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Alabama opioid crisis: A data-driven analysis of the impact of COVID-19 and policy responses

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Abstract

The opioid crisis has severely affected Alabama in the last decade with high prescribing rates, rampant opioid-involved overdoses, and rising treatment admissions. This study presents the calibration of a time-dependent system of ordinary differential equations model to Alabama data from 2015 through 2023 to investigate dynamics of opioid use pre- and post-COVID-19. Predicted is an increase in use disorders and opioid overdose deaths from 2024-2028, with heroin and fentanyl use disorder ramping up while prescription opioid use disorder slows down. Our policy intervention results suggest it is vital that policy related to long-term recovery, relapse prevention, and overdose-reversals be implemented in tandem, with unintended consequences illustrated otherwise. Threshold values key to epidemic outcomes in Alabama are estimated, which can inform policymakers on tangible goals to combat the crisis.

Contents

Introduction

Opioids are a class of natural, semi-synthetic, and synthetic drugs that are highly addictive and involved in the majority of drug overdose deaths in the United States [Nat25d]. Prescription opioids for pain (e.g. oxycodone, morphine), heroin, and illicitly manufactured fentanyl are examples of opioids that will be of focus in our study. Although fentanyl is also a prescription opioid to address pain, the fentanyl explicitly modeled in our study is only illicitly manufactured. Prescription opioid use is a risk factor for heroin use, and a subset of individuals with prescription opioid use disorder transition to heroin use disorder, driven by heroin's low cost and high availability [Nat25b, Nat25a]. However, heroin can be adulterated by illegally manufactured fentanyl, which can cause a fatal overdose with even a small dose [Nat25c]. Opioid use disorders, resulting from the addictive nature opioids, can be treated with behavioral therapy, medications that reduce opioid use and cravings (methadone, buprenorphine, or extended-release naltrexone), and medications that treat withdrawal symptoms (Lofexidine) [Nat23].

The national opioid epidemic before 2020 is often described in three waves [DBC18]. The first wave began in the 1990s with a sharp rise in prescription opioid use, followed by a second wave around 2010 marked by increased heroin use. The third wave began in late 2013, characterized by a surge in deaths linked to illicitly manufactured fentanyl and its analogues. Alabama was not spared from the epidemic's impact. In 2013, the state drew national concern when healthcare providers wrote 141.1 opioid prescriptions for every 100 residents—approximately 6.8 million prescriptions—making Alabama the highest-prescribing state in the nation and nearly doubling the national average rate of 79.3 [Nat22]. Although the state's prescribing rate declined annually from 2013 through 2022, the opioid crisis remained an ongoing issue [Uni]. By 2017, treatment admissions for opioid use surpassed those for alcohol use in Alabama, recorded by their drug of choice upon admission [Ala]. Opioid use treatment admissions increased as followed: from 5,259 in 2015 to 5,650 in 2016 to

6,851 in 2017 and then nearly doubled to 12,075 by 2018. This is compared to alcohol admissions, which were 5,947 in 2017 and 6,181 in 2018, almost half of opioid admissions. In 2021, Alabama saw 981 opioid overdose deaths, accounting for 70% of all overdose deaths in the state [Aland]. By 2022, Alabama's overdose death rate was more than double that of 2014, with the rise throughout the years mostly attributed to the increase in fentanyl related deaths.

In recent years, researchers have proposed that the COVID-19 pandemic marks the beginning of a fourth phase of the opioid epidemic [PS20]. An interrupted time series model study indicates that the pandemic significantly altered the trajectory of opioid-related deaths across all regions of the United States, lending support to this claim [LD24]. Several factors may explain this shift. During the pandemic, reduced access to in-person treatment and a rapid expansion of telehealth services transformed the landscape of substance use disorder care [Sub20c]. These changes raised concerns about higher relapse and overdose rates [CBJ20]. Yet, the period also saw some improvements, including the emergency expansion of Medicaid, relaxed restrictions on methadone distribution, and broader telemedicine access for individuals with opioid use disorder [HS20]. Together, these developments illustrate how the opioid crisis evolved under the unique pressures of the pandemic.

Several policy initiatives have been implemented both nationally and within Alabama to mitigate the harmful effects of the opioid crisis. One such initiative is the Alabama Prescription Drug Monitoring Program (PDMP), established in 2004 to improve oversight of controlled substance prescriptions and help identify potential cases of misuse or overprescribing [Dep19]. In 2016, national legislation was amended to allow licensed physicians and dentists to prescribe naloxone, while pharmacists and nurses were authorized to dispense it [Leg22]. Naloxone is a fast-acting medication that can rapidly reverse an opioid overdose by binding to opioid receptors and blocking the effects of drugs such as heroin, fentanyl, and prescription painkillers. To further expand access, first responders were provided free naloxone kits contingent upon completing a training course in their use.

In 2017, the opioid epidemic was officially declared a national public health emergency, underscoring the growing severity of opioid misuse and overdose deaths across the United States [Thend]. At that time, Alabama continued to have the highest opioid prescription rate in the nation, reflecting the state's persistent struggle with prescription drug dependency and overprescribing practices [Cen20b]. Nationally, overdose deaths involving synthetic opioids such as fentanyl surged dramatically, marking a turning point in the crisis as illicitly manufactured fentanyl became increasingly prevalent in drug supplies [Cen20a]. In response to these alarming trends, Alabama issued Executive Order No. 708 in August 2017, establishing the Alabama

Opioid Overdose and Addiction Council in order to develop a coordinated statewide strategy to address opioid misuse, improve prevention and treatment programs, and strengthen data collection and policy recommendations [The17]. This initiative represented a significant step in Alabama's commitment to confronting the crisis through collaboration between public health officials, law enforcement, medical professionals, and community organizations.

The national opioid crisis has been mathematically modeled to better understand its dynamics or potential intervention points [BPS19, GTM22], with some focusing solely on illicit opioid use dynamics [CW22, COW24], and the latter concluding that expanding accessibility to specialty treatment would be most beneficial. Many heroin models in particular have stemmed from the White and Comiskey ordinary differential equations model with susceptibles, drug users, and those in treatment [WC07]. Several studies have utilized mathematical modeling to explore the dynamics of the opioid crisis in specific regions, including at the state level (OH, KY, VA, PA, WV, ME, MA, TN, Province of BC in Canada) [PRH+21, BS23, Akr24, IMH+21, PLS21], as well as the county level (OH, MA) [KJH21, BGID17]. A few used Susceptible-Infected-Recovered (SIR) modeling [PLS21, BS23, Akr24]. Other works incorporated policy intervention in their work, informing harm reduction strategies specific to their region of study [BS23, Akr24, IMH+21, PLS21]. Moreover, mathematical modeling has been used to inform policy and intervention methods for the opioid crisis at the national level [LSS+22, KTR23, HJ20, BMH+20, DLB+24, NLB+25, HW21, PHB18, ABW25, MS79]. Of these, many utilize compartmental models [PHB18, ABW25, NLB+25, DLB+24, KTR23]. A few of the studies illustrate how certain national policies can have unintended harmful effects and that no single policy is effective in mitigating the opioid crisis, instead concluding that a combination of policy approaches is necessary for significant improvement [HW21, PHB18, ABW25], which will motivate our work in investigating simultaneous policy impact.

A focus in a few of these studies was fentanyl and how to best respond to the rise in fentanyl deaths in recent years [IMH+21, LSS+22]. That said, there is a call for more work that incorporates synthetic opioids, including fentanyl, due to the large proportion of overdose deaths they contribute to, as well as models that calibrate to local data [SKSM24]. Another work incorporating fentanyl consisted of a mathematical SIR-type model focused on the opioid crisis in Tennessee, a state similarly affected by opioid misuse and overdose deaths as Alabama [PLS21]. This work examined how individuals transition between different stages of opioid use —such as non-use, prescription use, dependence, and recovery—while incorporating Tennessee-specific data on prescribing rates, overdose mortality, and more. By calibrating the model to reflect state-level dynamics, which illustrated that heroin and fentanyl were sustaining the

epidemic in the time frame 2013-2018, the study provided valuable insights into the potential effectiveness of interventions. This resulted in recommendations for treatment availability and relapse support, as well as opioid overdose death prevention efforts.

To the best of our knowledge, there has been no mathematical work focused specifically on the Alabama opioid epidemic taking into account the peculiarities the state has (e.g. high prescribing rate compared to other states and nationwide), thereby providing a motivation for our work in which the previously mentioned SIR model [PLS21], which includes fentanyl, will be slightly modified to apply to Alabama in order to fill this specific regional gap in the literature. This will allow a capturing of regional heterogeneities in order to investigate the impact of recent national and localized policy responses in the state. This follows a recommended priority for opioid misuse studies to "incorporate data specific to the target population and period whenever possible" as stated in a comprehensive review of these types of studies [CJH+21].

1. Mathematical methodology

1.1. Mathematical model

The SIR-type model previously developed for Tennessee will serve as a foundational mathematical model for this application to Alabama [PLS21]. Although we do not outline all details of the original model formulation, we do remark on key components for readers to more easily refer to here.

The state variables of the model are disjoint population classes measured as portions of the entire population: susceptible individuals (S) who do not take opioids of any kind or that take illegally obtained opioids in a manner not constituting use disorder; prescribed opioid users (P) who take prescription opioids from a provider in a manner that does not constitute use disorder; prescription opioid use disorder individuals (A) who are not using heroin or fentanyl, including those who are within a year of their most recent use of prescription opioids; heroin or fentanyl use disorder individuals (H), including those within a year of their most recent use of heroin or fentanyl; and stably recovered individuals (R) who have not relapsed with opioid use for at least a year. For clarity on the disjoint nature of the classes, individuals in the A class *may or may not* be prescribed opioids depending on their opioid source(s) (e.g. doctor prescription, illicit market) but even if they are prescribed, we make the simplifying assumption in our model that they are taking them in a manner that falls under use disorder, and thus do not fall into the P class. We hold a similar assumption for those in the H class that are prescribed opioids, and thus they are not

included in the P class. We also note that the "or" we use in the definition of the H class and throughout the paper regarding that class is an inclusive "or," meaning that individuals may have use disorder with heroin, fentanyl, or both. We adopt mostly the same definitions of these compartments as the previous work [PLS21], although we replace the word "addicted" with (substance or opioid) "use disorder" throughout this work due to recent recommendations in appropriate language choice [Nat21] and to concur with the DSM-5 terminology [Amend]. In addition, we slightly modify the criteria for the A, H, and R classes. We consider an individual stably recovered if they do not relapse *within a year after usage* (from recovery and sobriety efforts that may or may not include treatment or groups), and individuals stay in the A or H class, respectively, until reaching that length of recovery. This is more stringent than the 4-week mark previously used and is supported by work suggesting that around the one-year mark is when the number of relapses for opioids slows down greatly [Sin11]. Due to this steadying out, one year is an appropriate updated definition. Moreover, we aim to improve the state variable definitions by explicitly accounting for individuals who illegally obtain any opioids (e.g. illicit market, stealing) and take them in a non-use disorder manner (e.g. occasional misuse). These individuals will be considered as susceptible individuals in our model since they are not prescribed opioids and do not have use disorder.

Finally, we remark on the hierarchy of opioids due to their potency in this work, starting with the least potent of prescription opioids, then heroin, then fentanyl. Thus, if an individual is using illictly obtained prescription opioids that are laced with fentanyl in a manner constituting use disorder, they will be counted only in the H class, and if there is a prescription opioid overdose containing fentanyl, it will be considered a fentanyl overdose due to the lethal nature of even a small amount [Unind]. Any mention of overdoses in this work inherently refers to opioid overdose deaths, as we do not consider non-fatal overdoses in our analysis. Moreover, if an individual with heroin use disorder is taking any prescription opioids from any source, they will be counted only in the H class.

One limitation of our model is the possible miscategorization of individuals in the use disorder classes (A and H) when we calibrate to data, as individuals who are not yet identified in the data as having a use disorder for a given year may be counted in the susceptible class (if they are only illegally obtaining their opioids) or in the prescribed opioid class (if they are prescribed opioids at all).

The model parameters represent births, deaths, and transition rates among classes, and are all per capita yearly rates that hold the same definitions as work in [PLS21]. A synopsis of their definitions are included in Tables 1 and 2, along with calculated parameter values from work in Appendix B and estimated parameter values based

Table 1: Definitions of model rates and the parameter values calculated and assumed for the model with $\alpha(t)$ as a piecewise linear function of time. Units are per capita yearly rates (1/year) except ω is dimensionless.

Rate	**Definition**	**Param.**	**Assumed Value**
μS, μP, μA, μH, μR	natural death and birth rates	μ	0.010
$\mu_A A$	rate of prescription opioid use disorder individuals overdosing	μ_A	0.003
$\mu_H H$	rate of heroin or fentanyl use disorder individuals overdosing	μ_H	0.036
ω	perturbation term for case of $A = H = 0$ in relapse rate	ω	$0.1{*}10^{-9}$

on our work in Sections 1.3 and 2.1. We assume the population is of constant size throughout the time frame of study and thus, the natural birth and death rate is considered equivalent in our work. The system of ordinary differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= -\alpha(t)S - \beta_A SA - \beta_P SP - \theta_1 SH + \epsilon P + \mu P + \mu A + \mu H + \mu R + \mu_A A + \mu_H H,\\
\frac{dP}{dt} &= \alpha S - \epsilon P - \gamma P - \theta_2 PH - \mu P,\\
\frac{dA}{dt} &= \gamma P + \sigma R\frac{A}{A+H+\omega} + \beta_A SA + \beta_P SP - \zeta A - \theta_3 AH - \mu A - \mu_A A,\\
\frac{dH}{dt} &= \theta_1 SH + \theta_2 PH + \theta_3 AH + \sigma R\frac{H}{A+H+\omega} - \nu H - \mu H - \mu_H H,\\
\frac{dR}{dt} &= \zeta A + \nu H - \sigma R\frac{A}{A+H+\omega} - \sigma R\frac{H}{A+H+\omega} - \mu R,
\end{aligned} \tag{1}$$

provides the adopted model from [PLS21], excluding time-dependency for μ_A, where $S+P+A+H+R = 1$ as proportions of the population and parameter information is in Tables 1 and 2. Discussion on time-dependent $\alpha(t)$, including its definition, will be had in Section 2.1. Initial conditions are all positive resulting in the solutions being nonnegative and bounded between 0 and 1 as shown in [PLS21].

As outlined in [PLS21], assuming all parameter values are constant, the disease-free equilibrium (DFE) for this model, in which disease represents opioid use disorder is this work, requires unrealistic assumptions of either $\alpha = 0$ or $\gamma, \beta_P = 0$. In either case, this leads to the scenario where individuals can enter the opioid use disorder classes only through interaction with those who already have opioid use disorder (as other pathways into the classes are shut down). There is a sense of "infectiousness," so to speak, where interaction with others is required; we utilize this result to move forward since our general mathematical model is the same for analysis

Table 2: Definitions of model rates and the parameter values estimated for the model with $\alpha(t)$ as a piecewise linear function of time. Units are per capita yearly rates (1/year) except the initial conditions S_0, P_0, A_0, H_0, and R_0 are dimensionless.

Rate or IC	**Definition**	**Param.**	**Estimated Value**
$\alpha(t)S$	rate of being prescribed opioids for susceptibles	(see m, b)	
m	slope of time-dependent piecewise linear α	m	-0.019
b	y-intercept of time-dependent piecewise linear α	b	0.287
ϵP	rate of finishing prescription opioids and returning to susceptible class	ϵ	1.68
γP	rate of prescribed opioid users developing a prescription opioid use disorder	γ	0.0123
$\beta_A SA$	rate of developing prescription opioid use disorder for susceptible individuals through illicit market or interactions with prescription opioid use disorder individuals	β_A	0.000898
$\beta_P SP$	rate of developing prescription opioid use disorder for susceptible individuals through leftover (e.g. from a family member, friend) or stolen prescriptions (e.g. from a pharmacy, family member)	β_P	0.00123
$\theta_1 SH$	rate of developing heroin or fentanyl use disorder for susceptible individuals through illicit market or interactions with heroin or fentanyl use disorder individuals	θ_1	0.0061
$\theta_2 PH$	rate of developing heroin or fentanyl use disorder for prescribed opioid individuals through illicit market or interactions with heroin or fentanyl use disorder individuals	θ_2	0.274
$\theta_3 AH$	rate of developing heroin or fentanyl use disorder for prescription opioid use disorder individuals through illicit market or interactions with heroin or fentanyl use disorder individuals	θ_3	5.02
ζA	rate of stable recovery for prescription opioid use disorder individuals	ζ	0.0454
νH	rate of stable recovery for heroin or fentanyl use disorder individuals	ν	0.00123
$\sigma R\frac{A}{A+H+\omega}$	rate of relapse for prescription opioid use disorder individuals	σ	0.412
$\sigma R\frac{H}{A+H+\omega}$	rate of relapse for heroin or fentanyl use disorder individuals	σ	0.412
S_0	initial condition for susceptible individuals	S_0	0.863
P_0	initial condition for prescribed opioid individuals	P_0	0.128
A_0	initial condition for prescription opioid use disorder individuals	A_0	0.00697
H_0	initial condition for heroin or fentanyl opioid use disorder	H_0	0.00182
R_0	initial condition for stably recovered individuals	R_0	0.0000305

purposes. This landscape allows us to compute the Basic Reproduction Number, $\mathcal{R}_0$, which in our context gives the expected number of secondary opioid use disorder instances that result from the introduction of opioid use disorder into a susceptible population; if the value is greater than 1, the epidemic is expected to grow (DFE unstable), but it dies out with a value less than 1 (DFE stable) [vW02]. Utilizing the Next Generation Matrix Method [vW08] and the calculated Next Generation Matrix applicable to our model [PLS21], we input our estimated model parameter values from Tables 1 and 2 (assuming the value of α to be the value of b, the initial value of $\alpha(t)$ in 2015) to obtain the eigenvalues for the Next Generation Matrix of 0.0084 and 0.95. The Basic Reproduction Number is given as the spectral radius of the Next Generation Matrix. Thus, $\mathcal{R}_0 = 0.95 < 1$, suggesting the opioid epidemic would not be self-sustaining under these assumptions, and that interactions with those specifically with heroin or fentanyl substance use disorder alone would not be sufficient to sustain the epidemic. The smaller value of $0.0084 < 1$ suggests that that interactions with prescription opioid substance use disorder individuals would not be sufficient to sustain the epidemic by itself either. This suggests that interactions with both opioid use disorders would be required to sustain the epidemic past 2015 in Alabama, which differs in conclusion than that of Tennessee over the time frame 2013-2018 [PLS21].

1.2. **Alabama data**

In order to estimate Alabama-calibrated parameters for this model, we estimated state-level data as shown in Table 3 from 2015 through 2023, noting the magnitude of values as proportions for model outputs may seem small but are significant as number of people. This required data acquisition and requests from a vast number of sources, including interpreting and transforming the data to align with relevant state variable definitions. Details of this process are given in Appendix A. We chose to work with this timefarme since the epidemic was clearly established in the state by then, including fentanyl, as well as available data. Here, we mention two important assumptions for clarity. Heroin and fentanyl use disorder are combined into the same class as in [PLS21] due to the lacing of heroin with fentanyl and the difficulty in isolating cause of death with multiple drugs present [Cen25]. Additionally, we make the simplifying assumption that if an individual died from an opioid overdose, it was due to a use disorder as there is not a way to parse out the data to know the opioid use history of the individual.

From the data in Table 3 and corresponding data visualizations shown in Figure 1, we make several key observations. First, prescription opioid use consistently de-

Table 3: The estimated number of unique individuals in various disjoint classes in Alabama from 2015 through 2023. Note: * indicates estimates utilizing relevant data from another year, † indicates estimates utilizing relevant data within the year, ∧ indicates reliance on national data information, and ⅄ indicates raw data. Sources: [U.S19, The25, HCB+17, RYJ+21, Ala25, Sub20f, Sub20e, Sub20d, Sub23a, Sub23b, Sub24b, Sub24c, Sub18a, Sub18b, Sub20a, Sub20b, Sub24a, Sub25, Sub16b, Sub16a, GCS+15, Sub21, Sub17, Ala19a, Har23, Cenndb, Cenndc]

Year	**Population 12+**	***H* Overdoses**	***A* Overdoses**	*H*	*A*	*P*
2015	4,130,653⅄	159†	122†	8,916†∧	39,855*†∧	1,511,233*†∧
2016	4,142,104⅄	221†	121†	9,497†∧	38,715†∧	1,468,392*†∧
2017	4,154,260⅄	243†	179†	10,272†∧	31,934†∧	1,437,197*†∧
2018	4,168,344⅄	229†	150†	10,029†∧	32,642†∧	1,278,347*†∧
2019	4,186,698⅄	278†	136†	7,719†∧	31,228†∧	1,206,805*†∧
2020	4,325,116⅄	493†	116†	10,873*†∧	40,510*†∧	1,137,333*†∧
2021	4,320,338⅄	878†	98†	15,578*†∧	92,613*†∧	1,171,648*†∧
2022	4,347,060⅄	850†	246†	16,410†∧	107,761†∧	1,148,687*†∧
2023	4,385,075⅄	-	-	9,360†∧	102,786†∧	1,152,064*†∧

clines for the years leading up to 2020 (pre-COVID-19 pandemic) and then seems to steady out and oscillate right around 1.15 million for the years following the onset of the pandemic. Furthermore, looking at the total number of prescribed users aged 12+ (including individuals with use disorders) in Table 4 (Alabama Unique Prescription Opioid Users (POU) Aged 12+) for the years after 2020, the number fluctuates, increasing and then decreasing every year, indicating that the aforementioned prescription change is mostly due to changes in prescribing practices and not use disorders. Potential reasons for the decrease in prescription opioid use may have come from ongoing efforts made by the PDMP to monitor and regulate opioid prescriptions, as well as efforts by the Alabama Medicaid Agency to consult with top prescribers in the state and enacting limits for supply days and dosages [Dep19].

We see that prescription opioid use disorder numbers decrease from 2015 to 2017, then mostly steady out until the onset of the COVID-19 pandemic, where we begin to see an estimated significant increase in the number of individuals with prescription opioid use disorder before a slight decrease in 2023. Heroin use disorder increases somewhat linearly from 2015 to 2017, steadies out in 2018, and dips in 2019, but then an estimated increasing trend is again seen at the onset of the pandemic from 2020 through 2022 (almost doubled in value compared to 2015 by this point) before approximately halving in 2023. Various factors may have played a role in the variation of these classes, such as tighter control on prescription opioids possibly contributing to accessing opioids elsewhere, in addition to awareness campaigns and recovery outreach efforts by the Alabama Opioid Overdose and Addiction Council starting in 2017 [Ala19b].

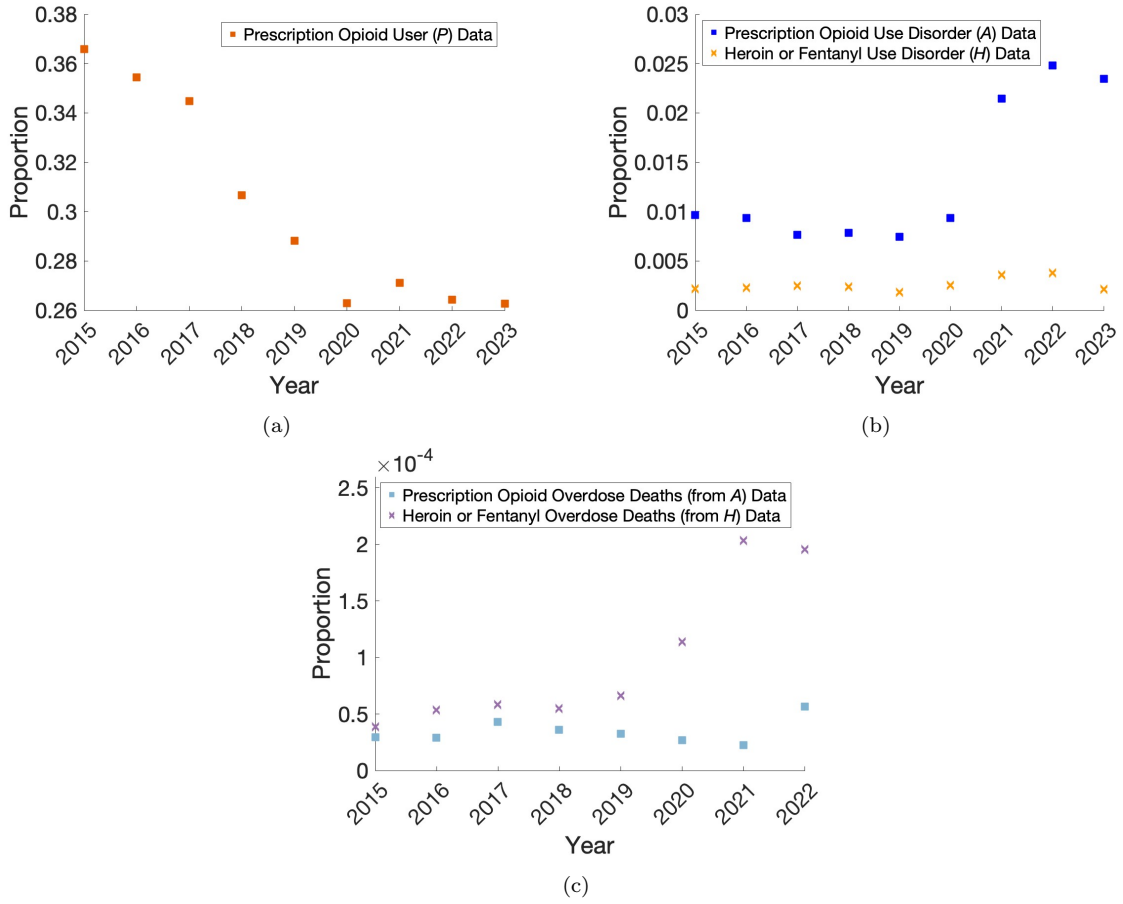

Figure 1: (a) displays the estimated number of unique prescribed individuals (P); (b) displays the estimated number of individuals with prescription opioid use disorder (A) and the estimated number of individuals with heroin or fentanyl use disorder (H); and (c) displays the estimated number of prescription opioid (A) overdose deaths and the estimated number of heroin or fentanyl (H) overdose deaths.

The prescription opioid overdose deaths are steady between 2015 and 2016 before reaching a local maximum in 2017 and then decreasing until 2022 where it then shoots up to a maximum for the entire study time frame. Overdose deaths from heroin, fentanyl, or both increase from 2015 to 2017, and then also reach a local maximum in 2017 before decreasing for the year 2018. From 2019-2021, the values increase, before dipping slightly in 2022.

Overall, it is worth noting that the years 2020-2022, the height of the COVID-19 pandemic before the Federal COVID-19 Public Health Emergency Declaration ended in May 2023 [Cen23b], display a significant estimated increase in the number of individuals with use disorder in our study. In addition, we see a steadying out of

the prescription opioid use values in this time frame following a consistent decline over several years, which motivates us to explore time-dependency pre- and post-COVID-19 in parameter estimation (Section 2.1).

1.3. **Parameter estimation**

Our system of differential equations model has 20 parameters and initial conditions to be estimated in which 4 have been calculated in Appendix B and displayed in Table 1. To estimate the unknown parameter and initial conditions in our model, we utilized ordinary least squares using 43 data points denoted by † in Table 3 for the P, A, H classes and the A and H overdoses. Specifically, we formulated an objective function to minimize defined as the sum of squared differences between the observed data (P_{data}, A_{data}, H_{data}, $A\text{overdose}_{data}$, $H\text{overdose}_{data}$) (denoted by † in Table 3 with sources) and the simulated outputs of the model (P_{sim}, A_{sim}, H_{sim}, $A\text{overdose}_{sim}$, $H\text{overdose}_{sim}$) for each data category, respectively weighted by each observed data sum squared (due to the significant differences in magnitude of the data and the inconsistent number of data points available for data types), and then square rooted as shown in Eq. 2:

$$\text{obj. funct.} = \frac{\sqrt{\sum_{i=1}^{9}(P_{sim}(i)-P_{data}(i))^2}}{\sqrt{\sum_{i=1}^{9}P_{data}(i)^2}} + \frac{\sqrt{\sum_{i=1}^{9}(A_{sim}(i)-A_{data}(i))^2}}{\sqrt{\sum_{i=1}^{9}A_{data}(i)^2}} + \frac{\sqrt{\sum_{i=1}^{9}(H_{sim}(i)-H_{data}(i))^2}}{\sqrt{\sum_{i=1}^{9}H_{data}(i)^2}} \quad (2)$$
$$+\frac{\sqrt{\sum_{i=1}^{8}(A\text{overdose}_{sim}(i)-A\text{overdose}_{data}(i))^2}}{\sqrt{\sum_{i=1}^{8}A\text{overdose}_{data}(i)^2}} + \frac{\sqrt{\sum_{i=1}^{8}(H\text{overdose}_{sim}(i)-H\text{overdose}_{data}(i))^2}}{\sqrt{\sum_{i=1}^{8}H\text{overdose}_{data}(i)^2}}.$$

To minimize this, we used the fmincon local solver within the MultiStart algorithm as part of MATLAB's Global Optimization Toolbox. We used 1000 starting points, specifying our initial starting point to be the average of the upper and lower estimated bound for all of the unknowns (see Appendix B for details on bound estimate calculations).

2. **Results**

2.1. **Parameter values and trajectories**

Utilizing the parameter estimation process outlined in Section 1.3 resulted in the values of 16 unknowns for the model: 11 parameters ($\alpha, \epsilon, \gamma, \beta_A, \beta_P, \theta_1, \theta_2, \theta_3, \zeta, \nu, \sigma$) and 5 initial conditions (S_0, P_0, A_0, H_0, R_0), since 4 parameter values ($\mu, \mu_A, \mu_H, \omega$) were calculated prior and displayed in Table 1 for a total of 20 model inputs. In this initial estimation process, we assumed all parameters were constant throughout the entire time frame. This resulted in an objective function value of 1.40. In this process,

we point out it was estimated that $P_0 \approx 0.24$ indicating that approximately 24% of Alabama's population aged 12+ was actively taking prescription opioids at the start of 2015. Although Alabama had a prescribing rate of 141.1 opioid prescriptions for every 100 residents two years prior ([Nat22]) as mentioned in the Introduction (which can occur due to factors such as "doctor shopping" to receive multiple prescriptions for the same individual or due to frequent refills for the same individual [Nat11]), it is estimated from Table 3 that throughout the *entire year*, 1,511,233/4,130,653 $\approx$ 37% of the population (unique individuals) was prescribed opioids at some point in 2015. With this in mind, it seems potentially unrealistic that 24% would be taking them at one point in time. In 2015, the national average days' supply of opioids prescribed was approximately 18 days (exactly 17.7) in length [GZB+17]. In Alabama, Blue Cross Blue Shield reported in 2015 that 6.5% of their members were on a long-duration opioid regimen [Blu17]. Taking Blue Cross Blue Shield members to be sufficiently representative of prescription users in Alabama for the purposes here, we find it unlikely that the model's estimate of 24% out of the entire population (which out of the 37% over the entire year that are taking prescription opioids yields a result of 65% of the individuals in Alabama that were prescribed opioids in 2015) were taking them at the very start of 2015. In an attempt to address this possibly unrealistic estimate, we were motivated by the trend we observed in the prescription opioid use data to consider a prescribing rate (α) as a linear function of time, as that might improve the fit of the model to the data.

We considered $\alpha(t)$ to be the linear function of time with unknown parameters m (slope) and b (y-intercept). Given the additional unknown parameter for slope, this resulted in estimating 12 parameters and 5 initial conditions. For m, we used bounds [-0.02,-0.000000001] and for b we used [0.2,0.5]. This way, the most extreme values that $\alpha(t)$ could be at the end of the 9 years of interest from 2015 through 2023 would be approximately the original bounds for α from Table 5. We obtained an objective function value of 1.37, and the estimated initial value of individuals in the P class in this case was indeed realistic, around 10%.

However, given that the prescribed opioid users in Table 3 decreases up until the start of the COVID-19 pandemic, 2020, and then remains relatively constant afterwards, we also considered a piecewise linear function of time for the prescription rate, α. To attempt to reflect the decrease from 2015-2020 and then the leveling out of the data for the individuals in the P class for the years 2021-2023, we incorporated a piecewise linear time-dependent prescribing rate $\alpha(t)$ (Eq.3), which linearly decreases from 2015 through the end of 2020 and then remains at the 2020 prescription rate value for the remaining years. We consider $t = 0$ to be the year 2015 so 2020 corresponds to $t = 5$ which is used in the second piece of the function:

$$\alpha(t) = \begin{cases} m * t + b & \text{if } t \leq 5, \text{ corresponding to years 2015-2020} \\ m * 5 + b & \text{if } t > 5, \text{ corresponding to years 2021 and after.} \end{cases} \tag{3}$$

We obtained an objective function value of 1.34 with the estimated parameters displayed in Table 2. We decided this model was the best model fit to the data overall due to reasons outlined in Appendix C informed by the Akaike Information Criterion (AIC) and realistic assumptions, including the output value of P_0 being around 13%. We note that due to the lower magnitudes of other classes (such as A and H) compared to the P class in the time frame, as well as the strongest confidence being in the trend of the P class, we did not consider other time-dependent parameters in this particular study.

Thus, Figure 2 displays the comparison between our estimated data from Table 3 to simulated data output from the model for the prescribed opioid user class (P) using the assumed parameters from Table 1, and the estimated parameters and initial values from Table 2. We illustrate the fit of data for the P class since the various models considered for constant and time-dependent α most strongly affect this class, showcasing the improved fit to the data for our model of choice where the prescription rate is a piecewise linear function of time. Moreover, the simulations for the S, A, H, and R classes were not drastically altered and retained their same shapes for all three model cases when compared to data, so we omit those figures.

To visualize the history and future trajectory of the state variables, especially for the opioid use disorder classes, we plotted the simulated outputs in Figure 3 from 2015 to the beginning of 2028. Figure 3a displays the overall decreasing trend of prescribed individuals after 2016, with the dashed line trajectory from 2024 to the beginning of 2028 anticipating that trend to continue. We observe the concave down shape of the A class in Figure 3b which suggests that aspect is slowing down, whereas for heroin and fentanyl substance use disorder, we see it is ramping up with a concave up shape (noting that although the concavity is not dramatic on the shared scale between the use disorders, it can be seen clearly on individual graphs). Altogether, the epidemic is expected to continue to worsen in this time frame studied until the beginning of 2028 as seen by the total proportion of opioid use disorders with an almost linearly increasing trend post-2024 in Figure 3b. In addition, looking at the cumulative overdoses since 2015 (Fig. 3c), we expect the rate of both the A overdoses and H overdoses to ramp up, which is a major concern, and it seems those from H are driving the overall increase in total overdose deaths. Although the proportions seem small, to give an idea of the magnitude, the cumulative number of individuals lost to total overdose deaths from A and H from this simulation from 2015 through

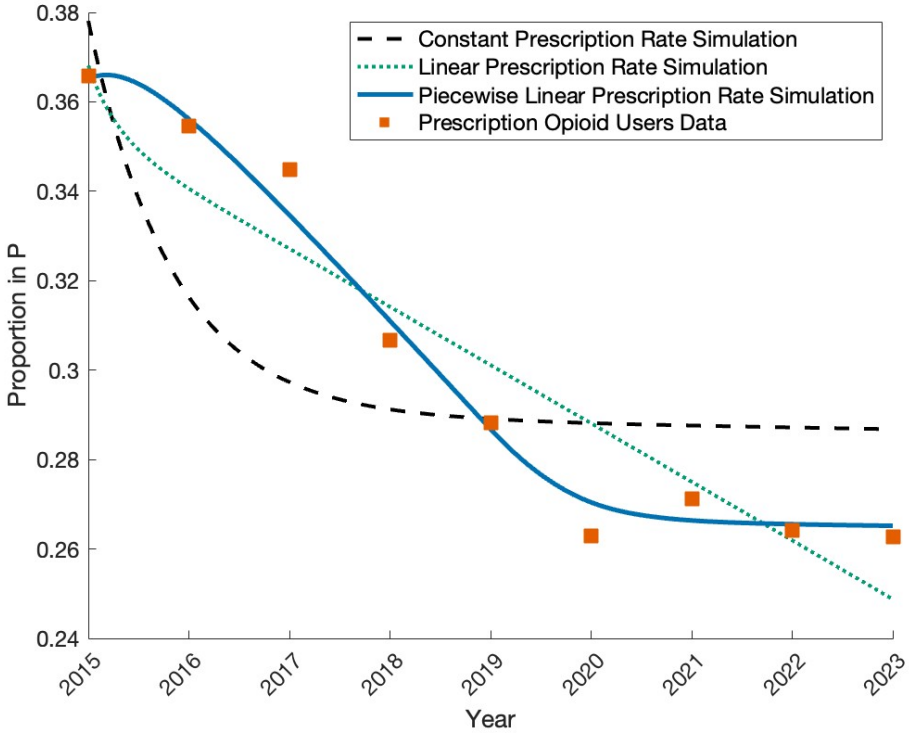

Figure 2: Comparison of the fit of prescription opioid user data from Table 3 (represented graphically by the proportion of unique individuals throughout the entire year) to the simulated output for the P class (with the output for each year connected for a smooth curve) for each of the model choices considered (all constant parameters, linear function of time prescription rate $\alpha(t)$, and piecewise linear function of time prescription rate $\alpha(t)$) in which the piecewise linear function of time was deemed the most appropriate model choice.

2023 was 5,199, with a predicted total cumulative overdose value from 2015 to the beginning of 2028 of 8,851.

2.2. **Impact of recent policy on the Alabama opioid epidemic**

Thus far, we have discussed the current outlook for the opioid crisis in Alabama for the near future. That said, policies and strategies have been and continue to be put in place with the intention of reducing the harmful impacts of the epidemic. We consider several in this section, both on the national and state level, in order to more closely investigate their impacts.

One policy focus that has been and continues to be a priority is getting individuals with opioid use disorder better access to quality treatment. On a national level, in 2023, the Biden Administration announced plans to improve opioid use disorder treatment by expanding access to medications for opioid use disorder and ensuring

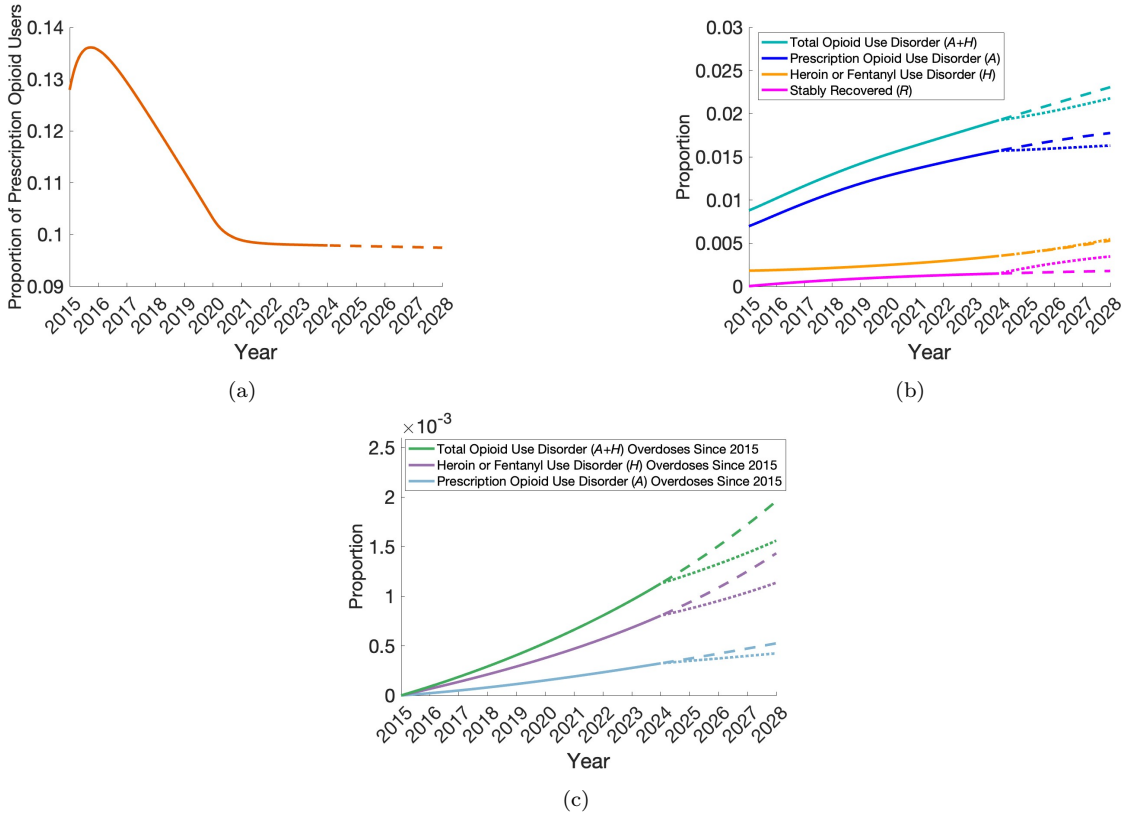

Figure 3: Model simulations and trajectories for the proportion of unique individuals in respective classes at any given time, for the model with $\alpha(t)$ as a piecewise linear function of time, as well as cumulative overdoses since 2015, utilizing estimated parameters from Table 2. Solid lines represent years of available data until the beginning of 2024, dashed $(--)$ lines represent trajectory predictions until the beginning of 2028, and dotted $(\cdots)$ lines represent the change in trajectory given approximately a 50% parameter change in $\zeta, \nu, \sigma, \mu_A$ and μ_H as discussed in detail in Section 2.2. (a) displays the P class simulation (b) displays A, H, and R classes, as well as total use disorder $(A + H)$ simulations and (c) displays the cumulative A overdoses, H overdoses, and total $(A + H)$ overdoses since 2015.

that every jail and prison across the nation can provide treatment for use disorder [Cen23a]. In 2025, the Office of National Drug Control Policy released the Statement of Drug Policy Priorities discussing their plan to provide treatment that leads to recovered individuals leading productive healthy lives [Off25], including expanding access to medications for opioid use disorder. In addition, they hope to improve the integration of mental health treatment with recovery and support services, mentioning support for strengthening peer recovery support services, including recovery community organizations, nationwide in hopes of improving the chances for stable recovery. By implementing these strategies, they work toward both increasing the rate of recovery while also decreasing the rate that recovered individuals return to

opioid use disorder.

At the state level, very similar approaches have been discussed. Alabama Legislature created the Oversight Commission on Alabama Opioid Settlement Funds (OCAOSF), which provided 4,094 treatment services in the year 2022 [Rey25]. Later, the Alabama Opioid Overdose and Addiction Council (OOAC) released their 2023 Annual Report stating their intention to continue to work to increase treatment and recovery [Ala23]. Their focuses included funding rides for individuals attending treatments, designating the outreach specifically to individuals in rural counties, and expanding access to recovery housing options for incarcerated individuals upon release. These efforts intend to reduce barriers and expand access for individuals in need of opioid treatment. They also plan to dedicate a workforce committee to develop recovery friendly workplace resources for workers with use disorders as well as mental illnesses, which could help to reduce the rate of relapse.

Another ongoing priority for opioid harm reduction efforts in Alabama is overdose reduction, with a large focus on reducing fentanyl deaths and expanding access to naloxone. In 2022, the OCAOSF distributed 1,252 Narcan Kits and 1,000 Fentanyl Test Strips [Rey25]. The OOAC 2023 Report indicated this to be an ongoing priority [Ala23]. They hope to expand overdose education and prescription nalaxone distribution through direct dispensing as much as state regulation allows. They also plan to explore how to effectively improve access to over-the-counter naloxone. On the national level, there has also been a prioritization for decreasing overdoses. In 2023 the Biden Administration announced plans to address the substance use disorder crisis with a focus on fentanyl [Cen23a]. They particularly wanted to focus on reducing overdoses by delivering naloxone to communities hit hardest by fentanyl, designating the Department of Health and Human Services to assist states in deciding where to allocate Opioid Response funds. The 2025 Office of National Drug Control Policy Statement of Drug Policy Priorities also indicated plans to focus on fentanyl and provide access to overdose prevention education and opioid overdose reversal medications like naloxone [Off25]. In doing so, they will encourage state and local jurisdictions to increase the availability of drug test strips and naloxone. Overall, these efforts intend to reduce the rate that individuals with opioid use disorder overdose.

We are particularly interested in investigating the impact of currently implemented policies as several of these are in their early stages or of recent emergence. To do so, we considered the state of the epidemic at the end of 2023 from our model simulations and projected out four years (until the beginning of 2028) with parameters of different values (Sect. 2.2) in order to compare to the expected trajectory of the epidemic.

Before diving in to that analysis, we briefly remark on our results from our global sensitivity analysis performed from 2024-2028 to determine how the variation in sizes

of the A and H classes in 2028 can be attributed to changes in certain parameters. First, a monotonic relationship was checked between parameters and outputs (A and H) which deemed Partial Rank Correlation Coefficient fitting to perform global sensitivity analysis, utilizing a Latin Hypercube Sampling method [MHRK08]. We ran the analysis over our time frame of interest from 2024-2028 with 200 parameter sets and parameter ranges varying $\pm 50\%$ of baseline values with the exception of m ($[-50\%, -2.9\%]$) and b ($[-50\%, 0\%]$) adapted to meet the $\pm 50\%$ range for α in 2024. We chose this timeframe in order to more practically connect to the time period of recent policy, to determine which parameters affect the use disorder classes most significantly. Since we cannot alter initial conditions at any given time, we don't consider those in our analysis and instead keep them fixed at $S_0 = 0.881, P_0 = 0.0979, A_0 = 0.0157, H_0 = 0.00353, R_0 = 0.00150$, the values of the classes at the end of 2023 from our simulations.

Results are given in Appendix D in which it was determined that the parameters with greatest impact on the A class in 2028 would be: ϵ, γ, and b, followed by ζ. For the H class, the parameters affecting it most in 2028 were: θ_3, μ_H, ϵ, and θ_2, although we mention that the increase of γ and b also increase H as they do A even though the PRCC values are smaller. These results suggest that the P class is a vital part of the story. Between A and H results, b ($y-$intercept of α), ϵ, γ, and θ_2 have an impact on one or both use disorders, which are all connected to the P class (being prescribed opioids, successfully finishing prescriptions, developing prescription opioid use disorder, or developing heroin or fentanyl use disorder, respectively). There have been efforts to control the number of prescription opioids which directly impacts the value of α, but it seems efforts to educate about opioid use disorder to prevent entry into A or H could be vital to be more on the preventative side.

Although the PRCC sensitivity analysis results are useful to know on a theoretical level, we choose to continue our analysis with parameters that are directly connected to currently implemented policy to see their impact on opioid use disorder and overdoses. These policies consist mainly of resources related to reactionary measures for the epidemic (e.g. helping those who already have use disorder to recover for the long-term, reducing fatality of overdoses). However, we will refer back to PRCC results for relevant connections in our work.

Treatment and Recovery Policy Efforts

Due to aforementioned policies striving to increase access to and availability of treatment, we investigated the effect that increasing ζ and ν in 2024, the recovery rates from the use disorder classes, has on the A and H use disorder classes by the beginning of 2028 as well as the cumulative overdoses from 2024-2028. It is imperative

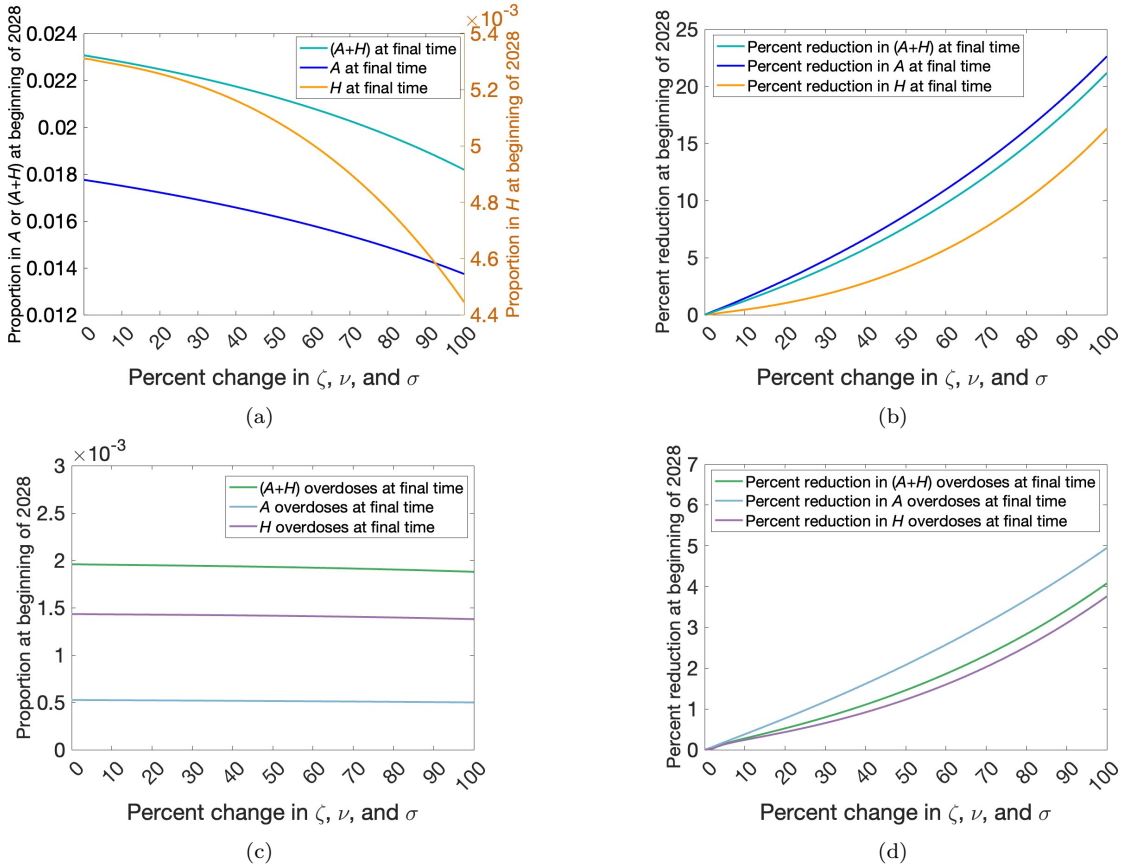

Figure 4: Model simulations (with $\alpha(t)$ as a piecewise linear function of time) of the projected impacts to proportions in 2028 in each category with parameters ζ, ν, and σ changing at various percentages as an intervention from 2024 to the beginning of 2028. (a) and (c) display the values of A and H in 2028 and their respective cumulative overdoses by 2028 given a certain percent change in the parameters; (b) and (d) display the percent reduction of A and H in 2028 and their respective cumulative overdoses by 2028 compared to baseline values with no intervention.

to change both parameters simultaneously, as efforts to increase treatment will be accessed by those who struggle with opioids in general. The simulation was run from the beginning of 2024 to the beginning of 2028 at various percentage reductions for both parameters (10%, 20%,..., 100%). This resulted in a decrease in the A class by the beginning of 2028 (as well as total overdoses from A over the time period) but interestingly enough an increase in the H class (as well as overdoses from H over the time period).

To further look into these dynamics, we changed ζ and ν individually to see the effects on the A and H classes. Increasing ζ led to an increase in the H class (as well as overdoses from H over the time period), most likely more because individuals were recovered and relapsing back into the H class, as well as a decrease in A; and

similarly, increasing ν led to an increase in the A class (as well as overdoses from A over the time period) and decrease in H. We note that these results align with the relationships shown between parameters and use disorder classes in our PRCC results. The two parameters combined as mentioned before, however, have an overall effect of an increase in the H class and not in the A class. This is a dangerous reality as an increase in the H class equates to dependence on a more potent drug, as well as greater risk for individuals as far as overdoses, so we conclude here that focusing efforts only on getting individuals into treatment is not sufficient in making strides to combat the epidemic, and in fact can lead to harmful unintended outcomes. Thus, we wish to explore further the effects on these classes from policy.

Due to efforts related to supporting stable recovery for individuals to help prevent relapse, we pair these policy efforts together with treatment policy efforts to see the effect of decreasing the rate of relapse into the A and H classes, σ, alongside increasing ζ and ν. Results for the combination of all three of these parameters changing is given in Figures 4a and 4b which displays both the A and H classes being reduced compared to the currently predicted values shown in Figure 3b (dashed lines that don't include specific interventions altering the system by 2028). The same is true for cumulative opioid overdose deaths from 2024-2028 (see Figures 4c and 4d as compared to (dashed line) trajectories in Figure 3c). Thus, our work here suggests that treatment alone will not lead to positive outcomes for the epidemic as a whole but instead treatment combined with efforts to support long-term recovery and prevent relapse are essential to help combat this crisis.

Overdose reversal policy efforts

Given the policies and resources devoted to preventing opioid overdose deaths outlined previously, we investigate the effect of reducing μ_A and μ_H, the overdose rates from the use disorder class, on the cumulative number of overdoses from 2024-2028. It is a natural consequence that if individuals are saved from an overdose or not overdosing at all, the A and H classes will rise given that individuals remain in the system, but we still include these results in Figures 5a and 5b for better comparison to our policy analysis in the next section. Results in Figures 5c and 5d display an anticipated significant decrease in the number of overdose deaths at any level of parameter change. The importance of these efforts is demonstrated clearly with juxtaposition to Figures 4c and 4d that had significantly less of an impact on total overdose deaths over the time period, reaching a maximum of a 4.08% reduction if all three ζ, ν, and σ are doubled, compared to an almost identical reduction in overdoses of 4.01% by reducing μ_A and μ_H by a mere 10%.

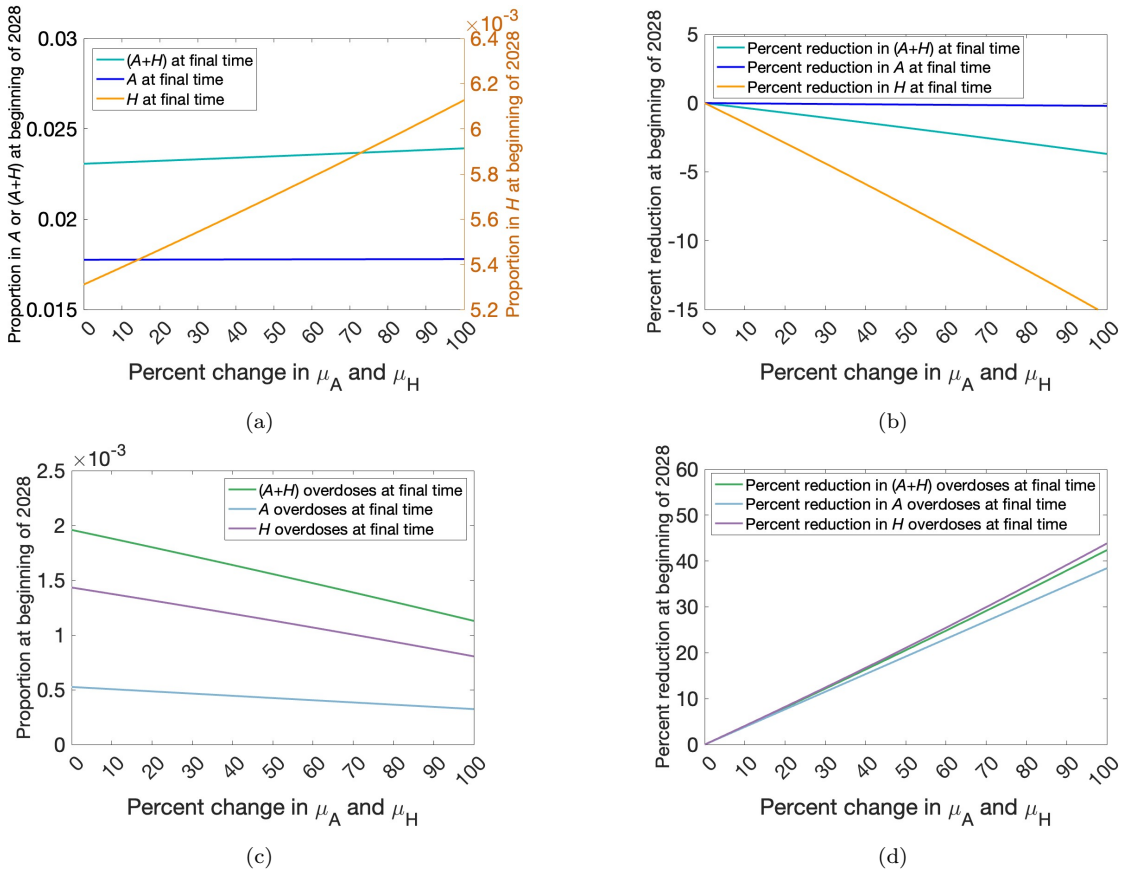

Figure 5: Model simulations (with $\alpha(t)$ as a piecewise linear function of time) of the projected impacts to proportions in 2028 in each category with parameters μ_A and μ_H changing at various percentages as an intervention from 2024 to the beginning of 2028. (a) and (c) display the values of A and H in 2028 and their respective cumulative overdoses by 2028 given a certain percent change in the parameters; (b) and (d) display the percent reduction of A and H in 2028 and their respective cumulative overdoses by 2028 compared to baseline values with no intervention.

Combined policy efforts

In reality, all of these policies are currently in motion and occurring simultaneously so we wish to see what effect the combined effort of these policies could have on the trajectories of the use disorders by 2028 and cumulative opioid overdoses from 2024-2028. Therefore, we increase ζ and ν while decreasing σ, μ_A, and μ_H at various levels with results shown in Figure 6.

We simulate the sizes of the A and H cumulative overdose proportion from 2015 to the beginning of 2028 in Figure 6c from these parameter changes and compare these sizes to their baseline sizes in Figure 3c by calculating percent reduction (Figure 6d). We observe the effect of the parameter changes on the number of overdoses in this case is effectively the same as when *only* the overdose rates are altered (Figs. 5c and 5d)

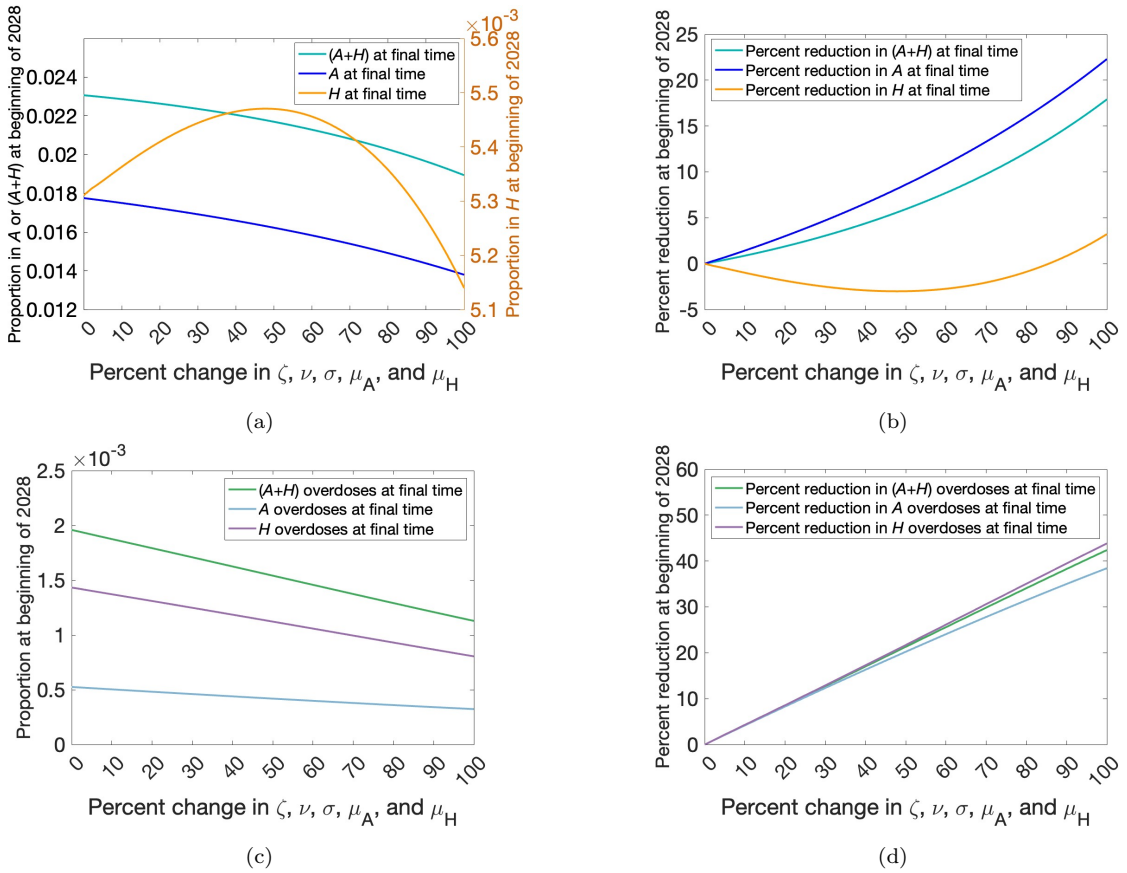

Figure 6: Model simulations (with $\alpha(t)$ as a piecewise linear function of time) of the projected impacts to proportions in 2028 in each category with parameters ζ, ν, σ, μ_A, and μ_H changing at various percentages as an intervention from 2024 through the beginning of 2028. (a) and (c) display the values of A and H in 2028 and their respective cumulative overdoses by 2028 given a certain percent change in the parameters; (b) and (d) display the percent reduction of A and H in 2028 and their respective cumulative overdoses by 2028 compared to baseline values with no intervention.

which suggests that the policies directly related to overdose-reversal drug availability and distribution, test strips for fentanyl, and education are the key to saving lives, as compared to only focusing on getting individuals into a long-term recovered state without relapse. This is further evidenced by the results in Figure 4d, in which the percent reduction of overdose deaths is more minimal. The results for percent change with overdoses is more straightforward in this policy intervention scenario than the story of the use disorder classes which we discuss now.

This is because, as a reminder, incorporating a decrease in overdose rates with no other interventions results in a natural increase of those with use disorder (and the number of individuals in the system as a whole). Under a combined policy effort, the A class actually decreases for all parameter percent change cases compared to the

baseline 2028 value, and the decrease in A is approximately the same as when only ζ, ν, and σ were changed, indicating that the recovery efforts overpower the natural increase of the A class from the reduction in overdoses. That said, we observe a slight increase in the H class compared to the baseline 2028 value for most parameter percent change cases, up until about the 90% mark (precisely 85.5%) in Figures 6a and 6b, after which the H class attains values lower than the baseline projected value of H. Since that goal of a parameter change is lofty at any given time, we investigate further.

We observe that the value of H at the beginning of 2028 reaches its maximum around the 50% mark for parameter change (precisely 47.7%) in Figures 6a (subsequently reaching its minimum in Figure 6b) which is a powerful threshold. This suggests any value greater than a 47.7% increase in the recovery rates and decrease in the relapse rate has a strong enough impact over the corresponding (same valued) decrease in overdose rates in order to see the H class begin to move in a direction of lower H values before reaching its baseline projected value at the 85.5% parameter change mark. This is key because Figure 3b suggests the trajectory of the epidemic is expected to increase through the beginning of 2028 (at the very least) and as discussed previously, is being driven mostly by those in the H class due to the concavity of the trajectory. This means actions that impact the H class in particular are of interest.

We specifically simulate the trajectories for use disorder classes, stably recovered, and overdose deaths to see how they are affected for the scenario where all five parameters are decreased or increased appropriately by 47.7% as shown in Figures 3b and 3c by the dotted lines, as compared to the dashed line trajectories (with no intervention). We can see a clear desirable impact on the A and R classes, as well as the total use disorder cases and overdose deaths, again pointing out that the H class overdoses are driving total overdoses the most. Moreover, we again put the proportion of total overdoses in terms of the number of lives lost or saved to give a better idea of the magnitude of change. For example, changing all the parameters by 47.7% would save approximately 778 lives in the time period from 2024 to the beginning of 2028. Subtracting this from a projected cumulative number of 3,652 lives with no intervention (from Fig. 3c), this would result in a predicted total number of overdoses of 2,874 in the time period instead which is still a significant number but a concrete improvement.

In summary, we observe quantitatively that the combined efforts of supporting recovery, preventing relapse, and overdose prevention predict a favorable effect as our results suggest that any level of parameter change is expected to decrease the total number of individuals with opioid use disorder (as well as cumulative overdose deaths

from the use disorder classes) by 2028. Some ways that the currently implemented and ongoing policy approaches could be strengthened in order to reach goals of significant parameter changes include creating more widespread campaigns and flyers to educate the general public on how to administer naloxone to prevent overdose deaths; building more treatment centers throughout the state to increase access, especially in rural areas; as well as increasing outreach efforts, support, and accessibility to community groups for individuals after they finish treatment to help prevent relapse.

3. **Discussion and conclusions**

This work explores the current state of the opioid epidemic in Alabama. Relying on state-level data extensively researched and estimated in order to calibrate an SIR-type mathematical model from 2015 through 2023, we believe the trajectory of the epidemic in the near future (until at least 2028) is not slowing down and is fueled mainly by heroin and fentanyl use disorder. The model chosen for this analysis, due to prescribing data trends, realistic assumptions, and AIC values, incorporated a piecewise linear function of time for the prescribing rate, $\alpha(t)$. Sensitivity analysis results suggested that rates related to the prescribed user class could be of benefit to focus policy efforts on. In this work, however, we mainly focus on the trajectory of the epidemic given currently implemented policy.

To help combat the crisis, current policy in Alabama includes efforts to increase treatment and relapse prevention measures in order to keep individuals in a recovered state, as well as provide resources for opioid-reversal drugs. Our results show that a combination of these efforts are essential to make strides in mitigating the epidemic, as targeting only one or two of them can lead to an increase in A or H which is undesirable. Changing all five parameters (ζ, ν, σ, μ_A, and μ_H) by any percent projects significant decrease in the total use disorder and overdose death numbers (compared to without intervention) which provides hope for this crisis that has faced the state for almost a decade. Within this process, however, we note that there are some parameter values that lead to an increase in the H class due to the efforts with overdose prevention. Thus, key conclusions include that at least an 85.5% increase or decrease mark is a crucial target value to meet for our parameters related to policy intervention with recovery, relapse prevention, and overdose prevention, to have the most influential impact on the epidemic. If that target is achieved, it is estimated the size of the H class will be less by the beginning of 2028 than the predicted baseline value currently, as well as the A class. However, due to the interplay between overdose prevention naturally causing an increase with those remaining in use disorder classes, there is a balancing effect right around the 47.7% mark for target parameter

changes where the H class reaches its maximum value and then decreases for any percent change value after that mark. This is a more reasonable target to strive for to have a positive impact on the size of the H class while also saving many lives through overdose prevention. Another important conclusion relates to reducing overdose deaths. Our work deemed that a reduction of overdose death rates by just 10% results in a decrease of total overdose deaths the same as if ζ, ν, and σ, rates related to recovery and relapse prevention were doubled, with the latter far more difficult to attain. Thus, we believe continuing education on overdoses, as well as the distribution and availability of naloxone in all areas, is essential.

This work may be of interest to other scholars interested in baseline estimates for opioid use disorders in this time frame in their own studies, or a methodology to estimate for other time frames. It can also inform policymakers on the impact of their work and provide informed goals to strive for. Limitations of the mathematical model utilized include homogeneity inside compartments. Future work could include a stratification of the susceptible class into low risk for use disorder (i.e. no opioid use at all) and higher risk (i.e. misuse of opioids through illegal channel) classes, as well as stratification of the prescribed opioid user class into classes of low risk (i.e. take prescribed opioids as directed) and higher risk (i.e. misuse prescribed opioids but not in a manner constituting use disorder). The model could also be calibrated to different age groups for comparison due to available data. In addition, the lack of available data at the state level rendered us unable to use a different modeling technique such as agent-based modeling and led us to rely on some national level assumptions. Although this work was focused on current actions being implemented to mitigate the epidemic, future work could include quantitative policy analysis surrounding the P class and it's parameters entering and exiting, as the LHS and PRCC results suggest potential there with mitigation of the epidemic. For example, since ϵ was an impactful parameter, more careful analysis incorporating data on lengths of prescriptions could be done. Work could also be done to explore other time-dependent parameters for the model, such as parameters for the overdose death rates or those affecting the use disorder classes specifically, especially once more data becomes available for the post-COVID-19 era. In addition, this model could be used in order to see the impact of epidemic mitigation policies that have parameters changing (increasing or decreasing appropriately) as time-dependent parameters from the time of implementation of a policy to several years out. It would also be of interest once more post-COVID-19 data is available to compare more lengthy pre- and post- COVID-19 trends, as both use disorders dipped in 2023 after significant increases, and it is not known whether that is an anomaly or the beginning of a trend in which time-dependent parameters related to the A and H class could be considered.

Acknowledgments and disclaimers

The authors would like to thank the Alabama Department of Public Health for their support with data requests through the Prescription Drug Monitoring Program and would also like to provide the disclaimer that any published findings and conclusions are those of the authors and do not necessarily represent the official position of the Alabama Department of Public Health.

A. Sources and assumptions with Alabama data

Total population 12 and older

Total Alabama Population shown in Table 4 gives estimates of the total population in Alabama each year as of July 1st from 2015−2023 [U.S19]. Given the majority of data used in this study was specific to individuals 12 years of age and older, we adjusted the population to represent this age group. To do so, we found the number of individuals in the age groups 0-4 and 5-11 in Alabama for each year by using data from the Kids Count Data Center and filtering for Child Population by Age Group in Alabama [The25]. We totaled those numbers to attain Alabama Population Age 0-11 (Table 4) and subtracted from the Total Alabama Population for each year to obtain Population 12 and Older (Table 3).

Overdose deaths from H or F

H or F overdose deaths represents the total number of overdose deaths due to heroin, fentanyl, or both. We began by finding the number of Overdose Deaths Involving F (Table 4) for the years $(2015 - 2022)$ [Ala19a, Har23]. For simplicity and due to the potency of the drug, we assumed that for any overdose death involving fentanyl, fentanyl was the cause of death.

To calculate Overdose Deaths Involving H (Table 4), we used the CDC WONDER database and filtered for any deaths by overdose (underlying cause of death) that involved heroin (multiple cause of death) [Cen25]. For underlying cause of death, we used codes X40–X44 (accidental poisonings), X60–X64 (intentional self-poisonings), X85 (assault or homicide by poisoning), and Y10–Y14 (poisonings with undetermined intent). Then for multiple cause of death, we used code T40.1 (poisoning by heroin) [Cennda, Cenndb, Cenndc].

However, we are careful to note that our Overdose Deaths Involving H (Table 4) counts individuals who overdosed with both heroin and fentanyl in their system.

Table 4: Accompanying data, calculations, and estimations of numbers of individuals in Alabama used in the process of calculating final estimates of Alabama data found in Table 3. Note: * indicates estimates utilizing relevant data from another year, † indicates estimates utilizing relevant data within the year, ∧ indicates reliance on national data information, and ⅄ indicates raw data. We also utilize the following for brevity: heroin (H), fentanyl (F), prescription opioid (PO), heroin use disorder (HUD), heroin users (HU), prescription opioid use disorder (POUD), and prescribed opioid users (POU). Sources: [U.S19, The25, HCB+17, RYJ+21, Ala25, Sub20d, Sub20e, Sub20f, Sub16b, Sub16a, GCS+15, Sub17, Sub18a, Sub18b, Sub20a, Sub20b, Sub24a, Sub25, Sub23a, Sub23b, Sub24b, Sub24c, Sub21, Sub17, Cenndb, Cenndc, Ala19a, Har23]

Alabama Data	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**
Population Data									
Total Alabama Population	4,852,347$^{\text{⅄}}$	4,863,525$^{\text{⅄}}$	4,874,486$^{\text{⅄}}$	4,887,681$^{\text{⅄}}$	4,903,185$^{\text{⅄}}$	5,033,094$^{\text{⅄}}$	5,049,196$^{\text{⅄}}$	5,076,181$^{\text{⅄}}$	5,117,673$^{\text{⅄}}$
Alabama Population Age 0-11	721,694$^{\text{⅄}}$	721,421$^{\text{⅄}}$	720,226$^{\text{⅄}}$	719,337$^{\text{⅄}}$	716,487$^{\text{⅄}}$	707,978$^{\text{⅄}}$	728,858$^{\text{⅄}}$	729,121$^{\text{⅄}}$	732,598$^{\text{⅄}}$
Population 12 and Older	4,130,653$^{\text{⅄}}$	4,142,104$^{\text{⅄}}$	4,154,260$^{\text{⅄}}$	4,168,344$^{\text{⅄}}$	4,186,698$^{\text{⅄}}$	4,325,116$^{\text{⅄}}$	4,320,338$^{\text{⅄}}$	4,347,060$^{\text{⅄}}$	4,385,075$^{\text{⅄}}$
H or F Overdose Death Data									
Overdose Deaths Involving F	59$^{\text{⅄}}$	140$^{\text{⅄}}$	161$^{\text{⅄}}$	121$^{\text{⅄}}$	193$^{\text{⅄}}$	428$^{\text{⅄}}$	830$^{\text{⅄}}$	835$^{\text{⅄}}$	-
Overdose Deaths Involving H	111$^{\text{⅄}}$	126$^{\text{⅄}}$	125$^{\text{⅄}}$	137$^{\text{⅄}}$	141$^{\text{⅄}}$	138$^{\text{⅄}}$	138$^{\text{⅄}}$	47$^{\text{⅄}}$	45
Intersect of Overdose Deaths Involving H & Synthetic Opioids	11$^{\text{⅄}}$	45$^{\text{⅄}}$	43$^{\text{⅄}}$	29	56$^{\text{⅄}}$	73$^{\text{⅄}}$	90$^{\text{⅄}}$	32	33$^{\text{⅄}}$
Overdose Deaths Involving H without Synthetic Opioids	100†	81†	82†	108†	85†	65†	48†	15†	12†
H or F Overdose Deaths	159†	221†	243†	229†	278†	493†	878†	850†	-
PO Overdose Death Data									
Opioid Related Deaths	281$^{\text{⅄}}$	342$^{\text{⅄}}$	422$^{\text{⅄}}$	379$^{\text{⅄}}$	414$^{\text{⅄}}$	609$^{\text{⅄}}$	976$^{\text{⅄}}$	1096$^{\text{⅄}}$	1198$^{\text{⅄}}$
PO Overdose Deaths	122†	121†	179†	150†	136†	116†	98†	246†	-
HUD Data									
Alabama HU Percentage	0.27%$^{\text{⅄}}$	0.31%$^{\text{⅄}}$	0.30%$^{\text{⅄}}$	0.33%$^{\text{⅄}}$	0.28%$^{\text{⅄}}$	-	-	0.44%$^{\text{⅄}}$	0.24%$^{\text{⅄}}$
Alabama HU	11,153$^{\text{⅄}}$	12,841$^{\text{⅄}}$	12,463$^{\text{⅄}}$	13,756$^{\text{⅄}}$	11,723$^{\text{⅄}}$	-	-	19,127$^{\text{⅄}}$	10,524$^{\text{⅄}}$
National HUD	661,920$^{\text{⅄}}$	701,120$^{\text{⅄}}$	730,240$^{\text{⅄}}$	589,120$^{\text{⅄}}$	490,560$^{\text{⅄}}$	691,000$^{\text{⅄}}$	990,000$^{\text{⅄}}$	900,000$^{\text{⅄}}$	587,000$^{\text{⅄}}$
National HU	828,000$^{\text{⅄}}$	948,000$^{\text{⅄}}$	886,000$^{\text{⅄}}$	808,000$^{\text{⅄}}$	745,000$^{\text{⅄}}$	902,000$^{\text{⅄}}$	1,089,000$^{\text{⅄}}$	1,049,000$^{\text{⅄}}$	660,000$^{\text{⅄}}$
National HUD/HU	79.94%$^{\text{⅄}}$	73.96%	82.42%$^{\text{⅄}}$	72.91%$^{\text{⅄}}$	65.85%$^{\text{⅄}}$	76.61%$^{\text{⅄}}$	90.91%$^{\text{⅄}}$	85.80%$^{\text{⅄}}$	88.94%$^{\text{⅄}}$
National $\text{HUD}_n/\text{HUD}_{n-1}$	-	105.92%$^{\text{⅄}}$	104.15%$^{\text{⅄}}$	80.67%$^{\text{⅄}}$	83.27%$^{\text{⅄}}$	140.86%$^{\text{⅄}}$	143.27%$^{\text{⅄}}$	90.91%$^{\text{⅄}}$	65.22%$^{\text{⅄}}$
HUD	8,916$^{\dagger\text{⅄}}$	9,497$^{\dagger\text{⅄}}$	10,272$^{\dagger\text{⅄}}$	10,029$^{\dagger\text{⅄}}$	7,719$^{\dagger\text{⅄}}$	10,873$^{*\dagger\text{⅄}}$	15,578$^{*\dagger\text{⅄}}$	16,410$^{\dagger\text{⅄}}$	9,360$^{\dagger\text{⅄}}$
POUD Data									
Alabama POUD Percentage	-	0.94%$^{\text{⅄}}$	0.77%$^{\text{⅄}}$	0.77%$^{\text{⅄}}$	0.75%$^{\text{⅄}}$	-	-	2.65%$^{\text{⅄}}$	2.46%
Alabama POUD (with HUD)	-	44,387$^{\text{⅄}}$	36,466$^{\text{⅄}}$	36,590$^{\text{⅄}}$	35,796$^{\text{⅄}}$	-	-	115,197$^{\text{⅄}}$	107,873$^{\text{⅄}}$
National POUD (with HUD)	2,323,320$^{\text{⅄}}$	1,998,420$^{\text{⅄}}$	1,912,920$^{\text{⅄}}$	1,931,160$^{\text{⅄}}$	1,557,240$^{\text{⅄}}$	2,300,000$^{\text{⅄}}$	5,020,000$^{\text{⅄}}$	5,577,000$^{\text{⅄}}$	5,344,000$^{\text{⅄}}$
National POUD	2,707,000$^{\text{⅄}}$	2,444,160$^{\text{⅄}}$	2,405,400$^{\text{⅄}}$	2,311,920$^{\text{⅄}}$	1,849,080$^{\text{⅄}}$	2,700,000$^{\text{⅄}}$	5,583,000$^{\text{⅄}}$	6,117,000$^{\text{⅄}}$	5,679,000$^{\text{⅄}}$
National POUD (without HUD)	2045580$^{\text{⅄}}$	1743040$^{\text{⅄}}$	1675160$^{\text{⅄}}$	1722800$^{\text{⅄}}$	1358520$^{\text{⅄}}$	2,009,000$^{\text{⅄}}$	4,593,000$^{\text{⅄}}$	5,217,000$^{\text{⅄}}$	5,092,000$^{\text{⅄}}$
National POUD (without HUD)/POUD (with HUD)	88.05%$^{\text{⅄}}$	87.22%$^{\text{⅄}}$	87.57%$^{\text{⅄}}$	89.21%$^{\text{⅄}}$	87.24%$^{\text{⅄}}$	87.35%$^{\text{⅄}}$	91.49%$^{\text{⅄}}$	93.54%$^{\text{⅄}}$	95.28%$^{\text{⅄}}$
National POUD_n(with HUD)/POUD_{n-1} (with HUD)	-	86.02%$^{\text{⅄}}$	95.72%$^{\text{⅄}}$	100.95%$^{\text{⅄}}$	80.64%$^{\text{⅄}}$	147.70%$^{\text{⅄}}$	218.26%$^{\text{⅄}}$	111.10%$^{\text{⅄}}$	95.82%$^{\text{⅄}}$
POUD	39,855$^{*\dagger\text{⅄}}$	38,715$^{\dagger\text{⅄}}$	31,934$^{\dagger\text{⅄}}$	32,642$^{\dagger\text{⅄}}$	31,228$^{\dagger\text{⅄}}$	40,510$^{*\dagger\text{⅄}}$	92,613$^{*\dagger\text{⅄}}$	107,761$^{\dagger\text{⅄}}$	102,786$^{\dagger\text{⅄}}$
POU Data									
Alabama POU Age 18+	1511398$^{\text{⅄}}$	1468246$^{\text{⅄}}$	1436089$^{\text{⅄}}$	1279674$^{\text{⅄}}$	1195060$^{\text{⅄}}$	1126726$^{\text{⅄}}$	1159563$^{\text{⅄}}$	1132654$^{\text{⅄}}$	1129117$^{\text{⅄}}$
Alabama POU Age 5-17	28104$^{\text{⅄}}$	27727$^{\text{⅄}}$	23625$^{\text{⅄}}$	19398$^{\text{⅄}}$	17809$^{\text{⅄}}$	16322$^{\text{⅄}}$	17973$^{\text{⅄}}$	21805$^{\text{⅄}}$	28736$^{\text{⅄}}$
National Total Opioid Prescriptions Age 0-5	634319$^{\text{⅄}}$	524432$^{\text{⅄}}$	394655$^{\text{⅄}}$	28841$^{\text{⅄}}$	-	-	-	-	-
National Total Opioid Prescriptions Age 6-9	562400$^{\text{⅄}}$	493823$^{\text{⅄}}$	388789$^{\text{⅄}}$	282695$^{\text{⅄}}$	-	-	-	-	-
National Total Opioid Prescriptions Age 10-14	1038889$^{\text{⅄}}$	901470$^{\text{⅄}}$	747044$^{\text{⅄}}$	564809$^{\text{⅄}}$	-	-	-	-	-
National Total Opioid Prescriptions Age 15-19	3418316$^{\text{⅄}}$	3098725$^{\text{⅄}}$	2719486$^{\text{⅄}}$	2260473$^{\text{⅄}}$	-	-	-	-	-
Patients Dispensed 1 Opioid Prescription	76.6%$^{\text{⅄}}$	78.4%$^{\text{⅄}}$	80.4%$^{\text{⅄}}$	82.6%$^{\text{⅄}}$	-	-	-	-	-
Patients Dispensed 2-4 Opioid Prescriptions	20.1%$^{\text{⅄}}$	18.8%$^{\text{⅄}}$	17.3%$^{\text{⅄}}$	15.5%$^{\text{⅄}}$	-	-	-	-	-
Patients Dispensed 5+ Opioid Prescriptions	3.2%$^{\text{⅄}}$	2.8%$^{\text{⅄}}$	2.3%$^{\text{⅄}}$	1.9%$^{\text{⅄}}$	-	-	-	-	-
Unique POU Out of Total Prescriptions	83.94%†	85.23%†	86.63%†	88.15%†	-	-	-	-	-
National Unique POU Age 0-5	532447†	446956†	341876†	25422†	-	-	-	-	-
National Unique POU Age 6-9	472079†	420869†	336795†	249186†	-	-	-	-	-
National Unique POU Age 10-14	872043†	768293†	647139†	497860†	-	-	-	-	-
National Unique POU Age 15-19	2869334†	2640940†	2355800†	1992532†	-	-	-	-	-
National Unique POU Age 0-19	745904†	4277058†	3681611†	2765001†	-	-	-	-	-
National Unique POU Age 5-19	4319946†	3919493†	3408110†	2744663†	-	-	-	-	-
National Unique POU Age 5-17	3172212†	2863117†	2465790†	1947650†	-	-	-	-	-
National Unique POU Age 5-11	927385†	817577†	664026†	453415†	-	-	-	-	-
(National Unique POU Age 5-11)/(National Unique POU Age 5-17)	29.23%†	28.56%†	26.93%†	23.28%†	-	-	-	-	-
Alabama POU Age 5-11	8216†	7918†	6362†	4516†	-	-	-	-	-
Alabama POU Age 5+	1539502$^{\text{⅄}}$	1495973$^{\text{⅄}}$	1459714$^{\text{⅄}}$	1299072$^{\text{⅄}}$	1212869$^{\text{⅄}}$	1143048$^{\text{⅄}}$	1177536$^{\text{⅄}}$	1154459$^{\text{⅄}}$	1157853$^{\text{⅄}}$
Alabama POU Age 5-11/ Alabama POU Age 5+	0.53%†	0.53%†	0.44%†	0.35%†	-	-	-	-	-
Alabama Unique POU Aged 12+	1531804*†	1488493*†	1452415*†	1292577*†	1206805*†	1137333*†	1171648*†	1148687*†	1152064*†
Alabama POUD that Obtained from Physician	20053†	19663*†	16154*†	16209*†	15858*†	20545*†	44842*†	51032*†	47788*†
POU	1,511,233$^{*\dagger\text{⅄}}$	1,468,392$^{*\dagger\text{⅄}}$	1,437,197$^{*\dagger\text{⅄}}$	1,278,347$^{*\dagger\text{⅄}}$	1,206,805$^{*\dagger\text{⅄}}$	1,137,333$^{*\dagger\text{⅄}}$	1,171,648$^{*\dagger\text{⅄}}$	1,148,687$^{*\dagger\text{⅄}}$	1,152,064$^{*\dagger\text{⅄}}$

Earlier we assumed that in any overdose involving fentanyl, the cause of death was fentanyl. That means, to find the number of heroin overdose deaths not involving fentanyl, it is necessary to remove any individuals who overdosed with both heroin and

fentanyl in their system. We note that the CDC WONDER umbrellas fentanyl under synthetic opioids (multiple cause of death code T40.4). That said, for simplicity we assumed that any overdose deaths involving both heroin and synthetic opioids involved fentanyl. Therefore, we found overdose deaths involving both heroin and fentanyl (Intersect of Overdose Deaths Involving H and Synthetic Opioids, Table 4) by using the same underlying death codes as before but this time filtering using multiple cause of death codes T40.1 AND T40.4 for each year. We then calculated Overdose Deaths Involving H without Synthetic Opioids (Table 4) by subtracting the Intersect of Overdose Deaths Involving H and Synthetic Opioids (Table 4) from Overdose Deaths Involving H (Table 4) [Cenndb, Cenndc]. Due to data limitations, we assumed here that any overdose death involving heroin without synthetic opioids was caused by heroin.

Therefore by totaling Overdose Deaths Involving F and Overdose Deaths Involving H without Synthetic Opioids in Table 4, we obtained H or F Overdose Deaths (Table 3).

PO overdose deaths (excluding overdoses involving H or F)

For PO Overdose Deaths (Table 3), we needed to find the total number of opioid related deaths, including, but not limited to, prescription opioids, heroin, and fentanyl, and then subtract off H or F overdose deaths (Table 4) since we assumed that in any overdose cases that involved either heroin or fentanyl, one of those substances was the cause of death.

To get the total number of Opioid Related Deaths (Table 4), we utilized the previously discussed overdose underlying death codes along with multiple cause of death codes T40.0 (opium), T40.1 (heroin), T40.2 (natural and semisynthetic opioids), T40.3 (methadone), T40.4 (synthetic opioids other than methadone), and T40.6 (other unspecified narcotics) [Cenndb, Cenndc]. Then, making the simplifying assumption that overdose deaths involving opioids without heroin or fentanyl were caused by prescription opioids, we calculated an estimate for PO Overdose Deaths 4 by subtracting H or F Overdose Deaths (Table 4) from total Opioid Related Deaths (Table 4).

HUD

Due to the lack of available data for HUD in Alabama, we first gathered heroin use data using state-specific tables from the National Survey on Drug Use and Health (NSDUH), which provided the percentage of Alabama's population aged 12+ that used heroin in the past year for each year from 2015 through 2019, 2022, and 2023 (Alabama

HU Percentage, Table 4) [Sub17, Sub18a, Sub18b, Sub20a, Sub20b, Sub24a, Sub25]. For the years 2020 and 2021, this data was not available. We calculated the number of Alabama HU (Table 4) for the years of available data by multiplying Alabama HU Percentage (Table 4) by the Population 12 and Over (Table 4) for each year.

Since we did not find Alabama-specific estimations for HUD, we used national-level information to estimate the percentage of heroin use that is HUD in Alabama. To begin, we found the total national number of heroin users and those with HUD for the years 2015 through 2023 using the NSDUH [Sub20d, Sub20e, Sub23a, Sub24b]. We note that the NSDUH underwent a major methodology change in 2020, shifting the criteria for substance use disorder from DSM-IV to DSM-5. Work by Goldstein et. al examined concordances between DSM-IV and DSM-5 substance use disorders and found that DSM-5 criteria yielded an estimate of 1.124 times larger than the estimate of DSM-IV criteria. The Substance Abuse and Mental Health Administration (SAMSHA) also studied the effect that changes from DSM-IV to DSM-5 had on specific use disorder measurements; when comparing weighted estimated percentages of HUD from NSDUHs for the years 2002-2012 using the different criteria, they found that both yielded an estimate of 0.1% of the total population. [Sub16a], so not much of a difference either.

Thus, for comparability of our HUD estimates before and after the 2020 methodology change, we adjusted any HUD data attained from the NSDUH for the years 2015 through 2019 by multiplying the estimates by 1.12. We chose to adjust data prior to the methodology change instead of the data for 2020 through 2023 because the DSM-5 criteria is the most current criteria for determining use disorder and we expect data following the year 2023 will continue to use it. Thus, National HUD (Table 4) for the years $2015 - 2019$ is 1.12 times the estimates provided by the NSDUH.

Next, we needed to find the national proportion of heroin use that is HUD, so we also obtained NSDUH estimates of National HU (Table 4) [Sub20e, Sub20d] and [Sub23a, Sub24b]. Then, we divided National HUD (Table 4) by National HU (Table 4) to get the national proportion of heroin use that is HUD. We made the simplifying assumption that Alabama has the same proportion of heroin users that have HUD as the national level does and applied the national proportion to our Alabama HU (Table 4) estimates. Multiplying National HUD/HU and Alabama HU from Table 4, we attained our Alabama HUD (Table 3) estimates for the years $2015 - 2019$, 2022, and 2023.

For the years 2020 and 2021, the NSDUH state-specific estimates were not available, so we extrapolated Alabama HUD (Table 4) estimates for those years. To do so, for 2020, we divided the 2020 value for National HUD (Table 4) by the 2019 estimate of National HUD (Table 4) to get a proportion National $\text{HUD}_{2020}/\text{HUD}_{2019}$ (Table

4), and then multiplied by the 2019 Alabama HUD estimate (Table 4) to estimate the 2020 Alabama HUD value (Table 4). Similarly, we estimated the 2021 Alabama HUD value (Table 4) by multiplying our 2020 Alabama HUD estimate (Table 4)by the National HUD_{2021}/HUD_{2020} proportion.

POUD (excluding individuals with HUD)

To find the number of individuals with POUD, we point out that an individual may have both HUD and POUD within the same year. Since any individual with HUD would have been counted in the H class, we needed to remove individuals with HUD from the number of individuals with POUD to obtain the count of the A class. We started by finding the overall number of individuals with POUD in Alabama for each year. Using the NSDUH state-specific tables, we obtained the estimated percentage of the population of individuals aged 12+ in Alabama that had a POUD in the past year for years 2016 through 2019, 2022, and 2023 (Alabama POUD Percentage, Table 4) [Sub17, Sub18a, Sub18b, Sub20a, Sub20b, Sub24a, Sub25]. The data was not available for the years 2015, 2020, and 2021.

Due to the change in NSDUH methodology for categorizing use disorder, we adjusted the data from 2015 through 2019, similar to our approach for HUD in which previous work determined that the DSM-5 criteria yielded an estimate 1.137 times the DSM-IV estimate for POUD (the work defined it as "opioids (other than heroin)," which we believe is a reasonable fit for our definition of prescription opioids) [GCS+15]. Work done by SAMSHA found that the pain reliever use disorder estimates using DSM-IV yielded an average of 0.7% and DSM-5 yielded an average of 0.8% of the population with POUD [Sub16b]. Dividing the DSM-5 estimate by the DSM-IV estimate, we found that the DSM-5 estimate was 1.143 times the DSM-IV estimate.

Thus, to calculate Alabama POUD (Table 4) for the years 2016 through 2019, we multiplied the Alabama POUD Percentage (Table 4) by the Population 12 and Older (Table 4) and then multiplied by 1.14, an average of the previous two estimates. For Alabama POUD for the years 2022 and 2023, we multiplied the Alabama POUD Percentage by Population 12 and Older since values were estimated already using DSM-5 criteria.

Once we had overall POUD numbers for Alabama, we removed individuals who also had HUD. We could not find Alabama data regarding the number of individuals who had both HUD and POUD, so we used the national proportion of prescription pain reliever use disorder that did not include heroin. We made an assumption that the proportion was the same in Alabama, and we used it to find the number of individuals in Alabama with POUD without HUD.

To find the national proportion of prescription pain reliever use disorder, which we take to be prescription opioids, that did not include HUD for each year, we used the NSDUH to attain the numbers for National POUD (Table 4) and National HUD (Table 4) for each year [Sub20e, Sub23a]. Since these data were from the NSDUH, we had to adjust the data for the years prior to 2020 similar to before due to methodology change. We adjusted the national pain reliever use disorder for the years 2015 through 2019 by multiplying the NSDUH estimates by 1.14. Since prescription pain reliever use disorder makes up a large proportion of overall opioid use disorder, we also adjusted opioid use disorder for the years 2015 through 2019 by multiplying the NSDUH data by 1.14. We then used these values along with National HUD (Table 4) that we calculated earlier to find POUD that did not include HUD.

To do so, we found National POUD without HUD (Table 4) by subtracting National HUD (Table 4) from National POUD (Table 4). Then, we divided National POUD without HUD (Table 4) by National POUD (with HUD) (Table 4) to get the national proportion of total POUD that does not include individuals who also have HUD. We applied that proportion to Alabama POUD (with HUD) (Table 4) to get Alabama POUD (Table 4) for the years 2016 through 2019, 2022, and 2023.

For the years 2015, 2019, and 2020, Alabama POUD estimates were not available. Thus, we followed a similar method to the one we used for extrapolating missing data estimates for HUD (Table 4). To estimate Alabama POUD (Table 4) for the year 2015, we did the following operation due to available data from 2016 and national data available, making the simplifying assumption that Alabama follows national trends due to lack of available data for the state:

$$\text{Alabama POUD}_{2015}\text{ (w/o HUD)}$$

$$= \text{Alabama POUD}_{2015}\text{ (w HUD)} * \frac{\text{Alabama POUD}_{2015}\text{ (w/o HUD)}}{\text{Alabama POUD}_{2015}\text{ (w/ HUD)}}$$

$$= \text{Alabama POUD}_{2016}\text{ (w/ HUD)} * \frac{\text{National POUD}_{2015}\text{ (w/ HUD)}}{\text{National POUD}_{2016}\text{ (w/ HUD)}} * \frac{\text{National POUD}_{2015}\text{ (w/o HUD)}}{\text{National POUD}_{2015}\text{ (w/ HUD)}}.$$

Then, to get 2020 Alabama POUD, we multiplied 2019 Alabama POUD (including HUD) by National POUD_{2020}/National POUD_{2019} and by the 2020 National proportion of POUD without HUD (Table 4). Similarly, for 2021 Alabama POUD, we multiplied 2020 Alabama POUD (including HUD) by National POUD_{2021}/POUD_{2020} and by the 2021 National proportion of POUD without HUD (Table 4).

POU (excluding individuals with POUD or HUD)

To find the number of POU in Alabama for each year, we note the possibility that individuals with HUD or POUD could have been prescribed opioids. That said, individuals with opioid use disorder have already been classified under either the A or H class, and we must remove any individuals who had either use disorder from our P class.

To do so, we obtained data from the Alabama PDMP on the overall unique number of individuals that were prescribed opioids in Alabama for each year (Alabama POU, Table 4) which included values for those aged 5 and older for each year from 2015-2024. However, we note that due to no data availability for the A and H classes in 2024 from the sources we were able to find, we were unable to use the 2024 data point for the P class [Ala25]. Since the age group of interest for our study was 12 and older, we first needed to remove individuals aged $5-11$ from the data before moving on to removing out individuals with opioid use disorder. The Alabama PDMP data was broken down such that the number of prescribed users age $5-17$ was given. Therefore, in order to remove individuals age $5-11$ from the data, first we calculated the national proportion of prescribed opioid users in the age group $5-17$ that were age $5-11$ using data from [RYJ+21] for the years of available data ($2015-2018$). This previous work had the total number of national prescriptions for the age groups $0-5$, $6-9$, $10-14$, and $15-19$ [RYJ+21]. These numbers represented the total national prescriptions, but we needed the number of unique prescribed users. In order to help with this, there was also data on the percent of patients under the age of 25 that were dispensed 1 prescription, $2-4$ prescriptions, and 5+ prescriptions. For simplicity in calculation and from lack of more specific data, we grouped these into 1, 3, or 5 prescriptions. We took the total number of national prescriptions for each age group for each year and multiplied it by (the percent of patients under 25 dispensed 1 prescription to get the unique number of individuals in the age group taking 1 prescription, plus $\frac{1}{3}$ times the percent of patients under 25 dispensed 3 prescriptions to get the unique number of individuals taking 3 prescriptions, plus $\frac{1}{5}$ times the percent of patients under 25 dispensed 5+ prescriptions to get the unique number of individuals taking 5 prescriptions) in order to determine the number of unique individuals prescribed opioids in each age group.

From here, however, we needed the national prescribed users aged $5-17$ to match the age group from Alabama PDMP. To calculate this, we began by totaling the national prescription users aged $0-19$ for each year and subtracting out $\frac{4}{5}$ of national prescribed users aged $0-5$ (wanting to be left only with age 5) and $\frac{2}{5}$ of national prescribed users aged $15-19$ (wanting only to be left with ages 15-17) for a result

of the total number of unique individuals aged 5-17 on the national level prescribed opioids. We then calculated national prescribed users aged $5-11$ by totaling $\frac{1}{5}$ of national prescribed users age $0-5$ plus national prescribed users age $6-9$ plus $\frac{2}{5}$ national prescribed users age $10-14$. Taking national prescribed users aged $5-11$ divided by national prescribed users age $5-17$, we got the national percentage of prescribed users that are age $5-11$ within the $5-17$ age group.

We used that proportion to find Alabama POU Age 5-11 (Table 4) for the years available, 2015-2018, by taking the National Unique POU Age 5-11 / National Unique POU Age 5-17 (Table 4) and multiplying by Alabama POU 5-17 (Table 4). In order to extrapolate the data for all of the remaining years, we divided Alabama POU Age 5-11 (Table 4) by Alabama POU Age 5+ from Table 4 (which is the total of Alabama POU 5-17 and Alabama POU 18+) to find the percentage of Alabama POU Age 5+ that were age 5-11 (which is shown in Table 4 by Alabama POU Age 5-11/Alabama POU Age 5+). These percentages averaged to about 0.5% across the years of available data. Therefore, for all of the years, we took 99.5% of Alabama Unique POU Age 5+ to obtain Alabama POU Aged 12+ (Table 4). This number still included individuals with HUD and POUD, so our next step was to remove those individuals.

Findings from the 2015 NSDUH indicated that 44.3% of adults reporting pain reliever use disorder obtained opioids for their most recent misuse from one or more physicians (which we will take to be that the individual was being prescribed) [HCB+17]. Using this statistic, we took 44.3% of Alabama POUD (including HUD) (which is an estimate of those in A or H during a given year) to get Alabama POUD that Obtained from a Physician. Then, to get Alabama POU (Table 4), we subtracted Alabama POUD that Obtained from a Physician (Table 4) from the total Alabama POU Aged 12+ (Table 4).

We note that the NSDUH combines data from two consecutive years and therefore, throughout all of our data estimation processes, we consistently chose the higher year to be the year we report the data on. For example, the NSDUH 2015-2016 report was data we estimated to be for 2016.

B. **Parameter calculations and bounds for parameter estimation**

μ, μ_H, and μ_A estimation

To find the natural death rate, we recorded the Alabama age-adjusted death rates (deaths per 100,000 people) for the years $2015-2023$ [Nat25e]. Taking the death rate for each year and applying it to Alabama residents aged 12+, we calculated the total number of deaths. We then removed opioid overdose deaths from the total deaths in those years, excluding 2023 due to data limitations, to obtain an estimated

natural deaths per year from 2015-2022. We then subtracted the natural deaths from the population and divided that number by the population to determine the proportion of the population that remains by the beginning of the next year for each year. Averaging those values we find this proportion to be 0.99. We assume an approximately constant proportion over this short time frame so as to include 2023 in our analysis, as well. This means that if we take T_0 to be the initial total population, we find the continuous-time natural death rate from the equation $0.990T_0 = T_0e^{-\mu t}$, yielding a natural death rate $\mu = 0.010$.

Similarly, we find the death rate of those with heroin or fentanyl use disorder. To do so, we make the assumption that individuals that overdose on heroin or fentanyl strictly come from the group of individuals that have heroin or fentanyl use disorder. Therefore, we calculate the proportion of the individuals with heroin or fentanyl use disorder that remain by the following year by subtracting overdose deaths from heroin, fentanyl, or both from the number of individuals with heroin or fentanyl use disorder and dividing this number by the number of individuals with heroin or fentanyl use disorder for each year. The average of these values yield 0.965. Using the equation $0.965H_0 = H_0e^{-\mu_H t}$, where H_0 represents the number of individuals with heroin or fentanyl use disorder for the initial year, we find $\mu_H = 0.036$.

Lastly, using the assumption that individuals that overdose on prescription opioids strictly come from the group of individuals that have POUD, we subtract prescription overdose deaths from the number of individuals with POUD and divide this number by the number of individuals with POUD for each year. The average proportion of individuals with POUD that remain by the beginning of the next year is 0.997. By taking $0.997A_0 = A_0e^{-\mu_A t}$, where A_0 represents the number of individuals with POUD for the initial year, we find $\mu_A = 0.003$.

These values are fixed throughout our parameter estimation process. Other parameters that must be estimated need to have reasonable bounds on them for the process, so we calculate bounds for the following parameters.

β_A and β_P bounds estimation

We wish to estimate reasonable ranges for the rates that individuals enter the A class through the illicit market, β_A, or through leftover or stolen prescriptions, β_P.

Previous studies have analyzed the results of the 2015 NSDUH regarding the source where individuals with pain reliever use disorder (which we take to mean prescription opioids in our context) obtained pain relievers for their most recent misuse [HCB+17, HWL+16]. While the statistics are similar between studies, for the purpose of our β_A and β_P estimations, we use [HWL+16] because it focuses on the age group

that we are interested in. In this source, we utilize information about those with POUD whose source was buying from a drug dealer or other stranger (13.4%) and whose source was obtained from friends or relatives (39%) which we will utilize for our estimates.

We began our estimation for β_A by calculating the POUD initiation rate, relying on the national percentage of the population that initiated pain reliever misuse (PRM) for the years $2016-2019$, 2022, and 2023 [Sub20f, Sub23b, Sub24c] multiplied by the proportion of pain reliever misusers in Alabama that have pain reliever use disorder for all the available years. Then, we multiply this by the percentage of individuals with POUD that obtain their pain relievers from a drug dealer or other stranger. Using this assumption we are able to estimate β_A by taking pain reliever use disorder initiation rate by the proportion of individuals with pain reliever use disorder who obtain from a drug dealer or other stranger and finding the average over the years (with i denoting year) as follows:

$$\beta_A = \frac{1}{\text{n years}} * \sum_{i=1}^{n} \frac{\text{PRM initiates}_i}{\text{Population (12+)}_i} * \frac{\text{POUD}_i}{\text{PRM}_i} * \frac{\text{0.134 obtain from drug dealer or other stranger}}{\text{POUD}} = \frac{0.000247}{\text{year}},$$

using 0.134 from [HWL+16] with drug dealer or other stranger as the source. Therefore, we choose the range for β_A to be $[0.00001, 0.001]$

Similarly, we estimate β_P, the rate that susceptible individuals develop POUD through leftover or stolen prescription opioids, except use the value of 0.39 from [HWL+16] for obtaining their pain relievers from friends or relatives, which yields the following:

$$\beta_P = \frac{1}{\text{n years}} * \sum_{i=1}^{n} \frac{\text{PRM initiates}_i}{\text{Population (12+)}_i} * \frac{\text{POUD}_i}{\text{PRM}_i} * \frac{\text{0.39 obtain from friends or relatives}}{\text{POUD}} = \frac{0.000718}{\text{year}}.$$

Therefore, we choose the range for β_P to be $[0.00001, 0.0015]$.

θ_1, θ_2, and θ_3 bounds estimation

To find θ_1, the rate that susceptible individuals develop heroin or fentanyl use disorder, we consider an estimate from 2013, where an estimated 0.02% of individuals with no prior non-medical pain reliever misuse transitioned to heroin on average for the years 2009-2011 [MGD13]. We made the assumption that individuals with no prior misuse of non-medical pain relievers represent susceptible individuals. Thus, we calculate:

$$\theta_1 * \frac{\text{HUD}}{\text{Population 12+}} = \frac{\text{HUD initiates}}{S} = \frac{\text{0.0002 HU initiates}}{S} * \frac{\text{HUD}}{\text{HU}}$$

$$\implies \theta_1 = \frac{\text{0.0002 HU initiates}}{S} * \frac{\text{HUD}}{\text{HU}} * \frac{\text{Population 12+}}{\text{HUD}}.$$

We do this for the years $2015 - 2023$ relying on estimates from Table 4, and average these values to get $\theta_1 \approx 0.06416$, resulting in a bounds range of [0.005,0.3], an order of magnitude above and below.

For θ_2, the rate that prescribed opioid users develop heroin or fentanyl use disorder, we used the same study which suggested that on average in $2009 - 2011$, 0.34% of prior non-medical pain reliever misusers with no dependence or abuse in the past year transitioned to heroin use [MGD13]. For the years $2016 - 2019$, 2022, and 2023, we calculated θ_2 in a similar manner as θ_1 as follows:

$$\theta_2 = \frac{\text{0.0034 HU initiates}}{\text{PRM-POUD}} * \frac{\text{PRM-POUD}}{\text{PU}} * \frac{\text{HUD}}{\text{HU}} * \frac{\text{Population (12+)}}{\text{HUD}}.$$

We took the average of the three years which yielded $\theta_2 \approx 0.111$, in which we chose bounds to be [0.001,0.4].

Lastly, for θ_3, the rate in which individuals with POUD develop heroin or fentanyl use disorder, we continue to consider the same national study [MGD13] where they found that 4.83% of people with pain reliever dependence or use disorder initiated heroin use on average for years $2009 - 2011$. We assume these individuals fall into the definition of our A class, and calculate θ_3 using the same method used before:

$$\theta_3 = \frac{\text{0.0483 HU initiates}}{\text{POUD}} * \frac{\text{HUD}}{\text{HU}} * \frac{\text{Population (12+)}}{\text{HUD}}.$$

Doing this for the years $2015 - 2019$, 2022, and 2023, and taking the average yields $\theta_3 \approx 16.1$ in which we chose bounds [5,25].

ν and ζ bounds estimation

It was found in 2023 that among adults with past year opioid use disorder, 35.6% received any treatment and only 22% received medication based treatment [JHB+23]. An estimated 40-60% of individuals who receive medication based treatment relapse within a year post treatment, which we will assume to be 50% for calculation purposes, and an estimated 90% of individuals relapse within a year after detoxification (non-medication based opioid use disorder treatment) [Rho17]. It is also noted that for individuals who discontinue medication, relapse rates jump back up to 90% .

We used these statistics to estimate both ν, the rate that individuals stably recover from the H class, and ζ, the rate that individuals stably recover from the A class. Since we used the same data for both, we chose the bounds to be the same. With this in mind, we estimated a relatively large upper bound and a relatively small lower

bound, to allow for error due to the possible difference in recovery related behaviors between the A and H class.

If only 22% of individuals with opioid use disorder received medication based treatment, then 13.6% of individuals with opioid use disorder received non-medication based treatment. Combining those numbers and the rate of relapse for each treatment type, we found $0.356 - [(0.22 * 0.5) + (0.136 * 0.9)] = 0.126$ to be the proportion of individuals with opioid use disorder that transition to the R class by the following year. This means that an estimated 87.4% of individuals with opioid use disorder do not transition to the R class by the following year. Because individuals who receive medication based treatment but discontinue medication have a 90% relapse rate, we consider 87.4% to be an underestimate of individuals with opioid use disorder that do not transition to the stably recovered class by the following year. Then, we also calculated an overestimate of individuals who did not meet our definition of recovered. To do so, we underestimated the proportion of individuals that recovered by taking $0.356 - (0.356 * 0.9) = 0.0356$, to find that an an overestimate of 96.4% of individuals with opioid use disorder do not meet our definition of recovered by the following year.

To estimate ν, we took $H' = -\nu H$ and solved to get $H = H_0 e^{-\nu t}$. For the upper bound, we took $0.874H_0 = H_0 e^{-\nu(1)} \implies \nu = 0.135$. Then, for the lower bound, we took $0.964H_0 = H_0 e^{-\nu(1)} \implies \nu = 0.037$. Therefore, we chose the bounds for ν to be [0.001, 0.2]. Since the information we used were for opioid use disorder as a whole, we chose the same bounds for ζ. All bound ranges are shown in Table 5.

Table 5: Reasonable Bound Estimates for the Model Parameters Used in Parameter Estimation

Parameter or IC	**Bounds**	**Reasoning for Bounds**
α	[0.1,0.5]	Estimate from [PLS21] based on y-intercept of time-dependent α
ϵ	[1,5]	Estimate from [BPS19, PLS21]
γ	[0.005,0.1]	Estimate from [BPS19, PLS21]
β_A	[0.00001, 0.001]	See Appendix B for detailed calculations
β_P	[0.00001, 0.0015]	See Appendix B for detailed calculations
θ_1	[0.005, 0.3]	See Appendix B for detailed calculations
θ_2	[0.001, 0.4]	See Appendix B for detailed calculations
θ_3	[5, 25]	See Appendix B for detailed calculations
ζ	[0.001, 0.2]	See Appendix B for detailed calculations
ν	[0.001, 0.2]	See Appendix B for detailed calculations
σ	[0.1, 2]	Estimate from [PLS21]
P_0	[0.001,0.37]	Maximum 37% of the population since during 2015, the estimated proportion of individuals prescribed opioids out of the entire population is $\frac{1,511,233}{4,130,653} \approx 0.37$ from Table 3
A_0	[0.0001,0.01]	Maximum 1% since during 2015, the estimated proportion of individuals with POUD out of the entire population is $\frac{39,855}{4,130,653} \approx 0.0096$ from Table 3
H_0	[0.00001,0.0025]	Maximum 0.25% of the population since during 2015, the estimated proportion of individuals with HUD out of the entire population is $\frac{8,916}{4,130,653} \approx 0.0022$ from Table 3
R_0	[0.00001,0.1]	Estimate from [PLS21]

C. **Comparing models**

Comparison of Models with AIC. The Akaike Information Criterion (AIC) is an estimator of the relative quality of statistical models for a given set of data [MC03]. It does so by balancing the change in the fit of the model to the data with the change in the number of parameters being estimated. When we add more parameters to improve the fit of the data, the AIC determines whether the benefit of the improvement in the data fit outweighs the negative consequence of estimating additional parameters. The score sums the lack of fit and the complexity of the model. It is given by:

$$AIC = N \ln \frac{SS}{N} + 2K.$$

Here, N is the number of data points the model is calibrating to, SS is the sum of squares of the differences between model simulated points and data points, and K is the number of parameters being estimated, including the value of $S(0)$ and SS since they are both being estimated. Our model has $N = 43$ data points. Additionally, for each model form that we investigated, we have the following number of "parameters" (parameters, initial conditions, and sum of squares) being estimated:

$$\begin{gathered}\text{All constant parameters: } 16 \implies K_1 = 16 + 1 = 17,\\ \text{Linear prescription rate } \alpha\text{: } 17 \implies K_2 = 17 + 1 = 18,\\ \text{Piecewise linear prescription rate, } \alpha\text{: } 17 \implies K_3 = 17 + 1 = 18.\end{gathered}$$

We note that the linear and piecewise linear alpha cases have the same number of unknown parameters since the piecewise linear function is structured to be a constant function after the year 2020.

In the case of small sample sizes and when the number of parameters being estimated is a significant portion of the sample size (and no bigger than half), it is recommended to use the corrected AIC score (AIC_C), which is intended to address potential overfitting [MC03]. Since our sample size N=43 is not very large and K ranges from 40% to 42% of this value, we instead use the AIC_C. In addition, our parameter estimation output was not simply SS but instead was an objective function value, OF given in detail in Section 1.3, and is substituted in for SS in the following corrected AIC score formula:

$$AIC_C = N \ln \frac{OF}{N} + 2K + \frac{2K(K+1)}{N-K-1}.$$

For our three model forms, we compare the following AIC_C values:

$$AIC_{\text{constant}} = 43 \ln \frac{1.398917168170849}{43} + 2(17) + \frac{2(17)(18)}{43-17-1} = -88.8,$$
$$AIC_{\text{linear}} = 43 \ln \frac{1.3671058241639311}{43} + 2(18) + \frac{2(18)(19)}{43-18-1} = -83.8,$$
$$AIC_{\text{piecewise}} = 43 \ln \frac{1.34360040474168}{43} + 2(18) + \frac{2(18)(19)}{43-18-1} = -84.5.$$

The lower the AIC score, the better the choice for model fit to the data. Although the model with all constant parameters provided the lowest score, we deemed it potentially unrealistic due the value of P_0 that it produced, and therefore decided the best fit, taking into account practicality of the situation, was the model taking $\alpha(t)$ as a piecewise linear function of time.

D. **Partial Rank Correlation Coefficient (PRCC) results**

LHS and PRCC Results. Here we report the results for our LHS and PRCC analysis in Table 6, with the values closest to -1 or 1 (and small $p-$values so statistically significant) having the largest impact (negative or positive correlation, respectively) on the A or H classes, reported in Section 2.2.

Table 6: Results from LHS and PRCC analysis run using 200 samples from 2024 to the beginning of 2028 with sensitivity to the A and H classes measured at the beginning of 2028. Values closest to -1 or 1 and with a small p-value (statistically significant) are of most interest.

Parameter	**PRCC Value for A**	**p-value**	**PRCC value for H**	**p-value**
m	0.321	3.52e-06	0.200	5.49e-05
b	0.744	1.70e-36	0.392	3.75e-16
ϵ	-0.810	7.70e-48	-0.544	0.309e-32
γ	0.869	2.04e-62	0.140	4.88e-03
β_A	0.109	0.126	-0.021	0.677
β_P	0.130	0.0672	0.0117	0.816
θ_1	-0.0836	0.239	0.0869	0.0825
θ_2	-0.0939	0.186	0.533	9.27e-31
θ_3	-0.520	3.21e-15	0.884	1.49e-133
ζ	-0.573	7.43e-19	0.224	6.13e-06
ν	0.0219	0.758	-0.158	0.150e-03
σ	0.434	1.40e-10	0.347	8.78e-13
μ	-0.292	2.73e-05	-0.392	3.80e-16
μ_A	0.184	9.14e-03	1.96e-03	0.970
μ_H	0.0855	0.229	-0.619	9.62e-44
ω	-0.0872	0.219	0.0383	0.445

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