

Starsim: A flexible framework for agent-based modeling of health and disease

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tl;dr version

- Starsim is an open-access modeling framework for making agent-based models of multiple diseases
- It's based on our previous disease-specific models for COVID, family planning, HPV, etc.
- It's designed to be easy to use: >200 people trained
- It's still in development, and we're actively seeking collaborators – get in touch with modeling questions!



Agent-based modeling training, Nairobi, April 2024

Code:

- Starsim: <u>https://starsim.org/</u>
- Covasim: http://covasim.org
- FPsim: http://fpsim.org
- HPVsim: http://hpvsim.org

Methods papers:

- Starsim: in prep!
- Covasim: Kerr et al 2021, <u>PLoS CB</u>
- FPsim: O'Brien et al 2023, <u>Nature WH</u>
- HPVsim: Stuart et al 2024, PLoS CB



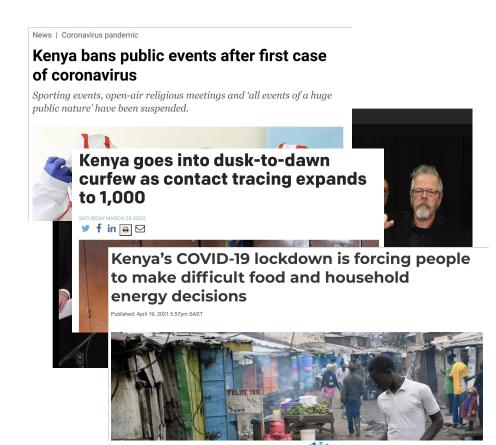
Outline

- Motivation & genesis: why / how did Starsim come about?
 - Origins in COVID-19
 - Expansion to other diseases/health areas
 - Evolution of an independent framework
- 2. Design and implementation
- 3. Application: Modeling co-circulating STIs
- 4. Summary

Motivation & genesis

Starsim's genesis

- Initially developed by the Institute of Disease Modeling, an embedded research group within the Gates Foundation
 - Provides internal support
 - Conducts scientific research
 - Develops open-source modeling tools
- In March 2020, urgent need for fast-paced modeling tools
 - IDM's existing models were not fast or nimble enough to adapt



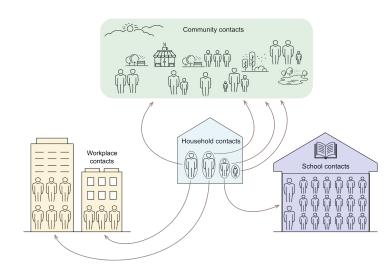
Modeling at pandemic pace required new tools

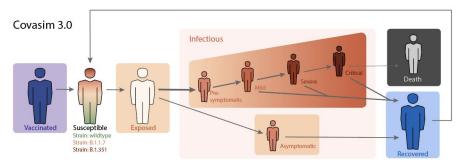
Covasim is an agent-based COVID-19 model purpose-built to explore complex scenarios

- Clear purpose: Simple design
- Changing questions: Flexible, easy to use
- Fast development: Pure python
- Rigorous science: calibration and local data

Fnabled focus on the science:

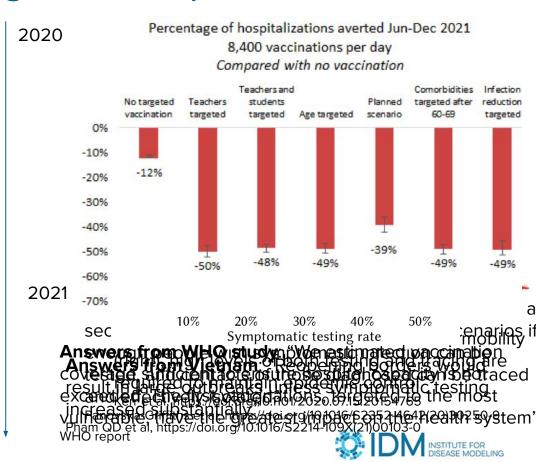
- Infection natural history
- Detailed contact networks
- Individual-level heterogeneity
- Modeling antibody-based immunity
- Co-transmitting variants of concern



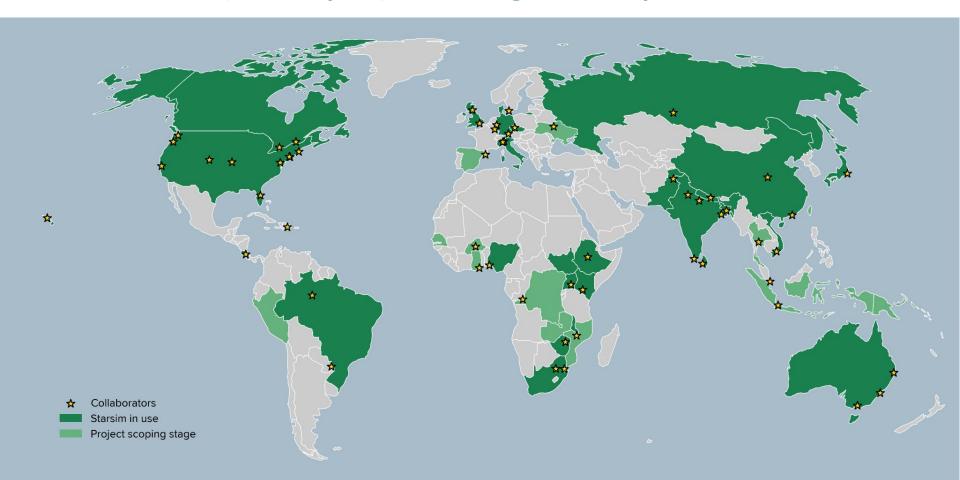


Many questions throughout the pandemic

How much testing & tracing do we need to do? How would this change if we opened up more? Is it OK to open schools? How can we do it safely? Is it OK to open borders? How can we do it safely? What will be the impact of new variants? What would be the impact of different vaccination roll-out strategies?

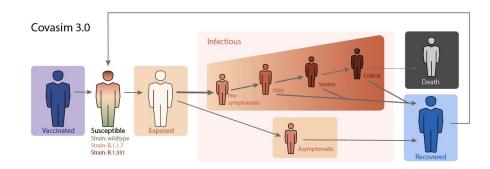


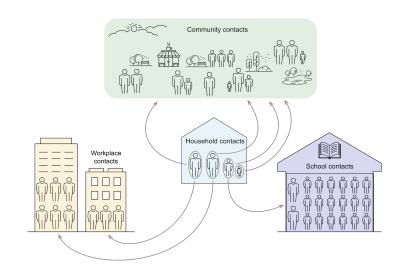
Covasim quickly spread globally



Covasim's structure

- Agent-based model: Simulates the state of individual people (agents) over time
- Fundamental calculation: the probability that a given agent, on a given time step, will change from one state to another, e.g.:
 - susceptible -> infected
 - undiagnosed -> diagnosed
 - o ill -> dead
- Transmission across networks

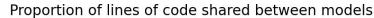


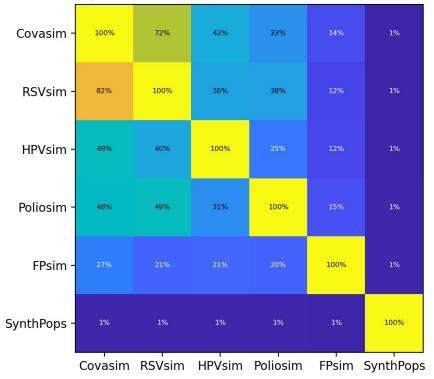


From Covasim to *sim

- Mature (released and in use)
 - Covasim (COVID)
 - **HPVsim** (human papillomavirus)
 - FPsim (family planning)
 - SynthPops (population modeling)
- Alpha (undergoing testing)
 - Poliosim (poliomyelitis)
 - o **STIsim**★ (all STIs + HIV)
- Pre-alpha (undergoing development)
 - o RSVsim★ (respiratory syncytial virus)
 - o **TBsim**★ (tuberculosis)
 - Typhoidsim★ (typhoid)

★ = Implemented with the Starsim framework







Design and implementation

Starsim architecture

Minimalist

A loose set of design principles and norms that underlie a suite of dynamic epi models

Intermediate

An interlocking set of modules that provide core functions to different epi models

Maximalist

A single unified codebase for dynamic modeling that covers many different aspects of health

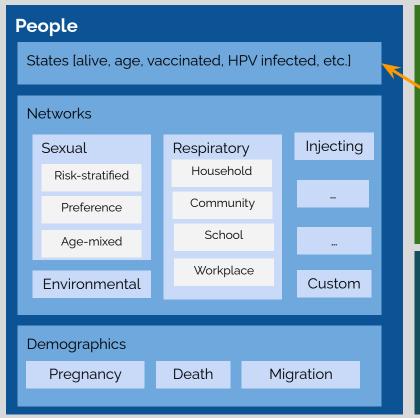
May 2023: Covasim, HPVsim, FPsim July 2024: We now think this is the sweet spot

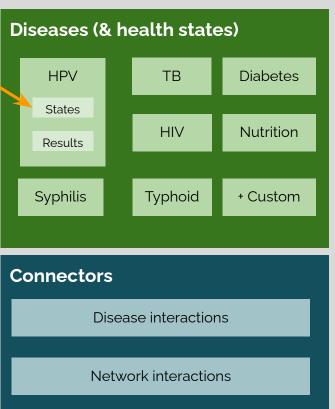
We originally thought this was the right approach

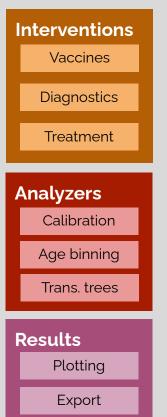


Starsim modular structure

Sim







Vision for Starsim

Starsim: IDM's next-generation agent-based model framework

To durably promote quantitative decision making...

We seek to build inclusive, collaborative, and open modeling communities...

Via tools that encourage innovation, scientific curiosity, and rapid exploration.

We take a **user-centric approach** to software design:

- 1. All aspects should be simple, intuitive, and accessible \rightarrow easier for ourselves and others
- Software should get out of the way of science, with simple solutions preferred → facilitates
 creativity and boldness in which scientific/policy questions to tackle
- 3. Embrace diverse users, from novice to elite \rightarrow we **cater to all levels** of technical expertise
- 4. Users trust us (rigor) and we trust them (power) \rightarrow we **don't need to control** every use case



Starsim's design philosophy

"Common tasks should be simple"

e.g.

- 1. Defining parameters
- 2. Running a simulation
- Plotting results

"...while uncommon tasks can't always be simple, but still should be possible" *e.g.*

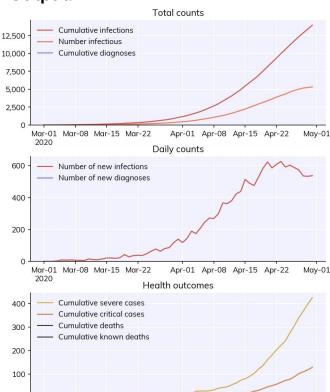
- Using a nonstandard distribution of viral load
- Writing a custom goodness-of-fit function
- 3. Defining a new population structure

code: import covasim as cv
sim = cv.Sim()
sim.run()
sim.plot()

Mar-01 Mar-08 Mar-15 Mar-22

2020

Output:



Apr-01 Apr-08 Apr-15 Apr-22

How **not** to write simulations in Python (or R)

- Slow implementation as "loop-de-loop":
 - On each timestep (n ≈ 700):
 - For each person (n ≈ 30,000):
 - For each state (n ≈ 30):
 - » Update! (1 billion times)
- Conceptually simple, fine in C++, but very inefficient in Python/R

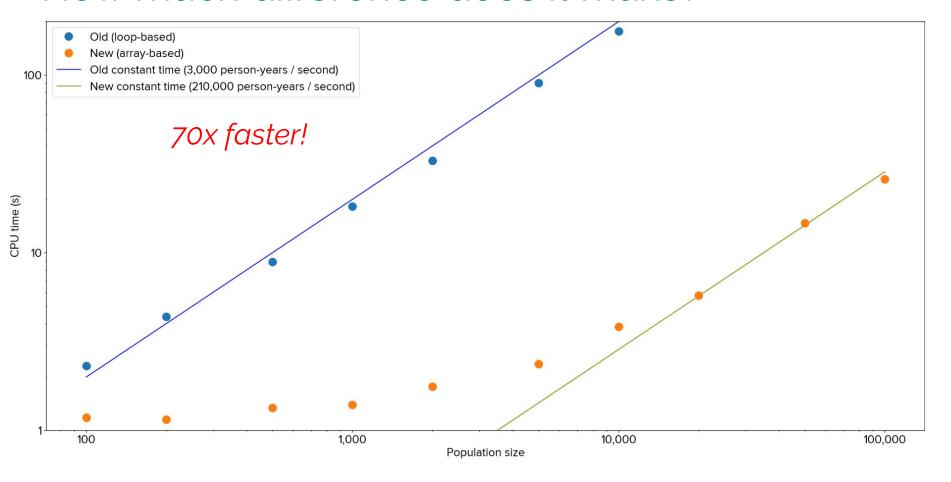
```
if self.alive: # Do not move through step if not alive
    self.age_person() # Age person in units of the timestep
    self.check mortality() # Decide if person dies
    if not self.alive:
        return self.step results
    if self.sex == 0 and self.age < self.pars['age limit fecundity']:</pre>
       if self.pregnant:
            self.check delivery() # Deliver with birth outcomes
            self.update pregnancy() # Advance gestation in timestep
            if not self.alive:
                return self.step_results
       if not self.pregnant:
            self.check_sexually_active()
           if self.pars['method_age']<=self.age<self.pars['age_lim_fecund']:</pre>
                self.update contraception(t, y)
            self.check lam()
            if self.sexually_active:
                self.check_conception() # Decide if conceives
            if self.postpartum:
                self.update postpartum() # Updates postpartum counter
        if self.lactating:
            self.update breastfeeding()
```

A better way to write simulations in Python

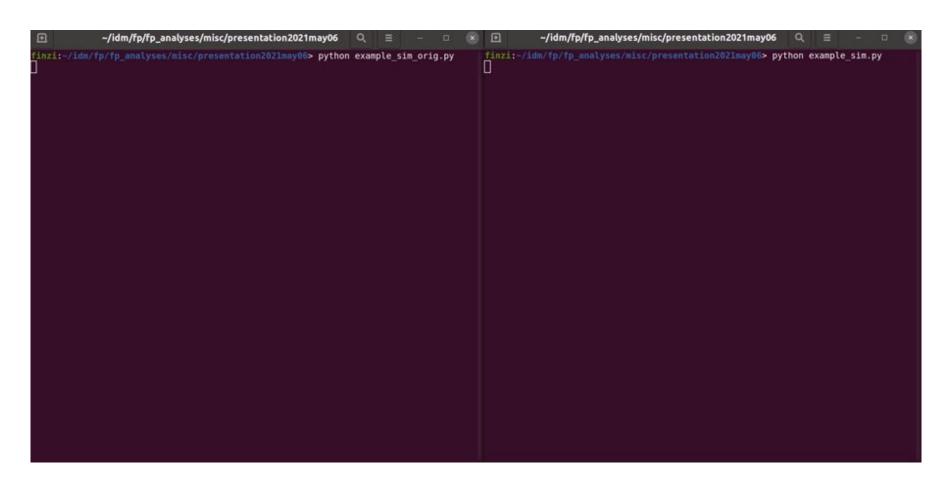
- Fast implementation via "arrayification":
 - On each timestep (n ≈ 700):
 - For each state (n ≈ 30):
 - Update everyone! (20,000 times)
- For loops become vector math, if statements become set operations
- Up to ~100x faster: as fast as C++ (plus shorter code!)

```
alive = self.alive.uids # "uids" is "universal identifiers"
self.age person(alive) # Age person in units of the timestep
self.check_mortality(alive) # Decide if person dies
within age = self.age < self.pars.age lim fecund # Within age limit
fecund = self.alive * (~self.sex) * within age.uids # sex==0 is female
preg = self.pregnant.uids
nonpreg = fecund - preg # Find the set difference
lact = self.lactating.uids
# Update everything
self.check delivery(preg) # Deliver with birth outcomes
self.update pregnancy(preg) # Advance gestation in timestep
self.check_sexually_active(nonpreg)
self.update contraception(nonpreg)
self.check lam(nonpreg)
self.update postpartum(nonpreg) # Updates postpartum counter
self.update_breastfeeding(lact)
self.check conception(nonpreg) # Decide if conceives
```

How much difference does it make?

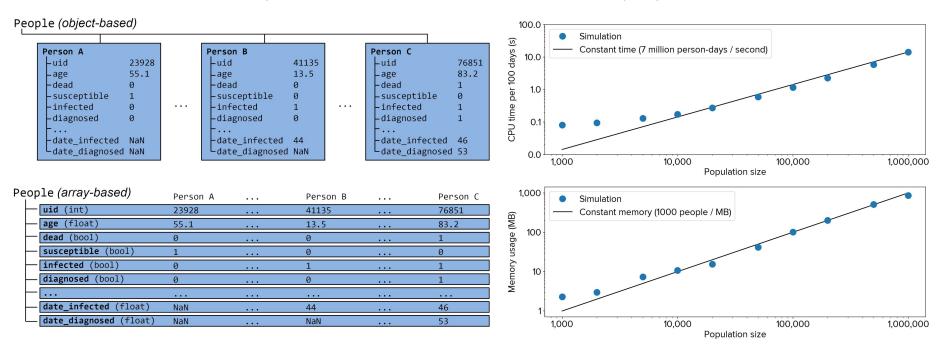


How much difference does it make?



Overall performance

- Implementation based on arrays (not objects) and Numba
- Pure Python, yet runs as fast as pure C/C++ models
- Feasible to run multiple realistic scenarios on standard laptop in minutes



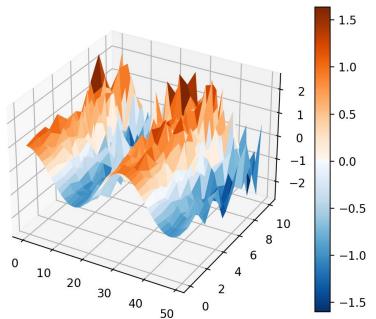


Powered by Sciris

Starsim uses <u>Sciris</u> to simplify common tasks







Instead of this:

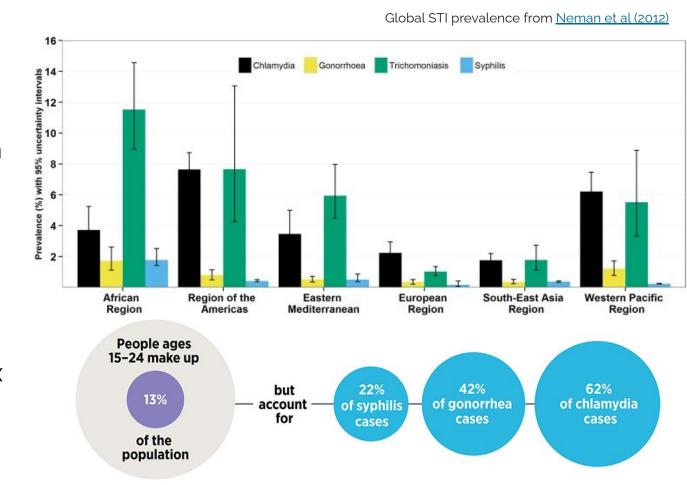
Do this:

Instead of this:		Do this:	
1 2	# Define random wave generator import numpy as np	1 2	# Define random wave generator import numpy as np
3 4 5 6	<pre>def randwave(std, xmin=0, xmax=10, npts=50): np.random.seed(int(100*std)) # Ensure differences between runs a = np.cos(np.linspace(xmin, xmax, npts)) b = np.random.randn(npts)</pre>	3 4 5 6	<pre>def randwave(std, xmin=0, xmax=10, npts=50): np.random.seed(int(100*std)) # Ensure differences between runs a = np.cos(np.linspace(xmin, xmax, npts)) b = np.random.randn(npts)</pre>
8	return a + b*std	8	return a + b*std
10	# Other imports	10	# Other imports
11 12 13 14 15 16	- import multiprocessing as mp - import pickle - import gzip - import matplotlib.pyplot as plt - from mpl_toolkits.mplot3d import Axes3D # Unused but must be imported	11	+ import sciris as sc
17		12	
18	# Start timing	13	# Start timing
19	- start = time.time()	14	+ T = sc.timer()
21	# Calculate output in parallel	16	# Calculate output in parallel
22	- multipool = mp.Pool(processes=mp.cpu_count())	17	+ waves = sc.parallelize(randwave, np.linspace(0, 1, 11))
23 24 25	<pre>- waves = multipool.map(randwave, np.linspace(0, 1, 11)) - multipool.close() - multipool.join()</pre>		
26		18	
27	# Save to files - filenames = []	19	<pre># Save to files + filenames = [sc.save(f'wave{i}.obj', wave) for i,wave in enumerate(waves)]</pre>
29 30 31 32 33	- filenames = [] - for i,wave in enumerate(waves): - filename = f'wave(i).obj' - with grip.GripFlle(filename, 'wb') as fileobj: - fileobj.write(pickle.dumps(wave)) - filenames.append(filename)	20	+ filenames = [sc.save(f wave(1):00] , wave) for 1, wave in enumerate(waves)]
34		21	
35	# Create dict from files	22	# Create dict from files
36 37 38 39 40	- dat_dict = {} - for fname in filenames: - with gzip.GzipFile(fname) as fileobj: - filestring = fileobj.read() - data_dict[fname] = pickle.loads(filestring)		+ data = sc.odict({fname:sc.load(fname) for fname in filenames})
41	# Create 3D plot	24	# Create 3D plot
43	- data = np.array([data_dict[fname] for fname in filenames])		+ sc.surf3d(data[:], cmap='orangeblue')
44 45 46 47 48 49 50 51	- fig = plt.figure() - ax = plt.axes(projection='3d') - ny,nx = np.array(data).shape - x = np.arange(nx) - y = np.arange(nx) - y = np.arange(nx) - x, y = np.meshgrid(x, y) - surf = ax.plot_surface(X, Y, data, cmap='coolwarm') - fig.colorbar(surf)	20	- Action (Action (Action) of the Country of the Cou
52		27	
53	# Print elapsed time	28	# Print elapsed time
	- elapsed = time.time() - start - print(f'Elapsed time: {elapsed:0.1f} s')	29	+ T.toc()

Application: Modeling co-circulating STIs

Global burden of STIs

- >1 million new
 STIs every day
- >1 million
 pregnant women
 with syphilis in
 2016; ~350,000
 adverse birth
 outcomes
- Burden varies by country/age/sex



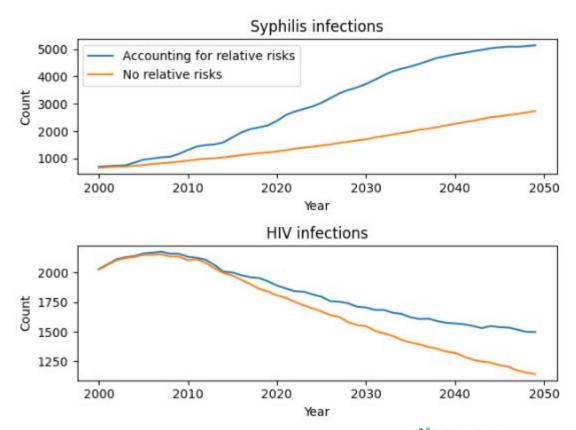
Example policy questions

- How many DALYs would be averted by improved syphilis diagnostics?
 - Better syphilis control → better HIV control: combined DALY impact
- What is the optimal combination of STI diagnostics and treatments to offer via antenatal clinics to minimize negative birth outcomes?
 - Need to consider cross-cutting interventions
 - Must capture co-transmission
- Which populations are contributing most to onward transmission of STIs, and should be prioritized for testing and treatment?
 - Need to capture transmission pathways and network effects



Modeling HIV and syphilis

- Syphilis infection increases the risk of HIV acquisition (~2.7x rel risk)
- Diagnosis of early syphilis carries a high risk of consequent HIV
- Accounting for these effects, we see increased transmission

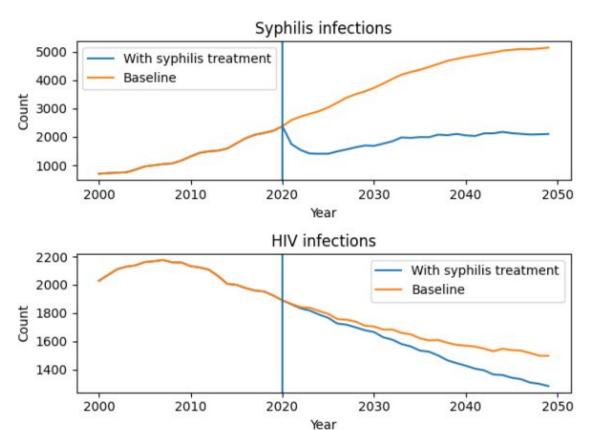




Modeling syphilis treatment and HIV

 Syphilis treatment can moderate HIV transmission

 Modeling the secondary effects of treatment for one disease on burden of related diseases captures the true impact





Summary

Limitations and discussion

- Have not spoken about calibration or validation, critical components of turning a modeling framework into a model
 - Starsim has built-in calibration methods, but your mileage may vary
- Starsim is still very much in development, please give us feedback and we welcome any and all collaboration!
- Underlying philosophy drove practical user-centric design decisions
- Next phases: Applications, ongoing refinement
- Open question: Should we think of Starsim as a general-purpose agent-based model?



Starsim access

Code:

Starsim: https://starsim.org/

Covasim: http://covasim.org

FPsim: http://fpsim.org

HPVsim: http://hpvsim.org

Documentation/tutorials:

- Starsim: http://docs.starsim.org

Covasim: http://docs.covasim.org

FPsim: http://docs.fpsim.org

HPVsim: http://docs.hpvsim.org

Methods papers:

Covasim: Kerr et al 2021, PLoS CB

- FPsim: O'Brien et al 2023, npj Women's Health

- HPVsim: Stuart et al 2024, PLoS CB

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Contributors 19



Thank you!

