HOW CAN AGENT-BASED MODELING SUPPORT PUBLIC HEALTH GOALS?

APPLICATIONS TO DEVELOPING INTERVENTIONS FOR REDUCING HEALTH INEQUITIES



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OUTLINE

- Agent-based modeling
- Team-based research for complex/interconnected problems in public health
- Applications
 - Hepatitis C
 - İmportance of retreatment
 - Computational discovery of combination interventions
 - Medication for Opioid Use Disorder (+ Hepatitis C)
- Additional Applications Overview
 - HIV in YBMSM + Justice Contexts (BARS)
 - Health Information Intervention (CommunityRx ABM)
 - COVID-19 Spread and Effectiveness of Interventions (CityCOVID)
- Ongoing work on Health Inequities
 - Justice Community Circulation Model (MAARC)
 - COVID-19 Social Determinants of Health (C3 DTI)
 - HIV Disparities in Racial, Ethnic and Sexual Minorities (ChiSTIG)



AGENT-BASED MODELS (ABMS)

Disaggregated description of complex systems:

- Method of computing the potential system-level consequences of the behaviors of sets of individuals
- Effects of interventions can be run with different assumptions







AGENT-BASED MODELS (ABMS)

Agents

- Agents have individual attributes
- Agents have individual behaviors
- Agents are autonomous (no central authority) so,
- Agents are decentralized
- Interactions
 - Agents have interactions
 - Can act on local Information
 - Not everyone interacts with everyone else, all of the time.
 - Agents live in a dynamic environment, which can define the possible interactions
 - Geographic, network-based, or other, abstract environments







AGENT-BASED MODELS (ABMS)

Emergence

- Even simple rules can lead to complexity
 - But modern ABMs have many, datadriven, complex rules
- Self-organization of patterns and structure
- Phenomena emerge in agent-based models that you **did not explicitly program** into the models







UTILITY OF AGENT-BASED MODELING IN PUBLIC HEALTH APPLICATIONS

- Analytical platform for integrating disparate data sources governing individuals, networks, geography, resources
- Can incorporate hypothesized causal mechanisms (theories) for complex processes at multiple and interacting scales (micro, meso, macro), which pose challenges to traditional epidemiologic and statistical methods
- Computational approach enables sensitivity analyses that can guide (expensive/difficult) data collection
- With improved methods for large-scale computation, ABMs can be used for uncertainty analyses of input parameters and outcomes of interest
- Evaluate interventions and combinations/sequences of interventions that would be difficult to implement (cost, effort, ethics, logistical considerations)
- Modeling can identify priority subpopulations for intervention focus



TEAM-BASED SCIENCE + DECISION SUPPORT

- Agent-based modeling is inherently interdisciplinary and team-based
- Modeling projects combine expertise across subject matter areas (e.g., for this lecture):
 - Hepatitis C
 - Opioid use disorder
 - HIV
 - COVID-19
 - Clinical
 - Public health
 - Epidemiology
- Supports increasingly complex/interconnected systems/problems faced in public health
- Exploits advances in simulation, machine learning and high-performance computing for application to public health



Simulation Technologies

repast

The Repast Suite

The Repast Suite is a family of advanced, free, and open source agent-based modeling and simulation platforms that have been under continuous development for over 15 years:

Repast Simphony 2.8.0, released on 23 October 2020, is a richly interactive and easy to learn Java-based modeling system that is designed for use on workstations and small computing clusters.

Repast for High Performance Computing 2.3.0, released on *26 November 2018*, is a lean and expert-focused C++-based modeling system that is designed for use on large computing clusters and supercomputers.

Learn Repast using the Repast Tutorials.

Watch the Repast team discuss the present and future of ABM as part of the CoMSES 2018 Virtual Conference:





Experiences in Developing a Distributed Agent-based Modeling Toolkit with Python

Nicholson T. Collier Decision and Infrastructure Sciences Argonne National Laboratory Lemont, IL USA ncollier@anl.gov Jonathan Ozik Decision and Infrastructure Sciences Argonne National Laboratory Lemont, IL USA jozik@anl.gov Eric R. Tatara Decision and Infrastructure Sciences Argonne National Laboratory Lemont, IL USA tatara@anl.gov

Collier, Nicholson, Jonathan Ozik, Eric Tatara. 2020. "Experiences in Developing a Distributed Agent-based Modeling Toolkit with Python." 9th Workshop on Python for High-Performance and Scientific Computing @ Supercomputing 2020.



Machine Learning for Simulations



* Ozik, Jonathan, Nicholson T. Collier, Justin M. Wozniak, Charles M. Macal, and Gary An. 2018. "Extreme-Scale Dynamic Exploration of a Distributed Agent-Based Model With the EMEWS Framework." IEEE Transactions on Computational Social Systems 5 (3): 884–95. https://doi.org/10.1109/TCSS.2018.2859189.

** Tatara, Eric, Nicholson T. Collier, Jonathan Ozik, Alexander Gutfraind, Scott J. Cotler, Harel Dahari, Marian Major, and Basmattee Boodram. 2019. "Multi-Objective Model Exploration of Hepatitis C Elimination in an Agent-Based Model of People Who Inject Drugs." In 2019 Winter Simulation Conference (WSC), 1008–19. https://doi.org/10.1109/WSC40007.2019.9004747.

*** Ozik, Jonathan, Nicholson T. Collier, Justin M. Wozniak, Charles M. Macal, and Mickaël Binois. "A Population Data-driven Workflow for Covid-19 Modeling and Learning." Finalists, Gordon Bell Special Prize for HPC-Based COVID-19 Research, Supercomputing 2020.



High-performance Computing





awarded in 2020 and 2021 to recognize outstanding research achievement towards the understanding of the COVID-19 pandemic through the use of high performance computing (HPC). The purpose of the award is to recognize the innovative parallel computing contributions towards the solution of the global crisis. See the <u>award website</u> for details, including deadlines.



Ozik, Jonathan, Nicholson T. Collier, Justin M. Wozniak, Charles M. Macal, and Mickaël Binois. "A Population Data-driven Workflow for Covid-19 Modeling and Learning." Finalists, Gordon Bell Special Prize for HPC-Based COVID-19 Research, Supercomputing 2020.



HEPATITIS C (HepCEP)



HepCEP Interdisciplinary Team

Harel Dahari



Jonathan Ozik



Basmattee Boodram



Marian Major



"Computational discovery of effective hepatitis C intervention strategies" NIH award R01GM121600 (NIGMS)



HEPATITIS C ELIMINATION IN PWID (HepCEP) ABM APPROACH

- ABM to simulate the PWID population in metropolitan Chicago including the social interactions that result in HCV infection
- •Use ABM to account for the complex interplay of demographic factors, risk behaviors, social networks, and geographic location for HCV transmission
- Goal: To identify and optimize detailed implementations of direct acting antiviral (DAA) therapy scale-up and treatment strategies needed for PWID
- HepCEP was developed with Repast HPC



Lines represent co-injection links and color indicates HCV infection state: blue, uninfected PWID or PWID successfully treated with DAAs; red, chronic HCV PWID; green, PWID who spontaneously cleared acute HCV infection







THE UNIVERSITY OF



HepCEP AGENTS AND NETWORKS

Agents:

- -32,000 PWID (sampled from 100,000 CNEP+ database, new PWID added as agents leave model)
- –Age, age started injecting drugs, gender, race, zip code, syringe source (harm reduction), HCV infection status, drug sharing network degree, and parameters for daily injection rates and syringe sharing

PWID networks:

- -Network formation is determined by the probability of two persons encountering each other in their neighborhood of residence, in outdoor drug purchasing market areas in Chicago, or random interaction with any other individual
- –Empirical data provides numbers of in-network PWID partners who provide syringes and out-network PWID partners who receive syringes from them (directionality determines HCV transmission)
- -Network connections have an average lifespan after which they are destroyed, and new connections are probabilistically formed



DATA SOURCES FOR PWID POPULATION



Gutfraind, Alexander, Basmattee Boodram, Nikhil Prachand, Atesmachew Hailegiorgis, Harel Dahari, and Marian E. Major. 2015. "Agent-Based Model Forecasts Aging of the Population of People Who Inject Drugs in Metropolitan Chicago and Changing Prevalence of Hepatitis C Infections." PLOS ONE 10 (9): e0137993. https://doi.org/10.1371/journal.pone.0137993.



- Project the frequency of retreatment and DAA cost needed to achieve WHO goals (90% reduction of chronic infection incidence by 2030)*
 - –While DAA treatment is highly efficacious, some payors still restrict access to DAAs** and prohibit DAA re-treatment of those who become re-infected once cured by DAA therapy.
- Treatment success, sustained virologic response (SVR), set at 90% (i.e., treatment failure 10%)
- Possible treatment adherence rates (i.e., DAA cure rates) of 60%-90% with DAA treatment enrollment rates of 2.5%-10%
- Retreatments per PWID of 0 (retreatment prohibited), 1, 2, 3, or no retreatment restriction were simulated.
- DAA cost is assumed \$25,000 (USD) per treatment.

^{*} Tatara, Eric, Alexander Gutfraind, Nicholson T. Collier, Scott J. Cotler, Marian Major, Basmattee Boodram, Jonathan Ozik, and Harel Dahari. 2019. "Agent-Based Modeling of Persons Who Inject Drugs in Metropolitan Chicago Suggests That Re-Treatment with Antivirals of Persons Who Are Re-Infected with Hep C Is Critical to Achieve the WHO Incidence Reduction Objective by 2030." BioRxiv, May, 653196. https://doi.org/10.1101/653196.

^{**} Ooka, K., J.J. Connolly, and J.K. Lim, Medicaid Reimbursement for Oral Direct Antiviral Agents for the Treatment of Chronic Hepatitis C. Am J Gastroenterol, 2017. 112(6): p. 828-832.



Activity timeline for a single agent in the HepCEP model who was allowed only 4 courses of DAA therapy. The colored bars indicate activities in which the agent is participating during the dates along the bottom of the timeline. The activity pattern shown in the figure are typical in some of HCV-positive agents that are selected for DAA treatment, cured, and re-infected multiple times. In this example, the agent was allowed to re-enroll in DAA treatment 3 times (total of 4 treatment courses), had a single occurrence of failed DAA treatment in year 2022 (orange bar) and eventually was re-infected ~1 year after SVR and remained chronically infected until 2030 (not shown).





Projected mean incidence of new HCV chronic infections among PWID relative to the predicted 2020 incidence during DAA rate (enrollment percent is DAA rate e.g., a therapy rate of 10% per year), with retreatment prohibition and a treatment adherence of 90%. The ribbons represent the 95% confidence interval around the mean of 20 simulation runs. The horizontal red dashed line represents the WHO 2030 goal of 90% reduction in the incidence rate.





Projected HCV mean incidence of new chronic infections among PWID relative to the predicted 2020 incidence during DAA rate (enrollment percent is DAA rate e.g., a therapy rate of 10% per year), without retreatment prohibition and treatment adherence of 60%-90%. The ribbons represent the 95% confidence interval around the mean of 20 simulation runs. The horizontal red dashed line represents the WHO 2030 goal of 90% reduction in the incidence rate.



Times Retreated	Total #	%	Cost (1K \$)
0	7,368	75.3	184,201
1	1,805	18.5	90,273
2	461	4.7	34,586
3	108	1.1	10,825
4	28	0.3	3,450
5	5	0.1	803
6	1	< 0.1	256
7	1	< 0.1	229
8	1	< 0.1	225
Totals:	9,779	100.0	324,847

DAA treatment rate of 7.5% per year when unlimited retreatment is allowed, and with treatment adherence of 90% can achieve WHO's 90% incidence reduction if retreatment is allowed, with an estimated cost of \$325 million

Compare with ODE approach predicting \$430M cost*

* Echevarria, Desarae, Alexander Gutfraind, Basmattee Boodram, Jennifer Layden, Jonathan Ozik, Kimberly Page, Scott J. Cotler, Marian Major, and Harel Dahari. 2019. "Modeling Indicates Efficient Vaccine-Based Interventions for the Elimination of Hepatitis C Virus among Persons Who Inject Drugs in Metropolitan Chicago." Vaccine 37 (19): 2608–16. https://doi.org/10.1016/j.vaccine.2019.02.081.



HepCEP OPTIMAL COMBINATION INTERVENTIONS

Direct acting antiviral treatment enrollment methods:

- -Random Recruitment: Select HCV-infected individuals from the PWID population. Individuals are selected until the daily enrollment target for the recruitment is met or no eligible PWID remain for recruitment that day
- -Harm Reduction Program (HRP): Similar to random recruitment, but individuals must be registered in a harm reduction program, such as syringe service program (SSP) that provides sterile syringe injection equipment along with risk reduction counseling to enrollees. PWID enrolled in these programs are considered a lower risk for HCV transmission than those with similar injection behaviors who are not enrolled.
- -Full Network: The network recruitment methods begin by selecting a PWID via the random recruitment method, then subsequently enrolling all other PWID who share syringes with the selected individual (personal injection network).
- -In-Partner Network: Similar to the full network recruitment, but this enrollment method only recruits a single social network "in" edge, i.e., a PWID who provides syringes to the originally selected individual.
- -**Out-Partner Network**: Similar to the full network recruitment, but this enrollment method only recruits a single social network "out" edge, i.e., a PWID who receives syringes from the originally selected individual.



HepCEP OPTIMAL COMBINATION INTERVENTIONS

- Multi-objective optimization of combination interventions (Tatara et al. 2019)
- Varying enrollment rates and the combined types of recruitment strategies while optimizing incidence and treatment count (i.e., cost)
- Produced Pareto front for non-dominated strategies using NSGA2 multi-objective optimization algorithm
- Combinations of "in-partner" and "full network" yield the best results that meet the 2030 WHO goal

Tatara, Eric, Alexander Gutfraind, Nicholson T. Collier, Scott J. Cotler, Marian Major, Basmattee Boodram, Jonathan Ozik, Harel Dahari. 2019. "Multi-objective model exploration of hepatis c elimination in an agent-based model of people who inject drugs," to appear in Winter Simulation Conference (WSC) 2019 Proceedings. National Harbor, Maryland, USA, 2019.



OPIOID USE DISORDER



Medication for Opioid Use Disorder (MOUD) and HepCEP

Team:

- Marynia Kolak (1)
- Qinyun Lin (1)
- Harel Dahari (2)
- Basmattee Boodram (3)
- John Schneider (4)
- Eric Tatara (5)
- Nicholson Collier (5)



5) Decision and Infrastructure Sciences Division, Argonne National Laboratory and Consortium for Advanced Science and Engineering, University of Chicago

- Funding:
 - NIH U2CDA050098: Methodology and Advanced Analytics Resource Center (MAARC)
 - NIH R01GM121600: Computational discovery of effective hepatitis C intervention strategies
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1) Center for Spatial Data Science, Division of Social Sciences, University of Chicago



2) Program for Experimental and Theoretical Modeling, Division of Hepatology, Department of Medicine, Stritch School of Medicine, Loyola University Chicago



4) Chicago Center for HIV Elimination, Department of Infectious Disease, UChicago Medicine



 Division of Community Health Sciences, School of Public Health, University of Illinois at Chicago

MOUD HepCEP Spatial Health Inequity

- Evaluated three MOUD interventions (Methadone [M], Naltrexone [N], Buprenorphine [B]) using different scenarios with varying levels of spatial health inequity, using the HepCEP model
- To approximate potential access to MOUD resources, we calculated distance to the nearest MOUD provider using 2019 locations from the Substance Abuse and Mental Health Services Administration (SAMSHA), with methadone sites cross-validated with locations on the current IDPH website.
- HepCEP agents periodically make decisions about continuing MOUD treatment
 - -Cadence of decision making is based on the typical requirements for clinic visits for each MOUD intervention (M: 7 days, B: 7 [or 30] days, N: 30 days)
 - -The decision to continue treatment is based on an agent's access to services, where better access increases average agent treatment duration
 - -Treatment results in fewer injection drug use events, which leads to a reduction in disease transmission
- Differentiated the access threshold in urban versus suburban settings, and by MOUD type



MOUD HepCEP Counterfactual Scenarios

- To understand how spatial distribution of MOUD locations affect health outcomes, we generate three counterfactual scenarios (CS)
 - –MOUD locations are reshuffled compared to the actual locations of resource (Real scenario)
 - -In all scenarios, the total amount of MOUD resources is limited
 - all three CS only reshuffle locations so that effects of spatial distribution of MOUD locations can be disentangled from the effect of the total amount of resources
- Spatially Random (CS1): MOUDs are randomly distributed
- Need-Based 1 (CS2): assign MOUDs proportional to the adult population (age 18 - 39) at risk of Hepatitis C for each zip code
- Need-Based 2 (CS3): assign MOUDs proportional to the PWID population for each zip code: the more PWID, the more MOUD for that zip code area



MOUD HepCEP Spatial Distribution

- Spatial distributions of MOUD resources under the different CS are substantially different from one another and from the Real scenario
- The figure shows how the number of B resources changes for each zip code area, when comparing the Real scenario with each CS
- More MOUD resources get assigned to South and West Chicago areas in the two Need-Based scenarios (CS 2 & 3).

Change in Number of MOUD resources – Buprenorphine from Real to each Counterfactual Scenario





MOUD HepCEP Access to Resources

- Access to MOUD resources changes greatly under different counterfactual scenarios
- The figure shows whether each zip code area has good access to the nearest Methadone MOUD resource – West and South Chicago areas have better access in the two Need-Based scenarios (CS 2 & 3) and worse access in the Spatially Random (CS 1) scenario when compared to the Real scenario



MOUD HepCEP Access to Resources

- The Table summarizes the number of zip code areas having good access versus not under each scenario
- Different spatial distributions optimize access to different types of medications

Good Access : Not	Real	Spatially Random	Need based 1	Need based 2
Methadone	237 : 61	200 : 98	241 : 47	201 : 97
Buprenorphine	296 : 2	298 : 0	294 : 4	278 : 20
Naltrexone	293 : 5	285 : 13	285 : 13	262 : 36

Total number of zip codes that had "good" access vs. not, for each scenario. **Bolded entries** indicate optimal scenario.



MOUD HepCEP Health Outcomes + Future

- Downstream health outcomes vary substantially in different experimental settings
- For example, with MOUD locations equally distributed through the area, the average treatment duration for Methadone would increase in 60% of zip code areas, and the average new HCV chronic infection rate would decrease in 33% of areas by 2030
- More investigation into new HCV chronic infections as an outcome are underway
- As health departments co-locate MOUD services with other existing clinical infrastructure, this work can inform optimal selection of locations and sites for integrated MOUD services based upon the spatial need and distribution of opioid users.





ADDITIONAL PUBLIC HEALTH APPLICATIONS AND ONGOING WORK



BARS HIV MODEL

- Black MSM are disproportionately impacted by HIV and criminal justice involvement, cycling between communities and criminal justice settings
- CJI can impact:
 - · Social and sexual network stability
 - Employment and housing opportunities
 - Access to medical care
- Disruption in the HIV prevention and care continuum via changes in post-incarceration ART and PrEP engagement
- Impact of incarceration and release on partners of those with CJI
- ABM can uncover emergent dynamics resulting from the intersection of CJI-related changes in network composition and HIV prevention/care continuum engagement

NIH/National Institute On Drug Abuse (R01DA039934): PIs John Schneider (UC), and Nina Harawa (UCLA), Kayo Fujimoto (UT Houston)





CommunityRx ABM

Understand the multi-level impact of a health information technology-based intervention on a community



NIH/National Institute of Aging (R01 AG 047869) : PI Stacy Lindau (UC)



CityCOVID: COVID-19 SPREAD AND EFFECTIVENESS OF INTERVENTIONS

CityCOVID model for Chicago, 2.7 M people (agents) move hourly between 1.2 M locations 2020-06-01

RELAXED



Ongoing ABM Work on Health Inequities

- NIH U2CDA050098: Methodology and Advanced Analytics Resource Center (MAARC): Justice Community Circulation Model: PIs John Schneider, Harold Pollack
- C3.ai Digital Transformation Institute: Modeling the Impact of Social Determinants of Health on COVID-19 Transmission and Mortality to Understand Health Inequities: PI Anna Hotton
- NIH R01MD014703: Simulation Modeling to Understand and Address HIV Disparities in Racial, Ethnic, and Sexual Minority Populations: PI Michelle Birkett (Northwestern University)



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