Beyond the Pathogen: Disease-Agnostic, Scalable Models for Public Health Preparedness and Decision-Making

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Why this Matters **Now**

Global Development Influencing Pathogen Amplification Spread and Reach

Where geography previously isolated most populations from exposure to many pathogens, an increasingly globalized world has enabled a rapid expansion in the reach and spread of infectious diseases.

Examples of Unexpected Occurrence of Pathogens in Naïve Areas That **Required a Public Health Response**

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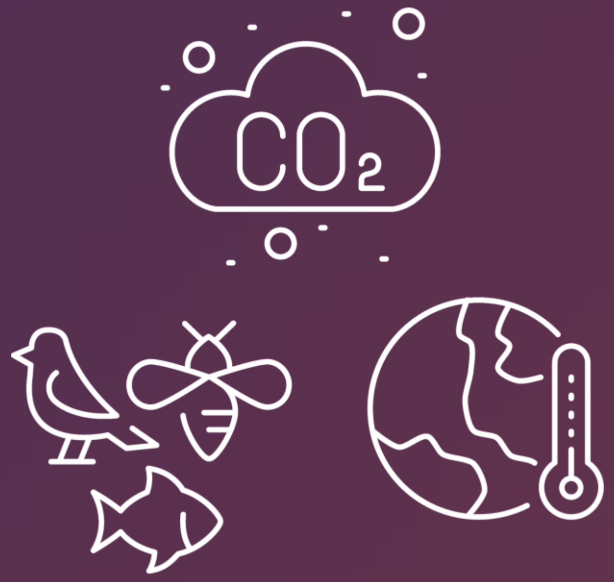
OUTBREAK	PREVIOUS GEOGRAPHIC DISTRIBUTION	NEW OCCURRENCE	PUBLIC HEALTH IMPACT
Nipah virus, 1994	Fruit bats in Malaysia	Malaysia and Singapore	105 human deaths, culling of 1.1 million pigs
Monkey pox virus, 2022	Central Africa	9 new countries, outside of Africa, experienced cases, including the United States, Spain, Brazil, and United Kingdom	28,379 cases in United States
Borrelia burgdorferi (Lyme disease)	Largely concentrated in select northeastern states (Connecticut, Delaware, Maryland, Massachusetts) and parts of Minnesota and Wisconsin	Now found in nearly every northeastern state, Wisconsin, and most of Minnesota	Number of reported cases has tripled in the United States in the past 20 years
Ebola virus, 2015	Central Africa	Western Africa	Estimated 11,017 deaths

Factors Influencing Distribution Patterns of Pathogens

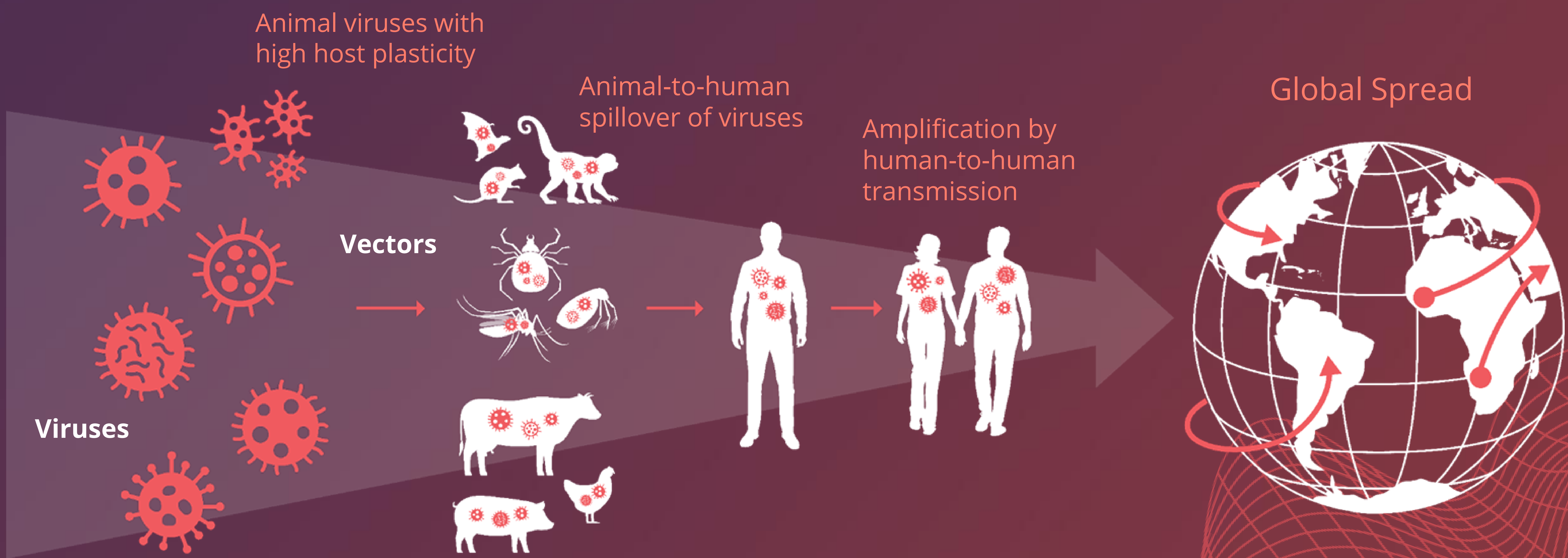


Worsening patterns of weather challenges can shift environments so that new areas become suitable for disease-carrying animals or insects.

Land use changes (like deforestation or farming) can push these animals closer to humans, increasing the chance of disease transmission.

Virus evolution (mutations and genetic changes) can make viruses infect new species, spread more easily, or evade control measures like biosecurity and testing.

Route of Entry and Amplification for Pathogen Emergence



Today's Webinar Objectives

- Identify the need for flexible, multi-scale modelling frameworks and the limitations of current modeling approaches
- Demonstrate RTI’s "on the shelf" modelling tools, which simulate disease spread and decision-making support
- Explain how synthetic populations, cost-effectiveness modeling, and geospatial data augments disease models
- Showcase real-world applications across pathogens with different transmission routes
- Demonstrate RTI's flexible, multiscale, integrated disease modelling approaches which can be used for public health preparedness and decision-making

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What can models give us?

- Forecast trends and identify patterns of disease transmission to guide public health action.
- Improve understanding of populations at highest risk.
- Identify “hot spots” for intervention.
- Estimate disease burden to assist with planning for treatment and health care resources.
- Provide cost analyses to compare differing public health responses.
- Test hypothetical “what if” scenarios quickly and efficiently.
- Identify transmission dynamics that may not be observable through traditional epidemiological methods.

Current Gaps and Challenges

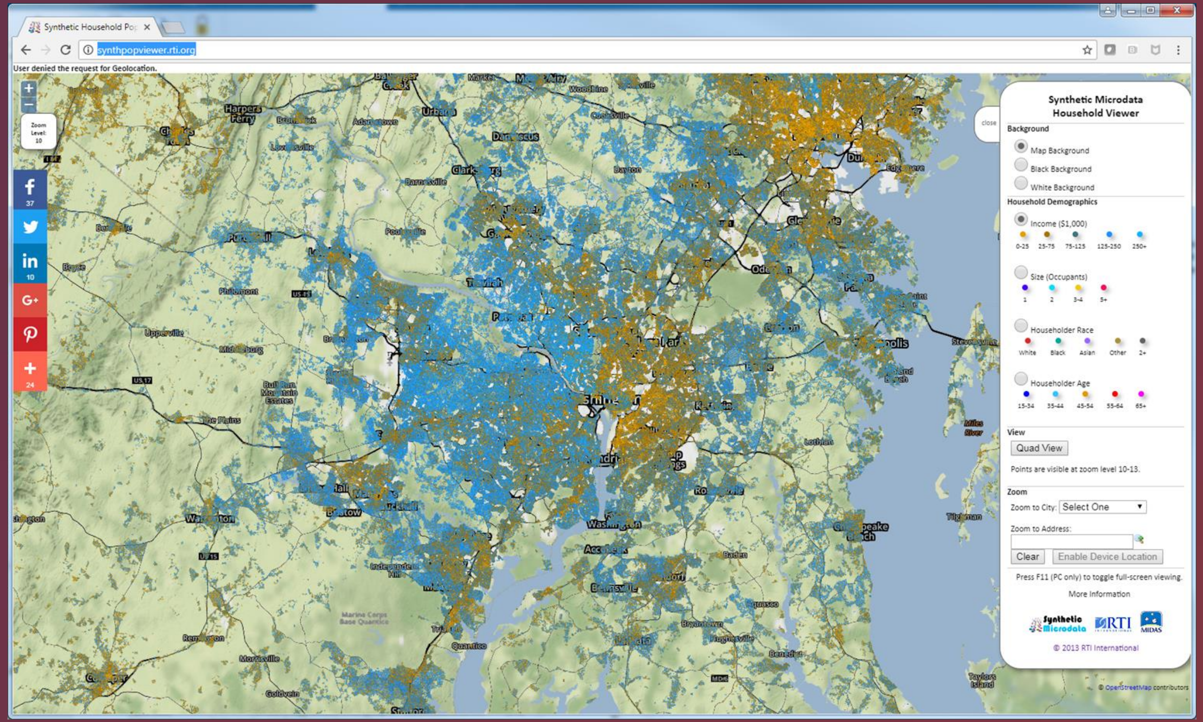
- Simulation-based models can capture complex health dynamics but are often built for a single health condition
- Disease models can be difficult to parameterize, share, and explain
- Forecasting models are often tailored to a particular setting or population, limiting generalizability

There is a call for modeling approaches that incorporate the following:

- **Multi-scale geospatial resolution** to track transmission patterns and deliver decision support to public health practitioners
- **Flexibility in model dynamics and parameterization** to account for unknown or emerging pathogens, new reservoirs, and changing environmental conditions
- **Multiple pathogens and transmission pathways** (droplet, aerosol, close contact, fomite), enabling rapid application across multiple diseases such as influenza, SARS-CoV-2, RSV, or measles by tailoring contact patterns and transmission parameters

What’s required to create flexible multi-scale models?

- NIH and CDC have invested in creation of geospatially explicit human and animal synthetic population datasets to facilitate global to local analyses in the US as well as for other countries
- These data are downscaled from publicly available Census data and enriched with other health survey information using advanced AI/ML and statistical methods
- *Agent input* refers to the population records on which individual public health models operate.
- Each record in a synthetic population dataset will typically contain detailed socio-demographic and behavior-related information (e.g., economic, education, and health status) in addition to probabilistic assignments to workplaces and schools or other key disease transmission locations important to a modeled disease dynamic.
- RTI maintains gold standard open-source synthetic population datasets and source code for parameterizing public health preparedness and decision-making solutions that require high temporal and/or spatial resolution to capture inherent heterogeneity at different scales.



RTI’s 2010 U.S. Synthetic Population Viewer
https://synthpopviewer.rti.org/

Spatial Cluster Analysis of Modeled Adult BMIs relative to the National Average Using NHANES and RTI’s Synthetic Population Data
https://synthpopviewer.rti.org/obesity

Rineer, J., Kruskamp, N., Kery, C., Jones, K., Hilscher, R., & Bobashev, G. (2025). A national synthetic populations dataset for the United States. Scientific data, 12(1), 144. https://doi.org/10.1038/s41597-025-04380-7

Wheaton, W., Cajka, J., Chasteen, B., Wagener, D., Cooley, P., Ganapathi, L., ... Allpress, J. (2009). *Synthesized population databases: A U.S. geospatial database for agent-based models*. RTI Press. RTI Press Methods Report No. MR-0010-0905. https://doi.org/10.3768/rtipress.2009.mr.0010.0905

Transmission Route:
Vector-Borne

Modelling Method:
Spatio-Temporal

Modeling Based on Environmental Mapping

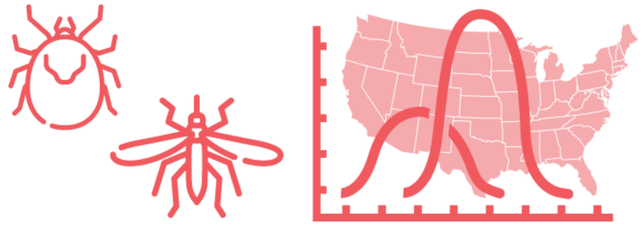
Temporal-spatial dynamic modeling as a tool to predict diffusion and persistence of tick-borne pathogens in the United States

Transmission Route:
Vector-Borne

Modelling Method:
Spatio-Temporal

Importance of Environmental Factors on Distribution of Pathogens

- Environmental characteristics of a location are strongly associated with the distribution patterns of pathogens.
- Different types of land cover can facilitate or inhibit pathogen spread.
- For zoonoses circulating in wild animal populations, environmental factors can affect the distribution of pathogen reservoirs.
- Environmental factors also have an important effect on the ecology of vectors (e.g., mosquitoes, ticks).
- Human populations and their behaviors are closely correlated with environmental factors, which can increase the risk of disease introduction, spread, and persistence.

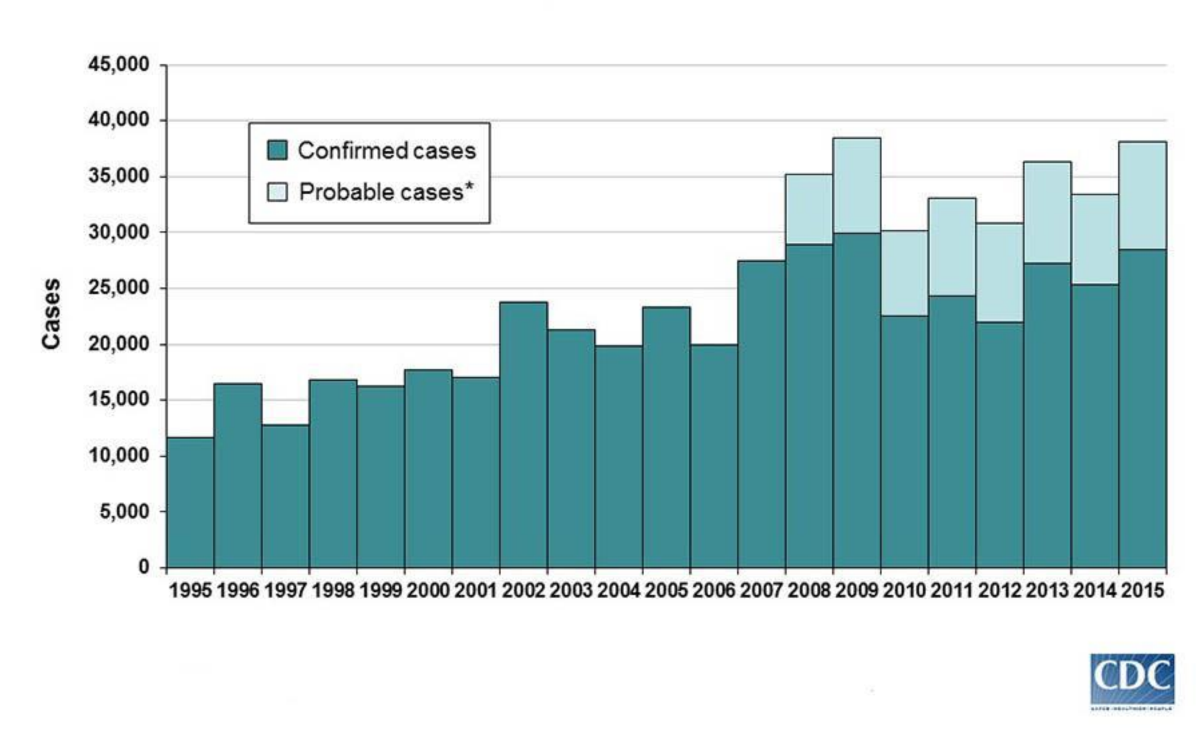


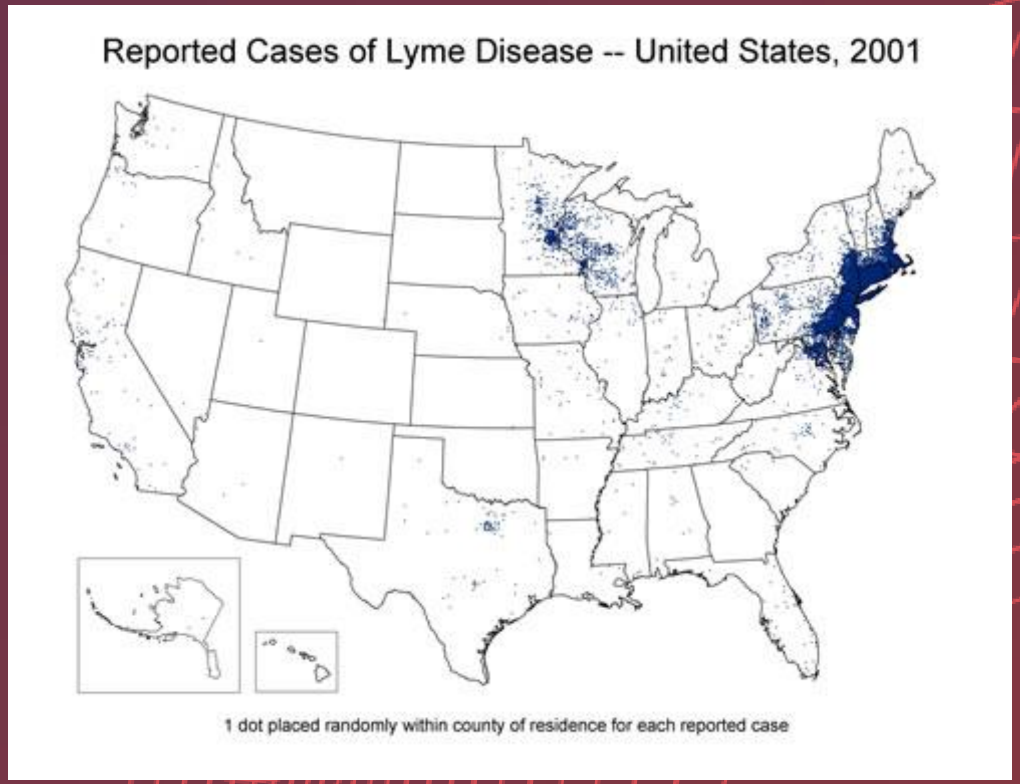
Transmission Route:
Vector-Borne

Modelling Method:
Spatio-Temporal

Expansion of Lyme Disease in the United States since 2000

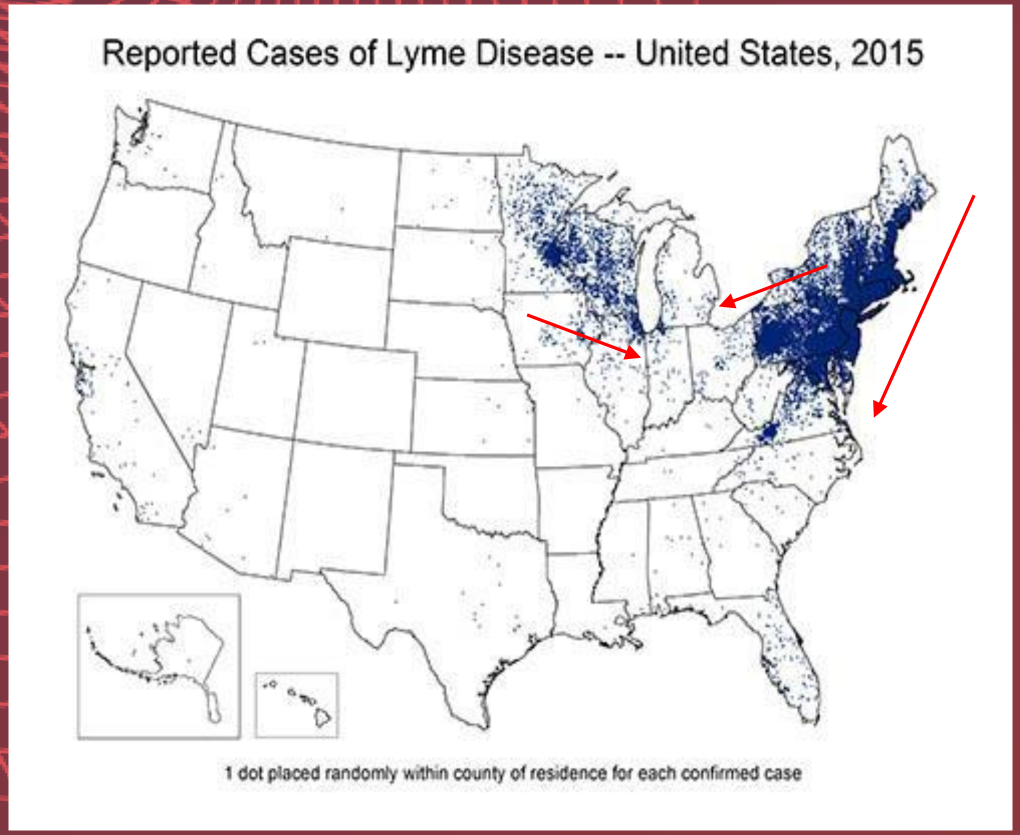
- Lyme disease:
  - Vector: Blacklegged (Ixodes) ticks
  - Habitat: Deciduous forests
  - Reservoirs: Wild animals
- Since 2000, Lyme disease has expanded in the United States.
- Diffusion started from Northeast states following three main routes.





Reported Cases of Lyme Disease -- United States, 2001

1 dot placed randomly within county of residence for each reported case



Reported Cases of Lyme Disease -- United States, 2015

1 dot placed randomly within county of residence for each confirmed case

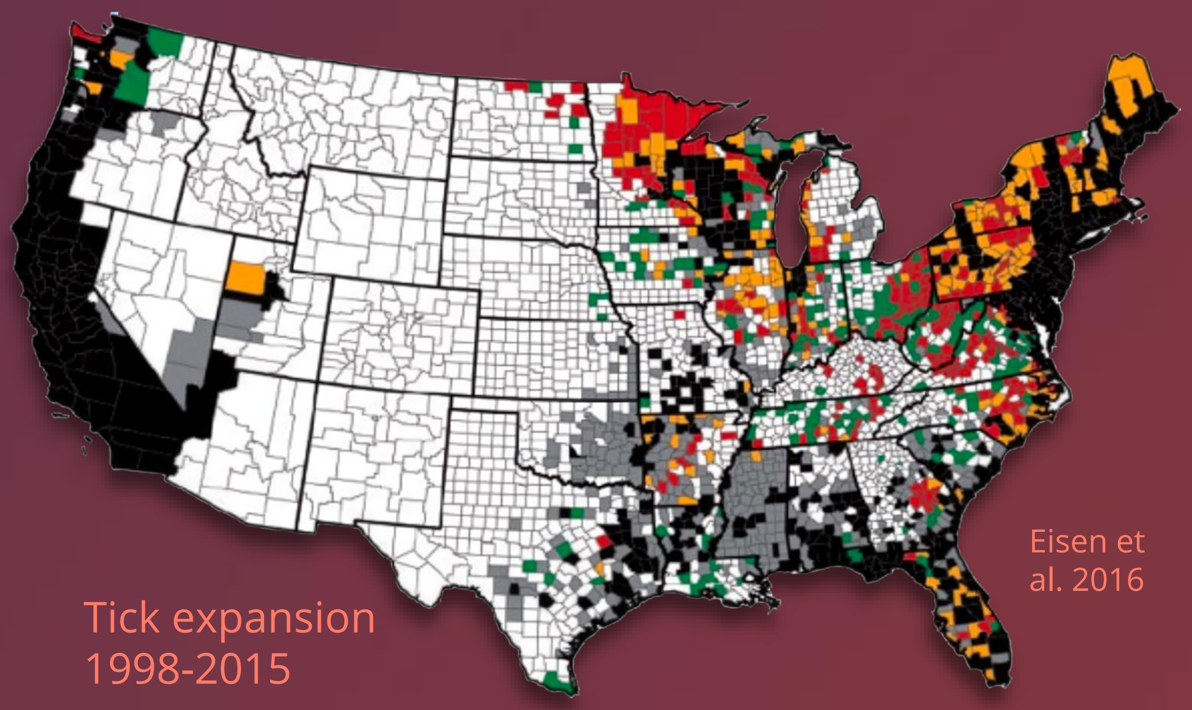
Transmission Route:
Vector-Borne

Modelling Method:
Spatio-Temporal

Modeling and Forecasting Spread of Lyme Disease in the United States

Aims of the model:

- Evaluate the importance of environmental factors
- Predict future diffusion of Lyme disease in the United States
- Build a space-time simulation framework to predict the spread of the pathogen



Tick expansion
1998-2015

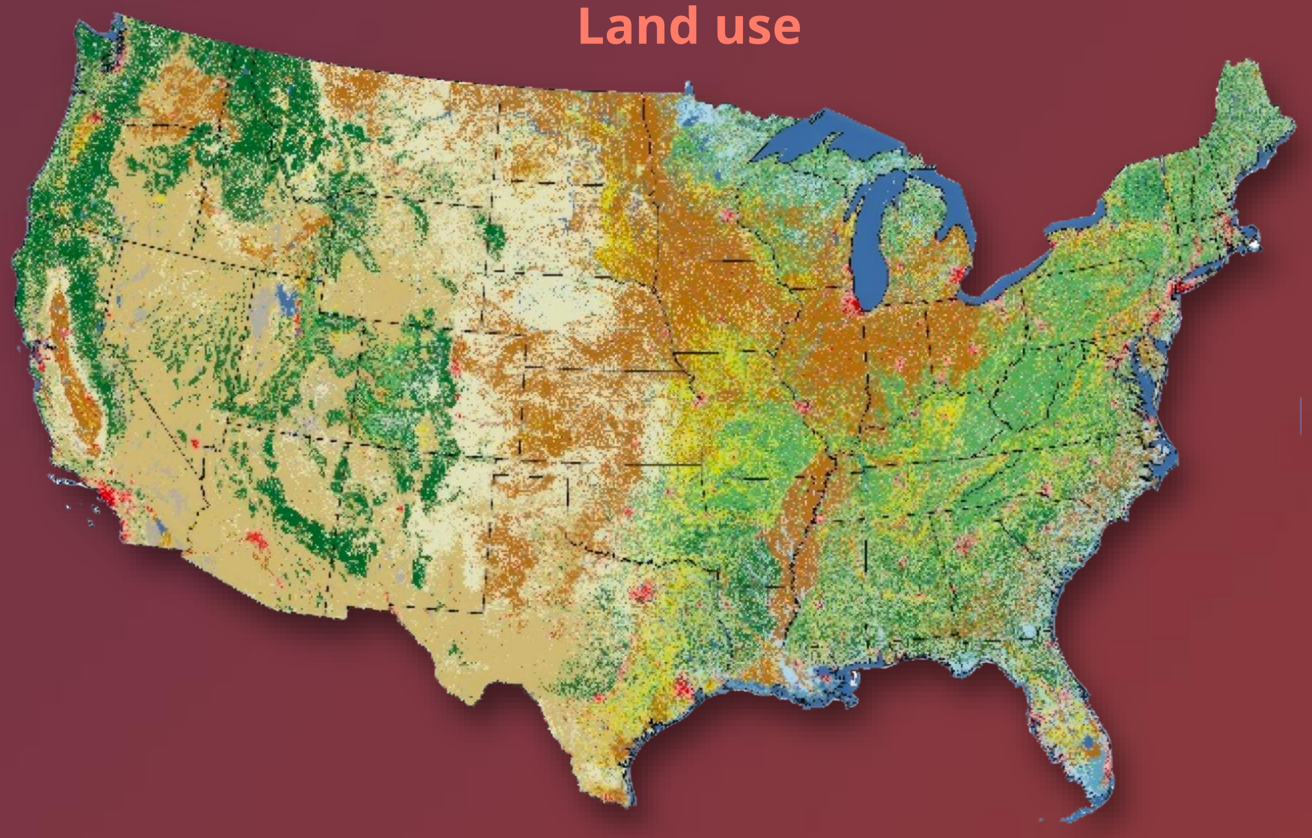
Eisen et
al. 2016

Reported Cases of Lyme Disease — United States, 2015

1 dot placed randomly within county of residence for each confirmed case

> 2017

Land use

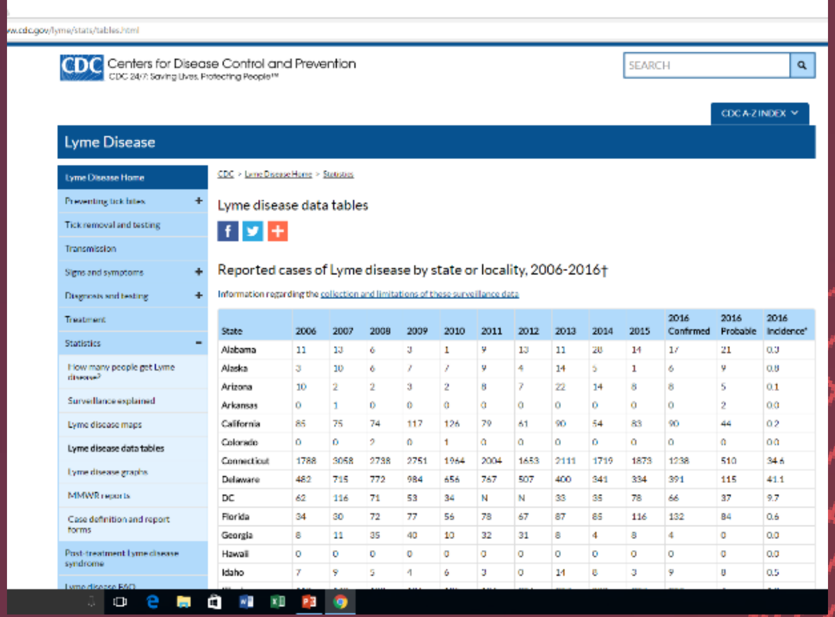


Transmission Route:
Vector-Borne

Modelling Method:
Spatio-Temporal

Lyme Disease Reported Cases and Environmental Data

- Data downloaded from CDC website:
  https://www.cdc.gov/lyme/stats/tables.html
- Confirmed and probable Lyme disease cases
- Land use to extract forest coverage (NOAA)
- Wild-urban interface
- Presence of the vector (Eisen et al., 2016)
- Elevation as DTM raster (NASA)
- County population (U.S. Census Bureau)

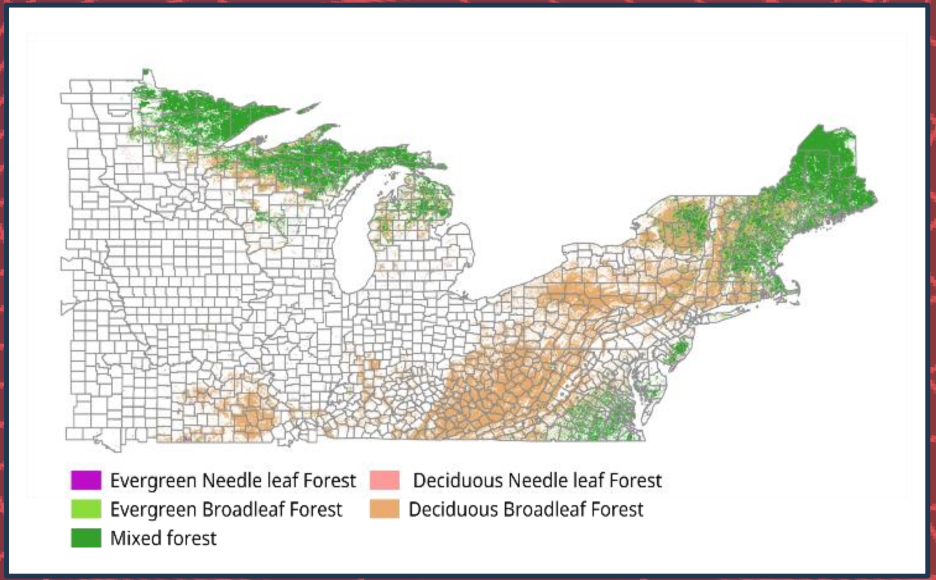


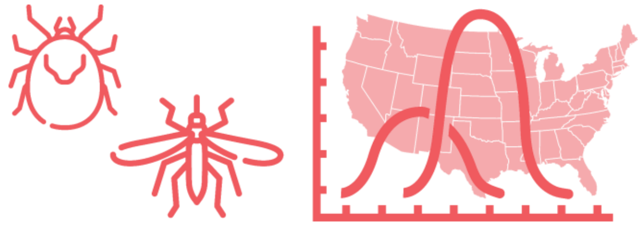
Lyme disease data tables

Reported cases of Lyme disease by state or locality, 2006-2016†

Information regarding the collection and limitations of these surveillance data

State	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016 Confirmed	2016 Probable	2016 Incidence*
Alabama	11	13	6	3	1	9	13	11	20	14	17	21	0.3
Alaska	3	10	6	7	7	9	4	14	5	1	6	9	0.8
Arizona	10	2	2	3	2	8	7	22	14	8	8	5	0.1
Arkansas	0	1	0	0	0	0	0	0	0	0	0	2	0.0
California	85	75	74	117	126	79	61	90	54	83	90	44	0.2
Colorado	0	0	2	0	1	0	0	0	0	0	0	0	0.0
Connecticut	1788	3058	2738	2751	1964	2004	1653	2111	1719	1873	1238	510	34.6
Delaware	482	715	772	984	656	767	507	400	341	334	391	115	41.1
DC	62	116	71	53	34	N	N	33	35	78	66	37	9.7
Florida	34	30	72	77	56	78	67	87	85	116	132	84	0.6
Georgia	8	11	35	40	10	32	31	8	4	8	4	0	0.0
Hawaii	0	0	0	0	0	0	0	0	0	0	0	0	0.0
Idaho	7	9	5	4	6	3	0	14	8	3	9	8	0.5



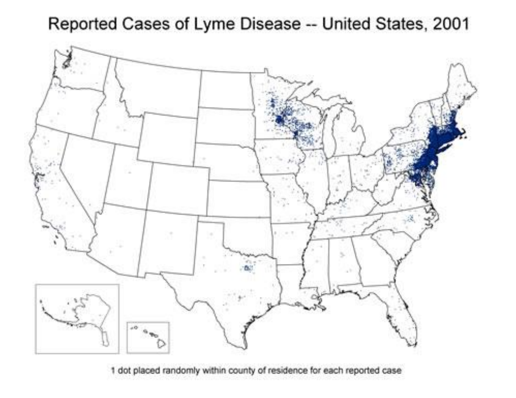


Transmission Route:
Vector-Borne

Modelling Method:
Spatio-Temporal

Dataset Assembly for Modeling

- New reporting counties per year from 2000 to 2015 (2016–2017 → model testing)
- County's forest coverage
- County's population
- Number of reporting 1st and 2nd degree neighbors
- Forest coverage of reporting 1st and 2nd degree neighbors (median value)



Reported Cases of Lyme Disease -- United States, 2001

1 dot placed randomly within county of residence for each reported case

2001

.....

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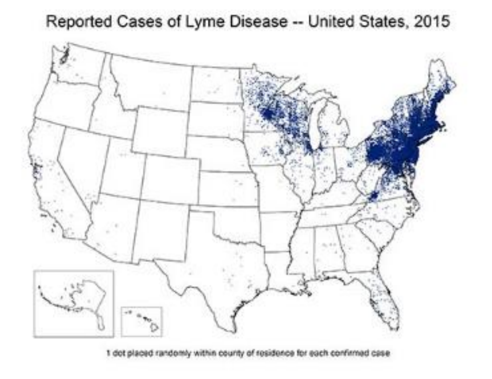
2014



Reported Cases of Lyme Disease -- United States, 2015

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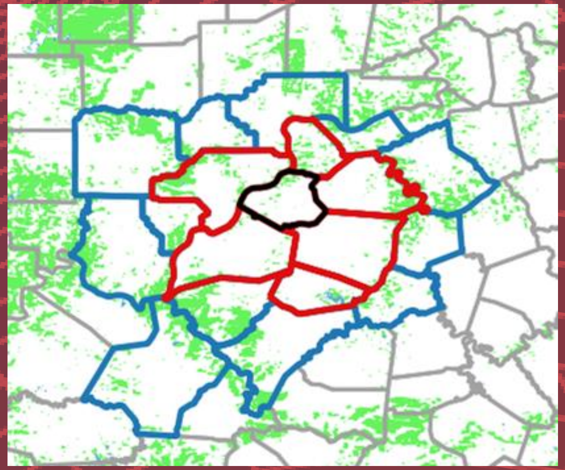
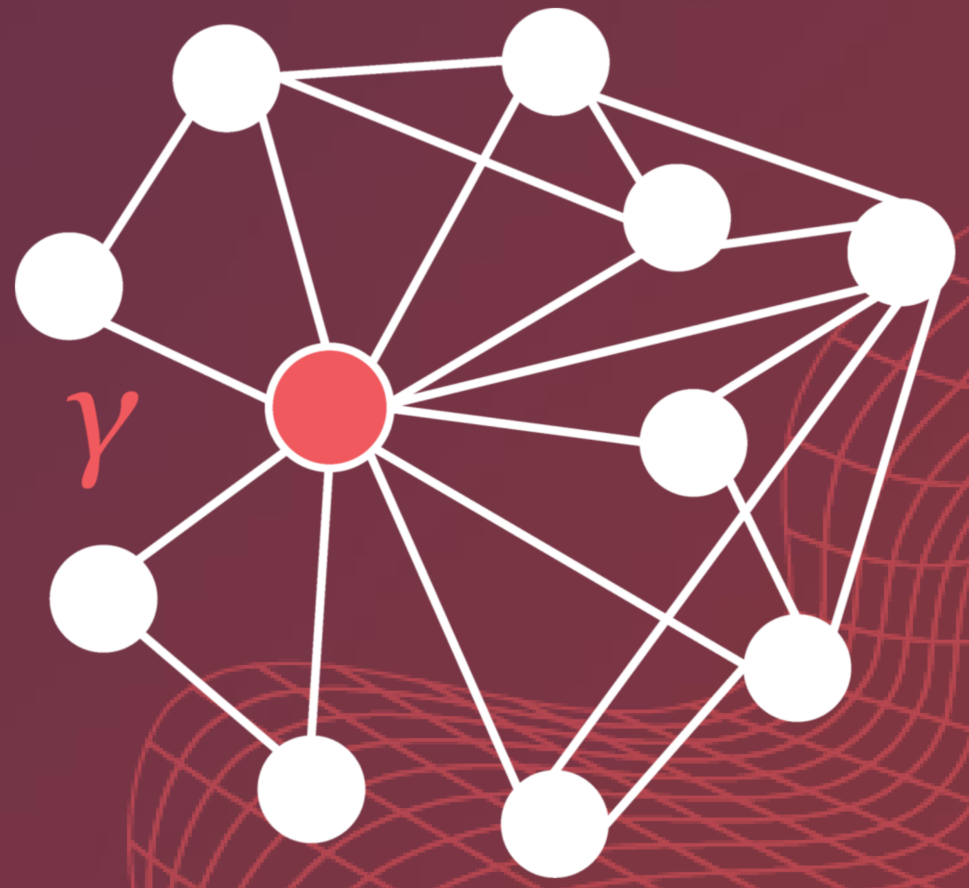


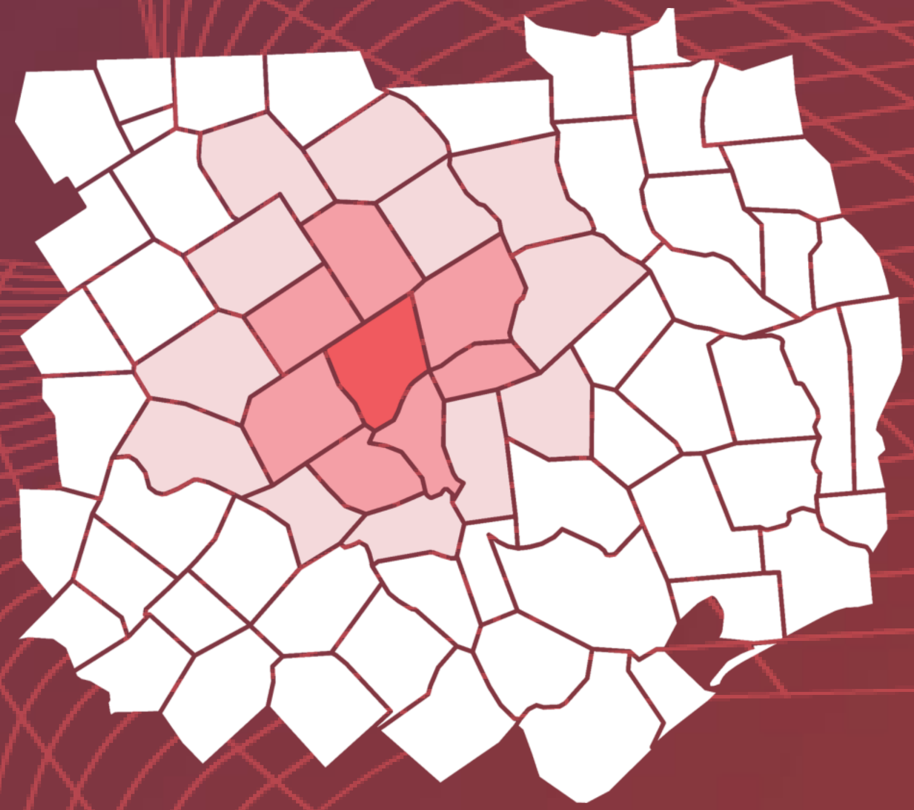
Transmission Route:
Vector-Borne

Modelling Method:
Spatio-Temporal

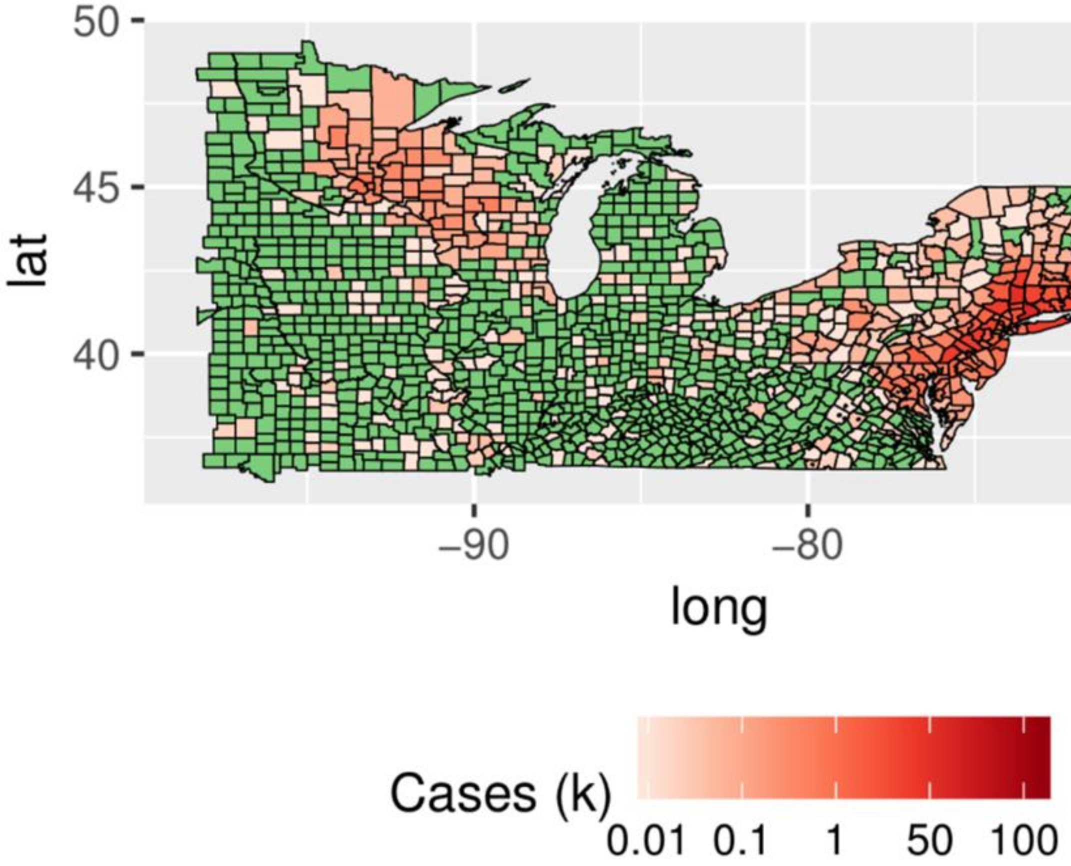
Diffusion Model

- County network based on 1st and 2nd degree neighbors
- Nodes and link = counties linked to their neighbors
- Each node characterized by county’s forest tract
- Probability (γ) of reporting Lyme disease for first time, prediction from logistic regression
- Starting from counties reporting in 2000
- Simulation 2001–2017 (16 years)
- Jackknife approach, 1,000 simulations per run
- Result: Probability of reporting from 2001 to 2017

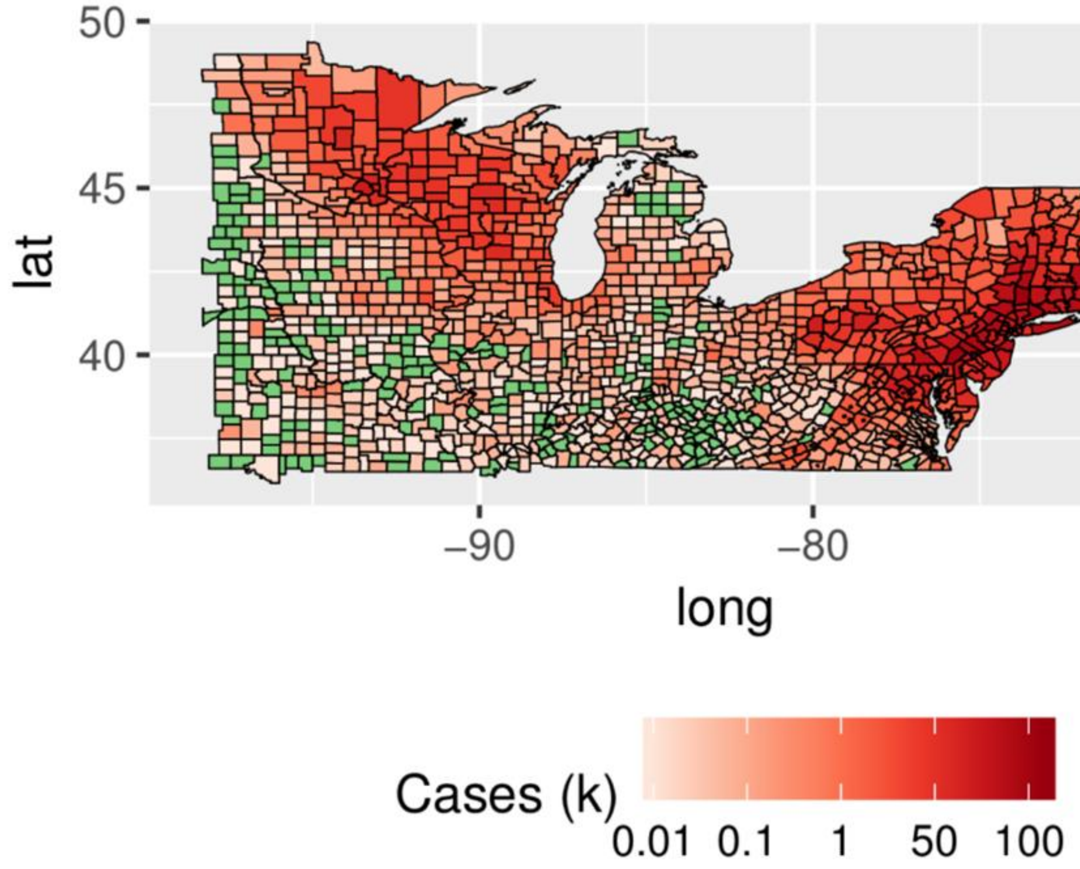


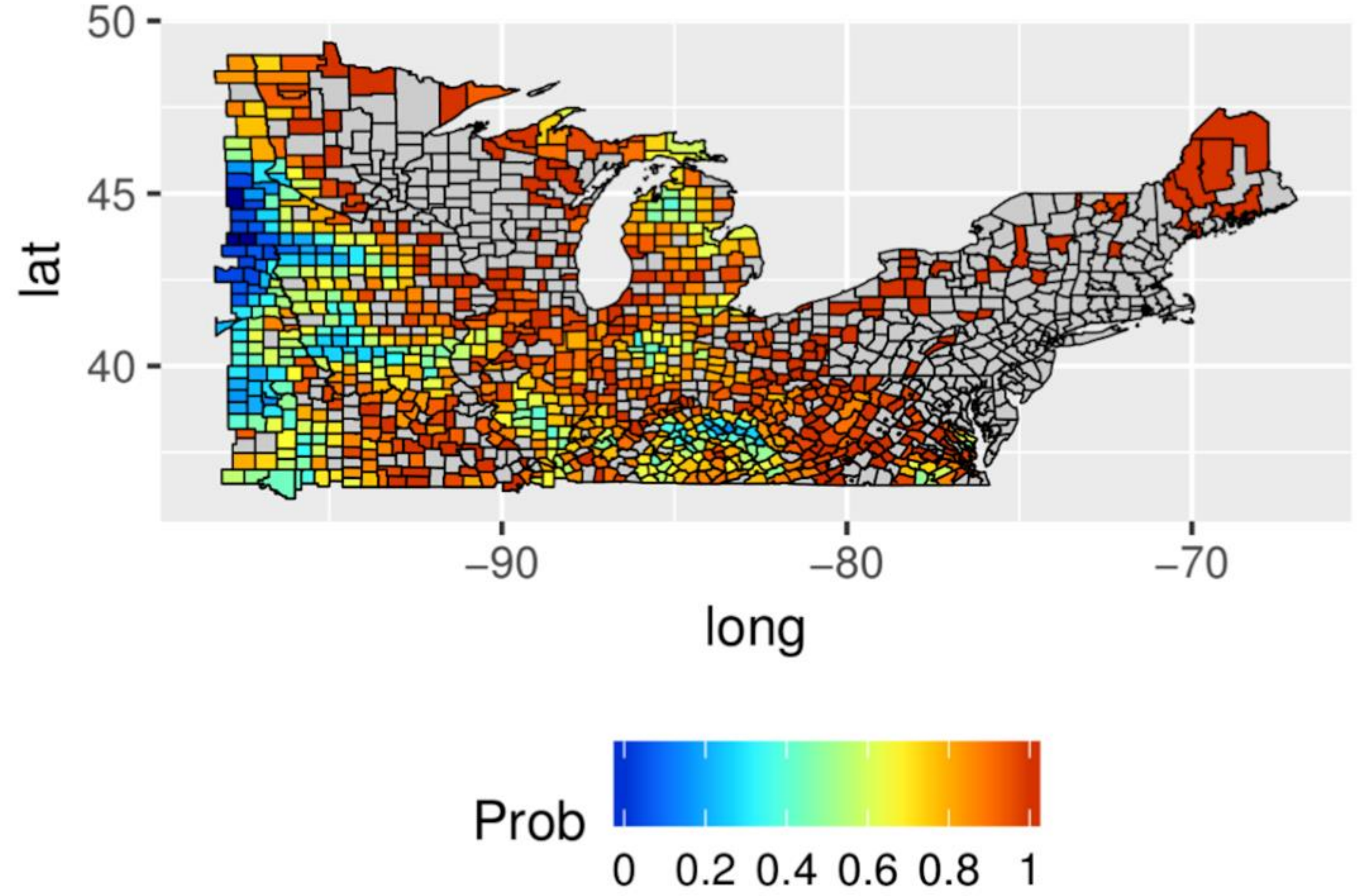


2000



2017





AUC of ROC curve = 82.3% (95% CI: 78.1–87.6 %)

- 162 free LD counties in 2017
- 30.1% (N=47) had a high (>0.8) probability

Transmission Route:
Human-to-Human

Modelling Method:
Individual-Based

RTI-Cassandra™

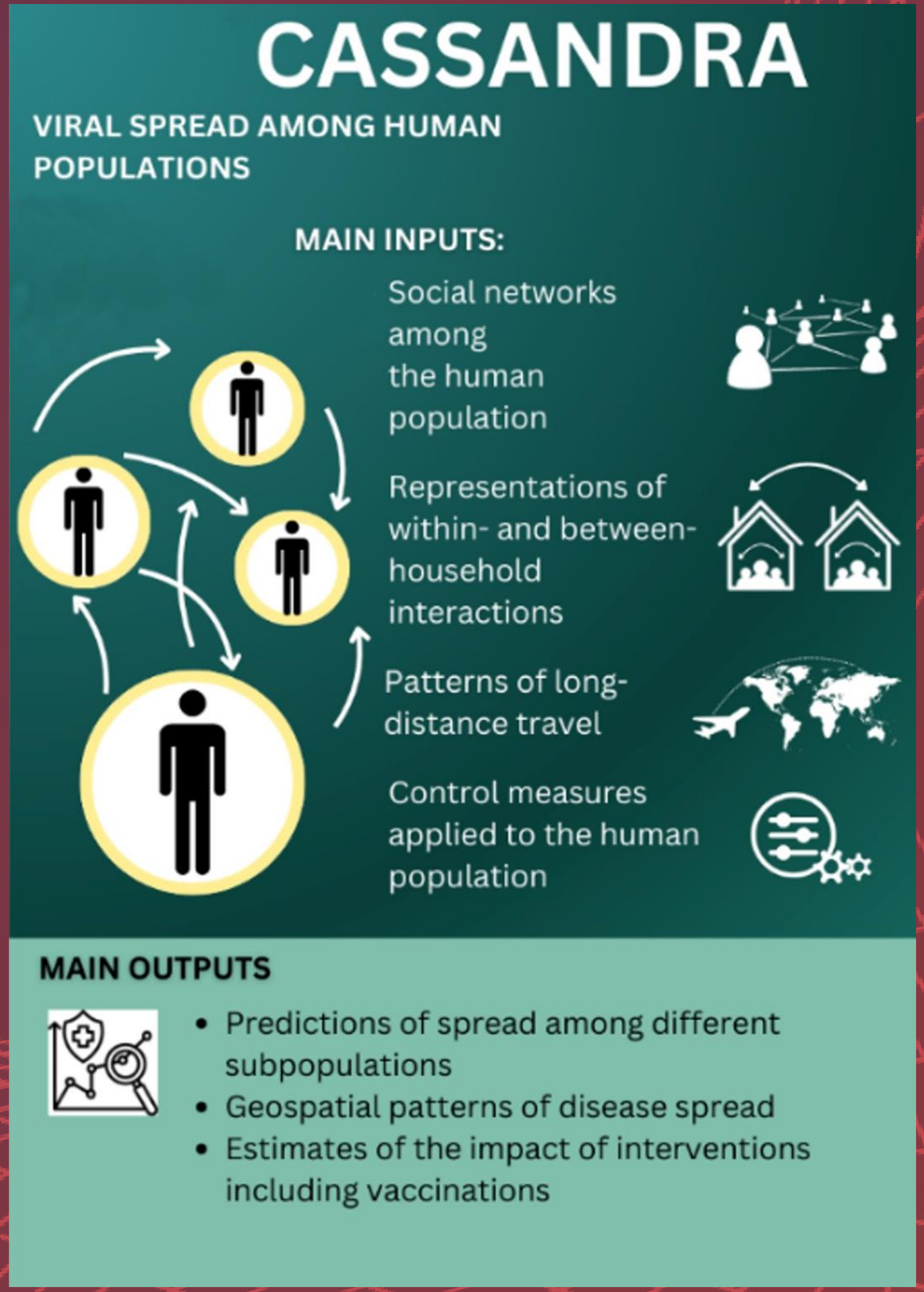
A novel modeling framework to support outbreak response

Transmission Route: Human-to-Human

Modelling Method: Individual-Based

RTI-Cassandra$^{\text{TM}}$ Modeling Framework

- Modeling framework to simulate spread of disease agents (virus, bacteria, protozoa) among human population
- **Spatially Explicit:** The model includes human mobility and environmental characteristics, which is essential for understanding how diseases spread geographically.
- **Individual-Based Model (IBM):** It accounts for variations in human interactions, including the number and duration of contacts.
- **Disease Transmission Modeling:** This feature allows the framework to simulate how diseases are transmitted within a population.
- **High Scalability:** The model can simulate disease spread at large scales, including national-level outbreaks.
- **High Speed:** Optimized to deliver rapid results (within about 1 week), which is crucial for decision-making in emergencies.
- **Already Deployed:** Used to model outbreaks due to novel and emerging and re-emerging diseases in DRC (Bisanzio et al., 2023) and Uganda (Bisanzio et al., 2025), Saudi Arabia (Bisanzio et al., 2022), Kenya (Bisanzio et al., in prep), and high-income countries (Bisanzio et al., 2022).



CASSANDRA

VIRAL SPREAD AMONG HUMAN POPULATIONS

MAIN INPUTS:

- Social networks among the human population
- Representations of within- and between-household interactions
- Patterns of long-distance travel
- Control measures applied to the human population

MAIN OUTPUTS

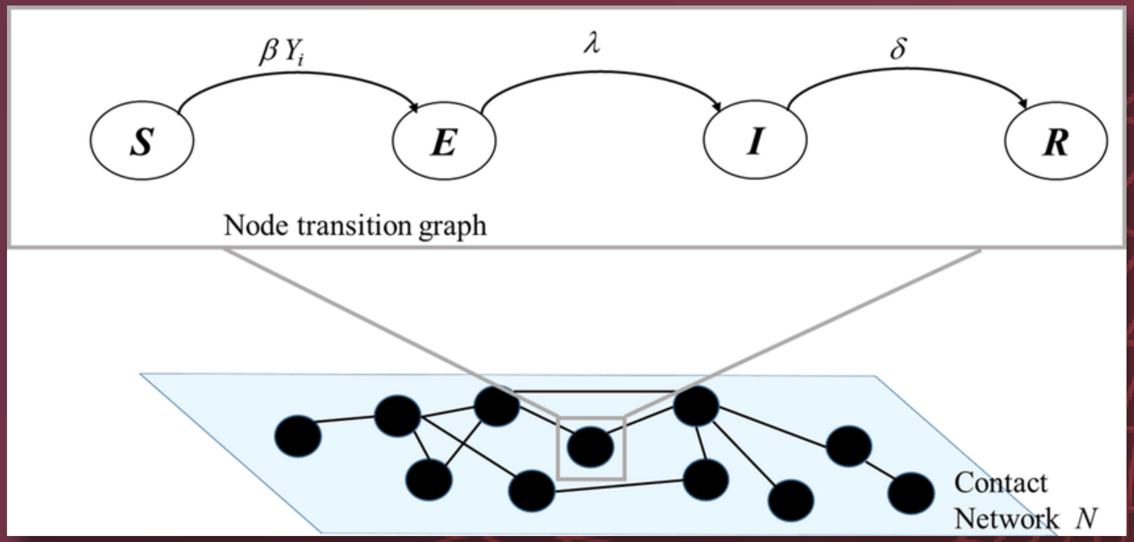
- Predictions of spread among different subpopulations
- Geospatial patterns of disease spread
- Estimates of the impact of interventions including vaccinations

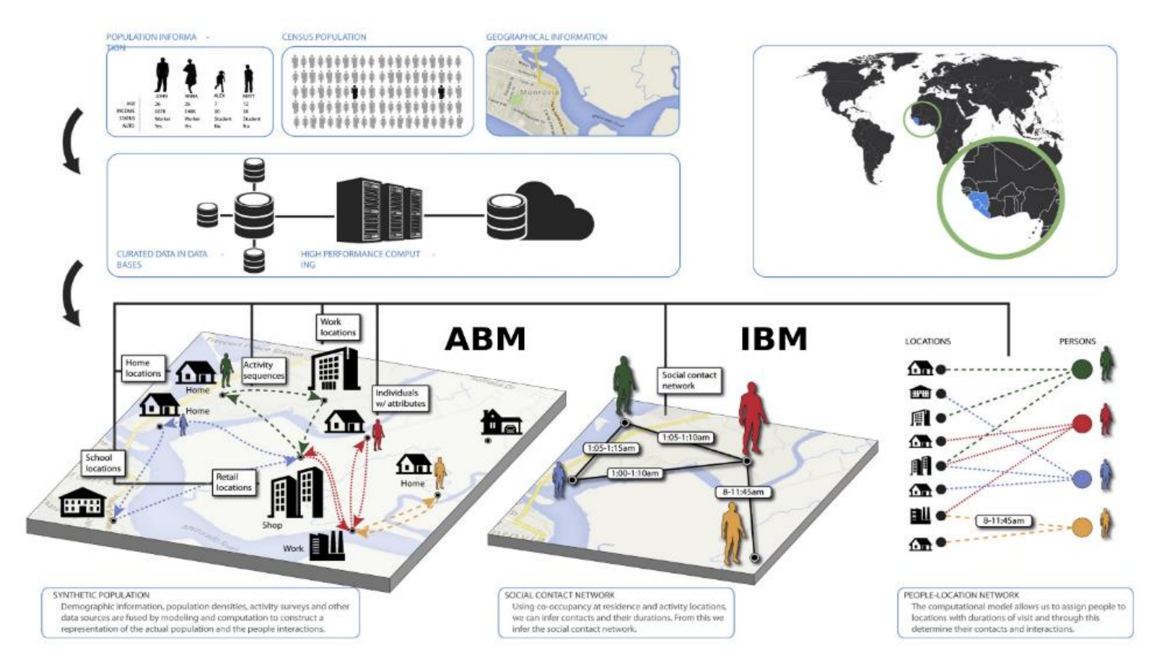
Transmission Route:
Human-to-Human

Modelling Method:
Individual-Based

Synthetic Population and its Social Network

- Model includes a synthetic population representing the target population (national or sub-national level)
- Modular structure allows user to turn on and off parts of the code (e.g., non-pharmaceutical interventions, vaccination, lockdowns, transmission dynamics)
- Age and sex of individuals based on country demography
- Account for interaction among people through social network
- Account for people migration using a gravity model adjusted by travel time based on recorded movement data (e.g., social network, survey)
- Unlike most other IBMs, Cassandra allows researchers to account for heterogeneity of agent interaction, infection exposure, and movement dynamics.





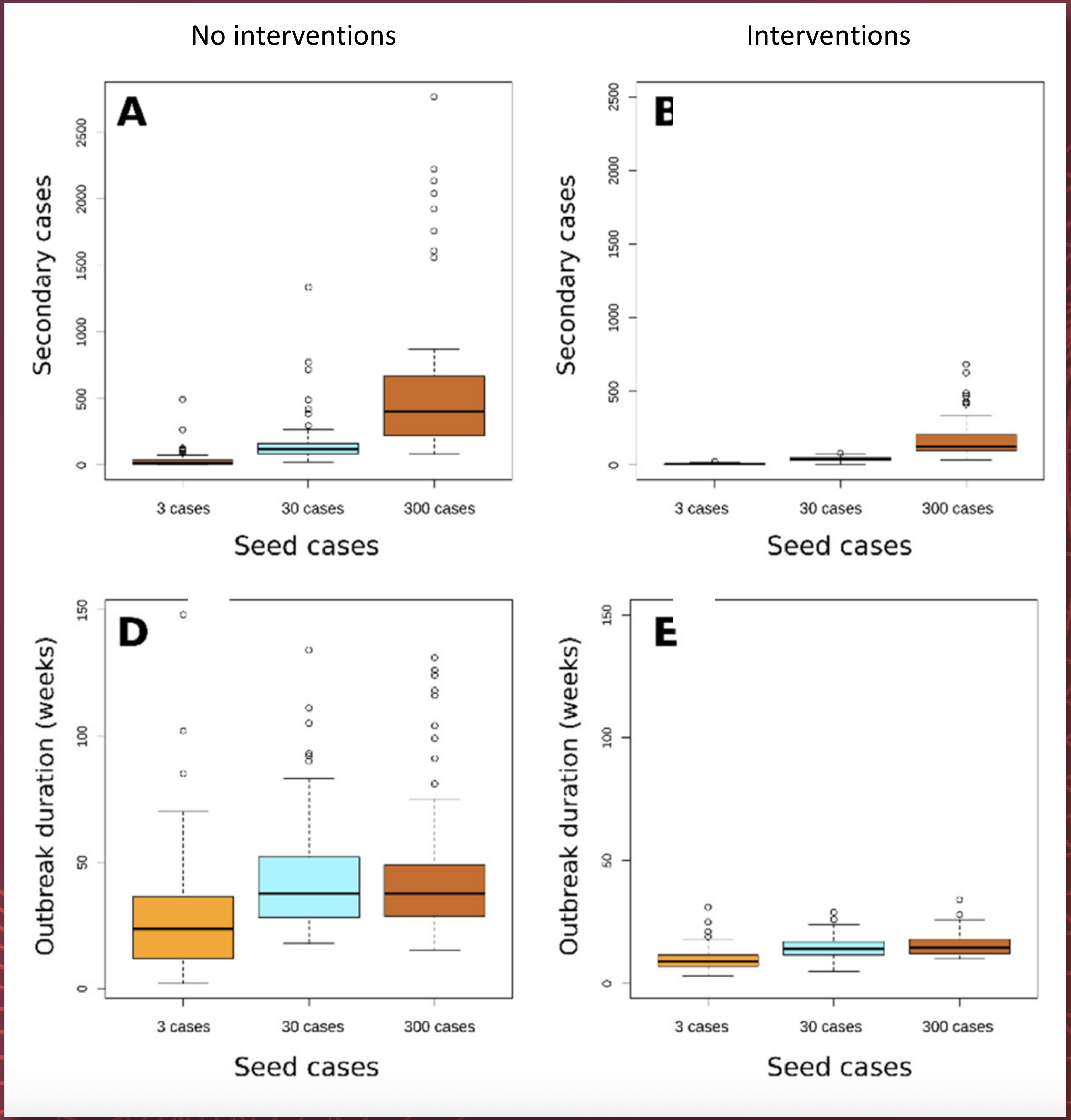
Venkatramanan et al., 2018

Transmission Route:
Human-to-Human

Modelling Method:
Individual-Based

Spread of Zoonotic mpox in High-Income Countries

- RTI-Cassandra$^{\text{TM}}$ was used to predict the spread of zoonotic mpox (clade I) in a synthetic population representing a high-income country (United States/Europe/Canada).
- The model estimated the epidemic due to introduction of imported cases from an endemic country or a country with an ongoing outbreak.
- The model was used to check the effect of response interventions deployed to reduce the spread of the mpox virus.
- The model was also recalibrated to simulate transmission of the novel clade II that caused the global outbreak during 2022.



Transmission Route:
Human-to-Human

Modelling Method:
Individual-Based

Modular Design for Rapid Response

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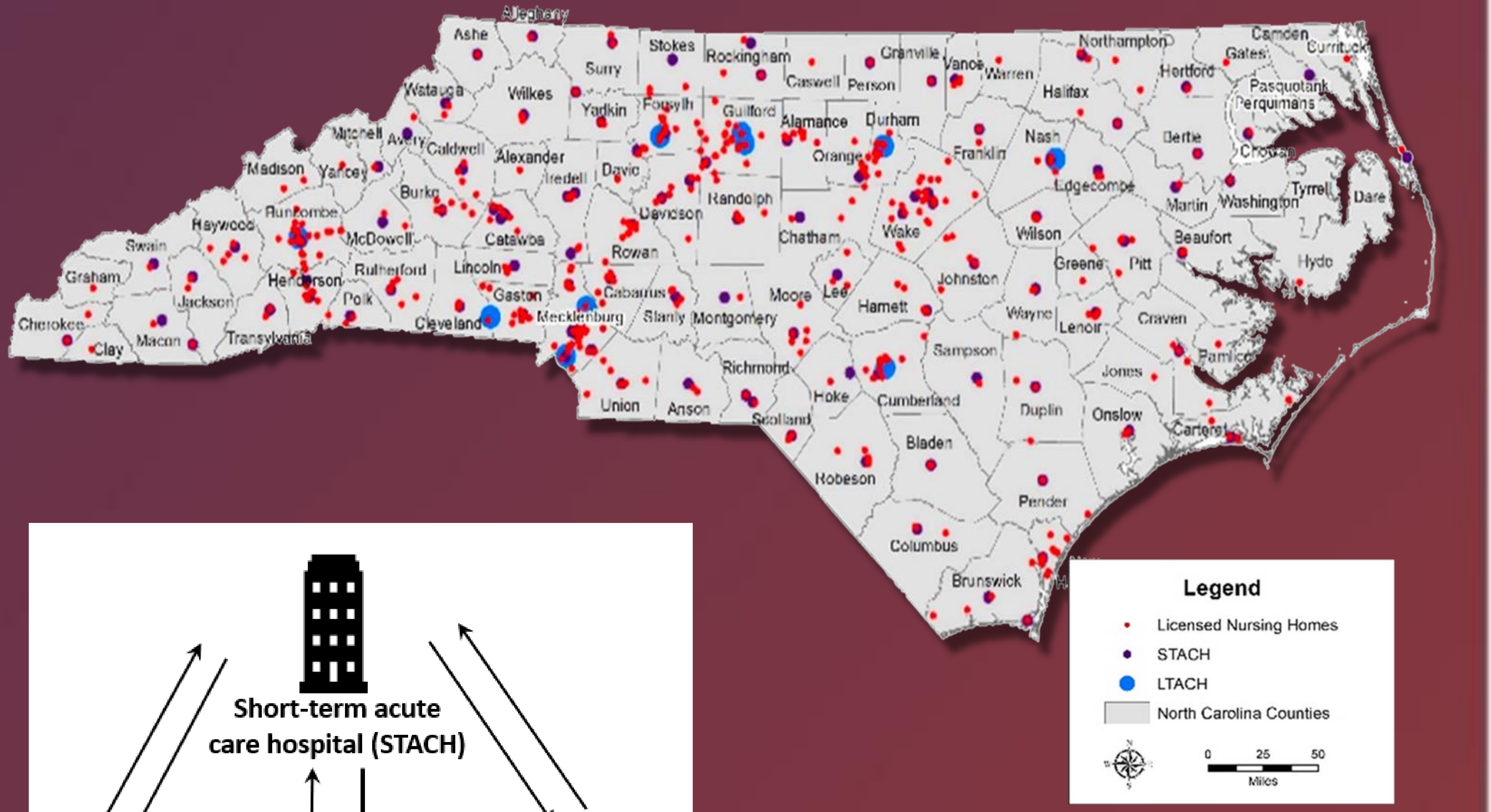
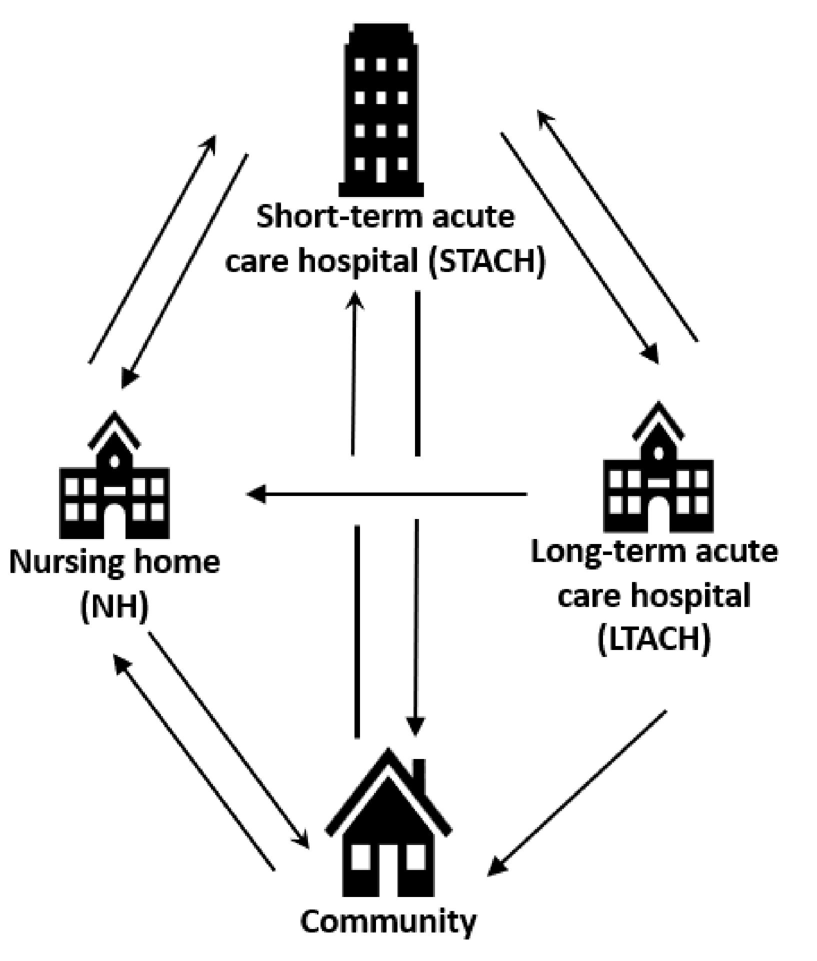
- Agent-based model of North Carolina for the Modeling Infectious Diseases in Healthcare Network (MInD – Healthcare)
- Calibrated to *C.difficile* infection surveillance data from National Healthcare Safety Network data
- Simulates agent movement from the community to facilities as patients, visitors, or healthcare workers
- Built using RTI's SynthPop™ of North Carolina (n=10.6 million individuals)





Transmission Route:
Human-to-Human

Modelling Method:
Individual-Based

Modular Design for Rapid Response

RTI INTERNATIONAL

- Starting in 2020, RTI began to modify the ABM of HAI in North Carolina to simulate SARS-CoV-2 and estimate hospital and ICU occupancy
- Monthly updates shared with NC Governor's Office and helped inform state response
- Used to evaluate testing policies and the number of undetected cases of SARS-CoV-2 admitted as inpatients under different testing policies for hospitals and nursing homes

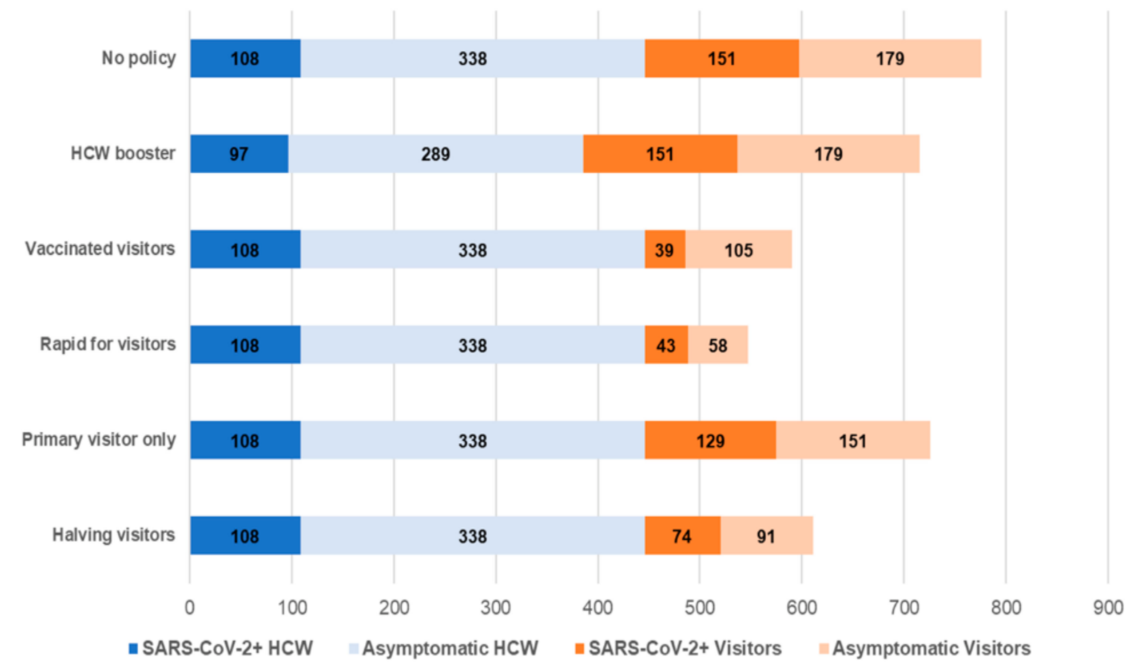


Figure 1. Average number of SARS-CoV-2 infected healthcare workers (HCW) or visitors entering nursing home facilities per day by policy.

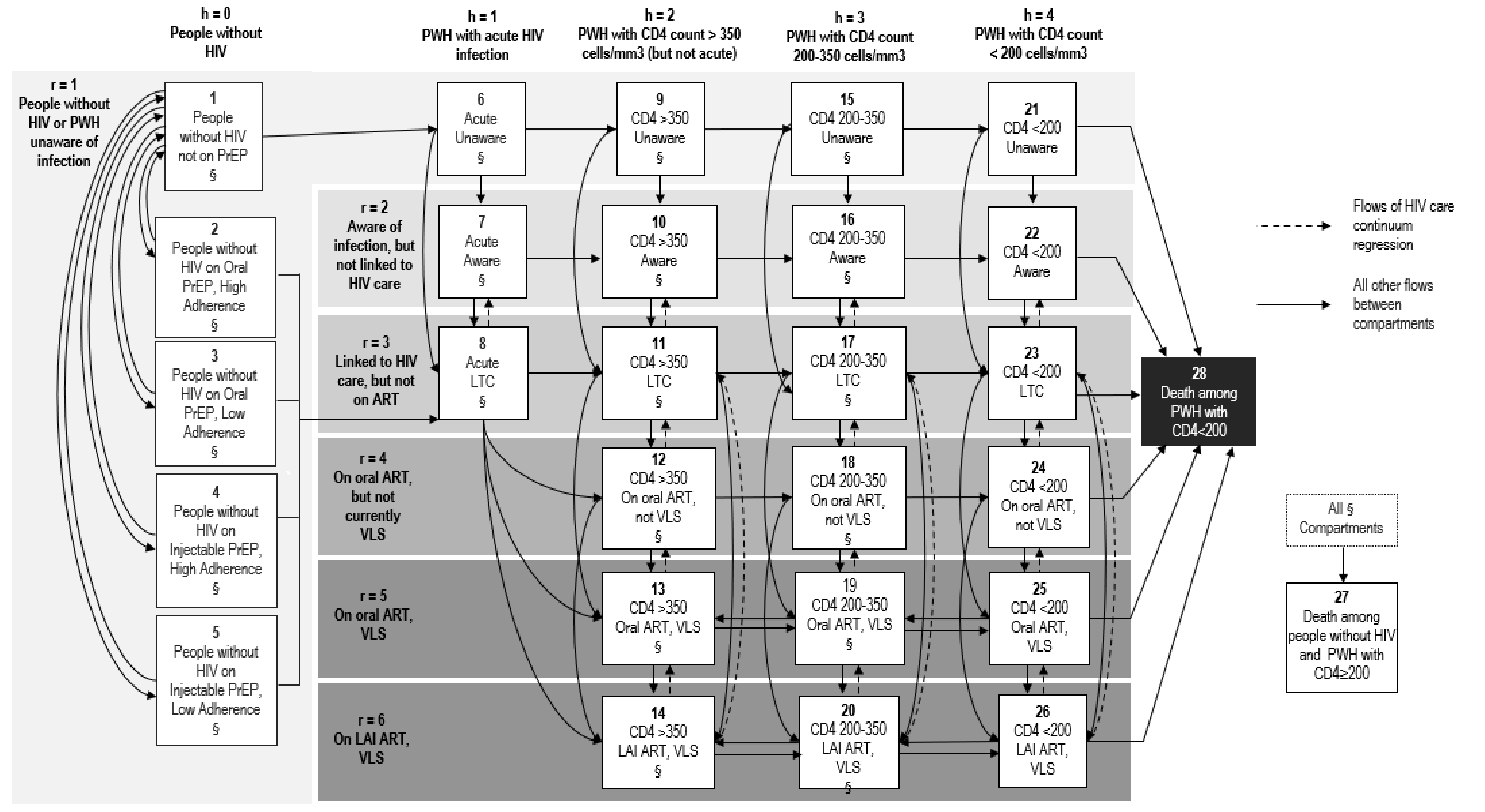
Source: Adams, J. W., Jones, K., Preiss, S., Hadley, E., & Segelman, M. (2023). Evaluating policies to decrease the risk of introducing SARS-CoV-2 infections to nursing home facilities. Journal of Applied Gerontology, 42(7), 1505–1516.

Transmission Route:
Human-to-Human

Modelling Method:
System Dynamics

What about the cost?

- Extensive experience incorporating costs within compartmental, system dynamics, and microsimulation models
- Outcomes like cost-effectiveness, incremental cost-effectiveness ratios, QALYs, and total societal cost related to disease burden
- Used to compare treatment or intervention approaches
- HIV Optimization and Prevention Economics (HOPE) model represents dynamics of HIV transmission and disease progression for the United States



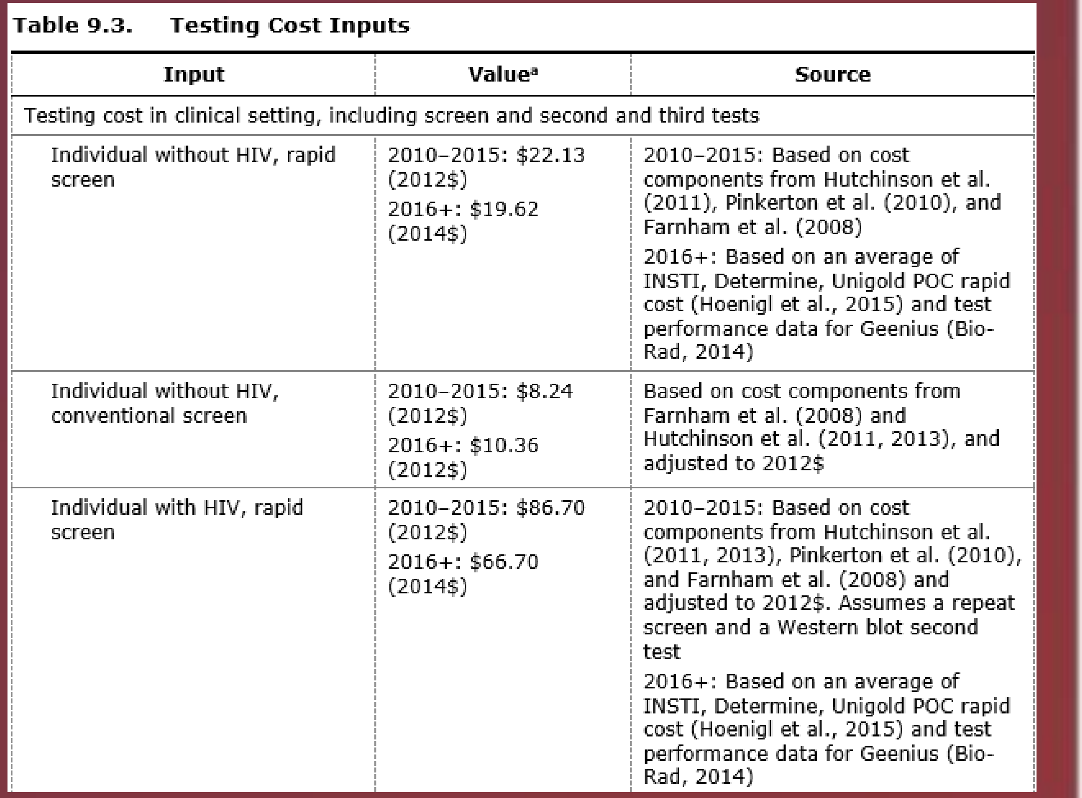


Table 9.3. Testing Cost Inputs

Input	Value[a]	Source
Testing cost in clinical setting, including screen and second and third tests		
Individual without HIV, rapid screen	2010–2015: $22.13 (2012$) 2016+: $19.62 (2014$)	2010–2015: Based on cost components from Hutchinson et al. (2011), Pinkerton et al. (2010), and Farnham et al. (2008) 2016+: Based on an average of INSTI, Determine, Unigold POC rapid cost (Hoenigl et al., 2015) and test performance data for Geenius (Bio-Rad, 2014)
Individual without HIV, conventional screen	2010–2015: $8.24 (2012$) 2016+: $10.36 (2012$)	Based on cost components from Farnham et al. (2008) and Hutchinson et al. (2011, 2013), and adjusted to 2012$
Individual with HIV, rapid screen	2010–2015: $86.70 (2012$) 2016+: $66.70 (2014$)	2010–2015: Based on cost components from Hutchinson et al. (2011, 2013), Pinkerton et al. (2010), and Farnham et al. (2008) and adjusted to 2012$. Assumes a repeat screen and a Western blot second test 2016+: Based on an average of INSTI, Determine, Unigold POC rapid cost (Hoenigl et al., 2015) and test performance data for Geenius (Bio-Rad, 2014)

Transmission Route:
Human-to-Human

Modelling Method:
System Dynamics

Cost-effectiveness Modeling

- Selected analyses conducted with the HOPE model:
  - Cost-effectiveness of testing the heterosexual population at different frequencies
  - Estimation of the HIV reproduction number for the US
  - Cost-effectiveness of PrEP in the U.S.
  - Optimal societal allocation of HIV prevention and treatment resources for young MSM in the US
- Recent analysis estimated how increased uptake of long-acting injectable antiretrovirals could decrease HIV incidence

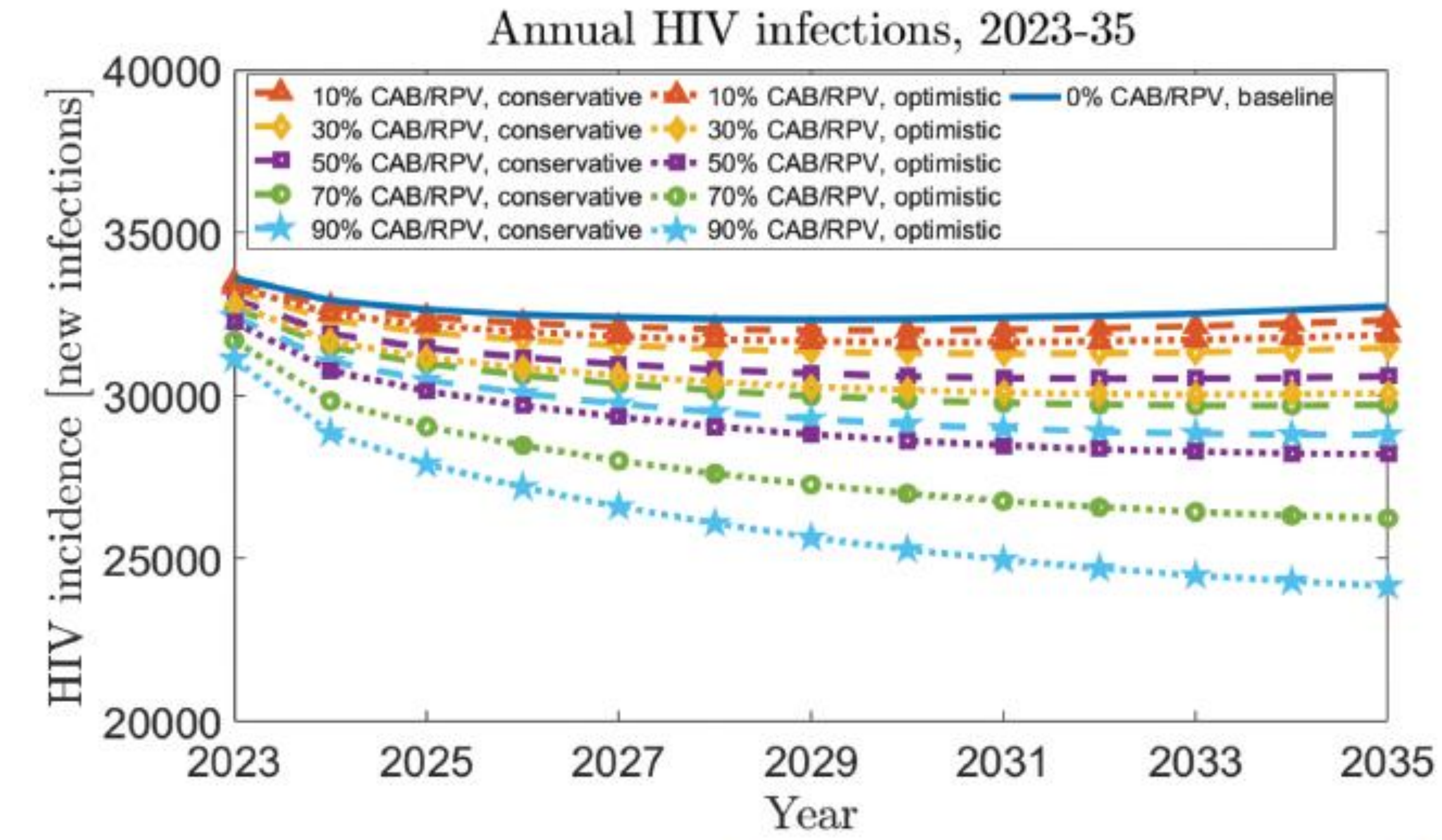


Fig. 1. HIV incidence for varying levels of CAB/RPV use in each scenario[†]. Note: for reasons of visibility the y-axis scale does not begin at zero. ART, antiretroviral therapy; B/AA, Black/African-American; CAB/RPV, cabotegravir-rilpivirine; H/L, Hispanic/Latino; O, other racial/ethnic groups besides B/AA and H/L; PWDH, people with diagnosed HIV; VLS, viral load suppression. [†]The *conservative* scenario refers to the scenario in which CAB/RPV increases the length of VLS upon cessation of use; the *optimistic* scenario refers to the scenario in which CAB/RPV is assumed additionally to improve overall ART adherence.

SOURCE: Viguerie, A., O'Shea, J., Johnston, M., Schreiber, D., Adams, J., Bates, L., ... & Farnham, P. G. (2022). Impact of increased uptake of long-acting injectable antiretroviral therapy on HIV incidence and viral suppression in the United States under 2021 FDA guidelines. *AIDS*, 10-1097.

Looking to the Future of Infectious Disease Modeling

- A flexible multi-scale modeling approach is essential to address fast-moving, complex health threats.
- Our work to date has emphasized the utility of and need for models that can be adapted quickly in response to new or emerging pathogens, changing environmental conditions, or innovations such as the availability of new treatment regimens or vaccines.
- Our modeling portfolio features a synthetic population that reflects the entire U.S. population; an adaptable microsimulation disease modeling tool; and our expertise in disease modeling, health economics, and implementation science.

Questions?

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