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Bayesian Calibration of a Simulation Model of Opioid Use Disorder

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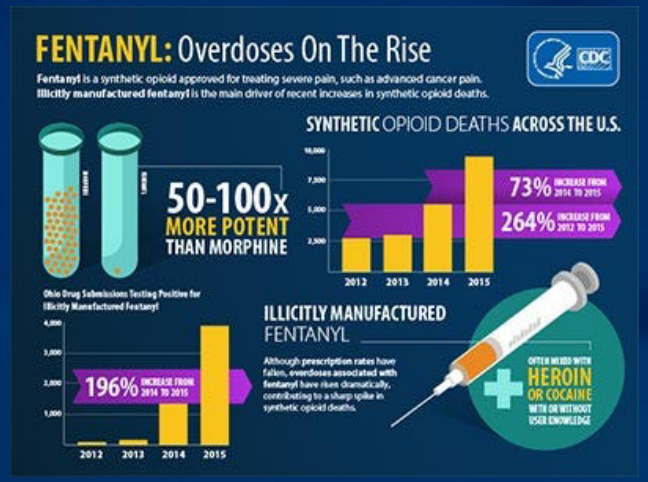
NIH National Institute on Drug Abuse
The Science of Drug Abuse & Addiction

Boston University School of Public Health

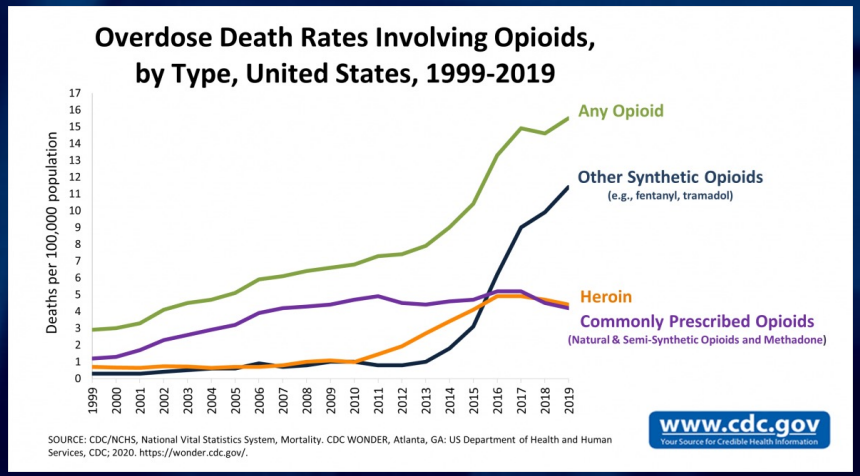
Boston University School of Medicine

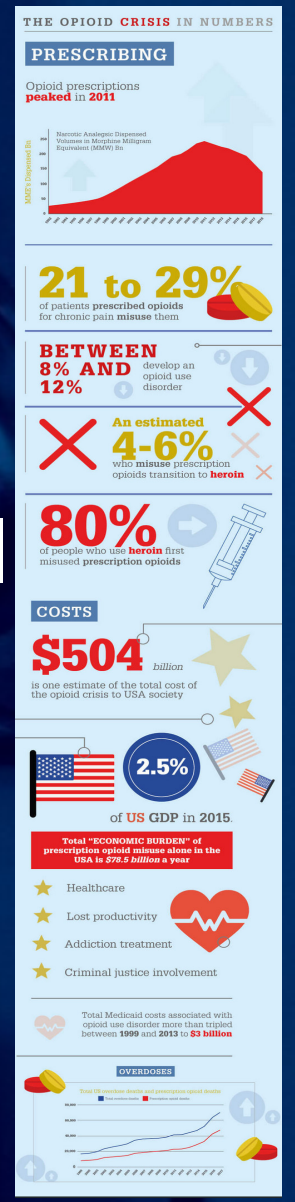
Opioid use disorder (OUD) is epidemic in the U.S.

www.poison.org



www.usatoday.com/





https://themedicinemaker.com/

Medications for Opioid Use Disorder

Buprenorphine

Buprenorphine is a schedule III opioid medication and a partial opioid agonist. It is an evidence based medication for opioid use disorder that mitigates risk of nonfatal and fatal overdose because of it's ceiling effect on respiratory depression. The most common formulations are sublingual as the monoproduct (i.e. Subutex) or in combination with naloxone (ie. Suboxone).

Methadone

Methadone is a full opioid agonist, which binds to the opioid receptor and can attenuate opioid withdrawal symptoms and be continued for maintenance treatment in an Opioid Treatment Program (OTP).

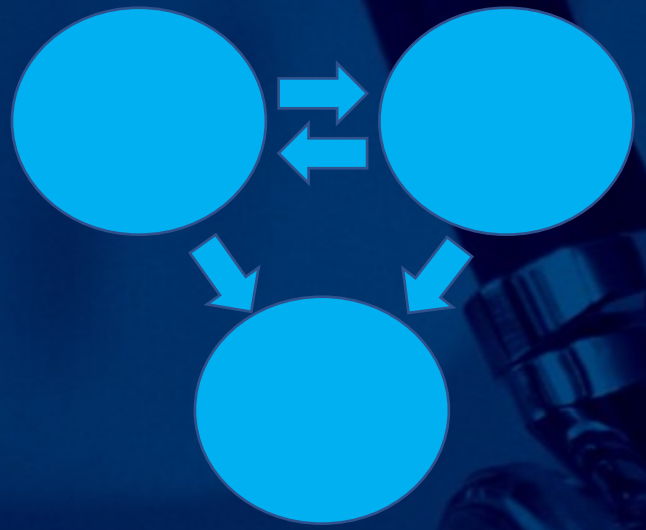
Naltrexone

Extended-release naltrexone is an opioid antagonist that is available as a monthly depot injection. It is an option for maintenance in patients who have been abstinent from opioids for a sufficient period (at least 7 days) to prevent adverse reactions and acute withdrawal.

"Patients treated with buprenorphine are less likely to overdose, die, use illicit opioids, develop Hepatitis C or HIV, suffer other infections complications, or have contacts with the criminal justice system."

Source: https://penncamp.org/

Simulation Models of OUD

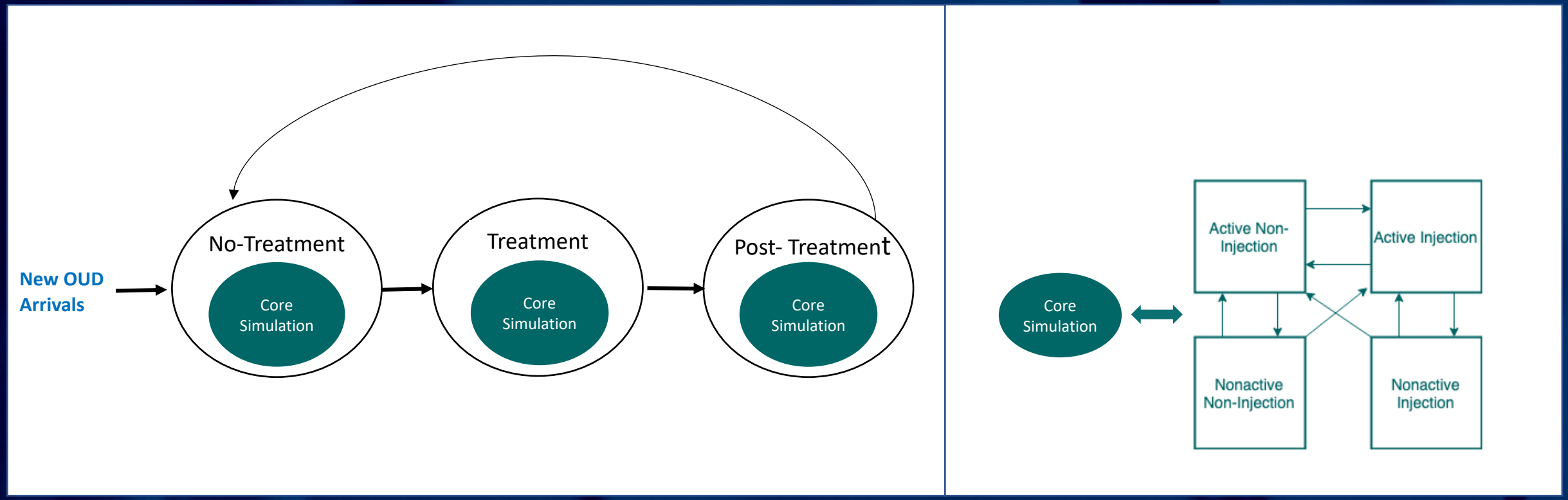


Simulation models of OUD aim at evaluating the impact of different care delivery and treatment strategies on population-level outcomes.

Researching Effective Strategies to Prevent Opioid Death (RESPOND) Model

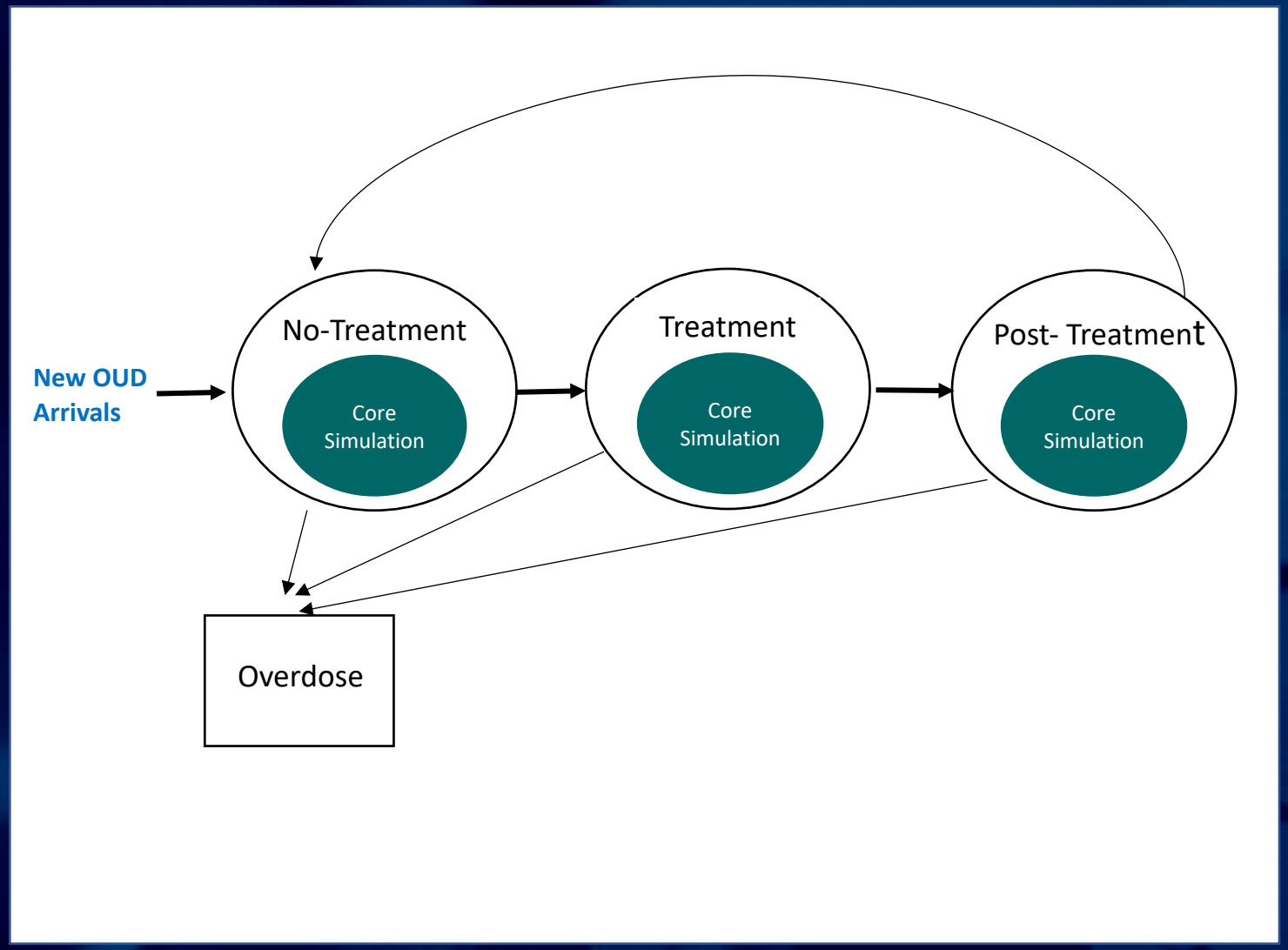
We developed the RESPOND model: a cohort-based state transition model to simulate the Massachusetts (MA) OUD population in order to inform policy priorities.

RESPOND Model



The treatment block is stratified by four types of treatments: Buprenorphine, Naltrexone, Methadone and Detox

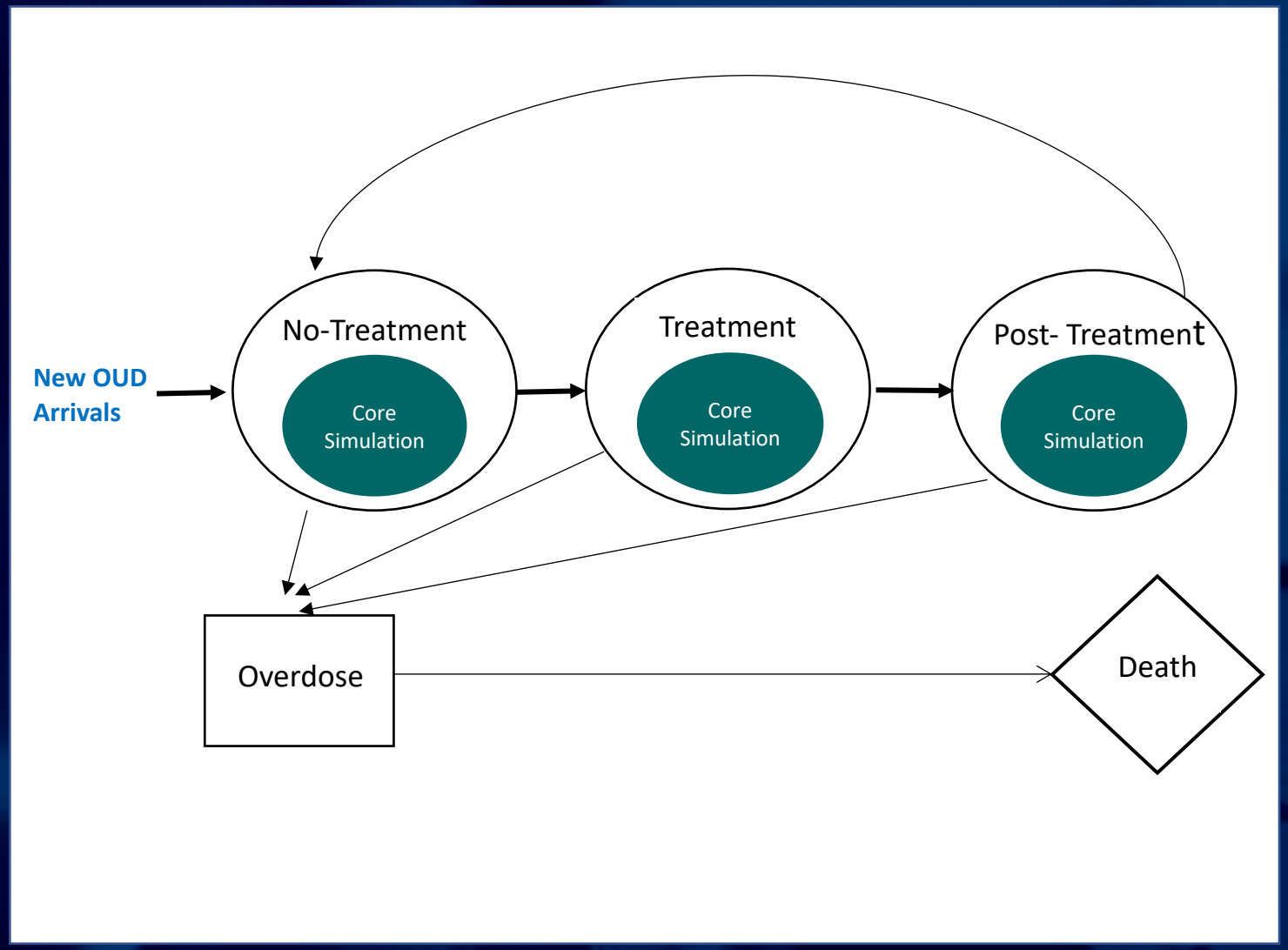
RESPOND Model



Modeling Overdoses

- A portion of active users can overdose in each block
- Overdose risk is stratified by age, sex and route of administration

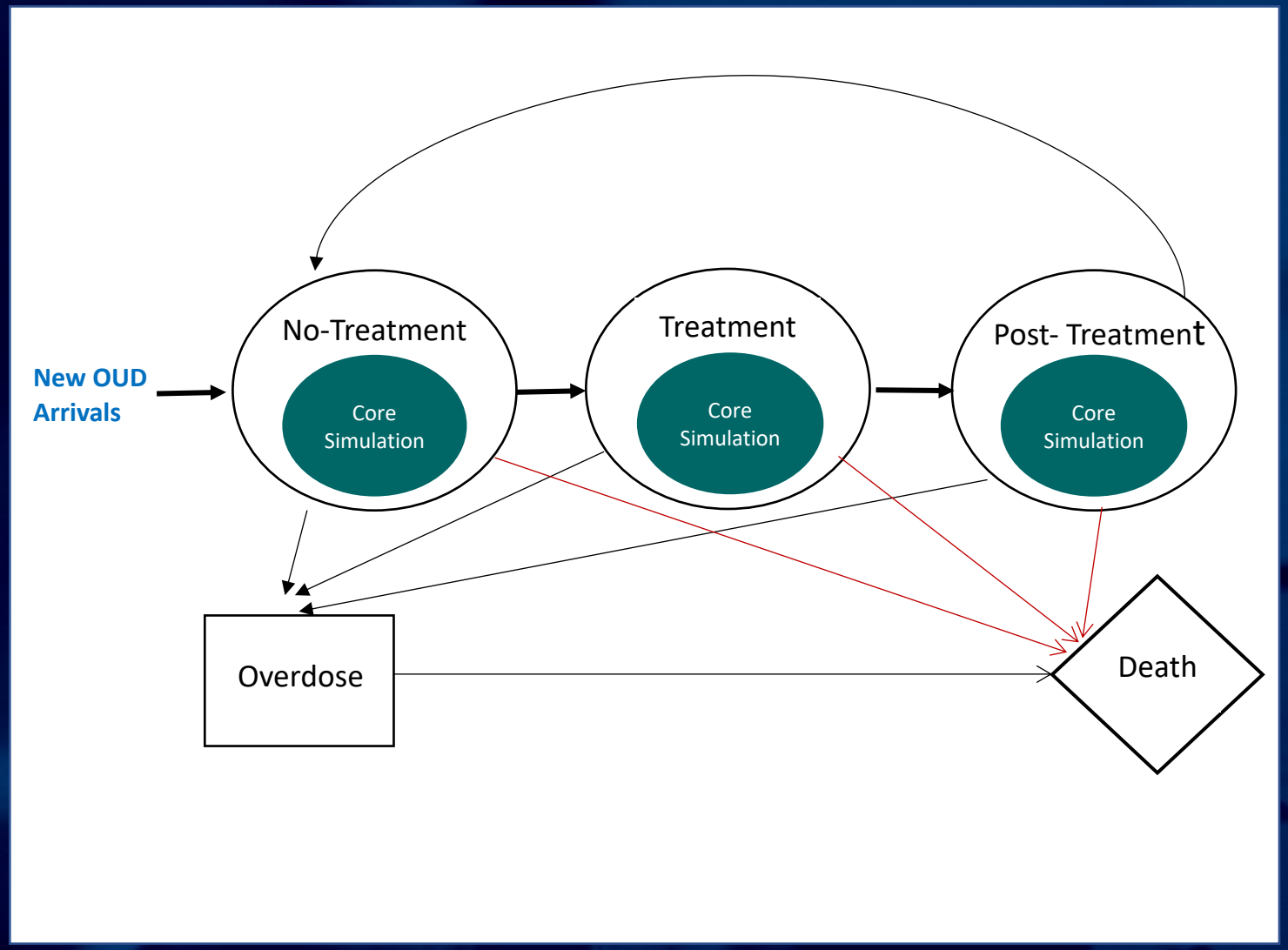
RESPOND Model



Modeling Deaths

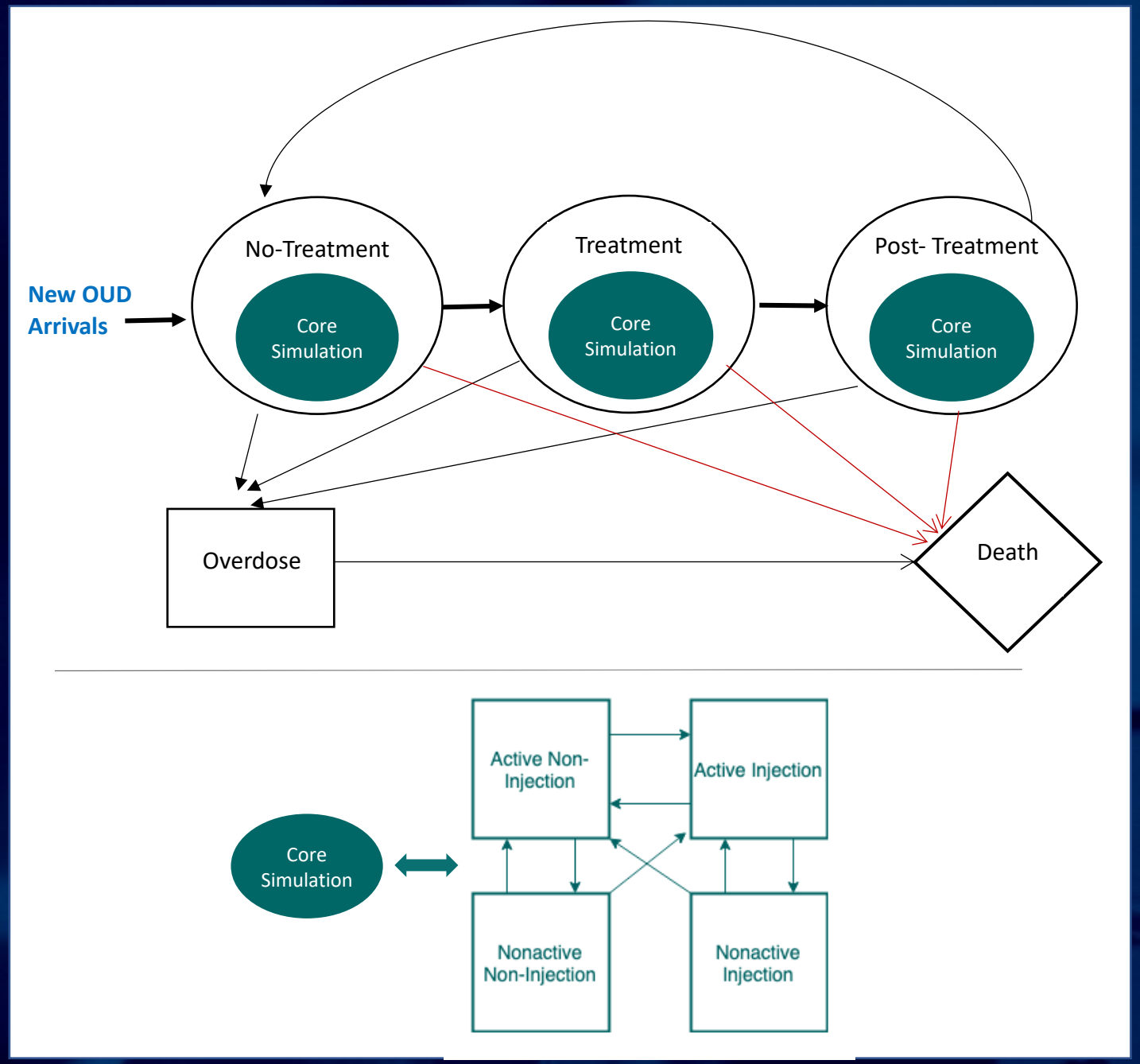
- Among those who overdose, there is a conditional probability of death due to overdose

RESPOND Model



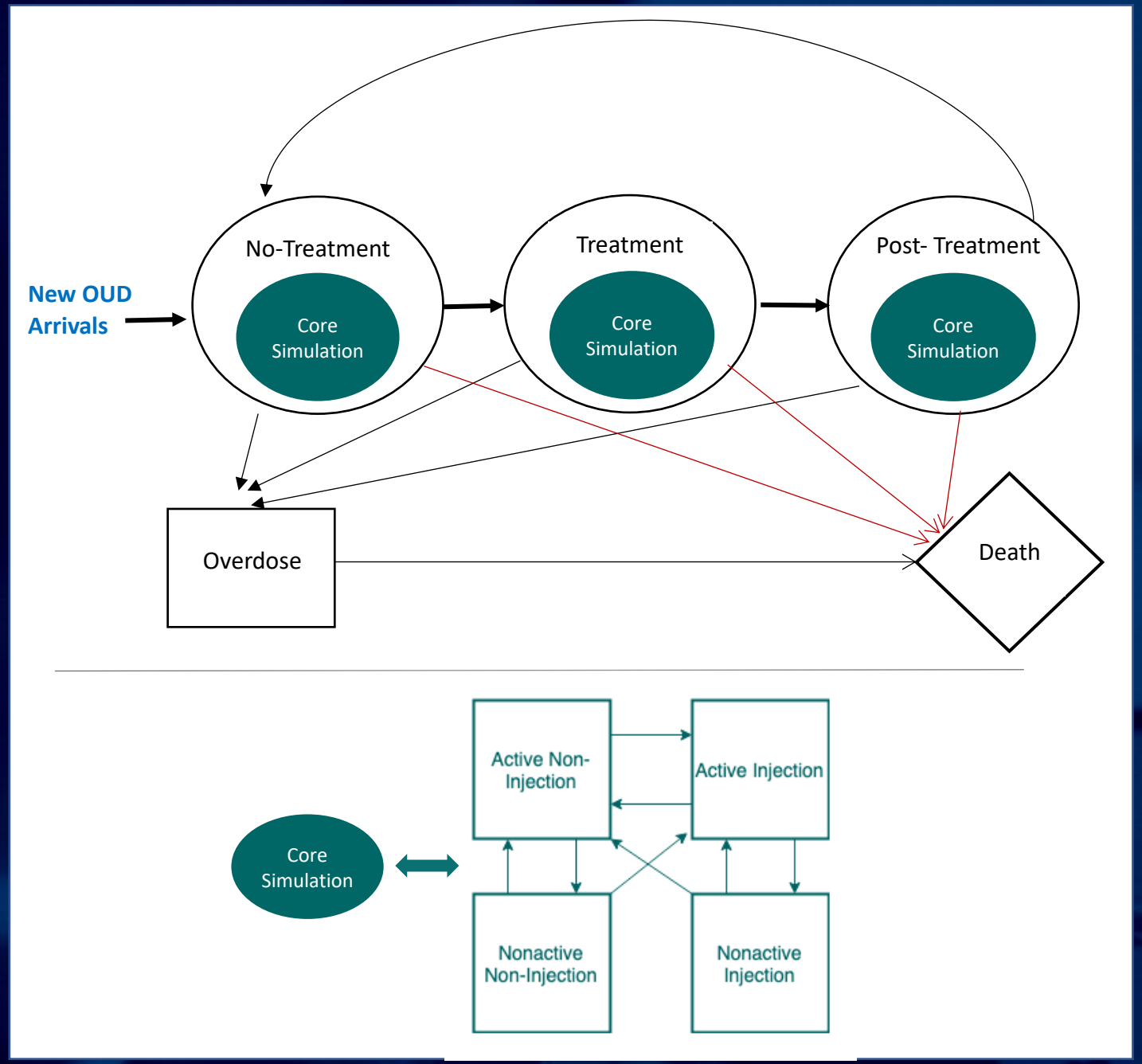
Modeling Deaths

- Among those who overdose, there is a conditional probability of death due to overdose
- Non-overdose related deaths are modeled using standard mortality rates (SMR)



Model Parameters

- New OUD arrivals
- OUD state transition probabilities
- Treatment and Post-treatment transition rates
- Overdose rates and fatal overdose proportions
- SMR



Model Parameters

- New OUD arrivals
- OUD state transition probabilities
- Treatment and Post-treatment transition rates
- Overdose rates and fatal overdose proportions
- SMR

Calibration Targets: Yearly OUD population sizes, fatal overdoses and admission to Detox

Data Sources

- The primary data source: Massachusetts Public Health Data Warehouse (PHD)

- Other sources: National Survey on Drug Use and Health (NSDUH), National Vital Statistics System, 2010 Census and Massachusetts Public Health Data Repository, National Institute of Drug Abuse (NIDA) Clinical Trials Network (CTN)

Model Calibration

- Calibration period is from year 2013-2015
- Targets:
  - Total OUD population count of year 2015 estimated from capture-recapture analysis [1]
  - Yearly fatal overdose counts for 2013-2015 from PHD
  - Yearly counts of admission to Detox for 2013-2015 from PHD
- Calibrated a selected set of model parameters

[1] Barocas, J. A., White, L. F., Wang, J., Walley, A. Y., LaRochelle, M. R., Bernson, D., Land, T., Morgan, J. R., Samet, J. H., and Linas, B. P. (2018). Estimated Prevalence of Opioid Use Disorder in Massachusetts, 2011–2015: A Capture–Recapture Analysis. American Journal of Public Health.

Bayesian Calibration Approach

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- Possible correlations between calibration targets complicate the data likelihood formulation of the RESPOND model

- Therefore, we used Approximate Bayesian Computation (ABC) employing Sequential Monte Carlo (SMC) posterior sampling to search for parameters

- SMC modifies ABC rejection sampling by using weights to enhance the performance of the search algorithm by decreasing/increasing the sampling rate from low-/high-probability regions iteratively

Calibration Results

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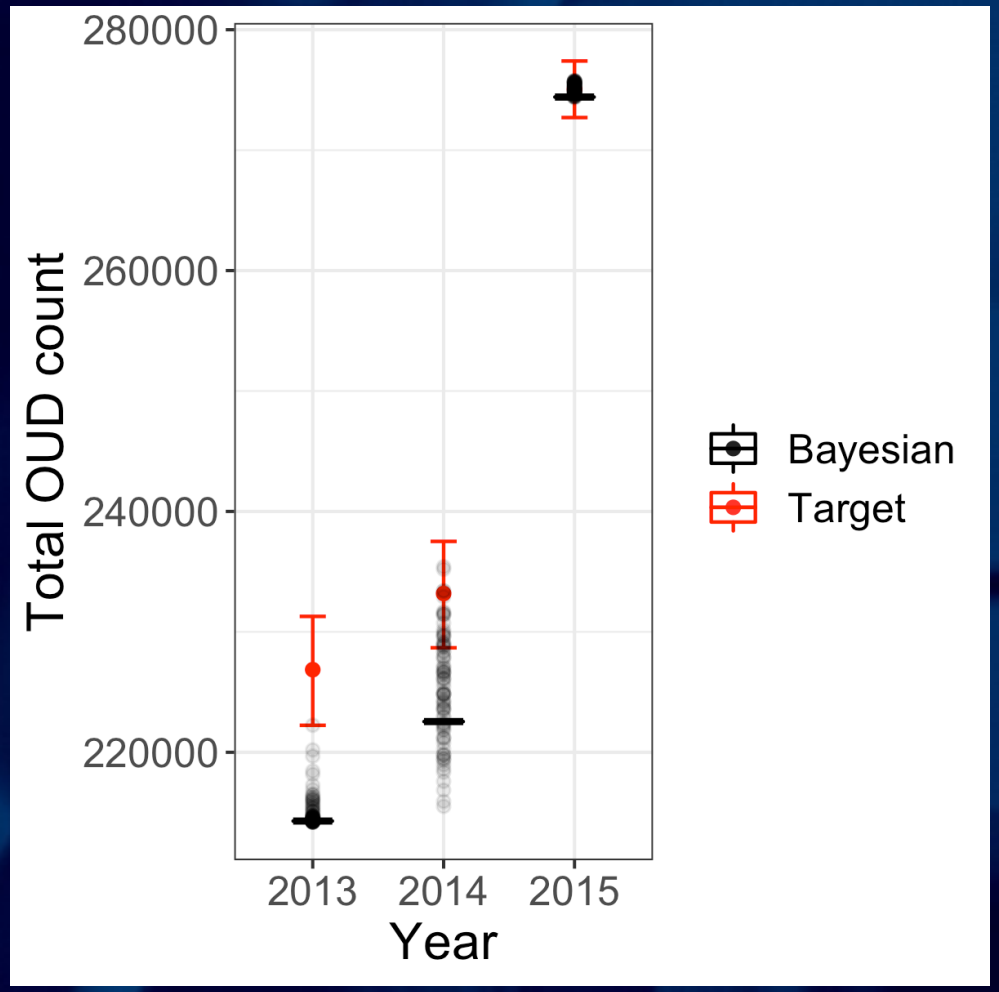
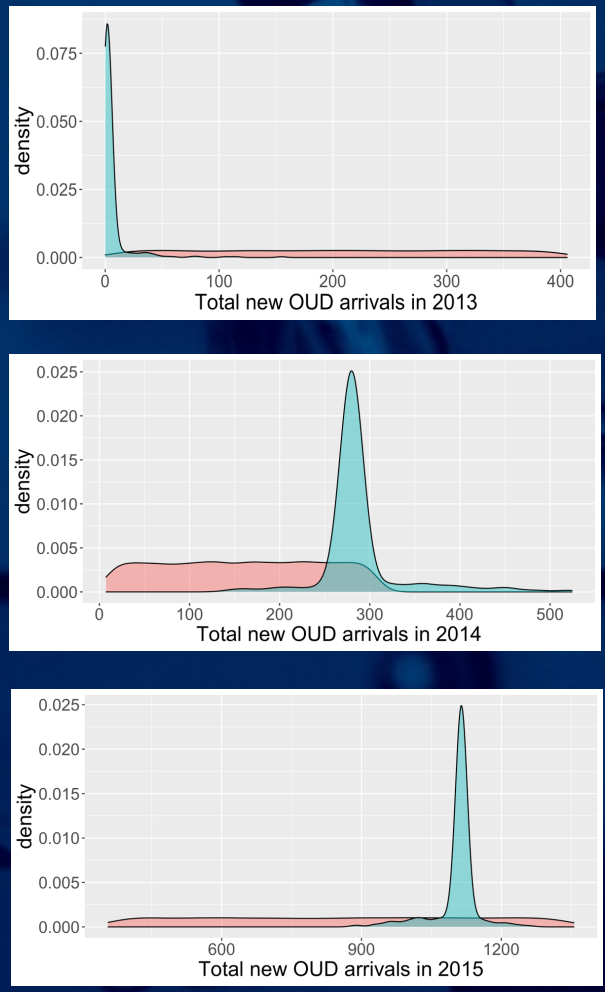
Target OUD Counts vs Calibrated Model Outcomes



Marginal Posteriors of New OUD Arrivals



Calibration Results

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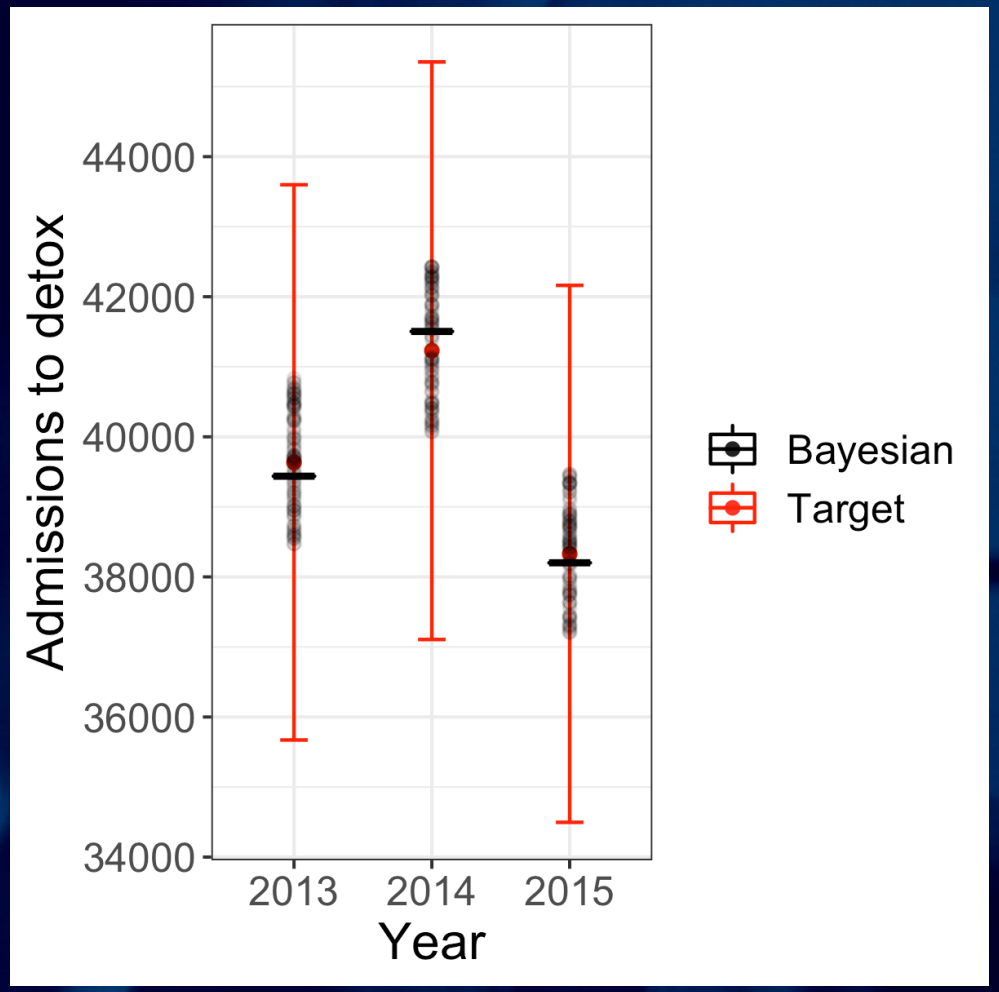
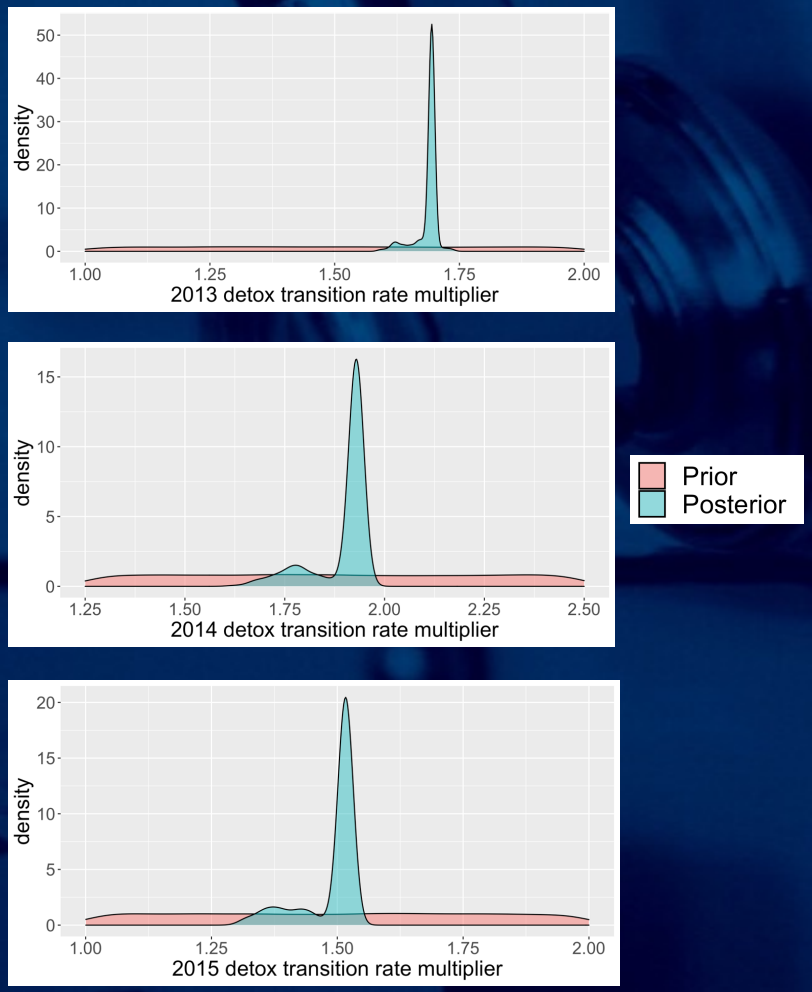
Target Detox Admissions vs Calibrated Model Outcomes



Marginal Posteriors of No-treatment to Detox Transition Rate Multipliers



Calibration Results

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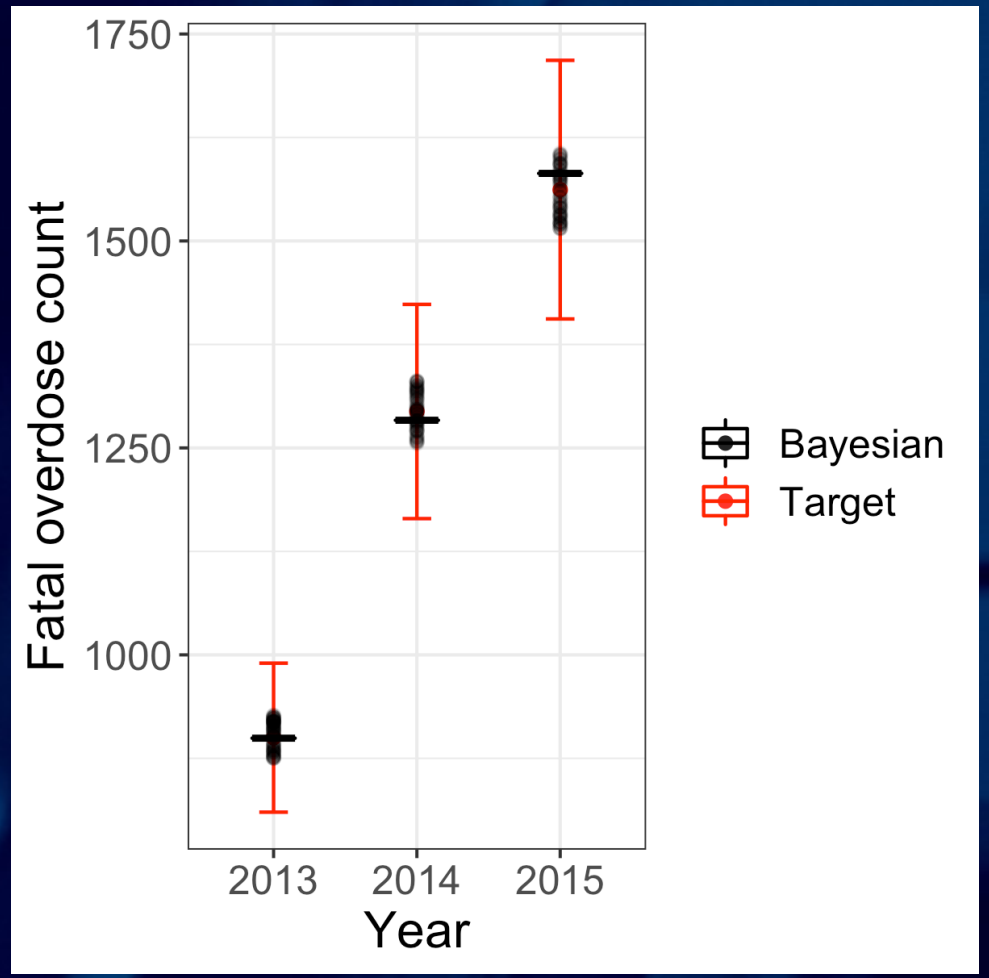
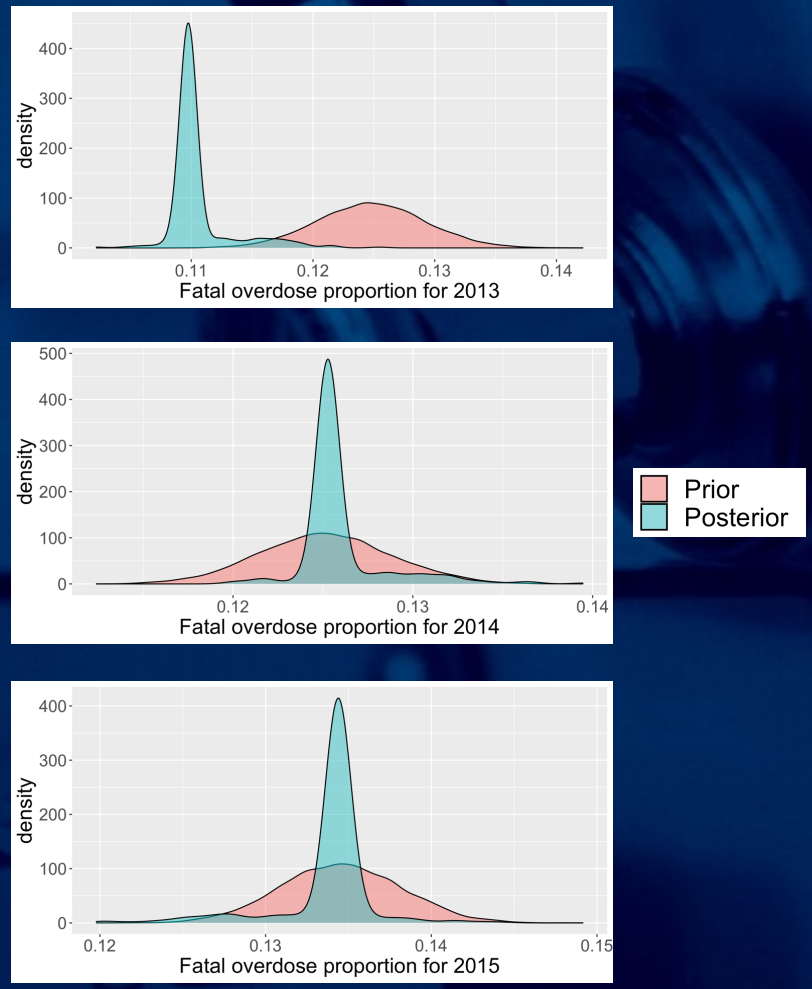
Target Fatal Overdose (FOD) Counts vs Calibrated Model Outcomes



Marginal Posteriors of of FOD Proportions



Calibration Results: Marginal Posteriors of Overdose Parameters

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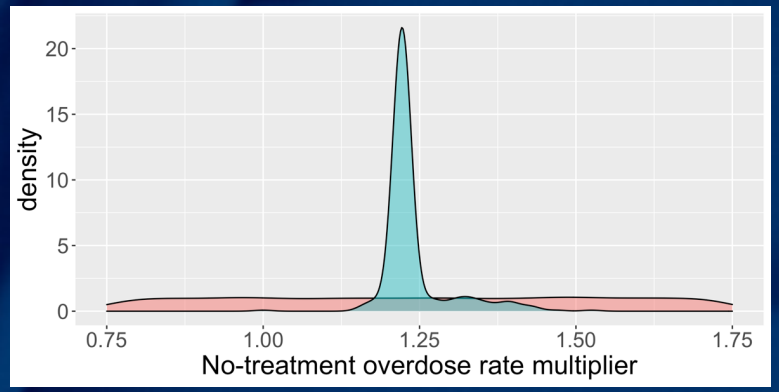

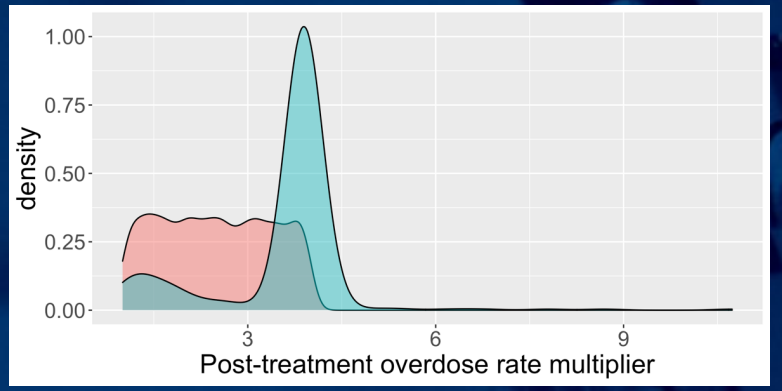

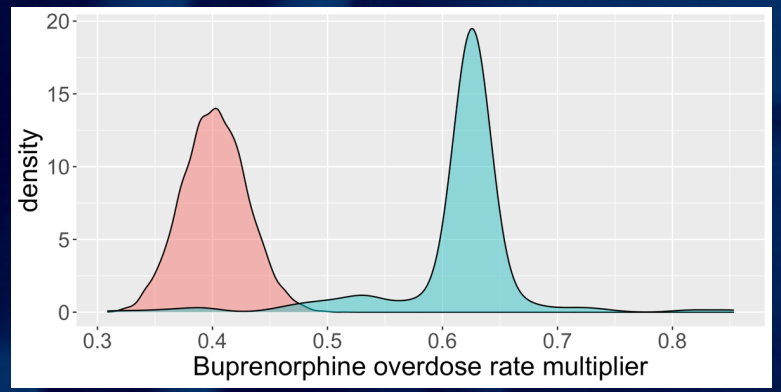

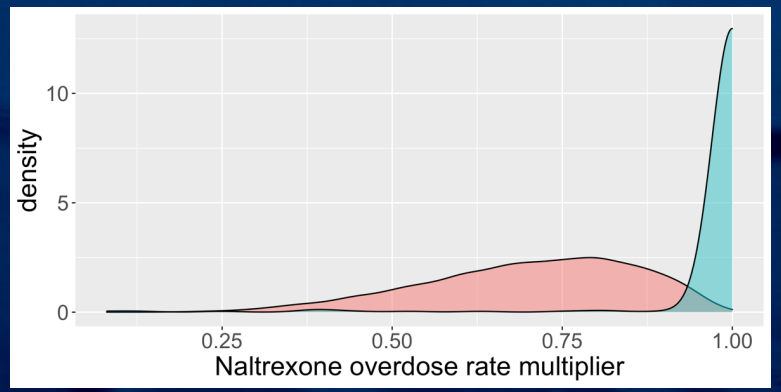

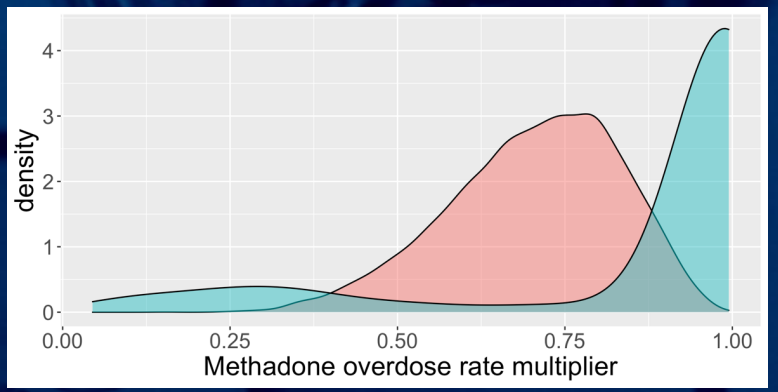

Conclusion and Future Work

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- We Calibrated the RESPOND model using a SMC ABC and the calibration helped us to reduce parameter uncertainty
- Bayesian calibration will be updated for new target data of years beyond 2015
- The calibrated model will be externally validated comparing model outputs to other data: all-cause mortality, active OUD counts, treatment admissions and overdoses (fatal + non-fatal)
- Calibrated RESPOND model will be employed to improve shared decision making of OUD


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Thank You!