Aging with HIV: Tailoring Care for Older Adults Living with HIV

Monica Gandhi MD, MPH

Director, UCSF Center for AIDS Research and Ward 86 HIV Clinic

Professor of Medicine, Division of HIV, ID and Global Medicine, UCSF

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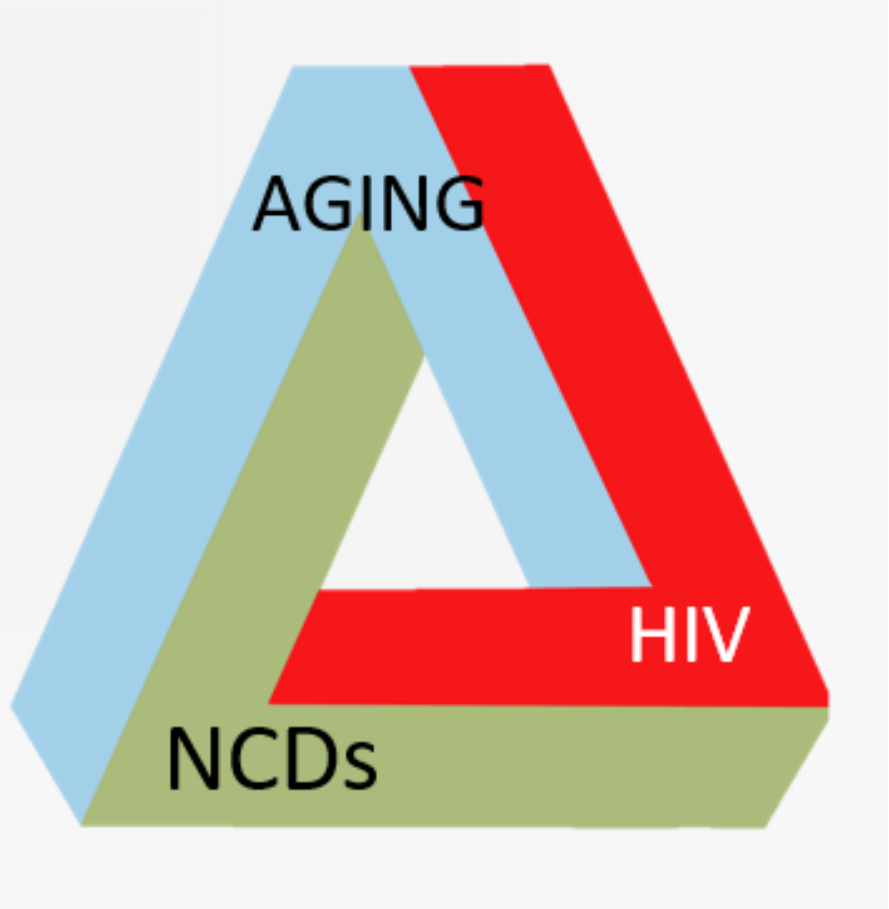
Continuum 2025 • June 10-12, 2025 • San Juan

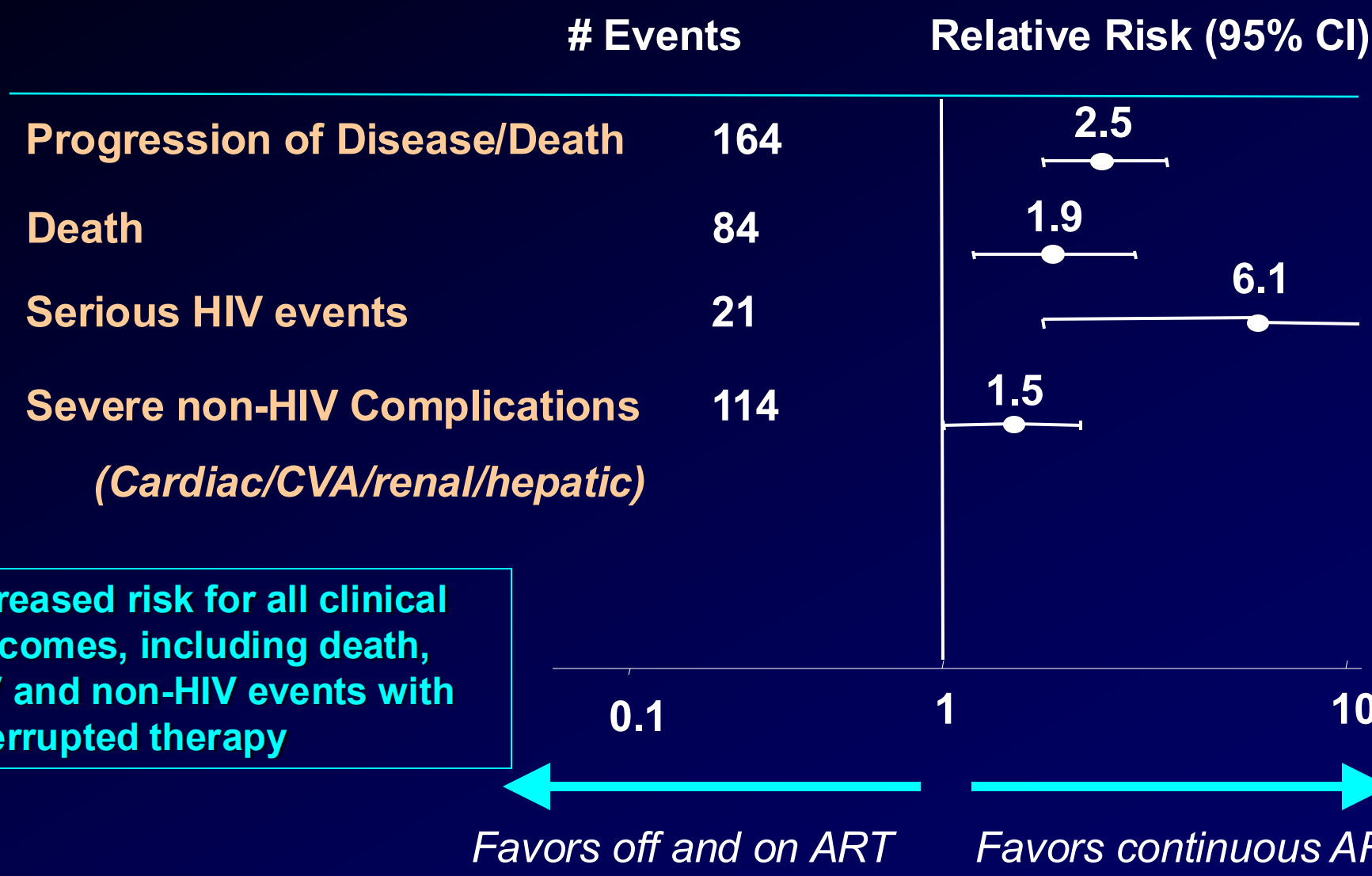
Objectives of talk

- Pathophysiology of aging in people living with HIV
- Aging of the epidemic
- Comorbidities and geriatric syndromes among people with HIV who are aging
- Clinical care programs
- Bone health, PrEP, STD prevention



SMART Study

One of first to show inflammation of untreated HIV



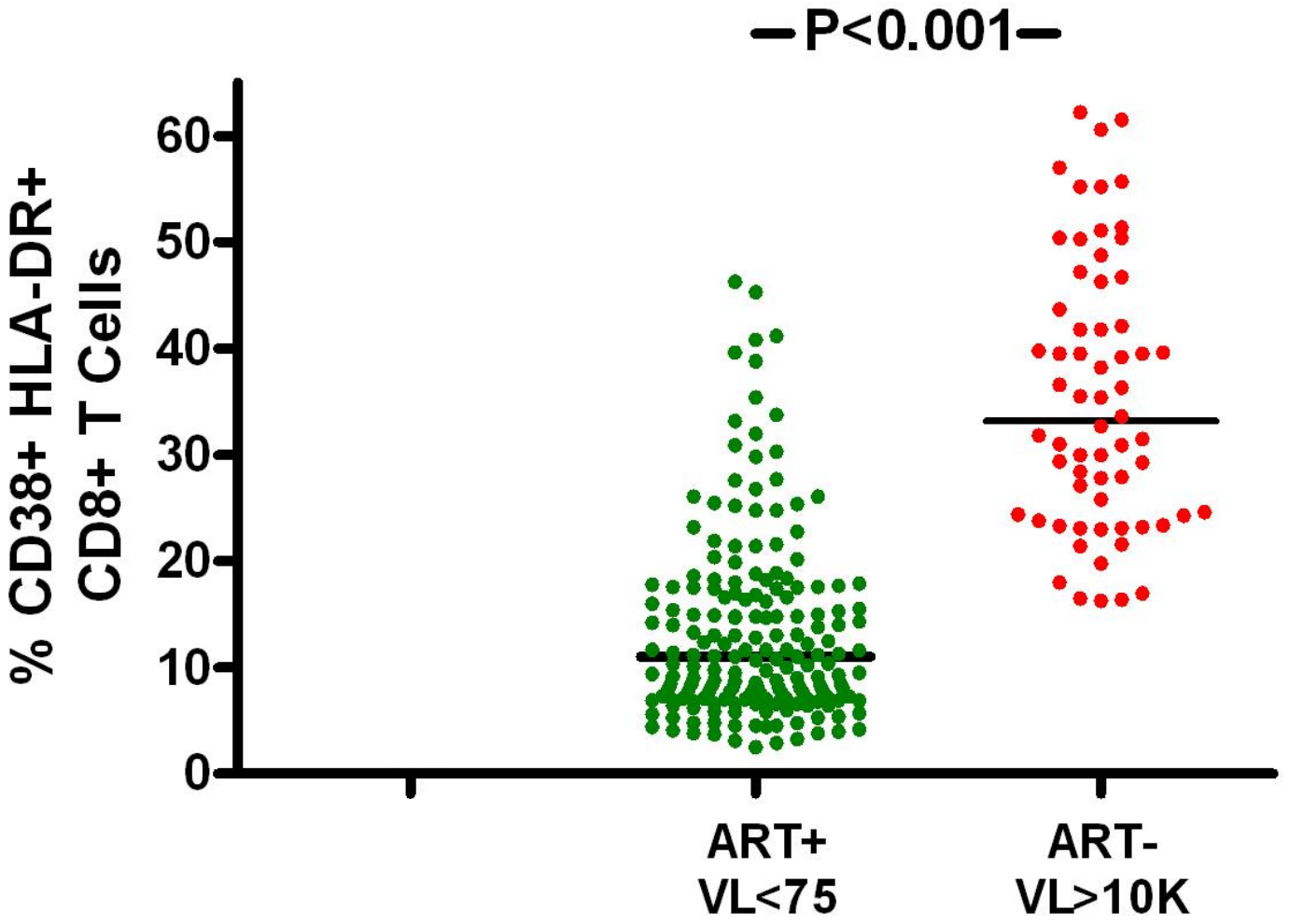
Study designed to look at off-and-on ART vs continuous ART (to spare toxicities) – almost all outcomes (including non-communicable diseases) favored continuous ART, launching discussions of HIV & inflammation

Increased risk for all clinical outcomes, including death, HIV and non-HIV events with interrupted therapy

The NEW ENGLAND JOURNAL of MEDICINE

El Sadr NEJM 2012

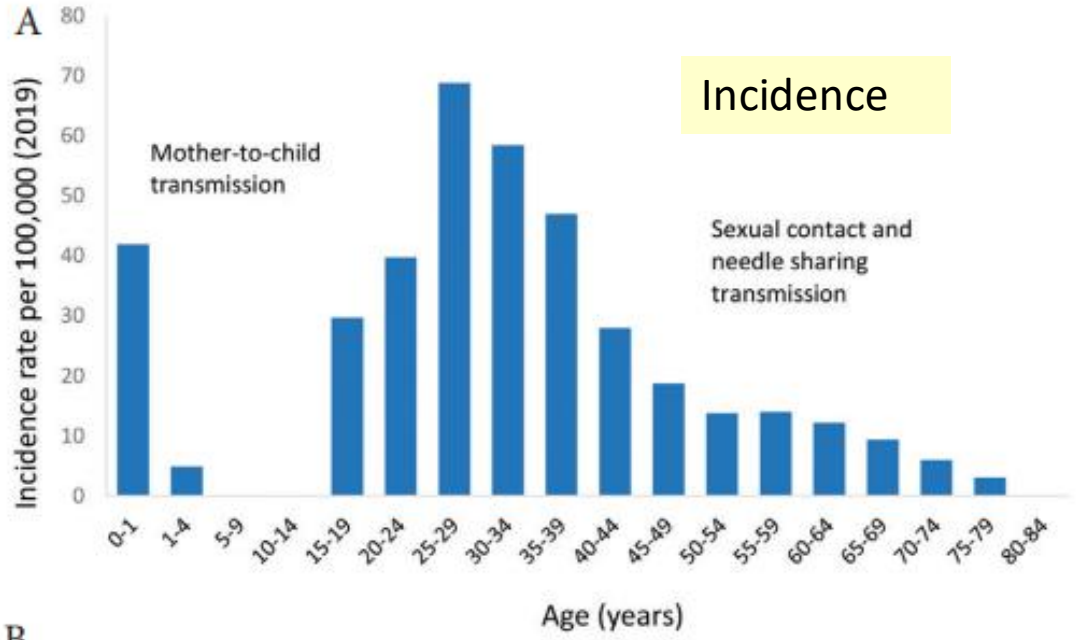
Immune Activation (T-cell) Declines with ART

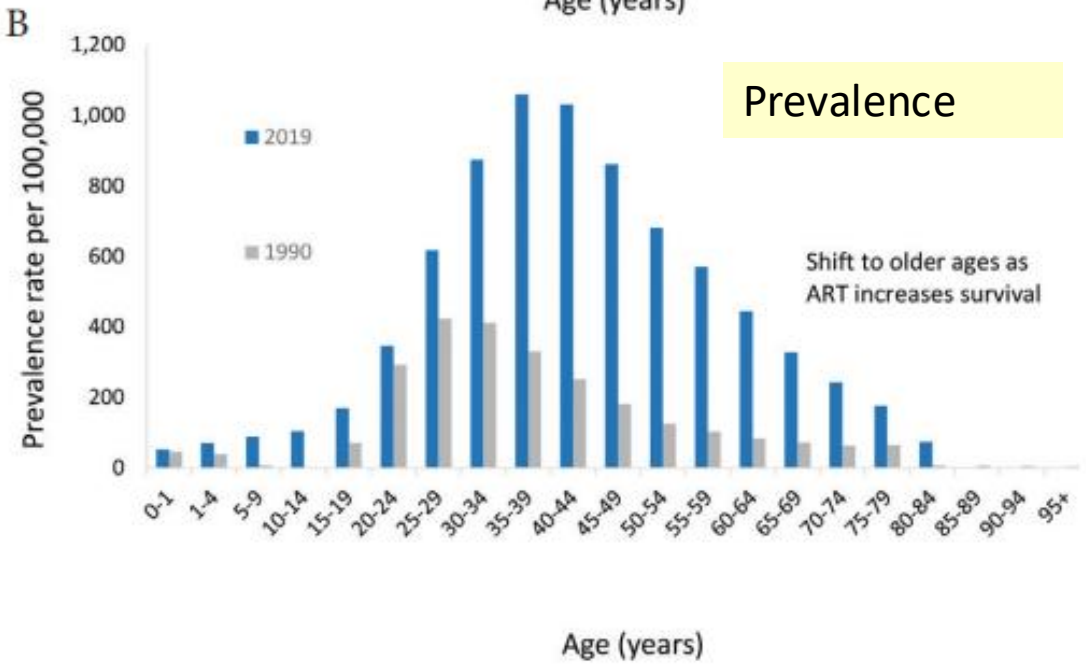


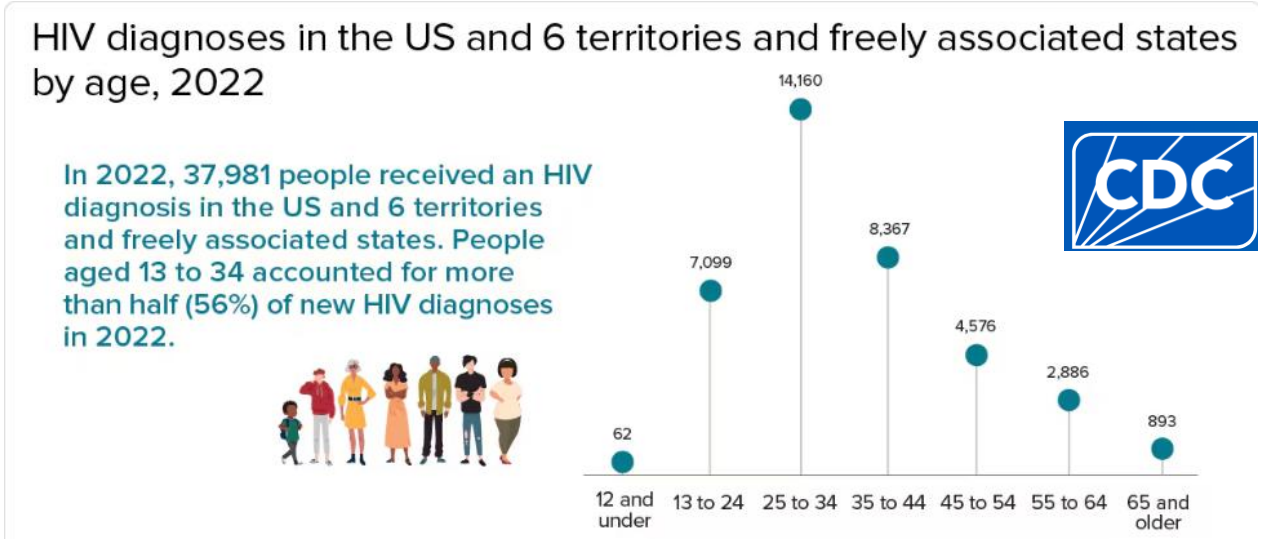
Inflammation, immune activation drive aging in HIV

ART decreases immune activation, but doesn't take it away (or aging phenotype) completely

Hunt et al, JID, 2003; PLoS One, 2011

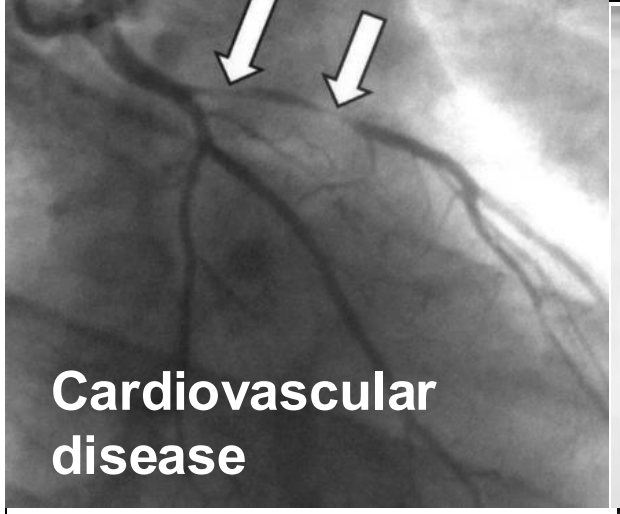


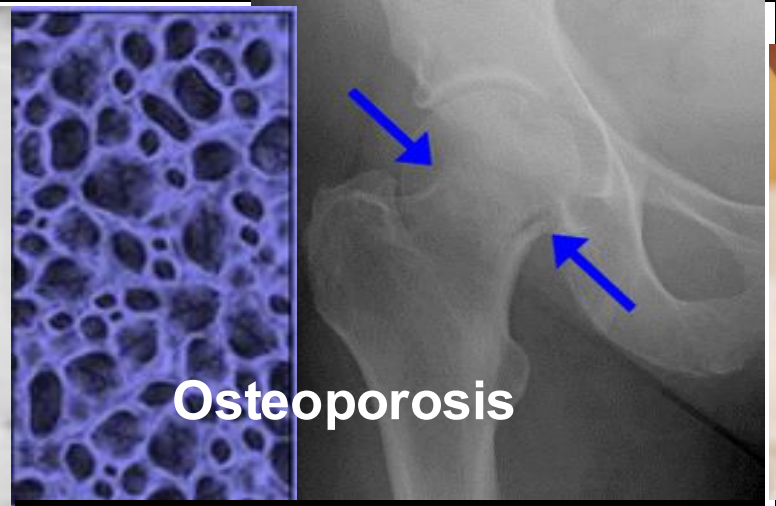


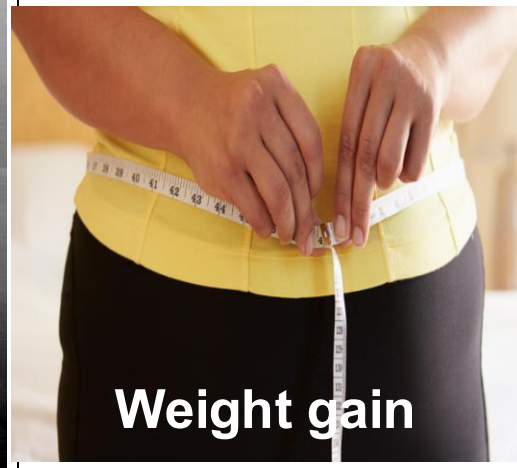


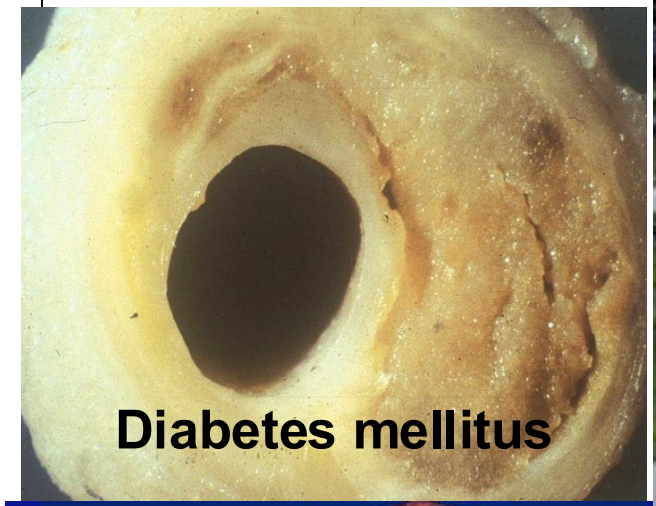
- HIV epidemic is aging
- Both new infections in older people and older people with HIV living longer due to ART
- >50% of PWH in U.S. over 50 years (20% worldwide)
- Very important to develop designated clinical programs for this group

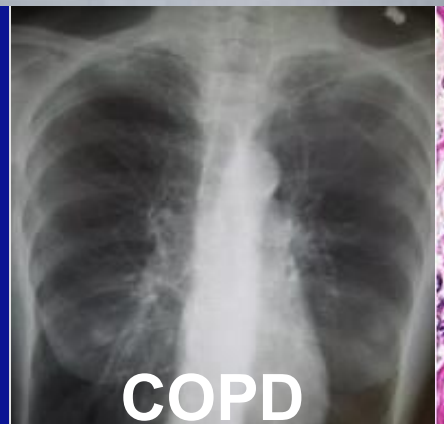
Govender. J of Epi and Global Health 2021

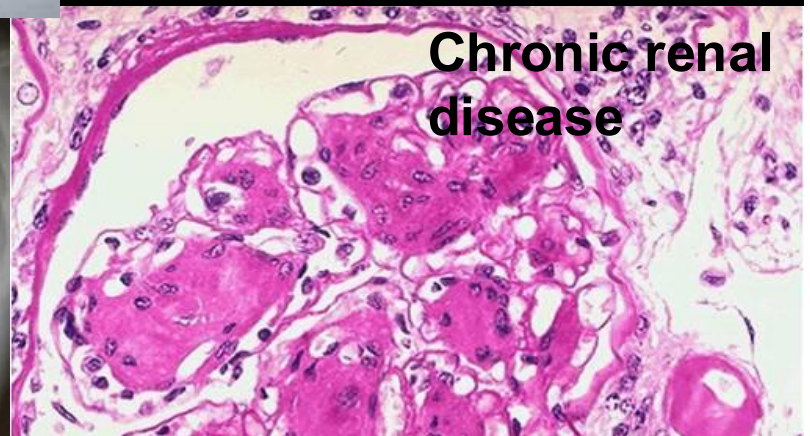








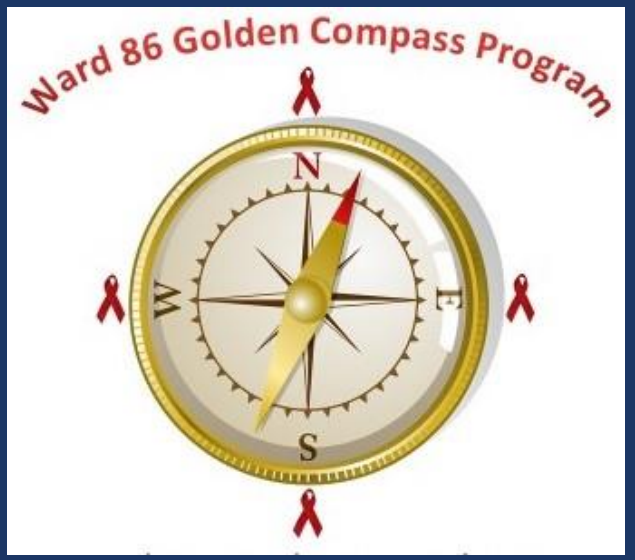




Diseases of aging (co-morbidities and geriatric syndromes) are many in people with HIV – design programs to tackle them

Slide courtesy Judith Currier MD

Steps leading up to development of designated HIV and Aging care program in San Francisco



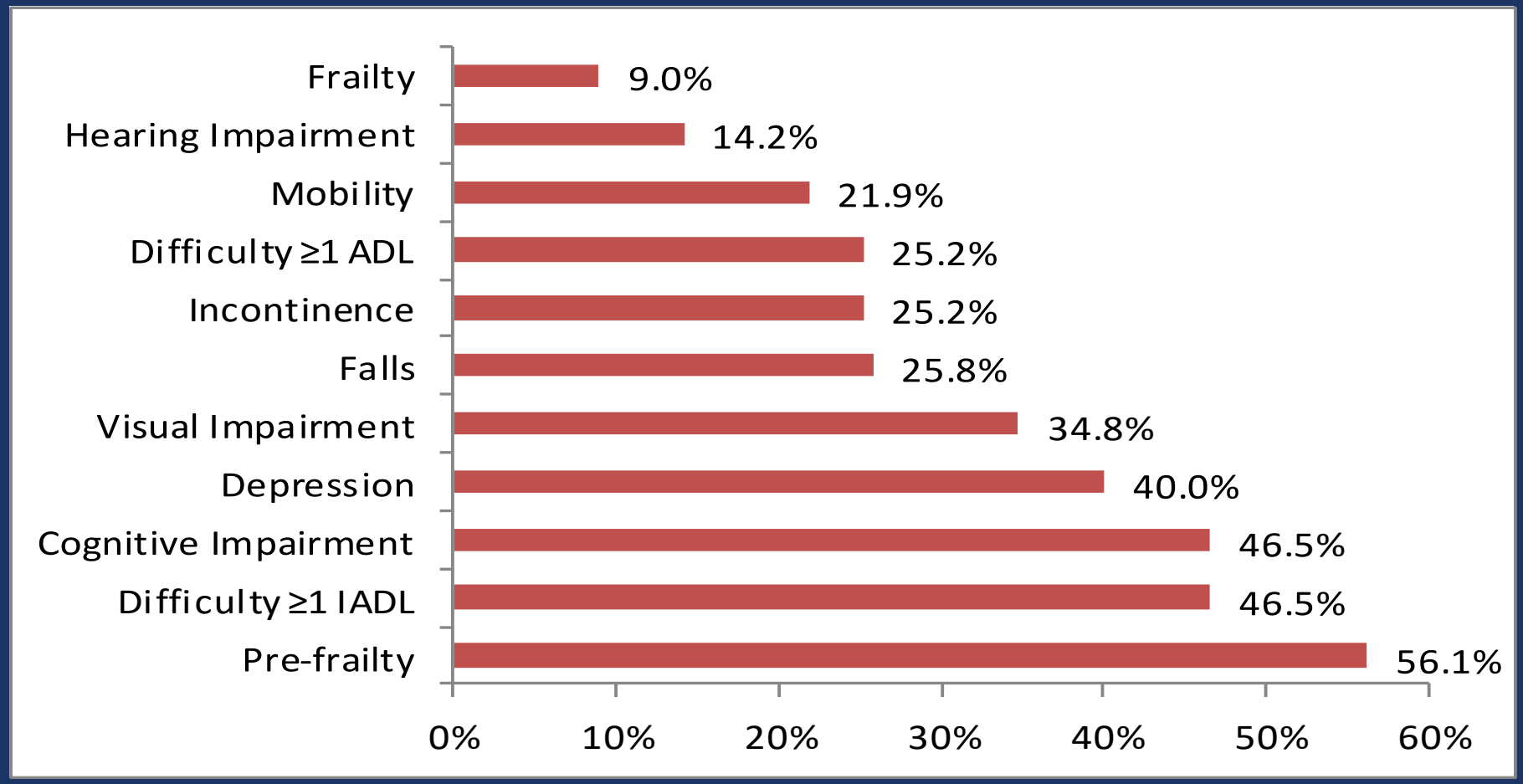
1) Community needs assessment
2) Literature review
3) Pilot program (Silver Project)
4) Focus groups with patients and providers

Community Perspective

2010 City Needs Assessment

2013 Long term survivors community forums

Research in San Francisco



Greene *JAIDS* 2015

Findings from Silver Project Geriatric Assessments (n=359)

≥1 Fall in past year	145 (40.4)
Dependent in ≥1 ADL	43 (12.2)
Dependent in ≥1 IADL	136 (38.9)
At least Mild Sx Loneliness	207 (57.9)
MOCA < 26	121 (33.7)
At least mild Depressive Sx	198 (55.1)

Greene M & John M *JAIDS* 2016

Medication Review: Polypharmacy

- 248 patients underwent medication review with pharmacist
- Average 14 medications
  - 11 non- HIV meds
  - 16% taking more than 20 meds

- 63% had at least one potentially inappropriate medication
- 9% had a contraindicated drug-drug interaction

McNicholl I *Pharmacotherapy 2017*

Patient and Provider Perspectives on Assessments

Patients

- Depression 63%
- HIV Med Adh 49%
- Social Support 49%
- Falls 43%
- Memory 43%
- Help ADLs 13=
- Anxiety 13=
- Gait 10=
- Chair Stands 9=
- Loneliness 9=

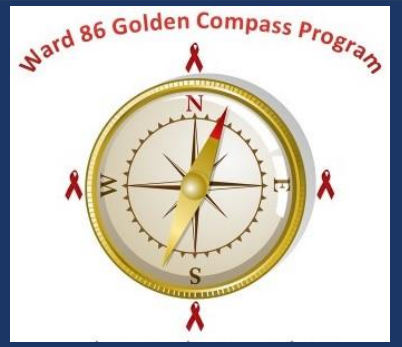
Providers

- Falls 9
- Memory 9
- Depression 6
- Function 6
- Loneliness 5
- HIV Med Adherence 5
- Social Support 5
- Gait 4
- Substance Use 3
- Chair Stands 3

Greene M, paper in revision

University of California, San Francisco
Division of Geriatrics

Focus Groups



- 2 Provider groups, 4 Patient Groups- MSM, Women, IDU, 70+ & outside
- Common themes: Need help navigating system, HIV and aging resources
- Name came from focus groups

Themes from Focus Groups

Northern Point: Heart and Mind

Themes: Provider concerns about cardiovascular disease; patients' desire for self-management of other co-morbid conditions, dual concerns of mental health and cognitive changes

Western Point: Dental, Hearing, Vision

Themes: Need to address aging concerns, link to ancillary services

Eastern Point: Bones and Strength

Themes: aging concerns of importance in HIV: falls, frailty, bone density, neuropathy, need for access to low cost exercise options

Southern Point: Network and Navigation

Themes: loneliness, isolation, wanting to form new connections with other older adults with HIV, navigating healthcare system

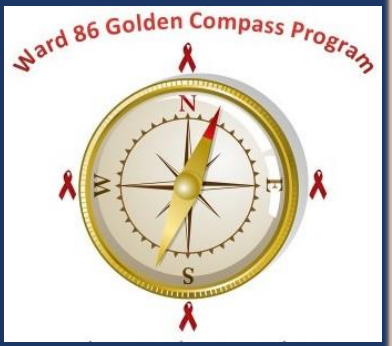
Greene M, paper in submission

North: HIV Cardiologist on-site, Brain Health Classes, Cognitive Eval/Resources

East: Acquired DEXA machine, Fall & Balance evaluations, Exercise classes Polypharmacy, Provider/Staff Education by Geriatrician, Geriatrician every other week on-site, polypharmacy

West: Ensure age-appropriate screening; Link to low cost eyeglasses, hearing aids, dental

South: Partnerships with community agencies, social support groups, social work services, Advanced Care Planning



The Geriatric 5Ms

Geriatric 5Ms	Description
Mind	Mentation Dementia Delirium Depression
Mobility	Impaired gait and balance Fall injury prevention
Medications	Polypharmacy, deprescribing Optimal prescribing Medication burden and adverse medication effects
Multicomplexity	Multimorbidity Complex biopsychosocial situation
Matters Most	Each individual's personal health outcome aims and care preferences

Molnar. Can Fam Physician. 2019;65:39.

Molnar. Can Fam Physician. 2019;65:39.

What's next for Golden Compass?

Continue to tackle issues most important for HIV and Aging

Next step: Endocrine (have one on site) due to diabetes, weight gain, metabolic, statins

What was the first data suggesting INSTIs are linked with weight gain? (CROI 2019)

Bourgi K et al. *Journal of the International AIDS Society* 2020, **23**:e25484
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25484/full | https://doi.org/10.1002/jia2.25484

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

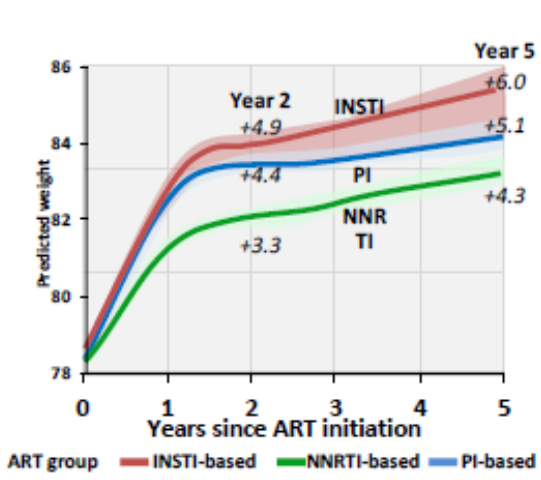
RESEARCH ARTICLE

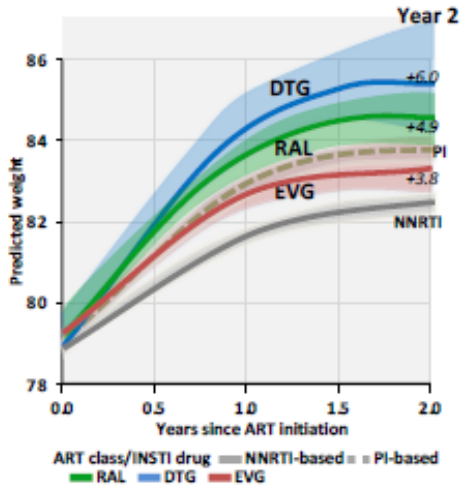
Weight gain among treatment-naïve persons with HIV starting integrase inhibitors compared to non-nucleoside reverse transcriptase inhibitors or protease inhibitors in a large observational cohort in the United States and Canada

Kassem Bourgi[1,2], Cathy A Jenkins[1], Peter F Rebeiro[1], Bryan E. Shepherd[1], Frank Palella[3], Richard D Moore[4],

Weight Gain and Integrase Inhibitors

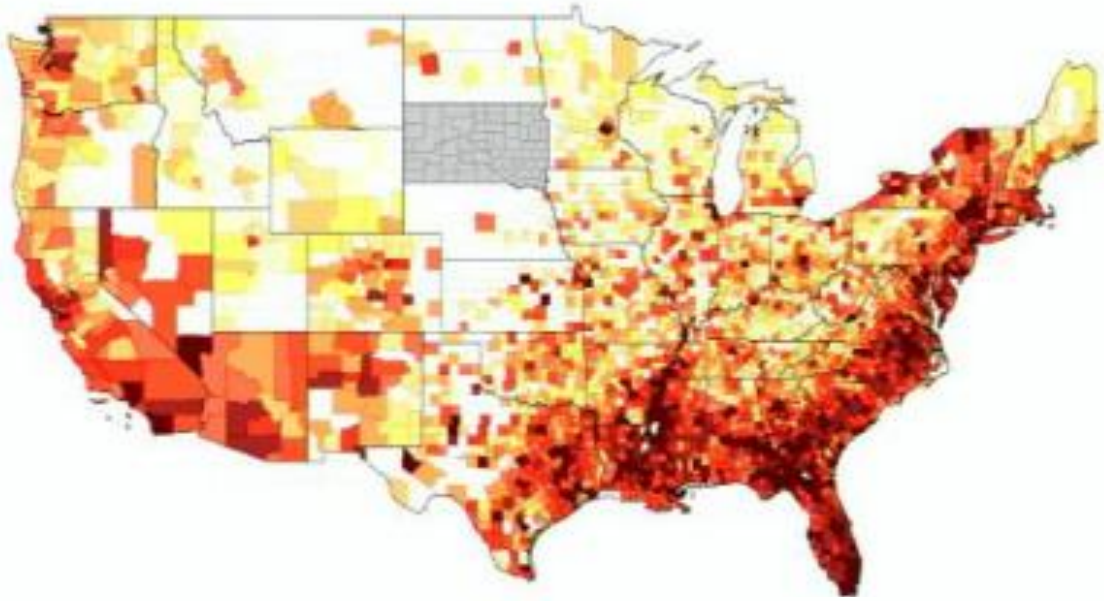
- NA-ACCORD: observational study of 24,001 participants initiating ART
  - INSTIs, PIs associated with greater weight increase than NNRTI
  - DTG and RAL associated with greater weight gain than EVG

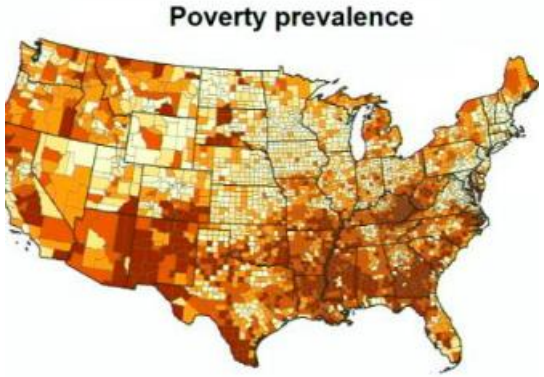




Bourgi K et al, CROI 2019, #670

Overlapping Epidemics: HIV, Obesity, Diabetes, and Cardiovascular Diseases in the US





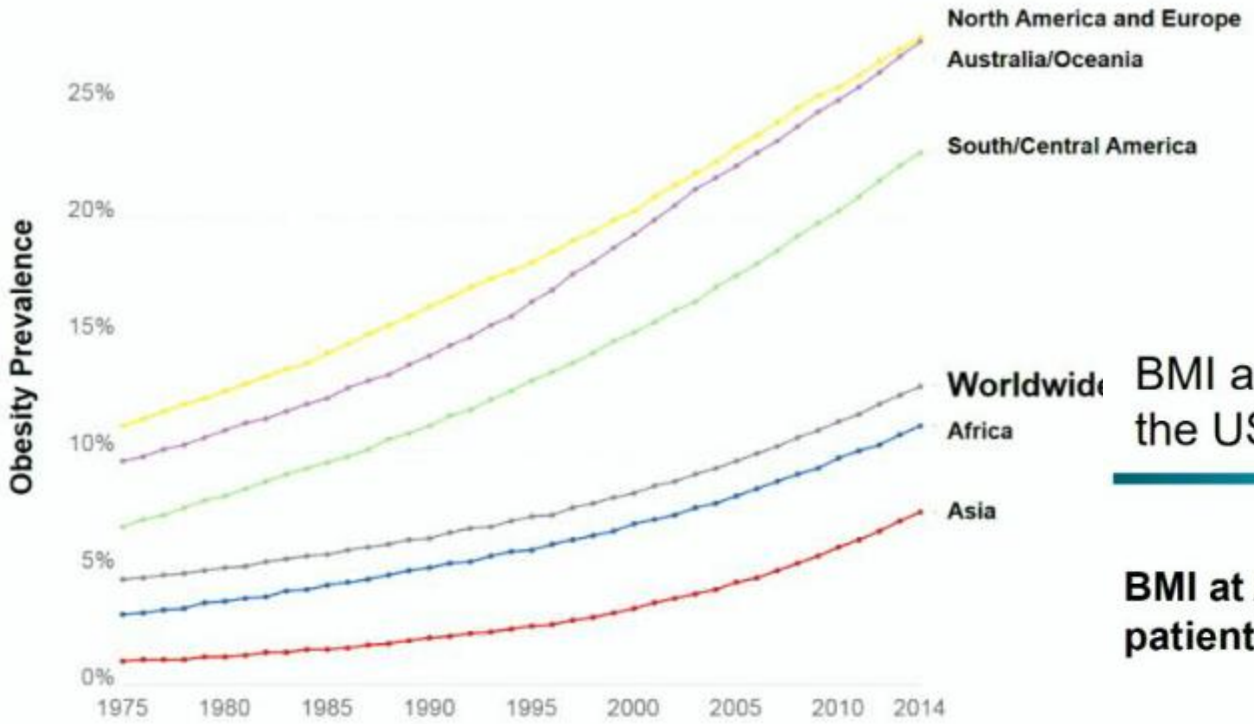
Focus at CROI 2019 on weight gain – both with INSTIs and independently rising

Koethe. CROI 2019

In NA-ACCORD data, 80% of 3-year weight gain occurred in 1st 12 months; more in white men and non-white women

Weight gain seems to rise more steeply among PWH than general population

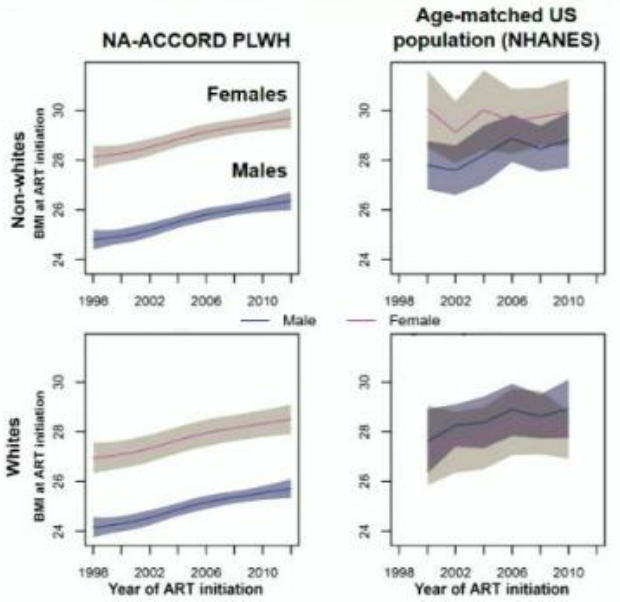
Obesity Prevalence is Rising Worldwide



BMI at ART Initiation has Risen More Steeply Compared to the US Population

BMI at ART initiation in 14,000 patients from 1998-2010

- **NA-ACCORD:** North American AIDS Cohort Collaboration on Research and Design
- **NHANES:** National Health and Nutrition Education Survey

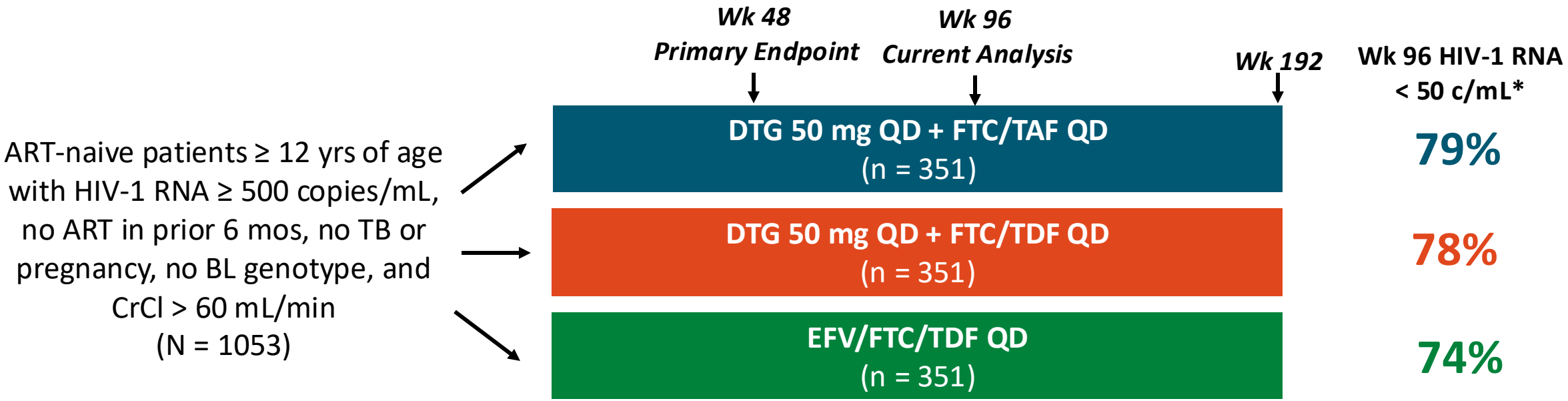


NA-ACCORD, *AIDS Res. Human Retrovir.* 2016

Koethe. CROI 2019

ADVANCE: Phase III Trial of First-line DTG + FTC/(TAF or TDF) vs EFV/FTC/TDF in South Africa

- Multicenter, randomized, open-label phase III trial conducted in South Africa



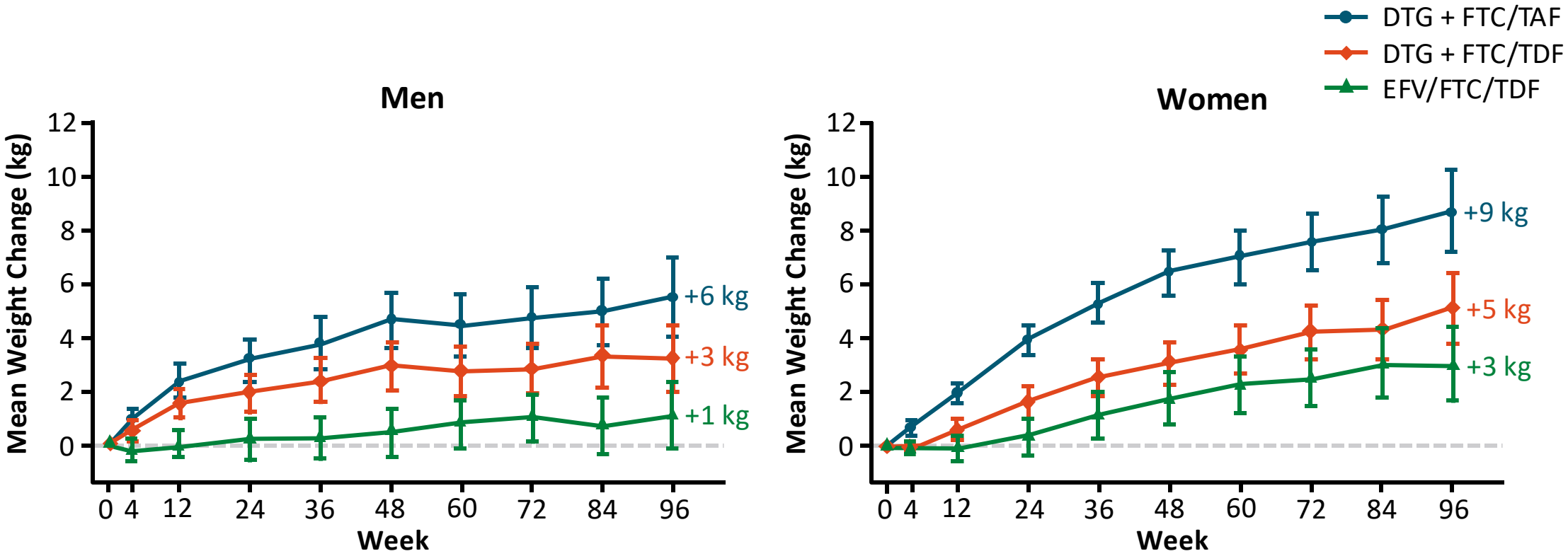
*Differences between arms not statistically significant.

- Primary efficacy endpoint: HIV-1 RNA < 50 copies/mL at Wk 48 by ITT (M = F) analysis
  - DTG + FTC/TAF and DTG + FTC/TDF noninferior to EFV/FTC/TDF at Wk 48: 84% vs 85% vs 79%
- Secondary endpoints: safety, weight gain

Sokhela. AIDS 2020. Abstr OAXLB01. Venter. NEJM. 2019;381:803.

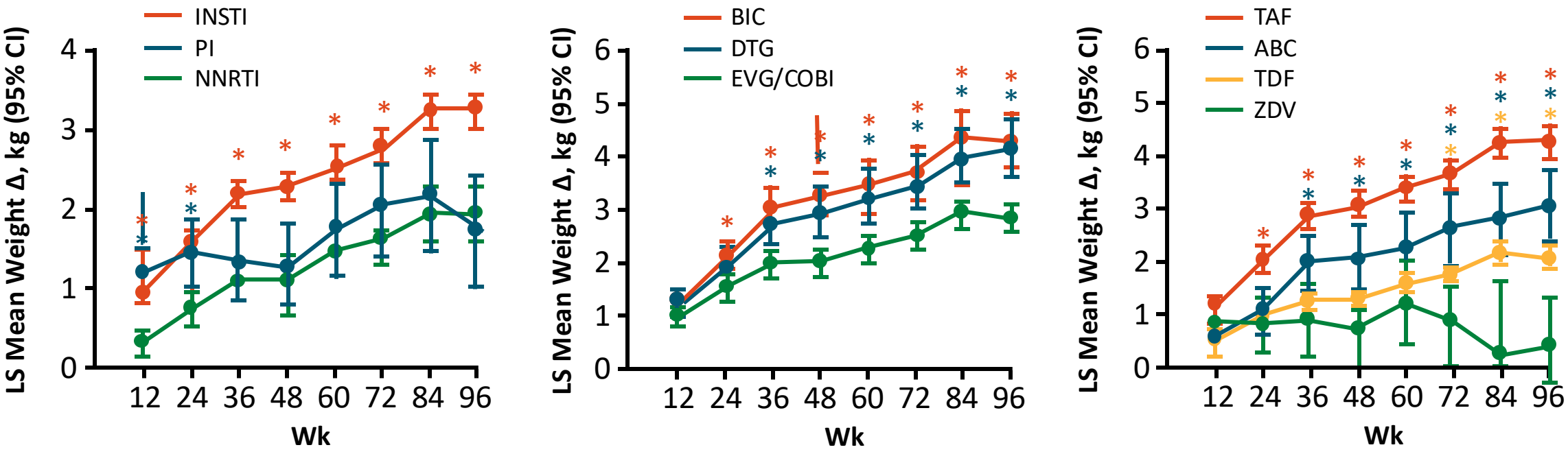
ADVANCE: Mean Weight Change by Sex up to 96 weeks

- Greater weight increase with DTG vs EFV, with TAF vs TDF; plateau in weight gain after Week 48 observed in men but not in women
  - Same patterns observed for percentage change in weight and change in BMI category over time



McCann. EACS 2019. Abstr PS3/3. Venter. NEJM. 2019;381:803.

Weight Gain Following ART Initiation by ARV Class and ARV Drug: BIC, DTG, TAF



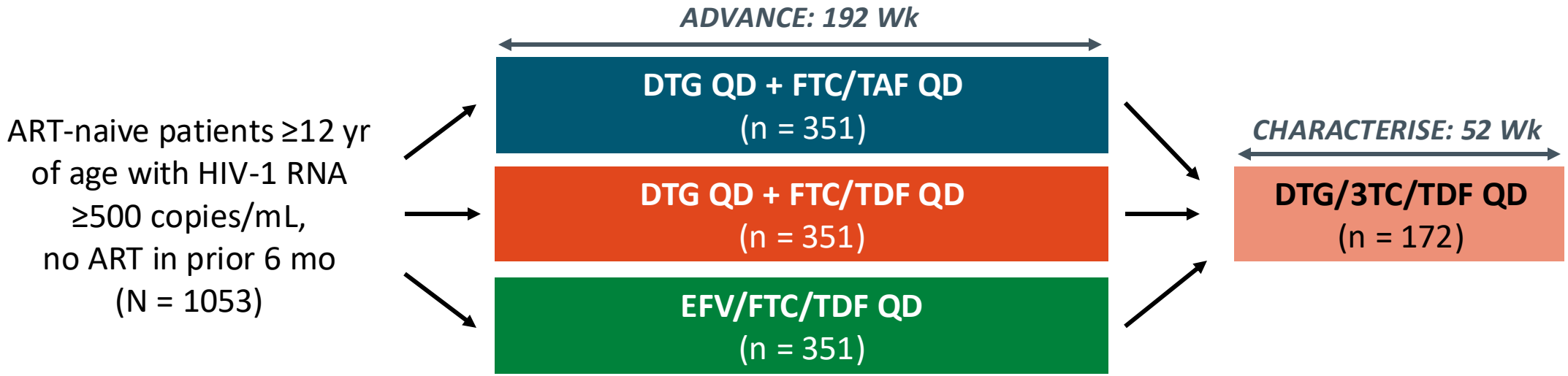
*8 RCTs of PWH treatment-naïve initiating ART between 2003 and 2015, >5000 participants & 10 000 person-years of follow-up

Color-coded to match respective comparators, denoting $P \leq .05$ vs NNRTI (first panel), EVG/COBI (second panel), or ZDV (last panel).

Sax. Clin Infect Dis. 2020;71:1379.

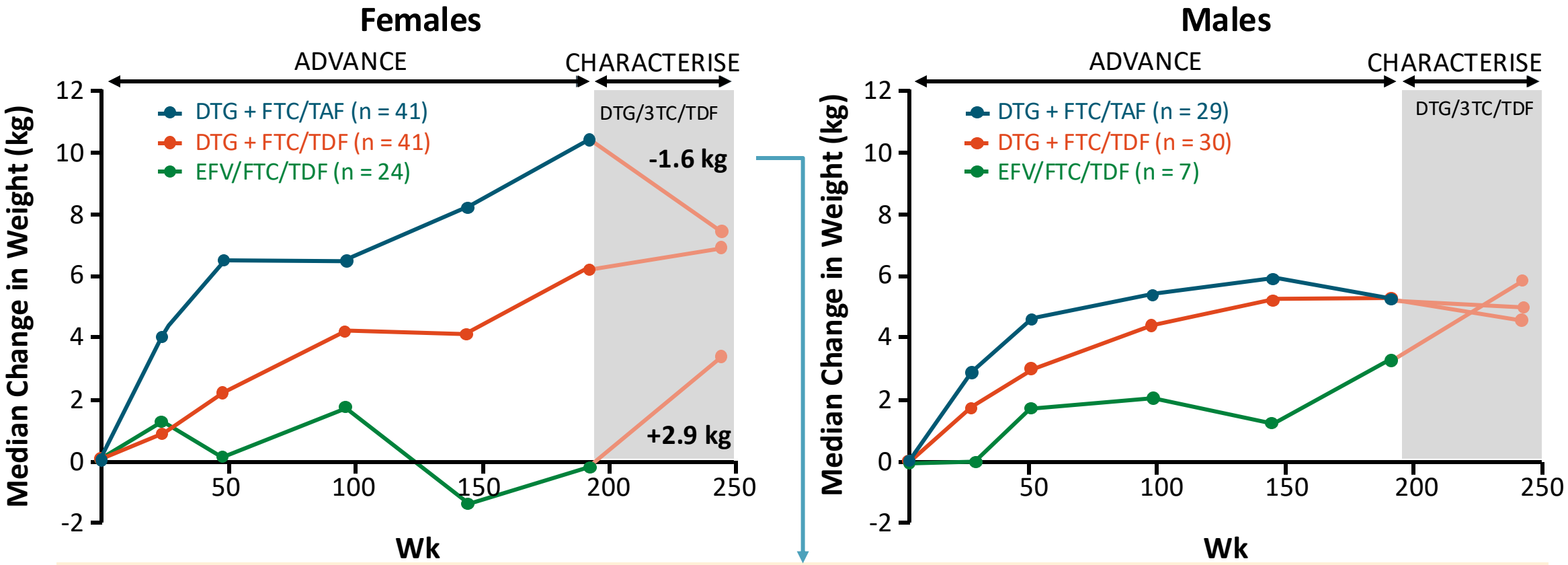
CHARACTERISE: Switch to DTG/3TC/TDF After ADVANCE Trial Participation

- **ADVANCE:** randomized, open-label phase III noninferiority trial in South Africa
  - HIV-1 RNA <50 copies/mL similar across treatment groups at Wk 48 (primary endpoint)[1] and through Wk 192,[2] but weight increases higher with DTG regimens: **+8.9 kg with DTG + FTC/TAF**, **+5.8 kg with DTG + FTC/TDF**, and **+3.3 kg with EFV/FTC/TDF** at Wk 192[2]
- **CHARACTERISE:** evaluation of weight and laboratory changes ≥52 wk after switch from ADVANCE trial to open-label DTG/3TC/TDF[3,4]



1. Venter. NEJM. 2019;381:803. 2. Venter. AIDS 2022. Abstr PELBB01.
3. **Bosch. CROI 2023. Abstr 167. 4**. Bosch. Clin Infect Dis. 2022;ciac949.

CHARACTERISE: Weight Change by Sex After Switch From ADVANCE Trial Regimens to DTG/3TC/TDF



In females, switch from **DTG + FTC/TAF** to **DTG/3TC/TDF** associated with median **1.6 kg weight loss**

Bosch. CROI 2023. Abstr 167.

What do we do about it with ART (exercise, nutrition, GLP-1 agonists)

- CHARACTERISE study suggest switching TAF to TDF will lead to weight loss on INSTI
- TANGO and SALSA studies – just dropping TAF doesn't seem to help

TANGO:

- **Switched from 3-4 drug TAF-containing regimen to DTG/3TC**
- **No h/o NRTI or INSTI mutations**
- **Noninferior**
- **No weight benefit to switch**
- **However, lipid benefit for 3 years to switch (better LDL, total chol on DTG/3TC)**

SALSA:

- **Switched from 3-4 drug regimen to DTG/3TC**
- **No h/o NRTI or INSTI mutations**
- **Noninferior**
- **No weight benefit to switch - Weight gain actually higher in DTG/3TC group but driven by those who switched from TDF and/or EFV**

Llibre J CID 2023; Osiyemi CID 2022

REPRIEVE

Randomized Trial to Prevent Vascular Events in HIV

Beyond diet, exercise, control other risk factors for cardiovascular disease; showed a 35% reduction in major adverse CV event among PWH with statin (clearly most important for moderate-high risk groups)

Clinical Infectious Diseases

MAJOR ARTICLE Clin Infect Dis. 2023 Sep 12;

Weight gain after antiretroviral therapy initiation and subsequent risk of metabolic and cardiovascular disease

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

Steven K. Grinspoon, M.D., Kathleen V. Fitch, M.S.N., Markella V. Zanni, M.D., Carl J. Fichtenbaum, M.D., Triin Umbleja, M.S., Judith A. Aberg, M.D., Edgar T. Overton, M.D., Carlos D. Malvestutto, M.D., M.P.H., Gerald S. Bloomfield, M.D., M.P.H., Judith S. Currier, M.D., Esteban Martinez, M.D., Ph.D., Jhoanna C. Roa, M.D., Marissa R. Diggs, B.A., Evelynne S. Fulda, B.A., Kayla Paradis, M.B.A., Stephen D. Wiviott, M.D., Borek Foldyna, M.D., Sara E. Looby, Ph.D., Patrice Desvigne-Nickens, M.D., Beverly Alston-Smith, M.D., Jorge Leon-Cruz, M.S., Sara McCallum, M.P.H., Udo Hoffmann, M.D., M.P.H., Michael T. Lu, M.D., M.P.H., Heather J. Ribaudo, Ph.D., and Pamela S. Douglas, M.D., for the REPRIEVE Investigators*

ABSTRACT

Participants who experienced >10% weight gain in 1st year of ART had an increased risk of DM (HR 2.01), metabolic syndrome (HR 2.24), and cardiometabolic outcomes (HR 1.54)

British guidelines- all PWH >40 – statin
US- ASCVD >2.5%

Bone health

Recommendations for Evaluation and Management of Bone Disease in HIV

Table 4. Bone Mineral Density T- and Z-Score Thresholds for Determination of Osteopenia and Osteoporosis

Population	Interpretation: Use of T-Score or Z-Score	Normal	Osteopenia	Osteoporosis
Postmenopausal women and men ≥50 y of age	T-score (compared with a young healthy adult)	≥ –1 SD	Between –2.5 and –1 SD	≤ –2.5 SD
All others	Z-score (age-, sex-, ethnicity-matched)	Low BMD for chronological age if ≤ –2 SD[a]		

Sources: [4, 8].

Abbreviations: BMD, bone mineral density; SD, standard deviation.

[a] In premenopausal women, men <50 years of age, and children, the diagnosis of osteoporosis should not be made by BMD criteria alone [4].

Thompson MA. Primary care guidance for persons with HIV.

Age is Not a Condom

PrEP in Older Adults

- CDC: Once daily, oral PrEP is recommended for adults at substantial risk* of acquiring HIV infection, **regardless of age**[1]
- **Cabotegravir (and lenacapavir in future, expecting approval June 19, 2025) may be better option given bone effects of tenofovir**
- DHHS: ***"Age alone should not exclude older adults from being evaluated for and offered PrEP."***[2]

MSM*[1]	Heterosexual Women and Men*[1]	Persons Who Inject Drugs*[1]
▪ Sexual partner with HIV ▪ Recent bacterial STI ▪ High number of sex partners ▪ History of inconsistent or no condom use ▪ Commercial sex work	▪ Sexual partner with HIV ▪ Recent bacterial STI ▪ High number of sex partners ▪ History of inconsistent or no condom use ▪ Commercial sex work ▪ In high HIV prevalence are or network	▪ Injecting partner with HIV ▪ Sharing injection equipment

1. CDC. PrEP Guidelines. 2017. 2. DHHS. ART Guidelines. December 2020. 3. Huang. MMWR. 2018;67:1147.

Slide credit: clinicaloptions.com

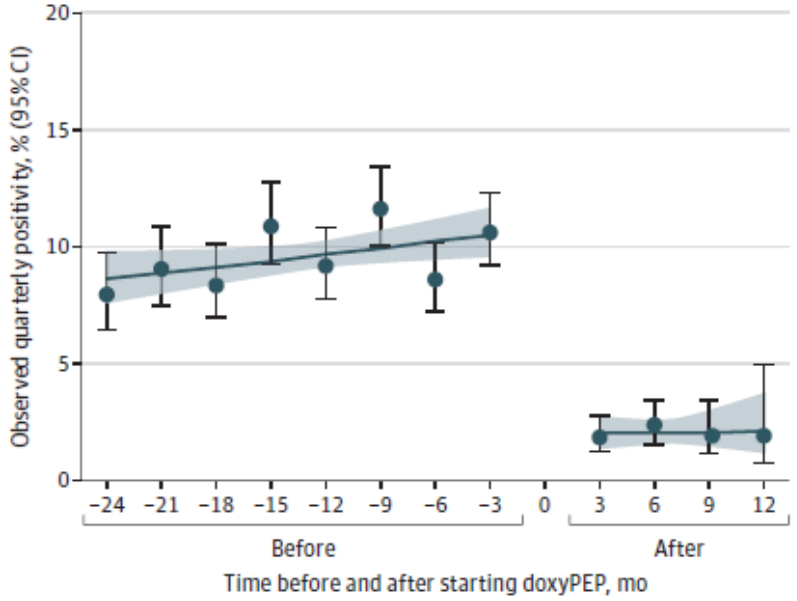
JAMA Internal Medicine | Original Investigation

Doxycycline Postexposure Prophylaxis and Bacterial Sexually Transmitted Infections Among Individuals Using HIV Preexposure Prophylaxis

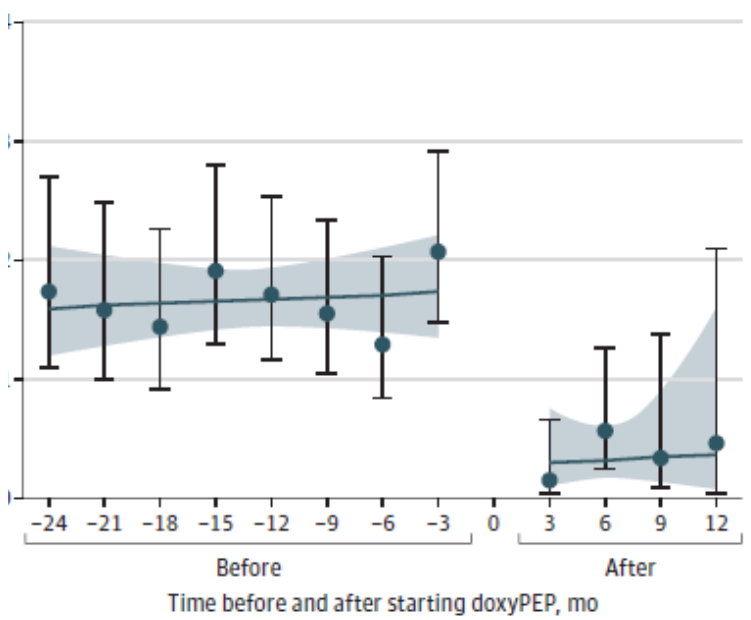
Michael W. Traeger, PhD, MSc; Wendy A. Leyden, MPH; Jonathan E. Volk, MD; Michael J. Silverberg, PhD; Michael A. Horberg, MD; Teaniese L. Davis, PhD; Kenneth H. Mayer, MD; Douglas S. Krakower, MD; Jessica G. Young, PhD; Samuel M. Jenness, PhD; Julia L. Marcus, PhD

- > 11, 000 Northern California Kaiser PrEP users
- 20% on doxyPEP, 98% male, ≈ 50% with an STI in prior year
  Chlamydia & syphilis: ↓ 80% quarterly
  Gonorrhea: no overall change, 20% ↓ in rectal & urethral
- No change in STIs for those not on doxyPEP

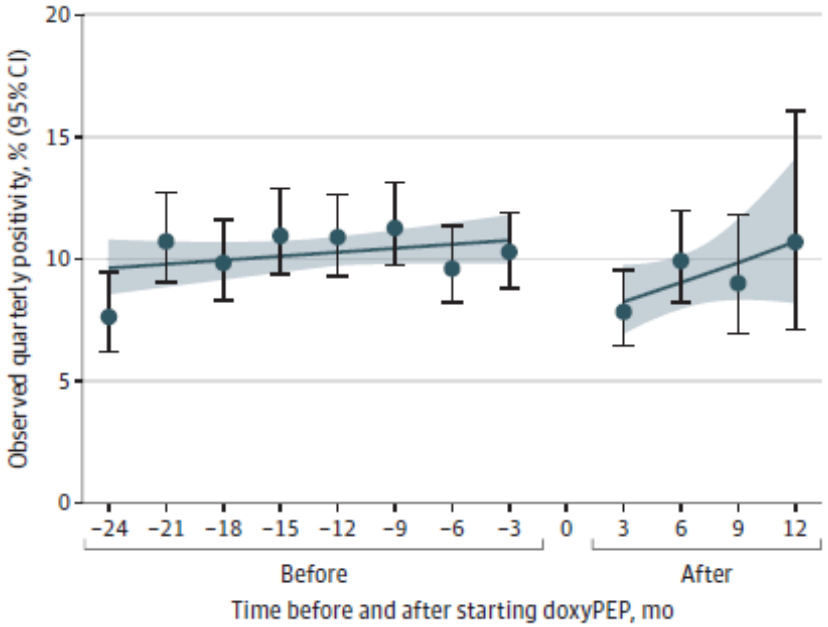
Chlamydia



Syphilis



Gonorrhea



Human Papillomavirus Vaccination (HPV)- can go up to 45 years & why not older?

- **Child vaccination (so recommendations for adults with HIV if not done)**
  - All adolescents 11-12 years old (usually middle school, can start at 9)
  - Number of doses dependent on age at initial vaccination
    - Age 9-14 years: 2-dose series at 0 and 6-12 months (interval >= 5 months)
    - Age 15 years or older: 3-dose series at 0, 1-2 months, and 6 months

- **HCw vaccination**
  - If adult with HIV only had 2 doses as child, get additional dose
  - All persons who didn't get as child should get 3 doses through 26 years of age as an adult
  - If didn't get before 26, can still give ages 27-45 (**encouraged in HIV**)

MMWR / August 16, 2019/ 68(32);698–702 MMWR / February 18, 2022 / 71(7);234-237 https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

Conclusion

#continuum2025

- Population of people living with HIV in the world is aging
- Need clinical care paradigms specifically focused on this group
  - Weight gain and metabolic effects
  - Polypharmacy
  - Cardiovascular disease
  - Exercise, frailty, bone health
  - Social groups, hearing, vision, dentistry
- PrEP needed at any age and STD prevention (vaccines, DoxyPEP)