Methods and Sources

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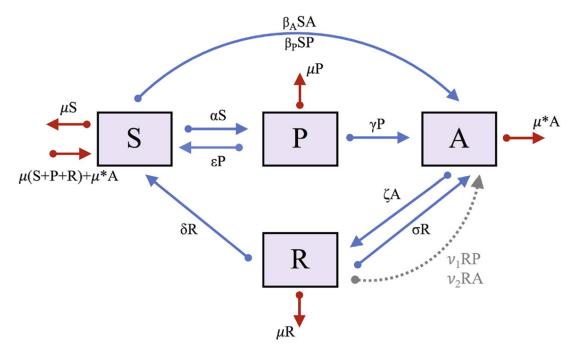
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The Previous Methodology

1. Prelude

- Battista, Strickland, Pearcy (2019):
 - Introduce the S,P,A,R model for the prescription opioid epidemic in the US (right).
 - Show the impossibility of reaching an addiction free equilibrium without significant decreases in the prescription rate.
 - Investigate the epidemic as a 5-dimensional dynamical system.
 - Investigate the impact of the parameter space using variance based sensitivity methods.



Data: Sources and Manipulations

a. Sourced Data: State

Rates/Value	New York State		
	Value	Source	
Addiction (γ)	0.00744	Battista et al. (2019)	
Relapse (σ)	0.9	Battista et al. (2019)	
Addiction if misuse of opioids	0.093	Battista et al. (2019)	
Prevalence of opioid misuse	0.039	NYS Opioid Report (2018)	
Regular use if any use	0.44	Kelly et al. (2008)	
Overdoses attributed to addicted class	0.546	Battista et al. (2019)	
Prescription Substance Abuse in the Northeast	0.019	Han et al. (2017)	

a. Sourced Data: Sub-state

Rate/Value	NYC		NYS/NYC	
	Value	Source	Value	Source
Prescription ($lpha$)	0.289	NODD	0.5229	NODD
Overdoses attributed to addicted class	0.546	Battista et al. (2019)	0.546	Battista et al. (2019
Natural death rate ($oldsymbol{\mu}$)	0.006312	NYS CHIRS	0.008903	NYS CHIRS
Population (2010-2017)	List	<u>US Census</u>	List	<u>US Census</u>
Overdoses (2010-2017)	List	NODD	List	NODD
Prescribed Users (2012- 2017)	List	NODD	List	NODD
Prescribed Users (2010)	722000	Epi Data Brief (2012)	-	-
People admitted to OASAS treatment (2010-2017)	List	NYS Opioid Report (2018)	List	NYS Opioid Report (2018)

b. Calculated Values:

Rate/Value	NYC		NYS/NYC	
	Value	Procedural Breakdown	Value	Procedural Breakdown
Addiction via illicit drugs sourced from the prescribed class (β_P)	0.0028	I	0.0028	1
Addiction via illicit drugs sourced from the prescribed class (β_A)	0.00223	II	0.00246	II
Prescribed class (2010)	0.0387	Ш	0.0638	IV

b. Calculated Values: Procedural Breakdown

- *I.* $\beta_P = \text{(prevalence of opioid misuse)} *P(Addiction|opioid misuse) = 0.039*0.093$
- II. β_A : Given I, OASAS treatment entries and actual overdoses attributed to opioids, found values of b_A that resulted in comparable values after running the model from 2010-2017. $\beta_A = E(b_A)$
- III. $P_{NYC}(2010) = \text{(prescribed users in 2010)} * \frac{P(\text{regular use}|\text{any use})}{(Population in 2010)}$
- IV. $P_{NYS/NYC}(2010)$: Using the same method for III for 2012-2017, Determined proportion for 2010 using a regression model P(t) ~ t given $R^2 = 0.975$

Formulas and Equations

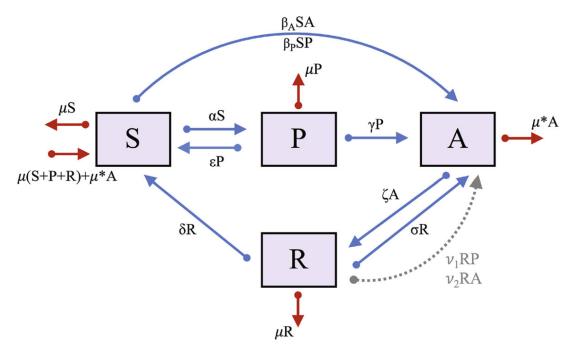
2. (a) Assumptions

- From Battista (2019):
 - Enforcing a conservative system in an attempt to simplify the model:

1.
$$S+P+R+A=1 \triangleleft t$$

2.
$$\dot{S} + \dot{P} + \dot{R} + \dot{A} = 0 \triangleleft t$$

- $3. \quad S, P, R, A \geq 0 \triangleleft t$
- Assuming a linear relapse rate (σ) , independent of the R and A class.



1)
$$\dot{S} = -\alpha S - \beta_A SA - \beta_P SP + \varepsilon P + \delta R + \mu (P + R) + \mu^* A$$

2)
$$\dot{P} = \alpha S - (\varepsilon + \gamma + \mu) P$$

3)
$$\dot{A} = \gamma P + \sigma R + \beta_A SA + \beta_P SP - (\zeta + \mu^*)A$$

4)
$$\dot{R} = \zeta A - (\delta + \sigma + \mu)R$$

2. (a) Assumptions: Our contribution

- A and R refer to any opioid substance abuse disorder.
 - Classify larger proportion of population as members of the classes.
 - Shifts β_A (addiction via illicit sourced drugs sourced from the addicted class) to include illicit opioids such as synthetic fentanyl, heroin, etc.
 - Wider net overall.
- Complete turnover of the R class:
 - $\delta + \sigma + \mu = 1$
 - Opioid treatment lengths range between 28-90 days.
 - Assuming that within a given year, anyone initially in the R class will have moved on.

Original Formulation:

1.
$$\dot{S} = -\alpha S - \beta_A SA - \beta_P SP + \epsilon P + \delta R + \mu(P + R) + \mu^* A$$

2. $\dot{P} = \alpha S - (\epsilon + \gamma + \mu) P$
3. $\dot{A} = \gamma P + \sigma R + \beta_A SA + \beta_P SP - (\zeta + \mu^*) A$
4. $\dot{R} = \zeta A - (\delta + \sigma + \mu) R$

Define for each class X some scaled value x such that:

•
$$X = x * x_c$$

• $\dot{X} = \frac{dx}{d\tau} * \frac{t_c}{x_c} = \dot{x} * \frac{t_c}{x_c}$ for $t = \tau * t_c$

Plugging in the scaled values:

1.
$$\dot{s} = -\alpha t_{c} s - \beta_{A} t_{c} a_{c} s a - \beta_{P} t_{c} p_{c} s p + \frac{[\epsilon t_{c} p_{c} p + \delta t_{c} r_{c} r + \mu t_{c} (p_{c} p + r_{c} r) + \mu^{*} t_{c} a_{c} a]}{s_{c}}$$

2. $\dot{p} = \frac{\alpha t_{c} s_{c}}{p_{c}} s - t_{c} (\epsilon + \gamma + \mu) p$

3. $\dot{a} = \frac{[\gamma t_{c} p_{c} p + \sigma t_{c} r_{c} r]}{a_{c}} + \beta_{A} t_{c} s_{c} s a + \frac{\beta_{P} t_{c} s_{c} p_{c}}{a_{c}} s p - t_{c} (\zeta + \mu^{*}) a$

4. $\dot{r} = \frac{\zeta t_{c} a_{c}}{r_{c}} a - t_{c} (\delta + \sigma + \mu) r$

Choose:

•
$$t_c = \frac{1}{\delta + \sigma + \mu}$$
 for $\delta + \sigma + \mu = 1$

•
$$p_c = \frac{1}{\beta_P}$$
, $a_c = \frac{1}{\beta_A}$, and $r_c = \frac{1}{\sigma}$

1.
$$\dot{s} = -(\alpha + \alpha + p)s + \frac{1}{s_c} \left[\frac{p}{\beta_P} (\epsilon + \mu) + \frac{r}{\sigma} (\delta + \mu) + \frac{\mu^* a}{\beta_A} \right]$$

2. $\dot{p} = \alpha \beta_P s_c s - (\epsilon + \gamma + \mu) p$
3. $\dot{a} = \beta_A r + \left(\frac{\beta_A}{\beta_P} \gamma + \beta_A s_c s \right) p + \left(\beta_A s_c s - (\zeta + \mu^*) \right) a$
4. $\dot{r} = \frac{\zeta \sigma}{\beta_A} a - r$ (IV)

• Choose $s_c = \frac{1}{\alpha}$:

1.
$$\dot{s} = -(\alpha + \alpha + p)s + \frac{\alpha p}{\beta_P}(\epsilon + \mu) + \alpha r \left(\frac{1}{\sigma} - 1\right) + \frac{\alpha \mu^* a}{\beta_A}$$

2. $\dot{p} = \beta_P s - (\epsilon + \gamma + \mu)p$

3. $\dot{a} = \beta_A r + \left(\frac{\beta_A}{\beta_P}\gamma + \frac{\beta_A}{\alpha}s\right)p + \left(\frac{\beta_A}{\alpha}s - (\zeta + \mu^*)\right)a$

4. $\dot{r} = \frac{\zeta\sigma}{\beta_A}a - r$

- Define $h = \frac{\beta_A}{\beta_P}$, $k = \frac{\beta_P}{\alpha}$, $\beta_P = \alpha k$, g = hk and $\beta_A = \alpha hk$:
 - **k:** ratio of the rate of addiction via illicit opioids sourced from the prescribed class to the prescription rate.
 - h: ratio of the rates of addiction via illicit opioids from the addicted class to the prescribed class
 - g: ratio of the rate of addiction via illicit opioids sourced from the addicted class to the prescription rate.

Scaled formulation of the system:

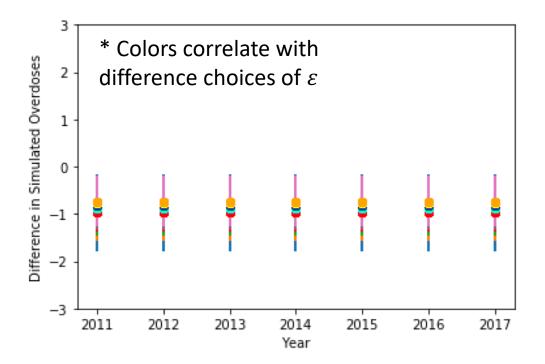
1.
$$\dot{s} = -(\alpha + \alpha + p)s + \frac{(\epsilon + \mu)}{k}p + \alpha(\frac{1}{\sigma} - 1)r + \frac{\mu^*}{g}a$$

2. $\dot{p} = \alpha ks - (\epsilon + \gamma + \mu)p$
3. $\dot{a} = \alpha gr + (h\gamma + gs)p + (gs - (\zeta + \mu^*))a$
4. $\dot{r} = \frac{\zeta\sigma}{\alpha g}a - r$ (VI)

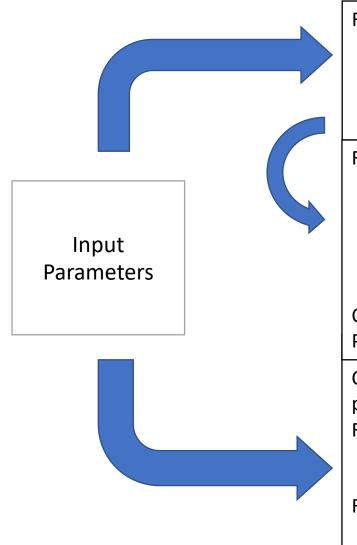
- As opposed to the original formulation, the scaled one focuses on ratios between different paths to opioid SUD (A class).
- Moreover, isolates an effect of the ratio between illicit prescribed drugs and non prescribed ones (a factor of interest with the rise of overdoses attributed to synthetic fentanyl in places like NYC).
- Depends on a smaller parameter space.

2. (c) Comparison

• Comparing the simulated overdoses from 2010-2017 for the same intervals of α , ε , ζ using Battista's formulation and our own, plotting the difference:



Pseudocode Breakdown



For α , ε , ζ in ranges:

For t in 2010-2016:

Solve ODE for t+1 (RK4)

Calculate $ORD_S(t)$

Calculate $d(ORD_S(t), ORD_A(t))$

For given α :

Find distance d s.t:

for sample of all $ORD_S(2017)$ and $n_{min} = 30$

fail to reject difference from $ORD_A(2017)$

for sample of $ORD_S(2017)\epsilon N_d(ORD_A(2017))$

 $n_{min} = 30 @ p < 0.1$

Collect samples $\triangleleft \alpha$

Perform ANOVA on α subsets

Create a Saltelli sample matrix given desired parameters and ranges.

For each row of the matrix (set of parameters):

For t in 2010-2020:

Solve ODE for t+1 (RK4)

For each population class in [S,P,A,R]:

Perform Sobol analysis

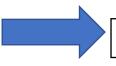
Find first order and total order sensitivities

Legend:

 $ORD_S(t)$: Simulated overdoses for year t

 $ORD_A(t)$: Actual overdoses for year t

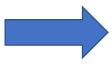
 $N_d(X)$: Neighborhood of radius d around value X



Plot $ORD_S(t)$ vs. Year



Plot ε $vs. \zeta$ for given α



Plot first order and total order sensitivities of populations to parameters