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Investigating the Net Benefit of a Clinical Algorithm Detecting Chemotherapy Patients' Risk of Emergency Care and Inpatient Hospitalization

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Background

- Emergency department (ED) visits and inpatient hospitalizations (IP) for patients undergoing chemotherapy treatment are common and potentially preventable. Hospitalization negatively affects patient experience, increases out-of-pocket costs, and delays cancer treatment
- Proactive clinic outreach to patients in the first two weeks after the initiation of chemotherapy, coupled with proactive symptom management, has been shown to reduce hospitalization. Deploying proactive symptom management throughout treatment according to a real-time, daily hospitalization risk prediction score may yield new opportunities to reduce hospitalization
- A recent study found that a deep learning algorithm, the Reverse Time Attention (RETAIN) model, displayed promising performance in its ability to predict dynamic hospitalization risk during chemotherapy using cancer-registry-linked insurance claims data. RETAIN predicts a patient's next-day likelihood of an ED visit (AUROC: 0.9) or an IP stay (AUROC: 0.88) in the six months following chemotherapy initiation
- In contrast to the AUROC performance metric, a net benefit function, and decision curve analysis accounts for the potential economic consequences of decisions made according to a prediction model. In this study, we assume the RETAIN model is coupled with proactive symptom management. Thus, a net benefit function can account for the costs of true positives (hospital costs avoided), false positives (unnecessary proactive symptom management), and false negatives (missed opportunities to reduce unplanned IP stay or ED visit)

OBJECTIVES AND AIMS

Aim: Evaluate the economic net benefit of a deep learning model predicting ED visits and IP stays for three strategies over a range of algorithm threshold probabilities.

Objectives: (1) Utilize decision curve analysis using three strategies:

1.Treat according to algorithm - Select patients for proactive symptom monitoring according the RETAIN prediction model

2.Treat all curve - Proactive symptom management given daily to all patients

3.Treat none curve - None of the patients receive the proactive symptom management

(2) Compare the population costs associated with the Treat according to algorithm (Strategy 1) vs the Treat-None (Strategy 3) at select thresholds for both ED Visits and IP stays

Methods

The current study uses the test set data from the original development of the RETAIN model.

Data Source: Data for this retrospective cohort study was sourced from the Hutchinson Institute for Cancer Outcomes Research (HICOR) database. The database links enrollment and claims data from Medicare and two commercial insurers, Premera Blue Cross and Regence Blue Shield, to the National Cancer Institute's SEER and the Washington State cancer registry records for the state.

Study Cohort: Our study included patients 18 years or older newly diagnosed with any primary tumor site, excluding leukemias and nonmelanoma skin cancers, between January 1, 2011 and June 30, 2018. The population was limited to those who were treated with their first course of systemic outpatient chemotherapy since diagnosis. Our inclusion criteria is consistent with Center for Medicare and Medicaid Services's Oncology Care Model.

Methods

Net Benefit Assumptions
Average IP stay cost: $24,770
Costs of IP proactive symptom management intervention: $200.00
Average ED visit cost: $1,300
Costs of ED proactive symptom management intervention: $65.00
Proactive symptom management intervention is 100% effective

Main Outcomes and Measures:

Net Benefit Function – captures the economic benefits minus the harms of each strategy for a given threshold probability. For example, in Strategy 1:

- Benefits = costs associated with RETAIN's true-positives *(hospitalizations prevented)* + true-negatives *(no costs)*
- Harms = costs associated with RETAIN's false-positives *(unnecessary proactive symptom management)* and false-negatives *(i.e., missed opportunities to prevent hospitalization).*

According the (Vicker's 2008), the net benefit can be calculated as:

$$\frac{True\ Positive\ Count - False\ Positive\ Count * (\frac{P_t}{1-P_t})}{Total\ Sample\ Size}$$

Where P_t is the threshold probability (i.e., odds cutoff) for a given intervention (proactive symptom management):

$$Odds\ (cutoff) = \frac{costs\ of\ False\ Positives - costs\ of\ True\ Negative}{costs\ of\ False\ Negatives - costs\ of\ True\ Positives}$$

Decision Curve – represents the Net Benefit Function calculated over the entire set of relevant threshold probabilities (potentially ranging from 0 – 100%) in 5% increments for three strategies:

1. Treat according to algorithm - Select patients for proactive symptom monitoring according the RETAIN prediction model
1. Treat all curve - Proactive symptom management given to all patients every day
2. Treat none curve - None of the patients receive the proactive symptom management

The strategy with the "highest curve" at a given threshold probability has the largest net benefit. Thus, the x-axis identifies the threshold probability with the largest net benefit for a given strategy.

The data was analyzed using STATA/IC 16.1 and RStudio.

Results

- The analytic dataset included 2,485 patients from 22 clinics in Washington state who experienced a total of 801 ED visits and 941 unplanned IP stays during the 6 months post-chemotherapy initiation. Patients were primarily aged 65 years and older (66%), Non-Hispanic white (89%), with a mix of cancers, and roughly half were diagnosed with stage III or IV (48%).
- On any given day, the likelihood of either an ED visit or IP stay was approximately 1%.
- The analytic dataset included a predicted risk score generated by the RETAIN model and the true outcome for each patient-day, yielding 84,352 patient day observations for the IP stay model and 88,464 for the ED visit model.

Figure 3: IP stay confusion matrix at the 5% threshold

Sensitivity: 95.6%; Specificity: 84.2%; Prevalence: 1.1%

Algorithm Results: 5% Threshold	Actual IP Stay	No IP Stay	Total
Positive	TP = 900	FP = 13,164	N = 14,064
Negative	FN = 41	TN = 70,247	N = 70,288
Total	N = 941	N = 83,411	N = 84,352

Figure 4: ED visit confusion matrix at the 5% threshold

Sensitivity: 93.3%; Specificity: 77.3%; Prevalence: less than 1%

Algorithm Results: 5% Threshold	Actual ED Stay	No ED Visit	Total
Positive	TP = 747	FP = 19,916	N = 20,663
Negative	FN = 54	TN = 67,747	N = 67,801
Total	N = 801	N = 87,663	N = 88,464

Figure 5: Population Costs associated with the Treat according to algorithm (Strategy 1) vs the Treat-None (Strategy 3) at Select Thresholds for IP stays

Avg. IP Stay Cost: $24,770		IP Table of Population-Level Strategy Costs		Intervention Cost: $200.00
Threshold	5%	10%	35%	50%
Costs According to Algorithm (Strategy 1)	($3,828,370)	($8,729,750)	($11,874,330)	($13,474,220)
Costs Treat None (Strategy 3)	($23,308,570)	($23,308,570)	($23,308,570)	($23,308,570)
Cost Savings	$19,480,200	$14,578,820	$11,434,240	$9,834,350

Figure 6: Population Costs associated with the Treat according to algorithm (Strategy 1) vs the Treat-None (Strategy 3) at Select Thresholds for ED Visits

Avg. IP Stay Cost: $24,770		IP Table of Population-Level Strategy Costs		Intervention Cost: $200.00
Threshold	5%	10%	35%	50%
Costs According to Algorithm (Strategy 1)	($1,413,295)	($1,224,665)	($1,034,605)	($1,026,090)
Costs Treat None (Strategy 3)	($1,041,300)	($1,041,300)	($1,041,300)	($1,041,300)
Cost Savings	($371,995)	($183,365)	$6,695	$15,210

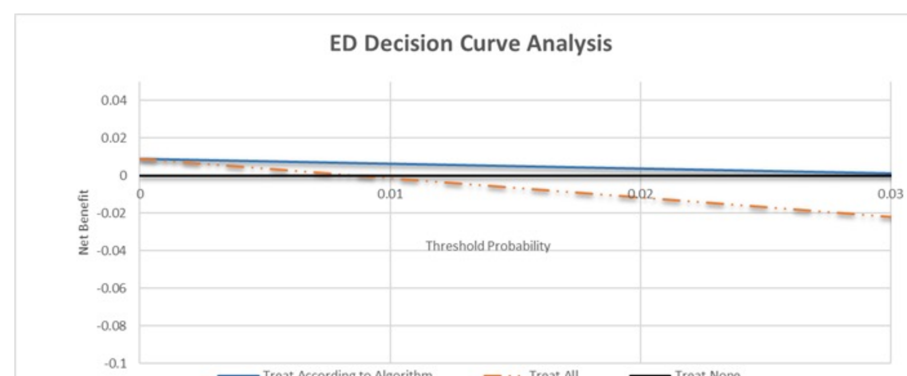

Figure 2: The graph gives the expected net benefit per patient relative to no nurse call intervention for any patient ("treat none"). Threshold probabilities are restricted as thresholds greater than 3% are of no benefit.

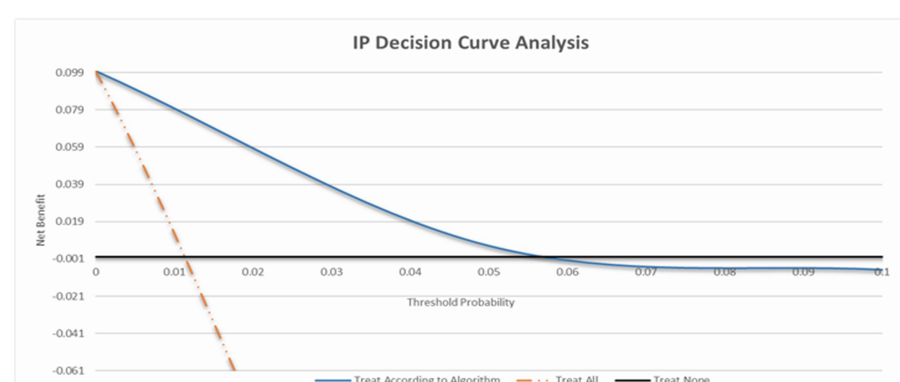

Figure 1: The graph gives the expected net benefit per patient relative to no nurse call intervention for any patient ("treat none"). Threshold probabilites are restricted as thresholds greater than 10% are of no benefit.

Results

We provide the following calculation for illustrative purposes. Net benefit of Strategy 1 – Strategy 2:

$$\frac{900 - 13{,}164 * (\frac{0.05}{1-0.05})}{84{,}352} - \frac{941 - 83{,}411 * (\frac{0.05}{1-0.05})}{84{,}352}$$

$$= 0.002 - (-0.04) = 0.042$$

Interpretation of net benefit:

- The net benefit of the RETAIN algorithm (i.e., 0.042) relative to treating all patients (Strategy 2) can be interpreted as:

$$0.042 \times \frac{100}{0.05/0.95}$$
$$= 80\ fewer\ false - positive\ results\ per\ 100\ patient\ visit\ days.$$

- This is equivalent to the algorithm leading to 80% fewer nurse call interventions compared to the strategy of calling all patients.
- The net benefit of none of the patients receiving proactive symptom management (Strategy 3) is zero across all algorithm threshold probabilities for IP visits.
- Note: The net benefit for ED visits for strategies, 1, 2, and 3 is negative for algorithm threshold probabilities greater than 5%.

Conclusion

- The RETAIN model was developed as a feasibility study using administrative claims data. Additional research with real-time data sources (EHR, PRO, biometric data) and interventions is required for real-time applications in clinical practice
- However, this study suggests that the strategy of selecting patients for proactive symptom monitoring according the RETAIN prediction model generates a higher net benefit relative to the Treat all and Treat none strategies at low probability thresholds for IP and ED visits
- At higher probability thresholds, the RETAIN prediction model did not provide any net benefit. Given the high costs of both IP and ED visits, future research should consider lower probability thresholds for algorithms targeting the proactive symptom monitoring of chemotherapy patients.

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Drug Prices and Crime: An Empirical Study Examining Northern Central America

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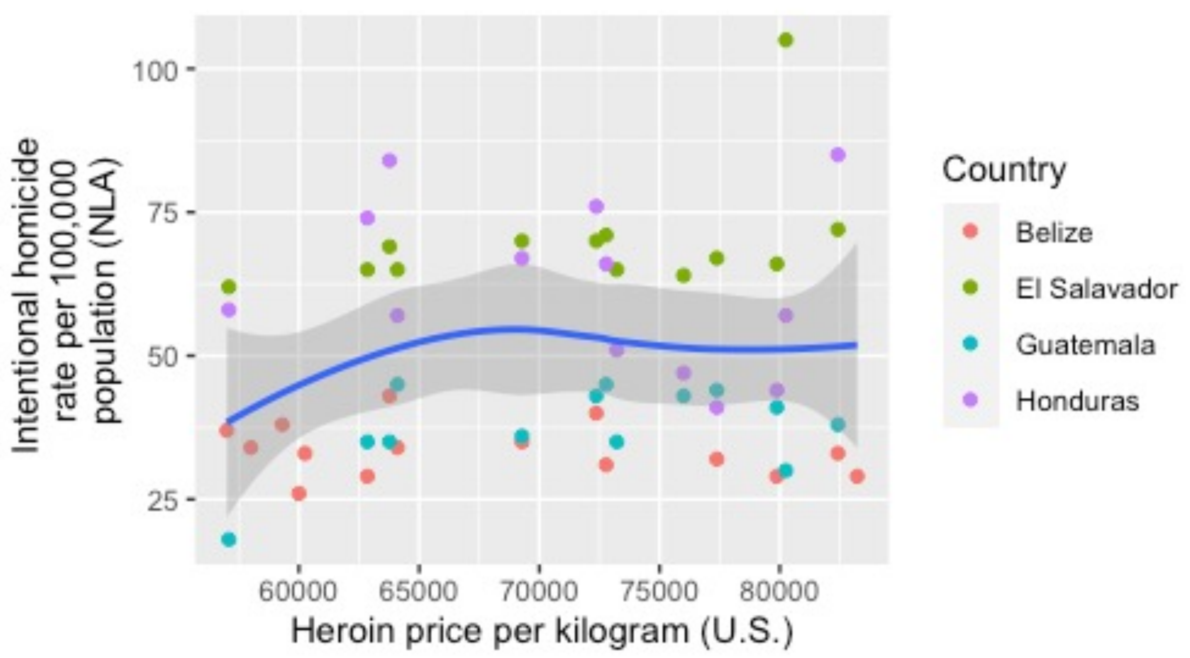
Background

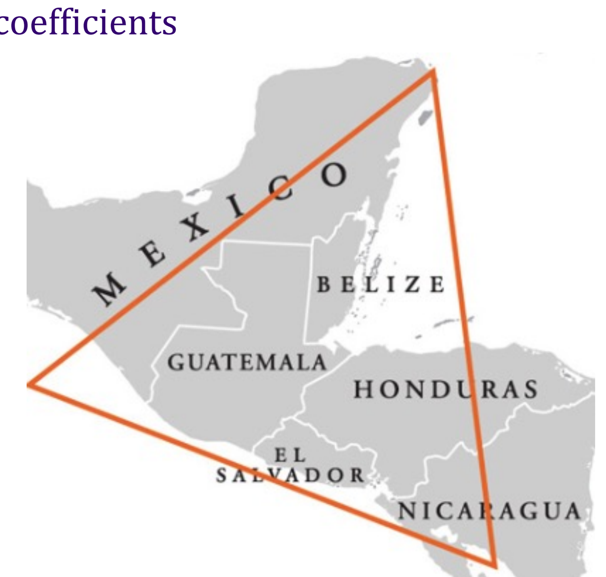
- Crime in Northern Central America (NCA) is a public health and societal issue that is persistent and costly
- The region has experienced the highest intentional homicide rates for nearly two decades (2004-2020) at 50 per 100,000 population (Figure 1)
- The regional concentration of homicidal risk factors includes notorious street gangs (or maras) and their interactions, contiguous factors related to drug trafficking and their spillover effects, economic forces, and regulatory inefficiencies that may confer positive and negative externalities, among others
- Sarrica (2008) hypothesized the price of illegal drugs affects the level of violent crimes

Figure 1: Rate of Intentional Homicides in Northern Latin America from 2004-2020



OBJECTIVES AND AIMS

Aim: To discover whether the prices of illegal drugs affect the level of intentional homicides in NCA
Objective: Use a two-stage least squares (2SLS) regression model that considers the time-varying omitted variables correlated with illegal drug prices not observable in the model and produces consistent coefficients



World Vision (2020)

Theoretical Framework

Becker's Crime and Punishment Model (1968):

$$u = pU(Y - f) + (1 - p)U(Y) \qquad (1)$$

where "u" is the individual's utility which is a function of the money they would receive from the crime "Y", the risk of being arrested "p", and the harm of the punishment "f". Sarrica (2008) acknowledges if the price of a drug rose (or fell), say in the next month (T + 1), the marginal monetary returns from any act of violence would increase (decrease);

$$Y = Y_{T+1} \geq Y_T \qquad (2)$$

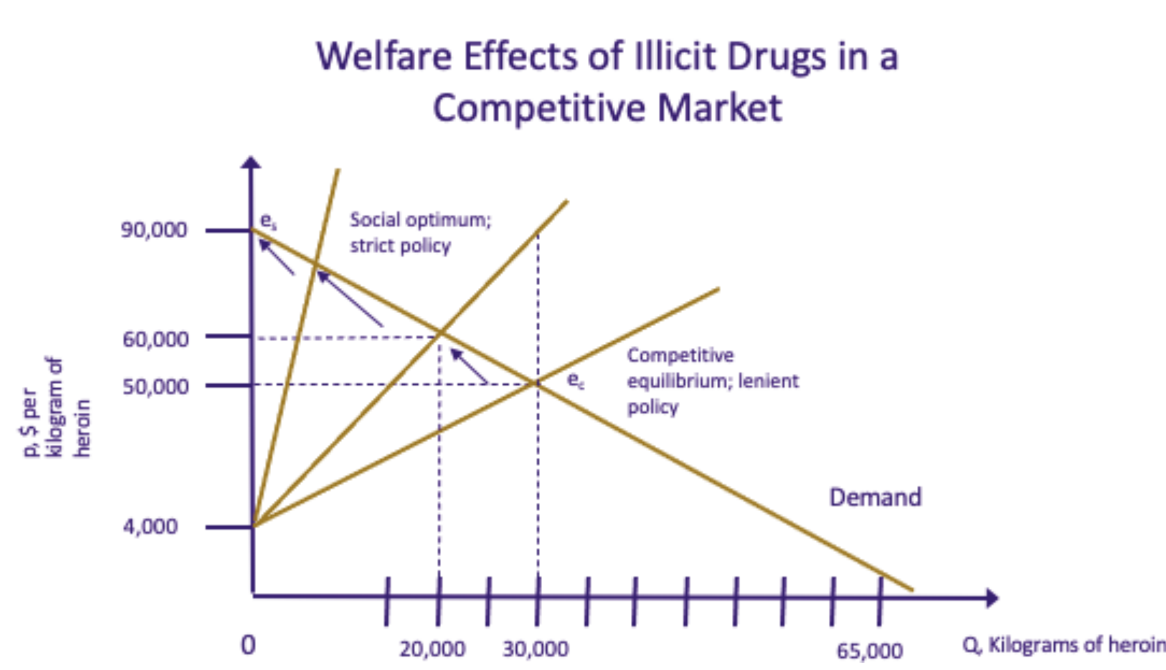
$$Y = Y_{T+1} < Y_T \qquad (3)$$

Crime will only occur when,

$$u_{T+1} > 0 \qquad (4)$$

A drug dealer will only commit a crime when the reward is greater than the punishment (i.e., marginal benefit > marginal cost)

Figure 2: Current Policy



MATERIALS AND METHODS

Two-Stage Least Squares introduced by Theil (1953) and Basmann (1957):

$$\ln(Hom.\ Rate) = \gamma_1 + \gamma_2 * \ln(h.Price) + \gamma_3 * \ln(c.Price) + \gamma_4 * \ln GDPpc + \varepsilon \qquad (5)$$

Instrumental Variable Requisites:

1. Uncorrelated with the errors (i.e., IV is exogenous)
2. Correlated with the regressors

First Stage:

$$\ln(\widehat{h.price}) = \theta_1 + \theta_2 * \ln(c.Price) + \theta_3 * \ln(GDPpc) + \delta_1 * \ln(OD\ deaths) + \upsilon \qquad (6)$$

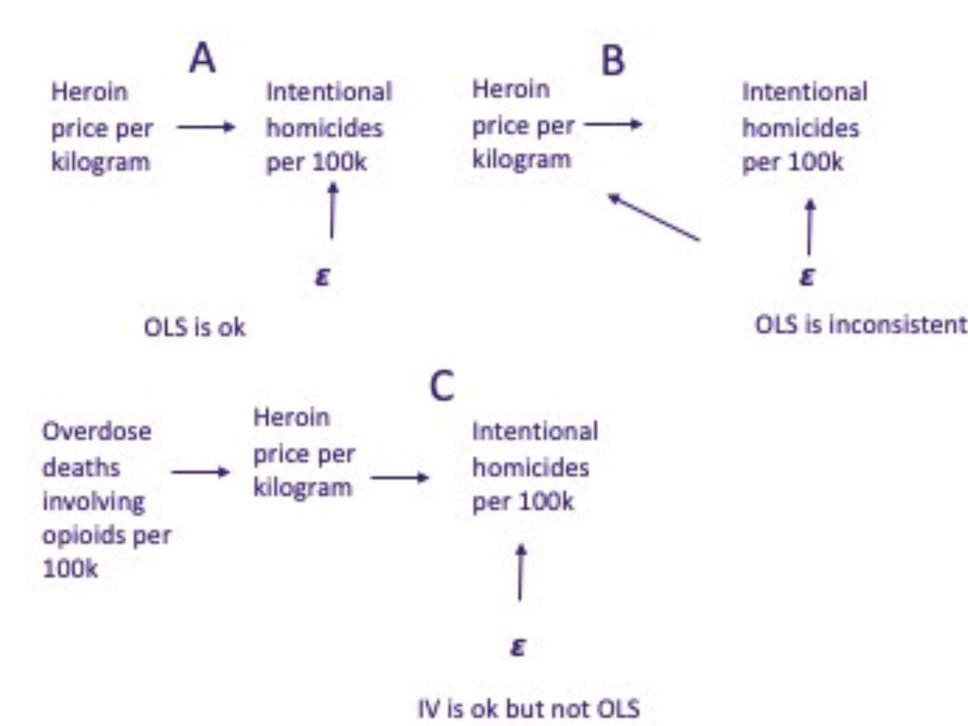
$$\ln(\widehat{c.price}) = \alpha_1 + \alpha_2 * \ln(h.Price) + \alpha_3 * \ln GDPpc + \eta_1 * \ln(c.price.gram) + \tau \qquad (7)$$

Second Stage:

$$\ln(Hom.\ Rate) = \gamma_1 + \gamma_2 * \ln(\widehat{h.Price}) + \gamma_3 * \ln(\widehat{c.Price}) + \gamma_4 * \ln GDPpc + \varepsilon \qquad (8)$$

With ε assumed to be i.i.d. N(0, σ_ε^2)

Figure 3: Illustrative example



Results

Table 1: Summary Statistics

	Intentional Homicides per 100,000 population	Heroin price per kilogram (U.S.)	Cocain price per kilogram (U.S.)	GDP per capita (PPP)	Cocain price per gram (U.S.)
Mean (SE)	50.17 (18.53)	$70,680 (8,135)	$34,217 (5,393)	$3,523 (1,046)	$187 (42)
Median	44	$72,369	$34,623	$3,574	$197
Range	18-105	$57,000-$83,221	$25,193-$43,533	$1,887-$6350	$119-$240
Skewness	0.62	-0.16	-0.31	0.43	-0.30
Kurtosis	2.8	1.76	2.08	3.45	1.63
Observations (n)	54	54	17	54	17

Years: 2004-2020
Source: World Development Indicators (WDI), Centers for Disease Control and Prevention (CDC), U.S. Customs and Border Protection (CBP), Drug Enforcement Agency (DEA)

Table 2: Log Homicide Equation: OLS, and 2SLS Models

	Dependent Variable: Log Homicide			
	OLS	2SLS		
log(heroin price)	0.076* (0.042)	0.257** (0.115)		
log(cocain price)	0.118 (0.228)	0.744 (0.651)		
log(GDP)	-0.195*** (0.064)	-0.226*** (0.072)		
Constant	3.371 (2.6)	-4.884 (7.75)		
Diagnostic Tests:	df1	df2	statistic	p-value
Weak instrument: log(heroin price)	2	49	40.25	<0.001
Weak instrument: log(cocain price)	2	49	41.3	<0.001
Wu-Hausman	2	47		0.045
Sargan	0	NA	NA	NA

*Note: *p<0.1; **p<0.05; ***p<0.01*

Conclusion

- Intentional homicide rates in NCA are partly explained by oscillating heroin prices per kilogram and GDP per capita
- The evidence suggests if current policy shifts towards the competitive equilibrium (Figure 2), the price of heroin may decline, in turn, reducing the rate of homicides in NCA

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