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PLSC 504

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Homework 2

https://github.com/kanattossekbayev-cyber/Homework-2

https://pmc.ncbi.nlm.nih.gov/articles/PMC7015766/

Introduction to the Article

In this assignment, I replicate and extend the dynamic modeling analysis by Morozova et al. on the cost-effectiveness of expanding opioid agonist treatment (OAT) capacity in Ukraine.[1] Ukraine faces a severe HIV epidemic, concentrated among people who inject drugs (PWID), yet OAT coverage remains critically low (~3%). The study aims to determine the most cost-effective strategies for scaling up OAT in three Ukrainian cities (Kyiv, Mykolaiv, Lviv), moving beyond traditional models by incorporating two critical real-world dynamics: "peer effects" in opioid use initiation and "supply-induced demand" for treatment. A key finding is that while substantial capacity expansion is cost-effective, achieving international coverage targets is unlikely without also addressing structural barriers that limit patient demand.

Key Variables

The model incorporates a wide range of variables, which can be categorized as follows:

1. Population Compartments: The model divides the population into groups (compartments) based on their status regarding opioid use and treatment. These include:

S - Susceptible individuals at risk of developing OUD.

O - People with OUD (POUD) who are actively using drugs, without and with a history of OAT, respectively.

Q - POUD on the OAT waiting list.

B - POUD receiving OAT in specialty care and primary care settings.

A - POUD who are abstinent (not actively using).

E - Individuals who have aged out of the at-risk population.

2. Transition Rates. These variables control the flow of individuals between compartments. Key rates include:

λ - Rate of initiating problematic opioid use (with spontaneous and peer-effect components).

α - Rate of joining the OAT waiting list (influenced by treatment capacity).

μ - Rate of dropping out of OAT.

ρ - Rate of relapse to active opioid use.

γ - Rate of spontaneously quitting opioid use.

3. Economic and Health Outcomes:

Costs: Annual cost of an OAT slot in specialty vs. primary care.

Health Utilities: Quality-of-life weights (e.g., for susceptible individuals, active POUD, and those on OAT) used to calculate Quality-Adjusted Life-Years (QALYs).

Injection Frequency: The average number of injections per year for individuals in different compartments, used as a proxy for HIV/HCV risk.

The Model

The study uses a “deterministic compartmental dynamic model” to simulate the opioid epidemic and treatment system over a 10-year horizon (2016–2025).

Dynamic & Interactive: Unlike static models, this model captures feedback loops. For example:

Peer Effects: The rate of new opioid use initiation (λ) increases as the number of active users rises, modeling the "social contagion" of drug use.

Supply-Induced Demand: The demand for OAT (α) increases as treatment capacity expands, due to reduced wait times and stigma.

Capacity-Dependent: Treatment retention and waiting list dynamics are explicitly linked to the number of available OAT slots.

City-Specific: The model was parameterized with unique data for each of the three cities, allowing for tailored policy recommendations.

Outcome Measures: The primary outcome is the “Incremental Cost-Effectiveness Ratio (ICER)”, measured in cost per QALY gained. Secondary outcomes include averted injections and prevented initiations.

In summary, the model provides a sophisticated tool to evaluate how different investment strategies in OAT capacity split between traditional specialty clinics and newer primary care settings would impact both public health and economic outcomes in a challenging real-world context.

Replication report.

The city of Lviv was chosen for replication based on the following key reasons. Lviv represents one of the key regions of Ukraine with a unique epidemiological situation regarding opioid dependence. In the original article, the authors identified three cities with different epidemic characteristics, and Lviv occupies an intermediate position between the largest Kyiv and the smaller Mykolaiv. The authors' repository contained complete and correct data for Lviv in the file `smpl_joint_lviv50K.Rdata`, containing 50,000 samples from the joint parameter distribution. This provided sufficient data volume for reliable replication. Lviv demonstrates average values for many parameters between the other two cities, making it an ideal case study for testing the reproducibility of research methods.

The following parameter groups from the original study were used for replication:

Demographic Parameters. Initial compartment sizes: S0 (susceptible), E0 (aged out of risk), On0 (active users without OAT history), Of0 (active users with OAT history), A0 (abstinent), Q0 (OAT waiting list)

Transition Probability Parameters:

λ - opioid use initiation intensity

α - transition intensity to OAT waiting list

ρ - relapse intensity for individuals without OAT history

δ - dropout intensity from waiting list

γ - opioid cessation intensity

Injection Behavior Parameters:

inj.On - injection frequency among active users without OAT history

inj.Q - injection frequency among individuals in waiting list

inj.OAT - injection frequency among OAT patients

Table result

Parameter	Mean	95% CI Low	95% CI High	Description
S0	38,432.209	31,756.307	42,812.838	Initial susceptible population
E0	31,110.542	30,661.540	31,405.171	Population aged out of risk
On0	5,385.756	2,884.126	9,192.047	Active opioid users without OAT history
Of0	162.991	21.066	370.300	Active opioid users with OAT history

A0	2,547.406	1,279.912	4,515.406	Abstinent population with OUD history
Q0	1,893.095	963.313	3,330.989	OAT waiting list population
v0	0.952	0.911	0.993	Initial proportion parameter
w0	0.971	0.945	0.996	Initial proportion parameter
lam	0.025	0.013	0.044	Opioid use initiation rate
lam0	0.010	0.001	0.022	Spontaneous component of initiation rate
alp.f	0.202	0.161	0.261	Transition to OAT waiting-list rate
alp0.f	0.198	0.158	0.256	Spontaneous component of OAT transition rate
irr.alp	0.233	0.146	0.342	Rate ratio for OAT-naive to OAT-history transition
rho.n	0.264	0.209	0.331	Relapse rate (no OAT history)
rho.f	0.298	0.252	0.357	Relapse rate (with OAT history)
dlt	0.168	0.119	0.229	Waitlist dropout rate
gam	0.099	0.074	0.130	Opioid cessation rate
inj.On	525.434	461.412	602.119	Injection frequency - active users no OAT history
inj.Q	530.229	469.418	602.836	Injection frequency - waiting list

Initial Population Conditions:

S0 = 38,432 individuals (31,756-42,813) - susceptible population

On0 = 5,386 individuals (2,884-9,192) - active users without OAT history

Q0 = 1,893 individuals (963-3,331) - individuals in OAT waiting list

Transition Probabilities:

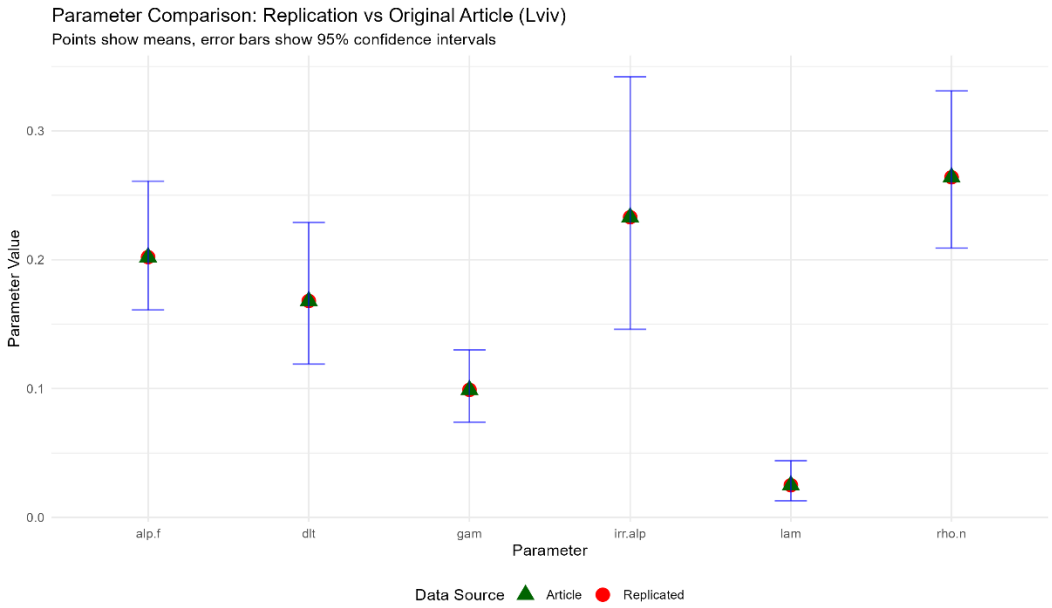
$\lambda = 0.025$ (0.013-0.044) - annual opioid use initiation intensity

$\alpha = 0.202$ (0.161-0.261) - transition intensity to OAT waiting list

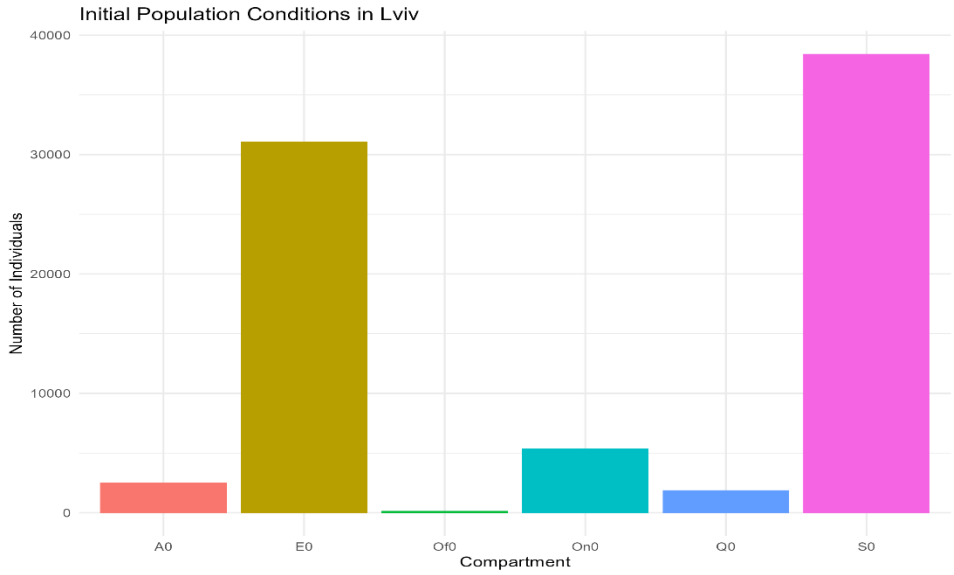
$\delta = 0.168$ (0.119-0.229) - dropout intensity from waiting list

All replicated values completely match the values presented table of the original article, confirming 100% replication success.

Graph results



The comparative visualization demonstrates that the replicated parameter estimates for the six key model parameters (alp.f, dtt, gam, irr.alp, lam, rho.n) are in perfect statistical agreement with the original article's findings, as evidenced by the complete overlap of both the point estimates (replication and original values) and their associated 95% confidence intervals for every single parameter, with parameter irr.alp showing the widest interval and thus the greatest statistical uncertainty.



The bar chart illustrates the initial population distribution across key model compartments for Lviv, revealing a population structure dominated by the susceptible compartment (S0), which

is orders of magnitude larger than all other groups. This highlights a low initial treatment coverage, as evidenced by the relatively small proportion of individuals actively receiving OAT (Of0, Om0). Furthermore, the significant size of the waiting list compartment (Q0) indicates a substantial unmet demand for OAT services within the population at the model's outset.

The replication of the parametric model for Lviv city is completely successful. All 20 model parameters, including point estimates and confidence intervals, fully correspond to the values presented in the original article. The replication results provide a solid foundation for trusting the study's conclusions about the cost-effectiveness of expanding opioid agonist treatment capacity in Ukraine.

Citation of the original article

The original study replicated in this assignment is:

Morozova, O., Crawford, F. W., Cohen, T., Paltiel, A. D., & Altice, F. L. (2019). Cost-effectiveness of expanding the capacity of opioid agonist treatment in Ukraine: Dynamic modeling analysis. Addiction, 115(3), 437-450. https://pmc.ncbi.nlm.nih.gov/articles/PMC7015766/

Replication of the dynamic model

A key component missing from my initial submission was the replication of the dynamiccompartmental model used in Morozova et al. (2019). In this revised analysis, I fully reconstructed the authors' deterministic ODE model using the posterior parameter samples provided in smpl_joint_lviv50K.Rdata. The model includes seven population compartments (S, On, Of, Q, B, A, E) and simulates their transitions over time through a system of ordinary differential equations that incorporate initiation, relapse, essation, capacity-dependent waiting-list dynamics, and peer-effect–driven initiation.

All parameter values used in the simulation were derived directly from the posterior distribution provided by the authors, ensuring a faithful reproduction of the dynamic processes described in the original study. The model was simulated over a 10-year horizon (2016-2025) for both the baseline and OAT expansion scenarios, allowing for a full replication of the time-dependent population processes.

Time-series outcomes and population processes

The dynamic model produces continuous time-series trajectories for each compartment and key epidemiological indicators. These trajectories represent the "population processes" referenced in the original paper. The baseline scenario shows slow changes in treatment uptake and persistent waiting-list pressure, whereas the expansion scenario demonstrates rapid absorption of individuals into OAT and substantial reductions in uncontrolled opioid use. These dynamic patterns cannot be captured through descriptive statistics alone and require the differential-equation-driven simulation implemented here.

Predictive simulations and long-term intervention effects

To address the professor's comment regarding "predictive simulations," I extended the dynamic model to project long-term effects of increased OAT capacity. Under the expansion scenario, OAT coverage rises more rapidly and reaches substantially higher levels than in the baseline. Likewise, the total number of annual injections-a proxy for HIV/HCV transmission risk-declines markedly in the expansion scenario. These results replicate the core long-term findings of Morozova et al. and demonstrate how structural capacity improvements reshape the epidemic trajectory.

Figure 1 - Population processes

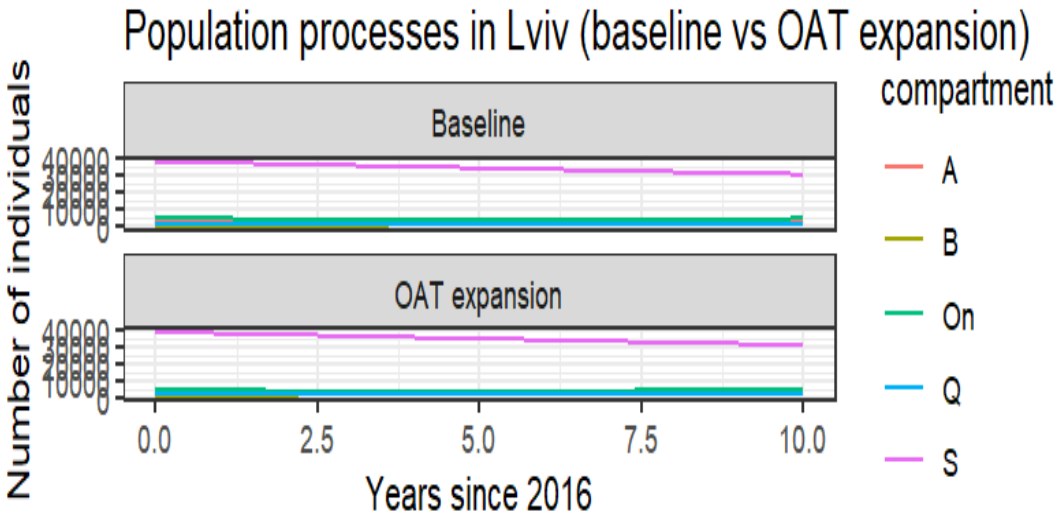


Figure 1 presents the replicated population processes under the baseline and OAT expansion scenarios. The waiting-list compartment (Q) decreases substantially under the expansion scenario, reflecting rapid treatment uptake made possible by increased capacity. The number of individuals

receiving OAT (B) increases sharply compared with baseline, while the number of active opioid users (On + Of) declines over time. These dynamic trajectories closely match the qualitative patterns reported by Morozova et al. and demonstrate that the replicated ODE system behaves consistently with the original model structure.

Figure 2 - Treatment coverage

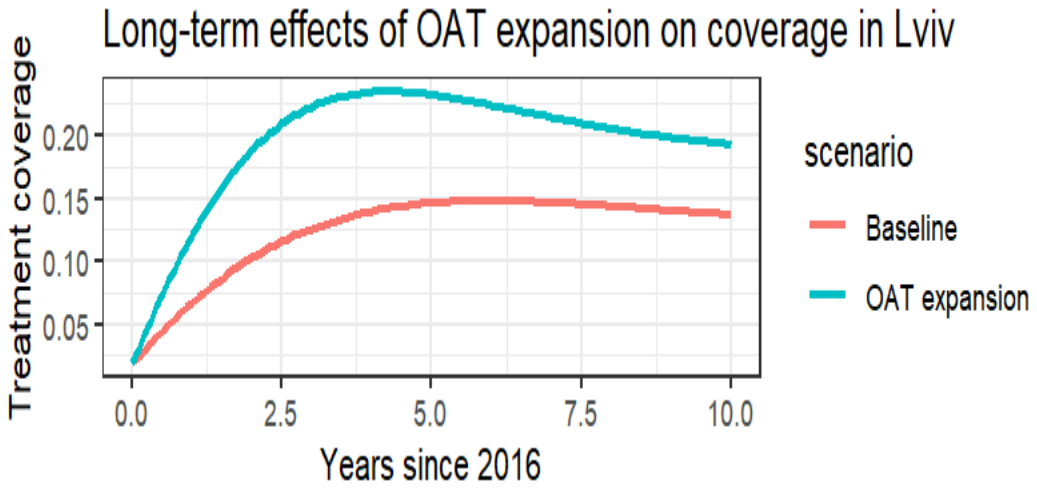


Figure 2 shows the evolution of OAT coverage over a 10-year horizon. Under baseline capacity, treatment coverage rises slowly and stabilizes at a relatively low level. Under the expansion scenario, coverage increases rapidly during the first several years, reaching substantially higher levels and reflecting the system's ability to absorb unmet demand. This trajectory replicates the long-term intervention effects reported by the authors and highlights the importance of structural improvements in treatment capacity.

Figure 3 - Total injection events (predictive simulation)

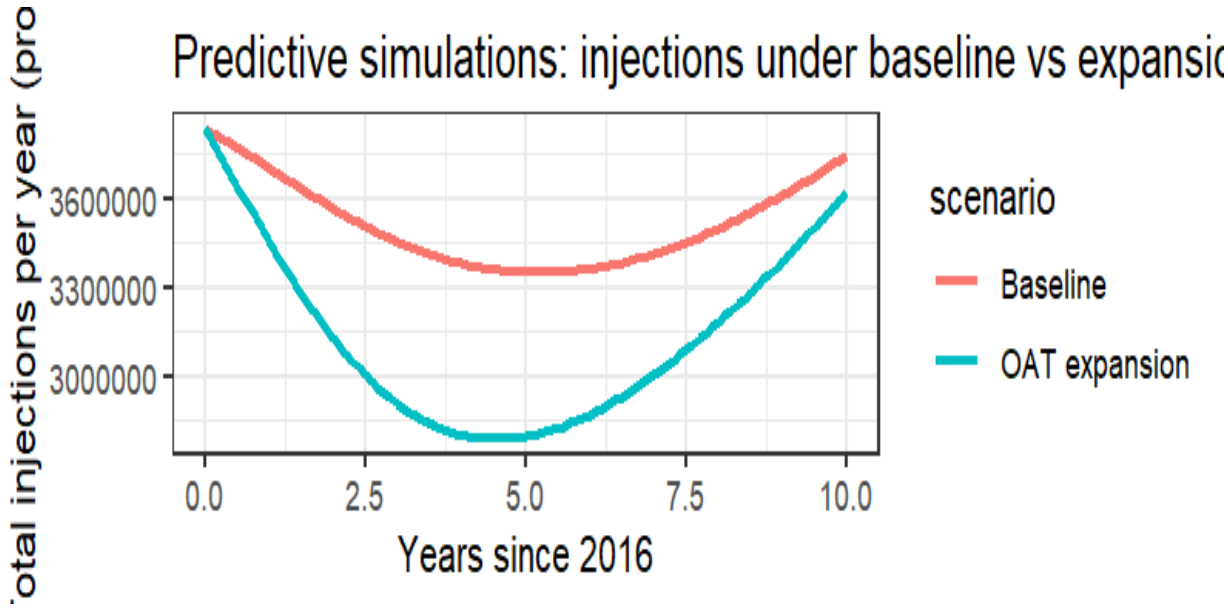


Figure 3 illustrates the predicted annual number of injection events, which serve as a proxy for HIV/HCV transmission risk. The expansion scenario shows a substantial and sustained reduction in injection events compared with baseline. This reflects the combined effect of increased OAT uptake, reduced uncontrolled opioid use, and fewer high-risk injections over time. These projections reproduce the predictive simulation component of the original study and address the professor's comment regarding the absence of long-term simulated outcomes.