

A Data-Driven Approach to Getting to Zero: Modeling Cost-Effectiveness of HIV Prevention and Treatment Strategies in Los Angeles County

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On behalf of the UCLA-USC-DHSP partnership team

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Agenda

- Information about the overall project, its goals and objectives
- Specifics about the modeling approach: methods, analyses
- Discussion of next steps and analyses to be conducted

UCLA-USC-DHSP partnership

- Generously supported by seed grant from the UCLA Center for AIDS Research (CFAR), UCLAAIDS Institute and the Keck School of Medicine of USC (*A collaboration to model the impact and cost-effectiveness of approaches to meet the Los Angeles County HIV/AIDS “Strategy for 2020 and Beyond”*)
- PIs: Corrina Moucheraud (UCLA), Sze-chuan Suen, USC
- Co-investigators: Arleen Leibowitz, Nina Harawa, Ian Holloway, Diane Tan (UCLA); Neeraj Sood (USC); Emmanuel Drabo (Johns Hopkins); Wendy Garland, Yuwen Yue (DHSP)

Why and when are models helpful?

- Diseases have complex dynamics
 - Entry and exit from the population
 - Demographically dependent rates of transition
 - Behavior may influence treatment uptake and adherence
 - Transmission patterns may vary across groups within the population
- Uncertainty in estimates
 - Prevalence, incidence, adherence to treatment
 - Transmission patterns may be unknown
- Variety of response approaches
 - Need to model different interventions

But, need policy recommendations!

How can we use models to inform decision-making?

- **Rigorously evaluate tradeoffs between costs and outcomes of alternative HIV treatment/prevention strategies**
 - Epidemic and health outcomes
 - Resource use (costs)
 - Cost and benefit tradeoffs of alternative interventions
 - Cost per infection averted, or HIV-related death averted
 - Incremental cost-effectiveness ratio (incremental cost per QALY gained)
- **Examine heterogeneities in disease risk and intervention effects**
 - e.g., across geographic or risk groups
- **Help identify combination and intensity of interventions that may help achieve the 2020 strategic goals**
 - Optimal combination of interventions

General approach to modeling

- **Apply systems science methods to model reality**
 - A model is a simplified representation (abstraction) of reality
 - Synthesize high-quality data and use this to compare hypothetical outcomes from “what if” scenarios
- **We are going to tell you about a model we’ve built – and one we are developing – and then discuss your ideas for how such models can be most useful for LAC**

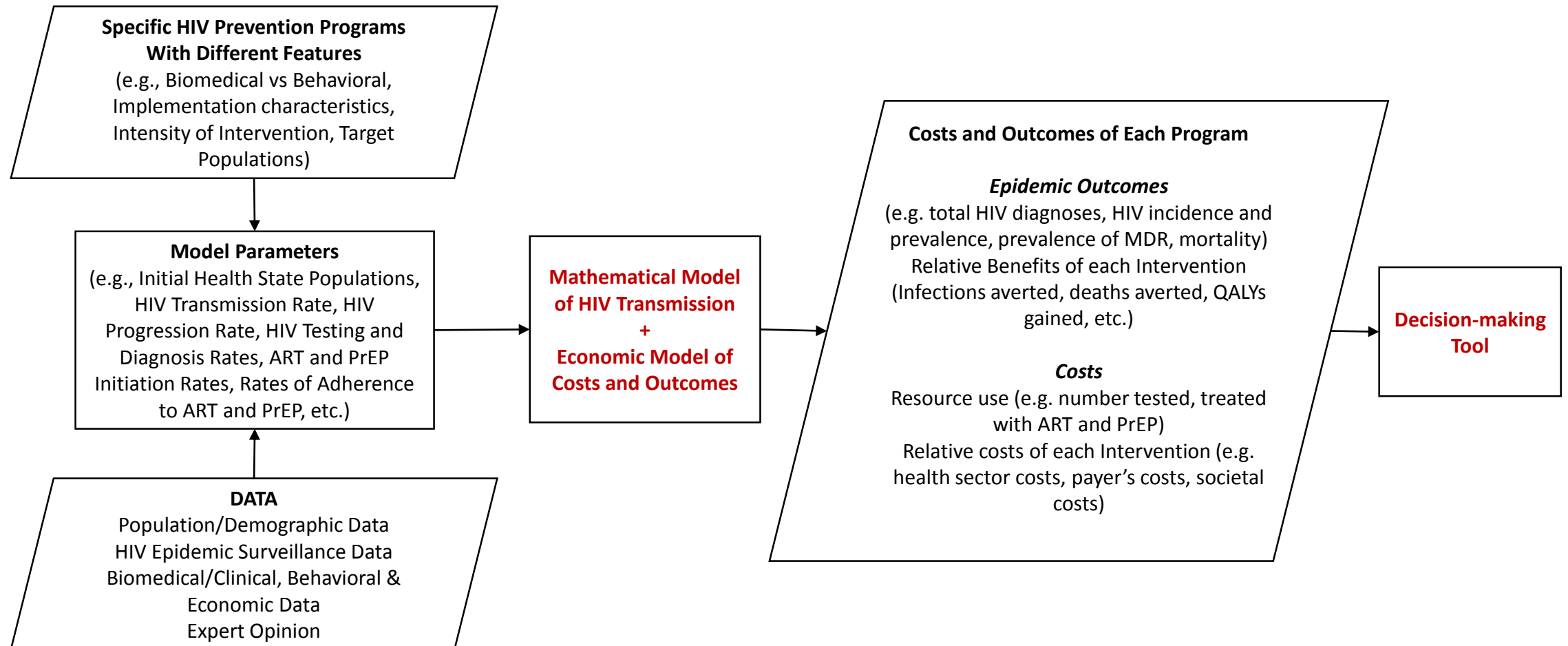
Model Overview

- **Model:** Compartmental model of HIV transmission & Economic model
 - Extension of model used in Sood et al. 2013 and Drabo et al. 2016
- **Population:** Los Angeles County MSM, aged 15–65 y
- **Evaluation Period:** 2013-2033
- **Outcomes and measures:**
 - Cumulative HIV incidence and HIV infections averted
 - Discounted costs and quality-adjusted life years (QALYs)
 - Incremental cost-effectiveness ratios (ICERs)

$$\bullet ICER_{i,j} = \frac{PV(Costs_j) - PV(Costs_i)}{PV(QALYs_j) - PV(QALYs_i)}$$

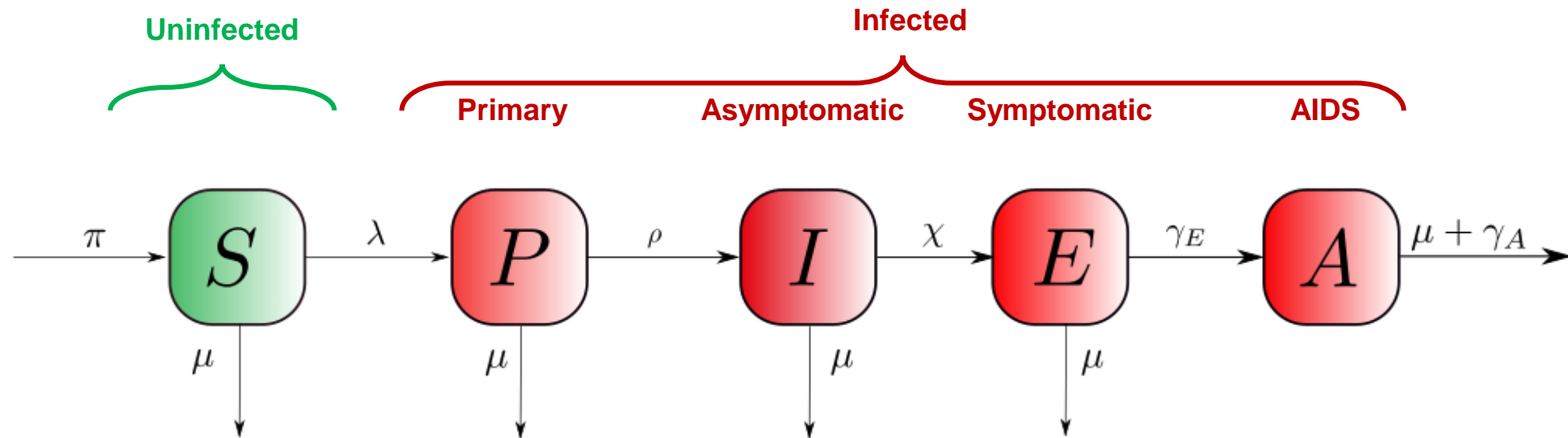
Structural Overview

- A mathematical model of HIV transmission among MSM (15-65 y) in Los Angeles County
- Economic model of costs and outcomes of HIV prevention strategies



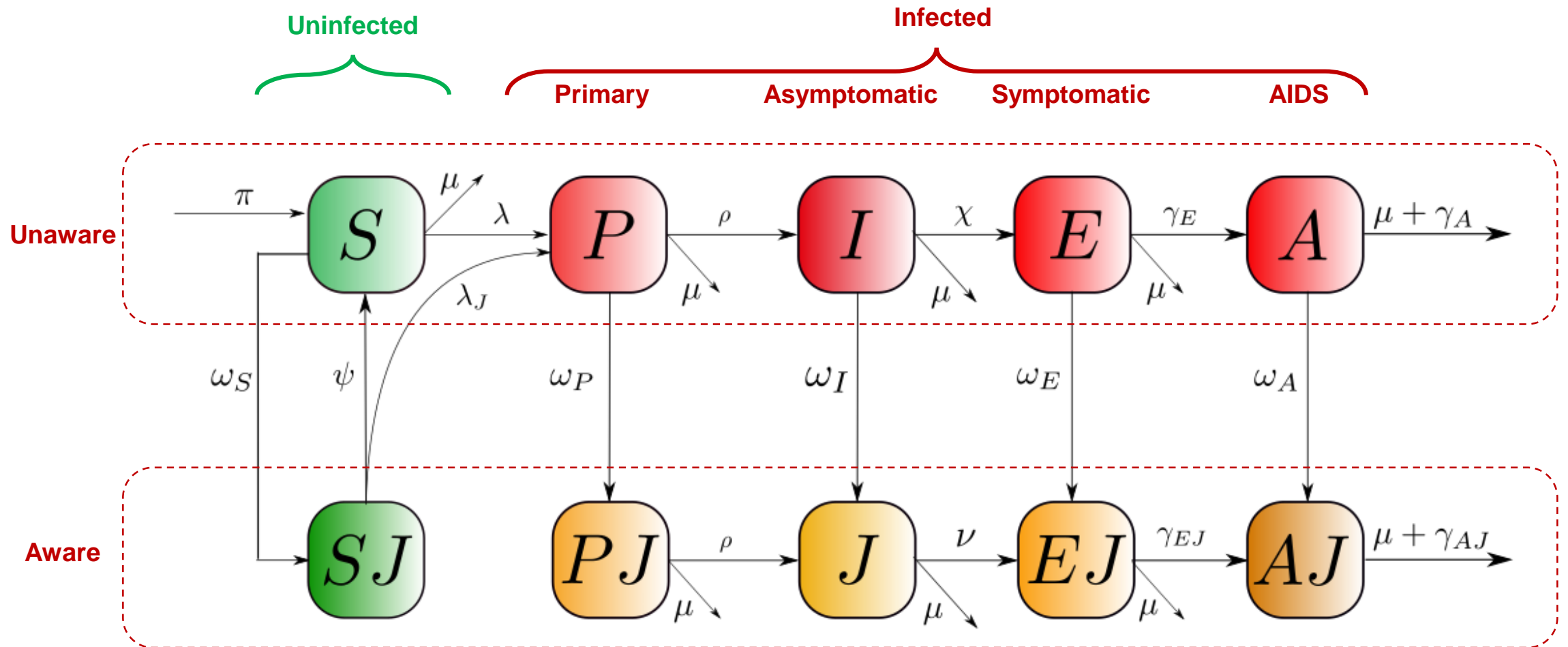
USC-LAC HIV Transmission Model – Overview

- Men enter model through aging and discovery of sexual orientation (rate π)
- They can transition between uninfected and infected health states at specific rates
- They exit the model through natural death or death from HIV complications (rates π and γ_A)



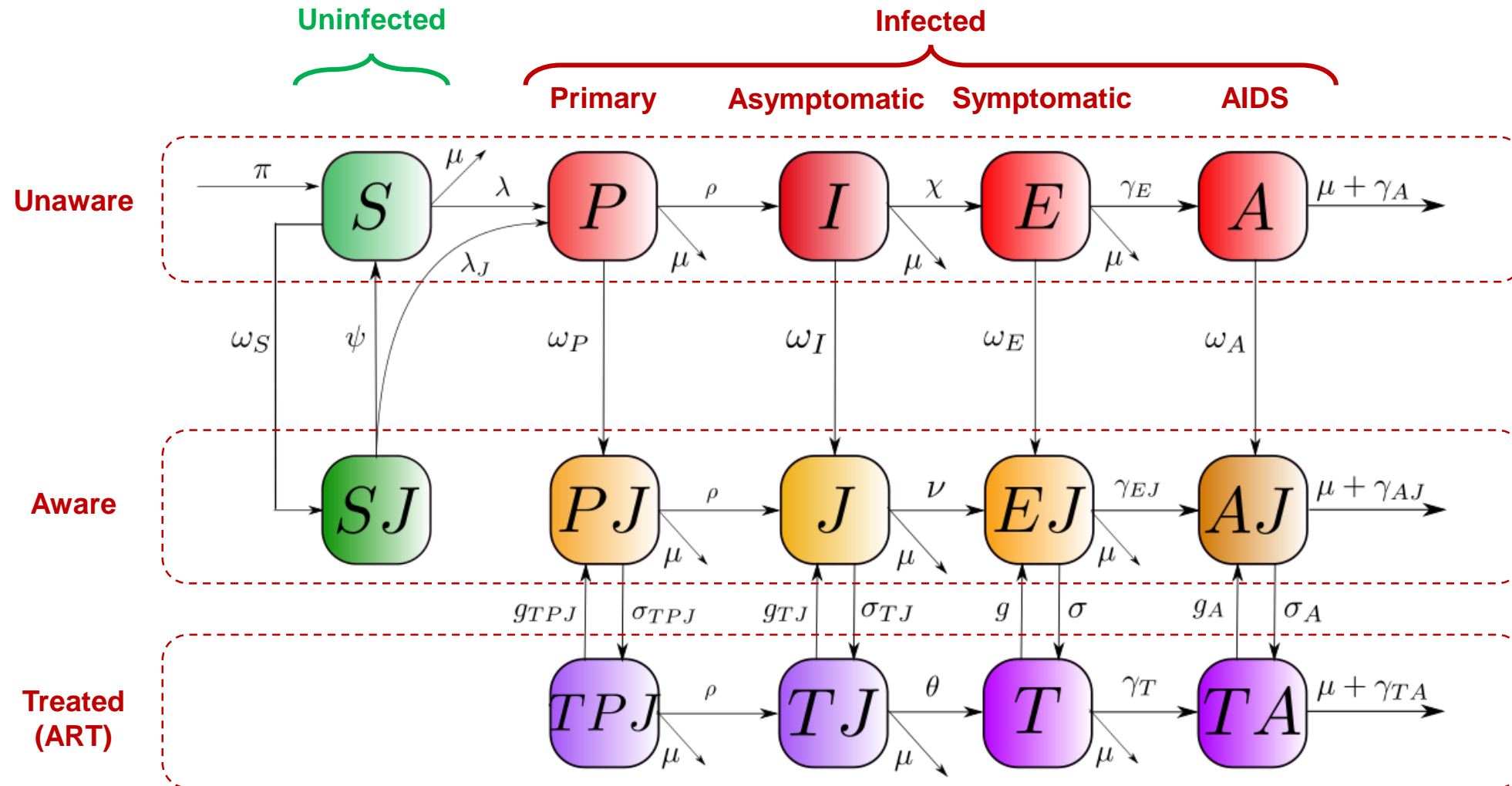
USC-LAC HIV Transmission Model – Overview

- MSM are also tracked based on their awareness of serostatus through testing



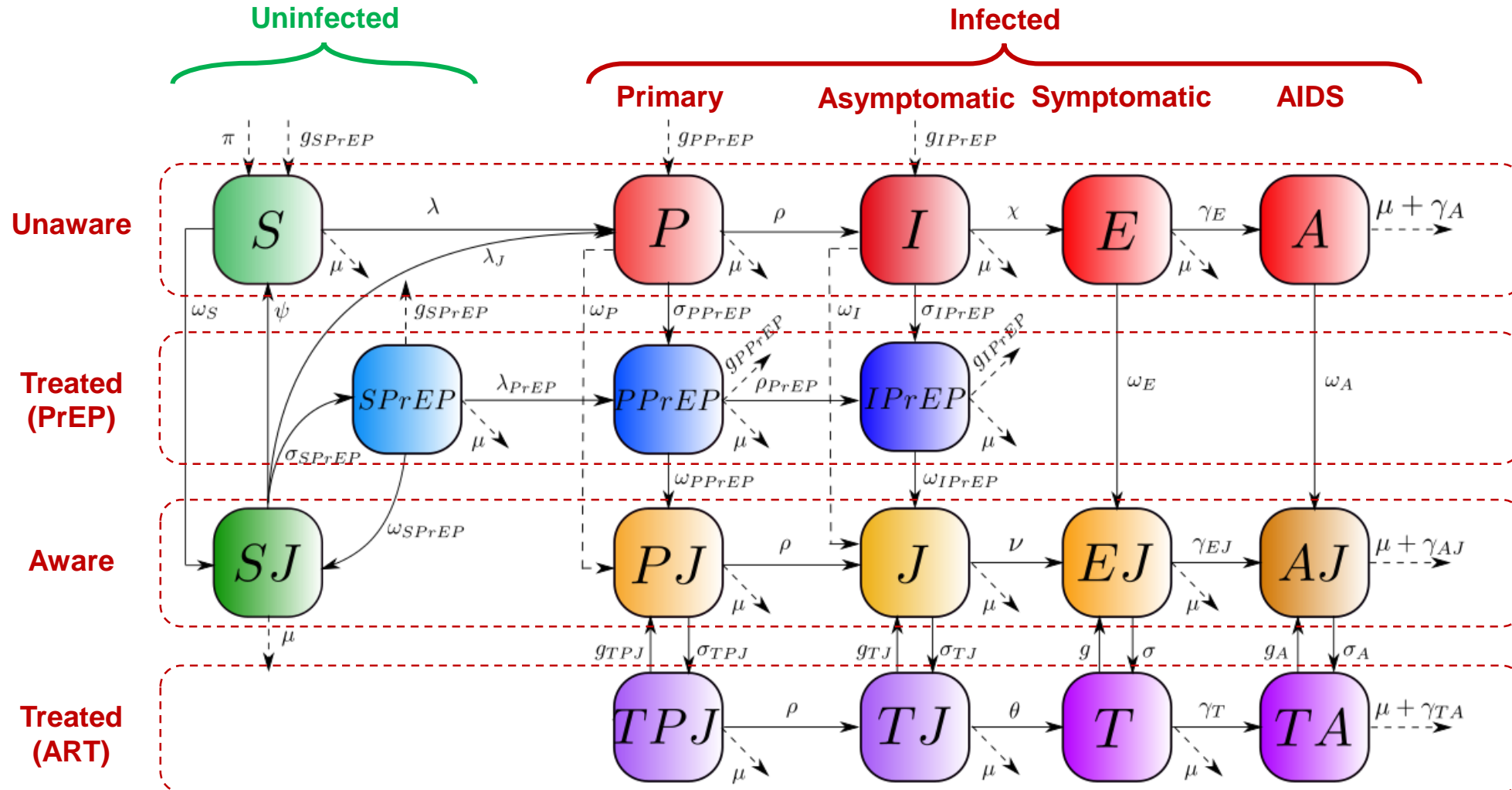
USC-LAC HIV Transmission Model – Overview

- MSM are also tracked based on their treated status ... ART



USC-LAC HIV Transmission Model – Overview

- MSM are also tracked based on their treated status ... ART and PrEP



Representation as a System of Ordinary Differential Equations (Partial List)

$$\dot{S} = (\pi + g_{PrEP}SPrEP + \psi SJ) - (\mu + \lambda_s + \lambda_r + \omega_S)S \quad (1)$$

$$\dot{SJ} = (\omega_S S + \omega_{SPrEP}SPrEP) - (\mu + \psi + \lambda_{J_s} + \lambda_{J_r} + \sigma_{SPrEP})SJ \quad (2)$$

$$SP\dot{r}EP = \sigma_{SPrEP}SJ - (\mu + \lambda_{sPrEP} + \lambda_{rPrEP} + g_{SPrEP} + \omega_{SPrEP})SPrEP \quad (3)$$

$$\dot{P}_s = (\lambda_s S + \lambda_{J_s} SJ + g_{PPrEP}PPrEP_s) - (\mu + \rho + \sigma_{PPrEP} + \omega_P)P_s \quad (4)$$

$$\dot{P}_r = (\lambda_r S + \lambda_{J_r} SJ + g_{PPrEP}PPrEP_r) - (\mu + \rho + \sigma_{PPrEP} + \omega_P)P_r \quad (5)$$

$$P\dot{J}_s = (\omega_P P_s + \omega_{PPrEP}PPrEP_s) - (\mu + \rho)PJ_s \quad (6)$$

$$P\dot{J}_r = (\omega_P P_r + \omega_{PPrEP}PPrEP_r) - (\mu + \rho)PJ_r \quad (7)$$

This is what the model looks like (in R)

```
RStudio
File Edit Code View Plots Session Build Debug Profile Tools Help
Go to file/function Addins
ds178_1 x HIV_Frontend.R x HIV_Model.R x
Source on Save Run Source
60
61 ## *****
62 ## Differential Equations
63 ## *****
64 ## Susceptible
65 dS = (pi + psi*SJ + PrEP.dummy*g.SPPrEP.S*SPPrEP) - (lambda.S.s + lambda.S.r + omega.S + sigma.S + mu)*S
66 dSJ = (omega.S*S + PrEP.dummy*g.SPPrEP.SJ*SPPrEP) - (lambda.SJ.s + lambda.SJ.r + psi + PrEP.dummy*sigma.SJ + mu)*SJ
67 dSPPrEP = PrEP.dummy*((sigma.S*S + sigma.SJ*SJ) - (lambda.SPPrEP.s + lambda.SPPrEP.r + g.SPPrEP.S + g.SPPrEP.SJ + mu)*SPPrEP)
68
69 ## Primary Stage
70 dPs = (lambda.S.s*S + lambda.SJ.s*SJ + PrEP.dummy*g.PPrEP.P*PPrEPs + q.P*Pr) - (rho.P.s + PrEP.dummy*sigma.P + omega.P + mu)*Ps
71 dPr = (lambda.S.r*S + lambda.SJ.r*SJ + PrEP.dummy*g.PPrEP.P*PPrEPr) - (rho.P.r + PrEP.dummy*sigma.P + omega.P + q.P + mu)*Pr
72
73 dPPrEPs = PrEP.dummy*((lambda.SPPrEP.s*SPPrEP + sigma.P*Ps) - (rho.PPrEP.s + g.PPrEP.PJ + g.PPrEP.P + r.PPrEP + mu)*PPrEPs)
74 dPPrEPr = PrEP.dummy*((lambda.SPPrEP.r*SPPrEP + sigma.P*Pr + r.PPrEP*PPrEPs) - (rho.PPrEP.r + g.PPrEP.PJ + g.PPrEP.P + mu)*PPrEPr)
75
76 dPJs = (omega.P*Ps + PrEP.dummy*g.PPrEP.PJ*PPrEPs + q.PJ*PJR) - (rho.PJ.s + sigma.PJ + mu)*PJs
77 dPJR = (omega.P*Pr + PrEP.dummy*g.PPrEP.PJ*PPrEPr) - (rho.PJ.r + sigma.PJ + q.PJ + mu)*PJR
78
79 dPTS = (sigma.PJ*PJs + sigma.PTD*PTDs) - (g.PT.PTD + rho.PT.s + r.PT + mu)*PTS
80 dPTR = (sigma.PJ*PJR + sigma.PTD*PTDr + r.PT*PTS) - (g.PT.PTD + rho.PT.r + mu)*PTR
81
82 dPTDs = (g.PT.PTD*PTS + q.PTD*PTR) - (rho.PTD.s + sigma.PTD + mu)*PTDs
83 dPTDr = (g.PT.PTD*PTR) - (rho.PTD.r + sigma.PTD + q.PTD + mu)*PTDr
84
85 ## Secondary Stage
86 dIs = (rho.P.s*Ps + PrEP.dummy*g.IPrEP.I*IPrEPs + q.I*Ir) - (omega.I + PrEP.dummy*sigma.I + chi.I.s + mu)*Is
87 dIr = (rho.P.r*Pr + PrEP.dummy*g.IPrEP.I*IPrEPr) - (omega.I + PrEP.dummy*sigma.I + chi.I.r + q.I + mu)*Ir
88
89 dIPrEPs = PrEP.dummy*((rho.PPrEP.s*PPrEPs + sigma.I*Is) - (g.IPrEP.IJ + g.IPrEP.I + r.IPrEP + mu)*IPrEPs)
90 dIPrEPr = PrEP.dummy*((rho.PPrEP.r*PPrEPr + sigma.I*Ir + r.IPrEP*IPrEPs) - (g.IPrEP.IJ + g.IPrEP.I + mu)*IPrEPr)
91
92 dIJs = (omega.I*Is + PrEP.dummy*g.IPrEP.IJ*IPrEPs + rho.PJ.s*PJs + q.IJ*IJr) - (chi.IJ.s + sigma.IJ + mu)*IJs
93 dIJr = (omega.I*Ir + PrEP.dummy*g.IPrEP.IJ*IPrEPr + rho.PJ.r*PJR) - (chi.IJ.r + sigma.IJ + q.IJ + mu)*IJr
94
95 dITS = (sigma.IJ*IJs + sigma.ITD*ITDs + rho.IT.s*PTS) - (g.IT.ITD + chi.IT.s + r.IT + mu)*ITS
96 dITr = (sigma.IJ*IJr + sigma.ITD*ITDr + rho.IT.r*PTR + r.IT*ITS) - (g.IT.ITD + chi.IT.r + mu)*ITr
97
98 dITDs = (g.IT.ITD*ITS + rho.PTD.s*PTDs + q.ITD*ITDr) - (sigma.ITD*ITDs + chi.ITD.s + mu)*ITDs
99 dITDr = (g.IT.ITD*ITr + rho.PTD.r*PTDr) - (sigma.ITD*ITDr + chi.ITD.r + q.ITD + mu)*ITDr
100
101 ## Symptomatic Stage
102 dEs = (chi.I.s*Is + q.E*Er) - (omega.E + gamma.E.s + mu)*Es
103 dEr = (chi.I.r*Ir) - (omega.E + gamma.E.r + q.E + mu)*Er
104
105 dEJs = (chi.IJ.s*IJs + omega.E*Es + q.EJ*EJr) - (gamma.EJ.s + sigma.EJ + mu)*EJs
106 dEJr = (chi.IJ.r*IJr + omega.E*Er) - (gamma.EJ.r + sigma.EJ + q.EJ + mu)*EJr
107
108 dETs = (chi.IT.s*ITS + sigma.EJ*EJs + sigma.ETD*ETDs) - (gamma.ET.s + g.ET.ETD + r.ET + mu)*ETs
109 dETr = (chi.IT.r*ITr + sigma.EJ*EJr + sigma.ETD*ETDr + r.ET*ETs) - (gamma.ET.r + g.ET.ETD + mu)*ETr
110
111 dETDs = (chi.ITD.s*ITDs + g.ET.ETD*ETs + q.ETD*ETDr) - (sigma.ETD*ETDs + gamma.ETD.s + mu)*ETDs
112 dETDr = (chi.ITD.r*ITDr + g.ET.ETD*ETr) - (sigma.ETD*ETDr + gamma.ETD.r + q.ETD + mu)*ETDr
113
114
115
```

Data

- **Demographic & epidemic data:**
 - LA County Division of HIV and STD Programs
 - LAC HIV Surveillance Reports
- **Transition rate values:**
 - LA County Division of HIV and STD Programs
 - Estimated from demographic and epidemic data
 - Extracted from medical clinical literature
 - Informed by expert opinion
- **Cost and health outcomes data:**
 - Economic and medical clinical literature
 - Federal Supply & Clinical Diagnostic Laboratory Fee Schedules

Surveillance data among MSM in LAC

REDACTED

Engaged = PLWH who have at least one care visit within the indicated year

VLS = PLWH at the end of indicated year whose last viral load was < 200 copies/mL

SVLS = PLWH with all VL tests in the indicated year was <200 copies/ml, regardless of number of VL tests(≥ 1).

Model Calibration and Validation

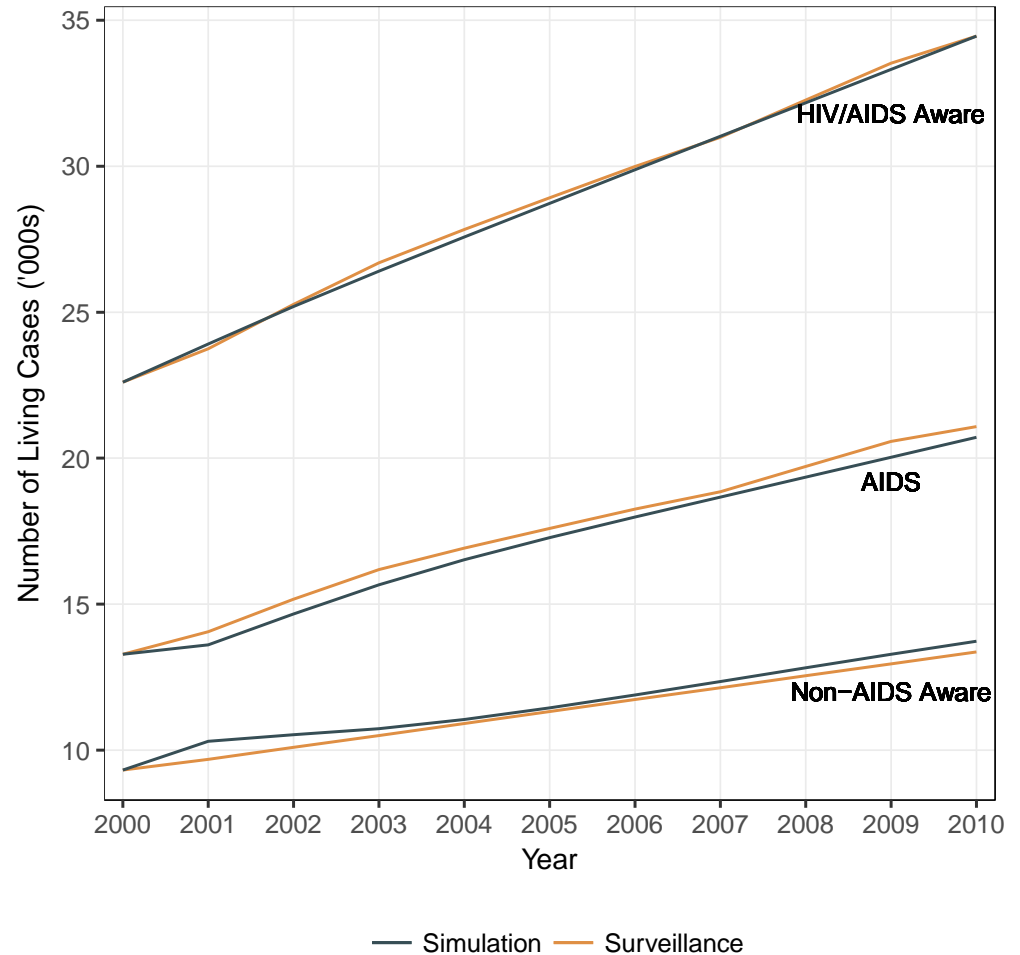
- Have uncertainty ranges on model inputs
 - What is the “best fitting” parameter set?
 - Just as in regressions, minimize the error with observed data
- Latin hypercube sampling (LHS) to pick input sample sets
- Calibration targets:
 - LAC surveillance data from 2000 to 2009
 - Unaware, infected prevalence
 - MDR prevalence

Calibration Procedure

1. Run 500,000 LHS simulations
2. Keep parameter sets where:
 - a. “HIV+ but unaware” population is 21-25% of the total HIV/AIDS population
 - b. MDR prevalence is 2-5% of the total population
3. Select top 1000 simulations with lowest prevalence error: smallest sum of squared errors on estimates of total numbers of PLHWA in LAC surveillance data in 2000 to 2009
 - Use these simulations to create narrower parameter ranges
4. Run additional 500,000 LHS simulations
5. Drop simulations that do not match criteria a and b
6. Retain simulations where predicted AIDS cases and non-AIDS HIV-aware cases are both <5% different from the 2009 surveillance data.
7. Of remaining simulations, choose input set that minimizes the prevalence error
 - This is the “Best Run”: input set is used for base case analysis

Model Calibration and Validation

- Calibration: Latin-hypercube sampling method and best-fit approach
- Validation: Compare model's prediction to reported HIV/AIDS prevalence



Next Steps: Scenarios for Analysis

- PrEP Uptake
- Risk Compensation
- Treatment Uptake
- Care Coordination
- Expanded Testing
- Behavioral Nudges
- Social Programs (housing, etc.)

Results from Prior Analysis with the Same Model

- Sood et al (2013) and Drabo et al (2016)
- Scenarios with enhanced:
 - Testing
 - Test and Treat
 - PrEP

Cumulative HIV Incidence For Different Strategies

- PrEP and Test-and-Treat are very effective at reducing HIV transmission
- But they do not eliminate HIV

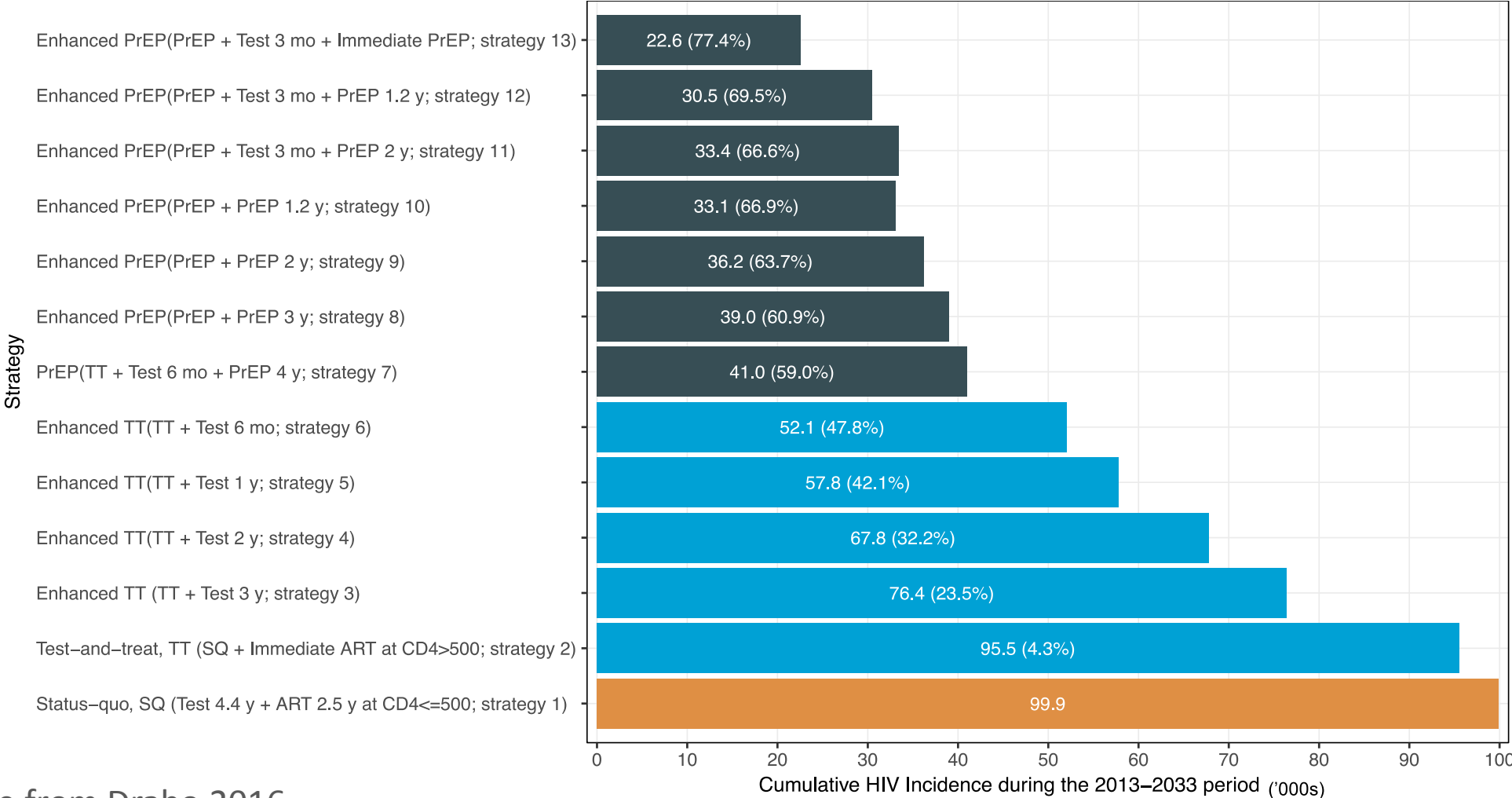
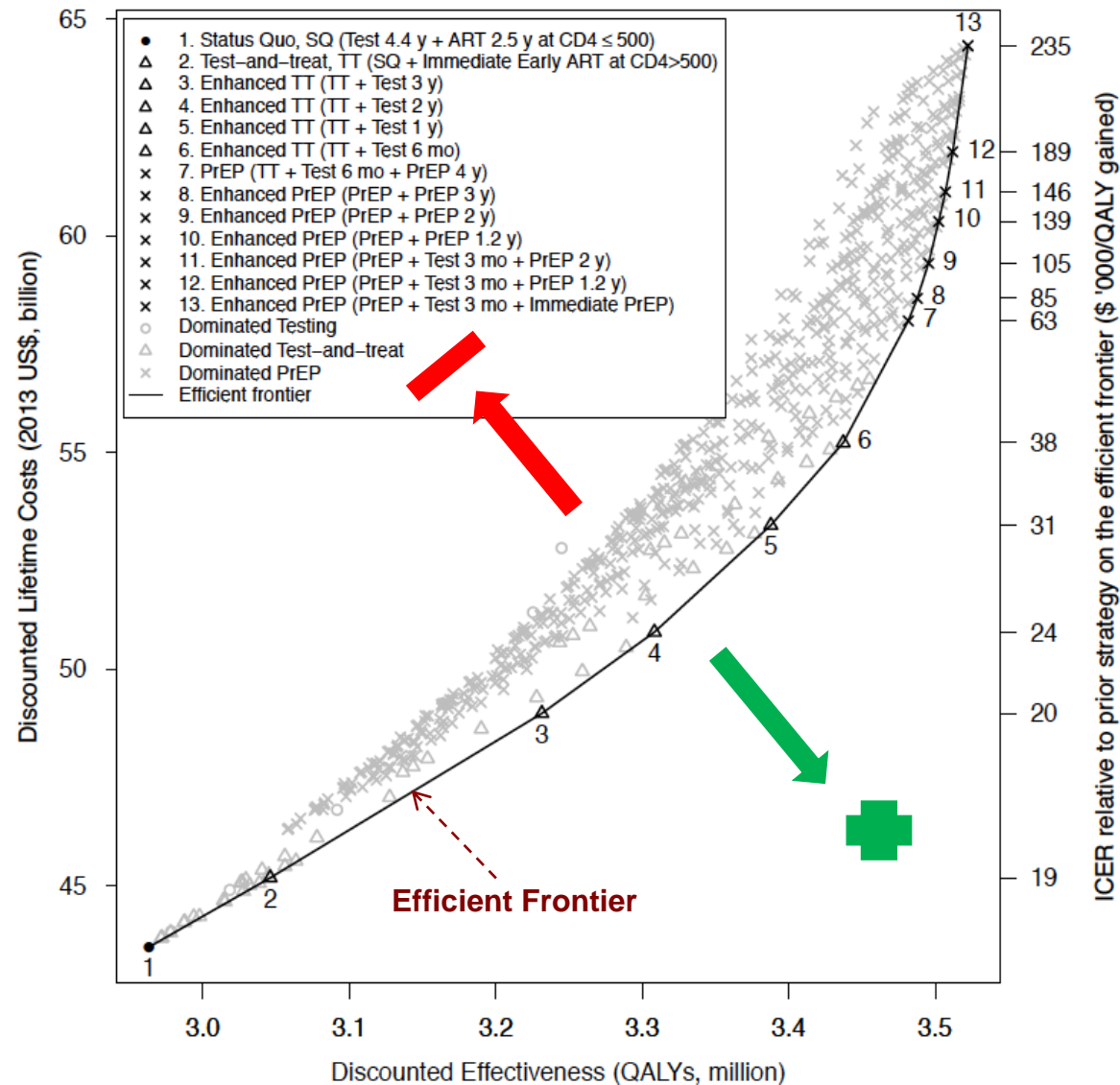


Figure from Drabo 2016

Informing Decision-Making – Efficient Frontier



- Strategies that yield the highest value (lowest cost per QALY) for a defined level of societal WTP
- Slope of the line between 2 points represents the ICER of these strategies relative to each other
- Steeper slopes mean high ICERs

Figure from Drabo 2016

Sensitivity Analysis

- One- and multi-way sensitivity analyses
 - Bootstrapping and probabilistic sensitivity analyses
- Relative effectiveness of PrEP is sensitive to
 - Initial disease prevalence
 - PrEP and ART initiation rates
 - Adherence to PrEP and ART
 - Sexual mixing rates
- All cost-effectiveness profiles improve with ART price reductions

PrEP (TT + Test 6 mo + PrEP 4 y) Relative to Status Quo

- ICERs sensitive to PrEP & ART coverage rates and rates of adherence

Epidemic Parameters

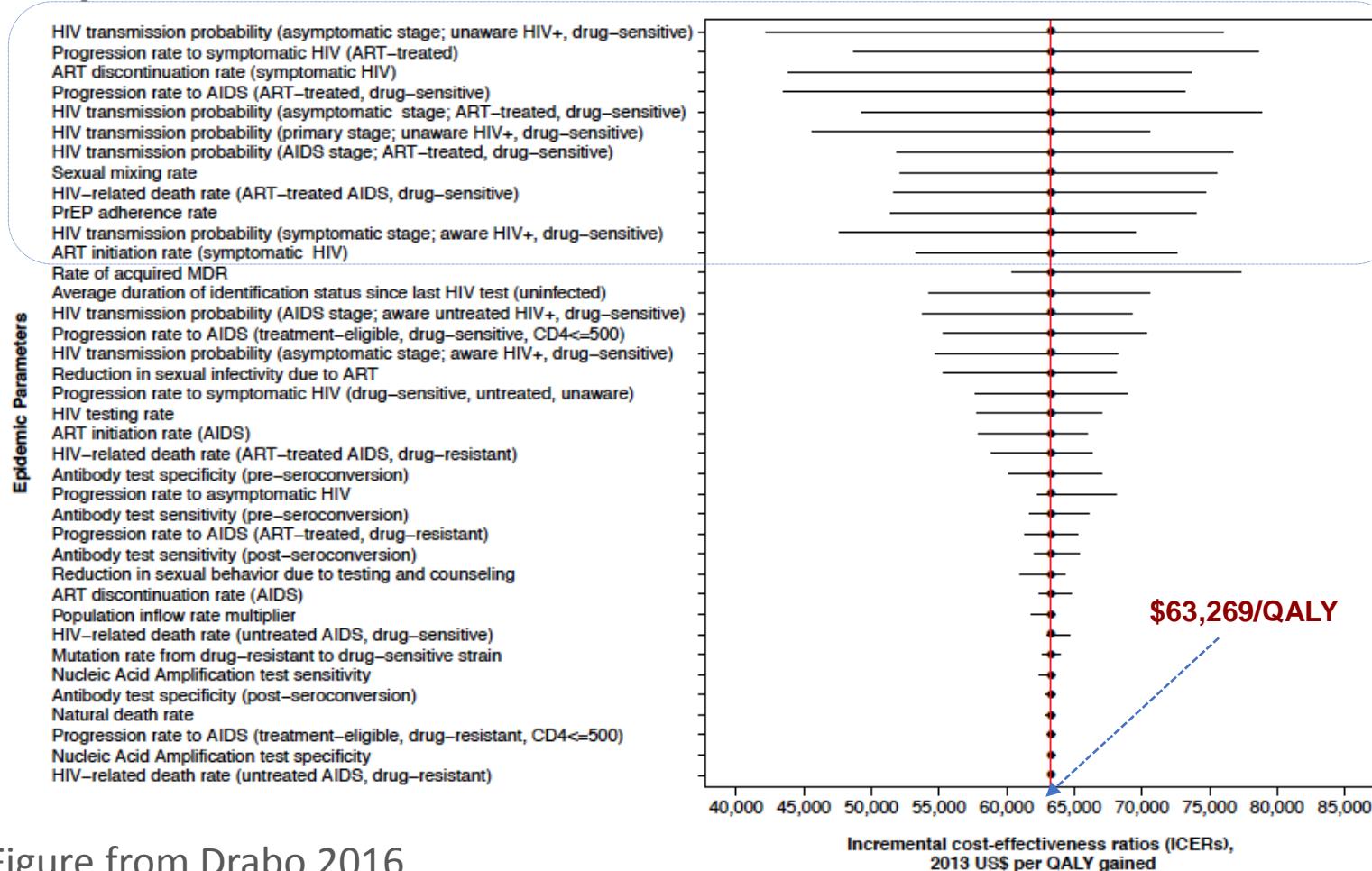


Figure from Drabo 2016

Geographical Stratification

- What mix of interventions is appropriate for different health districts, based on differences in the epidemic (better to invest in scaling up testing vs. PrEP, etc.)?
 - Need geographical stratification of the model
- This analysis may:
 - Guide resource allocation & programmatic decisions
 - Help us understand effects of local outbreaks
- Data from LA County Division of HIV and STD Programs

What is different about the stratified model?

- Requires disaggregated data
 - Locally-specific input parameters: disease and transmission characteristics, baseline coverage of programs
- Requires a different model structure
 - Each compartment needs to be replicated for each health district
 - Flow rates can now also be unique to a health district
- Analysis focuses on intra-health district comparisons between scenarios
 - In area A, is intervention X or Y more impactful / cost-effective?
- Can also re-aggregate back to county level
 - e.g., budget impact analysis (how much would it cost to implement this package of “best” approaches across the county, and what gains would we see for LAC)

Selected Geographical Data from LACDHSP

Redacted

Conclusions

- Models are only abstractions of reality – but, due to real-world complexities, can be very helpful for priority-setting and policy-making
- These models require many high-quality data sources for inputs, and detailed attention to construction
- Choice of scenarios, and of key outcomes for comparison during analysis, is critical
- We look forward to hearing your ideas & thoughts about how this model can be helpful to key stakeholders in LAC!

Thank You!