_k$$

- ΔE_k is a vector of proxy variables
- Several issues arise
  - Proxies capture difference components of economic conditions
  - But probably correlated
  - How to aggregate "effects"
- Lubotsky-Wittenberg (2006) method: optimal weighting of coefficients to minimize attenuation bias

▸ LW method

Incomplete Drug Reporting on Death Certificates

- Drugs unspecified (ICD-code T-50.9) on 1/5 to 1/4 of death certificates
- Two-stage correction procedure used
- Year-specific probit model for deaths with specified drug involvement
  - Dependent variable indicates specific drug involvement
  - Explanatory variables: sex, race/ethnicity, marital status, education, age, location & day-of-week of death, census region
- Probit model gives prediction equation
- Apply predicted drug involvement where not specified

Selection on Unobservables (Oster, 2016)

- "Short" Regression: $\Delta M_k = \Delta \mathbf{E_k} \beta + \lambda_k$
  - β^o, R^o are regression coefficient & R^2 from short regression
- "Long" Regression: $\Delta M_k = \Delta \mathbf{E_k} \beta + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \varepsilon_k$
  - $\tilde{\beta}$, $\tilde{R}$ are regression coefficient & R^2 from long regression
- Omitted variables bias often assumed small if $\tilde{\beta}$ similar to β^o
- But (probably) not true if: $\tilde{R}$ similar to R^o

Selection on Unobservables (Oster, 2016)

- β^o, R^o are regression coefficient & R^2 from short regression
- $\tilde{\beta}$, $\tilde{R}$ are regression coefficient & R^2 from long regression
- Selection-adjusted treatment effect β^* computed using β^o, R^o, $\tilde{\beta}$, $\tilde{R}$ & assumed values of δ & R_{max}
  - R_{max} is R^2 from hypothetical regression capturing all determinants of M

    ($R_{max} < 1$ if measurement error in M)
  - δ : relative importance of selection on observables & unobservables

    $\delta = 1$: observables & unobservables equally important

    $\delta < 1$: observables more important
- Assumptions: $\delta = 0.5$, $R_{max} = 0.75$
- Also calculate δ^*, R^*_{max} giving zero treatment effect

▸ Oster

Robustness Checks

- 1990-2000 vs. 1999-2015 Δ in economic conditions
  - EP ratios rather than unemployment rates as proxy
  - 1999 levels rather than 1999-2015 changes
- Unweighted vs. Weighted estimates
- Unadjusted vs. Adjusted mortality rates
- IV (GMM) rather than LW estimates
- Different starting/ending years & sub-periods
- Population subgroups, rural vs. urban locations
- Alternative definitions of suicides, alcohol-related deaths

Dependent Variables

Δ in Drug Death Rates per 100,000 (2015 vs. 1999)	Mean	SD
All Drugs	10.37	9.06
Opioid Analgesics	3.58	4.22
Illicit Opioids	6.27	6.67
Drug, Suicide, Alcohol (DSA)	15.39	12.38
Nondrug DSA	5.02	7.35
Nondrug Suicide	2.76	5.67
Alcohol	2.26	4.21

Economic Proxies

Δ 2015 vs. 1999	Mean	SD
Poverty Rate (3-year average ending in 1999 or 2015)	**2.93**	**2.47**
Median Household Income, 2015$ (3-year average ending in 1999 or 2015)	**-2,817**	**5,586**
Median Home Price, 2015$ %Δ (2011-2015 average vs. 2000)	**17.85**	**22.31**
Unemployment Rate (3-year average ending in 1999 or 2015)	**1.77**	**1.56**
Instrumented Import Employment Share (2011 vs. 1999)	**1.57**	**2.03**

Population Shares (1999 & 2015)

Females

Hispanics

Non-Hispanic Blacks

Other Race (Non-Hispanics)

15-24 Year Olds

24-34 Year Olds

34-44 Year Olds

44-54 Year Olds

54-64 Year Olds

64-74 Year Olds

≥ 75 Year Olds

Some College (≥25 years old)

College Graduate (≥25 years old)

Female-headed Household (2000, 2010)

Foreign born (2000, 2011-2015)

Other Covariates (1999 & 2015)

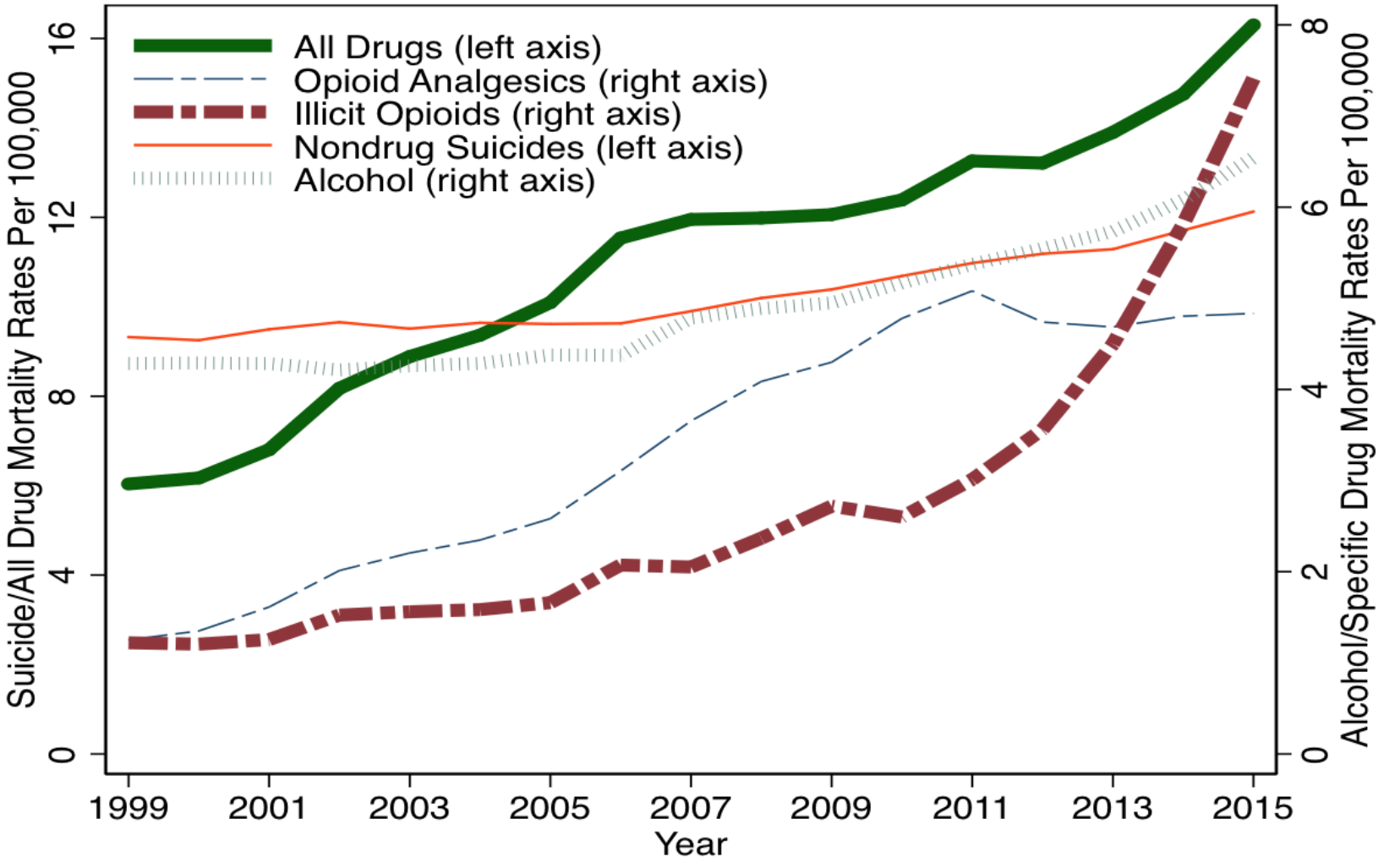
Medical/Policy Variables

- Active Nonfederal MD's per 1000
- Hospital beds per 1000
- State Law Legalizing Marijuana for Medical or Recreational Uses
- State Prescription Drug Monitoring Program

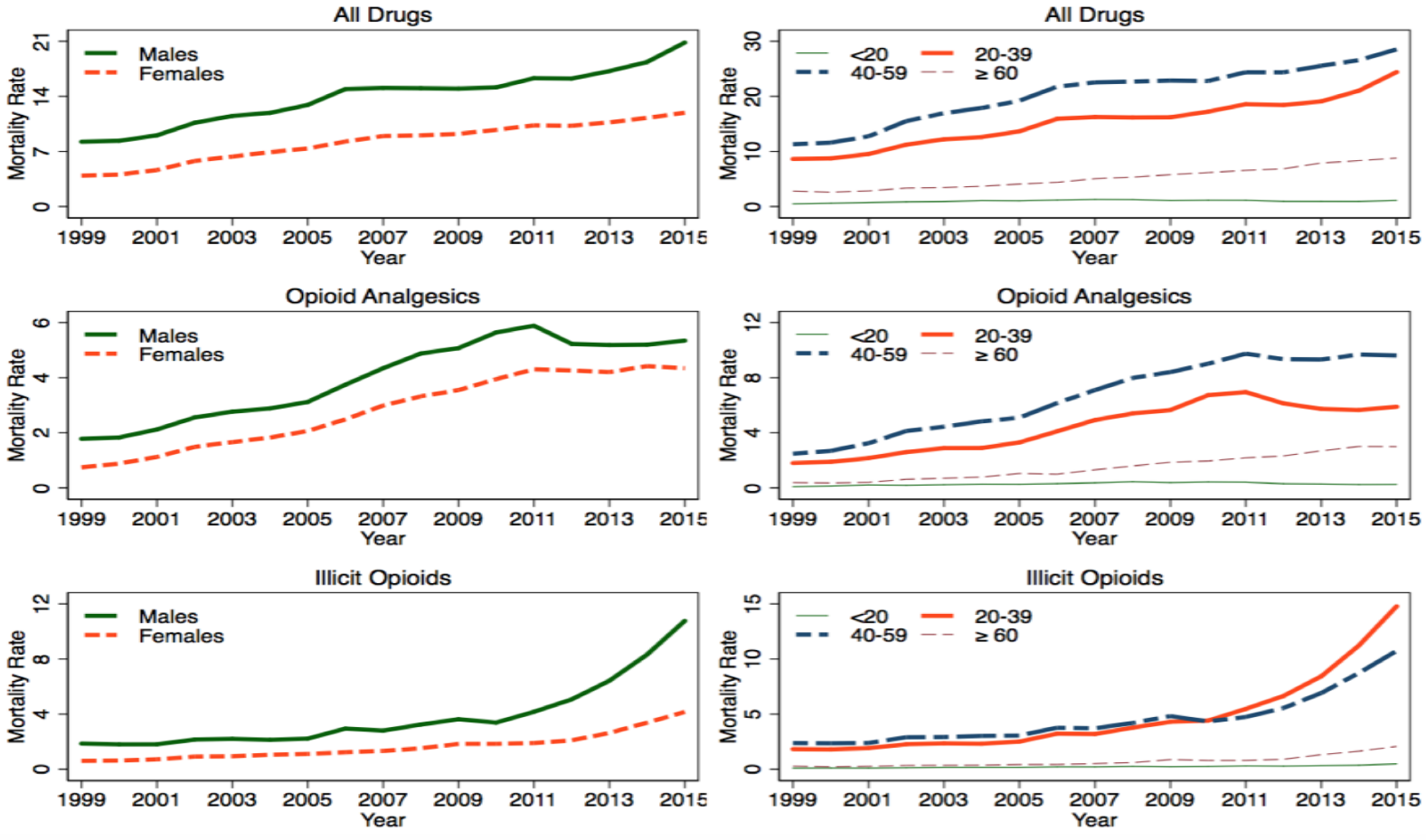
Urban-Rural Status Share (2013)

- Metropolitan Area: Population 250,000 - 999,999
- Metropolitan Area: Population <250,000
- Urban Area: Population ≥20,000, adjacent to metropolitan area
- Urban Area: Population ≥20,000, not adjacent to metro area
- Urban Area: Population 2,500 - 19,999, adjacent to metro area
- Urban Area: Population 2,500 - 19,999, not adjacent to metro area
- Rural Area: Population <2,500, adjacent to metro area
- Rural Area: Population <2,500, not adjacent to metro area

Mortality Rate Trends

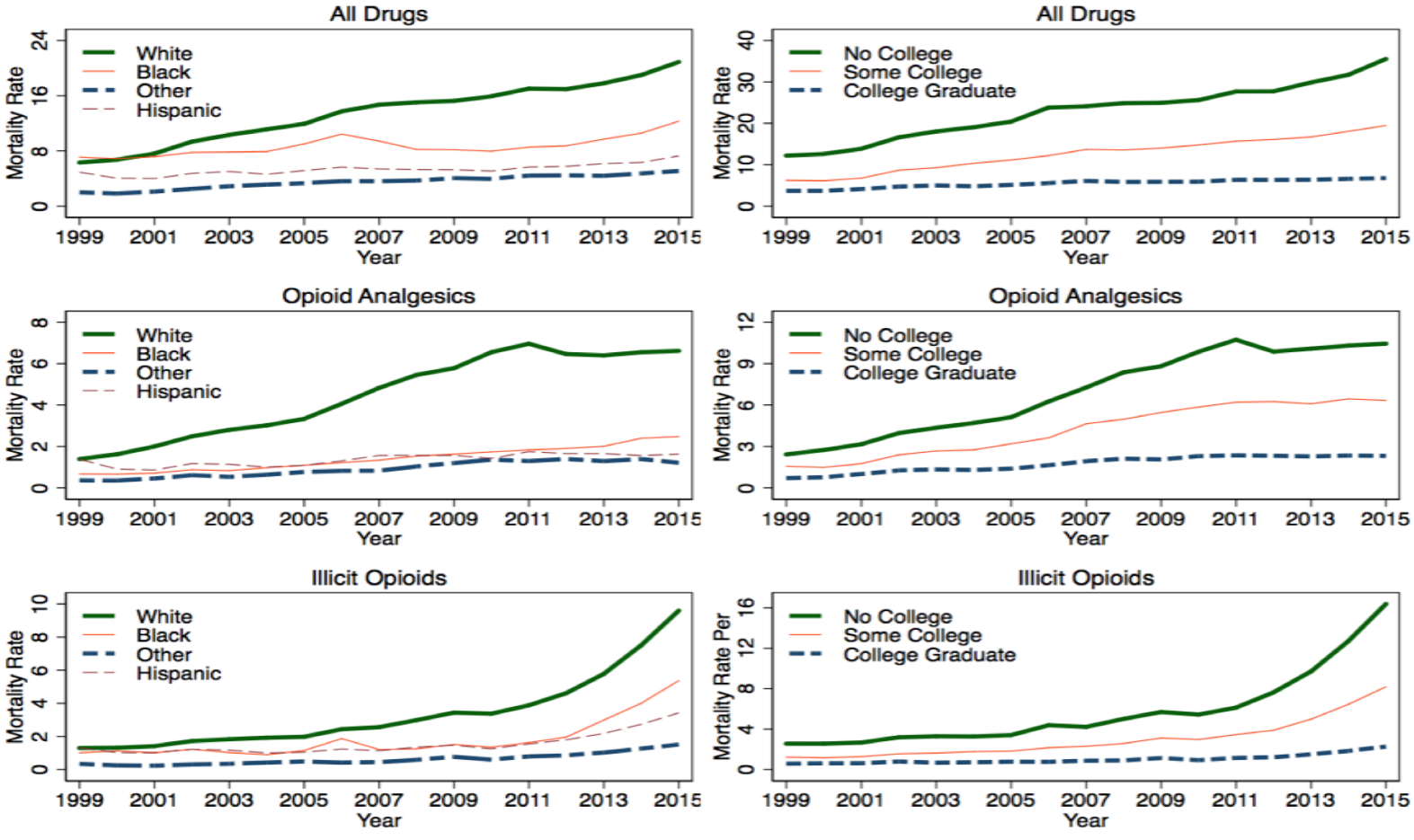


Drug Mortality Rates by Sex & Age



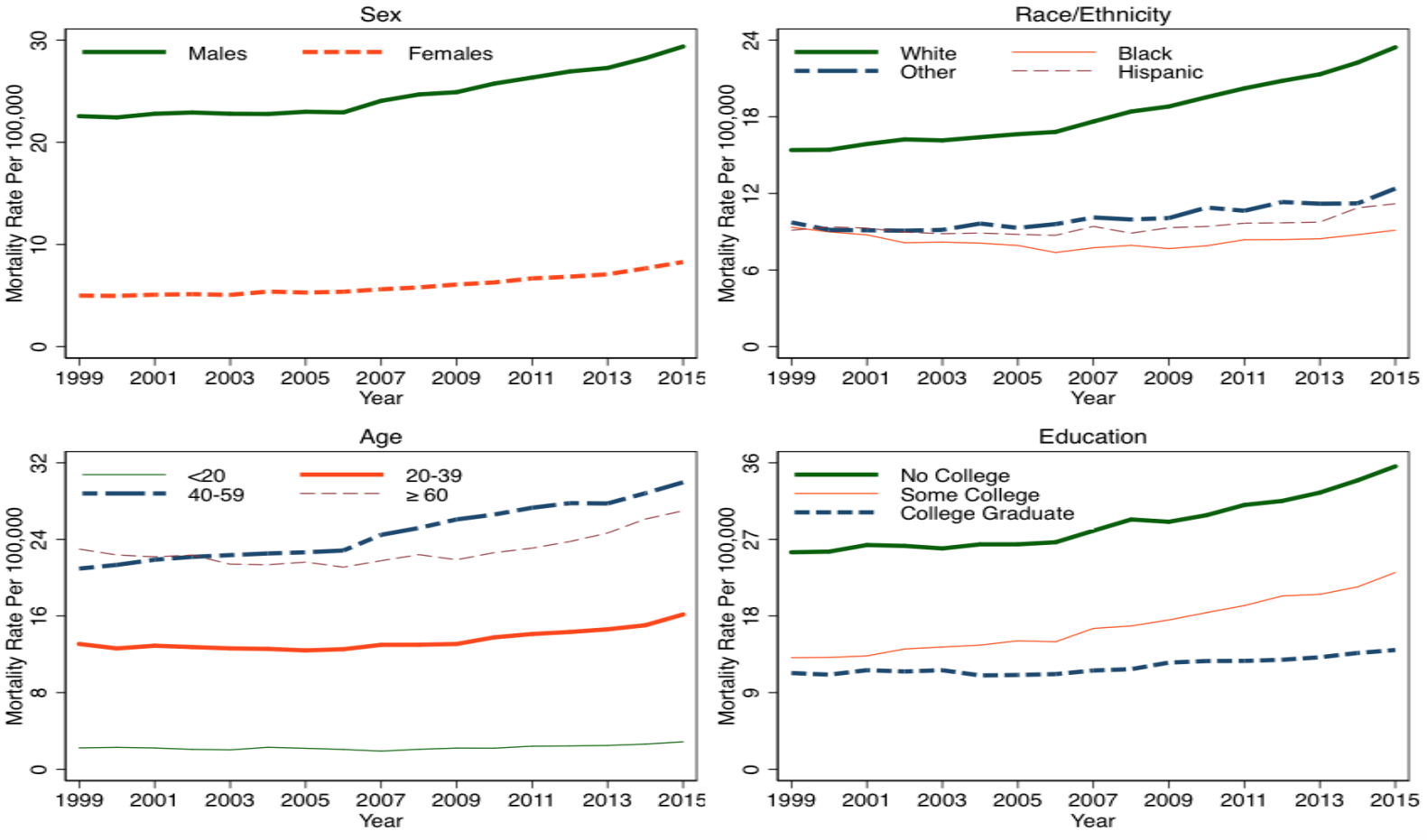
age & sex patterns vary by drug type

Drug Mortality Rates by Race/Ethnicity & Education



- $>$ for whites, less educated

Nondrug DSA Mortality Rates



- much $>$ for males, more concentrated on older groups

Δ in 1999-2015 Death Rates: No Extra Controls

Economic Proxy	All Drugs	Opioid Analgesics	Illicit Opioids	DSA
Proxies Included Separately				
Poverty Rate Δ	2.205***	0.798***	1.334***	2.320***
	(0.560)	(0.242)	(0.446)	(0.752)
Med HH Income Δ	2.068***	0.679***	1.136**	2.515***
	(0.546)	(0.254)	(0.496)	(0.773)
Med Home Price Δ	2.289***	0.908**	1.158*	2.840***
	(0.649)	(0.354)	(0.627)	(0.680)
Unemp Rate Δ	1.370***	0.295**	1.069***	1.144
	(0.464)	(0.131)	(0.253)	(0.765)
Import Exposure Δ	0.572	0.398**	0.168	0.570
	(0.414)	(0.182)	(0.328)	(0.511)
Dep. Var. Mean [SD]	10.37	3.58	6.27	15.39
	[9.06]	[4.22]	[6.67]	[12.38]

- Income, Home Price changes "reverse coded"
- Positive coefficient $\Longrightarrow$ worse econ. conditions, mortality $\uparrow$ (except suicide/alcohol)

Δ in Various Death Rates: No Extra Controls

	All Drugs	Opioid Analgesics	Illicit Opioids	DSA
Multiple Proxy Estimate	2.949*** (0.798)	1.164*** (0.239)	1.710*** (0.428)	3.256 (2.395)
Dep. Var. SD	9.06	4.22	6.67	12.38
% Δ Explained	32.5%	27.6%	25.6%	26.3%
R^2	0.082	0.059	0.051	0.060

Proxy effects weaker than when entered individually (correlated)

▸ Correlations

But MP estimates stronger than individual econ. conditions

▸ Additional Coefficients

Δ in Drug Death Rates, Various Controls

Economic Proxy	(a)	(b)	(c)
Multiple Proxy Estimate	2.949***	0.431	0.792*
% of Total Δ Explained	32.5%	4.8%	8.7%
R^2	0.083	0.431	0.441
P-Value	<0.001	0.496	0.003
Additional Controls	None	X_{1999}, ΔX	X_{1999}, ΔX^I

- Adding covariates attenuates proxy coefficients (confounding)
- More so when ΔX than ΔX^I controls included
- % Explained attenuated 73%-85% by inclusion of controls
- Important confounding factors: sex, race/ethnicity, % foreign-born

▸ Additional Coefficients

Various Death Rates: % Δ Explained

	(a)	(b)	(c)
All Drugs			
P-Value	<0.001	0.496	0.003
Multiple Proxy Estimate	2.949***	0.431	0.792*
% of Total Δ Explained	32.5%	4.8%	8.7%
Opioid Analgesics			
P-Value	0.001	0.695	0.037
Multiple Proxy Estimate	1.164***	0.197	0.306*
% of Total Δ Explained	27.6%	4.7%	7.3%
Illicit Opioids			
P-Value	<0.001	0.373	0.289
Multiple Proxy Estimate	1.710***	0.305	-0.101
% of Total Δ Explained	25.6%	4.6%	-1.5%
DSA			
P-Value	<0.001	0.604	0.106
Multiple Proxy Estimate	3.256	-0.343	0.351
% of Total Δ Explained	26.3%	-2.8%	2.8%
Additional Controls	None	X_{1999}, ΔX	X_{1999}, ΔX^{I}

- Supplementary covariates attenuate MP estimates: 73%-100% for fatal overdoses

Robustness Checks

- Unweighted observations, unadjusted mortality rates, 1990-2000 Δ in economic conditions ▸ Estimates
- Different start/end year ▸ Estimates
- IV (GMM) estimates ▸ Estimates
- Sub-Periods ▸ Estimates
- Population subgroups ▸ Estimates
- Rural vs. urban locations ▸ Estimates
  - $>$ Δ death rates explained in metropolitan than rural counties

Selection on Unobservables

Type of Drug/ Covariates	Unadjusted Estimate	Adjusted Estimates δ=0.5, R_{max}=0.75 β^*	% of Δ Explained	δ^*	R^*_{max}
All Drugs					
X_{1999}, ΔX	0.431	-0.720	-7.9%	0.187	0.551
X_{1999}, ΔX^I	0.792	-0.135	-1.5%	0.427	0.705
Opioid Analgesics					
X_{1999}, ΔX	0.197	-0.551	-13.1%	0.132	0.441
X_{1999}, ΔX^I	0.306	-0.210	-5.0%	0.297	0.597
Illicit Opioids					
X_{1999}, ΔX	0.305	-0.148	-2.2%	0.336	0.660
X_{1999}, ΔX^I	-0.101	-0.519	-7.8%	<0.00	$< \tilde{R}$
DSA					
X_{1999}, ΔX	-0.343	-2.159	-17.4%	<0.00	$< \tilde{R}$
X_{1999}, ΔX^I	0.351	-1.164	-9.4%	0.116	0.479

- Treatment effect eliminated with limited remaining confounding

Drug Environment Hypothesis: Approach

- Drug use & risks changed dramatically over analysis period
- Demand-side causes unlikely to predict corresponding Δ in composition & risk of deaths
  - Persons self-medicating for despair switch to more readily available drugs

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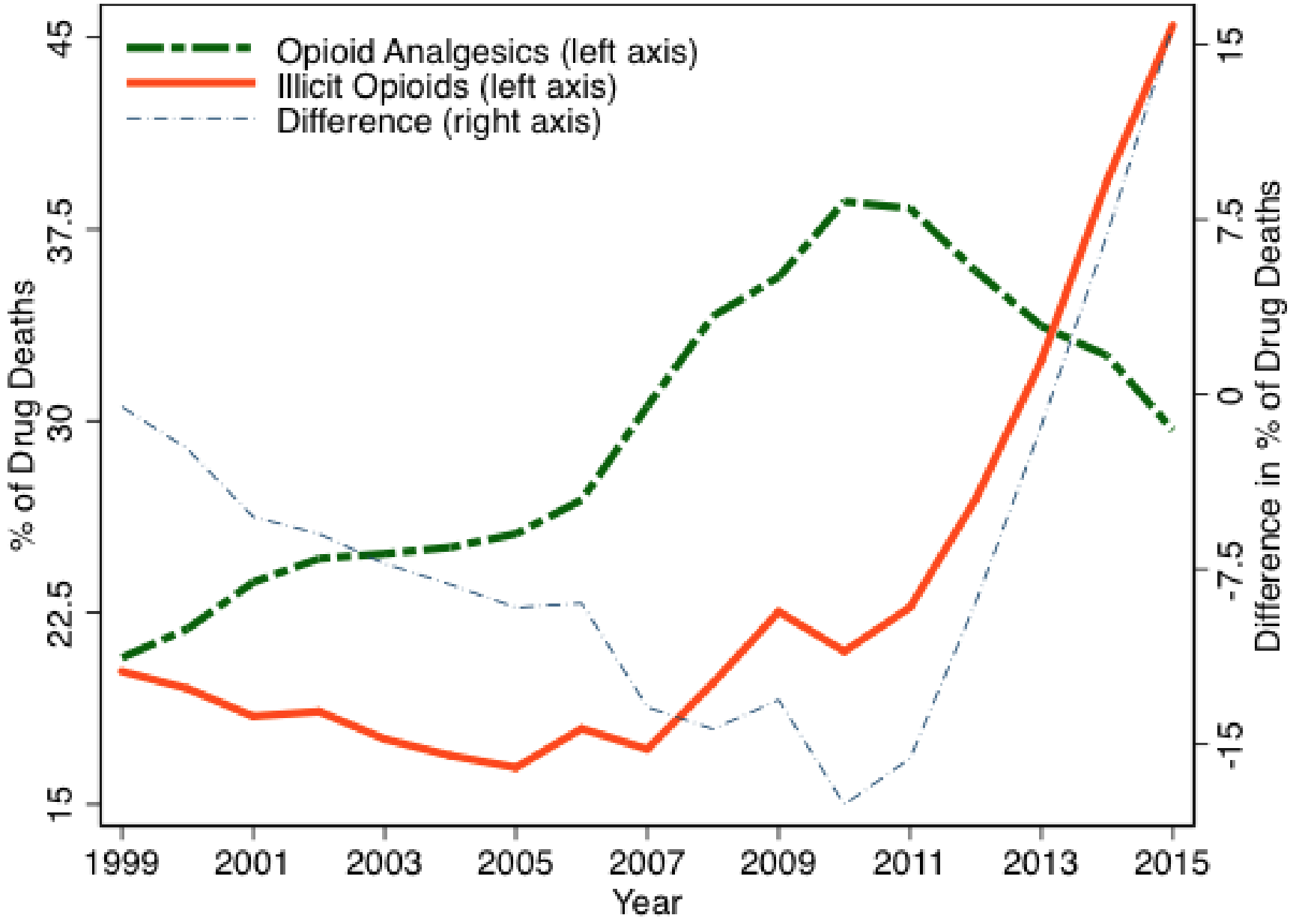
  - Persons self-medicating for despair switch to more readily available drugs
- Drug environment hypothesis predicts shifts in share/risk of death as supply & price change
  - Younger adults & men relatively likely to use illicit drugs
  - Older adults & women more often use legal drugs

% Drug Deaths by Opioid Type



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- Drug environment hypothesis predicts shifts in share/risk of death as supply & price change
  - Younger adults & men relatively likely to use illicit drugs
  - Older adults & women more often use legal drugs
- Expect death share/rate: older adults & women$\uparrow$ (or not $\downarrow$) from 1999-2010
- Expect death share/rate: younger adults & men $\uparrow$ after 2011
- Additional information from other drug categories ▸ Mortality Rates

Methods

$$S_{gkt} = X_{kt}\beta + F_k\kappa + T_t\tau + \omega_{gkt} \tag{5}$$

- Panel data model estimated here
- S_{gkt} = Mortality share: group g, county k, time t
- F_k = County fixed-effect
- T_t = General year effect
- $\hat{\tau}$= secular change in drug deaths by population group
  - could be drug environment or other time-varying factors
  - but sharp breaks/reversals probably indicate Δ in drug environment

Test of Trend Breaks

$$S_{gkt} = X_{kt}\beta + F_k\kappa + Trend_t\phi + Post_t\pi + \omega_{gkt} \quad (6)$$

- *Trend* = linear trend (0 in 1999, 16 in 2015)
- *Post* = trend spline: 0 in initial sample years, 1, 2, etc. after break/reversal (e.g. >2010)
- $\hat{\phi}$ = trend in deaths for group g from 1999-2010
- $\hat{\phi} + \hat{\pi}$ = group-specific trend after 2010

Relative Δ in group-specific mortality rates

- Changes relative to a reference group (e.g. males vs. females)

$$M_{gkt} = F_k\kappa + T_t\tau + (T_t \times G_g)\theta + \zeta_{gkt} \tag{7}$$

- Observations for $\geq$2 population groups in each year
- $\hat{\theta}$ shows relative treatment vs. control group mortality rate differences for year t
- Also estimate trend-spline model

$$M_{gkt} = F_k\kappa + T_t\tau + Trend_{gt}\phi + Post_{gt}\pi + \zeta_{gkt} \tag{8}$$

- $\hat{\tau}$ = reference group time effect
- $\hat{\phi}$ = initial treatment group mortality rate trend differential
- $\hat{\phi} + \hat{\pi}$ = differential in later periods

Other Changes

- Year & county fixed-effects reduce need for supplementary covariates
- & annual data lacking for some of them
  - unemployment & poverty rates, median incomes controlled for
  - results not sensitive to inclusion of other controls
  - effects subsumed in year coefficients for treatment vs. control group comparisons

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  - results not sensitive to inclusion of other controls
  - effects subsumed in year coefficients for treatment vs. control group comparisons
- Separate estimates by sex & age (20-39 vs. 40-59)
- Standard errors clustered by county

Overall Drug Deaths as Proxy for Drug Environment

- Abrupt mortality increases almost certainly reflect supply-side factors
  - No reason to expect sudden changes in demand
  - (Not true for gradual trends)
- County opioid analgesic mortality rates regressed on MME per capita (from ARCOS)
  - higher opioid analgesic prescriptions "explain" 85% of rise in associated deaths from 2000-2011

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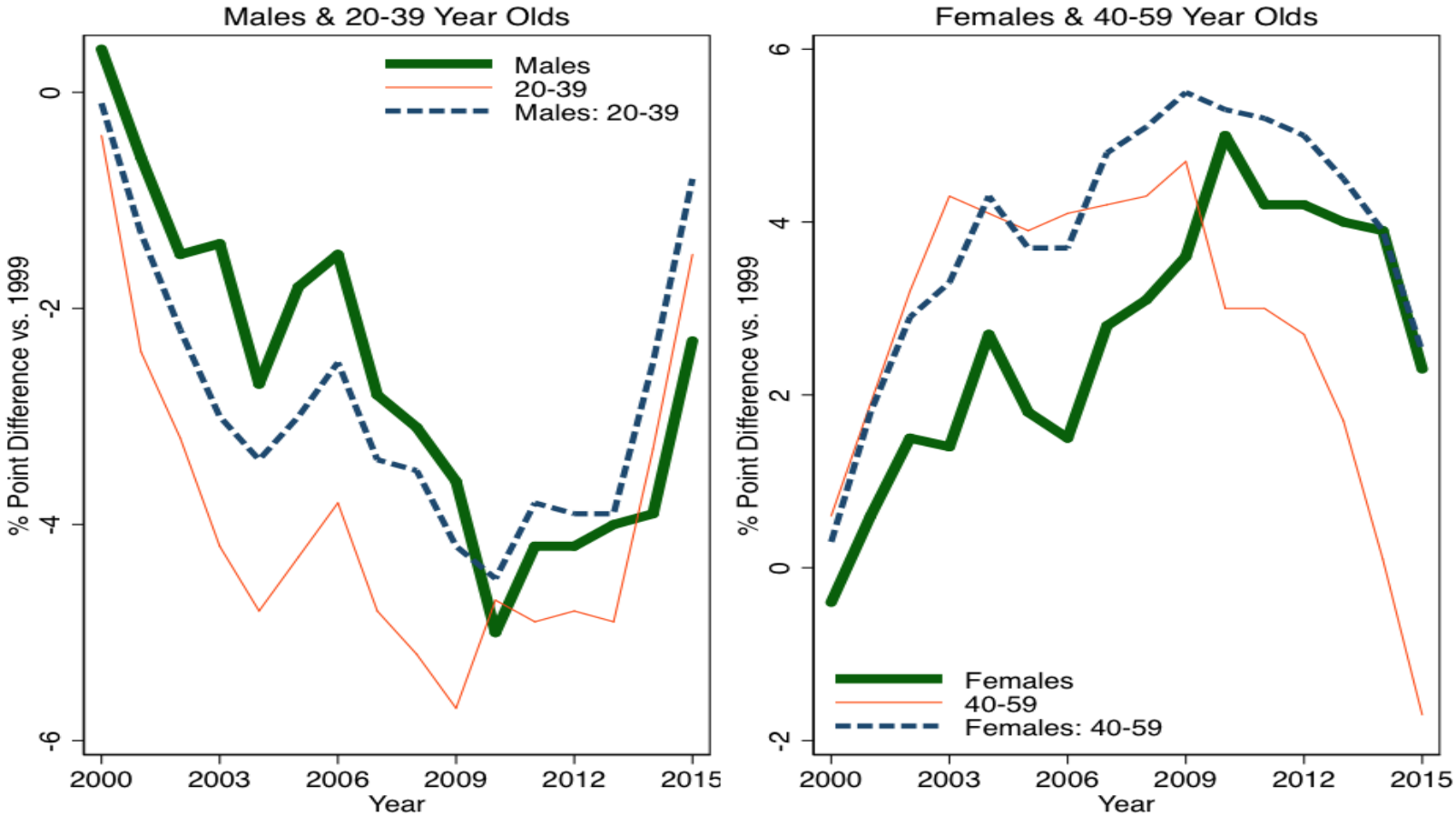
- County opioid analgesic mortality rates regressed on MME per capita (from ARCOS)
  - higher opioid analgesic prescriptions "explain" 85% of rise in associated deaths from 2000-2011
- Past year heroin use trends line up with fatal heroin overdoses
- Fentanyl reports also mirror patterns of death

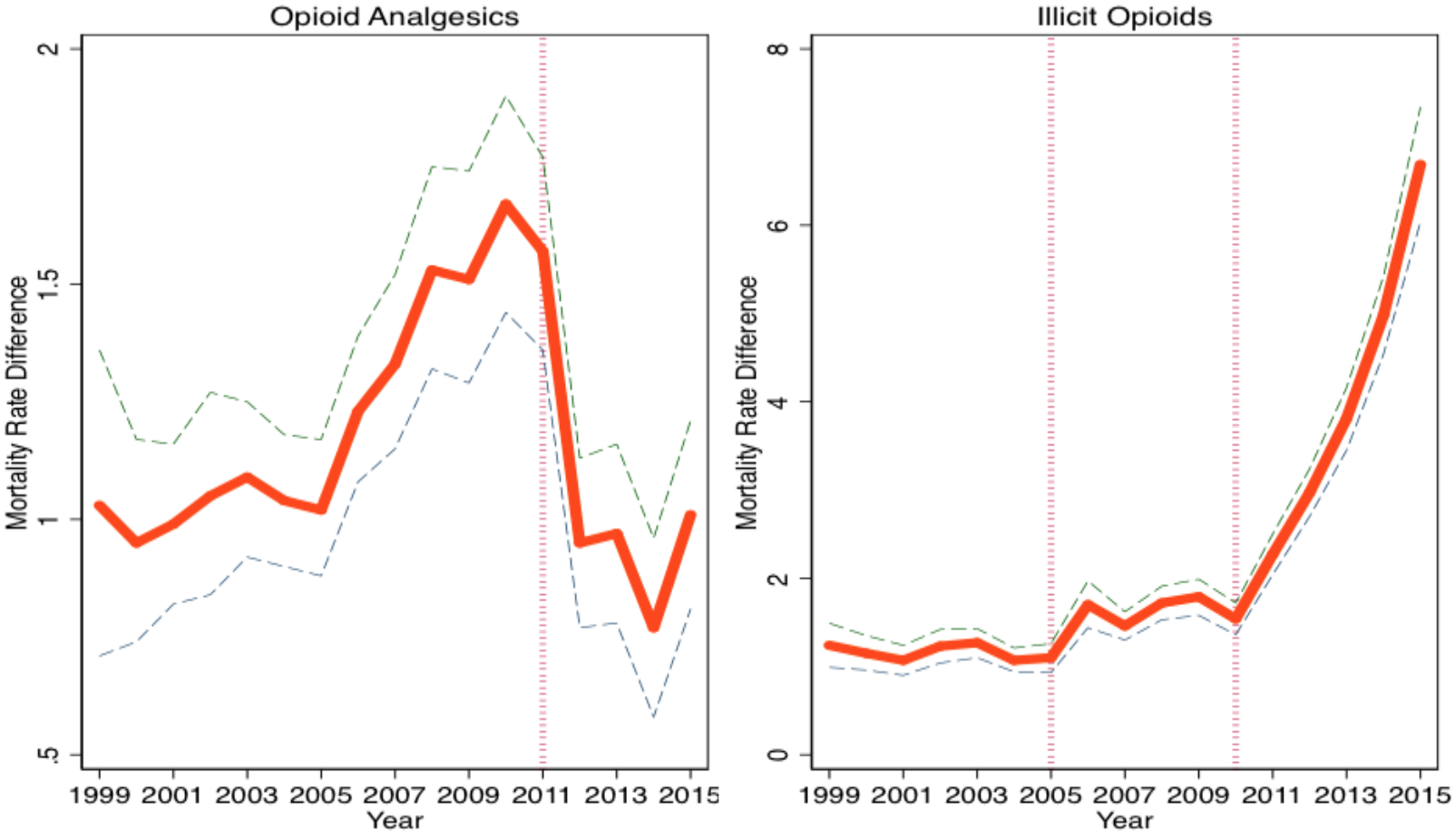
Δ in Mortality Shares



- Regression-adjusted estimates (show Δ since 1999)
- Initial fall then rise in male/young adult share

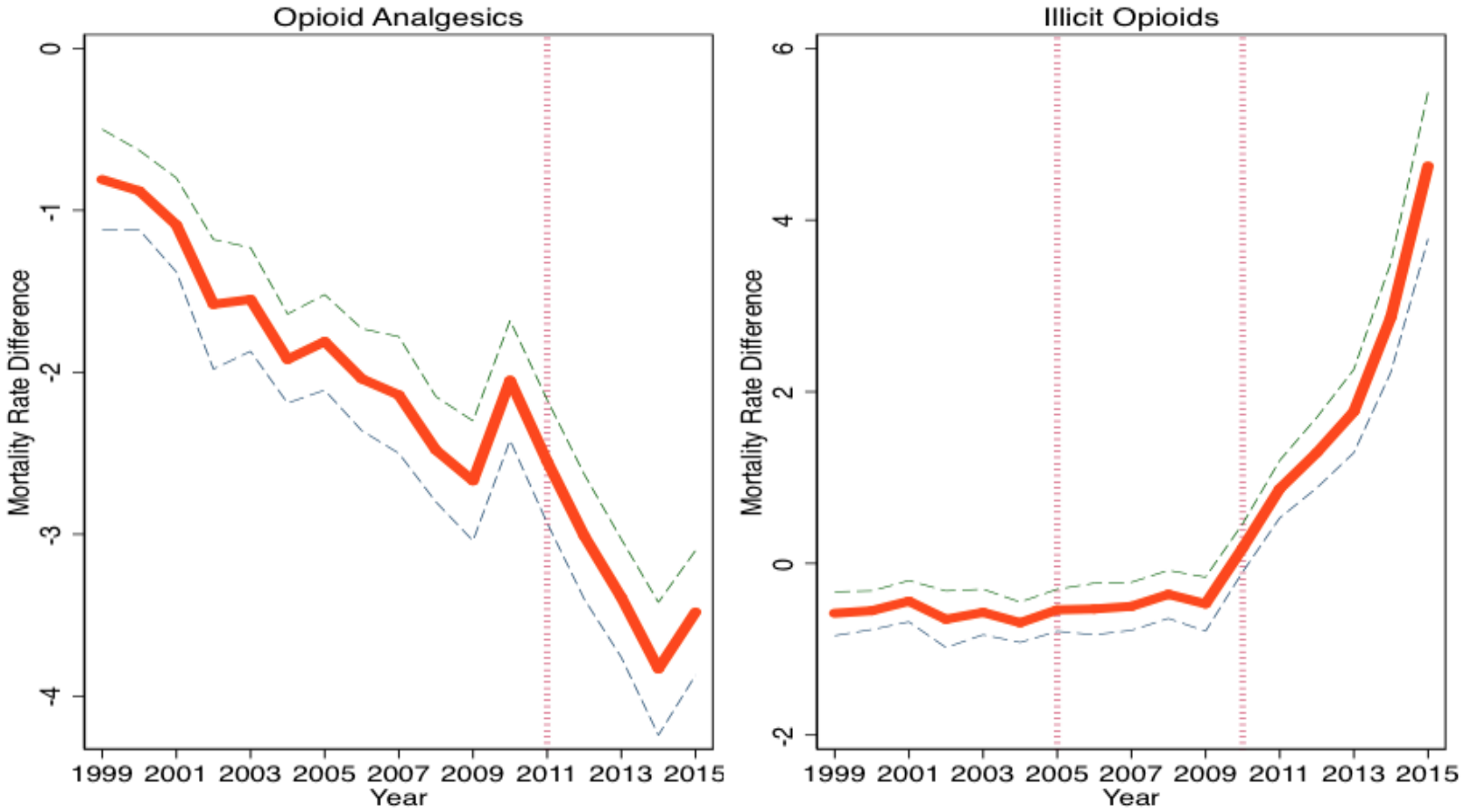
▸ Trend Spline Estimates

Mortality Rate Difference by Sex



- Relative male illicit opioid mortality rates rise starting in 2006, rapidly after 2010

Mortality Rate Difference by Age



- Relative 20-39 year old illicit opioid mortality rates rise starting in 2006, rapidly after 2010
- Also confirmed for heroin, synth opioids, cocaine, methadone

▸ Trend Spline Estimates

What Have We Learned

- Counties with (relative) economic decline did experience higher drug death rate growth
- Much of this reflects observed confounding factors
  - 73% - 85% of raw correlation attenuated for drug deaths
- Changes in economic conditions explain $< 1/10$ of observed increase in drug death rates
  - even less of Δ for opioid analgesic or illicit opioid mortality
  - None of Δ for suicide/alcohol deaths
  - Could modestly underestimate or overstate total contribution
  - But most of change is due to other factors
- Accounting for selection on unobservables eliminates estimated effects

What Have We Learned (cont.)

- Evidence consistent with importance of drug environment
  - 1999-2011: opioid analgesic deaths $\uparrow$
  - 2010-2015: illicit opioid deaths $\Uparrow$, opioid analgesics flat
- Share of male & young adult drug deaths $\uparrow$ after 2010
- Also consistent patterns for relative changes for other drugs

Some Implications

- Rising drug deaths not primarily due to medium-term changes in economic conditions
  - possibly affected by longer-term economic/social changes
    - hard to explain Δ in group death shares by demand-factors
  - but also by short-term differences in drug environment
- Potential gains for policies focused on drug environment

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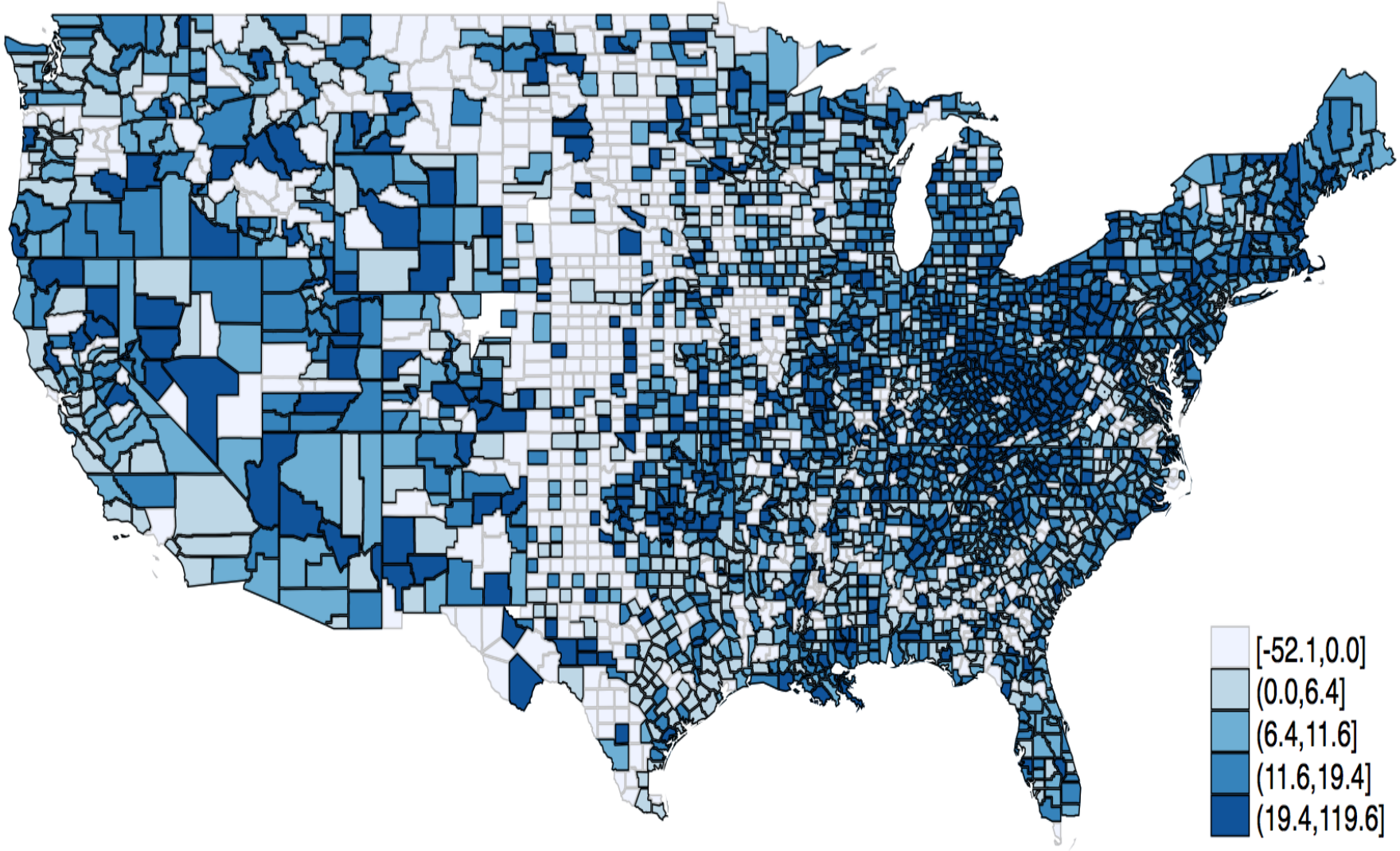
    - hard to explain Δ in group death shares by demand-factors
  - but also by short-term differences in drug environment
- Potential gains for policies focused on drug environment
- Fatal drug epidemic not just about opioids
  - movement from opioid analgesics to illicit opoiods
  - rapid recent growth in cocaine deaths
  - steady increase in stimulant deaths

EXTRA SLIDES

Δ Drug Mortality Rates: 1999-2015



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Instrumented covariate changes (ΔX^I)

- Based on starting year values & census division changes
- Continuous variables:

$$\Delta X_k^I = X_{k0} \times \frac{X_{d1} - X_{d0}}{X_{d0}} \tag{9}$$

d indicates census division

- Binary policy variables:
  - $\Delta X_k^I = 0$ if $X_{k0} = 1$
  - if $X_{k0} = 0$:

$$\Delta X_k^I \mid_{(X_{k0}=0)} = (X_{d1} - X_{d0}) \mid_{(X_{d0}=0)} \tag{10}$$

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Lubotsky-Wittenberg (2006) Method

$$\Delta M_k = \beta \Delta E_k^* + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \varepsilon_k \tag{11}$$

- E_k^* is a latent variable. Instead, observe proxies E_{kj},where

$$\Delta E_{kj} = \rho_j \Delta E_K^* + \mu_{kj} \tag{12}$$

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- Key Assumptions:
  - ΔE_k^* uncorrelated with ε_k
  - all μ_{kj} uncorrelated with ΔE_k^* & ε_k
- Unrestricted covariances between μ_{kj}, can be nonzero
  - unlike IV, factor/principal components analysis

LW Method (cont.)

- (2) & (3) cannot be directly estimated. To minimize attenuation bias estimate

$$\Delta M_k = \sum_{j=1}^{m} \beta_j \Delta E_{jk} + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \varepsilon_k \tag{13}$$

- & calculate weighted sum of proxy coefficients

$$\hat{\beta} = \sum_{j=1}^{m} \frac{cov(\Delta M, \Delta E_j)}{cov(\Delta M, \Delta E_1)} \hat{\beta}_j \tag{14}$$

LW Method (cont.)

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- & calculate weighted sum of proxy coefficients

$$\hat{\beta} = \sum_{j=1}^{m} \frac{cov(\Delta M, \Delta E_j)}{cov(\Delta M, \Delta E_1)} \hat{\beta}_j \tag{14}$$

- Weights depend on covariances between proxy and outcome
  - E_1 is "base" proxy (here use proxy with largest magnitude in regression without additional covariates $\hat{\beta}_j$ as E_1)
  - $\hat{\beta}$ has same scale as $\hat{\beta}_1$
  - Measures effects up to a normalization

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Oster Method: Details

- "Short" Regression: $\Delta M_k = \Delta \mathbf{E_k} \beta + \lambda_k$
  - β^o, R^o are regression coefficient & R^2 from short regression
- "Long" Regression: $\Delta M_k = \Delta \mathbf{E_k} \beta + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \varepsilon_k$
  - $\tilde{\beta}$, $\tilde{R}$ are regression coefficient & R^2 from long regression
- Hypothetical Regression:
  $\Delta M_k = \Delta \mathbf{E_k} \beta + X_{k0}\gamma_1 + \Delta X_k \gamma_2 + \mathbf{W}_k \psi + \mu_k$
  - $\mathbf{W}$, orthogonal to $\mathbf{X_0}$, and $\Delta \mathbf{X}$, and captures remaining determinants of M
  - R_{max} is R^2 from this regression
  - $R_{max} < 1$ if measurement error in M
- δ : relative importance of selection on observables & unobservables

$$\delta = \frac{\sigma_{WE} / \sigma_W^2}{\sigma_{XE} / \sigma_X^2}$$

  - $\delta = 1$: observables & unobservables equally important
  - $\delta < 1$: observables more important

Oster Method Details (cont.)

- Estimate $\beta^o, R^o, \tilde{\beta}, \tilde{R}$ from short and long regressions
- Selection-adjusted treatment effect:

$$\beta^* \approx \tilde{\beta} - \delta(\beta^o - \tilde{\beta}) \left[\frac{R_{max} - \tilde{R}}{\tilde{R} - R^0} \right] \tag{15}$$

- Adjustments attenuate MP estimate more for:
  - large δ (unobservables more important)
  - large $R_{max} - \tilde{R}$ (unexplained variance)
  - large $\beta^o - \tilde{\beta}$ (in absolute value): more attenuation when adding covariates
  - small $R^{o-}\tilde{R}$: R^2 increases little from short to long regression
- Assume values for $\delta = 0.5, R_{max} = 0.75$

Oster Method Details (cont.)

- Selection-adjusted treatment effect:

$$\beta^* \approx \tilde{\beta} - \delta(\beta^o - \tilde{\beta}) \left[\frac{R_{max} - \tilde{R}}{\tilde{R} - R^0} \right]$$

- Selection on unobservables yielding zero treatment effect:
-

$$\delta^* \approx \left(\frac{\tilde{\beta}}{\beta^o - \tilde{\beta}} \right) \left[\frac{R_{max} - \tilde{R}}{\tilde{R} - R^0} \right] \tag{16}$$

- R_{max} yielding zero treatment effect:

$$R^*_{max} \approx \tilde{R} + \left(\frac{\tilde{\beta}}{\delta(\beta^o - \tilde{\beta})} \right) (\tilde{R} - R^o) \tag{17}$$

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Correlations Between Economic Proxies

	Poverty	Income	Home Prices	Unemployment	Imports
Poverty	1.000				
Income	-0.702	1.000			
Home Prices	-0.530	0.641	1.000		
Unemployment	0.487	-0.436	-0.284	1.000	
Imports	0.154	-0.074	-0.098	0.101	1.000

Return

Δ in 1999-2015 Death Rates: No Extra Controls

Economic Proxy	All Drugs	Opioid Analgesics	Illicit Opioids	DSA
Proxies Included Together				
Poverty Rate Δ	1.102**	0.519**	0.782*	0.793
	(0.515)	(0.259)	(0.403)	(0.599)
Med HH Income Δ	0.206	-0.097	-0.043	0.751
	(0.671)	(0.329)	(0.543)	(0.951)
Med Home Price Δ	1.465*	0.710*	0.626	1.959**
	(0.805)	(0.409)	(0.668)	(0.883)
Unemp Rate Δ	0.307	-0.143	0.536	-0.146
	(0.452)	(0.213)	(0.365)	(0.669)
Import Exposure Δ	0.212	0.269	-0.065	0.214
	(0.392)	(0.177)	(0.343)	(0.470)
R^2	0.082	0.059	0.051	0.060
Multiple Proxy Estimate	2.949***	1.164***	1.710***	3.256
	(0.798)	(0.239)	(0.428)	(2.395)

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Δ in Total Drug Death Rate, Various Controls

Economic Proxy	(a)	(b)	(c)
Poverty Rate Δ	1.102**	0.638	0.736**
	(0.515)	(0.397)	(0.361)
Med HH Income Δ	0.206	-0.604	0.171
	(0.671)	(0.434)	(0.393)
Med Home Price Δ	1.465*	0.337	0.115
	(0.805)	(0.441)	(0.350)
Unemployment Rate Δ	0.307	0.160	-0.185
	(0.452)	(0.257)	(0.312)
Import Exposure Δ	0.212	-0.283	-0.302
	(0.392)	(0.237)	(0.262)
R^2	0.083	0.431	0.441
P-Value	<0.001	0.496	0.003
Multiple Proxy Estimate	2.949***	0.431	0.792*
	(0.798)	(0.488)	(0.436)
Additional Controls	None	X_{1999}, ΔX	X_{1999}, ΔX^{I}

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Robustness Checks

	All Drugs		Opioid Analg		Illicit Opioids	
	(a)	(b)	(a)	(b)	(a)	(b)
Main Model						
MP Estimate	0.431	0.792*	0.197	0.306*	0.305	-0.101
	(0.488)	(0.436)	(0.185)	(0.170)	(0.407)	(0.310)
% Δ Explained	4.8%	8.7%	4.7%	7.3%	4.6%	-1.5%
Unweighted						
MP Estimate	1.208***	0.503	0.344*	0.301*	0.740**	-0.004
	(0.423)	(0.378)	(0.182)	(0.176)	(0.323)	(0.274)
% Δ Explained	9.2%	3.8%	4.9%	4.3%	10.0%	-0.1%
Unadjusted Mortality Rates						
MP Estimate			0.217*	0.330***	0.198*	-0.270***
			(0.131)	(0.104)	(0.103)	(0.086)
% Δ Explained			5.3%	8.1%	3.1%	-4.2%
1990-2000 Δ in Economic Conditions						
MP Estimate	1.208***	0.503	0.344*	0.301*	0.740**	-0.004
	(0.423)	(0.378)	(0.182)	(0.176)	(0.323)	(0.274)
% Δ Explained	9.2%	3.8%	4.9%	4.3%	10.0%	-0.1%
Additional Controls	ΔX	ΔX^I	ΔX	ΔX^I	ΔX	ΔX^I

▸ Return

GMM (IV) Estimates

Economic Proxy	All Drugs	Opioid Analgesics	Illicit Opioids	All DSA
GMM Estimates				
Poverty Rate Δ	-0.038 (0.559)	0.186 (0.303)	-0.414 (0.494)	-0.659 (0.698)
Med HH Income Δ	0.853 (0.625)	0.281 (0.292)	0.287 (0.538)	0.200 (0.694)
Med Home Price Δ	0.232 (0.666)	0.320 (0.354)	-0.276 (0.679)	-0.378 (0.791)
Unemp Rate Δ	0.358 (0.966)	0.489 (0.473)	-0.009 (0.795)	-0.009 (1.156)
Import Exposure Δ	2.263 (2.067)	0.709 (0.817)	1.149 (1.479)	1.790 (2.282)
MP Estimate	0.431 (0.488)	0.197 (0.185)	0.305 (0.407)	-0.343 (0.583)

- Each proxy instrumented by all others, 1999 covariates included
- GMM & multiple proxy estimates mostly similar except import exposure (all DSA deaths most different)
- 1^{st}-stage F-Stat: 72.5, 129.0, 23.6 & 33.0 for poverty, incomes, home prices & unemployment; 5.4 for import exposure

GMM (IV) Estimates with $\Delta X'$ Controls

Economic Proxy	All Drugs	Opioid Analgesics	Illicit Opioids	All DSA
GMM Estimates				
Poverty Rate Δ	0.940***	0.330**	-0.264	0.761*
	(0.282)	(0.147)	(0.275)	(0.389)
Med HH Income Δ	1.039***	0.388**	0.050	0.414
	(0.321)	(0.169)	(0.263)	(0.449)
Med Home Price Δ	1.387***	0.534***	-0.066	1.235**
	(0.492)	(0.190)	(0.314)	(0.582)
Unemp Rate Δ	1.789***	0.478**	-0.012	1.391**
	(0.485)	(0.229)	(0.366)	(0.674)
Import Exposure Δ	3.123**	1.249***	-0.100	2.180
	(1.232)	(0.467)	(0.725)	(1.342)
MP Estimate	0.792*	0.306*	-0.101	0.351
	(0.436)	(0.170)	(0.310)	(0.987)

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Different Starting/Ending Years

Model	(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)	(i)	(j)
	1999-2015		**2000-2015**		**2001-2015**		**2002-2015**		**2003-2015**	
MP Estimate	0.431	0.792*	0.381	0.534	1.585	0.932	1.206	0.831	1.882*	1.452
% Δ Explained	4.8%	8.7%	14.4%	6.2%	18.7%	11.0%	14.3%	9.8%	22.5%	17.4%
	1999-2011		**1999-2012**		**1999-2013**		**1999-2014**		**1999-2015**	
MP Estimate	0.413	0.769**	0.360	0.654**	0.386	0.634**	0.248	0.688**	0.431	0.792*
% Δ Explained	5.6%	10.3%	5.1%	9.2%	5.3%	8.8%	3.2%	8.7%	4.8%	8.7%
Additional Controls	**ΔX**	**ΔX'**	**ΔX**	**ΔX'**	**ΔX**	**ΔX'**	**ΔX**	**ΔX'**	**ΔX**	**ΔX'**

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Selected Time Periods

	Opioid Analgesics		Illicit Opioids	
1999-2015				
MP Estimate	0.197	0.306*	0.305	-0.101
	3.58 [4.22]		6.27 [6.67]	
% of Δ Explained	4.7%	7.3%	4.6%	-1.5%
1999-2011				
MP Estimate	0.105	0.266		
	3.81 [4.76]			
% of Δ Explained	2.2%	5.6%		
2006-2015				
MP Estimate			0.326	0.248
			5.42 [6.15]	
% of Δ Explained			5.3%	4.0%
Additional Controls	ΔX	ΔX^I	ΔX	ΔX^I

- Initial year: 1999, 2006; final year: 2011, 2015
- No evidence of substantially greater treatment effects

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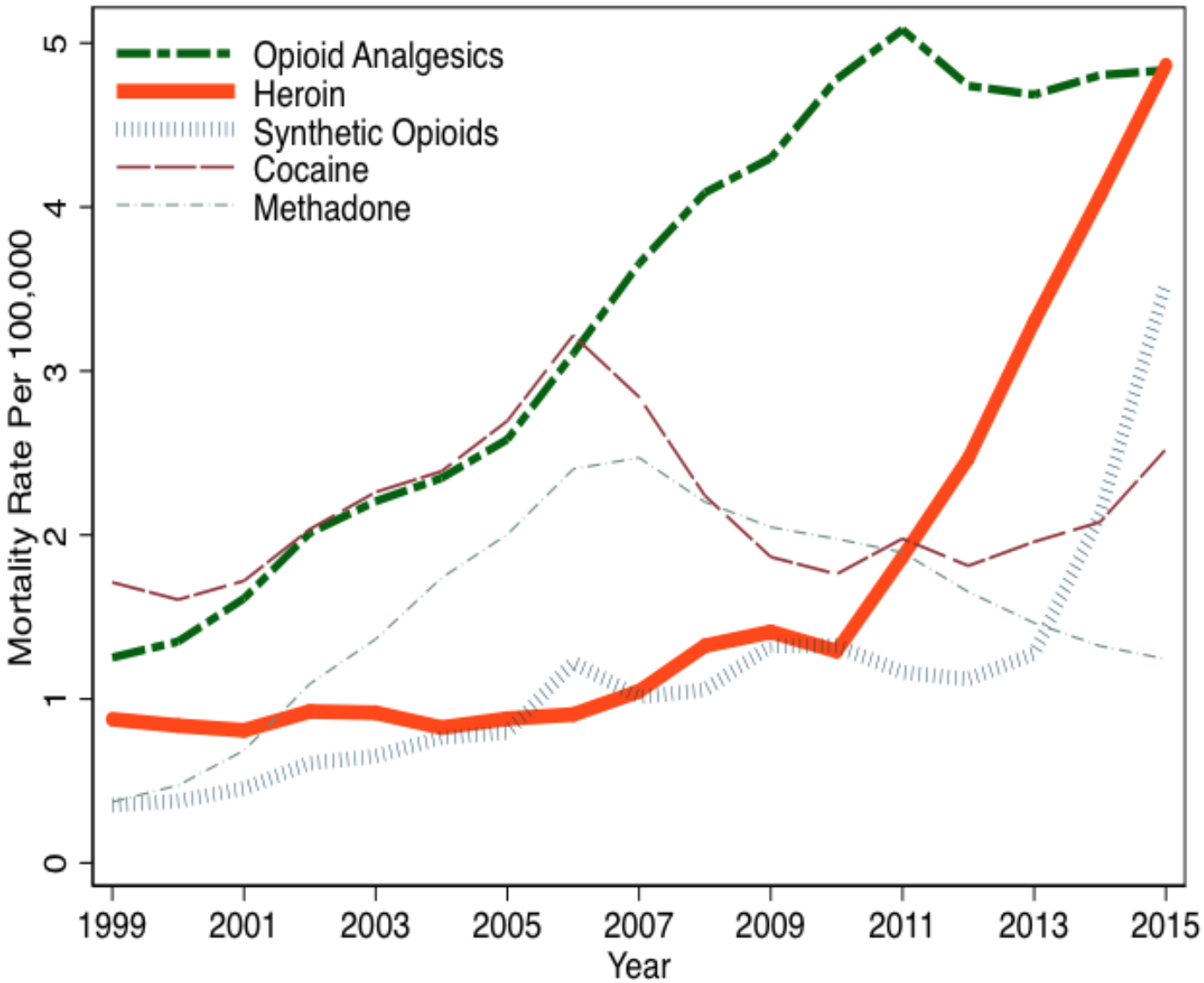
Selected Drug Mortality Rates



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Subgroups: % Δ Explained

Group	All Drugs		Opioid Analg		Illicit Opioids		DSA	
All	4.8%	8.7%*	4.7%	7.3%*	4.6%	-1.5%	-2.8%	2.8%
Males	0.3%	8.6%*	3.5%	6.8%	-0.6%	-3.6%	-5.2%	2.2%
Females	9.6%**	6.6%**	4.4%	5.5%	16.0%**	4.1%	2.5%	3.8%
Whites	7.2%	17.1%***	8.4%*	17.3%***	3.3%	3.4%	4.8%	17.2%***
Nonwhites	1.7%	6.1%	0.2%	2.6%	0.5%	1.1%	6.1%	10.9%
Age 20-59	3.2%	8.5%**	3.0%	7.4%**	4.4%	-0.5%	-3.1%	3.1%
White: 20-59	7.7%	18.3%***	7.1%	17.4%***	4.1%	6.0%	3.4%	14.8%**
White: 45-54	3.4%	11.4%*	6.3%	13.0%**	2.6%	3.3%	1.6%	7.9%
≤ H.S.	4.2%	2.9%	6.0%	3.8%	2.0%	-6.3%	0.9%	-0.1%
Some Col	5.3%	4.4%**	6.0%	1.8%	3.4%	0.1%	-1.2%	-0.5%
Col Grad	3.0%	6.7%	0.3%	4.5%	1.6%	2.6%	0.1%	6.5%
Controls	ΔX	ΔX^I	ΔX	ΔX^I	ΔX	ΔX^I	ΔX	ΔX^I

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Group Share of Drug Deaths (Regression-Adjusted)

Regressor	Males	Age: 20-39	Males: 20-39	Age: 40-59	Females: 40-59	Females: 20-39	Males: 40-59
Trend	-0.34***	-0.49***	-0.36***	0.34***	0.49***	-0.13***	-0.15***
	(0.06)	(0.07)	(0.06)	(0.07)	(0.05)	(0.04)	(0.06)
Post	0.49***	1.35***	0.96***	-1.59***	-1.11***	0.36***	-0.47***
	(0.13)	(0.14)	(0.12)	(0.24)	(0.15)	(0.07)	(0.15)
Intercept	64.72***	40.83***	28.34***	49.20***	17.59***	12.43***	31.60***
	(0.36)	(0.48)	(0.39)	(0.39)	(0.31)	(0.24)	(0.32)

- Male, 20-39 year old mortality shares fall through 2010
- Then rise rapidly

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Treatment vs. Reference Group Δ in Deaths

(Regression-Adjusted)

Regressor	Sex-Specific (Reference Group: Females)		Age-Specific (Reference Group: 40-49 Year Olds)	
	Opioid Analgesics	Illicit Opioids	Opioid Analgesics	Illicit Opioids
Trend	0.05*** (0.01)	0.03*** (0.01)	-0.15*** (0.02)	0.03*** (0.01)
Post	-0.24*** (0.03)	0.88*** (0.05)	-0.11** (0.05)	0.84*** (0.06)
Group Main Effect	0.92*** (0.11)	1.13*** (0.10)	-0.92*** (0.15)	-0.66*** (0.12)

- Male, 20-39 relative mortality rates Δ little through 2010 or 2011
- But illicit opioid rates grow rapidly after that

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Urban vs. Rural Counties

	All Drugs		Opioid Analg		Illicit Opioids	
	(a)	(b)	(a)	(b)	(a)	(b)
Metropolitan Counties						
MP Estimate	0.541	1.207**	0.376	0.517**	0.353	0.007
	(0.646)	(0.544)	(0.234)	(0.212)	(0.675)	(0.644)
% Δ Explained	6.4%	14.2%	10.5%	14.5%	5.3%	0.1%
Urban Counties						
MP Estimate	0.393	-0.018	0.176	0.509	0.676	-0.345
	(1.125)	(1.145)	(0.469)	(0.466)	(0.656)	(0.573)
% Δ Explained	3.7%	-0.2%	3.0%	8.6%	10.5%	-3.5%
Rural Counties						
MP Estimate	0.091	0.061	0.167	0.271	0.107	0.200
	(16.535)	(18.130)	(1.229)	(1.056)	(0.450)	(0.411)
% Δ Explained	0.6%	0.4%	1.9%	3.2%	1.6%	3.0%
Additional Controls	ΔX	ΔX^I	ΔX	ΔX^I	ΔX	ΔX^I

- Generally bigger effects in metropolitan (not rural) counties

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