

US federal cocaine essential ('precursor') chemical regulation impacts on US cocaine availability: an intervention time-series analysis with temporal replication

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ABSTRACT

Background and Aims Research shows that essential/precursor chemical controls have had substantial impacts on US methamphetamine and heroin availability. This study examines whether US federal essential chemical regulations have impacted US cocaine seizure amount, price and purity—indicators of cocaine availability. **Design** Autoregressive integrated moving average (ARIMA)-intervention time-series analysis was used to assess the impacts of four US regulations targeting cocaine manufacturing chemicals: potassium permanganate/selected solvents, implemented October 1989; sulfuric acid/hydrochloric acid, implemented October 1992; methyl isobutyl ketone, implemented May 1995; and sodium permanganate, implemented December 2006. Of these chemicals, potassium permanganate and sodium permanganate are the most critical to cocaine production. **Setting** Conterminous United States (January 1987–April 2011). **Measurements** Monthly time-series: purity-adjusted cocaine seizure amount (in gross weight seizures < 6000 grams), purity-adjusted price (all available seizures), and purity (all available seizures). Data source: System to Retrieve Information from Drug Evidence. **Findings** The 1989 potassium permanganate/solvents regulation was associated with a seizure amount decrease (change in series level) of 28% ($P < 0.05$), a 36% increase in price ($P < 0.05$) and a 4% decrease in purity ($P < 0.05$). Availability recovered in 1–2 years. The 2006 potassium permanganate regulation was associated with a 22% seizure amount decrease ($P < 0.05$), 100% price increase ($P < 0.05$) and 35% purity decrease ($P < 0.05$). Following the 2006 regulation, essentially no recovery occurred to April 2011. The other two chemical regulations were associated with statistically significant but lesser declines in indicated availability. **Conclusions** In the United States, essential chemical controls from 1989 to 2006 were associated with pronounced downturns in cocaine availability.

Keywords Cocaine, drug price, drug purity, drug seizure amount, environmental prevention, policy, potassium permanganate, precursor chemicals, regulation, time-series analysis.

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INTRODUCTION

Since the 1980s, the United Nations has encouraged nations to control commercial chemicals used in methamphetamine, heroin and cocaine manufacture, with the goal of limiting the drugs' availability [1–3] and thus their attendant consequences. Research on the policy's impact, however, has begun relatively recently. The first study assessing its impact on methamphetamine was published

in 2003 [4]; that for heroin in 2013 [5]. We know of no study evaluating the policy's impact on cocaine.

Commercial chemical control constitutes a form of environmental drug prevention—rather than targeting individual drug users, traffickers or producers, it seeks to alter the environment in which they function [5–10]. Here we evaluate a natural experiment in such control/prevention for cocaine: whether US cocaine availability was impacted by US federal regulation of cocaine manufacturing

chemicals, including the oxidizing agents potassium permanganate and sodium permanganate—cocaine's so-called 'choke chemicals' (i.e. central to and difficult to replace in the cocaine production process [11–14]), of which the United States is a leading producer [15–17].

US cocaine chemical regulations

To date, four US regulations have targeted cocaine manufacturing chemicals. The first, implemented 30 October 1989, regulated potassium permanganate and the solvents methyl ethyl ketone (MEK), toluene, ethyl ether and acetone [18]. The second, implemented 22 October 1992, regulated sulfuric acid and hydrochloric acid [19]. The third, implemented 19 May 1995, regulated methyl isobutyl ketone (MIBK), a solvent whose use in cocaine manufacturing increased following the 1989 regulation [20]. The fourth, implemented 18 December 2006, targeted sodium permanganate, a direct potassium permanganate substitute [21].

Of these chemicals, potassium permanganate and sodium permanganate, being choke chemicals, may be most critical to realizing impacts on cocaine availability [11–14]. Potassium permanganate's regulation in the United States is of particular interest, as the world's largest potassium permanganate producer is a US company [15–17]. Sodium permanganate manufacture was relatively limited in the 1980s/90s. However, around the early 2000s, the aforementioned company increased its annual manufacture of sodium permanganate by several-fold, perhaps with the eventual goal of phasing out potassium permanganate production in favor of sodium permanganate [17,21]. At that time, sodium permanganate was unregulated and untracked in the United States [17] and, according to Echeverry at the Universidad de Los Andes, Bogotá, a 'crucial input' to cocaine production [22]. (The US International Trade Commission, prompted by the Drug Enforcement Administration [DEA], assigned sodium permanganate a tracking code in 2005 [17]; see Supporting information, Table S1 for potassium permanganate commercial uses.)

All the targeted chemicals, as per their regulation, were classified as List II chemicals (ones that, in addition to legitimate uses, are used in controlled substance manufacture in violation of the Controlled Substances Act [23]). Thresholds were set for each to specify regulated transactions. For example, the sodium permanganate regulation established transactions ≥ 55 kg and ≥ 500 kg, respectively, as that chemical's thresholds for regulated domestic and international transactions [21]. Chemical distributors were required to register with the DEA and keep records on regulated transactions. Should a chemical distributor place public health and safety at risk, the DEA was empowered to revoke its license [18,21,23,24].

Cocaine manufacture

Cocaine, produced primarily in Bolivia, Colombia and Peru [25], has no single manufacturing method [26,27]. That said, the following illustrates uses of the US-targeted chemicals. Sulfuric acid is often used to dissolve coca paste (a chunky, off-white to light brown, putty-like substance). Potassium permanganate (a dry product) combined with water or sodium permanganate (a liquid product) can be mixed with the dissolved coca paste to help produce cocaine base. Ethyl ether, methyl ethyl ketone (MEK), methyl isobutyl ketone (MIBK) or toluene can be used to dissolve the cocaine base. In turn, the dissolved cocaine base can be mixed with hydrochloric acid dissolved in acetone; from this, cocaine hydrochloride (the powder form of the drug distributed to users) eventually precipitates [12,26,28] (NB: cocaine essential chemicals are sometimes called precursor chemicals. Essential chemicals, however, are reagents and catalysts that do not become part of a final product's molecular structure. In contrast, precursor chemicals, for example, ephedrine and pseudoephedrine in methamphetamine manufacture, become part of the final product's molecular structure [29–31]).

Cocaine chemical control: related findings

Operation Purple, an international chemical monitoring program, and one supported by Bolivia, Colombia and Peru, began in 1999 [11,32,33]. Its concept is that countries exporting potassium permanganate notify importing countries of all proposed transactions involving 100+ kg of the chemical. The importing country verifies legitimate end-use prior to shipment, and authorized shipments are then tracked from origin to final end-use [11]. Operation Purple reportedly had initial success which diminished by 2002 [32].

Controls on acetic anhydride, a heroin production choke chemical, were associated with a substantial impact on US heroin availability [5]. Ephedrine/pseudoephedrine controls were associated with impacts on methamphetamine availability and the drug's consequences, including arrests, hospitalizations and treatment demand [4,34–42].

Indicators of illicit drug availability

An illicit drug's availability can manifest in the physical amount of the drug in an area, its quality and its affordability. In theory, and other things being equal, when a drug's physical amount (physical availability) increases/decreases, the amount seized by the government should follow suit, rendering drug seizure amount a positive correlate of availability [5]. When traffickers reduce a drug's purity by adding diluents/adulterants (drug cutting), its quality (qualitative availability) declines, rendering purity a positive correlate of availability [5]. When

prices rise, affordability (economic availability) of a drug decreases, rendering price a negative correlate of availability [5,43,44].

Indicator impact patterns

Impacts on availability due to essential/precursor chemical control ought to differ from those due to domestic criminal justice interdiction. Chemical control impacts should be associated with declines in drug production, and thus decreases in seizure amount and purity and a rise in price. A seizure amount decrease is the opposite of what would be expected to follow from an increase in domestic criminal justice interdiction (at least in the short term). Expected directions of seizure amount, purity and price changes (SAPP patterns) associated with drug production versus domestic criminal justice interdiction are shown in Table 1 [5].

Study approach

This study uses autoregressive integrated moving average (ARIMA)-intervention time-series analysis to examine whether the US regulations impacted cocaine availability—cocaine seizure amount, purity and price—in the conterminous US (all 48 contiguous states and the District of Columbia).

Drug availability in drug portal areas can differ from that in other areas [45]. Consequently, drug availability series are also presented for the southeast US (AL, AR, FL, GA, LA, MS, NC, SC and TN) and southwest US (AZ, CA, CO, NM, NV, TX and UT) (Supporting information, Fig. S1), as cocaine enters the US in large part through these two areas/portals [45]. Comparison series are also presented: marijuana, heroin and methamphetamine seizure amounts and prices; and heroin and methamphetamine purities.

Table 1 Drug seizure amount^a, purity and price (SAPP) patterns typically expected to follow increases/decreases in drug production and domestic criminal justice interdiction.

	Seizure amount	Purity	Price
Increase in			
Drug production	↑	↑	↓
Domestic criminal justice interdiction	↑	↓	↑
Decrease in			
Drug production	↓	↓	↑
Domestic criminal justice interdiction	↓	↑	↓

^aPurity-adjusted seizure amount (i.e. seizure amount sans diluents and adulterants). ↑ = increase. ↓ = decrease. A drug production or domestic criminal justice intervention sometimes impacts only a subset of the three indicators listed. In that case, the subset impacted can be expected to change as described in the Table.

METHODS

System To Retrieve Information from Drug Evidence (STRIDE)

Data came from STRIDE, an administrative system/repository for data on drug evidence seized/collected/purchased during investigations by the DEA, the Federal Bureau of Investigation, other federal organizations and some state and local enforcement agencies. This study analyzes exhibits submitted by federal agencies (the terms exhibits and seizures are used interchangeably here). STRIDE exhibit information includes drug type, date, location, amount, purity and price.

Cocaine purity was assessed using median purity of exhibits per month. Price was purity adjusted (e.g. a 25% pure 2-g gross weight seizure that cost US\$200 would have a purity-adjusted price of US\$400 per gram), set to 2010 US dollars using the Consumer Price Index for all urban consumers (seasonally adjusted), and reported as the median purity-adjusted price of seizures per month [46]. Seizure amount was assessed using the monthly amount (weight) of cocaine seized sans diluents/adulterants (purity-adjusted seizure amount) [5]. Conterminous US purity, price and amounts were reported for all and gross weight < 10 g exhibits; amounts were also reported for gross weight exhibits < 100 g and < 6000 g.

ARIMA-intervention analysis

ARIMA models facilitate appropriate handling of drift, trends (including local trends), outliers, seasonality and serially correlated errors in a series [47–49]. During January 1987–April 2011 there were 292 monthly periods, a relatively long series. Recognizing this, the period January 1987–December 2000 (168 months) was used for the ARIMA-intervention analysis of the 1980s/90s regulations. The period January 2000–April 2011 (136 months) was used for the ARIMA-intervention analysis of the 2006 regulation.

Regarding impact start-times, each US cocaine essential chemical regulation was implemented in the latter half of a calendar month. This places the 30-day period (actual month) following each regulation implementation across two adjacent calendar months. If an impact was not indicated by the ARIMA-intervention analysis for the first calendar month, the subsequent calendar month was examined as the start month. If no impact was indicated for either, an approximate 1-month lag was examined using the next calendar month. This approach follows previous essential/precursor chemical control evaluations [4,5,34–39,41].

The series were non-stationary, and consequently first-order differenced for modeling [50]. Seizure amount series were log-transformed to address temporal changes in variance [50]. The autocorrelation and partial autocorrelation

functions of the complete differenced series were used to identify the ARIMA models [50]. An iterative outlier detection and adjustment procedure was used to obtain joint estimates of model parameters and outlier effects [51,52]. For each model, Box–Ljung Q-tests did not reject the hypothesis that the first 24 autocorrelations were jointly zero. Analyses were performed with the SCA Statistical System [53].

RESULTS

Conterminous US: seizure amount time-series description

The series of conterminous US purity-adjusted cocaine amounts from all seizures is shown in Fig. 1. Amounts in this series might have declined at the time of the 2006 sodium permanganate regulation, and perhaps at the times of the 1989 potassium permanganate/solvents regulation and 1992 acids regulation (Fig. 1). The

series, however, has substantial fluctuation, limiting its usefulness/interpretability.

The series of purity-adjusted cocaine amounts in gross weight seizures < 6000 g (second graph in Fig. 1) has substantially less fluctuation, but still includes most (94.3%) of the seizures. It exhibits a decrease at the time of the 1989 potassium permanganate/solvents regulation. Recovery occurred in 1–2 years. Amounts dropped sharply at the time of the 1992 acids regulation, and remained lower until the late 1990s. Amounts changed little at the time of the 1995 MIBK regulation. They dropped at the time of the 2006 sodium permanganate regulation, and remained lower to the series end (April 2011).

The < 10-g series (an approximate retail level series containing 35.1% of the seizures) exhibited changes at the times of the interventions roughly similar to that of the < 6000-g series, except that it also indicated a decline at the time of the 1995 MIBK regulation (Fig. 1). (For

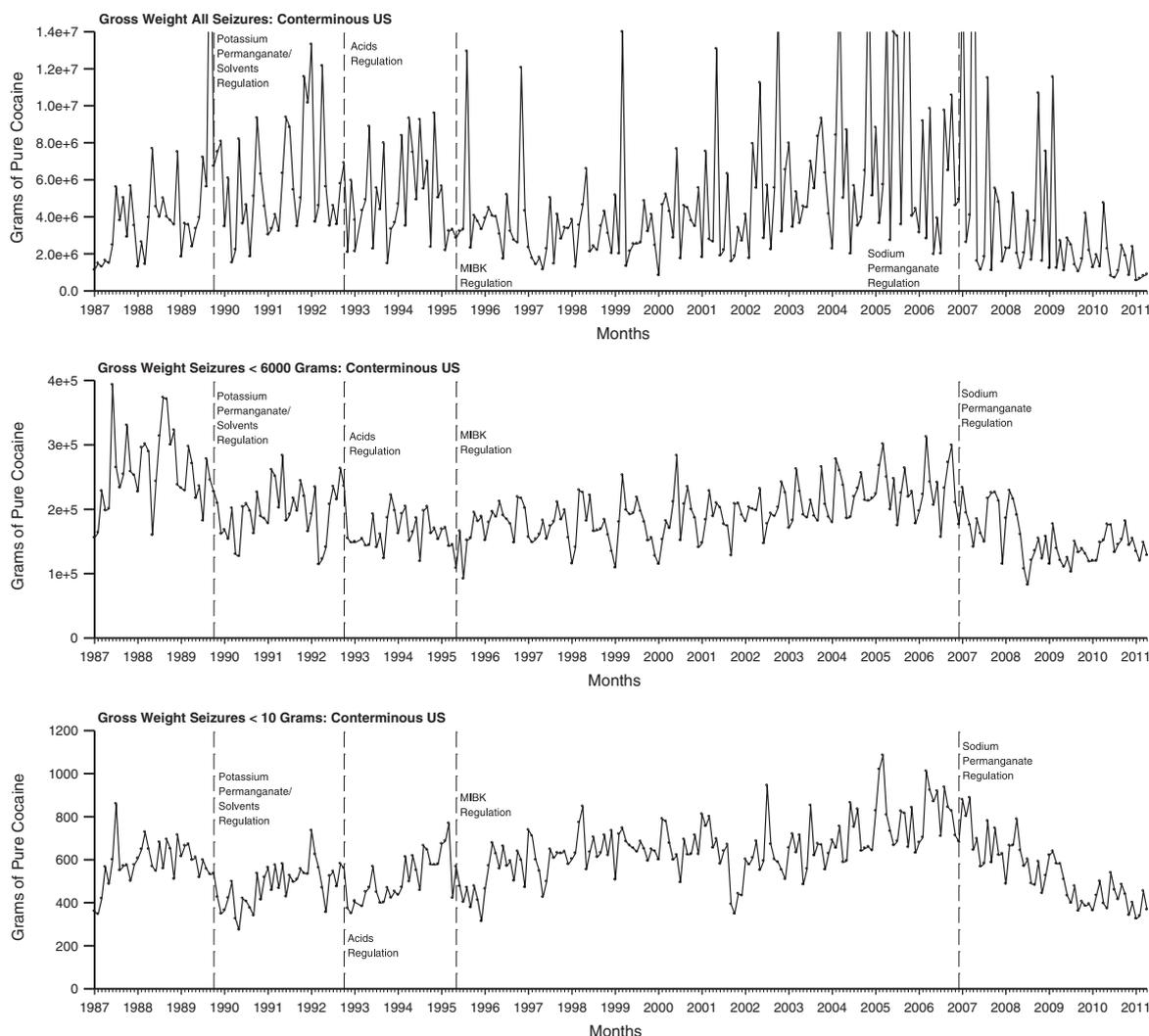


Figure 1 US cocaine essential chemical regulations: conterminous US monthly totals of pure cocaine^a in all seizures, seizures with gross weight < 6000 g, and seizures with gross weight < 10 g (January 1987–April 2011). ^aPurity-adjusted seizure amount

exhibit *ns* used to construct this study's series, see Supporting information, Table S2.)

Conterminous US: price time-series description

Conterminous US median cocaine price increased sharply around the time of the 1989 regulation, but recovered by 1991 (Fig. 2). Price increased just before and again after the 1992 regulation. Median price increased at the time of the 1995 regulation, but recovered by 1998. Price rose at the time of the 2006 regulation and remained elevated to the series end.

Conterminous US: purity time-series description

Conterminous US median cocaine purity dropped at the time of the 1989 regulation, but generally recovered in 1–2 years (Fig. 3). Little change in purity occurred at the times of the 1992 and 1995 regulations. Following the 2006 regulation, purity declined to and remained at the study period's lowest levels (NB: while not the analytical focus here, in 1999, Operation Purple's start year, an approximate 3-year elevation in price and decrease in purity began; Figs 2, 3).

Descriptive overview

Taking the conterminous US seizure amount, price and purity series collectively, the major downturns in US cocaine availability during the study period occurred at the times of essential chemical controls (Figs 1–3). The largest was

at the time of the 2006 regulation, followed by the 1989 regulation.

ARIMA-intervention modeling

The general initial ARIMA-intervention analysis model for the first three regulations was:

$$(1 - B)Y_t = C + \left(\frac{\omega_1}{1 - \delta_1 B}\right)(1 - B)I_{1t} + \left(\frac{\omega_2}{1 - \delta_2 B}\right)(1 - B)I_{2t} + \left(\frac{\omega_3}{1 - \delta_3 B}\right)(1 - B)I_{3t} + (1 - \theta_1 B)(1 - \theta_{12} B^{12})a_t$$

where B is the backshift operator such that $BY_t = Y_{t-1}$; C is a constant term which represents the overall trend of the series (with adjustments for intervention effects); a_t s are independently normally distributed random errors; ω_1 , ω_2 and ω_3 represent the effects of the 1989 potassium permanganate/solvents, 1992 acids and 1995 MIBK interventions, respectively; δ_i represents the impact dampening rate of an intervention effect; θ_1 is a non-seasonal moving average parameter; θ_{12} is a seasonal moving average parameter. Consistent with other chemical control analyses [4,5,34,36–40], I_{1t} , I_{2t} and I_{3t} are step functions for the 1989, 1992 and 1995 interventions, respectively (as such, ω represents a series level change)—(analysis period: January 1987–December 2000). In the final models, estimates for

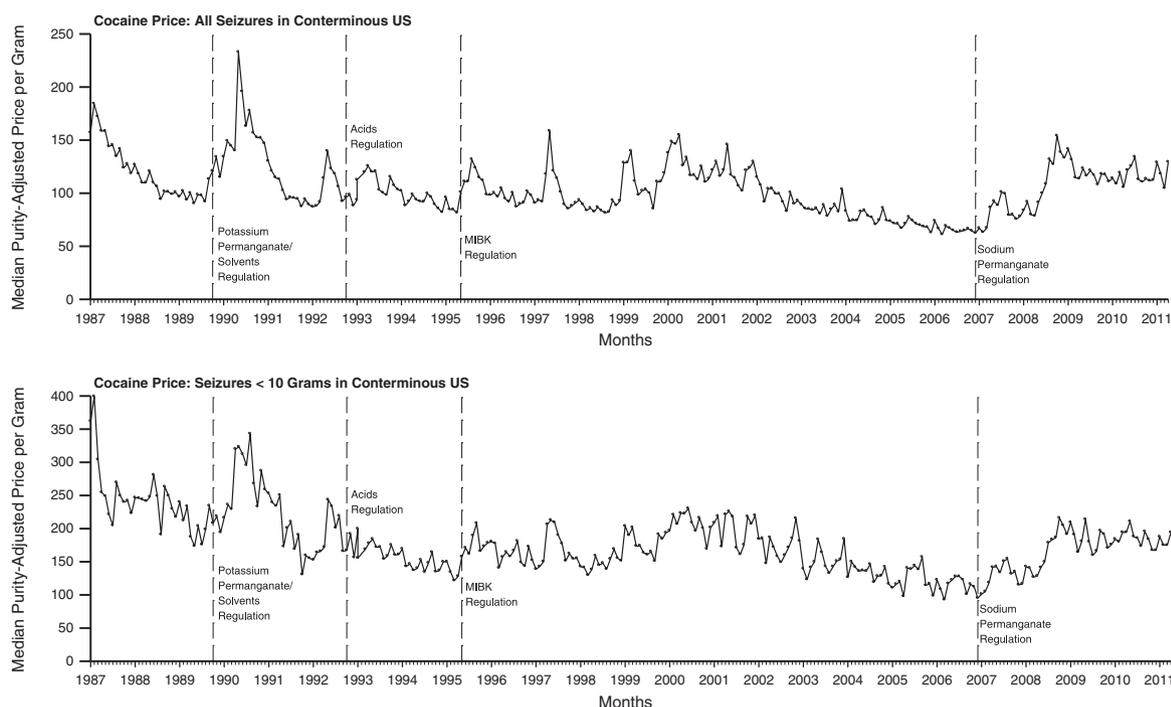


Figure 2 US cocaine essential chemical regulations: conterminous US monthly median cocaine purity-adjusted price^a for all seizures and for seizures with gross weight < 10 g (January 1987–April 2011). ^aAdjusted to 2010 US dollars

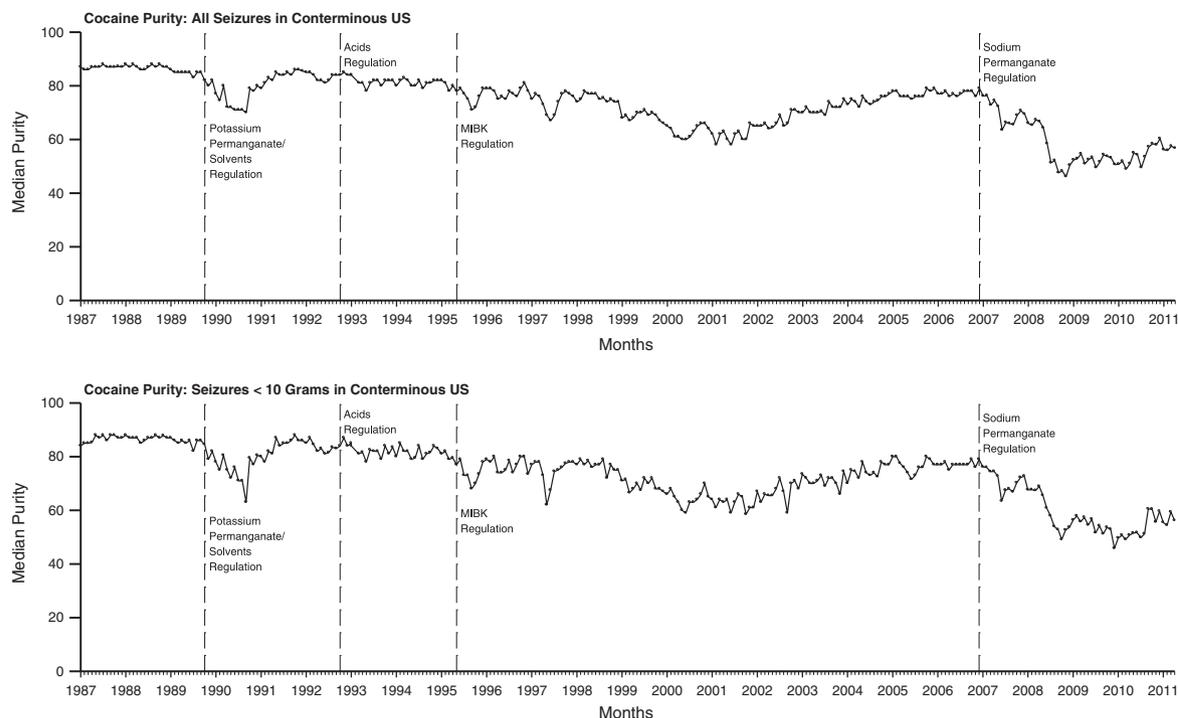


Figure 3 US cocaine essential chemical regulations: conterminous US monthly median cocaine purity for all seizures and for seizures with gross weight < 10 g (January 1987–April 2011)

C and θ_{12} were retained if statistically significant. An estimate for δ was retained if it and its respective estimate for ω were statistically significant [50]. A non-seasonal autoregressive parameter, ϕ_1 , and a seasonal autoregressive parameter, ϕ_{12} , were considered if warranted by model diagnostics.

The initial model for the 2006 sodium permanganate regulation was:

$$(1 - B)Y_t = C + \left(\frac{\omega_1}{1 - \delta_1 B} \right) (1 - B)I_{1t} + (1 - \theta_1 B)(1 - \theta_{12} B^{12})a_t$$

defined as earlier, except that ω_1 represents the effect of the 2006 intervention; and I_{1t} is a step function for that intervention (analysis period: January 2000–April 2011).

The formula $\omega/(1 - \delta)$ was used to assess the impact size of statistically significant series level shifts. δ ranges from 0 to 1; the closer to 1, the more slowly (gradually) the impact is realized. When δ was not found to be statistically significant (but its respective ω was), δ was set to 0 (an abrupt impact) during re-estimation.

The conterminous US seizure amount series for exhibits < 6000 g, and the median purity-adjusted price and median purity series for all available exhibits are modeled. Each model's pre-intervention period for a regulation is the time from the series' beginning to the regulation's start; the post-intervention period is the time from the regulation's start to the series' end.

Conterminous US purity-adjusted seizure amount had significant abrupt declines at the times of the 1989, 1992 and 2006 regulations (Table 2). Regarding price, gradual significant increases began at the times of the 1989 and 2006 regulations; an abrupt increase occurred at the time of the 1995 regulation. Regarding purity, an abrupt decline occurred at the time of the 1989 regulation; a gradual decline began at the time of the 2006 regulation.

The percentage change from pre-regulation series level to post-regulation series level is shown for statistically significant impacts in Table 2. All four regulations were associated with a substantial percentage change ($\geq 25\%$) in one or more of the three availability indicator series. The largest impacts occurred in association with the 1989 and 2006 regulations; both were associated with pronounced impacts on seizure amount and price; the 2006 regulation was also associated with a large impact on purity. The percentage change computation method is presented in Supporting information, Table S3.

As supplementary material, results from ARIMA-intervention analyses of the conterminous US retail series (<10 g) are presented in Supporting information, Table S4.

Southeast US and southwest US

At the times of the regulations, the southeast US and the southwest US experienced changes in cocaine

Table 2 US 1989, 1992, 1995 and 2006 cocaine essential chemical regulation impacts on cocaine seizure amount^a, price^b and purity^c in the conterminous United States (US): model parameter estimates.

	Parameter	Purity-adjusted seizure amount			Purity-adjusted price			Purity		
		Est	(95% CI)	% change	Est.	(95% CI)	% change	Est.	(95% CI)	% change
Series period (January 1987–December 2000)										
1989 potassium permanganate/solvents regulation	ω_1	-0.32**	(-0.59, -0.06)	-28%	15.52**	(2.73, 28.31)	+36%	-3.21**	(-6.08, -0.33)	-4%
	δ_1	- ^d	-	-	0.57**	(0.13, 1.01)	-	-	-	-
1992 acids regulation	ω_2	-0.34**	(-0.60, -0.07)	-29%	5.56	(-8.62, 19.74)	-	0.16	(-2.72, 3.04)	-
1995 MIBK regulation	ω_3	-0.08	(-0.35, 0.18)	-	21.13***	(7.02, 35.24)	+25%	-1.68	(-4.57, 1.20)	-
ARIMA	θ_1	0.65***	(0.54, 0.77)	-	0.29***	(0.14, 0.44)	-	0.14*	(-0.01, 0.30)	-
Series period (January 2000–April 2011)										
2006 sodium permanganate regulation	ω_1	-0.25**	(-0.47, -0.03)	-22%	6.18**	(0.97, 11.39)	+100%	-1.80**	(-3.58, -0.02)	-35%
	δ_1	-	-	-	0.91***	(0.81, 1.00)	-	0.93***	(0.85, 1.01)	-
ARIMA	θ_1	0.70***	(0.57, 0.82)	-	0.47***	(0.31, 0.62)	-	0.18**	(0.01, 0.34)	-
	ϕ_{12}	0.30***	(0.14, 0.46)	-	-	-	-	-	-	-

The seizure amount series was log-transformed. Est. = estimate; CI = confidence interval; ω_j = intervention impact; δ_j = impact rate; θ_1 = non-seasonal autoregressive parameter; ϕ_{12} = seasonal autoregressive parameter; MIBK = methyl isobutyl ketone; ARIMA = autoregressive integrated moving average. For the 1992 and 1995 regulations, gradual impacts were not found; consequently, δ_2 and δ_3 are not listed. ^aMonthly totals of pure cocaine in seizures < 6000 g gross weight; ^bmedian price per pure gram adjusted to 2010 US dollars; all seizures; ^cmedian purity; all seizures; ^ddashes (-) indicate that the parameter estimate was not in the model. * $P < 0.10$; ** $P < 0.05$; *** $P < 0.01$.

availability indicators that roughly approximated those for the conterminous US (Fig. 4). (A mid-wholesale level, < 100 g—a market level above retail but below that of upper wholesale—was used for the southeast and southwest US seizure amount series because extensive fluctuation occurs in the upper wholesale range.)

Southeast and southwest US ARIMA-intervention models are shown in Supporting information, Tables S5–S6.

Comparison series

Seizure amount and price for marijuana, a drug not targeted by chemical controls, changed little at the

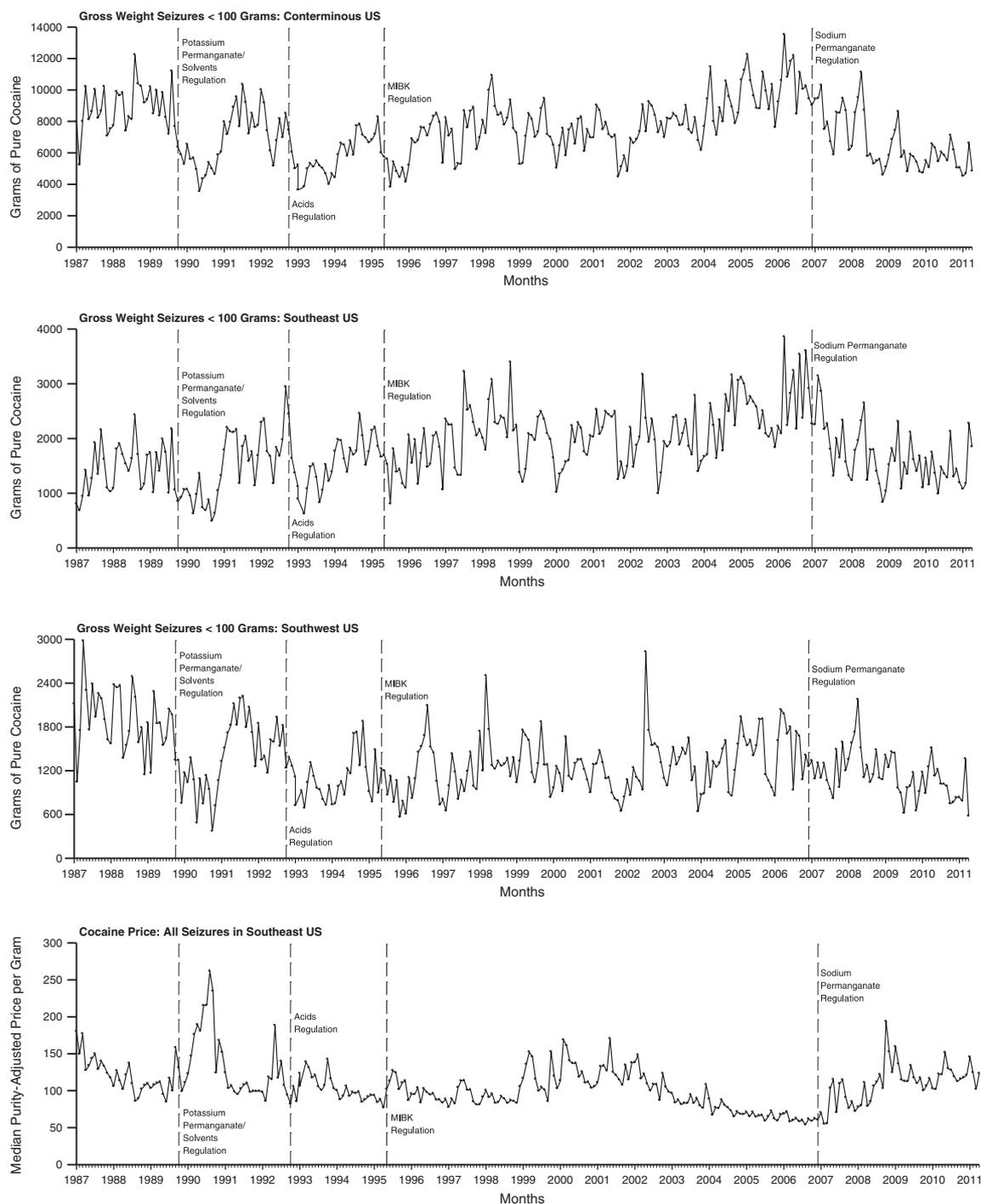


Figure 4 US cocaine essential chemical regulations: monthly totals of pure cocaine seized^a, monthly median cocaine purity-adjusted price^b, and monthly median purity in the southeast US and southwest US (January 1987–April 2011). Cocaine purity-adjusted price in the US southwest is generally lower than that in the conterminous US and the southeast US (cf. [45]). ^aPurity-adjusted seizure amount in gross weight exhibits < 100 g. ^bAdjusted to 2010 US dollars

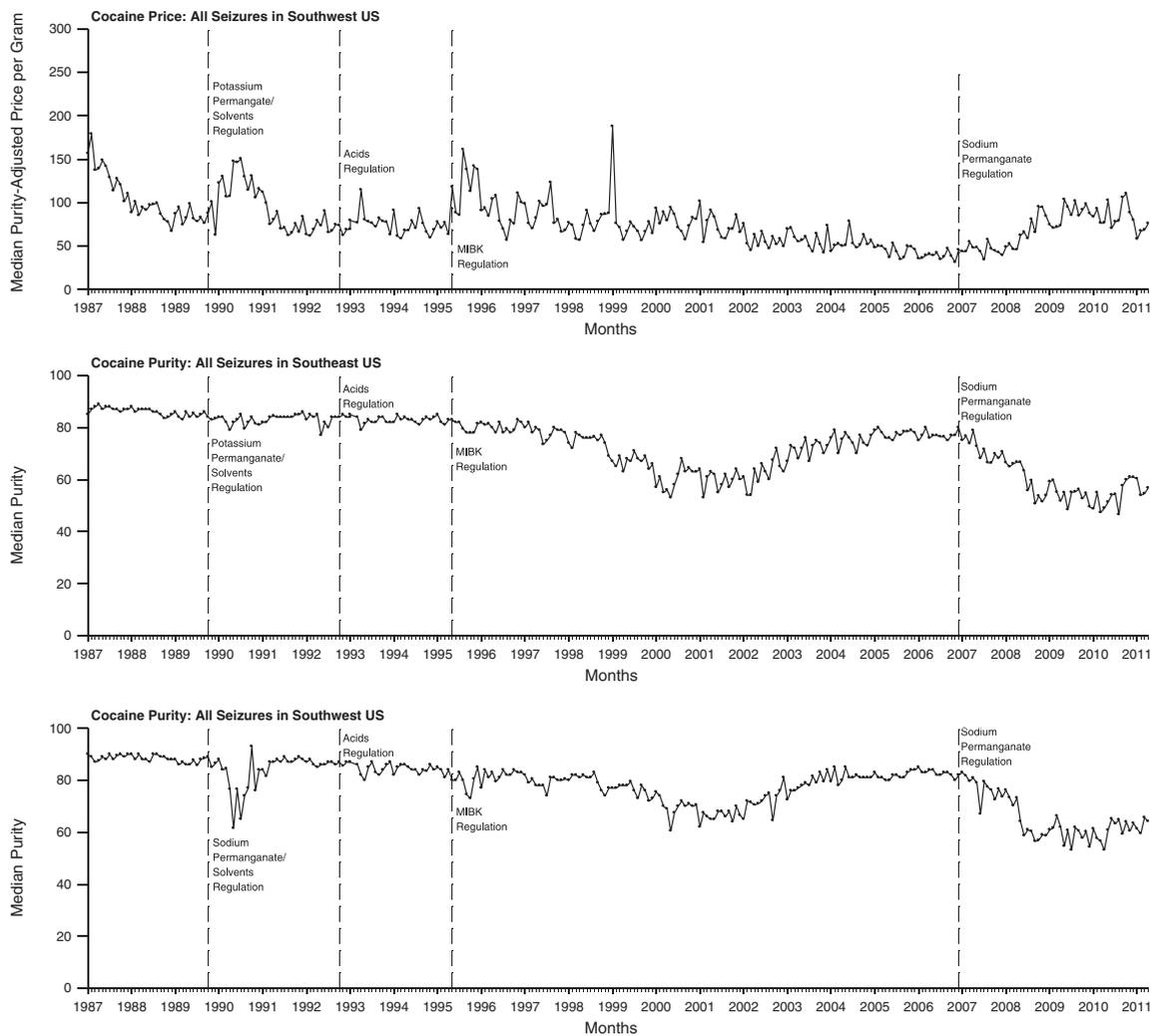


Figure 4 (Continued)

times of the cocaine regulations (Figs 5, 6). Cocaine, heroin and methamphetamine were all targeted by essential/precursor chemical controls in late 1989; their availability dropped simultaneously (Figs 5–7). Later, when cocaine and methamphetamine were targeted by temporally distinct chemical controls, their availability dropped at those distinct times. During the study period, the largest downturns in methamphetamine and heroin availability occurred at the times of their essential/precursor controls [5,38,39,41]. (The seizure amount series in Fig. 5 were constructed using approximate mid-wholesale levels.)

DISCUSSION

All four US cocaine essential chemical regulations were associated with downturns in conterminous US cocaine availability, the most pronounced of which occurred in association with the 2006 sodium permanganate regulation: cocaine seizure amount dropped

22%, price rose 100% and purity dropped 35%. The 2006 impacts continued to the study period end (April 2011). Research is now needed to determine how long reduced availability will continue.

The 1989 potassium permanganate/solvents regulation was associated with the second most pronounced downturn in conterminous US cocaine availability: cocaine seizure amount dropped 28%, price rose 36% and purity dropped 4%. Recovery following the regulation occurred within 2 years.

In association with the 1995 MIBK regulation, price in the conterminous US rose 25%. It recovered in approximately 3 years. At the time of the 1992 acids regulation, no impacts on price or purity were found; seizure amount dropped 29% and recovered 6–7 years later.

Seizure amount, purity and price (SAPP) patterns

Impacts found here (seizure amounts and purity declined and price rose) were consistent with SAPP patterns (Table 1) expected to follow drug production

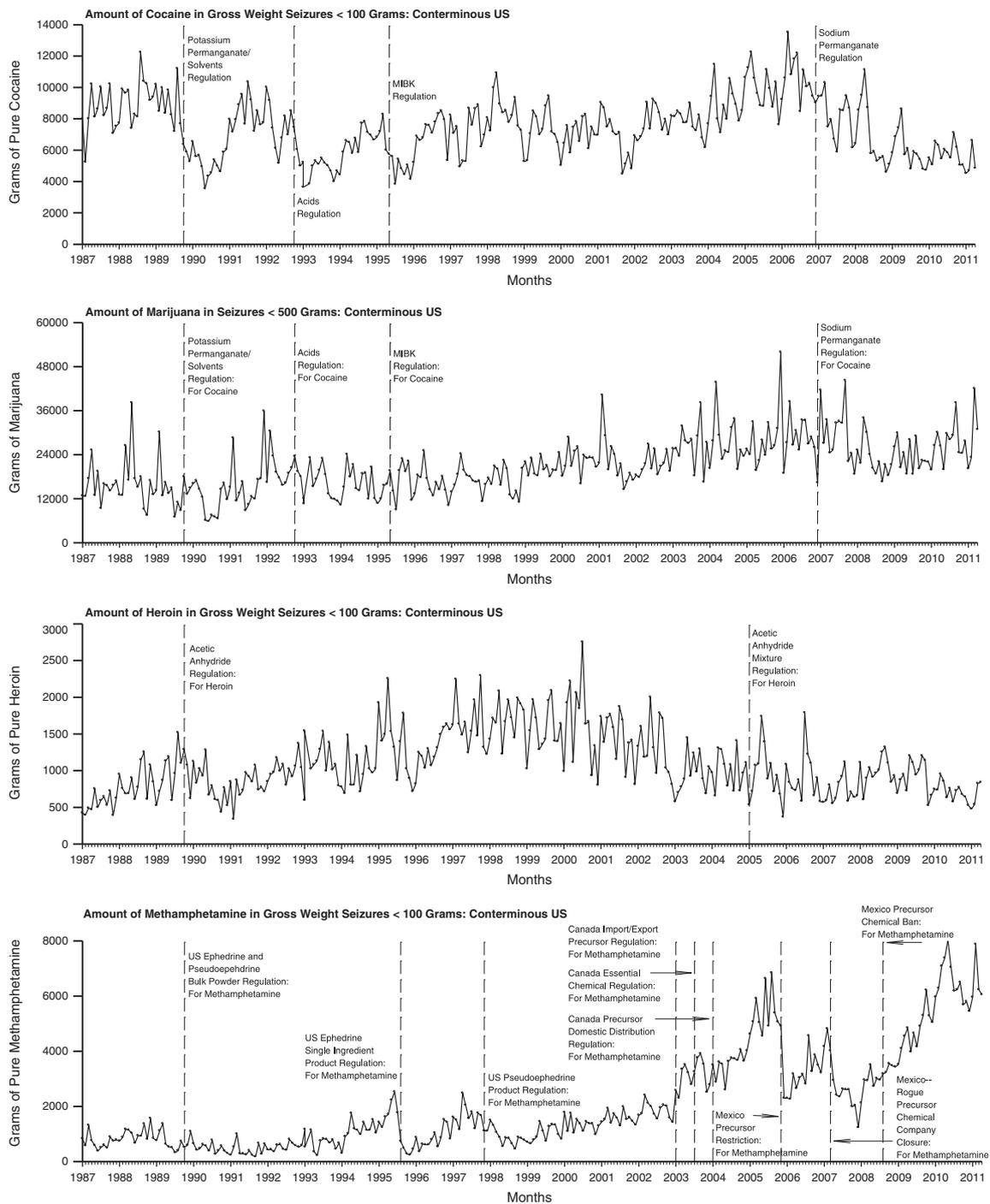


Figure 5 Essential/precursor chemical controls and monthly totals of cocaine^a, marijuana^b, heroin^a and methamphetamine^a seized in the conterminous US (January 1987–April 2011). Cocaine chemical regulations are listed in the cocaine and marijuana graphs; heroin chemical regulations are listed in the heroin graph [5]; and methamphetamine controls are listed in the methamphetamine graph [38,39,41]. Following Mexico's controls, multiple types of methamphetamines (including relatively low potency types such as *l*-methamphetamine and racemic methamphetamine) became commonplace [41]. This limits comparisons of the methamphetamine series prior to Mexico's controls with that post-Mexico's controls. ^aMonthly totals of pure cocaine, heroin and methamphetamine, respectively, in cocaine, heroin and methamphetamine exhibits with gross weight < 100 g. ^bMonthly totals of marijuana in exhibits with gross weight < 500 g

interventions such as chemical controls [5], and inconsistent with those expected from US domestic law enforcement interdiction.

Comparison series

The marijuana seizure amount and price series changed little at the times of the cocaine chemical regulations,

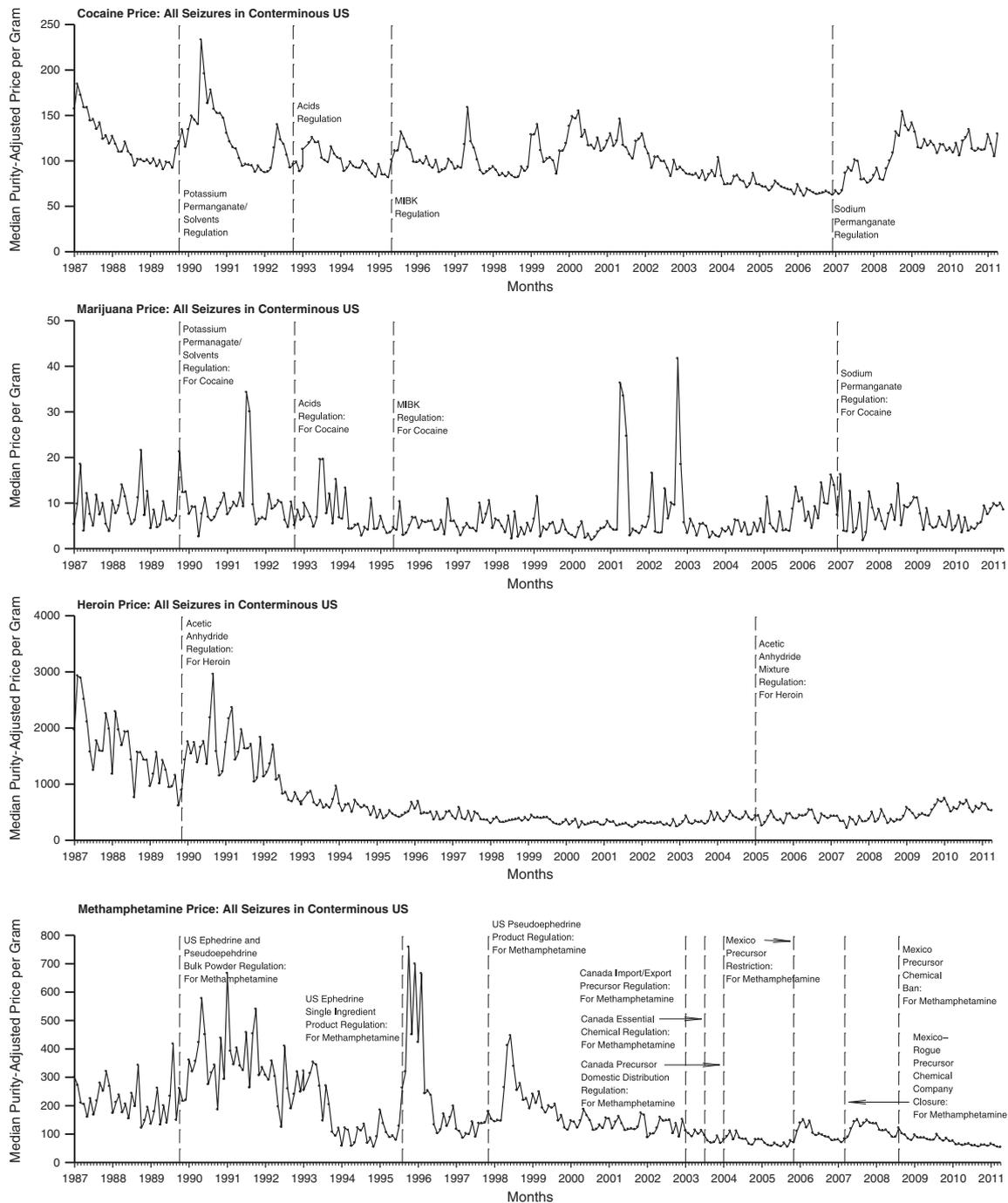


Figure 6 Essential/precursor chemical controls and monthly median cocaine, marijuana, heroin and methamphetamine price^a in the conterminous US (January 1987–April 2011). Cocaine chemical regulations are listed in the cocaine and marijuana graphs; heroin chemical regulations are listed in the heroin graph [5]; and methamphetamine controls are listed in the methamphetamine graph [38,39,41]. Following Mexico's controls, multiple types of methamphetamines (including relatively low potency types such as *l*-methamphetamine and racemic methamphetamine) became commonplace [41]. This limits comparisons of the methamphetamine series prior to Mexico's controls with that post-Mexico's controls. ^aMedian purity-adjusted price for cocaine, heroin and methamphetamine. Price for all four drugs was adjusted to 2010 US dollars

suggesting that neither general drug control nor system-wide changes in STRIDE accounted for the impacts found. When chemical controls targeted cocaine, methamphetamine and heroin simultaneously (October 1989), availability of all three drugs dropped. When later targeted

at different times, cocaine and methamphetamine dropped at those distinct times. As such, chemical controls predicted the temporal convergence and divergence of availability changes in multiple major illicit drugs, a drug policy finding unique to date.

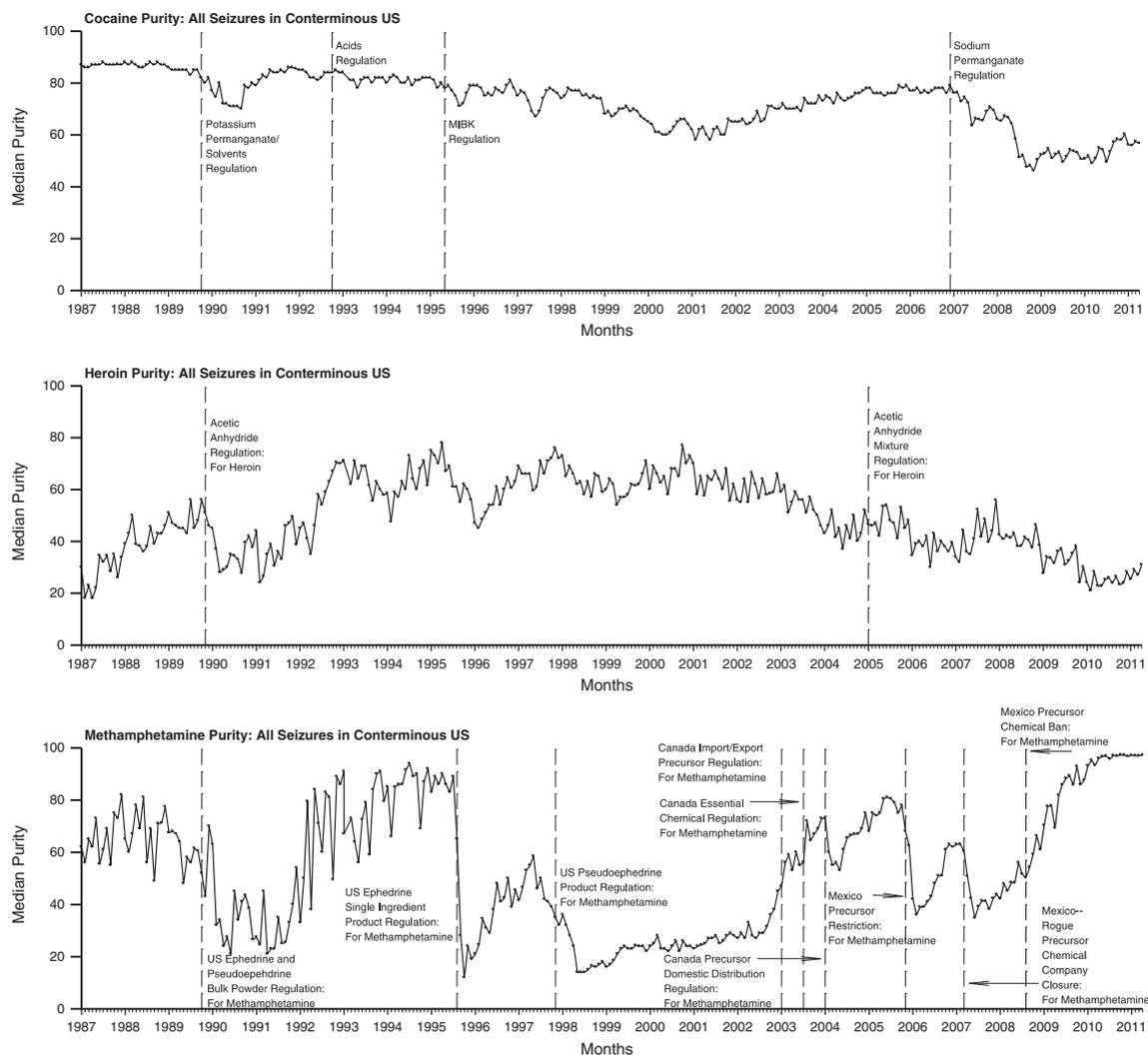


Figure 7 Essential/precursor chemical controls and monthly median cocaine, heroin and methamphetamine purity in the conterminous US (January 1987–April 2011). Cocaine chemical regulations are listed in the cocaine graph; heroin chemical regulations are listed in the heroin graph [5]; and methamphetamine controls are listed in the methamphetamine graph [38,39,41]. Following Mexico's controls, multiple types of methamphetamines (including relatively low potency types such as *l*-methamphetamine and racemic methamphetamine) became commonplace [41]. This limits comparisons of the methamphetamine series prior to Mexico's controls with that post-Mexico's controls

Cocaine manufacturing efficiency

Cocaine essential chemical controls, when effective, should reduce cocaine manufacturing efficiency (cf. [54]). After increasing during 2002–06, cocaine manufacturing efficiency (as measured by overall yield: ratio of cocaine manufactured to coca bush cultivation) declined substantially in 2007 and remained lower to 2011 [25,55] (recall that sodium permanganate was regulated in December 2006). Coca cultivation seems an unlikely explanatory factor; it did not decrease in 2007 [56]. Cocaine laboratory seizures also seem unlikely; they changed relatively little from 2006 to 2007 [56].

Change in cocaine essential chemical exports

The DEA estimated that, in 1988, US companies supplied 55% of the potassium permanganate, MEK, toluene, ethyl

ether and acetone used in Colombian cocaine manufacture. In 1990, following the chemicals' October 1989 regulation, that estimate shifted to 15% [57]. During 2005–11, US sodium permanganate exports peaked at 1.5 million kg in 2006 (effectively the year before the chemical's December 2006 regulation), then decreased to 0.96 million kg by 2011 [58].

Operation Purple and the 2006 US sodium permanganate regulation

Albeit speculative, Operation Purple's initial impact [32] might have been undermined temporarily by the unregulated upsurge in US sodium permanganate production during the early 2000s (Operation Purple began in 1999). Once the US 2006 regulation was implemented, such undermining may have been largely curtailed. If so, a

substantial drop in US cocaine availability, as seen with the regulation, would be expected.

Impact start times

As with previous federal chemical control studies, impacts began relatively immediately, suggesting that producers lacked chemical stockpiles sufficient to delay the impacts' initiation [4,5,34,36–39].

Design considerations

This study used intervention (interrupted) time-series analysis with replication and comparison series, a powerful quasi-experimental design [59–61]. Quasi-experimental designs can lend support to, but do not prove, a causal hypothesis, however. Accordingly, it is possible that the impacts found here could have been due to factors in addition to or other than US essential chemical regulation.

In late 1989, US government efforts to interdict boat/plane cocaine shipments in the Caribbean increased [62] —a consideration here as the potassium permanganate/solvents regulation was implemented in October 1989. The main US portal for Caribbean transshipped cocaine is the southeast US, particularly Florida [45]. Authors have suggested that traffickers, in response to the Caribbean effort, redirected cocaine shipments through Mexico, a land route to the southwest US [62]. If correct, southeast US cocaine availability should have declined beginning in late 1989, accompanied by growth in southwest US cocaine availability. Instead, the present study found that both areas experienced pronounced declines in cocaine seizure amount, pronounced rises in price and comparable recovery points—findings consistent with essential chemical regulation, not an interdiction operation directed at a selected portal.

Peru initiated a force-down/shoot-down policy against drug trafficker aircraft in March 1995 [54,63], 2 months before the May 1995 MIBK regulation. Granting the possibility that the policy had a lag before realizing an effect, it may have contributed to the cocaine price rise that occurred at the time of the MIBK regulation.

We know of no other law enforcement events which began approximately at the times of the US cocaine chemical regulations. The regulations were not coordinated with non-chemical-control drug activities/policies [18–21].

STRIDE's use in research has been questioned because it is an administrative system, lacks probabilistic sampling and involves black market acquisitions [64]. Such caveats, while important to note, do not establish the absence of construct validity (i.e. the absence of STRIDE's ability to reasonably represent drug prevalence/availability change) [41]. Instead, construct validity is assessed most effectively via pattern matching; that is, by examining whether a measure's patterns match what would be expected if it

reflected a construct [60]. A growing literature indicates that various STRIDE measures have had construct validity regarding drug prevalence/availability; in particular, seizure amounts, prices and purities have changed/varied as predicted by multiple drug hypotheses [5,41].

Next steps

Research is needed on whether cocaine availability changed outside the United States, and whether cocaine use and consequences were impacted (NB: kilograms of cocaine seized in Europe rose during 2002–06 (47 052, 91 895, 71 709, 106 063 and 120 567, respectively), then dropped during 2007–09 (76 858, 54 316 and 49 100, respectively) [65,66] (sodium permanganate regulation: December 2006). Cocaine users and use in Milan declined during 2007–10 [67]. US cocaine users and treatment admissions declined during 2007–11 [68,69]—see Supporting information, Figs S2 and S3. Cocaine/heroin-related arrests dropped sharply in California at the time of the 1989 regulation [34]. A cost-benefit analysis of the US regulations would be informative.

Cocaine essential chemical control issues

In Colombia, there have been attempts to manufacture potassium permanganate illicitly [70,71]. In Peru, some producers may be using ethanol as a potassium permanganate substitute [27]. Chemical diversion from domestic sources in Colombia, Peru and Bolivia and alternative source nations continues [14,72]. Multiple Chinese companies produce potassium permanganate; taken collectively, their production has surpassed US production [17]. China has chemical regulations and participates in Operation Purple, but reportedly lacks infrastructure to adequately monitor its chemical production/trade [32,72].

CONCLUSION

Essential chemical control was associated with the primary downturns in US cocaine availability during the past quarter-century. This finding—consistent with chemical control research on methamphetamine and heroin—renders essential/precursor chemical control the first policy with such a demonstrated breadth of impact across major illicit drugs.

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Declaration of interests

None.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site:

Figure S1 The conterminous United States (US) and its southwest US and southeast US areas.

Figure S2 Past month use of cocaine: persons aged 12 or older in the United States (2002–2012).

Figure S3 Annual counts of cocaine treatment admissions in the United States (2001-2011).

Table S1 Common commercial uses of potassium permanganate.

Table S2 Number of STRIDE seizures used to construct this study's series.

Table S3 Computation of percent change estimates.

Table S4 US 1989, 1992, 1995 and 2006 cocaine essential chemical regulation impacts on cocaine purity-adjusted seizure amount, purity-adjusted price and

purity in the conterminous US—seizures with gross weight < 10 grams: model parameter estimates.

Table S5 US 1989, 1992, 1995 and 2006 cocaine essential chemical regulation impacts on cocaine purity-adjusted seizure amount, purity-adjusted price and purity in the southeast US: model parameter estimates.

Table S6 US 1989, 1992, 1995 and 2006 cocaine essential chemical regulation impacts on cocaine purity-adjusted seizure amount, purity-adjusted price and purity in the southwest US: model parameter estimates.