Agent-based Modeling to Support Ending the HIV Epidemic in Chicago:

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FOR DRUG ABUSE AND HIV

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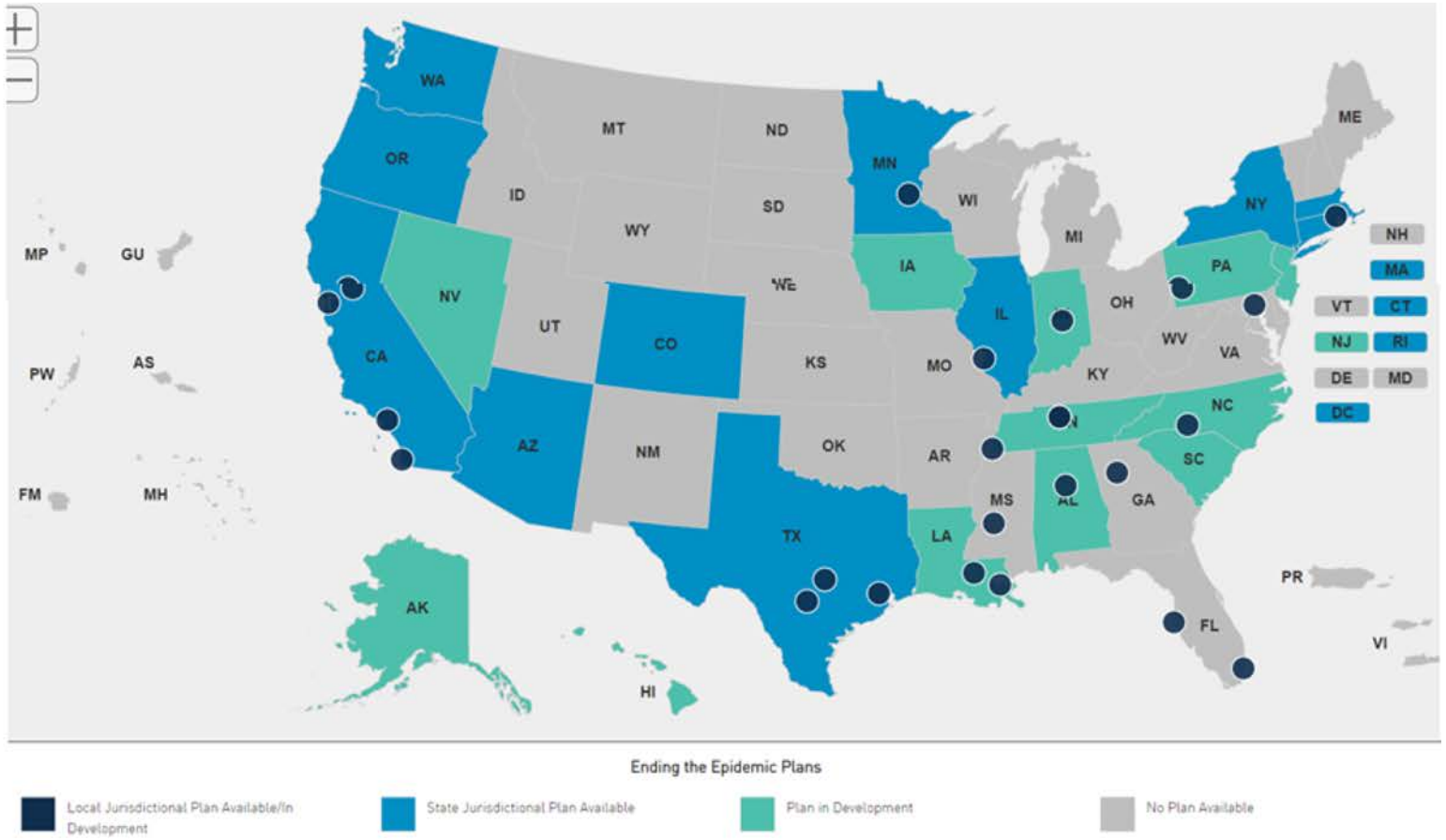
Outline

- Background and purpose of our ABM
- What are Agent-based models, and why are they relevant for prevention
- Overview of the Chicago HIV spread Model for MSM
- Model validation
- Virtual experiments
- Potential application to local EHE initiatives
- Next steps and future directions

ENDING THE HIV EPIDEMIC: JURISDICTIONAL PLANS

An increasing number of cities, counties, and states are developing plans to "End the Epidemic" in their jurisdiction. These plans are dynamic and will be updated as progress continues. Click on the map below to access the current versions. If you



https://www.nastad.org/maps/ending-hiv-epidemic-jurisdictional-plans

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Ending the HIV Epidemic: A Plan for America

HHS is proposing a once-in-a-generation opportunity to eliminate new HIV infections in our nation. The multi-year program will infuse 48 counties, Washington, D.C., San Juan, Puerto Rico, as well as 7 states that have a substantial rural HIV burden with the additional expertise, technology, and resources needed to end the HIV epidemic in the United States. Our four strategies – diagnose, treat, protect, and respond – will be implemented across the entire U.S. within 10 years.

GOAL:

75% reduction in new HIV infections in 5 years and at least **90%** reduction in 10 years.

Our goal is ambitious and the pathway is clear – employ strategic practices in the *places* focused on the right *people* to:

- **Diagnose** all people with HIV as early as possible after infection.
- **Treat** the infection rapidly and effectively to achieve sustained viral suppression.
- **Protect** people at risk for HIV using potent and proven prevention interventions, including PrEP, a medication that can prevent HIV infections.
- **Respond** rapidly to detect and respond to growing HIV clusters and prevent new HIV infections.
- **HIV HealthForce** will establish local teams committed to the success of the Initiative in each jurisdiction.

The Initiative will target our resources to the 48 highest burden counties, Washington, D.C., San Juan, Puerto Rico, and 7 states with a substantial rural HIV burden.

*2016-2017 data

Geographical Selection:
Data on burden of HIV in the US shows areas where HIV transmission occurs more frequently. More than 50% of new HIV diagnoses* occurred in only 48 counties, Washington, D.C., and San Juan, Puerto Rico. In addition, 7 states have a substantial rural burden – with over 75 cases and 10% or more of their diagnoses in rural areas.

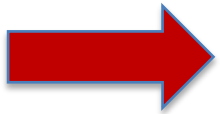
Ending the HIV Epidemic | www.HIV.gov

Designing a Model for Local Public Health Impact

- Understand local public health prevention/care portfolio and future priorities
  - On-going conversations with health department leadership
  - Participation in GTZ Illinois strategic planning and implementation
- Tailor model to reflect local epidemic and GTZ goals/strategies
- Run model and obtain real-world validation
- Plan for dissemination and sustainment

GTZ Illinois Strategic Plan

Goal: 100 new HIV infections or less by 2030



> "Ultimately, GTZ-IL paves the path toward a day in which zero people will contract HIV in Illinois and every person living with HIV will get the care they need to thrive."

+ Increase by 20 percentage points the number of people living with HIV who are virally suppressed. HIV treatment helps people living with HIV stay healthy. Moreover, if their viral load is undetectable because of successful treatment with HIV medications, they cannot transmit the virus sexually (U=U).

+ Increase by 20 percentage points the number of people vulnerable to HIV who use pre-exposure prophylaxis (PrEP). When used consistently and correctly, PrEP is a pill and program that is nearly 100% effective at preventing an HIV-negative person from contracting HIV sexually.

Pathway to GTZ Illinois

- What combination of prevention and care interventions (Combination Prevention) allow us to reach a functional end to the epidemic?
- What combination prevention can eliminate racial HIV disparities
- What combination prevention interventions targets need to be reached?
- What are the most effective implementation strategies?

An agent-based model (ABM) is a virtual representation of a system defined by individual level behaviors

- A system is modeled as a collection of autonomous decision-making entities called agents
- Each agent individually assesses its situation and makes decisions based on a set of rules
- Agent behavior can be internal, an interaction with the environment, or an interaction with another agent.
- By repeatedly having agents interact, these models capture emergent (system level) behavior, which can be:

- Path dependent	- Non-linear	- Memory driven
- Adapted to local circumstances	- Temporally correlated	

ABM is a unique tool for decision support

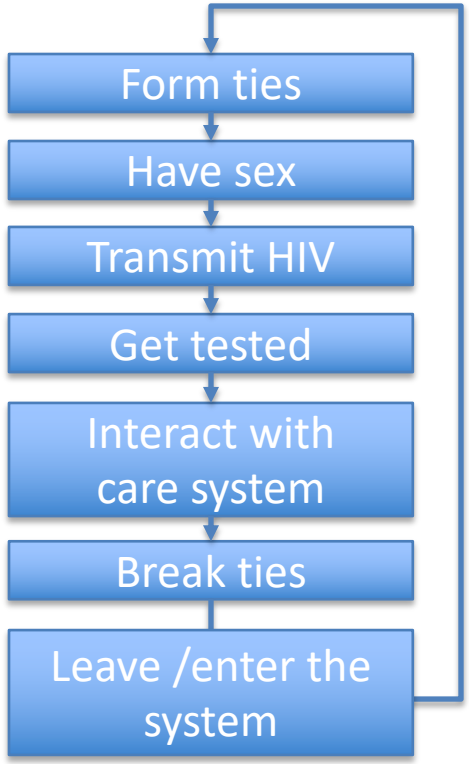
- ABM embraces heterogeneity by describing the model using individual level characteristics
- ABM provides a natural way of describing a system, giving agency to the appropriate entities, allowing for easier translation into practical settings
- ABM naturally includes a time dimension, setting it up particularly well for making predictions
- ABM allows for easy perturbation, enabling one to study ‘what-if’ scenarios, and do experimentation on the effect of interventions

Model Scope

- We created a model that reflects Chicago's HIV epidemic based on the following:
  - Men-who-have-sex-with-men (MSM) only, as they account for over 2/3 of new HIV diagnoses
  - Transmission occurs as a result of unprotected sex as this accounts for 91% (CDPH, surveillance data (2015)) of the new HIV diagnoses among MSM
  - Focuses on sexually active population of MSM, ages 13-85
  - MSM represent 6.3% of the total population (AIDSVU, 2013), resulting in ~ 65,000 MSM residing in Chicago

The Chicago HIV model consists of five modules

1. **Demographics** module: Describing the population characteristics
2. **Partnership dynamics** module: Describing the formation and dissolution of the sexual activity networks
3. **HIV transmission** module: Describing the mechanisms by which sex in serodiscordant pairs can result in transmission of HIV
4. **Prevention and treatment** module: Describing the ways by which individuals interact and move through steps of the prevention and care continuum
5. **Intervention** module: describing how the model is perturbed during intervention

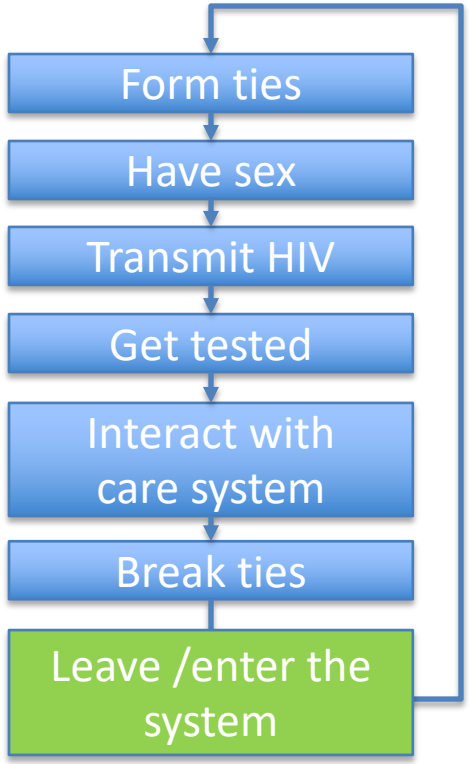


- All modules, except 3, must be informed by local data

1. Demographic Module

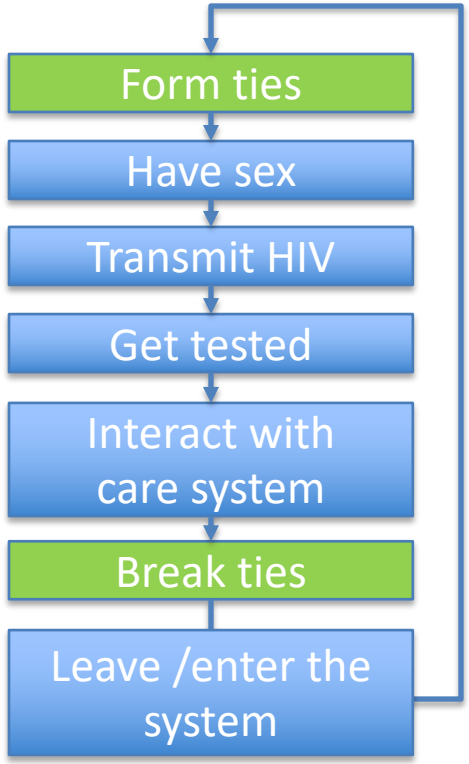
- Individual level demographic characteristics are based on data from CDPH
- We model Chicago on a 1:10 scale representing the city by 6500 agents
- Individuals die
  - As a result of HIV-related causes
  - Other causes
- People age out of the model's age range
- People become of age to be considered

Each of these rates are based on field data, and as it turns out they result in a fluctuating but relatively stable population of ~6500 agents in the model



2. Partnership Dynamics Module

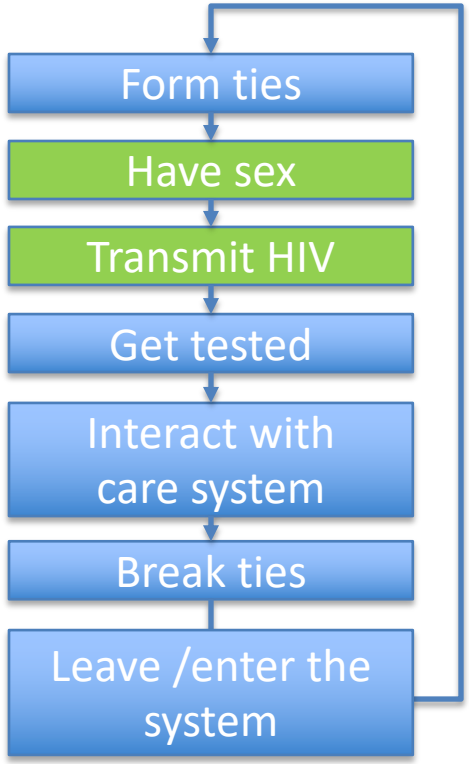
- The partnership dynamics model is based on RADAR cohort study (PI Mustanski)
- RADAR is longitudinal cohort study among ~1300 MSM in Chicago. It collects individual level sexual activity and risk information among this cohort, which we use in our model.
- Our model distinguishes two types of ties:
  - Casual ties (one-time encounters with duration of one week)
  - Main ties (relationships with a duration longer than a week, for which the duration is based on the distribution of durations in field data)
- It determines the formation of ties, partnership characteristics, and sexual activity within these ties for a cross-section of race/ethnicity, age, and HIV-status.



3. HIV Transmission Module

Once the partnership network is updated, sexual activity takes place within each tie.

- For each sex act, there is a stochastic HIV spread mechanism that is impacted by the following 8 factors:
  - Base risk
  - The viral-load of HIV-positive partner
  - If the HIV-positive partner is in the acute stage of HIV infection
  - The circumcision of the HIV-negative partner
  - The PrEP use and adherence of the HIV-negative partner
  - The CCR5 mutations of the HIV-negative partner
  - Whether a condom was used
  - **The socio-economic opportunity as a risk factor**



3.1 The socio-economic risk factor

To address the disparities, a proxy for socio-economic opportunity was included into the model:

- This proxy was based on the neighborhood of residence
- And serves as a factor by which the risk of contracting HIV is perturbed
- The proxy value is based on normalized indicator of a linear regression model in which the DV was local HIV incidence:

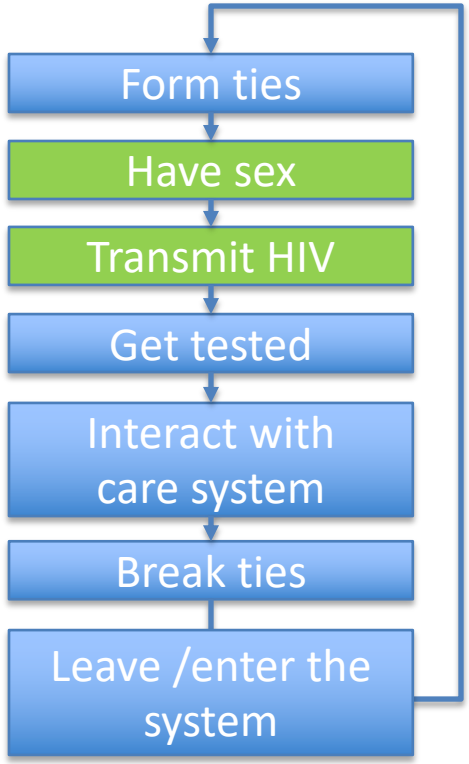
  The best performing model was one using only one variable:

  – local HIV prevalence

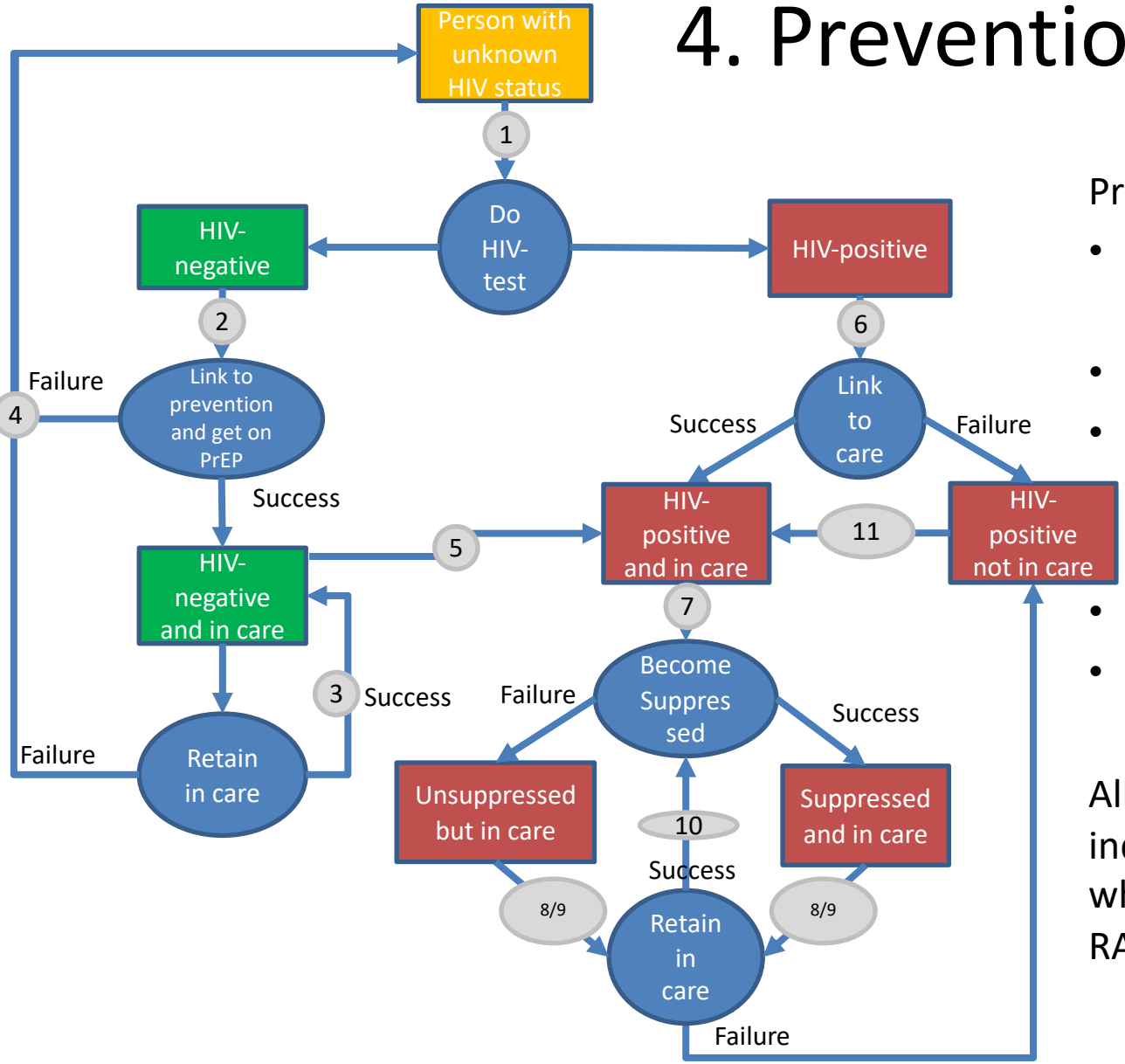
  Other more complex models tested integrated:

  – Prevalence of other STIs (chlamydia, gonorrhea, syphilis)

  – Economic hardship index factors



4. Prevention and treatment module



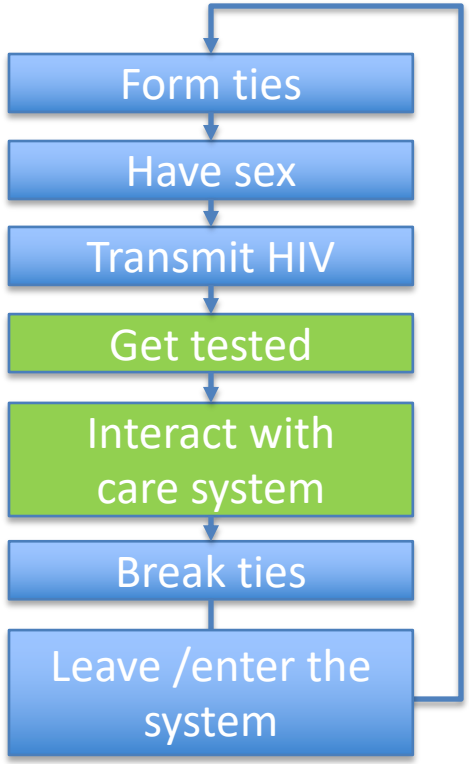
Primary mechanisms:

- Going in for testing [1]

- PrEP linkage for HIV-negatives [2]
- Retention in care for HIV-negatives [3]

- Linkage to care for HIV-positives [6]
- Becoming virally suppressed [7]
- Retention for HIV-positives [8/9/10]

All rate for treatment (of HIV+ individuals) is based on local CDPH data, whereas preventive care was based on RADAR cohort data



Model Data Sources: Maximize Use of Local Data

Module	Dimension	Data Origin			Data Source
		LHD data	Local network data	Other non-local estimates	
Demographics	MSM population estimate	✓			AIDS VU and Chicago Census Data
Demographics	HIV status (HIV-, HIV +aware and unaware)	✓			CDC estimates applied to Chicago data
Demographics	Death HIV-			✓	CDC
Demographics	Circumcision			✓	CDC/NCHS
Demographics	Births	✓			Chicago health atlas
Demographics	HIV dignoses and prevalence	✓			Chicago HIV surveillance registry/data reports
Demographics	Race	✓			Chicago HIV surveillance registry/data reports
Demographics	Age	✓			Chicago HIV surveillance registry/data reports
Demographics	Neighborhood characteristics and STI rates	✓			Chicago HIV surveillance registry/data reports
Demographics	Death HIV+	✓			Chicago HIV surveillance registry/data reports
Demographics	CCR5			✓	Jenness (2016)
Prevention/Treatment	Rate of Testing	✓			CDC/NHBS
Prevention/Treatment	ART status	✓			Chicago HIV surveillance registry/data reports
Prevention/Treatment	HIV linkage, retention, adherence levels and effectiveness	✓			Chicago HIV surveillance registry/data reports
Prevention/Treatment	Linkage, adherence, and retention measures	✓			Chicago HIV surveillance registry/data reports
Prevention/Treatment	PrEP adherence levels			✓	Jenness (2016)
Prevention/Treatment	PrEP use, linkage, retention		✓		RADAR cohort study
Partnership Dynamics	Tie formation rates		✓		RADAR cohort study
Partnership Dynamics	Partner characteristics		✓		RADAR cohort study
Partnership Dynamics	Sexual Behaviors		✓		RADAR cohort study
Partnership Dynamics	Sex-Role		✓		RADAR cohort study

Validating model behavior: three measures

- We base our model on field data which should yield realistic mechanisms and dynamics
- However there is always a need to validate model behavior.
- The model is set up using 2015 data, and consequently we tested if simulated behavior corresponded with 2016 emergent properties
- Three measures of alignment were used:
  1. Overall number of newly diagnosed incidence cases
  2. The distribution of newly diagnosed incidence cases by age
  3. The distribution of newly diagnosed incidence cases by race/ethnicity

Number of new diagnoses annually

CDPH data on incidence

2016 CDPH data suggest that 601 new diagnoses among MSM in Chicago + on top of that an additional 23 cases occurred among MSM/IDU

So **624** new diagnosed cases

Modelled data on Incidence

Our model estimates a mean of

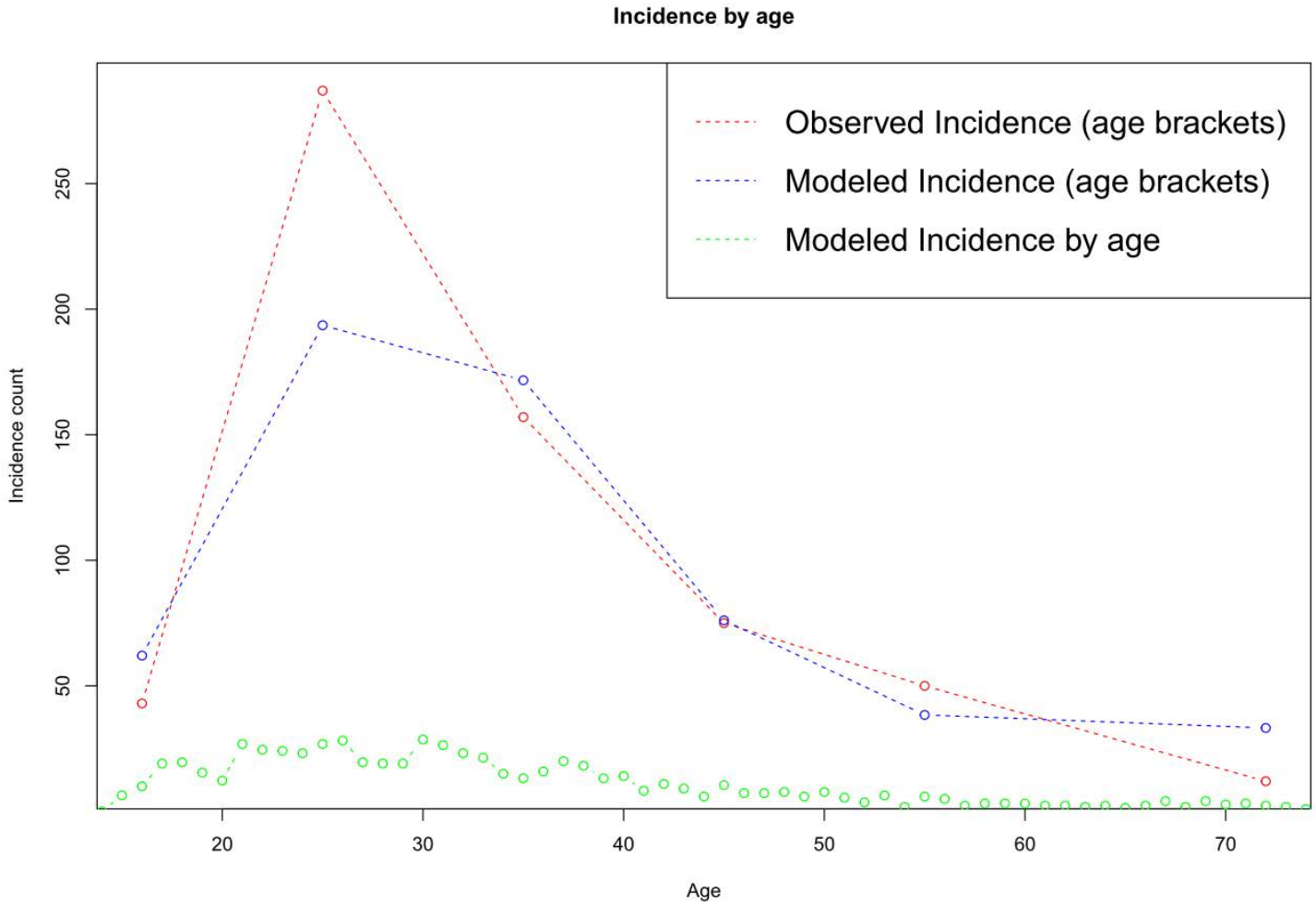
575.0 (95% conf int. 518.4 - 631.7)

new diagnosed cases among this population

- Our model does a reasonable job at capturing the system level dynamics, if anything it seem to be slightly underestimating incidence
- These result are obtained without doing any fitting of the model, relying only on local input data

Distribution of new diagnoses by age

- Overall, there is strong resemblance across the observed and modeled distribution over of incidence over age
- We do significantly under-estimate the peak in the 20-29 age bracket
- And over-estimates the incidence in the tails, were we have relatively fewer input data points



The distribution of new diagnoses by race/ethnicity

- We find substantial underestimation of incidence among Blacks
- We find substantial overestimation of incidence among whites (and Others)

- Only considering the individual risk factors does not explain the observed disparity in incidence
- Our model is missing some of the drivers of disparities in the system

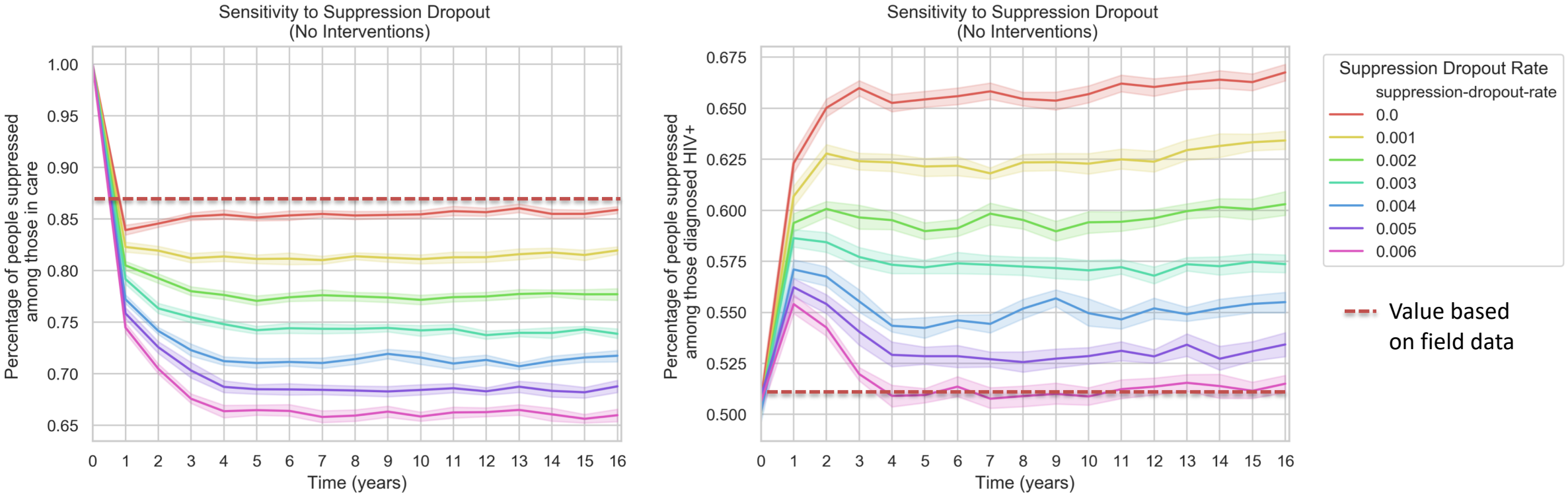
		Incidence rate (cases per person)
Black NH	Reality	**0.0176**
	Modeled	0.0101
White NH	Reality	**0.0051**
	Modeled	0.0076
Hispanic	Reality	**0.0081**
	Modeled	0.0086
Other	Reality	**0.0041**
	Modeled	0.0055

Validating treatment module behaviors

- Earlier presentation of model to CDPH resulted in discussion and a closer inspection of the treatment module.
- More specifically, while the ART module was based on data newly infected individuals, there was potential over-estimation of viral suppression levels in the HIV+ population.
- A more detailed inspection revealed that suppression level of people living with HIV (PLWH) was extremely high (~66%) compared to the observed (~53%).
- To address this we included a probability by which people in care, can (temporarily) become unsuppressed.

Validating treatment module behaviors

- This rate however identifies a tradeoff between matching the suppression levels of those in care (left) and matching the suppression levels of all people living with HIV (right).
- We decided to use a rate that minimizes the error in the combination of both, and preformed sensitivity analysis for the alternative fit



5. Intervention module

Virtual experiment to explore intervention impact

- Focused specifically on the two focus areas of the GTZ plan which correspond to the Prevent and Treat pillars of the EHE initiative.
- Identified six steps along the continuum we will use as levers (intervention targets):

PrEP care for HIV negatives (Prevention)

- Linkage to PrEP (this includes boosting awareness and access)
- Adherence to PrEP
- Retention in PrEP care

ART care for HIV positives (Treat)

- Linkage to HIV care
- Adherence to ART for people in care
- Retention in HIV care

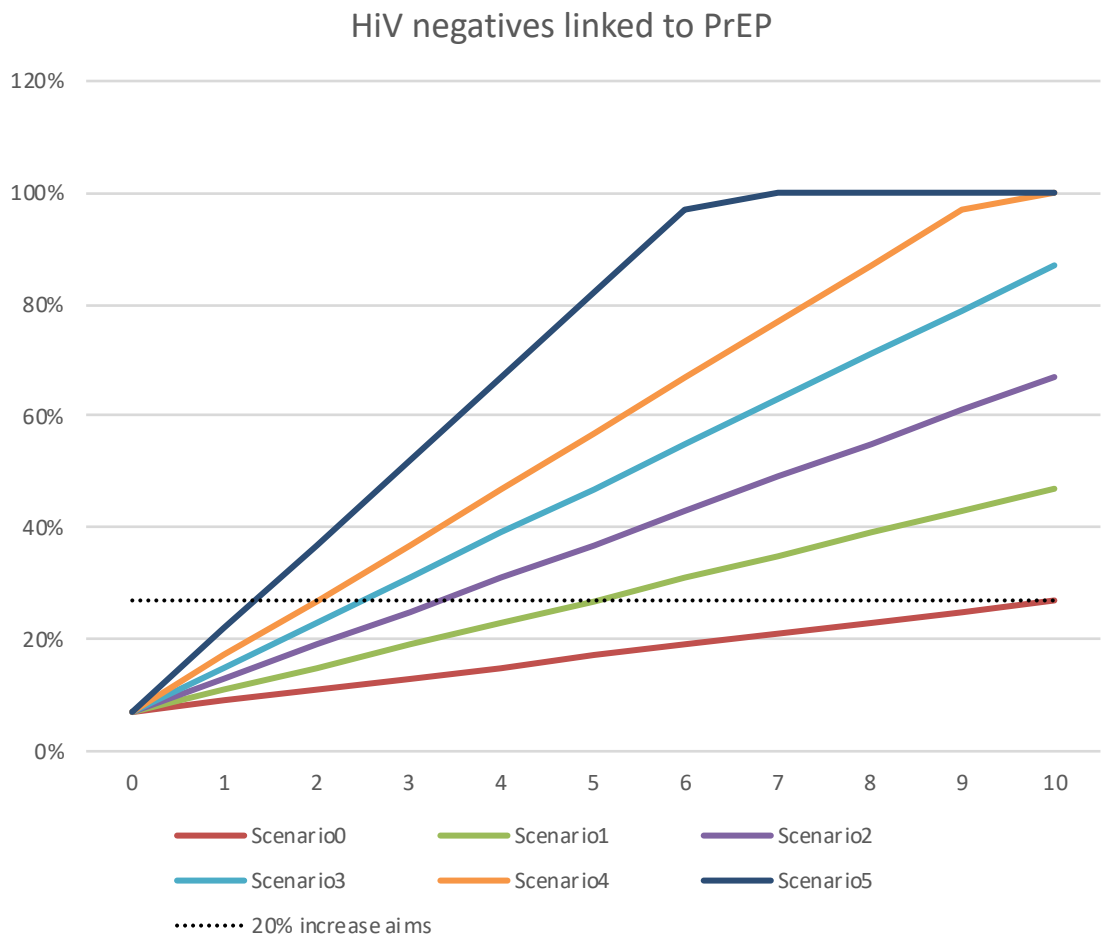
➢ We focus on the pre-implementation decision making, as such, modeling does not yet consider specific interventions to impact these levers

PrEP linkage

(Varying rates of increasing linkage over time)

Currently **7%** of MSM linked to PrEP

- **Scenario 0 (baseline):** 2pp annual increase.
  20% linkage increase achieved in 10 years
- **Scenario 1 (minimal):** 4pp annual increase.
  20% linkage increase achieved in 5 years
- **Scenario 2 (minor):** 6pp annual increase.
  20% linkage increase achieved in 3.33 years
- **Scenario 3 (moderate):** 8pp annual increase
  20% linkage increase achieved in 2.5 years.
- **Scenario 4 (extreme):** 10pp annual increase.
  20% linkage increase achieved in 2 years
- **Scenario 5 (max):** 15pp annual increase.
  20% linkage increase achieved in 1.33 years



Baseline rates are based on RADAR data

PrEP Retention

(Retention in care is increased once, at initiation)

Currently **53.5%** of MSM on PrEP are retained in PrEP service annually

Scenario 0 (baseline):

53.5% of MSM are retained annually

Scenario 1:

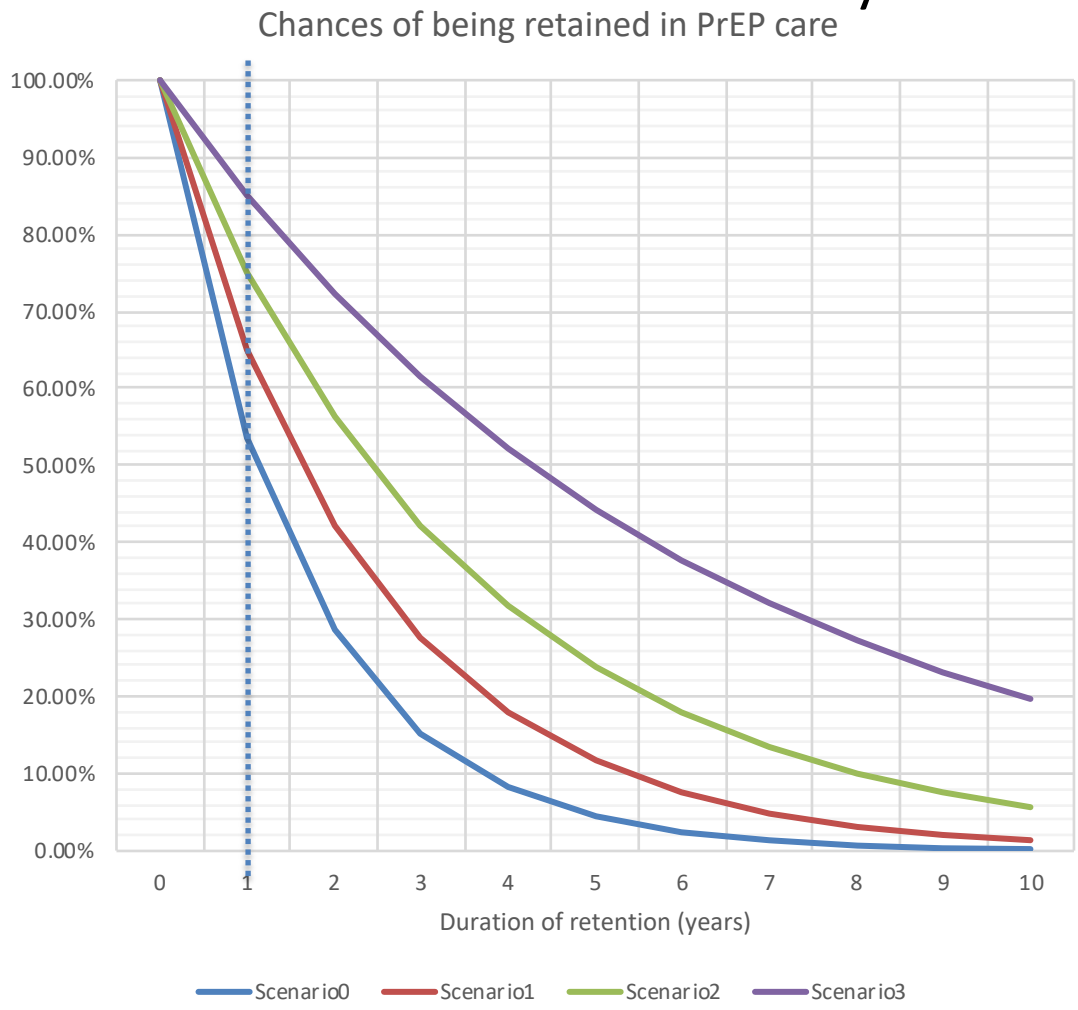
11.5 percentage point increase in retention rate from baseline (65% total)

Scenario 2:

21.5 percentage point increase in retention rate from baseline (75% total)

Scenario 3:

31.5 percentage point increase in retention rate from baseline (85% total)



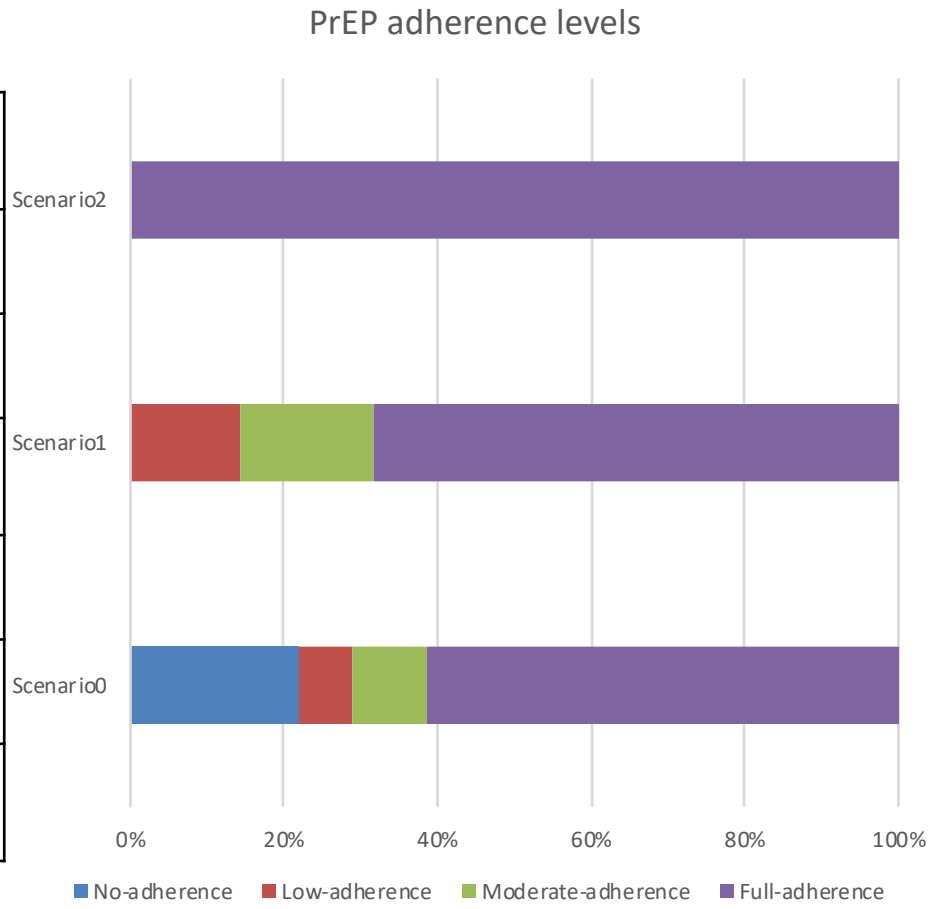
Baseline rates are based on RADAR data

PrEP Adherence

(Varying levels of adherence result in varying levels of risk)

Currently the mean risk reduction for PrEP users is **69.1%**

	Scenario0 (Baseline)	Scenario1	Scenario2
No-adherence	22.1%	0.0%	0.0%
Low-adherence	7.0%	14.4%	0.0%
Moderate-adherence	10.0%	17.4%	0.0%
Full-adherence	61.9%	69.2%	100.0%
Mean risk reduction	**69.1%**	**84.3%**	**95.0%**



Baseline data are based on EPiModel data

Linkage to HIV care

(rates of linkage are changed once, upon initiation)

Currently the mean linkage to care is **~90%**

Number of MSM recently diagnosed with HIV consequently get a CD4/viral load test.

Scenario 0 (baseline): See table below, variation by race/ethnicity and age

	Blacks	Whites	Hispanic	Other
Ages 13 to 33	87.70%	92.05%	91.68%	86.09%
34 y/o and over	87.69%	93.87%	94.20%	93.85%

Scenario 1:

100% of newly diagnosed are linked to care

Baseline data are based on CDPH data

Retention in HIV care

(rates of retention are increased once, upon initiation)

Currently, **72.46%** are retained in care

The percentage of individuals retained in care for 3 care visits. Data not readily available for ART adherence. Percentages vary by race and age.

Scenario 0 (baseline):

72.46% are retained for 3 care visits

Scenario 1:

77.41% of individuals are retained (5 percentage point increase in retention from baseline)

Scenario 2:

85.25% of individuals are retained (12.8 percentage point increase in retention from baseline)

Scenario 3:

96.71% of individuals are retained annually (24 percentage point increase in retention from baseline)

Baseline data are based on CDPH data

Viral suppression (assumed ART adherence)

(Variations in the rate of becoming suppressed are implemented as an annual increases in the probability of becoming suppressed)

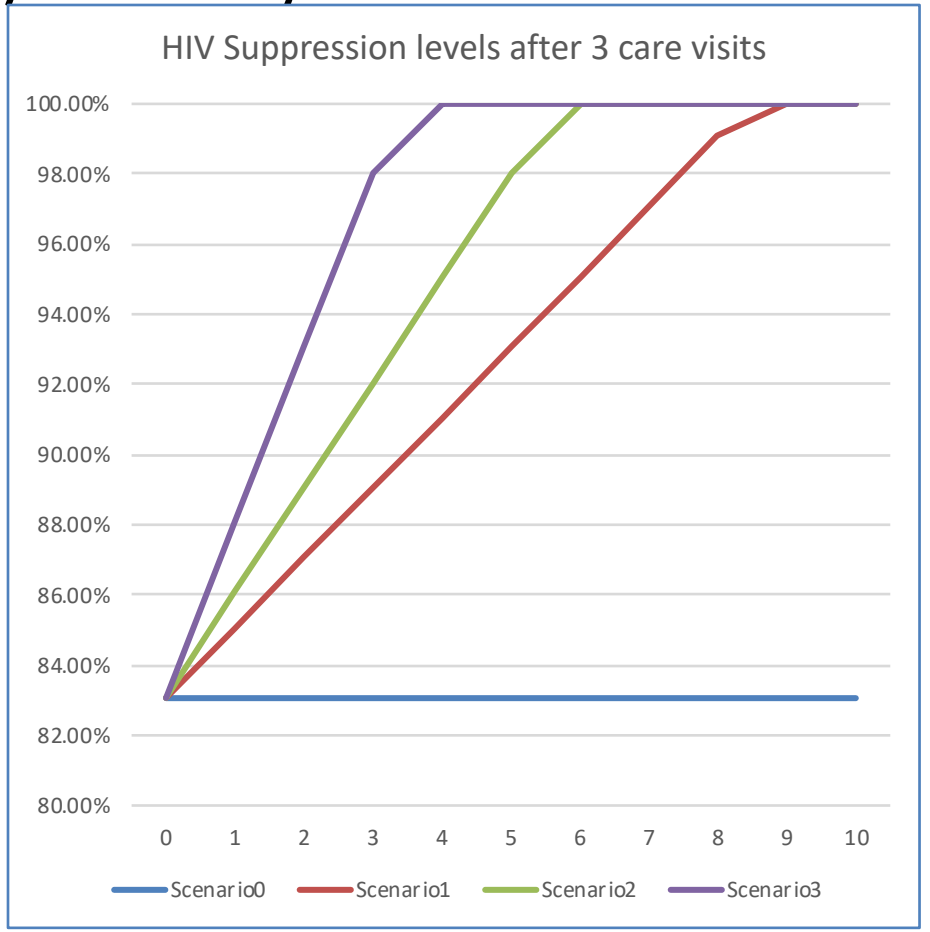
Current this probability is steady at **83.06%**

When we speak of viral suppression we in fact measure the chance that an MSM will become suppressed while being in care for 2 years.

This effect is assumed to be caused by varying levels of adherence to ART

In our scenarios we increase this chance by

- 2% annually (in scenario1)
- 3% annually (in scenario2)
- 5% annually (in scenario3)



Baseline data are based on CDPH data

Experimental setup for a population of 6500 MSM (1:10)

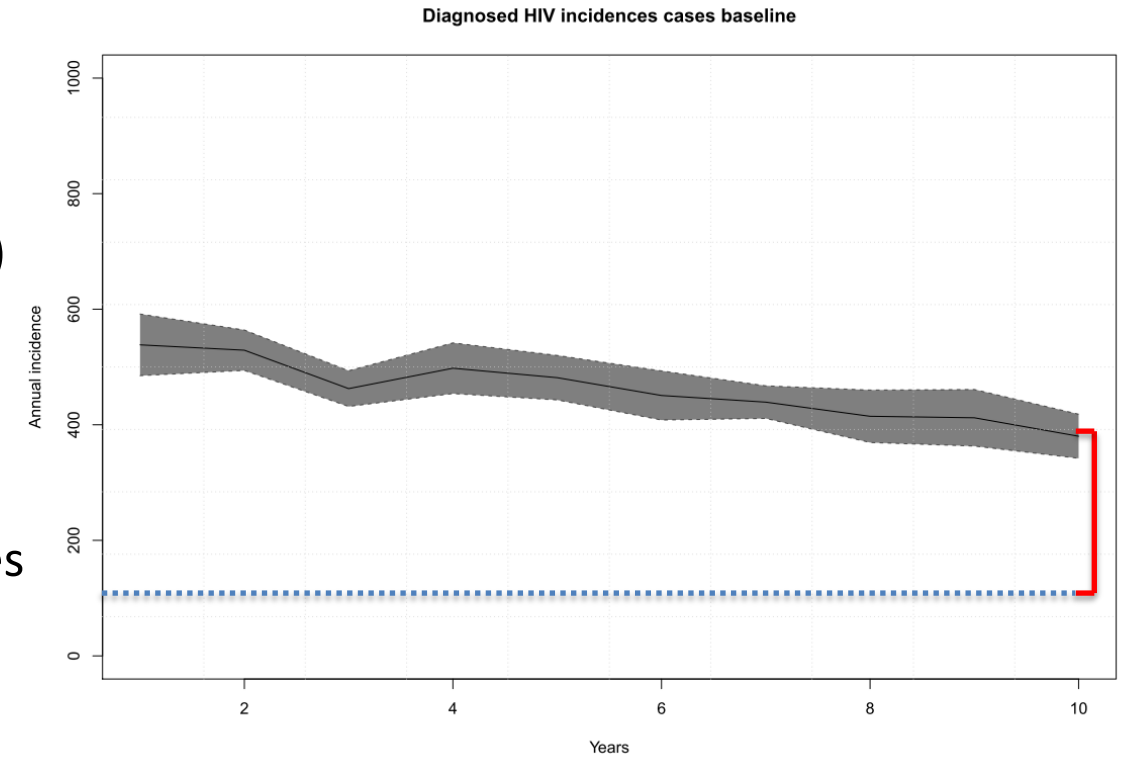
- 6 levels of Linkage to PrEP
- 3 levels of Adherence tp PrEP
- 4 levels of Retention in PrEP care
- 2 levels of Linkage to care
- 4 levels of Adherence to care (rate of viral suppression)
- 4 levels of Retention in care

2304 intervention scenarios (6x4x3x2x4x4)

As results are stochastic each scenario is repeated 22 times

Totaling over 50k simulation runs

Each scenario runs simulates a period of ten years, at which point the annual number of new diagnoses are calculated



Analyzing the experimental results

- We use partitioning trees as our main analysis methodology.

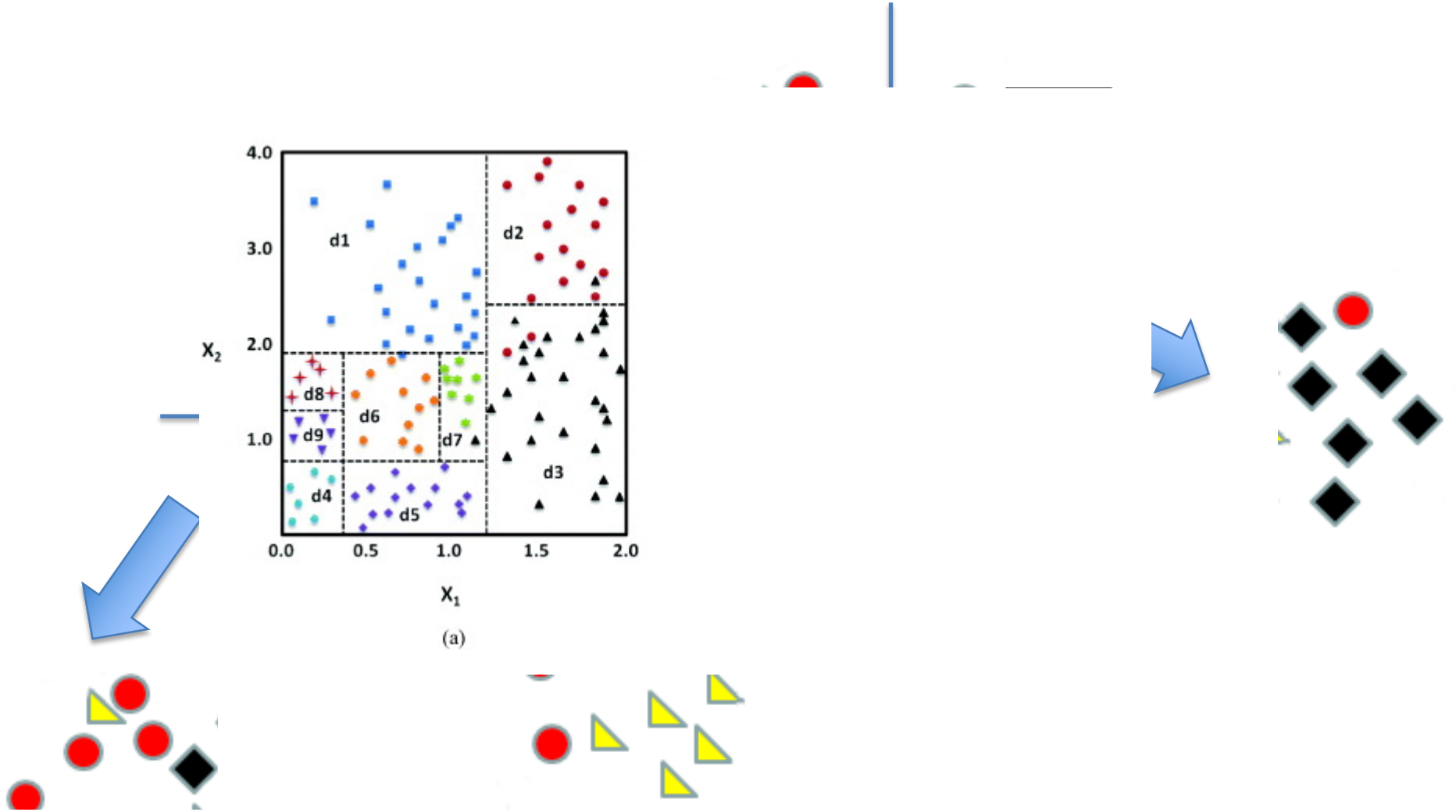
We choose this methodology as it:

a) Allows the consideration of multiple intervention dimensions at the same time

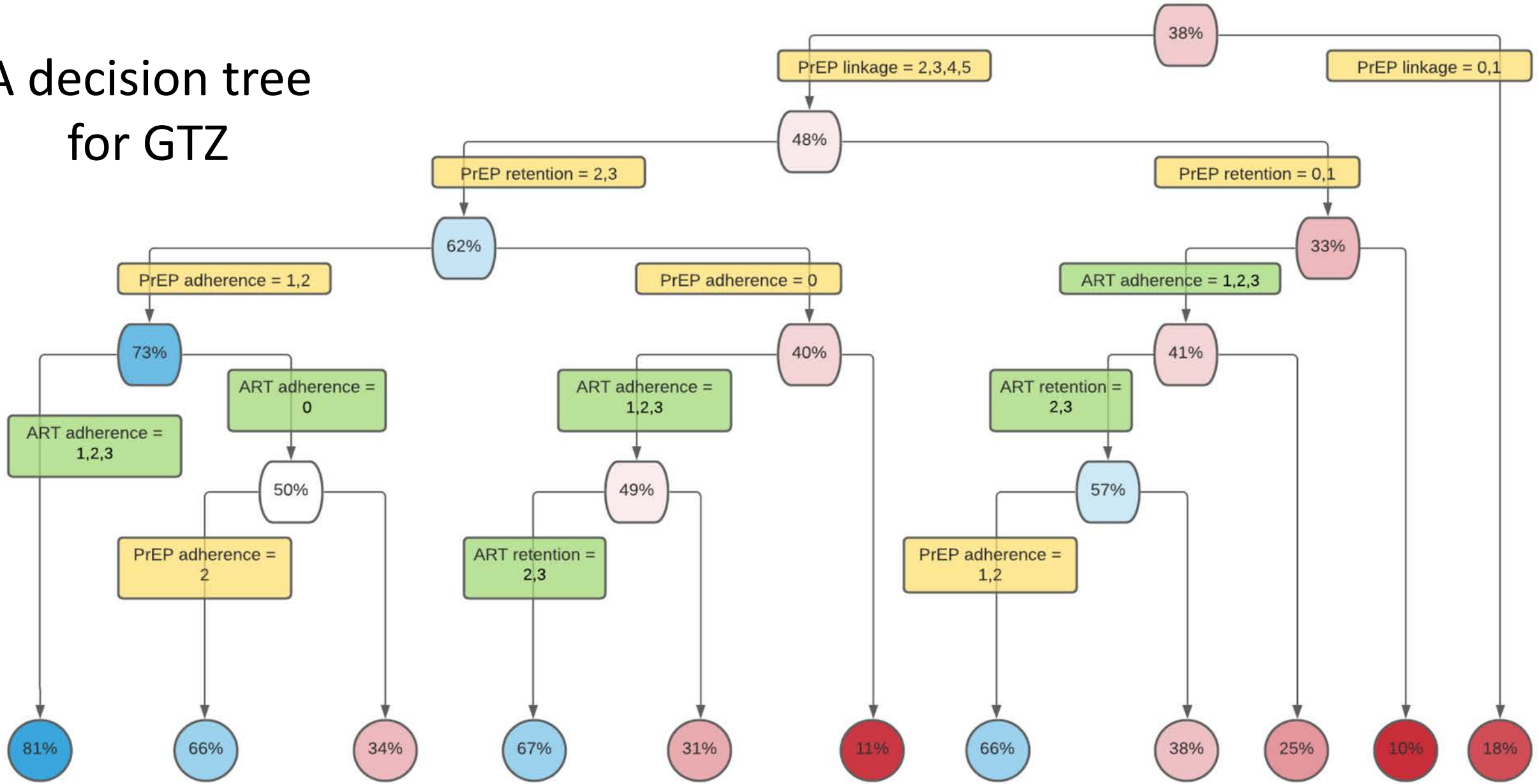
b) Allows for graphical representation of our results which improves interpretability

c) Translates naturally in a decision tree, which is a powerful tool for decision support

How do partitioning trees work?



A decision tree for GTZ

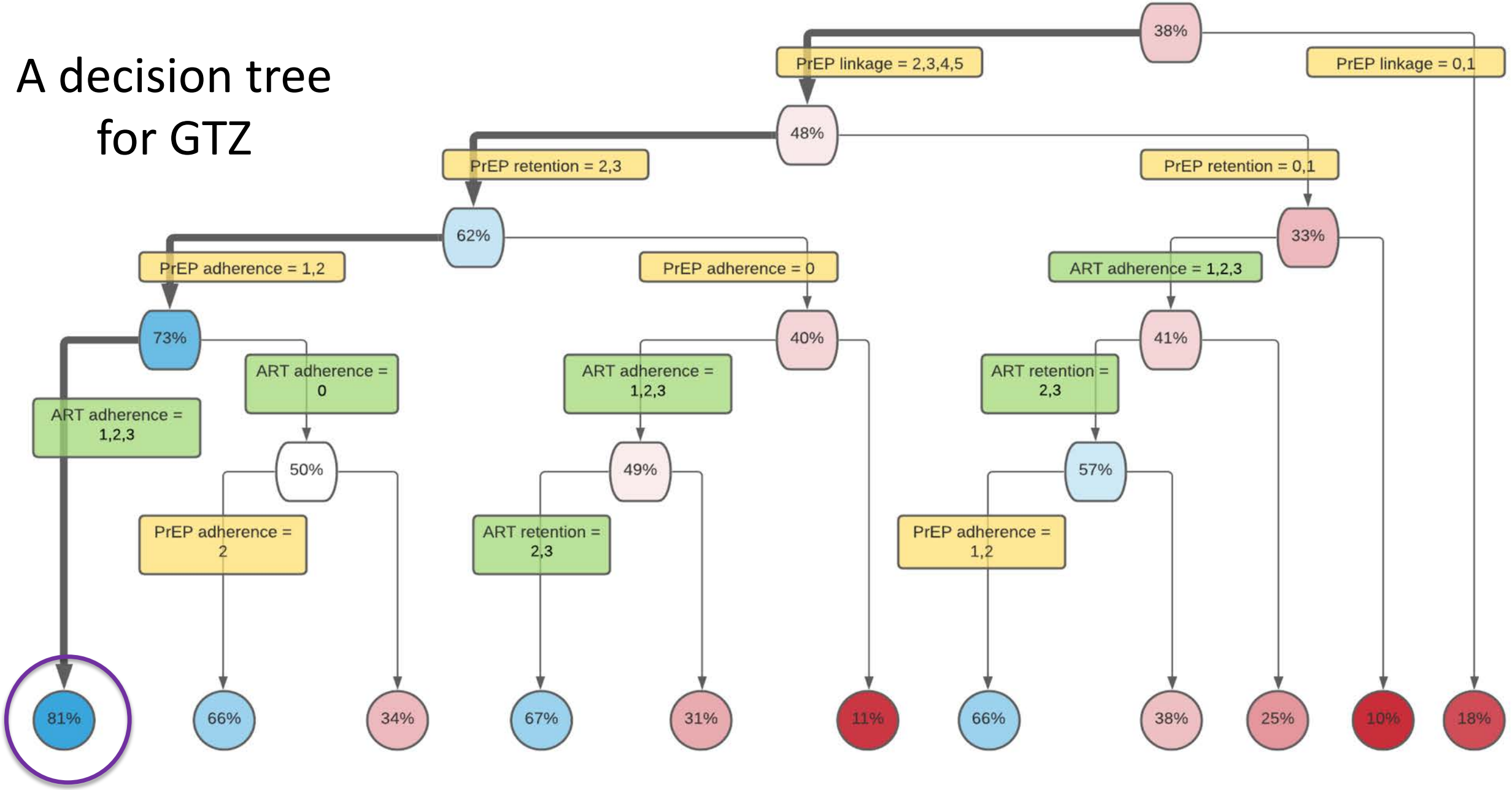


A decision tree for GTZ

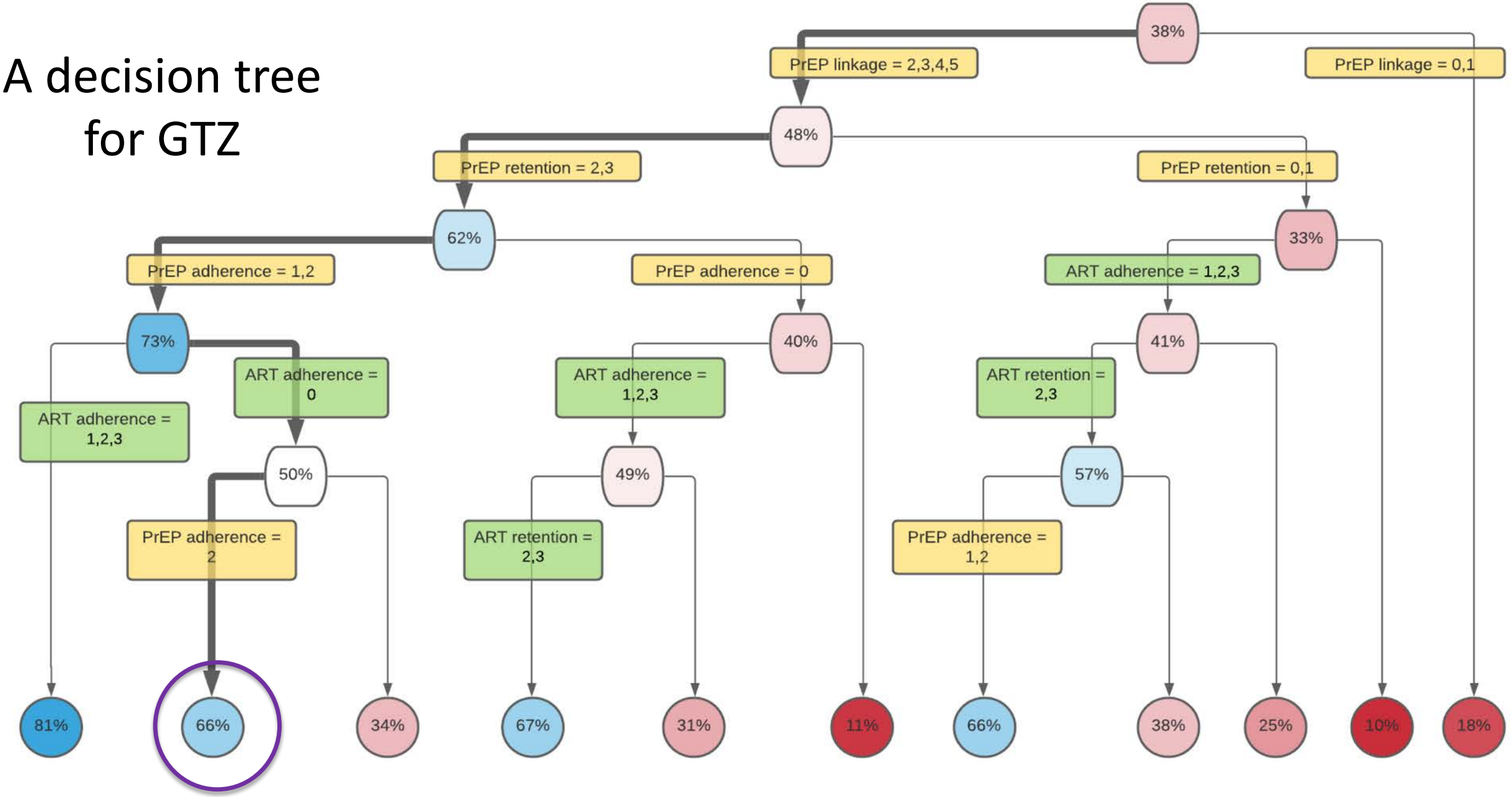
Prevention and Treatment Targets (Levers)

	Prevention			Treatment		
	PrEP Linkage (Years to 20% increase)	PrEP Retention	PrEP Adherence	Linkage to Care	Retention in Care	ART Adherence (Viral Suppression)
Baseline	**10**	**54%**	**Non-adherent: 22%; Low: 7%; Moderate: 10%; Full: 62%**	**90%**	**73%**	**83%**
Scenario 1	5	65%	Non-adherent: 0%; **Low: 14%; Moderate: 17%; Full: 69%**	100%	77%	85%
Scenario 2	3.3	75%	Non-adherent: 0%; Low: 0%; Moderate: 0%; **Full: 100%**		85%	86%
Scenario 3	2.5	85%			97%	88%
Scenario 4	2					
Scenario 5	1.3					

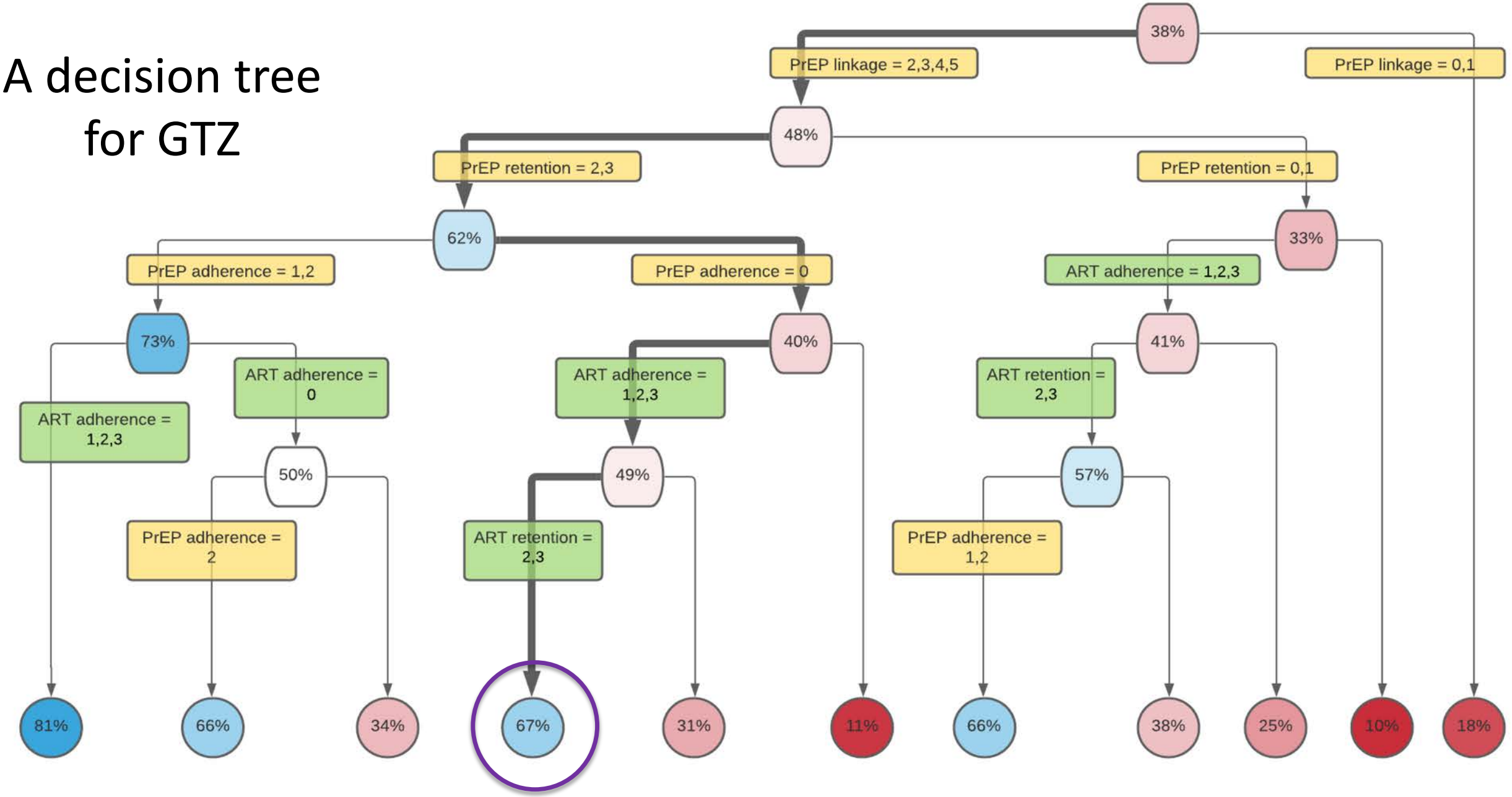
A decision tree for GTZ



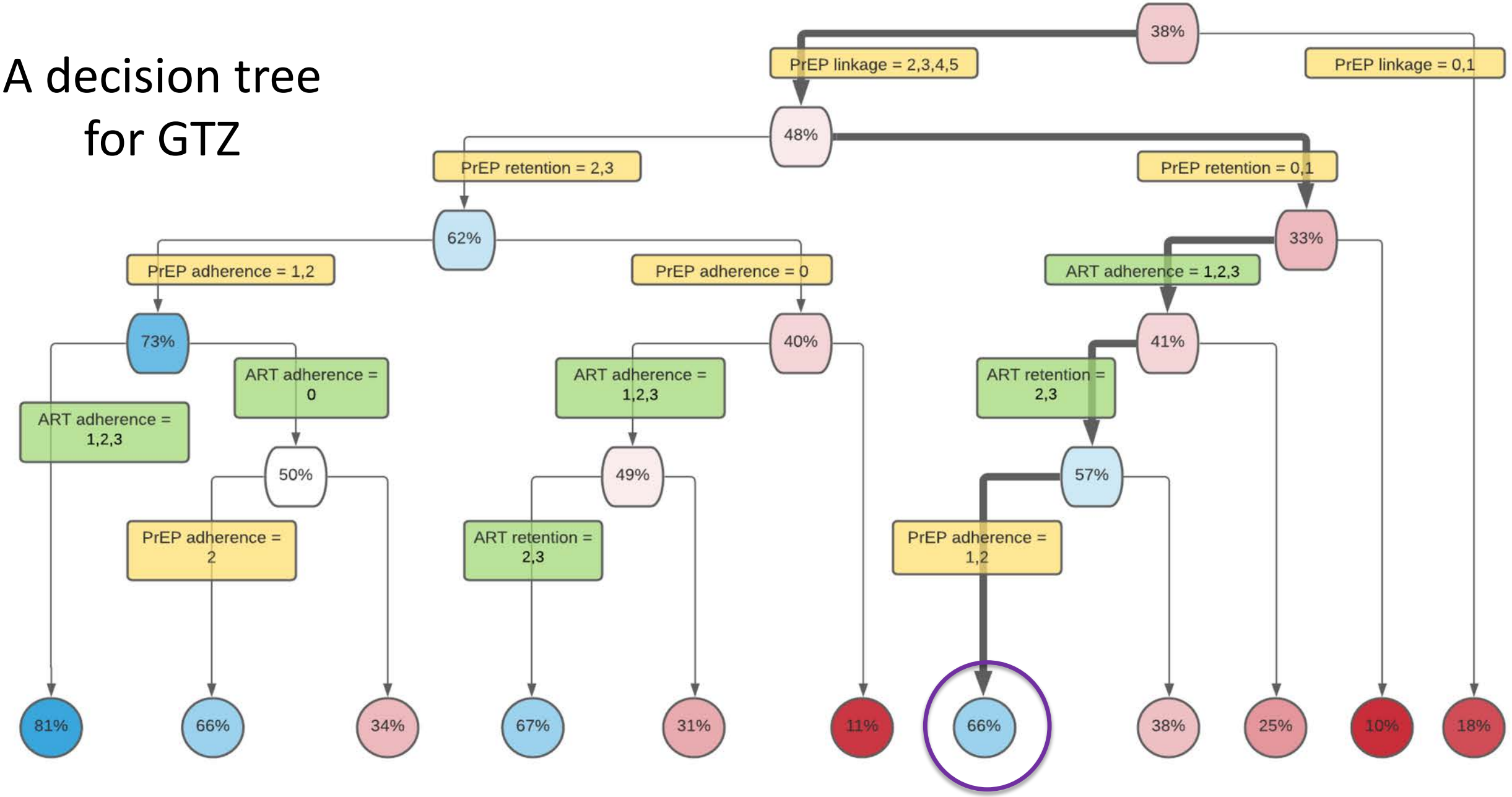
A decision tree for GTZ



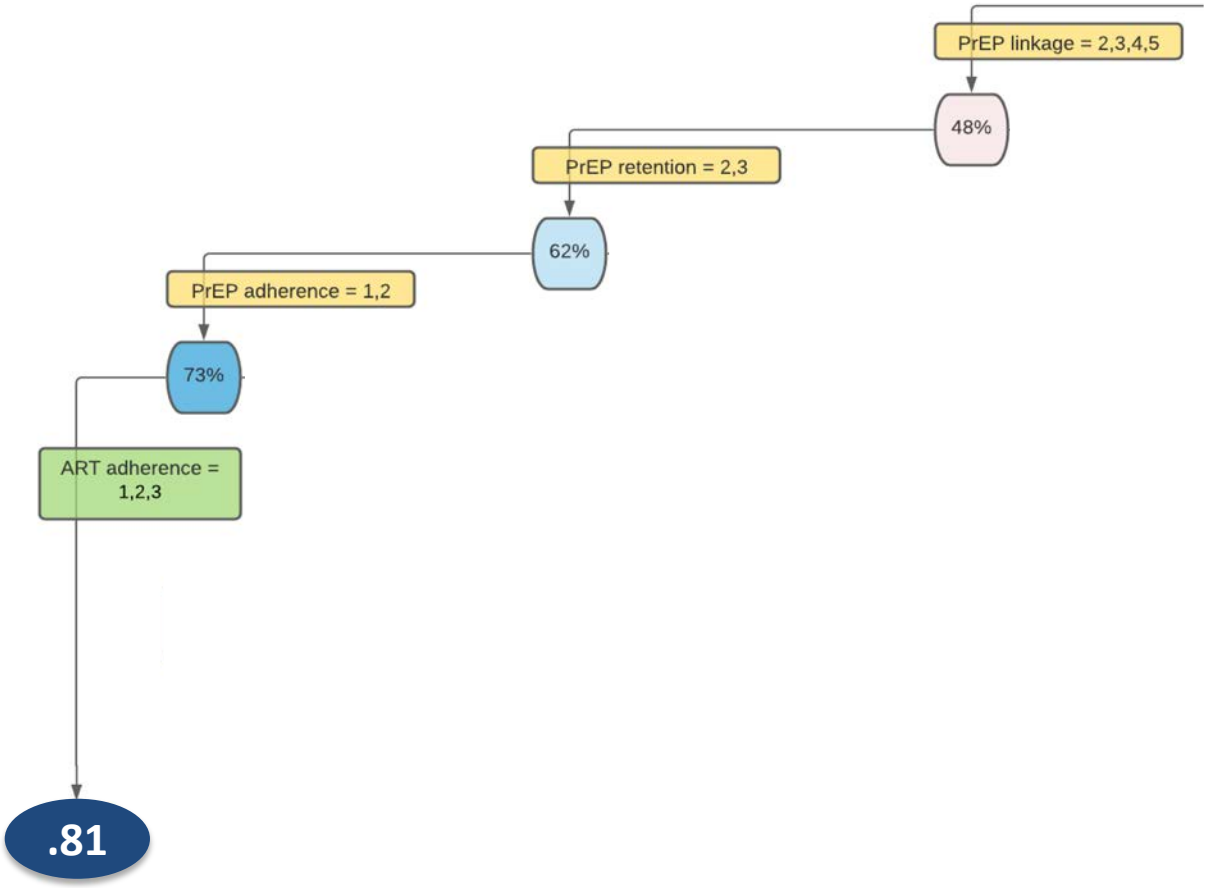
A decision tree for GTZ



A decision tree for GTZ



Effective Combination Prevention Toward GTZ Goal



81% of all simulations that achieve targets in this pathway reach GTZ goal:

PrEP

* **Linkage by 20% in ≤ 3 years**
* **Retention to at least 75%**
* **Full or < 30% low-moderate adherence**

ART

* **At least 85% of those in care for 2 years will become suppressed (adherent)**
* Baseline linkage
* Baseline retention

Other Pathways

66% of all simulations that achieve targets in this pathway reach GTZ goal:

PrEP

* Increase linkage by 20% in ≤ 3 years
* Increase retention to at least 75%
* **Achieve full adherence**

ART

* Baseline linkage
* Baseline retention
* **Baseline adherence**

67% of all simulations that achieve targets in this pathway reach GTZ goal:

PrEP

* Increase linkage by 20% in ≤ 3 years
* Increase retention to at least 75%
* **Baseline adherence**

ART

* Baseline linkage
* **At least 85% are retained in care**
* At least 85% of those in care for 2 years are suppressed

66% of all simulations that achieve targets in this pathway reach GTZ goal:

PrEP

* Linkage by 20% in ≤ 3 years
* **Baseline (53%) - 65% are retained**
* Full or < 30% low-moderate adherence

ART

* Baseline linkage
* **At least 85% are retained in care**
* At least 85% of those in care for 2 years will become suppressed

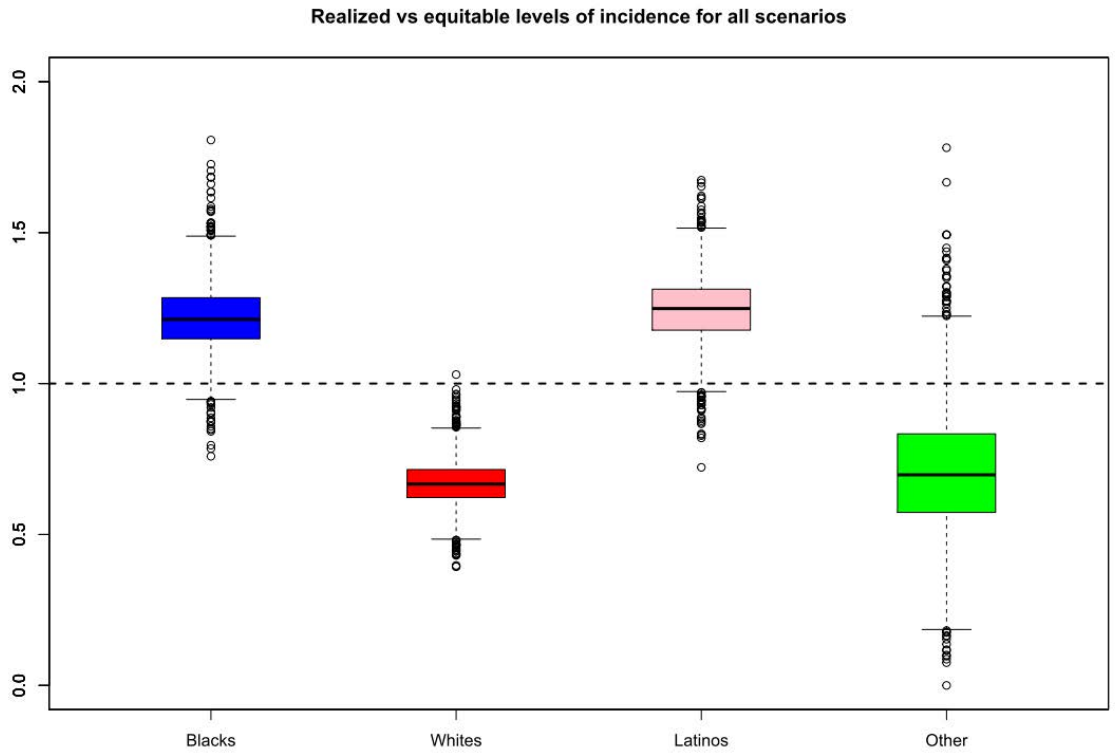
Considerations for Combination Prevention Approaches

- There are multiple combinations of targets for prevention and care continuum steps to achieve the GTZ goal, some more likely to achieve it than others
  - The most effective pathway involves high levels of all PrEP continuum steps, and moderate ART adherence
  - Achieving high levels of PrEP linkage in the first few years is central to all viable pathways
- Increasing linkage to care does not seem to have a strong impact given existing high levels
- Retention in care needs to exceed baseline if not possible to impact current levels of PrEP adherence

What does our model tell us about racial disparities?

We compared the rate of incidence in the model by race (and normalize over the total population)

- Substantial disparities that are present at the model initialization,
- Blacks and Latinos are disproportionally affected
- These effect are likely underestimated, given our model performs poorly in capturing the disparities from onset
- Disparities remain fairly constant throughout the 10 year simulation window



Model development next steps

Version 1.1:

- Revamp the ART treatment module using new data from CDPH

Version 2.0:

- Expand to address racial/ethnic and other HIV disparities
- Expand the population in the model (e.g. cis-women)

Version 3.0:

- Update the input data and integrate ongoing data updates
- Explore and incorporate other interventions that address social determinants of health that impact HIV

Next Steps For Public Health Application

- Need for feedback and input continues!
  - Inform ways to make model usable and readily available for users
  - On-going model validation with input from CDPH
  - Adapt model for use in other jurisdictions
    - Identify alternative data sources for partnership/network dynamics
    - Identify other key stakeholders and potential users
    - Develop SAS programs and guidance to facilitate obtaining data for model
  - Identify interventions considered in EHE jurisdictional plans that address the model's prevention and care continuum steps
  - Identify intervention strategies

Q & A

Selected Readings

- Benbow N, Aaby D, Rosenberg E, Brown C. (2020) County-level factors affecting Latino HIV disparities in the United States. *PLoS One*. doi: 10.1371/journal.pone.0237269.
- Vermeer, W., Hjorth, A., Jenness, S. M., Brown, C. H., & Wilensky, U. (2020). Leveraging modularity during replication: Lessons from replicating a complex agent-based model for HIV prevention. Journal of Artificial Societies and Social Simulation, To Appear.