



# People Aging with HIV in the US: A Simulation Modeling Approach

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*Funded by: NIA R01AG069575, the Jerome and Celia Reich HIV Scholar Award, HU CFAR*



# Disclosures

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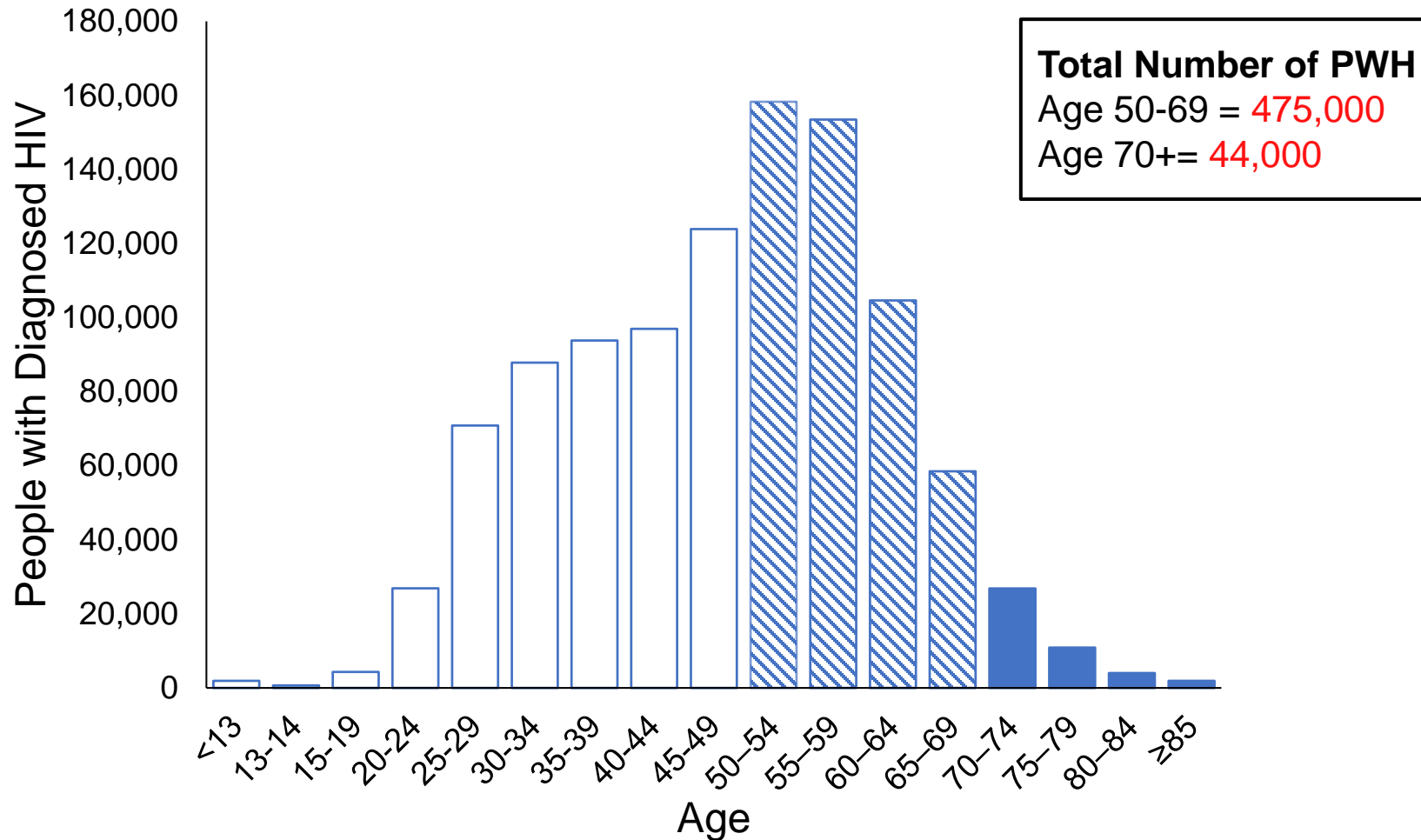
- Co-author at UpToDate.com

# Outline

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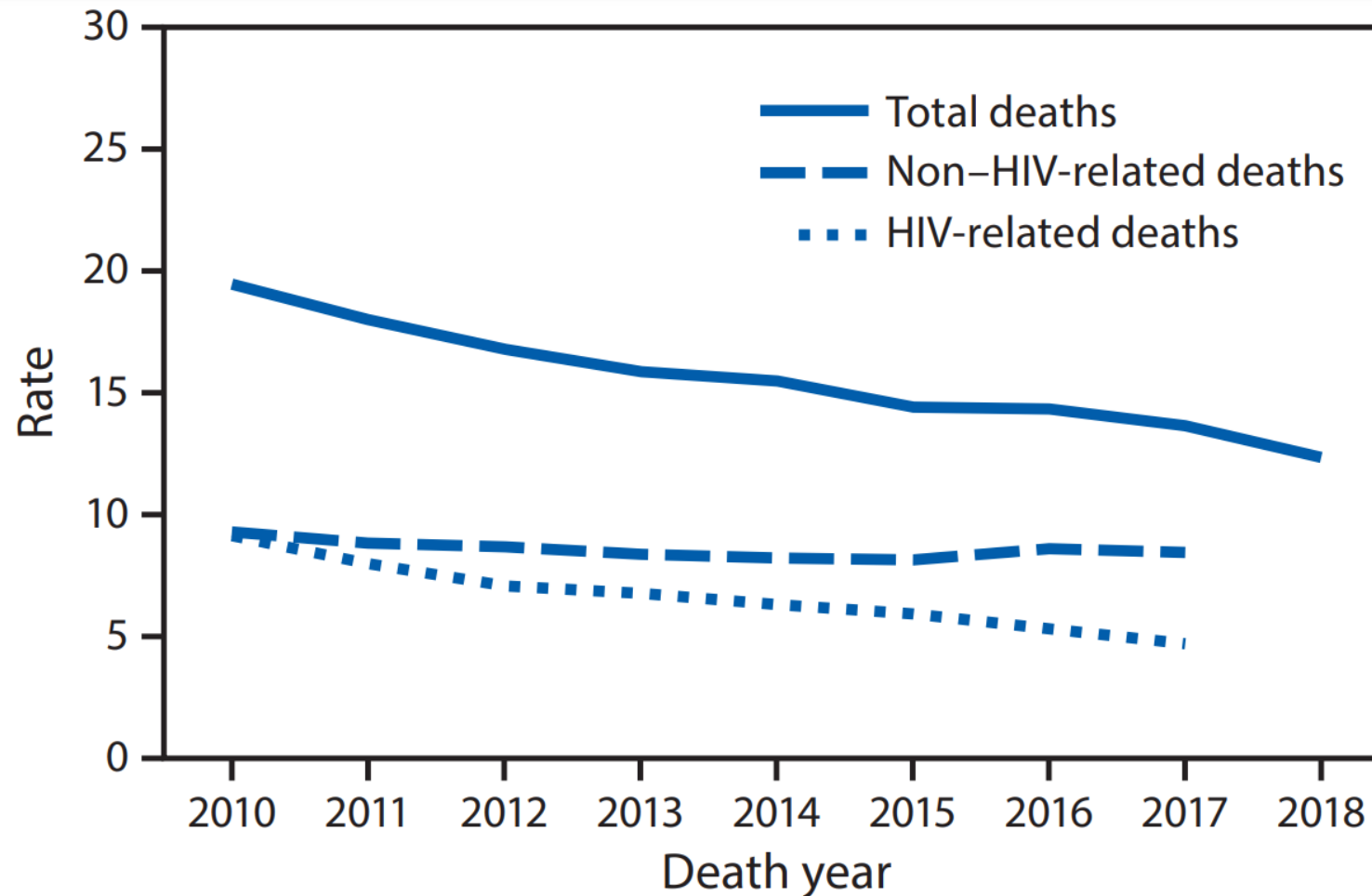
- **Background**
- Simulation modeling
- Model projections
  - MSM aging with HIV
  - Age-associated dementia
- Costs
- Conclusions

# Age distribution of PWH in the US, 2018



# Declining HIV-related mortality, 2010-2018

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# Multimorbidity, polypharmacy, and frailty

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- Multimorbidity is common and is rising among PWH
  - Traditional and HIV-related risk factors contribute to multimorbidity
- Polypharmacy includes risks of adverse events and drug-drug interactions
- Among PWH >50y, frailty is common (10.9%) and pre-frailty very common (47.2%)
  - Similar in frequency to community-dwelling adults >65y

# People aging with HIV in the US

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- Life expectancy of PWH who are engaged in care and virologically suppressed is near normal, but age-associated co-morbidities are rising
- Given trends in multimorbidity, additional clinical complexity and costs are anticipated in the future
- Simulation modeling can be used to project the future burden of co-morbidities among people aging with HIV

# People aging with HIV in the US

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# What can we do in simulation modeling?

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- Use existing data to project longer-term clinical and economic outcomes
- Investigate the impact of uncertainty in data on outcomes of interest
- Examine which parameters have the greatest influence on outcomes
- Estimate the value of specific interventions

“All models are wrong, but some are useful.”

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– George Box

# Cost-effectiveness of preventing AIDS complications (CEPAC) model\*

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- CEPAC is a simulation model of HIV disease and treatment that incorporates CD4, HIV RNA, ART, opportunistic infections, and age-associated comorbidities

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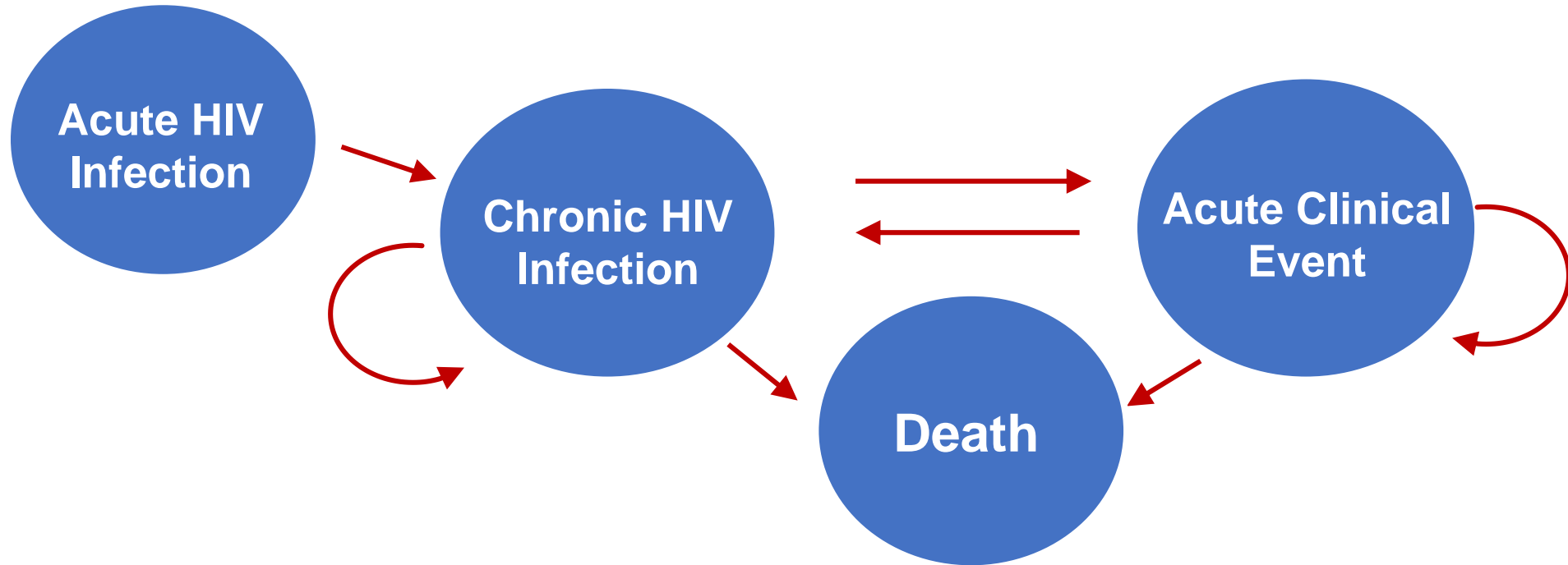
# Cost-effectiveness of preventing AIDS complications (CEPAC) model\*

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- CEPAC is a simulation model of HIV disease and treatment that incorporates CD4, HIV RNA, ART, opportunistic infections, and age-associated comorbidities
- Data are from public use datasets, observational cohorts, and clinical trials
- Model outcomes are reported in projected life expectancy, detailed clinical outcomes, and costs

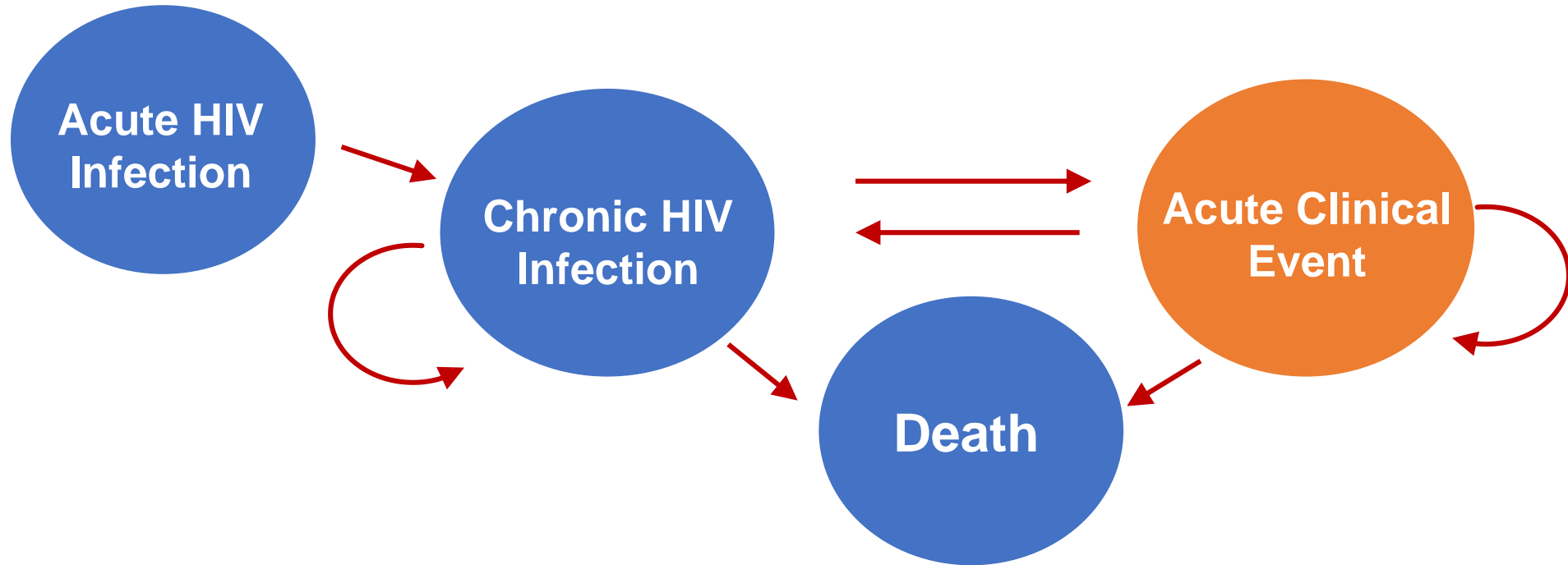
# The CEPAC microsimulation model

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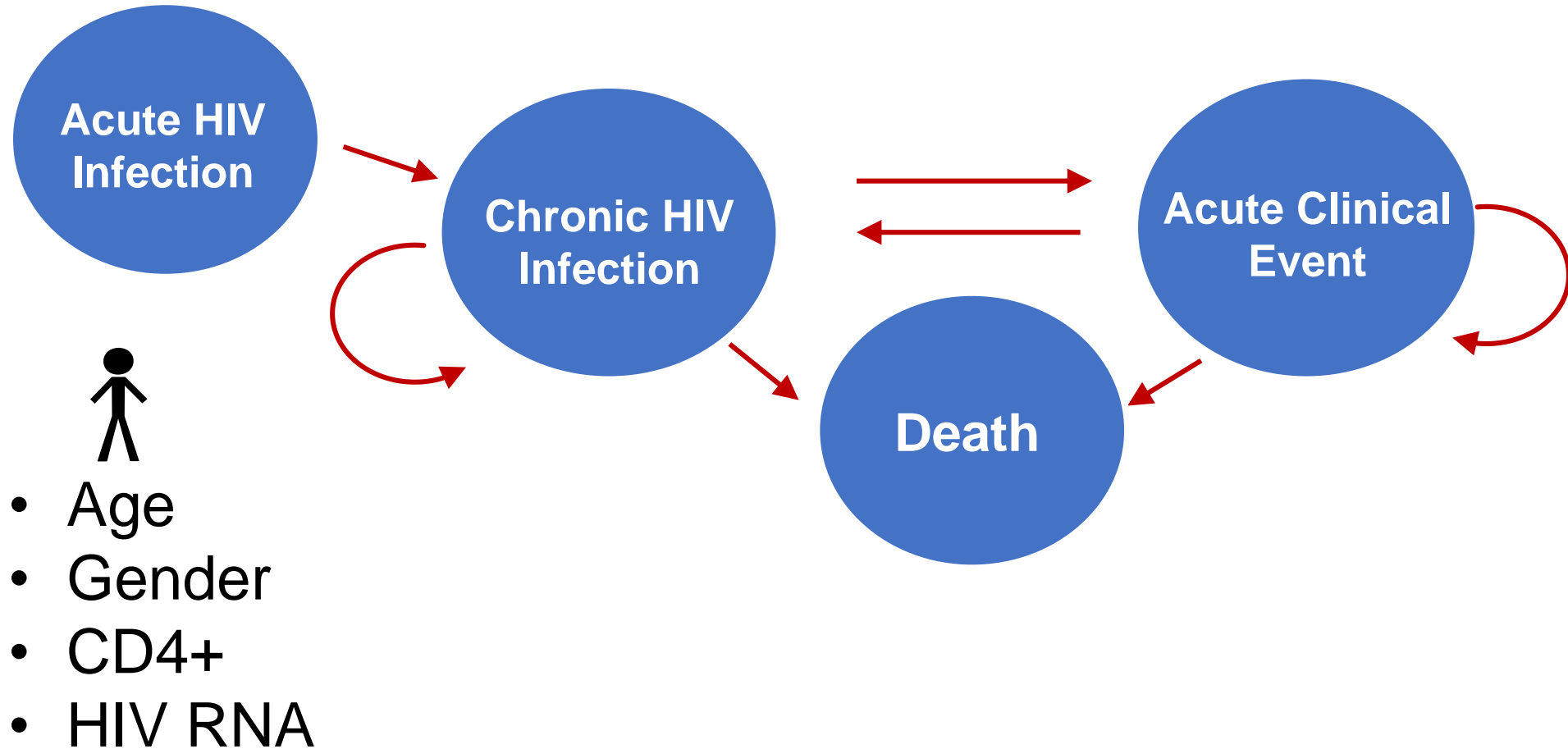


- Opportunistic infections
- Age-associated co-morbidities



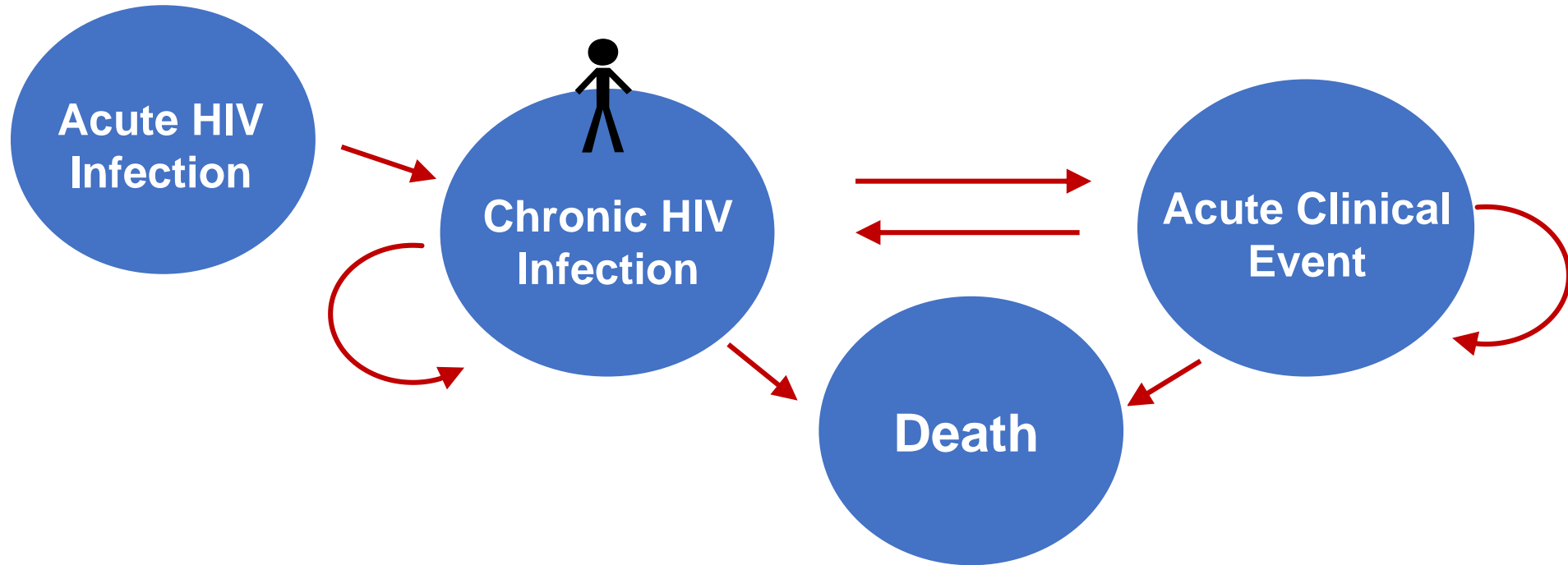
# The CEPAC microsimulation model

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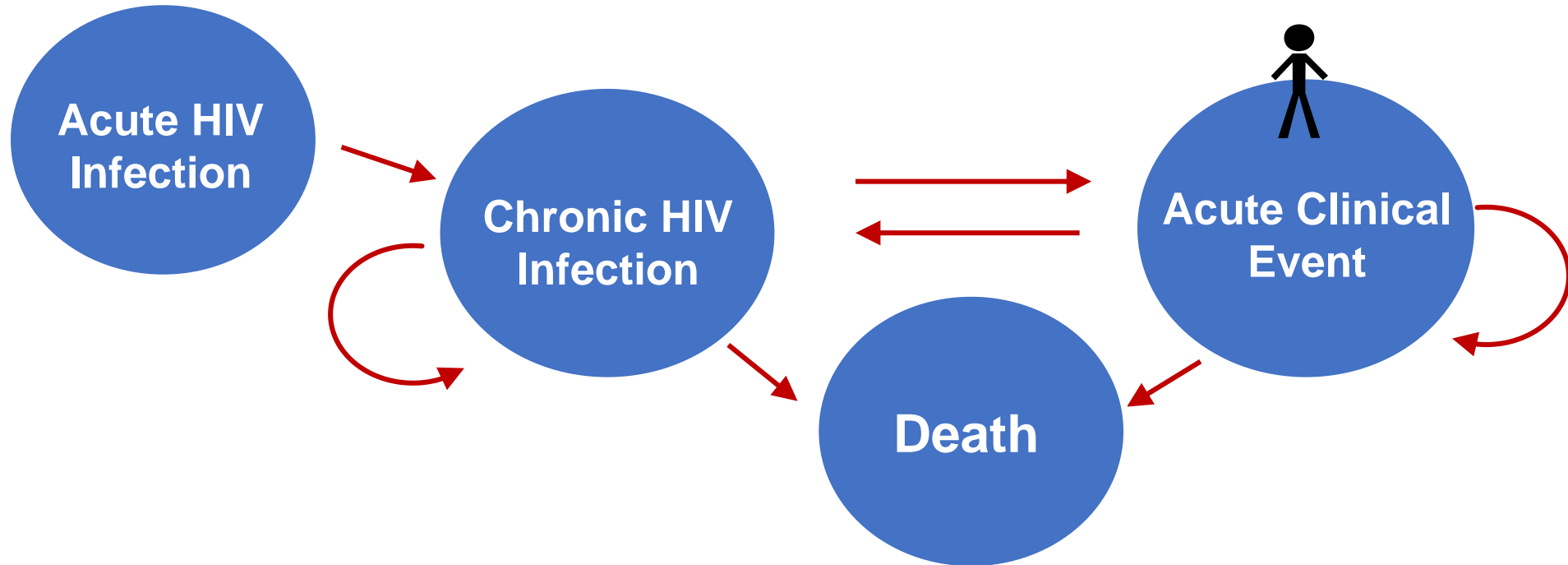
# The CEPAC microsimulation model

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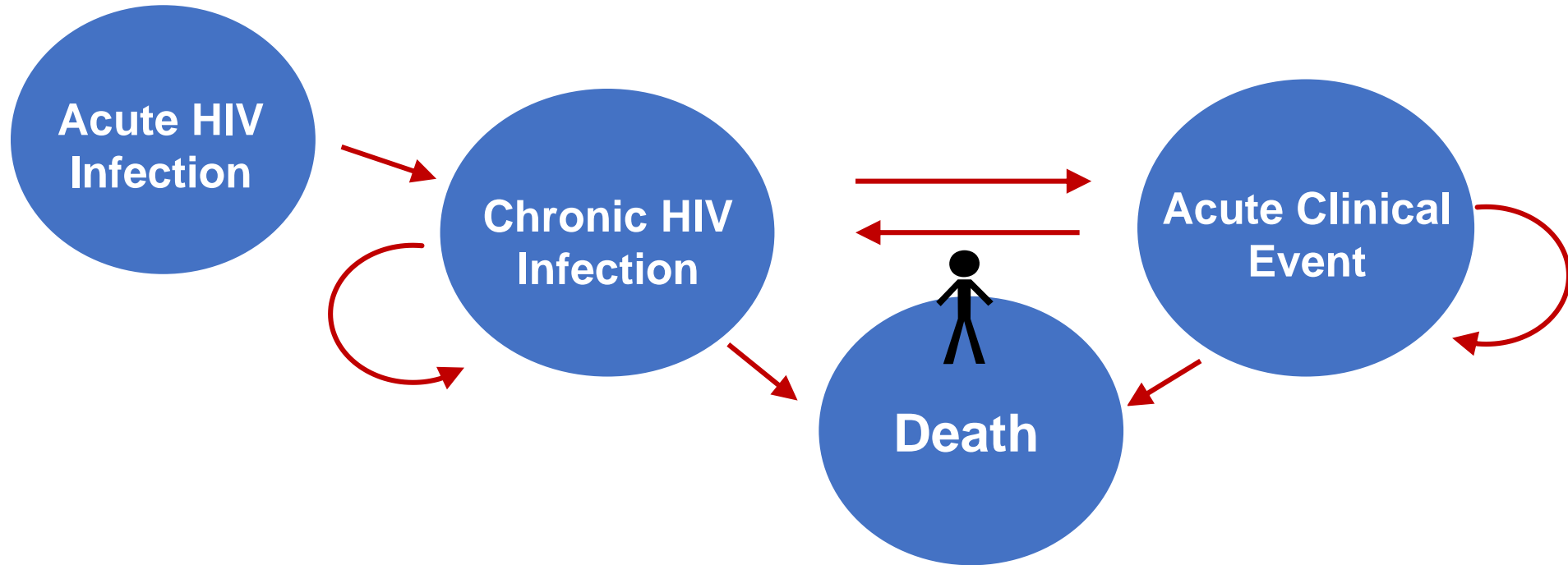
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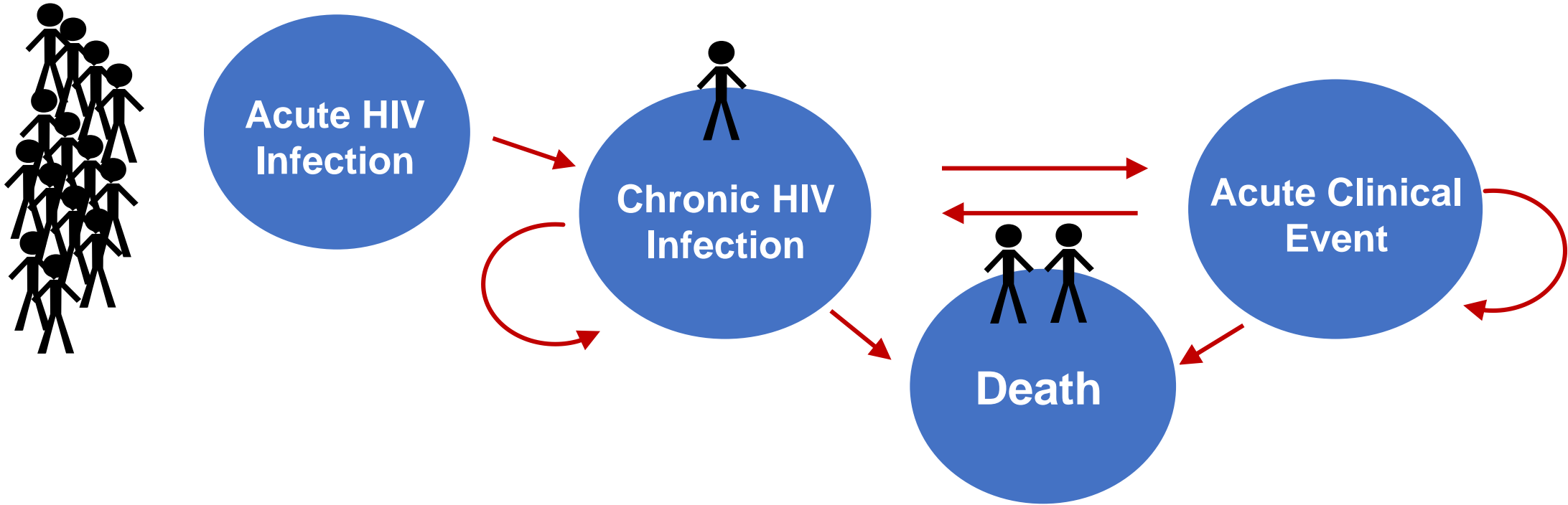
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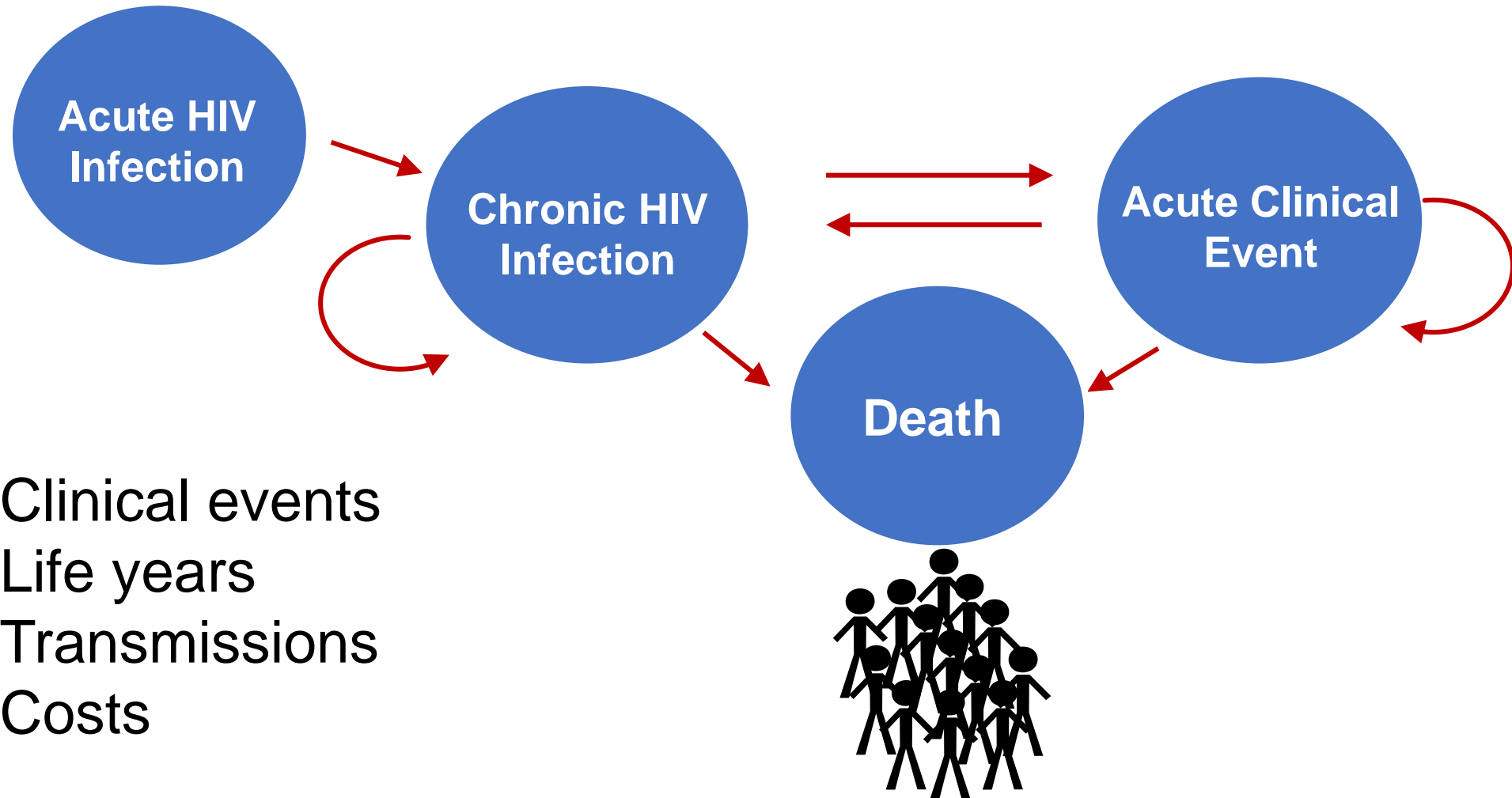
# The CEPAC microsimulation model

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# CEPAC model outcomes

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- Clinical events
- Life years
- Transmissions
- Costs



# CEPAC investigators

CEPAC Adult (US and International) <ul style="list-style-type: none"><li>• South Africa, Cote d'Ivoire, India, Brazil</li><li>• Zimbabwe, Botswana, Mozambique</li></ul>	Ken Freedberg
Aging and co-morbidities	Emily Hyle
Smoking & TB	Krishna Reddy
CEPAC Pediatrics & Perinatal Transmission	Andrea Ciaranello & Caitlin Dugdale
CEPAC Adolescents & Young Adults	Anne Neilan
HBV natural history and treatment	Amir Mohareb & Emily Hyle

# CDC HIV testing recommendations (1993, 1996, 2001)

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**Revised Guidelines for HIV Counseling,  
Testing, and Referral**

and

**Revised Recommendations  
for HIV Screening  
of Pregnant Women**

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Centers for Disease Control and Prevention (CDC)  
Atlanta, GA 30333



- Routine HIV screening in settings prevalence  $\geq 1\%$
- Targeted testing based on risk assessment
- Prevention counseling required



SPECIAL ARTICLE

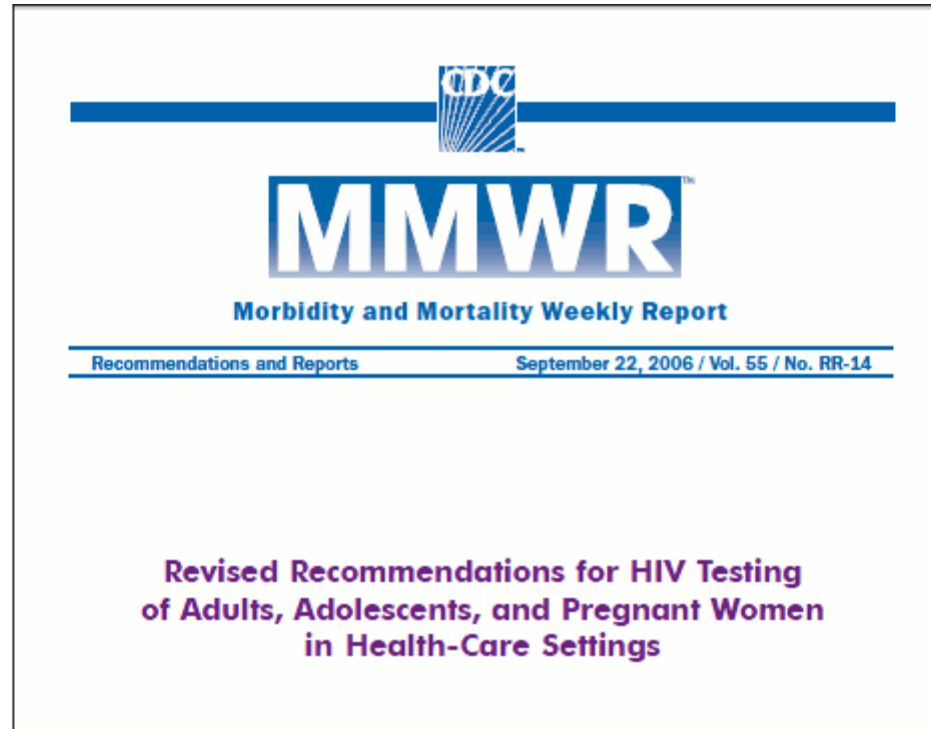
Expanded Screening for HIV in the United States  
— An Analysis of Cost-Effectiveness

A. David Paltiel, Ph.D., Milton C. Weinstein, Ph.D., April D. Kimmel, M.Sc.,  
George R. Seage III, Sc.D., M.P.H., Elena Losina, Ph.D., Hong Zhang, S.M.,  
Kenneth A. Freedberg, M.D., and Rochelle P. Walensky, M.D., M.P.H.

SPECIAL ARTICLE

Cost-Effectiveness of Screening for HIV  
in the Era of Highly Active Antiretroviral Therapy

Gillian D. Sanders, Ph.D., Ahmed M. Bayoumi, M.D., Vandana Sundaram, M.P.H.,  
S. Pinar Bilir, A.B., Christopher P. Neukermans, A.B., Chara E. Rydzak, B.A.,  
Lena R. Douglass, B.S., Laura C. Lazzeroni, Ph.D., Mark Holodniy, M.D.,  
and Douglas K. Owens, M.D.



## Screening for HIV Infection

- In all health-care settings, screening for HIV infection should be performed routinely for all patients aged 13–64 years. Health-care providers should initiate screening unless prevalence of undiagnosed HIV infection in their patients has been documented to be  $<0.1\%$ . In the absence of existing data for HIV prevalence, health-care providers should initiate voluntary HIV screening until they establish that the diagnostic yield is  $<1$  per 1,000 patients screened, at which point such screening is no longer warranted.

# Should We Be Testing for Baseline Integrase Resistance in Patients Newly Diagnosed With Human Immunodeficiency Virus?

**Yiannis Koullias,<sup>1,2</sup> Paul E. Sax,<sup>2,3</sup> Naomi F. Fields,<sup>4</sup> Rochelle P. Walensky,<sup>2,3,4,5</sup> and Emily P. Hyle<sup>2,4,5</sup>**

<sup>1</sup>Department of Medicine, Brigham and Women's Hospital, <sup>2</sup>Harvard Medical School, <sup>3</sup>Division of Infectious Diseases, Brigham and Women's Hospital, and <sup>4</sup>Medical Practice Evaluation Center, Department of Medicine and <sup>5</sup>Division of Infectious Diseases, Massachusetts General Hospital, Boston



## Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

- Standard genotypic drug-resistance testing in ARV-naive persons involves testing for mutations in the reverse transcriptase (RT) and protease (PR) genes.
- If transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern, providers should ensure that genotypic resistance testing also includes the integrase gene.

**Annals of Internal Medicine**

ORIGINAL RESEARCH

# **Cost-Effectiveness of Long-Acting Injectable HIV Preexposure Prophylaxis in the United States**

## **A Cost-Effectiveness Analysis**

**Anne M. Neilan, MD, MPH; Raphael J. Landovitz, MD, MSc; Mylinh H. Le, BA; Beatriz Grinsztejn, MD, PhD; Kenneth A. Freedberg, MD, MSc; Marybeth McCauley, MPH; Nattanicha Wattananimitgul, BA; Myron S. Cohen, MD; Andrea L. Ciaranello, MD, MPH; Meredith E. Clement, MD; Krishna P. Reddy, MD, MS; Emily P. Hyle, MD, MSc; A. David Paltiel, PhD; and Rochelle P. Walensky, MD, MPH**

# Outline

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- Background
- Simulation modeling
- Model projections
  - **MSM aging with HIV**
  - Age-associated dementia
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# MSM aging with HIV in the US

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- To project the burden of age-associated comorbidities among people with HIV in the US, we first must examine the face validity of model-projected numbers and age distribution of people aging with HIV
- We focused initially on MSM with HIV as the largest group of people with HIV engaged in care in the US

# Objective

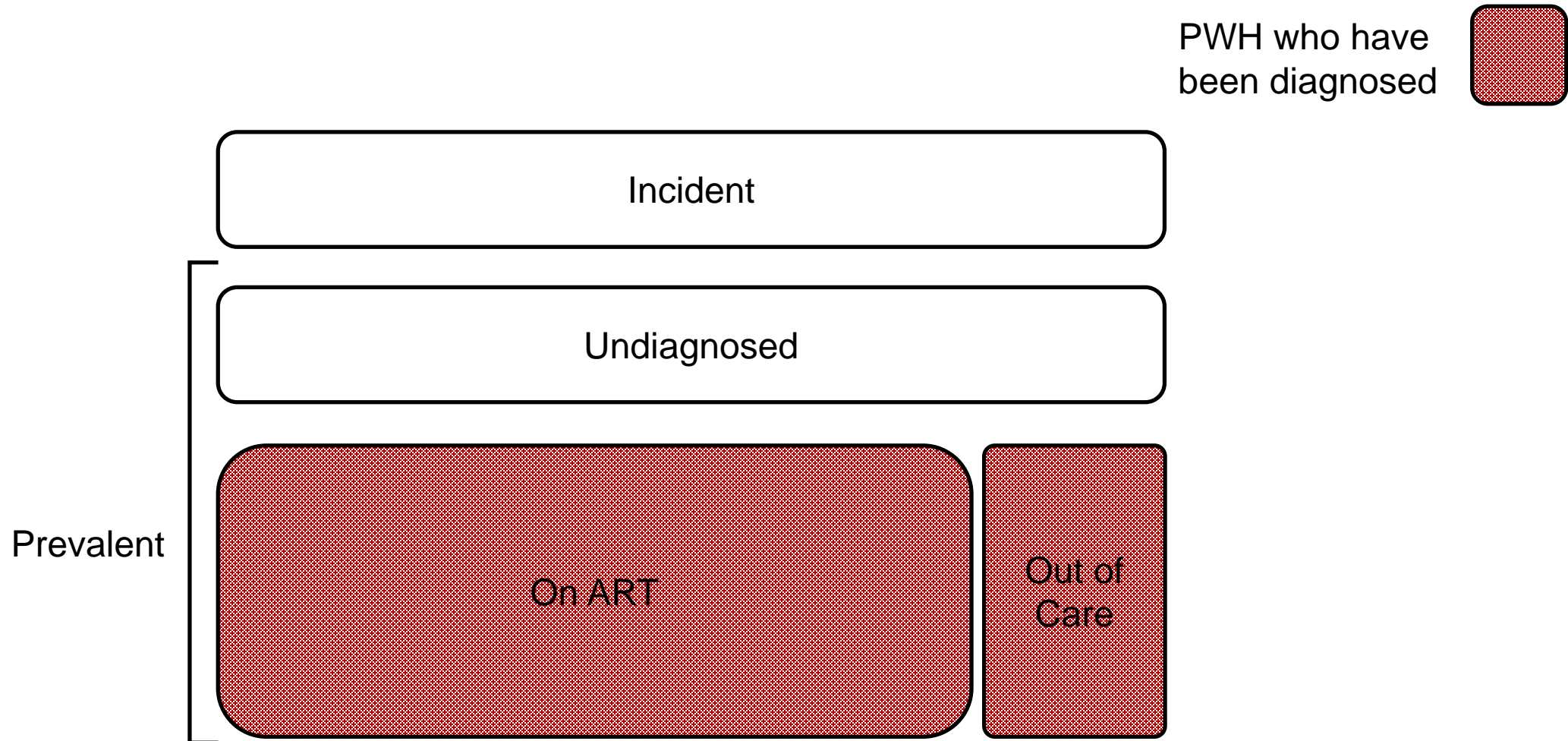
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- To use CEPAC to project the numbers and age distribution of MSM on ART from 2021 to 2031



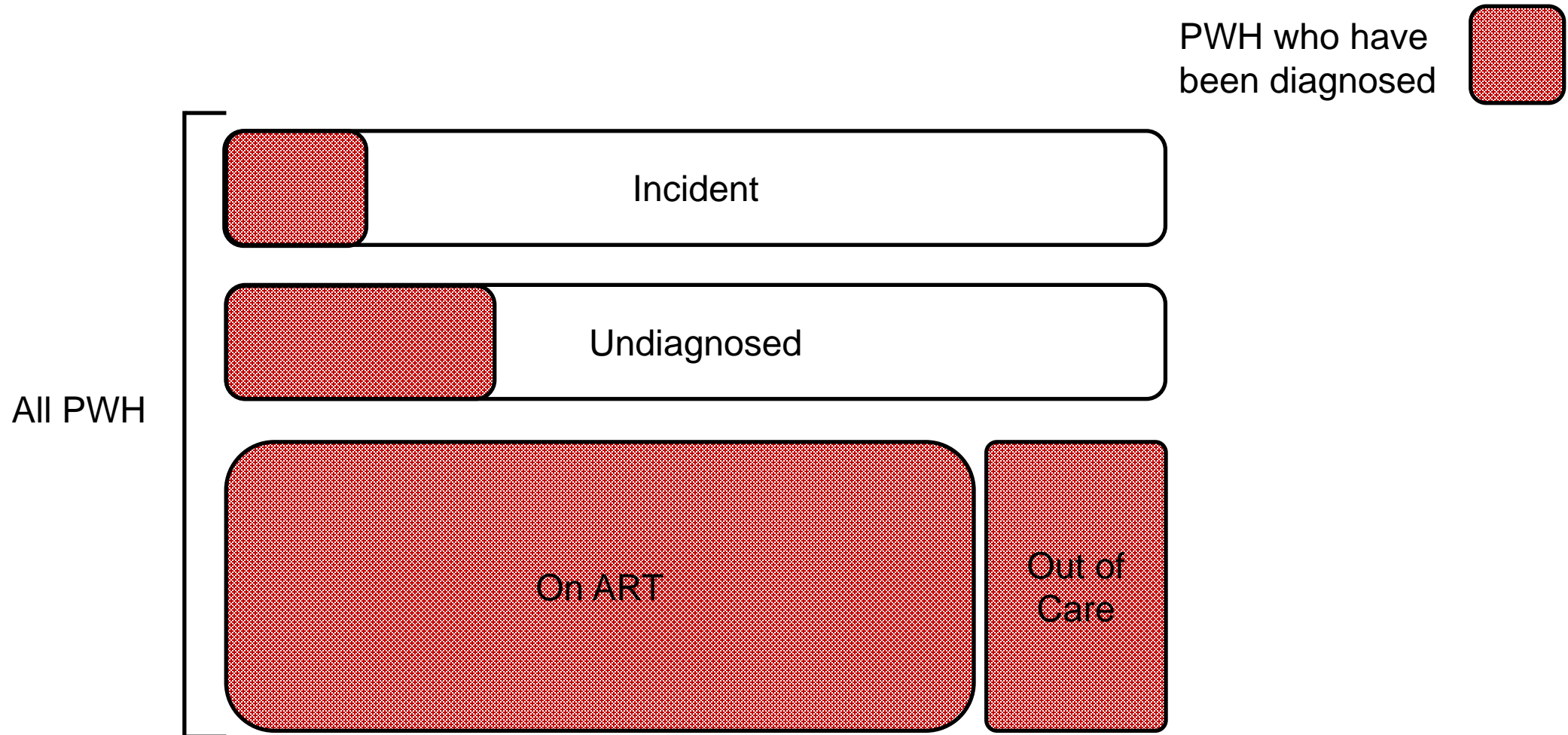
# Simulating the HIV care continuum

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# Progression along the HIV care continuum

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# Cohort characteristics at model start

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<b>Cohort</b>	<b>Initial CD4 count, mean cells/<math>\mu</math>l (SD)</b>	<b>Initial age, mean years (SD)</b>	<b>Cohort size, n</b>
Incident	667 (134)	33.7 (10.7)	Determined by transmissions

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On ART (in care)	600 (313)	45.7 (11.7)	370,000

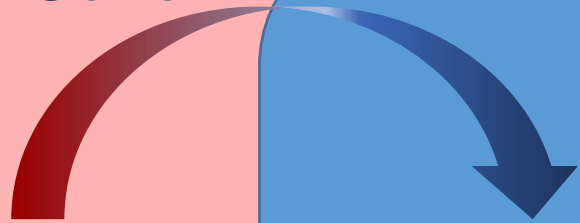
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On ART (in care)	600 (313)	45.7 (11.7)	370,000
Off ART (out of care)	325 (53)	45.7 (11.8)	124,000

# PWH Out of Care

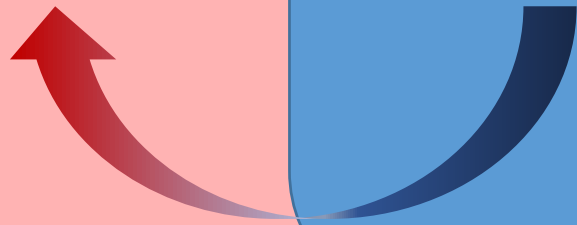
Return  
to Care



PWH In Care  
and On ART



Diagnosis  
& Linkage

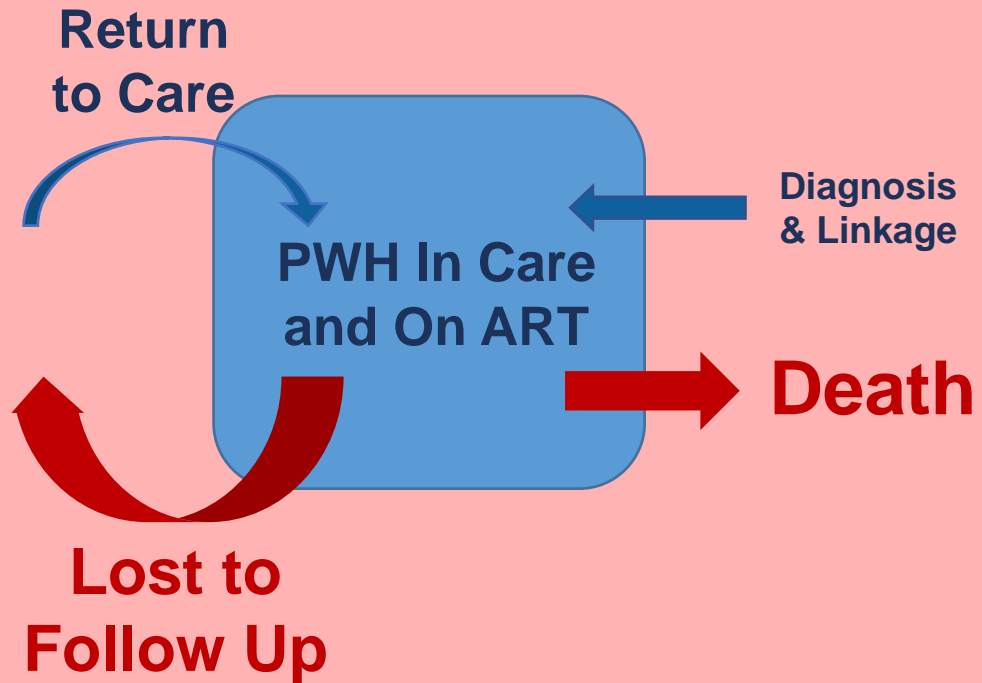


Lost to  
Follow Up

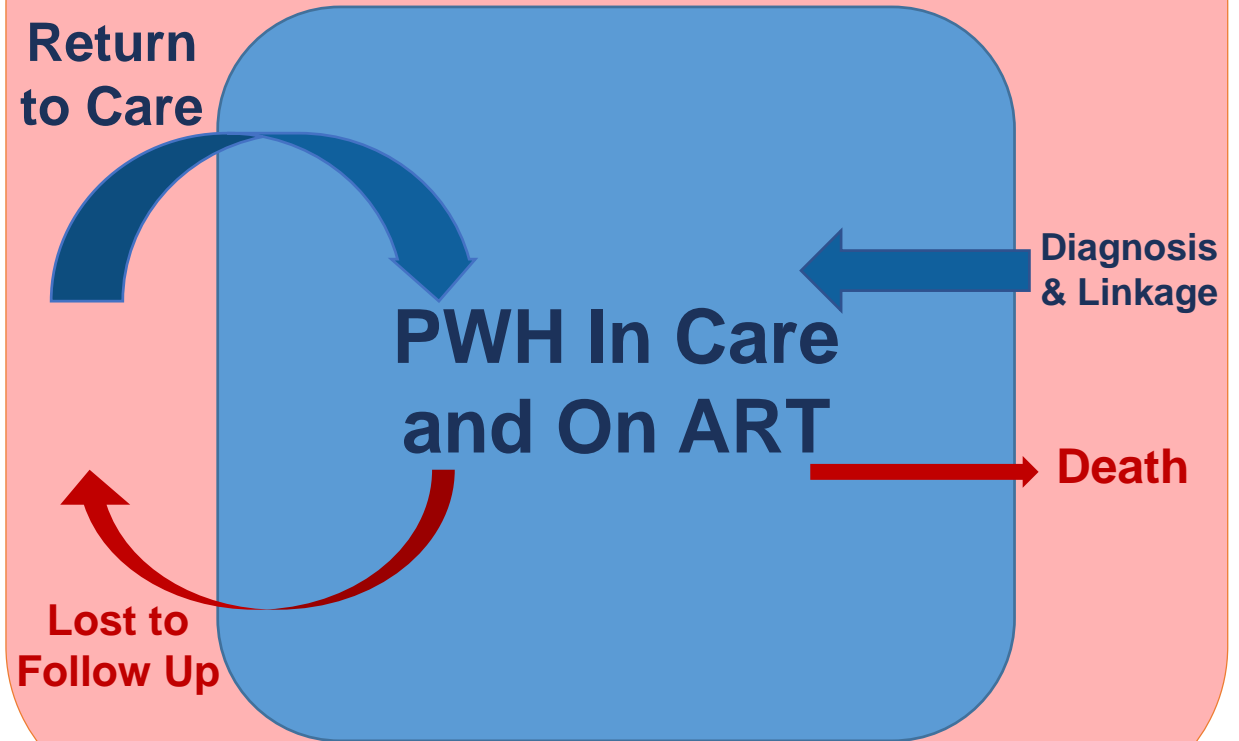


Death

## PWH Out of Care



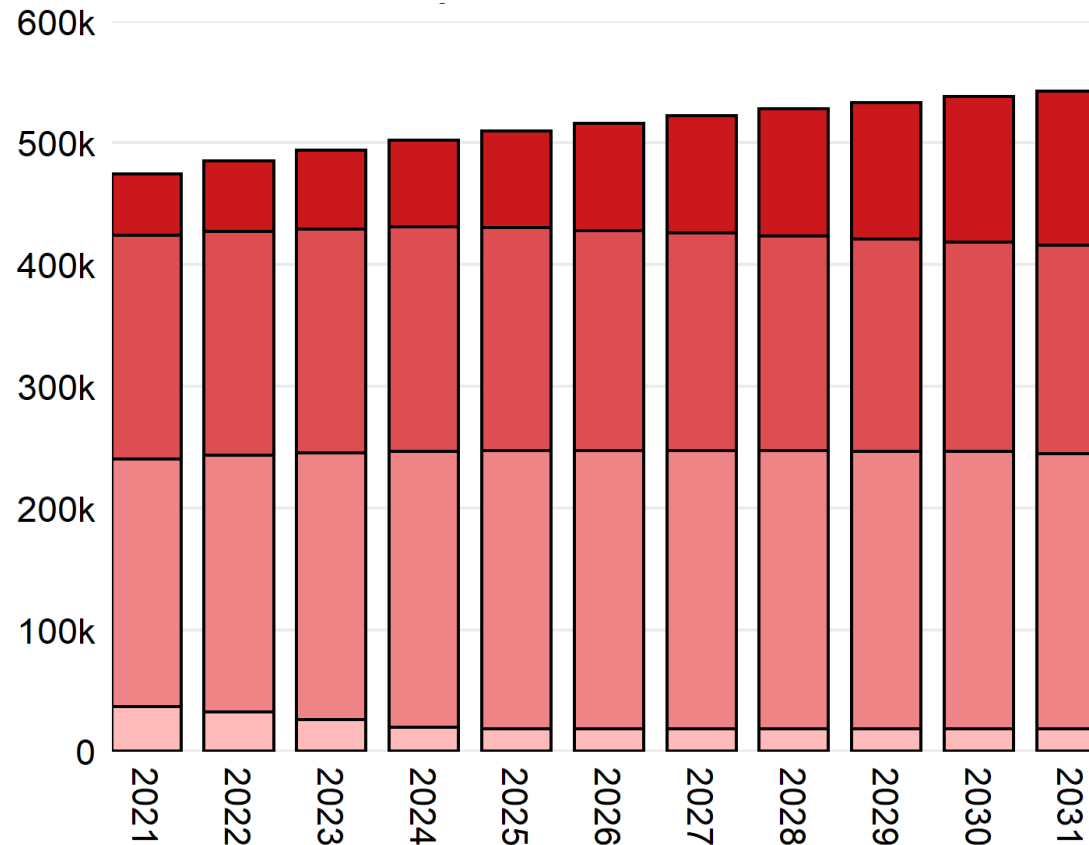
## PWH Out of Care





# CEPAC-US: Projected numbers of MSM on ART

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Age Groups of MSM on ART:

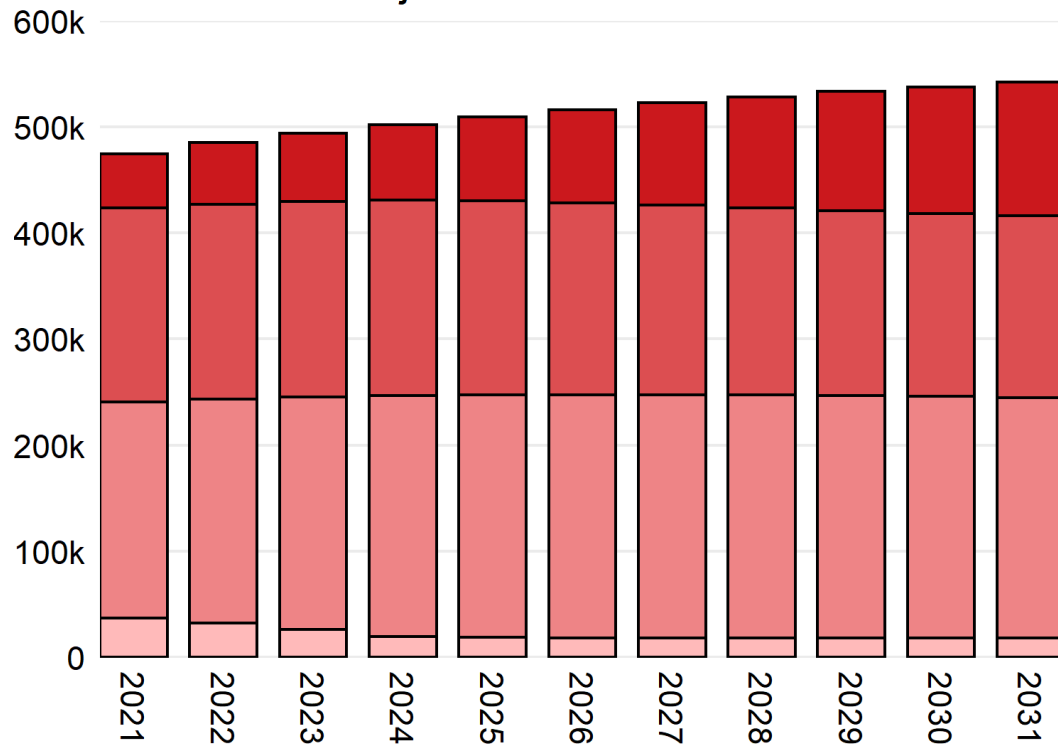


# Results: CEPAC-PEARL Collaboration

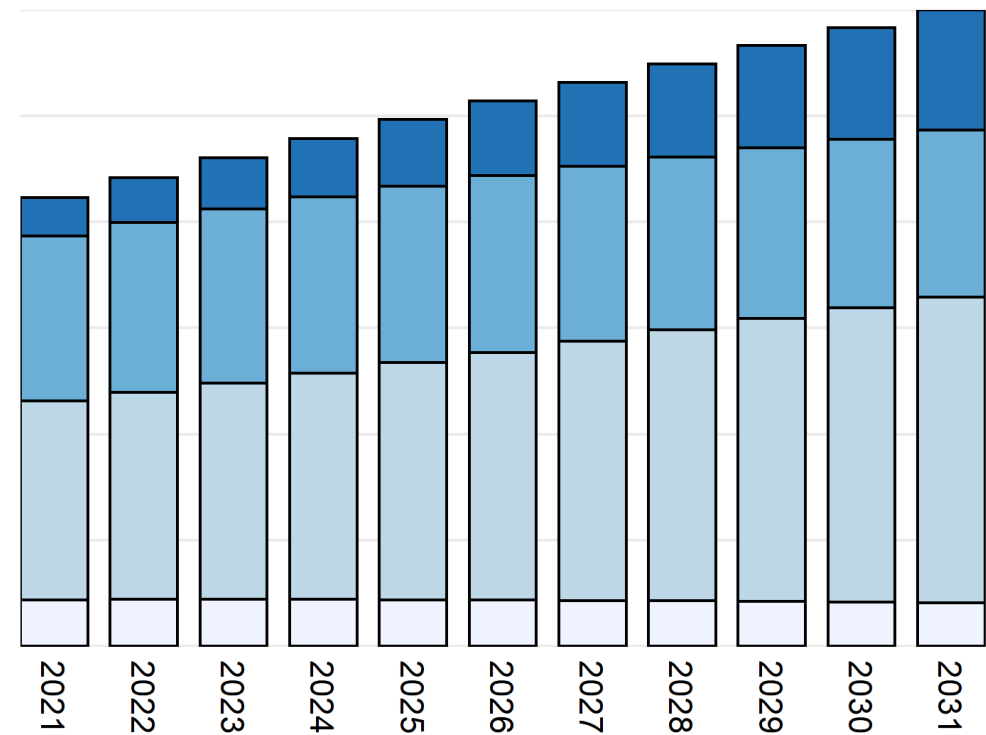
Age Groups of MSM on ART:



CEPAC-US: Projected Numbers of MSM on ART



PEARL: Projected Numbers of MSM on ART



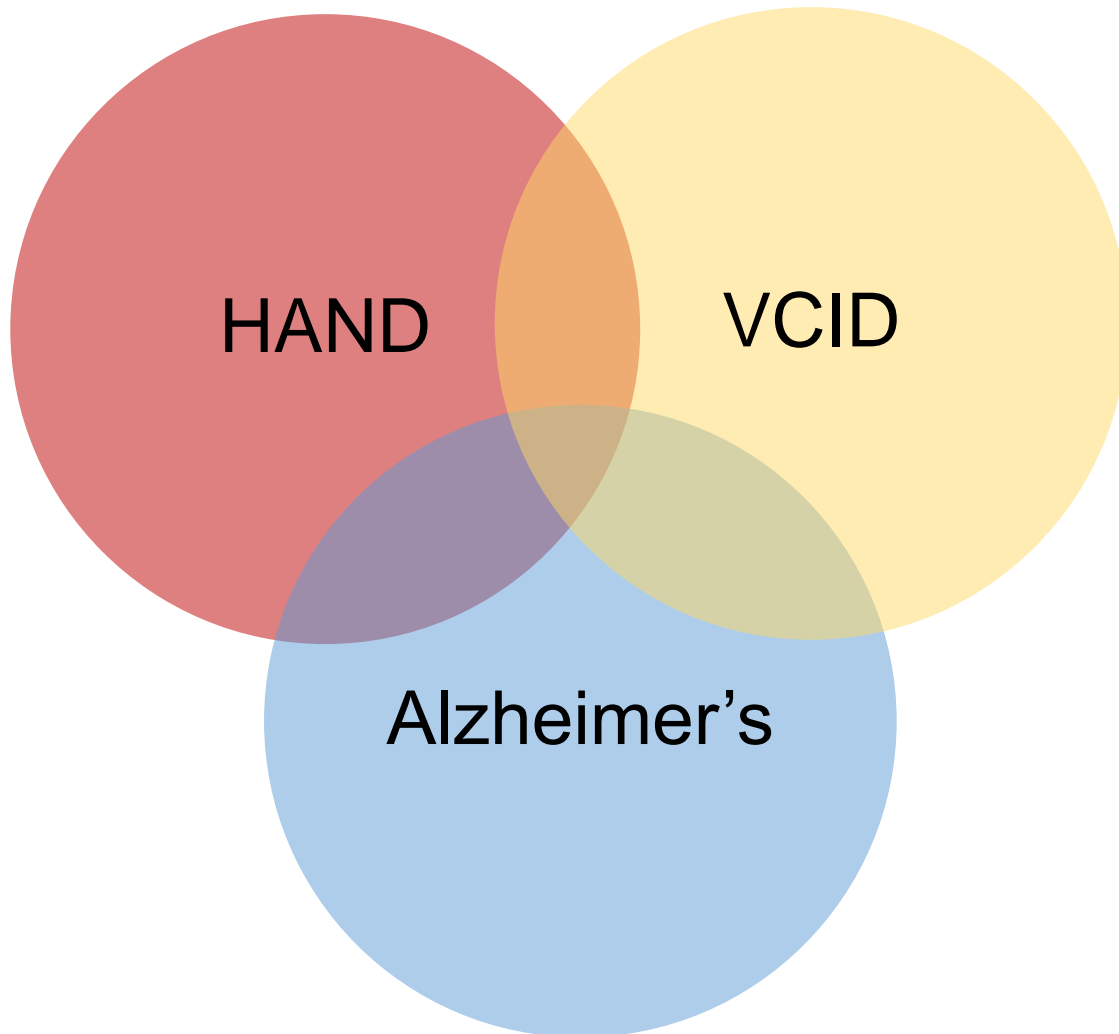
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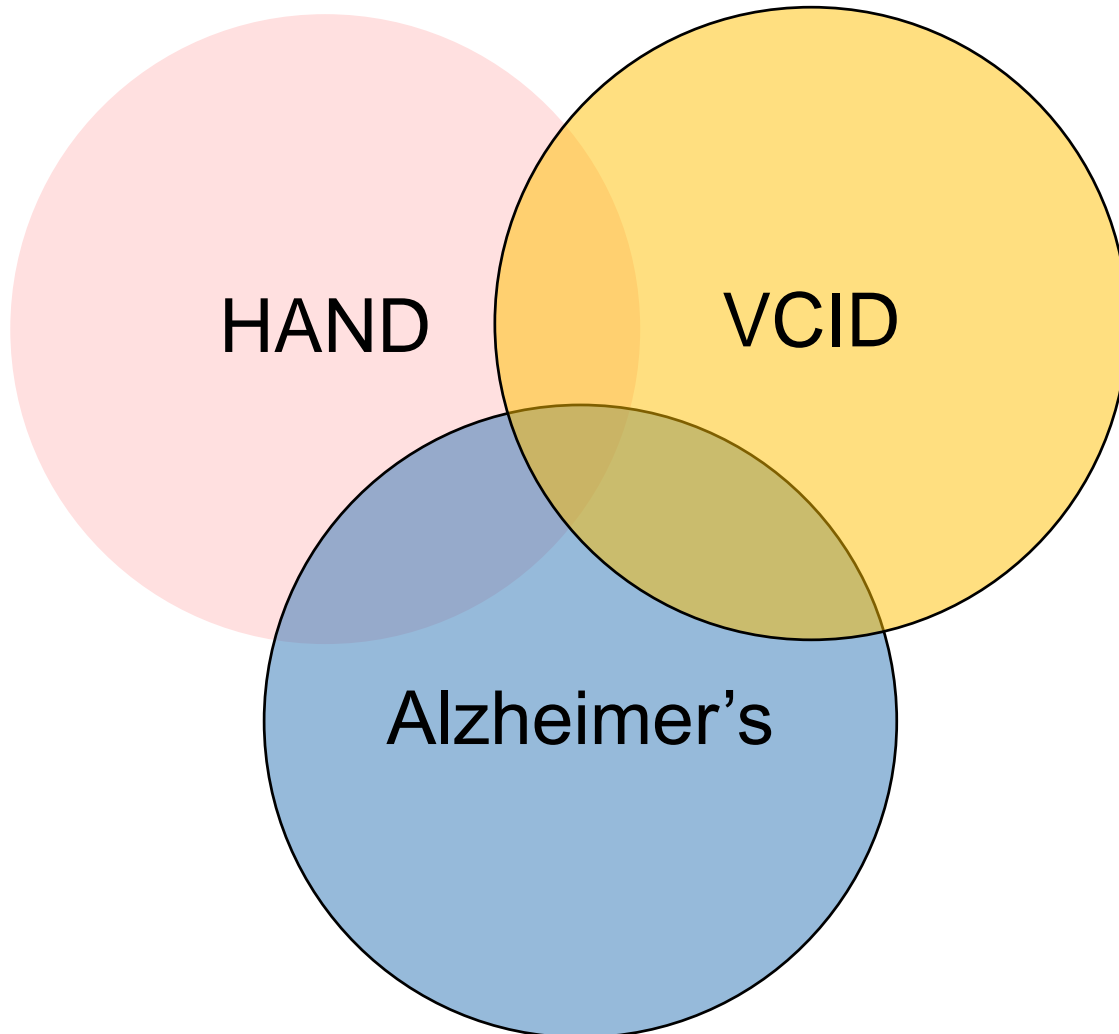
# PWH and Dementia

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# PWH and Dementia

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We focused on the anticipated burden of age-associated dementias among people aging with HIV in the US

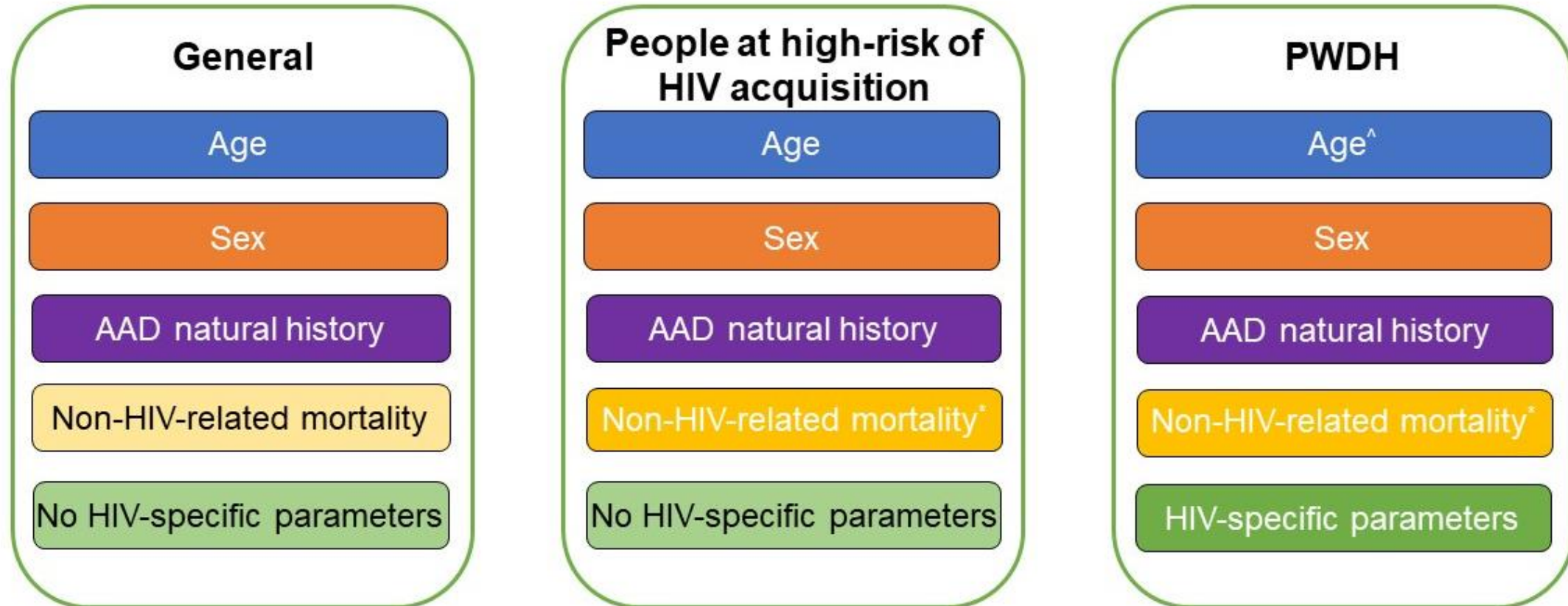
# Objective

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- To compare the cumulative incidence of age-associated dementias (AAD) among 3 populations:
  - General US population
  - People at high risk for HIV acquisition
  - People with diagnosed HIV (PWDH)

# Comparison of simulated cohorts

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\*Higher relative mortality risk from major HIV transmission categories were incorporated for the populations at high risk of and with HIV

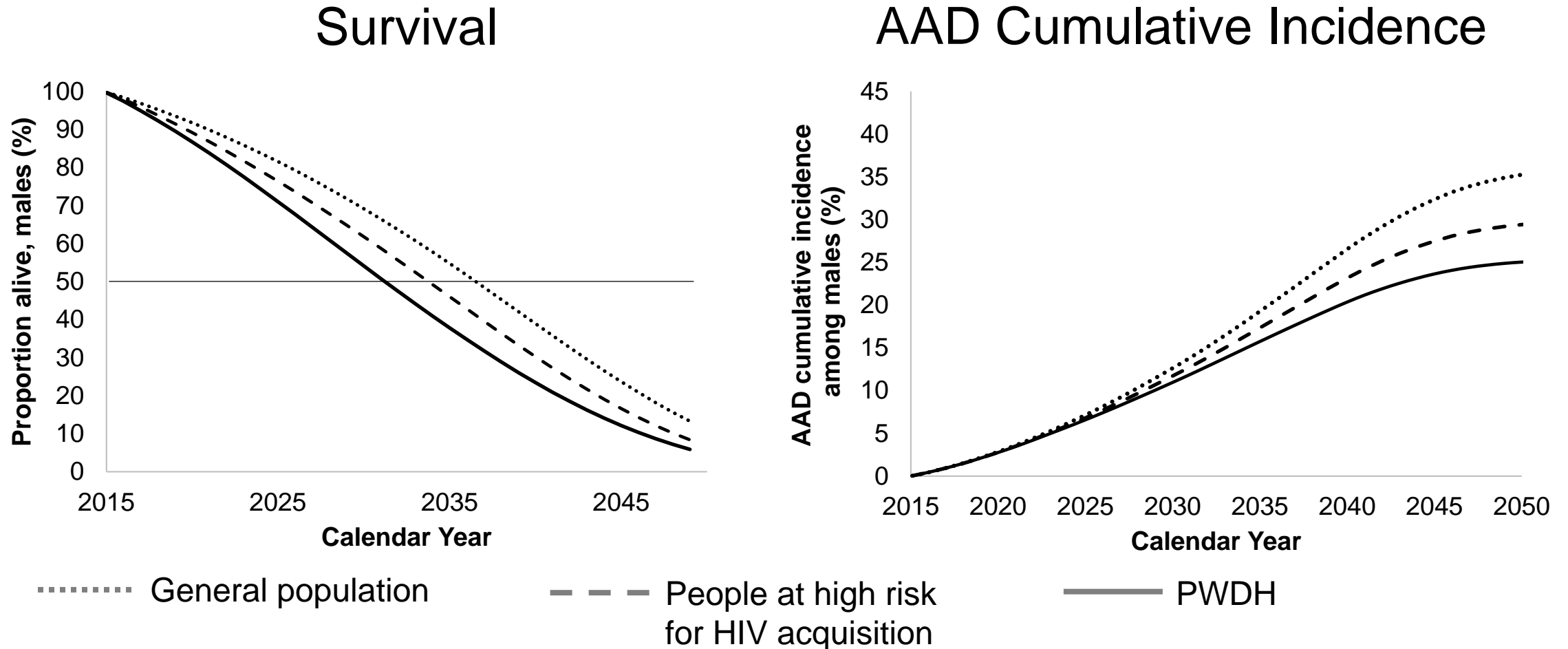
# Model input parameters

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- People aged 55 without AAD at model start
- Developed age- and sex-stratified AAD incidence and mortality rates from general population in the US
- Estimated the HIV care continuum and virologic suppression among PWDH from CDC sources



# CEPAC-projected AAD outcomes (males)

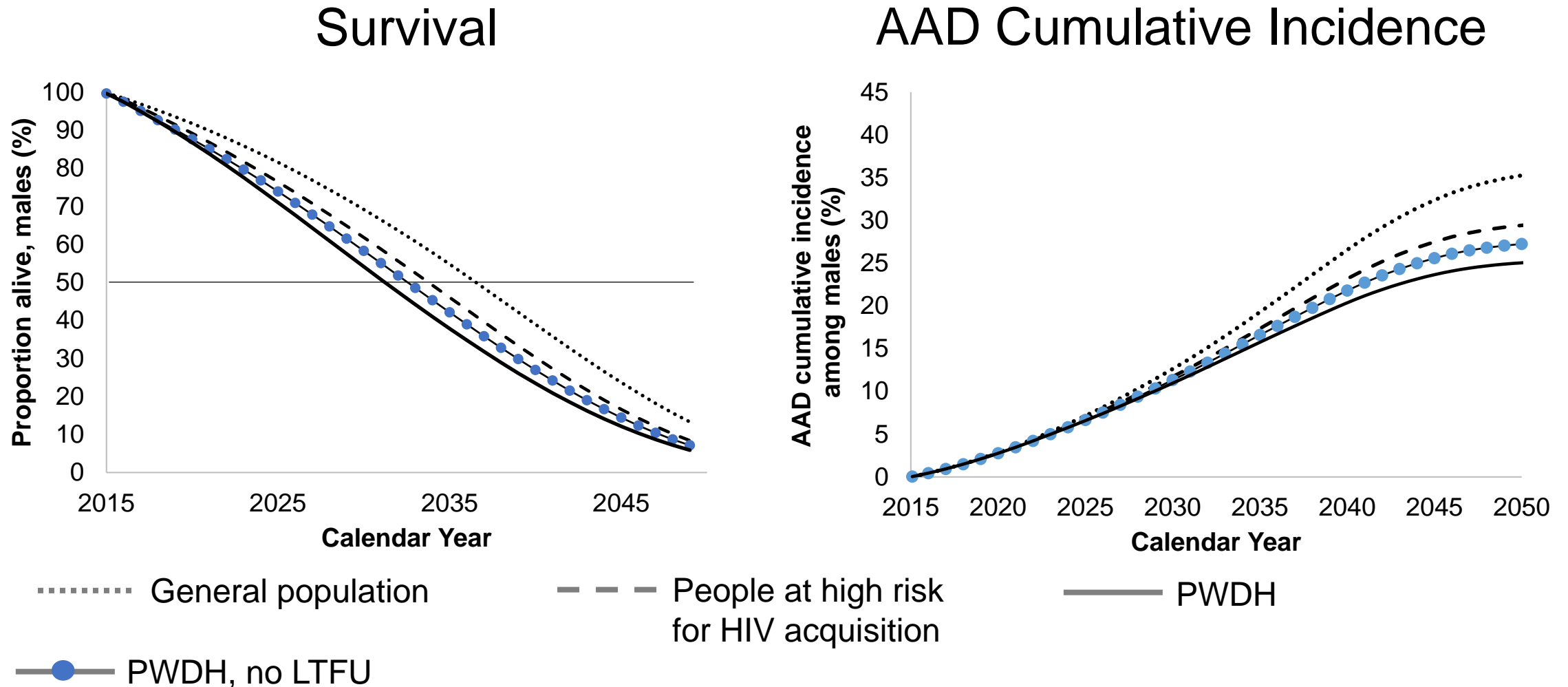


# Sensitivity analyses

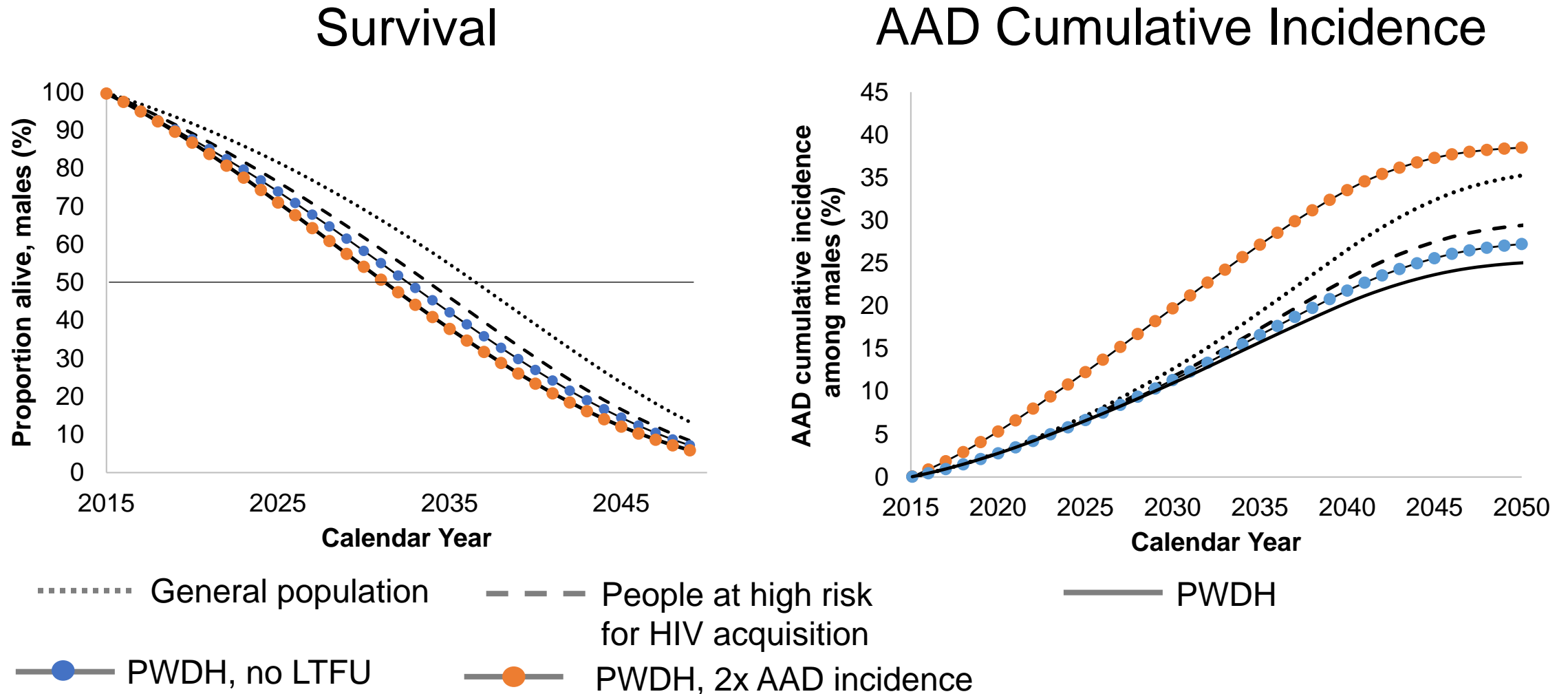
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- HIV-focused parameters
  - No loss to follow-up (LTFU)
- AAD-focused parameters
  - 2x AAD incidence
  - Premature aging
    - 2x AAD incidence
    - Mortality shifted 5y earlier

# CEPAC-projected AAD outcomes: sensitivity analysis (males)

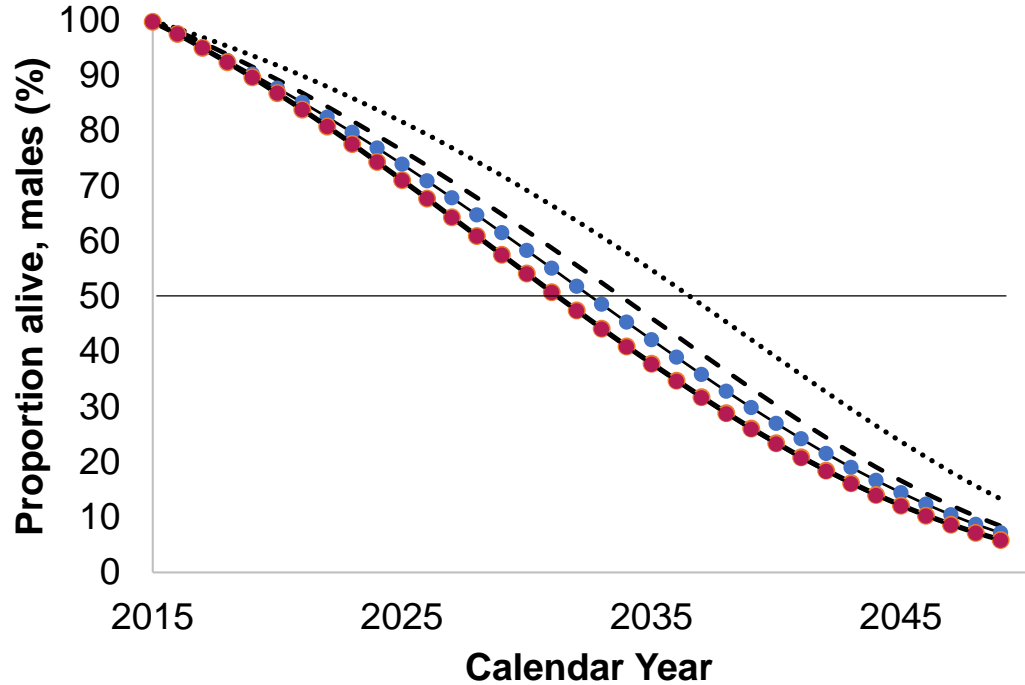


# CEPAC-projected AAD outcomes: sensitivity analysis (males)

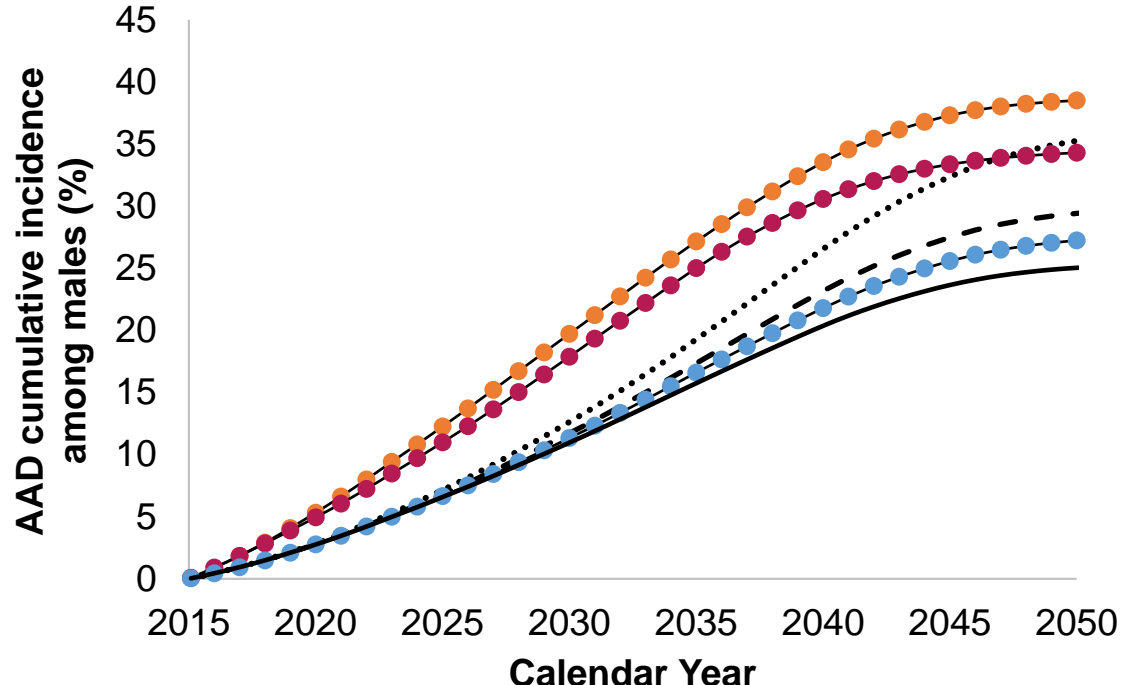


# CEPAC-projected AAD outcomes: sensitivity analysis (males)

## Survival



## AAD Cumulative Incidence



- ..... General population
- People at high risk for HIV acquisition
- PWDH
- PWDH, no LTFU
- PWDH, 2x AAD incidence
- PWDH, 5y premature aging

# Next steps

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- Account for HIV-specific causes of dementia
- Incorporate multimorbidity with a focus on comorbidities that can be synergistic with dementia and HIV:
  - Cardiovascular disease
  - Depression
- Include dementia screening, treatment, and costs

# Future work

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- To examine the future impact of co-morbidities and geriatric syndromes among people with HIV, including costs, to anticipate future health systems needs
- To investigate the clinical implications and cost-effectiveness of different interventions to prevent or treat age-associated co-morbidities

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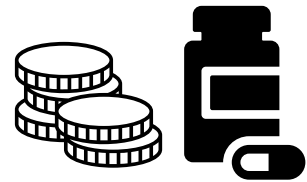
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  - Age-associated dementia
- **Costs**
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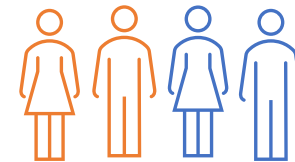
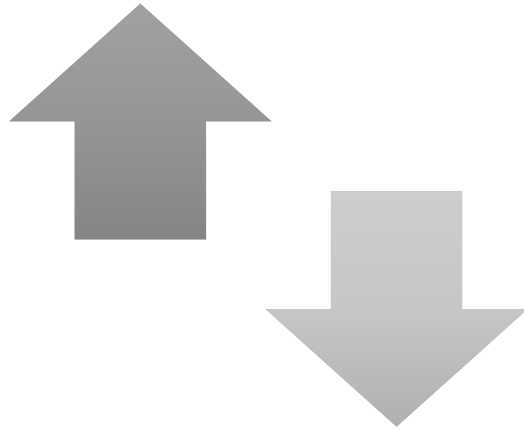
# ART costs in the US

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- Among all well-resourced countries, the US has the highest ART costs and the lowest rate of HIV viral suppression



\$3-4,000 out-of-pocket per year



Only 66% virally suppressed

# DHHS ART guidelines

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## Recommended Initial Regimens for Most People with HIV

- Have demonstrated durable virologic efficacy
- Favorable tolerability and toxicity profiles
- Ease of use

## Recommended Initial Regimens in Certain Clinical Situations

- Effective and tolerable, but have some disadvantages or have less supporting data from randomized clinical trials
- In certain clinical situations, one of these regimens may be preferred

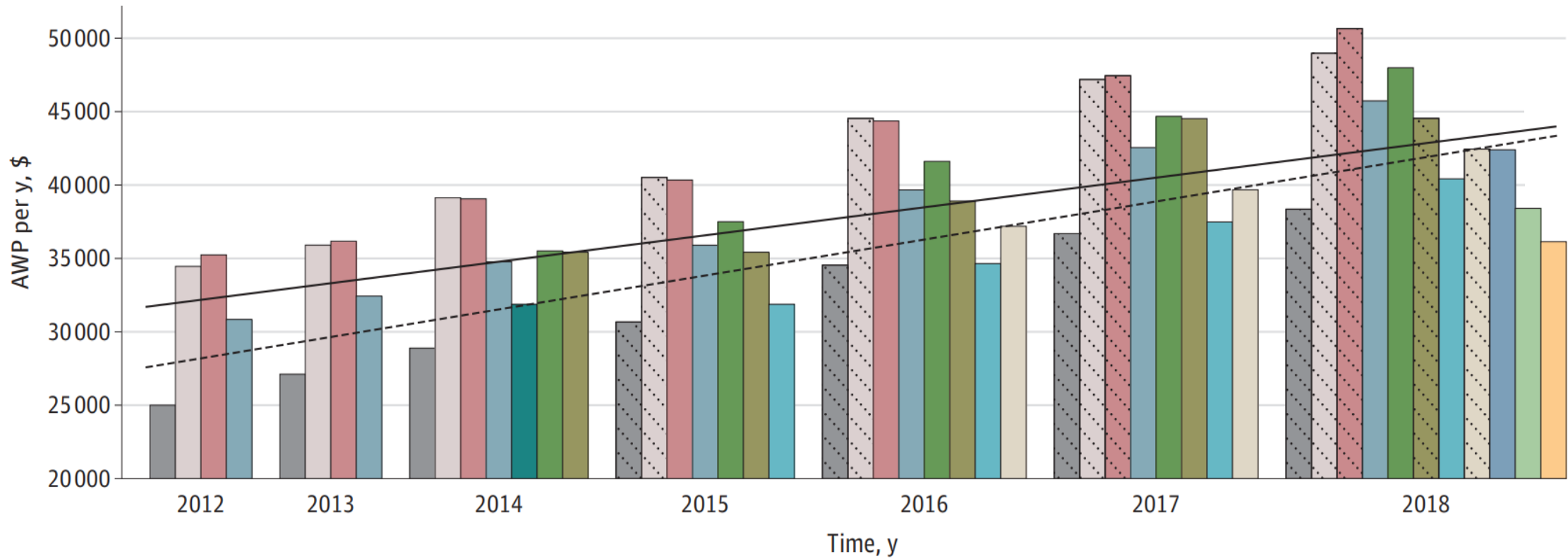
# Rising ART costs in the US

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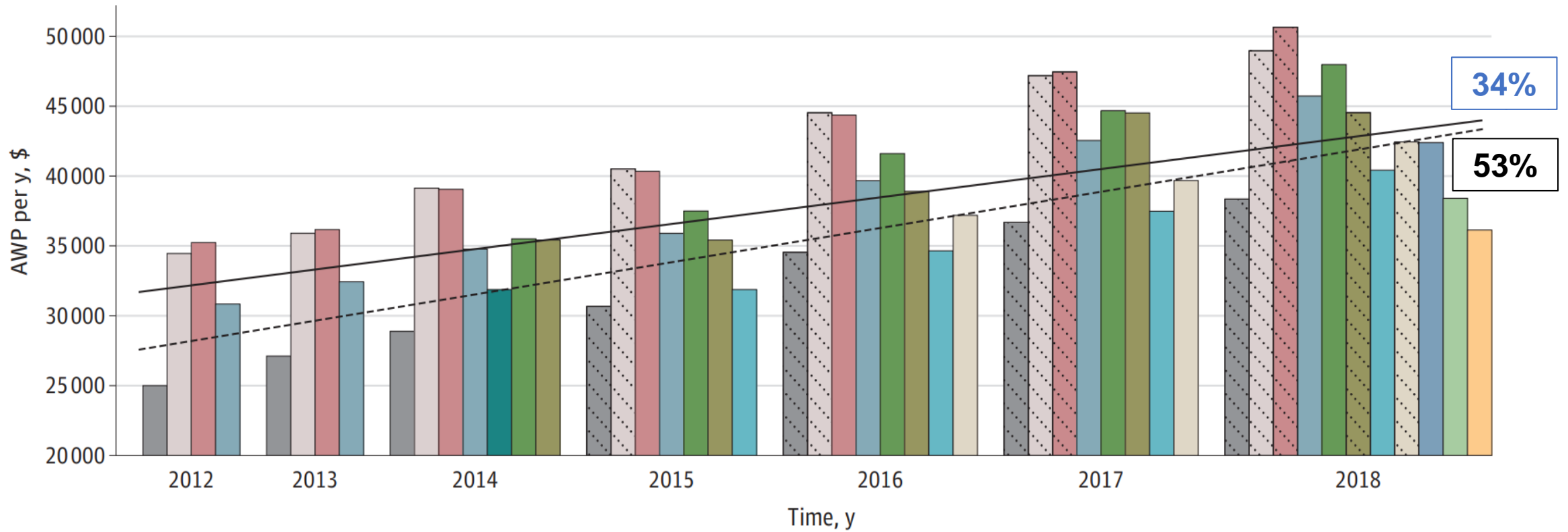
- To characterize changes in initial ART regimen costs over time, focusing on recommended regimens for:
  - Most people with HIV
  - Certain clinical situations
- Obtained the annual, average wholesale price of ART regimens recommended by the DHHS guidelines (2012-18)

# Annual ART average wholesale prices (AWP)

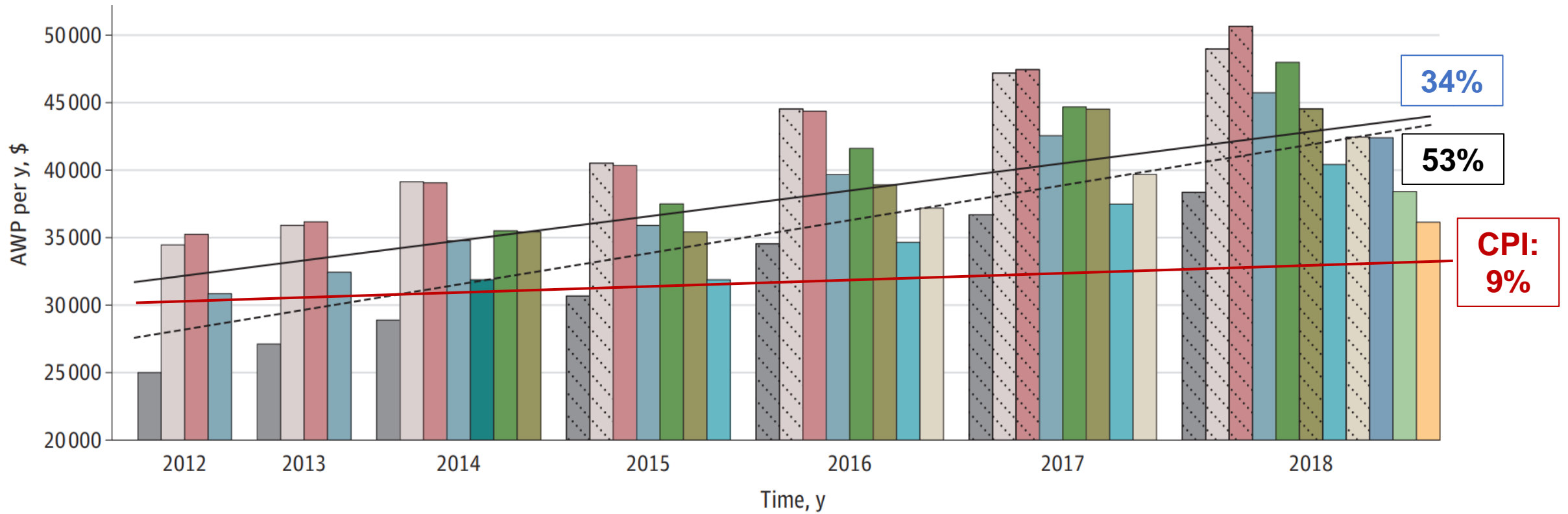
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# Annual ART average wholesale prices (AWP)



# Annual ART average wholesale prices (AWP)



# Who pays for ART among aging PWH?

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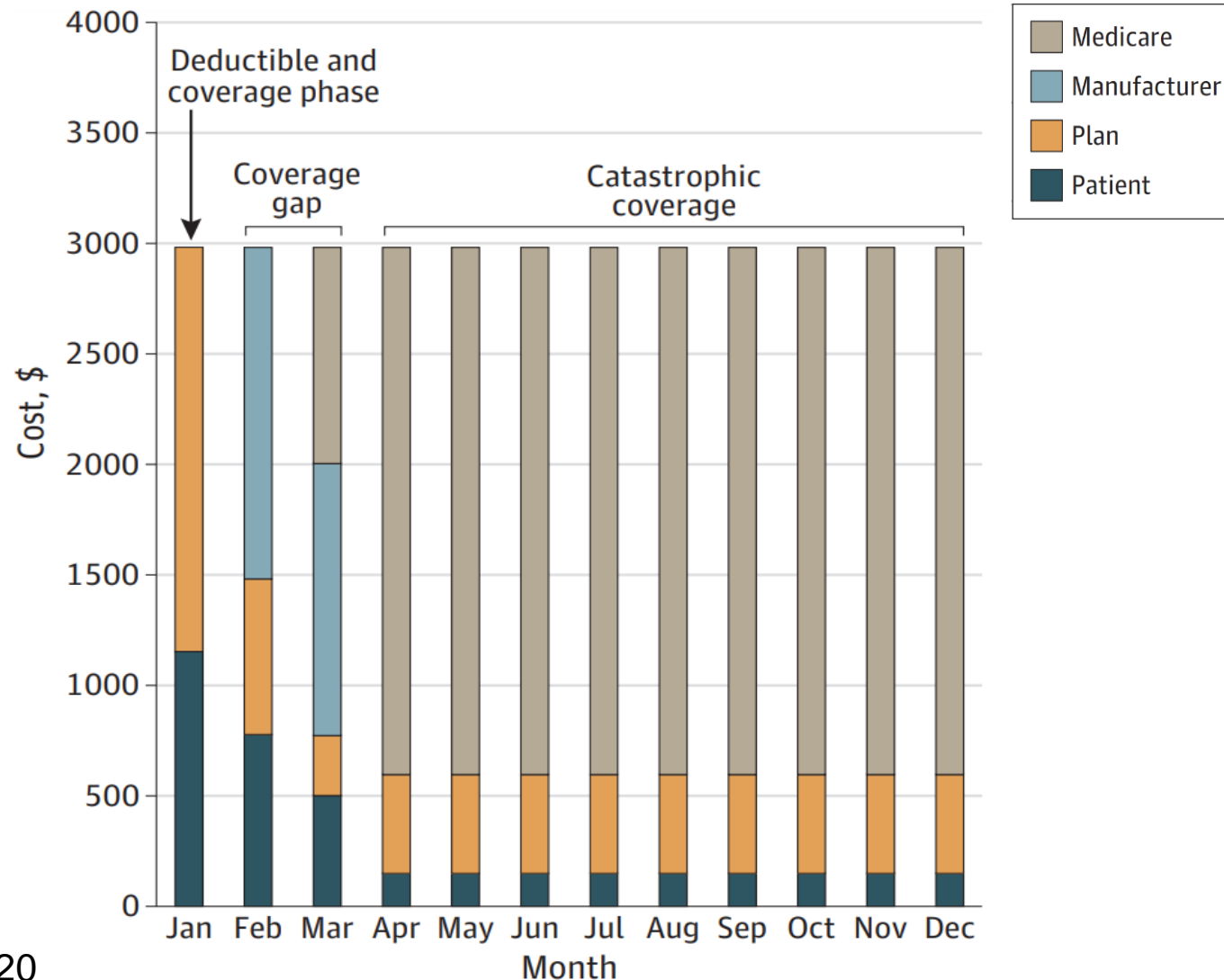
# Medicare Part D

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- Approximately 25% of PWH in clinical care are enrolled in Medicare
  - Most are also enrolled in Medicare Part D for prescriptions
- Complicated cost-sharing structure in Medicare Part D obscures who bears the burden of high ART costs



# Part D cost-sharing between patients, insurance plans, manufacturers, and Medicare for ART



# Inequities in Medicare Part D cost-sharing

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- With standard coverage, annual out-of-pocket costs are substantial (\$3,300-\$4,400/year)

# Inequities in Medicare Part D cost-sharing

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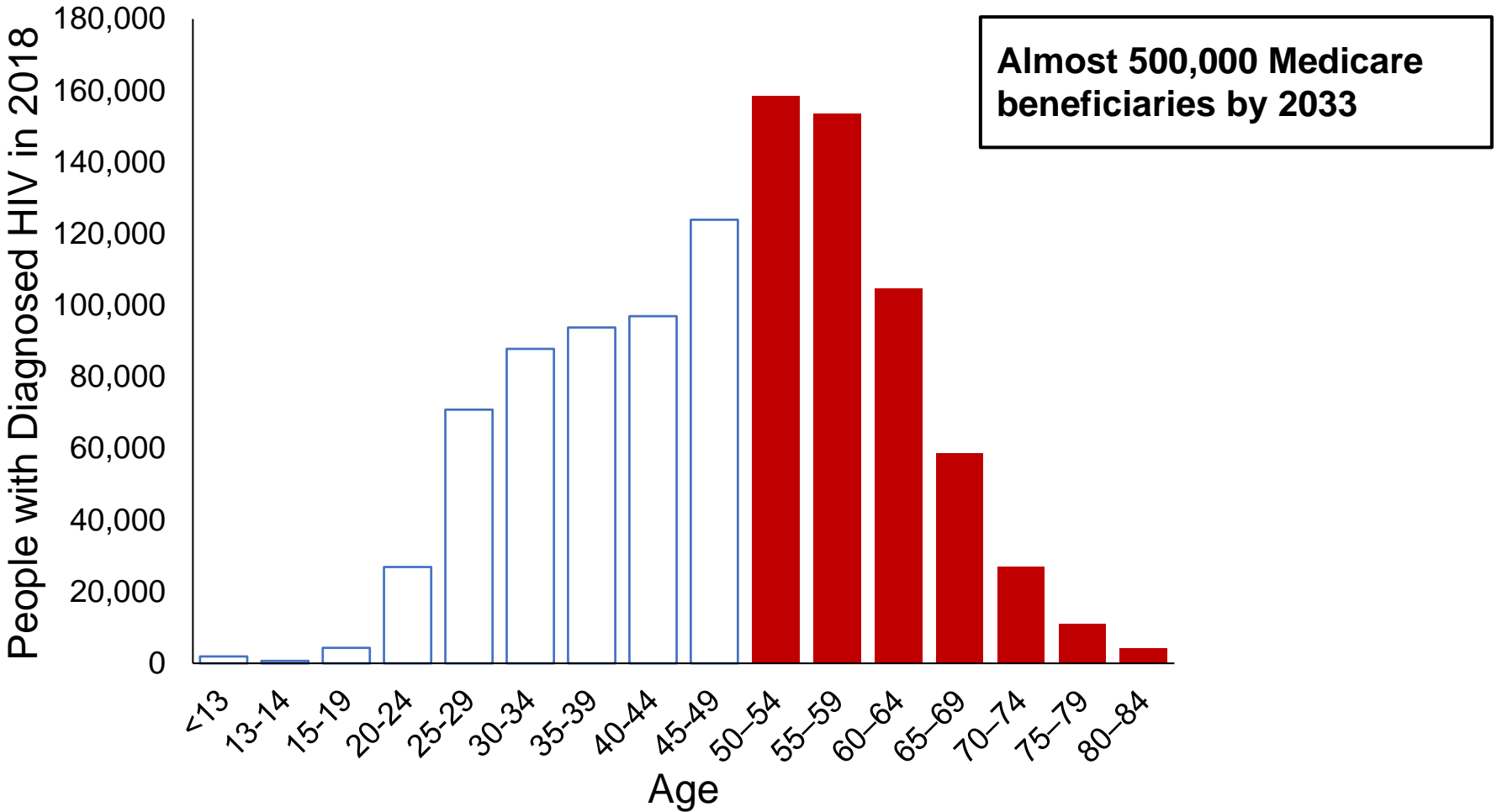
- With standard coverage, annual out-of-pocket costs are substantial (\$3,300-\$4,400/year)
- Low-income subsidies (LIS) are available but vary depending on person's income
  - At \$135%-150% of federal poverty level, Medicare beneficiaries would pay 15% of ART costs

# Inequities in Medicare Part D cost-sharing

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- With standard coverage, annual out-of-pocket costs are substantial (\$3,300-\$4,400/year)
- Low-income subsidies (LIS) are available but vary depending on person's income
  - At \$135%-150% of federal poverty level, Medicare beneficiaries would pay 15% of ART costs
- Higher ART prices result in greater costs assumed by Medicare beneficiaries or government payers (Ryan White; Medicare)

# Anticipated growth in Medicare beneficiaries with HIV by 2033



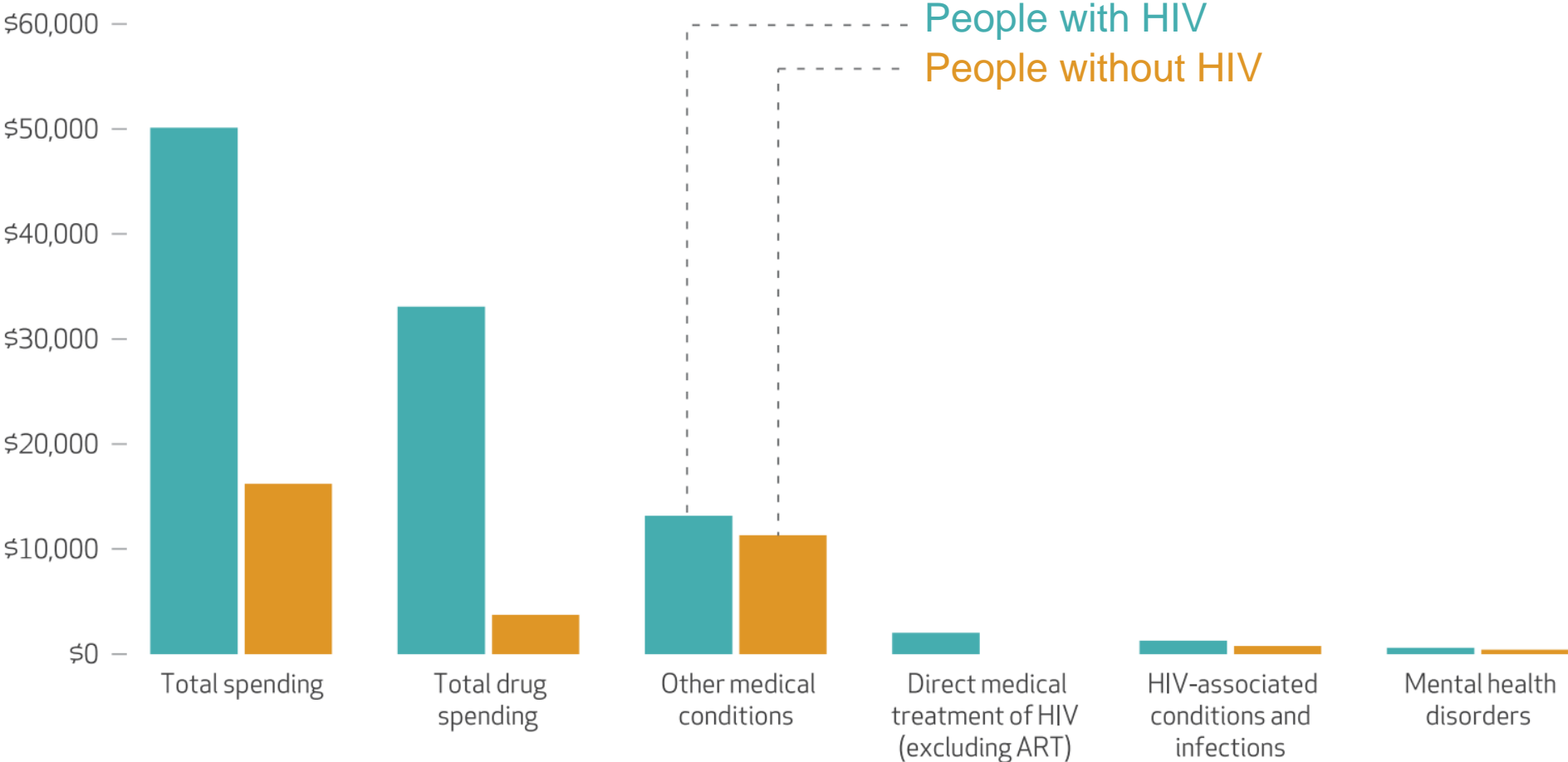
# Association of HIV with health care spending among Medicare beneficiaries

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- Utilizing 2016 Medicare claims data, we compared Medicare spending among:
  - People without HIV (n=4.5 million)
  - People with HIV (n=21,564)

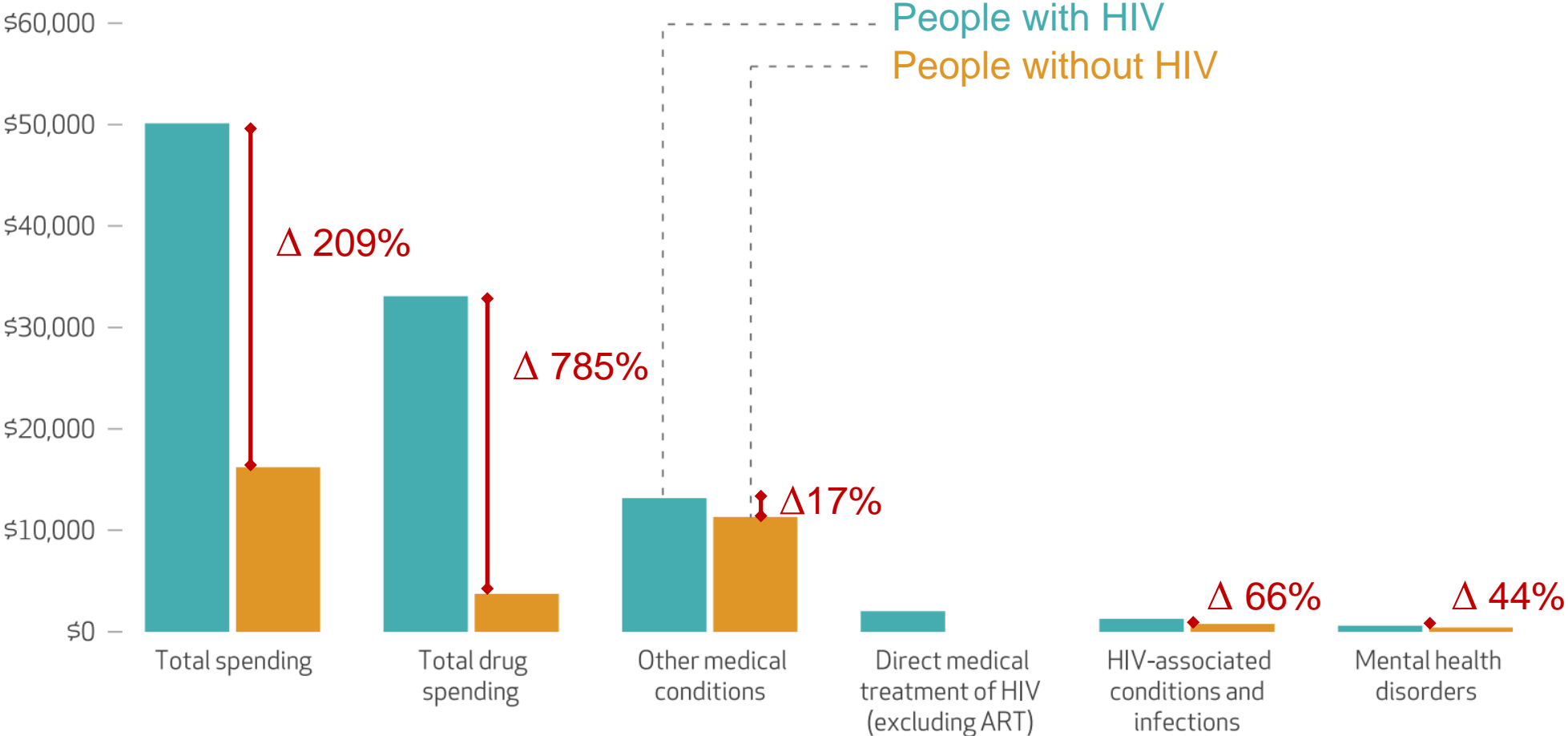
# Overall Medicare spending for people with and without HIV

Mean risk-adjusted spending (per person)



# Overall Medicare spending for people with and without HIV

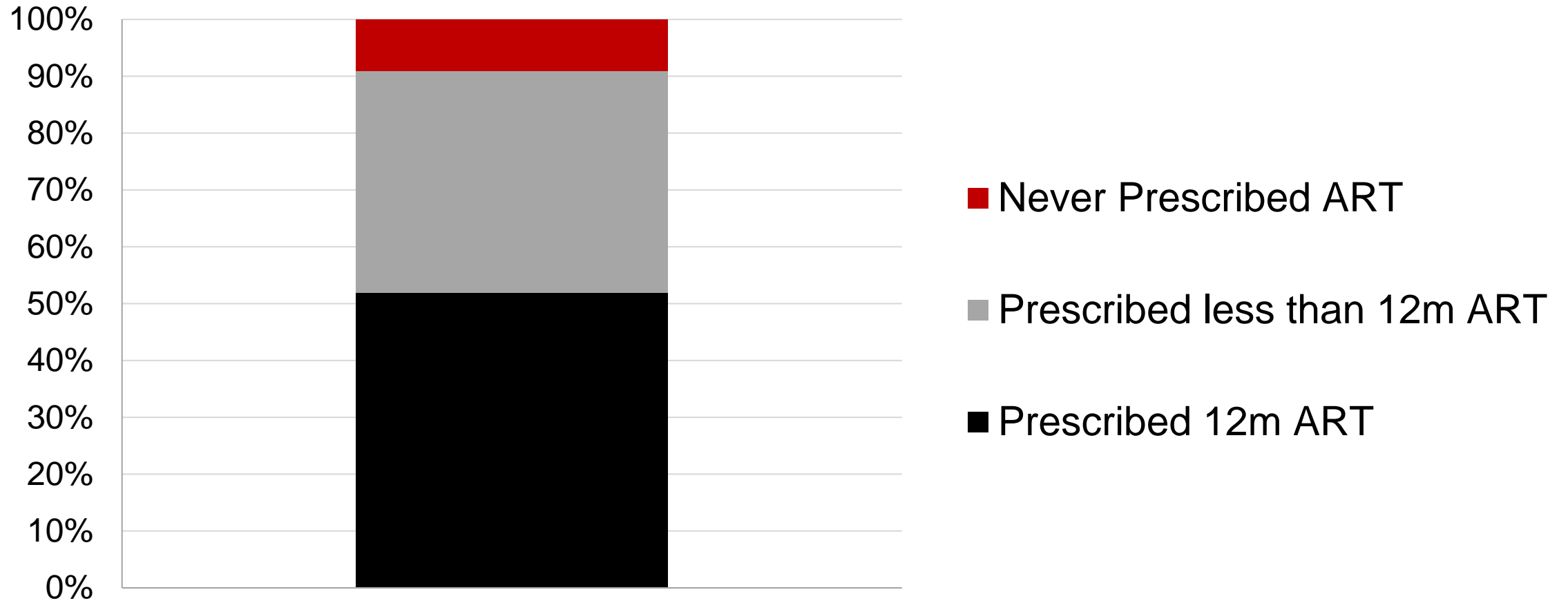
Mean risk-adjusted spending (per person)





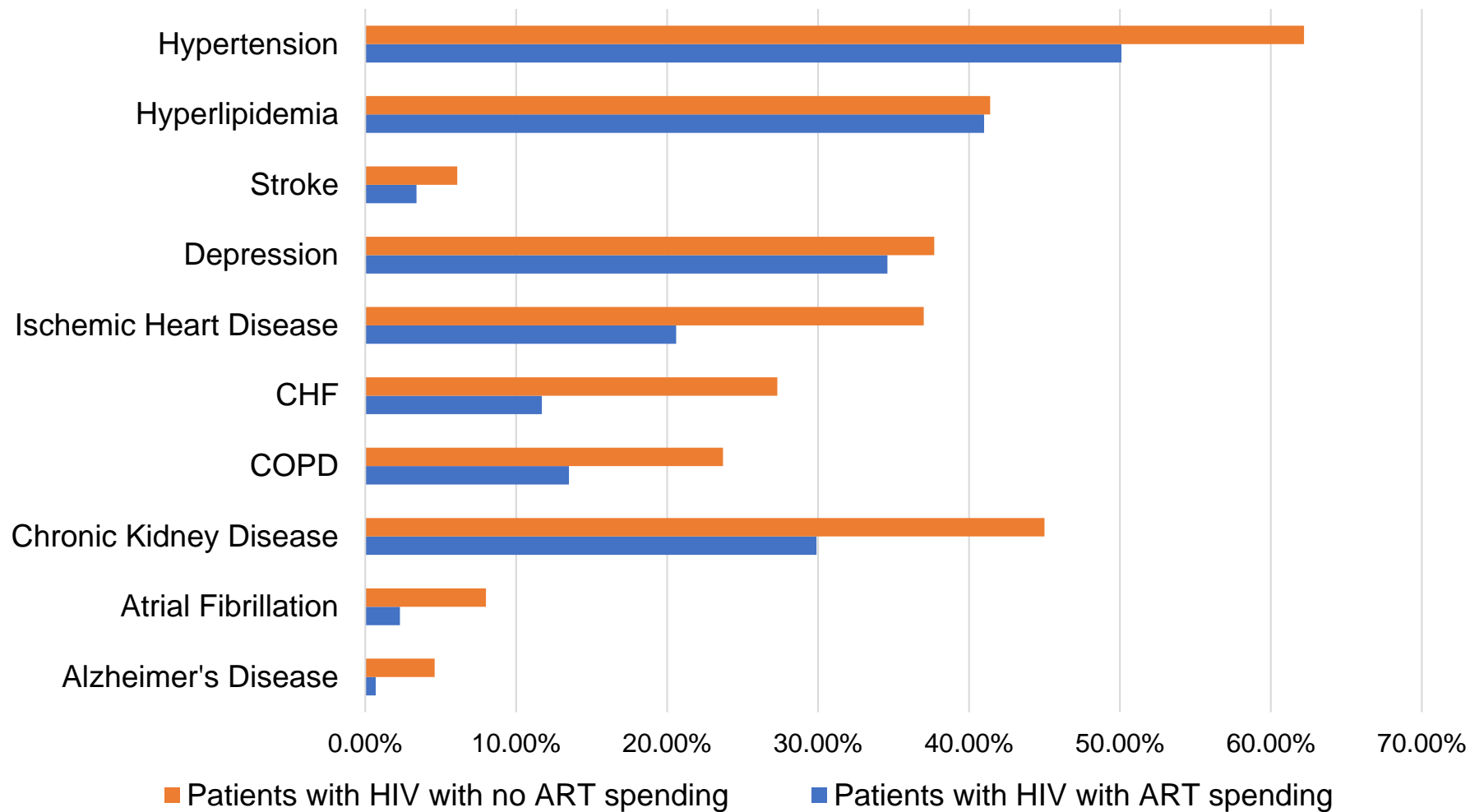
# Not all Medicare beneficiaries with diagnosed HIV are prescribed ART

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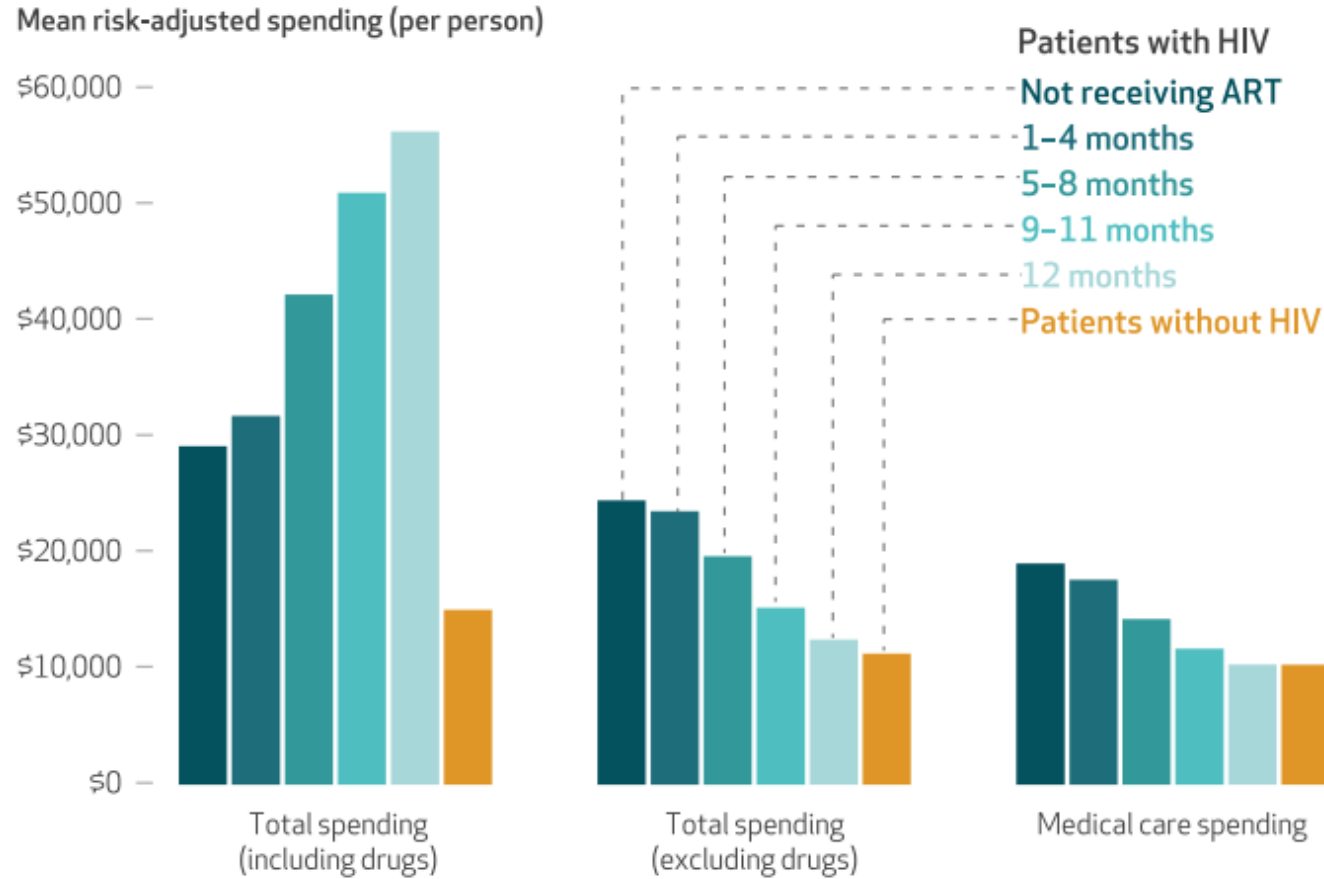


# More comorbidities among Medicare beneficiaries not prescribed ART

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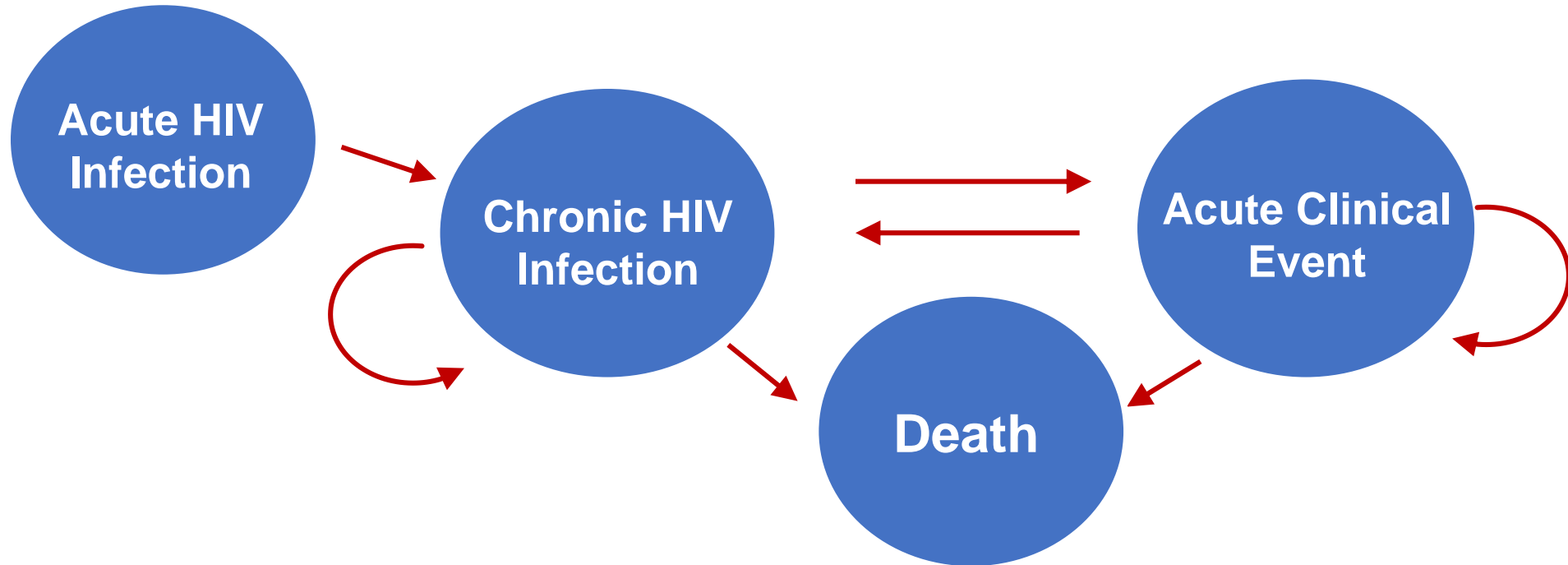
# Medicare spending by HIV status and months since ART initiation



People prescribed ART had less Medicare spending on mental health and other medical comorbidities

# Incorporating costs in CEPAC

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- Estimated costs of care can be used to populate the model
- Each clinical event is associated with a cost that includes any relevant visits, labs, medications

# How will we use model-projected costs?

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- Project the total direct medical costs incurred by PWH over a specific time-frame for HIV and non-HIV-related clinical care
- Compare the costs of different sub-populations of PWH
- Compare the clinical outcomes and costs of different interventions to examine the “cost-effectiveness” of one intervention compared with others

# Outline

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- Background
- Simulation modeling
- Model projections
  - MSM aging with HIV
  - Age-associated dementia
- Costs
- **Conclusions**

# Conclusions

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- People aging with HIV will grow in number given the effectiveness of ART
- Multimorbidity is a major issue and will increase as people age
  - Screening and treatment strategies are essential
  - Costs will grow with a direct impact on PWH due to out-of-pocket costs, as well as on taxpayers
- Simulation modeling is a method to examine and investigate interventions that are clinically effective and cost-effective



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# Thank you

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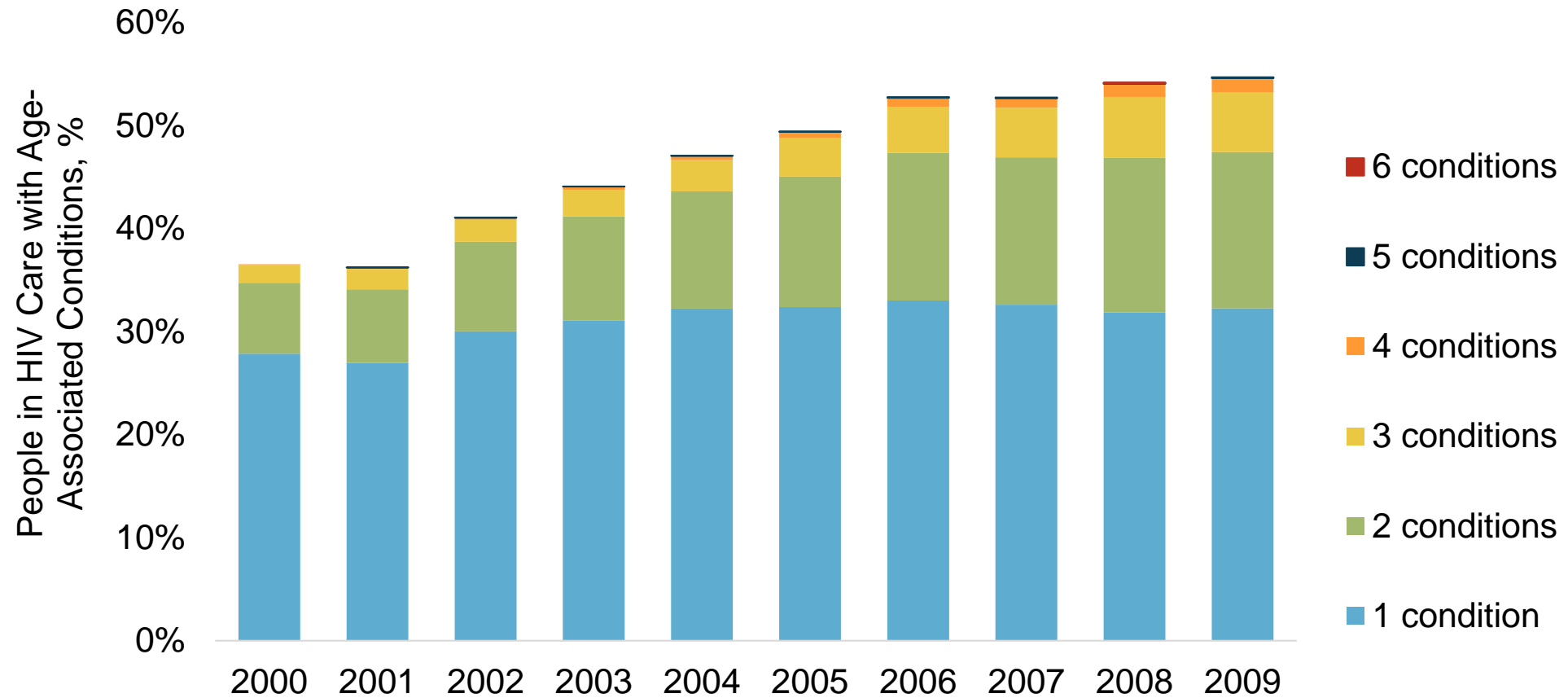
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**Additional slides**

# Increasing multimorbidity among PWH in care

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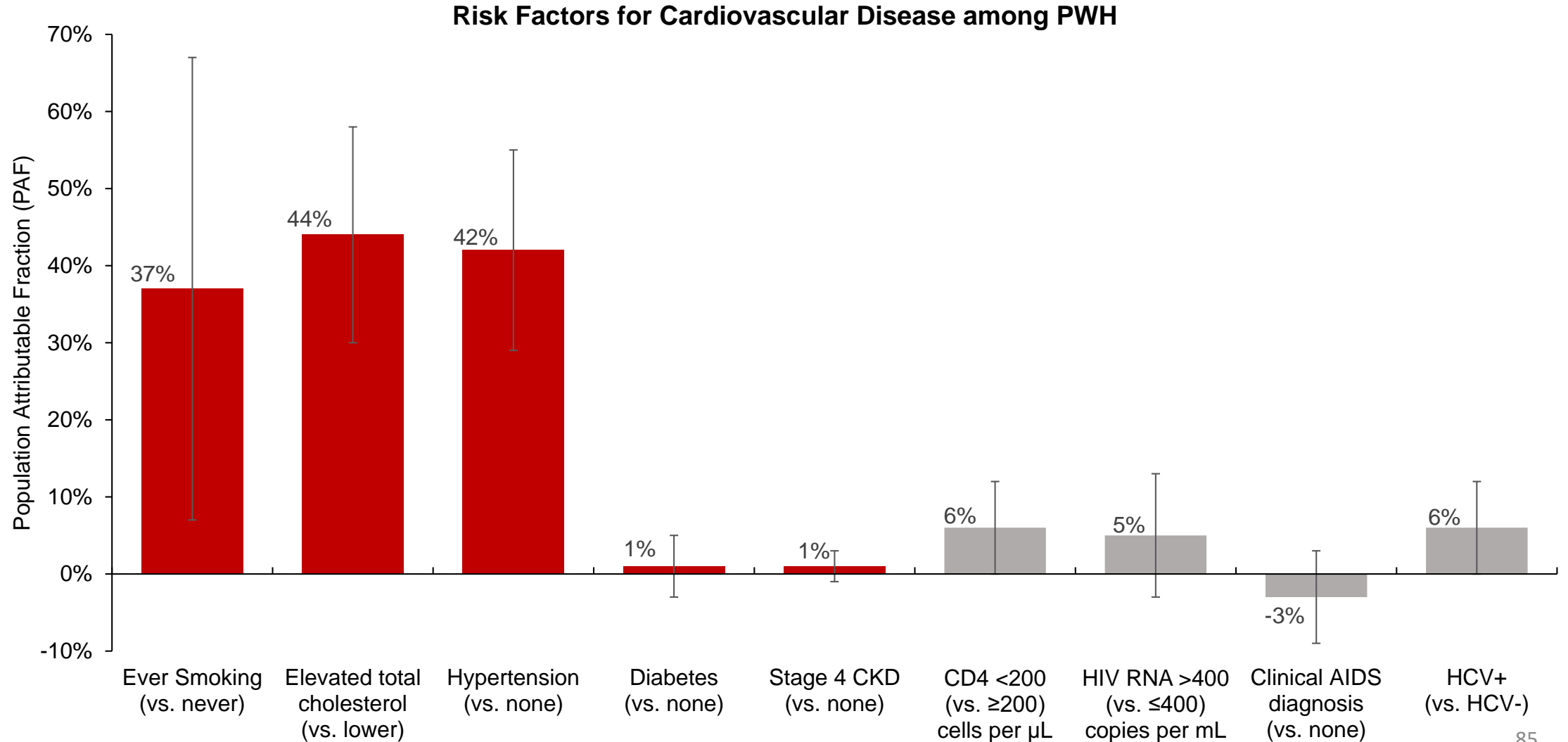


# “Traditional” risk factors are important

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- Compared with HIV-related risk factors for non-communicable diseases, traditional risk factors contribute markedly to risk:
  - smoking, dyslipidemia, hypertension, and chronic hepatitis C infection
- A substantial proportion of these comorbidities could be prevented with increased targeted interventions and screening

# “Traditional” risk factors are important



# CEPAC-US: Age distribution among MSM on ART

