Using agent-based modeling to understand HIV transmission, care, and prevention

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Outline

- **Introduction** – why mathematical modelling in epidemics
- **Overview of EMOD**
- **Overview of STI-HIV model in EMOD**
- **Results**:
  - Role of voluntary male medical circumcision (VMMC) in reducing HIV incidence and ensuring a sustainable response
  - PrEP
- **Conclusions**

Introduction – why mathematical modelling in epidemics

Understand health care system

Number on treatment by demographic

Suppression rates, fate of those LTFU

Measured incidence patterns

Challenges of new assays

Biases from sampling, consent

TRIANGULATE
in an epidemiologically consistent way

Impact on survival and transmission

Cohort studies of survival, suppression

Transmission studies controlling for suppression

Measured mortality

Challenges of assigning cause of death as conditions change

INSTITUTE FOR DISEASE MODELING
INTELLECTUAL VENTURES

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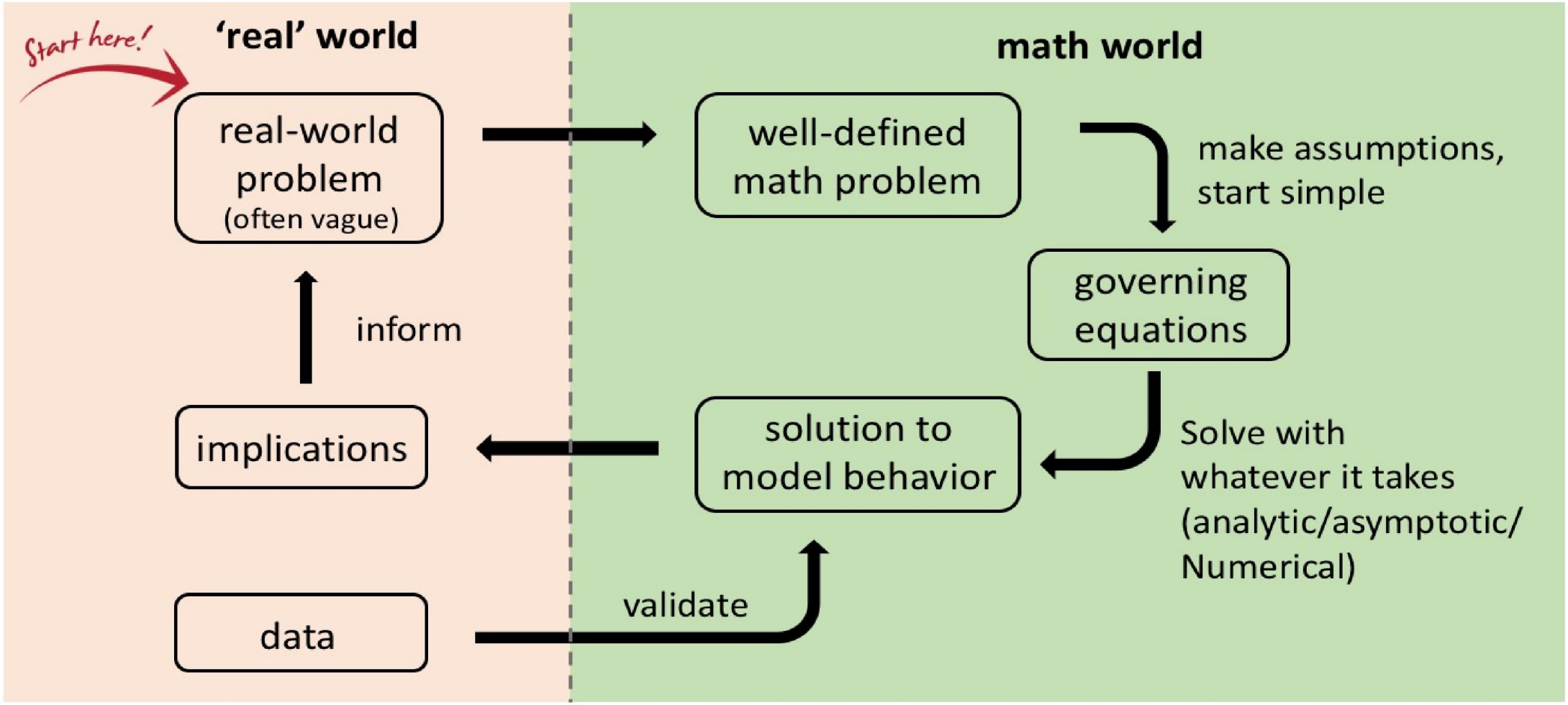
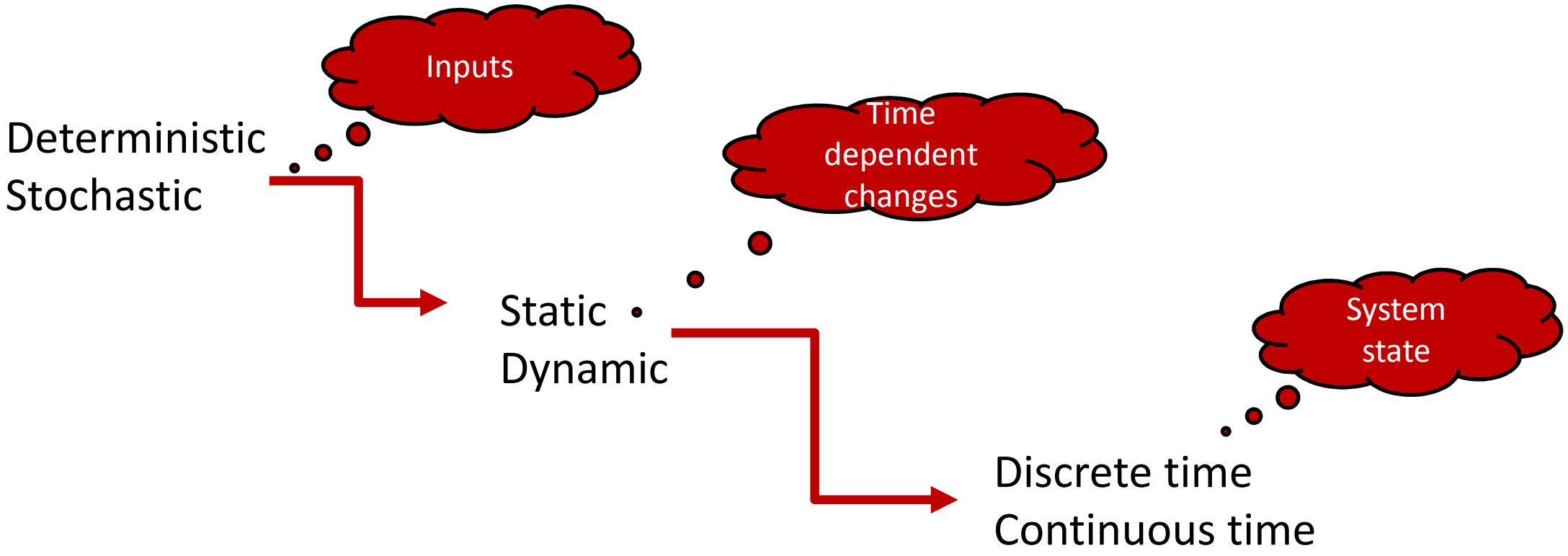
Typical mathematical modeling process



http://www.vcyang.com/model_flowchart/

Mathematical Models

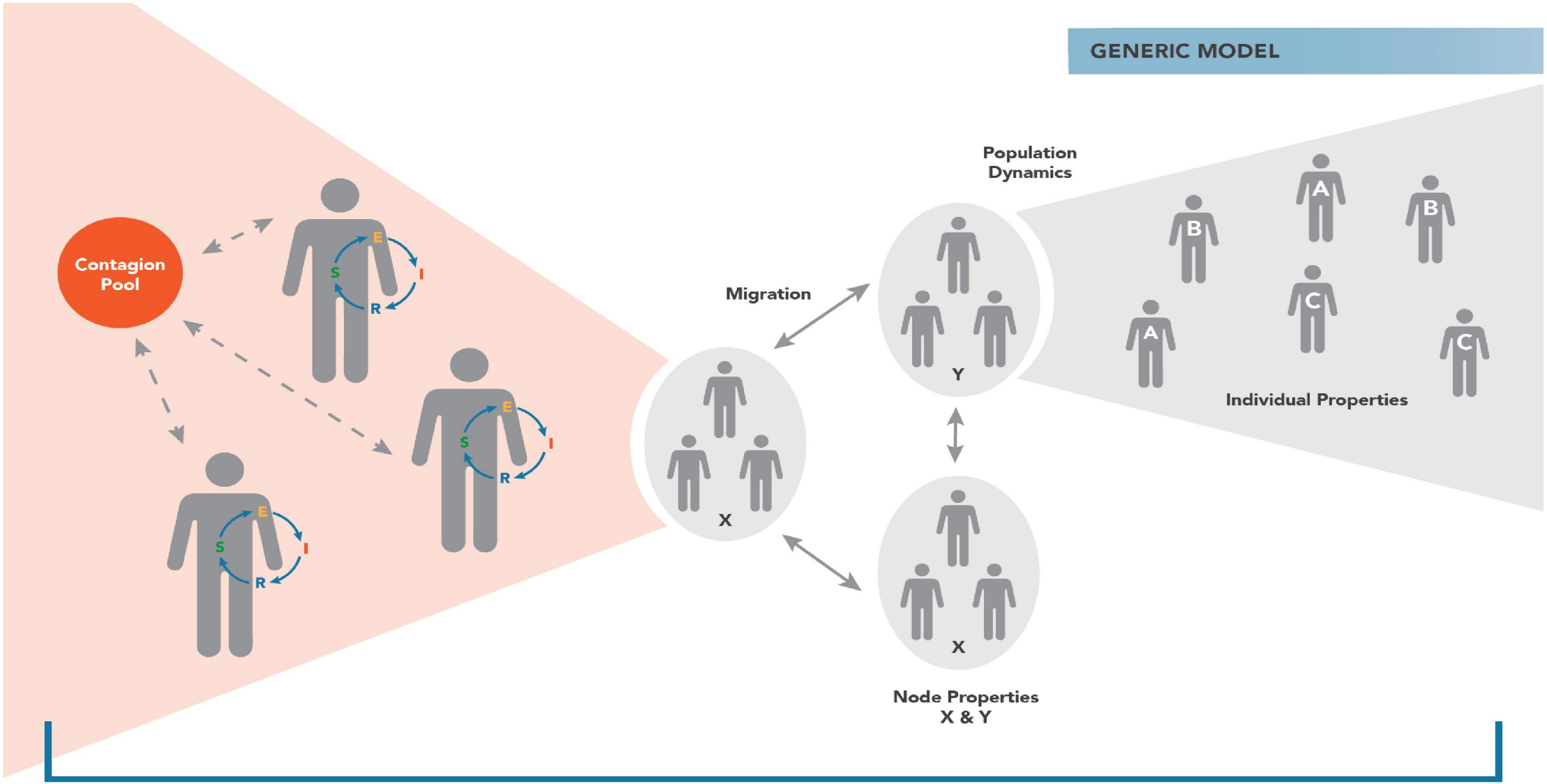


- Mathematical models are further classified into compartmental or agent-based models.

EMOD: Institute for Disease Modeling (IDM)

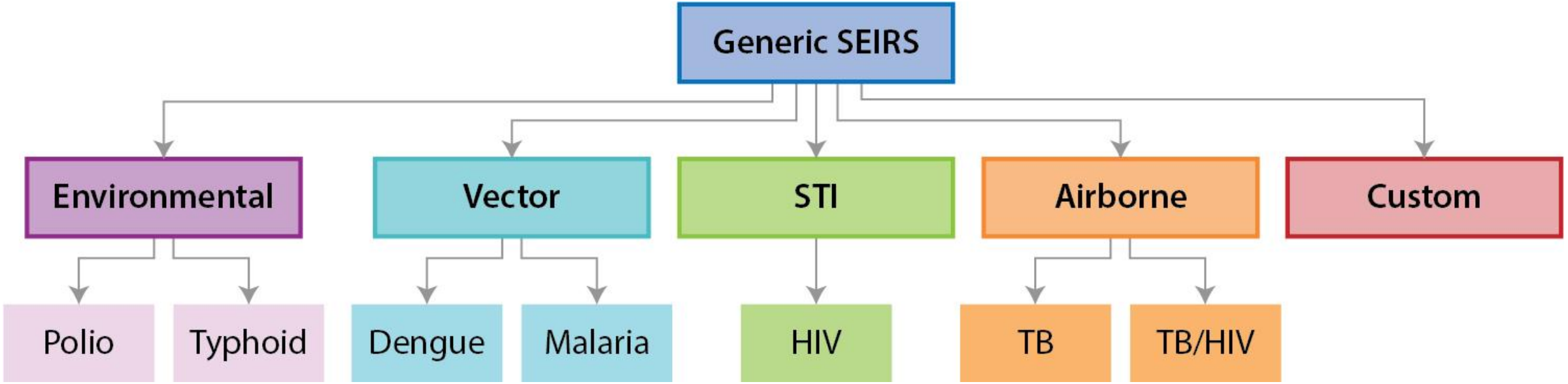
- Founded in 2007 to support Gates Foundation initiative to eradicate malaria
- Not-for-profit research group hosted within a private company, Intellectual Ventures
- Grew to ~100-person institute dedicated to quantitative analysis for global disease control and eradication
    - 2/3 research and policy “think tank”
    - 1/3 software “startup”
- Create professionally built and tested, re-usable tools
- Give them away for free: www.idmod.org and www.github.com/InstituteForDiseaseModeling

Overview of EMOD



Bershteyn et al., *Pathogens and Disease,* 2018.
https://europepmc.org/abstract/med/29986020

Overview of EMOD



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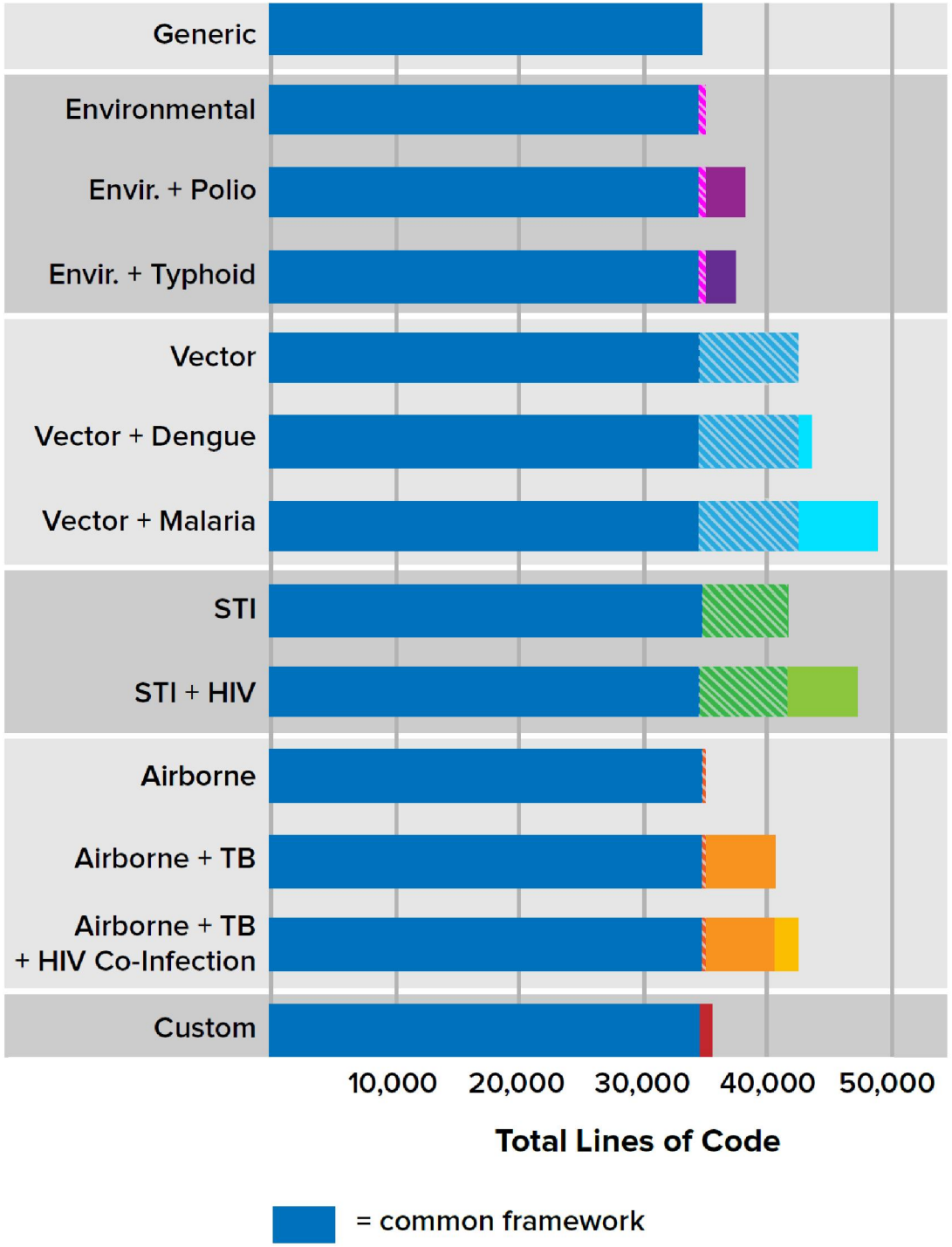
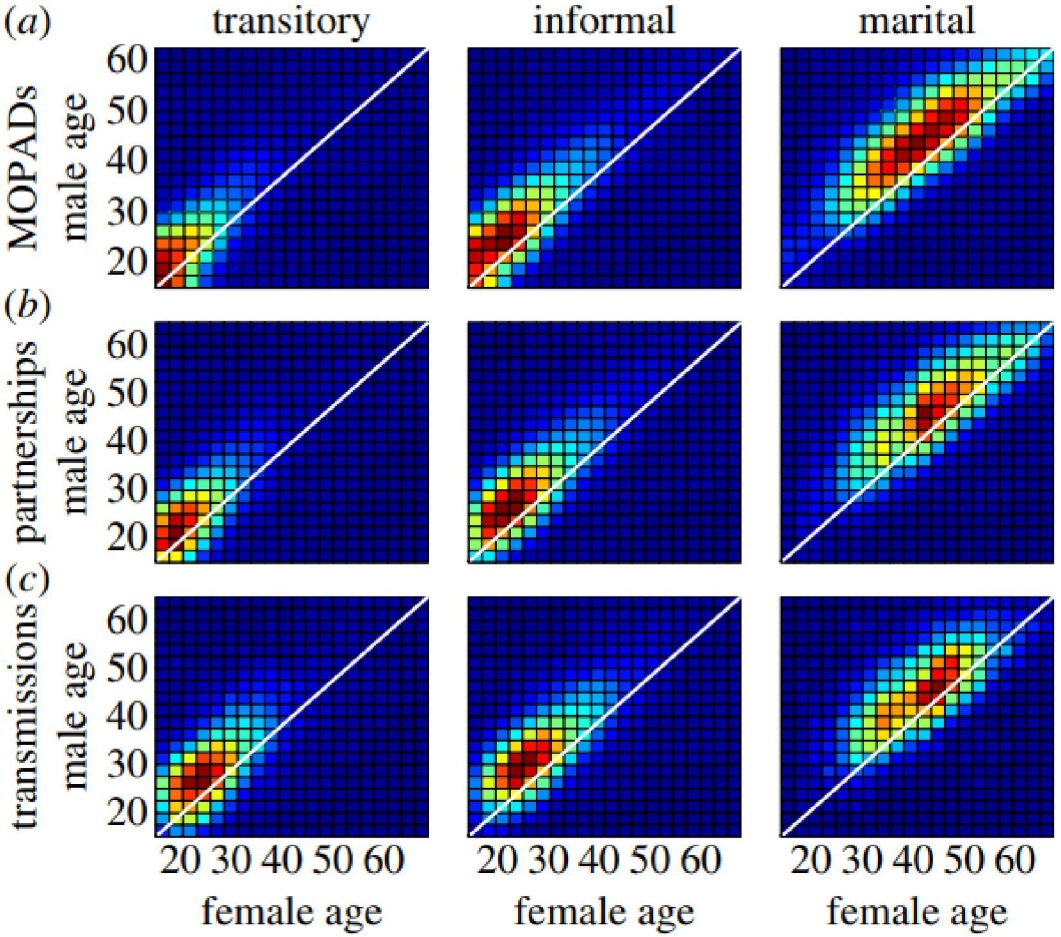


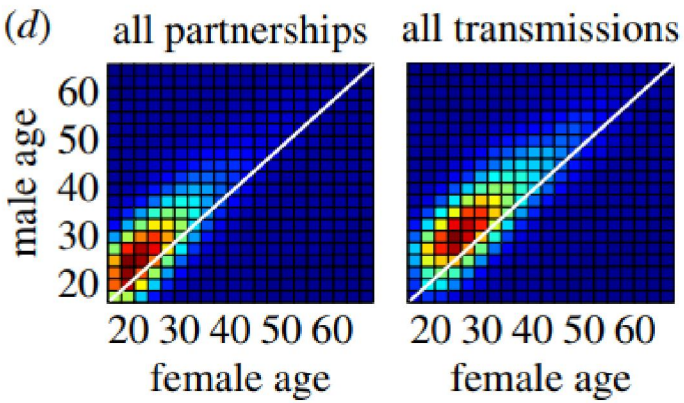
Shared across EMOD

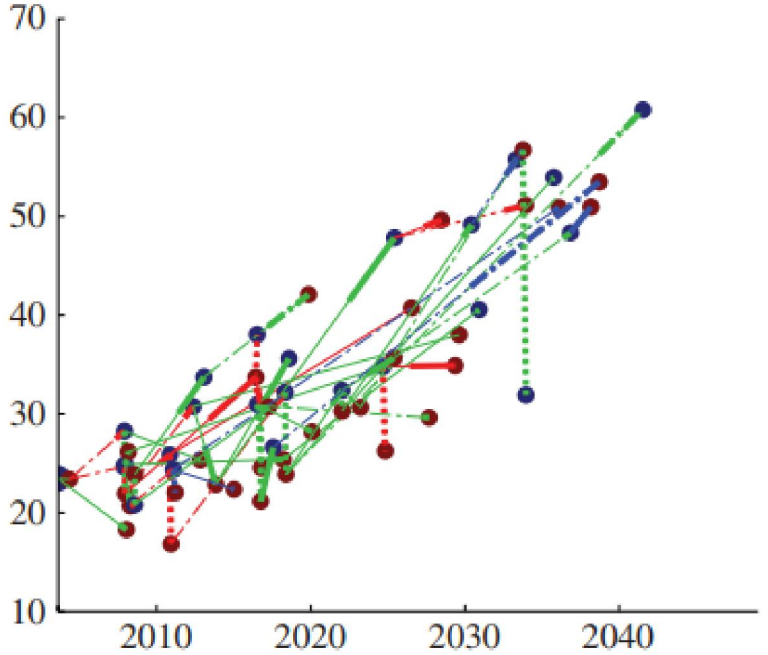
www.github.com/InstituteForDiseaseModeling

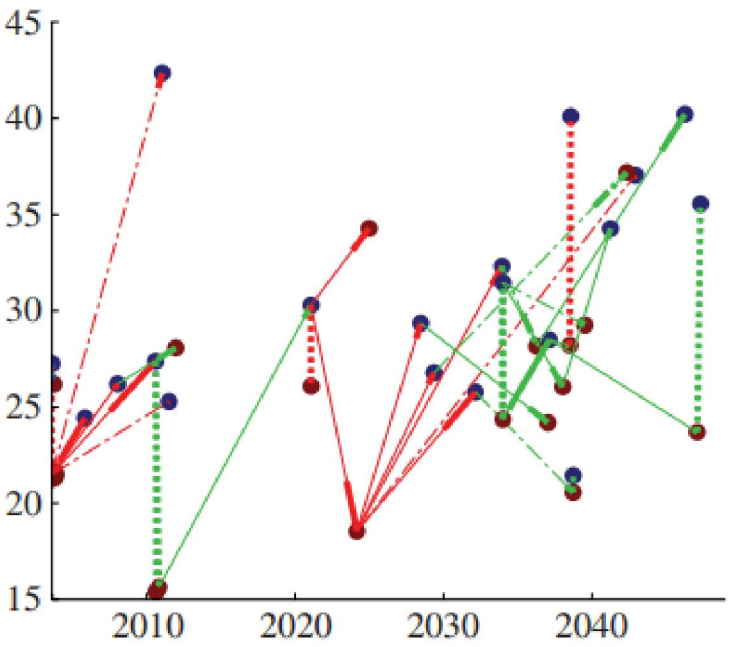
- > 600 regression tests
- > 140 scientific feature tests
  - "black box" testing
  - E.g. Kolmogorov-Smirnov test of a statistical distribution after random perturbation
- > 40 component tests
  - a.k.a. unit tests, instantiates a subset of the code base in isolation
  - "white box" testing
  - examine software components that are not user-facing, such as unique identifiers for individuals
- Extensive online documentation
  - Tutorials www.idmod.org
  - Parameter definitions, units, and ranges

Bershteyn et al., *Pathogens and Disease,* 2018
https://europepmc.org/abstract/med/29986020

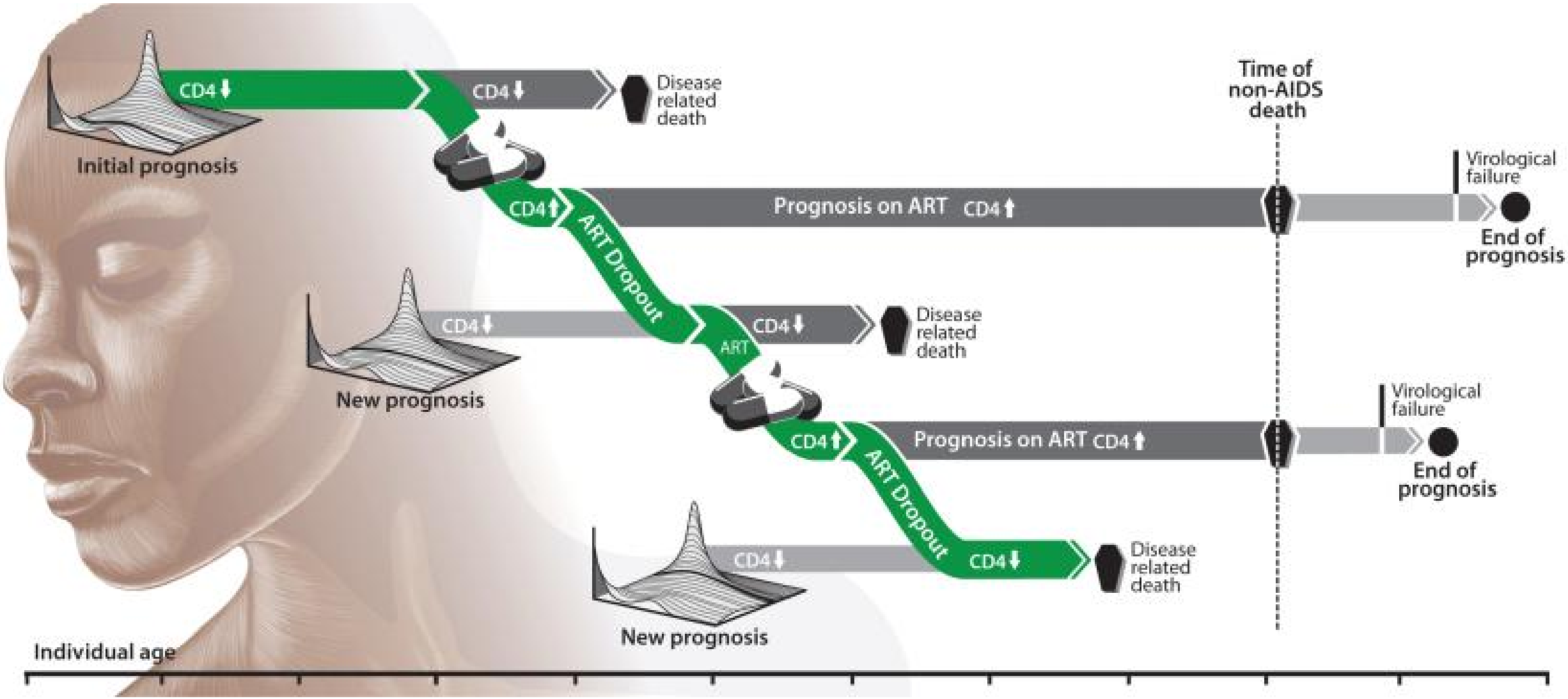


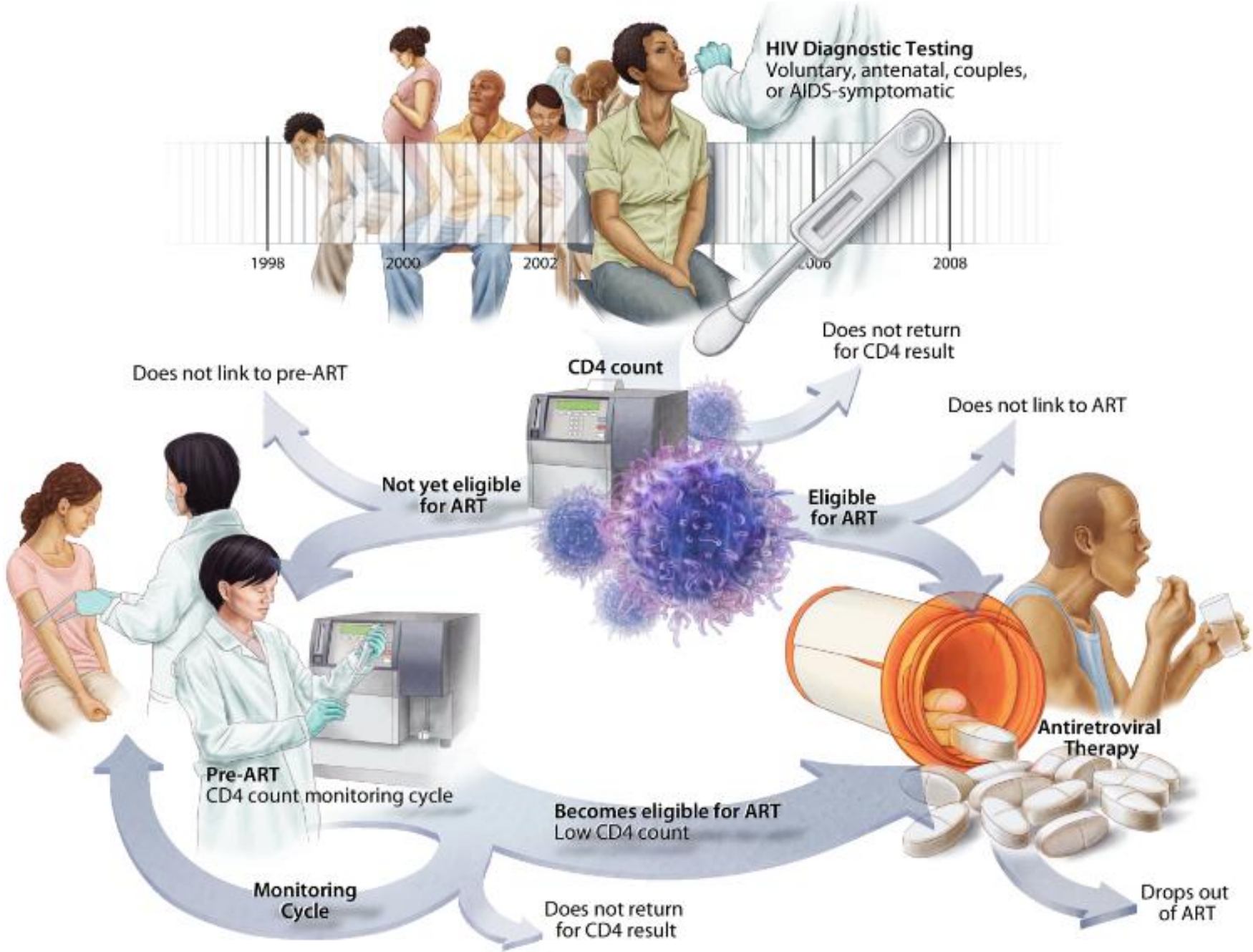




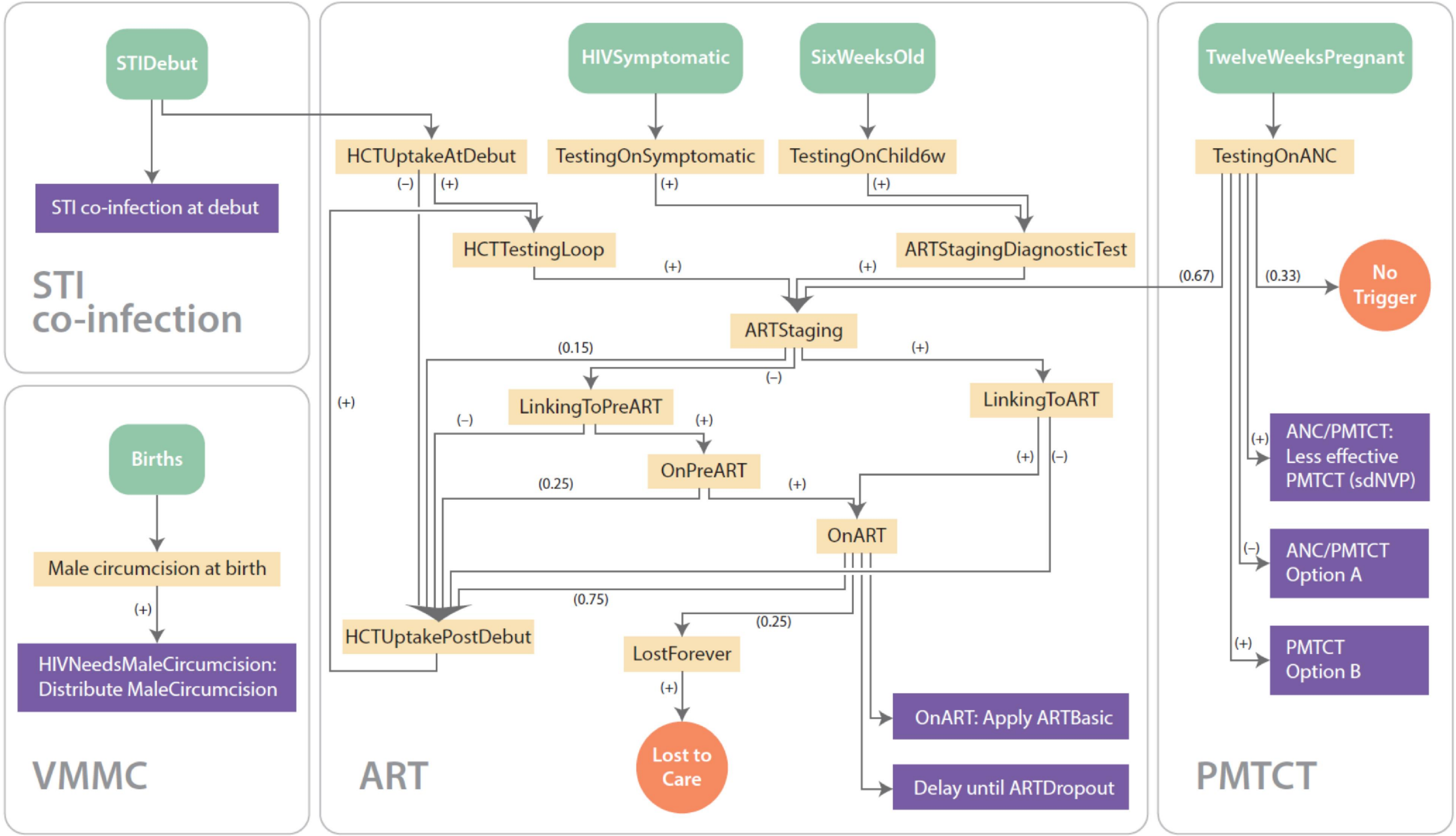


Bershteyn et al, *J. Royal Soc. Interface* 2013


CD4
Initial prognosis
CD4
Disease related death
Time of non-AIDS death
CD4
ART Dropout
Prognosis on ART CD4
Virological failure
End of prognosis
CD4
New prognosis
CD4
Disease related death
ART
CD4
ART Dropout
Prognosis on ART CD4
Virological failure
End of prognosis
CD4
New prognosis
CD4
Disease related death
Individual age



Klein, Bershteyn, and Eckhoff, *AIDS* 2014.


STIDebut
STI co-infection at debut
STI co-infection
Births
Male circumcision at birth
(+)
HIVNeedsMaleCircumcision: Distribute MaleCircumcision
VMMC
HIVSymptomatic
SixWeeksOld
HCTUptakeAtDebut
TestingOnSymptomatic
TestingOnChild6w
(–)
(+)
(+)
(+)
HCTTestingLoop
ARTStagingDiagnosticTest
(+)
(+)
ARTStaging
(0.15)
(+)
(–)
(+)
LinkingToPreART
LinkingToART
(–)
(+)
(+)
(–)
OnPreART
(0.25)
(+)
OnART
(0.75)
(0.25)
HCTUptakePostDebut
LostForever
(+)
Lost to Care
OnART: Apply ARTBasic
Delay until ARTDropout
ART
TwelveWeeksPregnant
TestingOnANC
(0.67)
(0.33)
No Trigger
(+)
ANC/PMTCT: Less effective PMTCT (sdNVP)
(–)
ANC/PMTCT Option A
(+)
PMTCT Option B
PMTCT

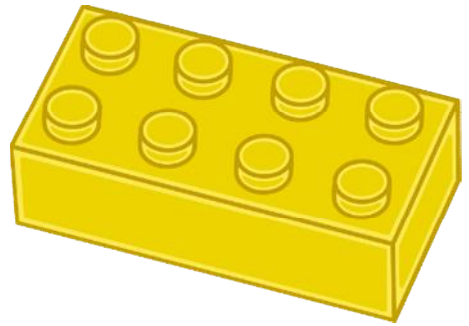
Connecting blocks using triggers

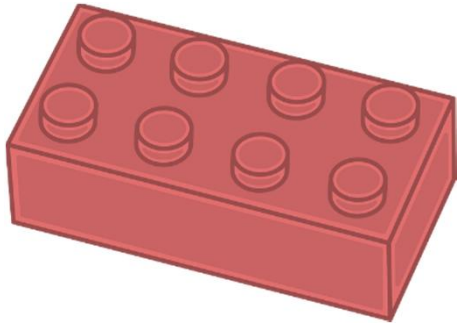
Inside the model

Broadcasts an event

e.g., pregnancy, new infection, AIDS symptoms

Listens for the event

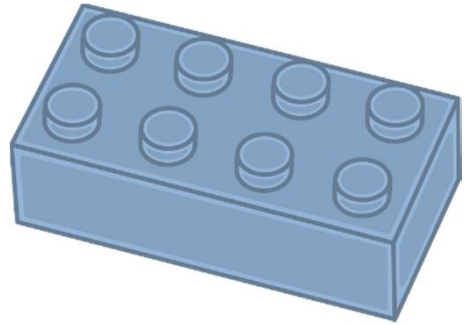




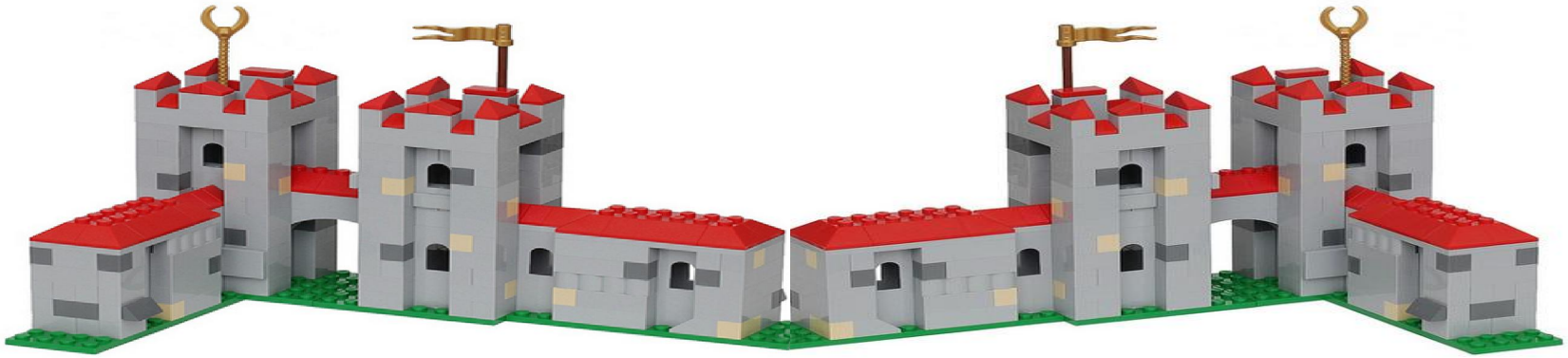
Broadcasts an event

e.g., MyCustomEvent

Listens for the event



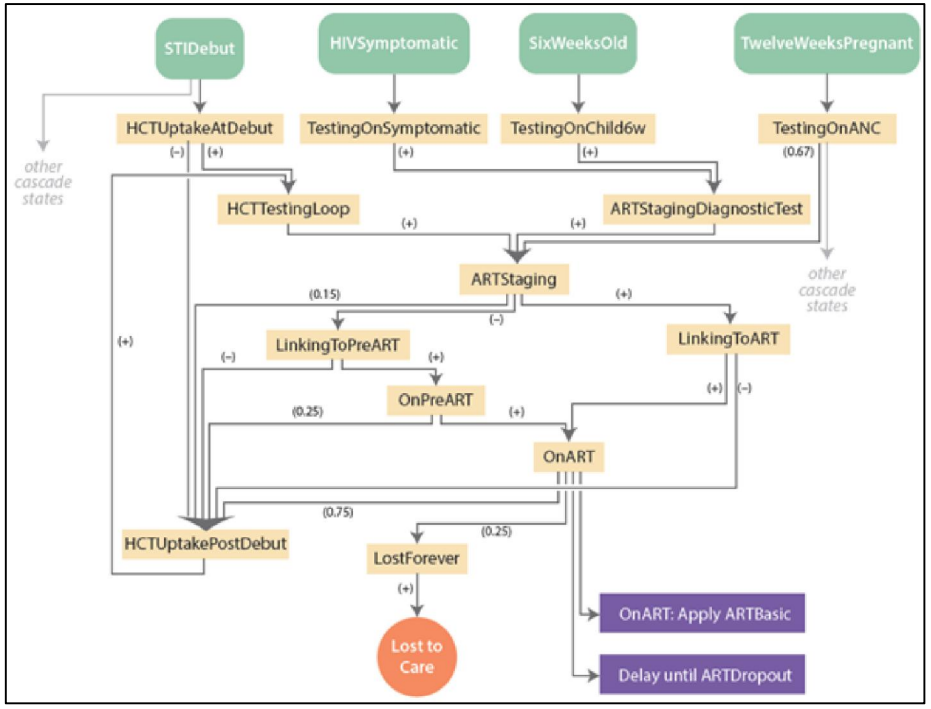
Build up complex health care systems

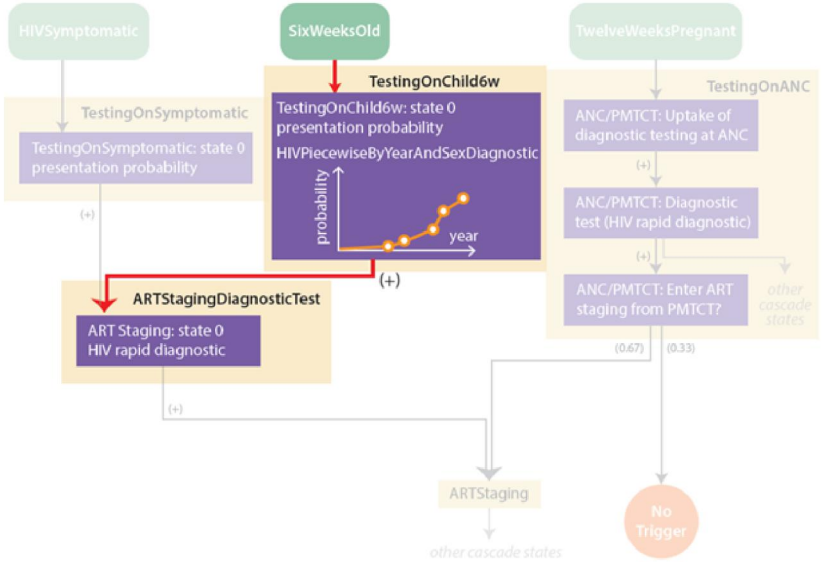


Building Blocks of the Health Care System

Image credit:“ Brand new bricks ” by fdecomite, CC BY 2.0 .

{ When
{ Who
{ Why
{ What
Tx, Dx, Prevention, Delay, Filter, f(t) }
}
}
}



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{
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    },
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        "Intervention_Config": {
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            "Property_Restrictions_Within_Node": [
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                }
            ],
            "Trigger_Condition_List": [
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            ],
            "Actual_IndividualIntervention_Config": {
                "class": "HIVPiecewiseByYearAndSexDiagnostic",
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                    "Values":[0,    0.03, 0.1,  0.2,  0.3365]
                },
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                    "CascadeState:OnART",
                    "CascadeState:LinkingToART",
                    "CascadeState:OnPreART",
                    "CascadeState:LinkingToPreART",
                    "CascadeState:ARTStaging",
                    "CascadeState:TestingOnSymptomatic"
                ],
                "Positive_Diagnosis_Event": "ARTStagingDiagnosticTest",
                "New_Property_Value": "CascadeState:TestingOnChild6w"
            }
        }
    }
},
```

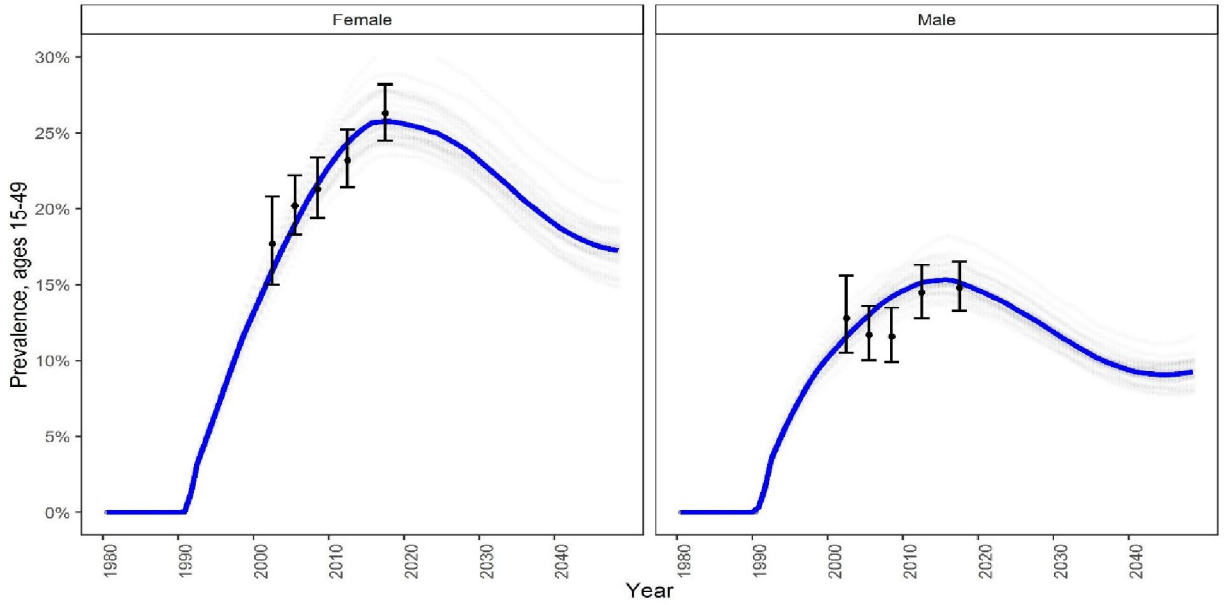

When

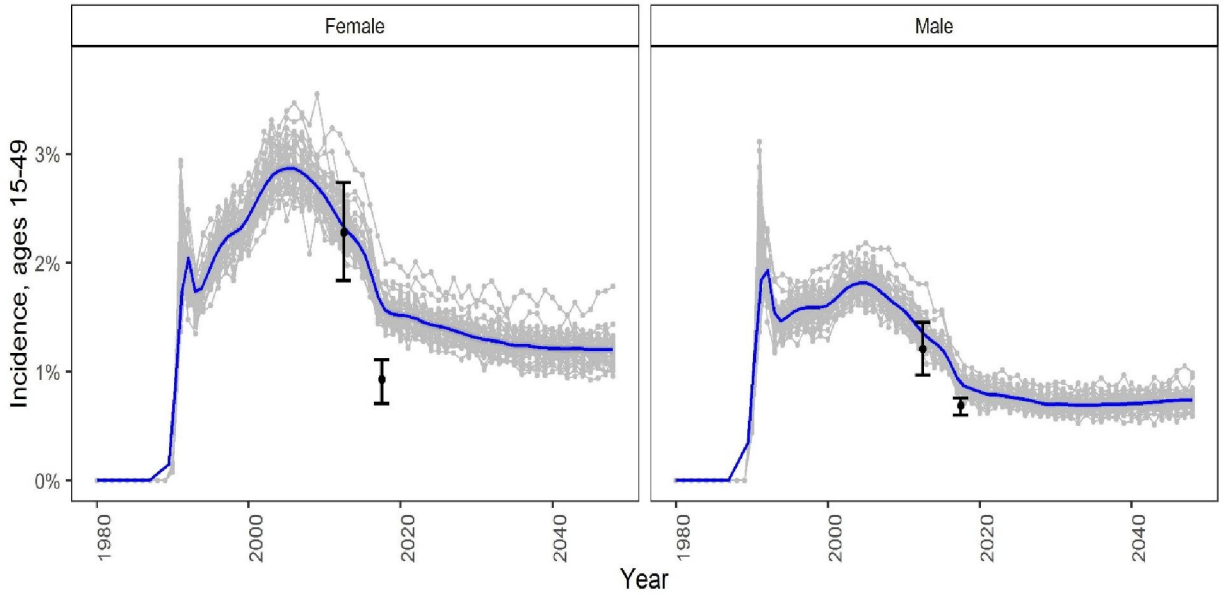
Who

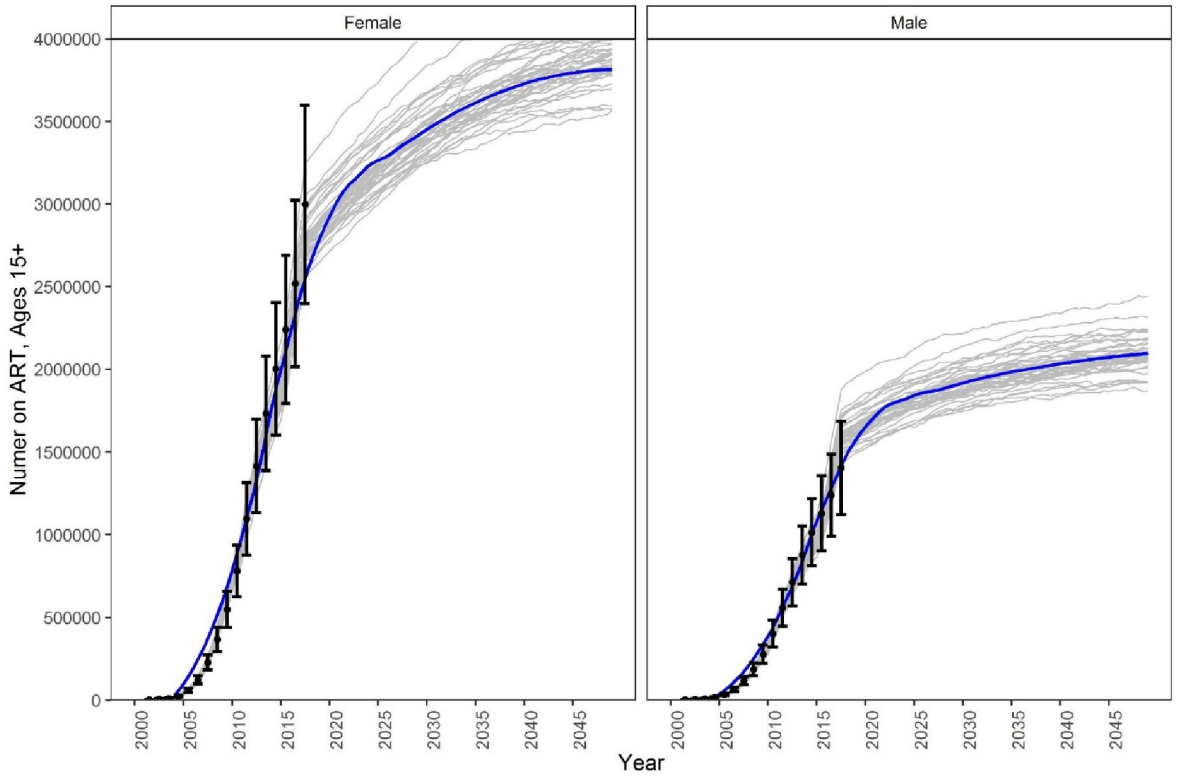
Why

What

Example of model calibration: SA national







Conclusions

- Individual-based modeling can be used to evaluate interventions like ART, VMMC, and PrEP in the context of setting-specific transmission
- New tools and strategies will be needed to dramatically reduce HIV incidence and burden for long-term epidemic control, EMOD can be used to test the new tools and strategies
- EMOD is a resource to the community to test hypotheses, understand broader implications of new evidence, and evaluate intervention strategies

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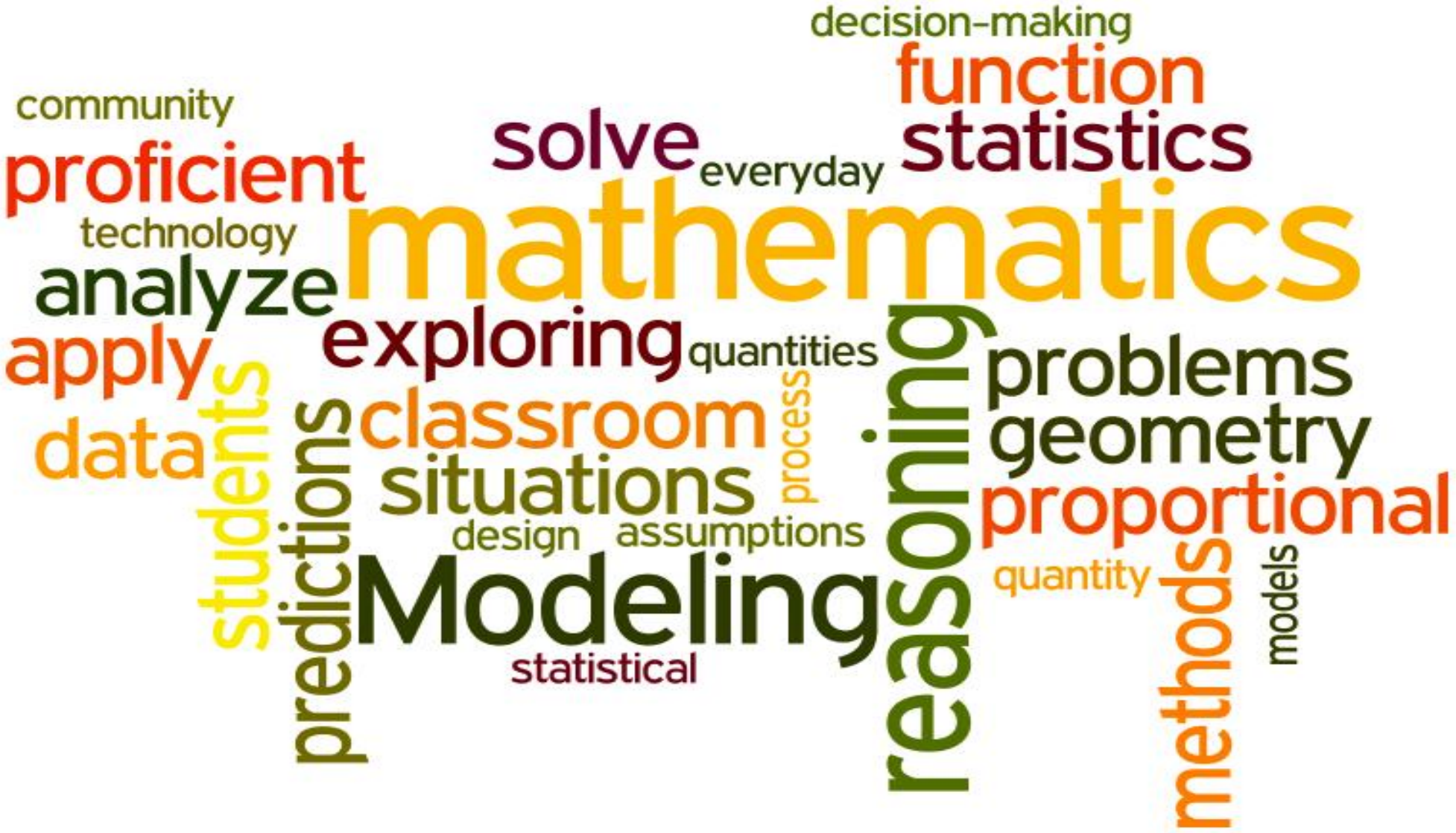
Thank you… and happy to take questions