CROI 2024 Update: Co-Occurring Conditions

Raaka Kumbhakar, MD, MPH
Clinical Assistant Professor
Department of Medicine, Division of Allergy and Infectious Diseases
University of Washington

Last Updated: 3/19/24

Disclosures

No conflicts of interests or relationships to disclose

MWAETC

Disclaimer

Funding for this presentation was made possible by U1OHA29296 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. *Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.*

AETC AIDS Education & Training Center Program Mountain West

Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities

MWAETC

CROI Updates: Co-Occurring Conditions

- Updates in anal cancer screening strategies
- Review updates in metabolic complications of HIV
  - Use of semaglutide
- Updates in HBV vaccination
  - BEe-HIVe Arm A results

MWAETC

Anal Dysplasia Screening

MWAETC

Anal Cancer in PWH

- Incidence of anal cancer is high among PWH; particularly among MSM
- ANCHOR: Treating anal HSIL reduces incidence of anal cancer (57% reduction)
- **HRA (high resolution anoscopy) is gold standard for HSIL detection….**
  …..but availability is limited
- Need practical strategies to approach anal cancer screening in PWH
  - Prioritization of referrals by demographics, low CD4 nadir, cytology/high risk HPV (HR-HPV)

Palefsky et al. NEJM 2022; Martin-Iguacel et al, CROI 2024 (poster)

MWAETC

Evaluation of Performance of Different HRA Triage Strategies in MSM LWH

Determine "best" strategy for HRA triage in MSM living with HIV (LWH) to efficiently allocate HRA resources

	Median (±SE)
Age (years)	47 (±10.7)
CD4 nadir (cells/uL)	350 (±241)
Current CD4 (cells/uL)	800 (±272)
CD4/CD8	1.03 (±0.39)
HIV RNA (copies/mL)	<37

180 MSM LWH had anal cytology, anal HPV, and HRA collected on same day

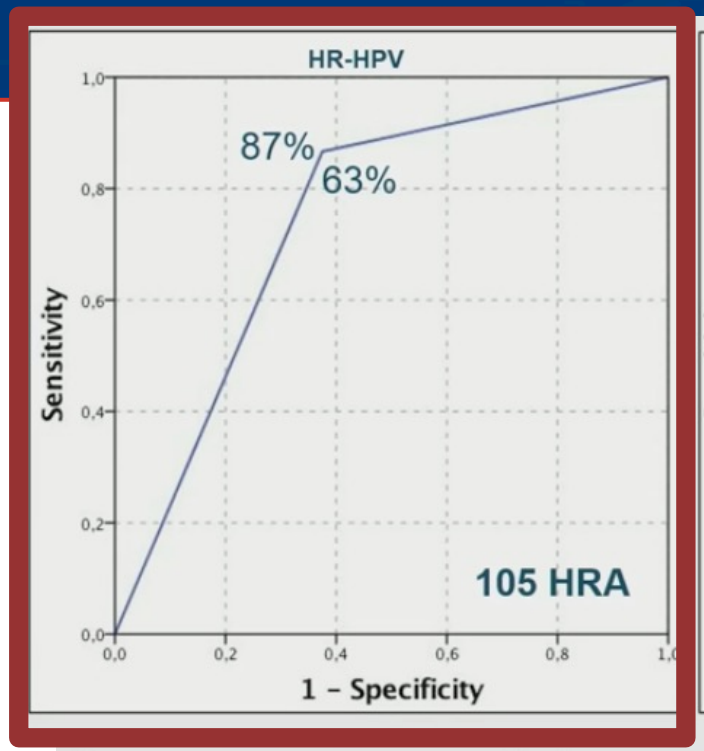
Results	Percent
Cytology	
NILM	10%
ASC-US	14%
LSIL	69%
ASC-H	5%
HSIL	2%
HR-HPV*	75%
HRA	43% HSIL

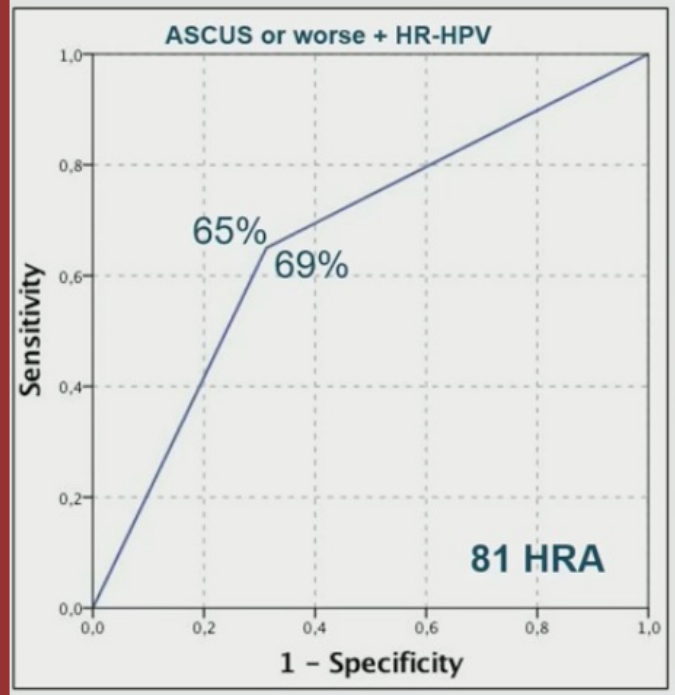
*Of HR-HPV, 54% HPV-16

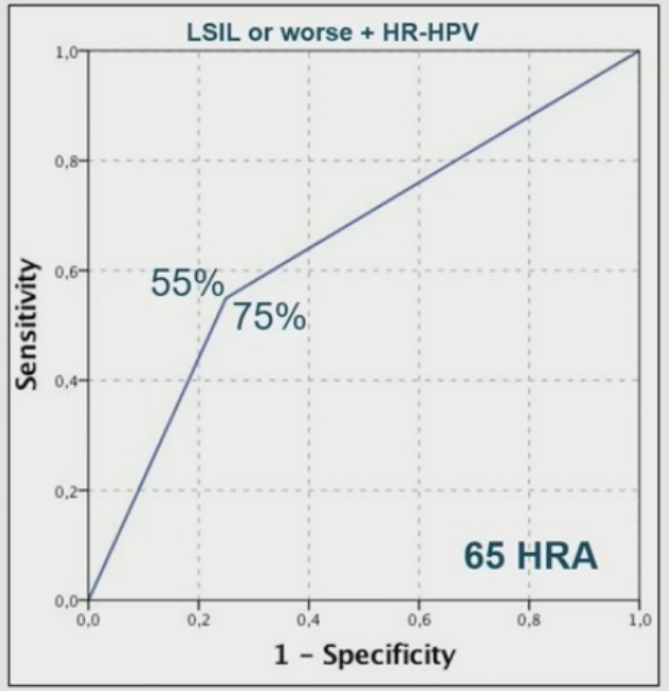
Cavallari et al. CROI 2024

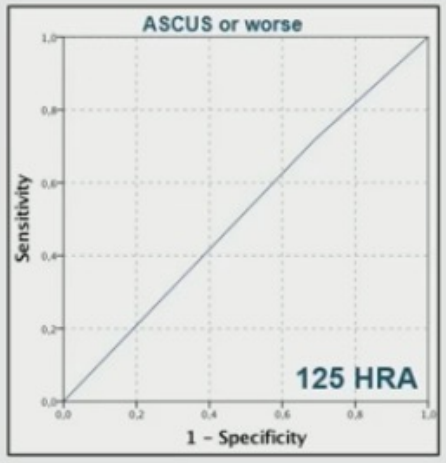
MWAETC

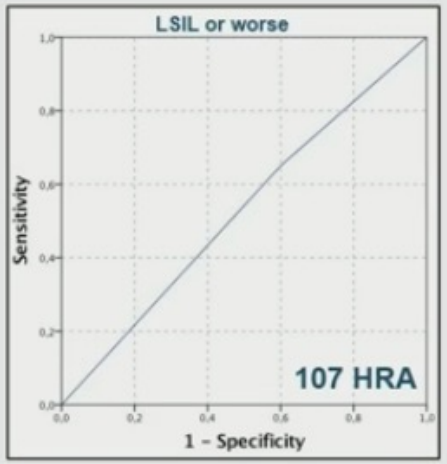
Results

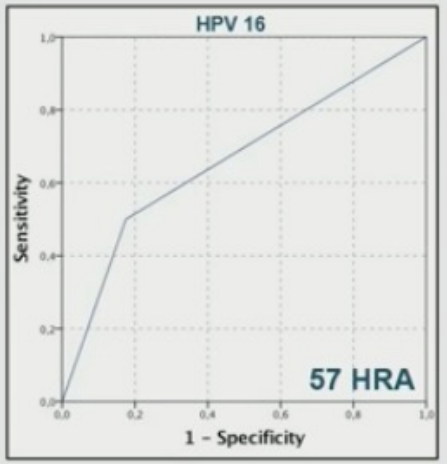


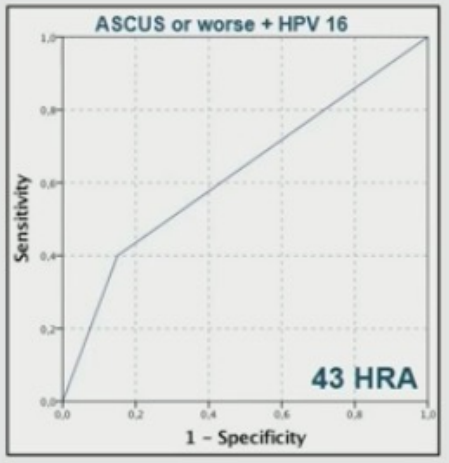












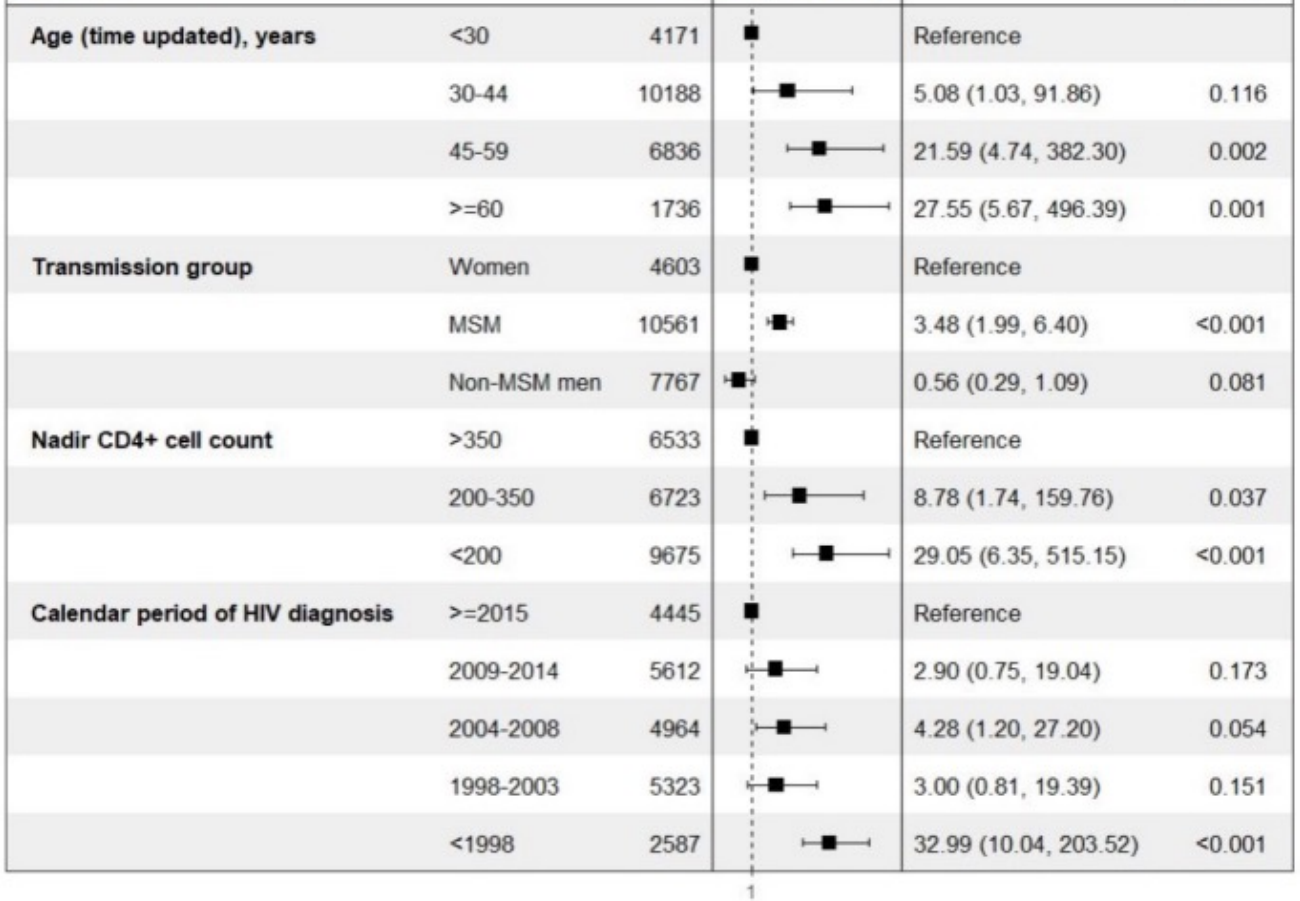
Cavallari et al. CROI 2024

CD4 Nadir and anal cancer risk

- PWH with nadir CD4 <200 had highest anal cancer risk (aIRR 29 v nadir > 350)
- PWH with nadir CD4 > 350 with similar risk as compared to general population
- Age, MSM, and nadir CD4 count strongest association w/anal cancer risk in PWH

Figure 2. Risk factors for anal cancer in the multivariable model.

Variable		N	Adjusted IRR	p-value
Age (time updated), years	<30	4171	Reference	
	30-44	10188	5.08 (1.03, 91.86)	0.116
	45-59	6836	21.59 (4.74, 382.30)	0.002
	>=60	1736	27.55 (5.67, 496.39)	0.001
Transmission group	Women	4603	Reference	
	MSM	10561	3.48 (1.99, 6.40)	<0.001
	Non-MSM men	7767	0.56 (0.29, 1.09)	0.081
Nadir CD4+ cell count	>350	6533	Reference	
	200-350	6723	8.78 (1.74, 159.76)	0.037
	<200	9675	29.05 (6.35, 515.15)	<0.001
Calendar period of HIV diagnosis	>=2015	4445	Reference	
	2009-2014	5612	2.90 (0.75, 19.04)	0.173
	2004-2008	4964	4.28 (1.20, 27.20)	0.054
	1998-2003	5323	3.00 (0.81, 19.39)	0.151
	<1998	2587	32.99 (10.04, 203.52)	<0.001



IRR adjusted for calendar time, age (time-updated), risk group and nadir CD4⁺ cell count

Martin-Iguacel et al. CROI 2024

MWAETC

Anal Self-Sampling for HR-HPV Detection

- Access to HRA, cytology limited in certain settings (such as sub-Saharan Africa)
- Evaluation of anal self-sampling (ASS) for HR-HPV detection as compared to anal swab by practitioner (ASP) in 188 MSM (67% with HIV) in Togo
  - Practitioner conducted anal exam and anal cytology post self-sampling
- Acceptability: 99% found ASS procedurally easy; 60% would prefer ASS to ASP (19% with no preference)
- Performance: 6% v 4% of ASS samples uninterpretable

Charpentier et al. CROI 2024

MWAETC

Anal Self-Sampling for HR-HPV Detection

- Substantial agreement between methodologies for HR-HPV (89.7%, k = 0.66) and HPV16 (90.3%, k = 0.75)
- At least one HR-HPV detected in 83% of ASS and 77% of ASP samples
- HPV16 detected in 28% of ASS and 26% of ASP

High concordance between sampling methods; high acceptability, ease of ASS

ASS may help achieve anal cancer screening targets, especially in LMIC

Charpentier et al. CROI 2024

MWAETC

Takeaways

- In discussion of how to develop guidance for HRA referral, consider:
  - HPV testing (HR-HPV types 16 and 18), inclusive of self-sampling
  - Anal cytology in combination
  - Nadir CD4, Age, MSM

MWAETC

Metabolic Complications

GLP-1 Receptor Agonists

- Mechanism: Promote insulin release and suppress hepatic glucose output

- Semaglutide
  - DM: 2% decrease in A1c, 6.4 kg weight loss, 26% decrease in MACE events
  - Without DM: 3-4 kg weight loss, 20% decrease in MACE events

- **Semaglutide in PWH?**

Marso et al. NEJM 2016
Lincoff et al. NEJM 2023

MWAETC

SLIM LIVER

- Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is common among people with HIV
  - GLP-1 (semaglutide) associated with metabolic improvements including improved hepatic steatosis

- Semaglutide for MASLD in HIV:
  - **ACTG A5361 (SLIM LIVER)**: single arm, open label, phase IIb study of **effects of semaglutide on hepatic steatosis**
    - MRI proton density fat fraction (MRI-PDFF) quantified intrahepatic trigylceride content (IHTG)

- 49 PWH suppressed on ART w/ elevated minimum waist circumference, insulin resistance, and ≥ 5% IHTG on MRI-PDFF

- Initiated on semaglutide, uptitrated over 24 weeks: 0.25 mg sc weekly → 0.5 mg → 1.0 mg)
  - MRI-PDFF performed again at week 24

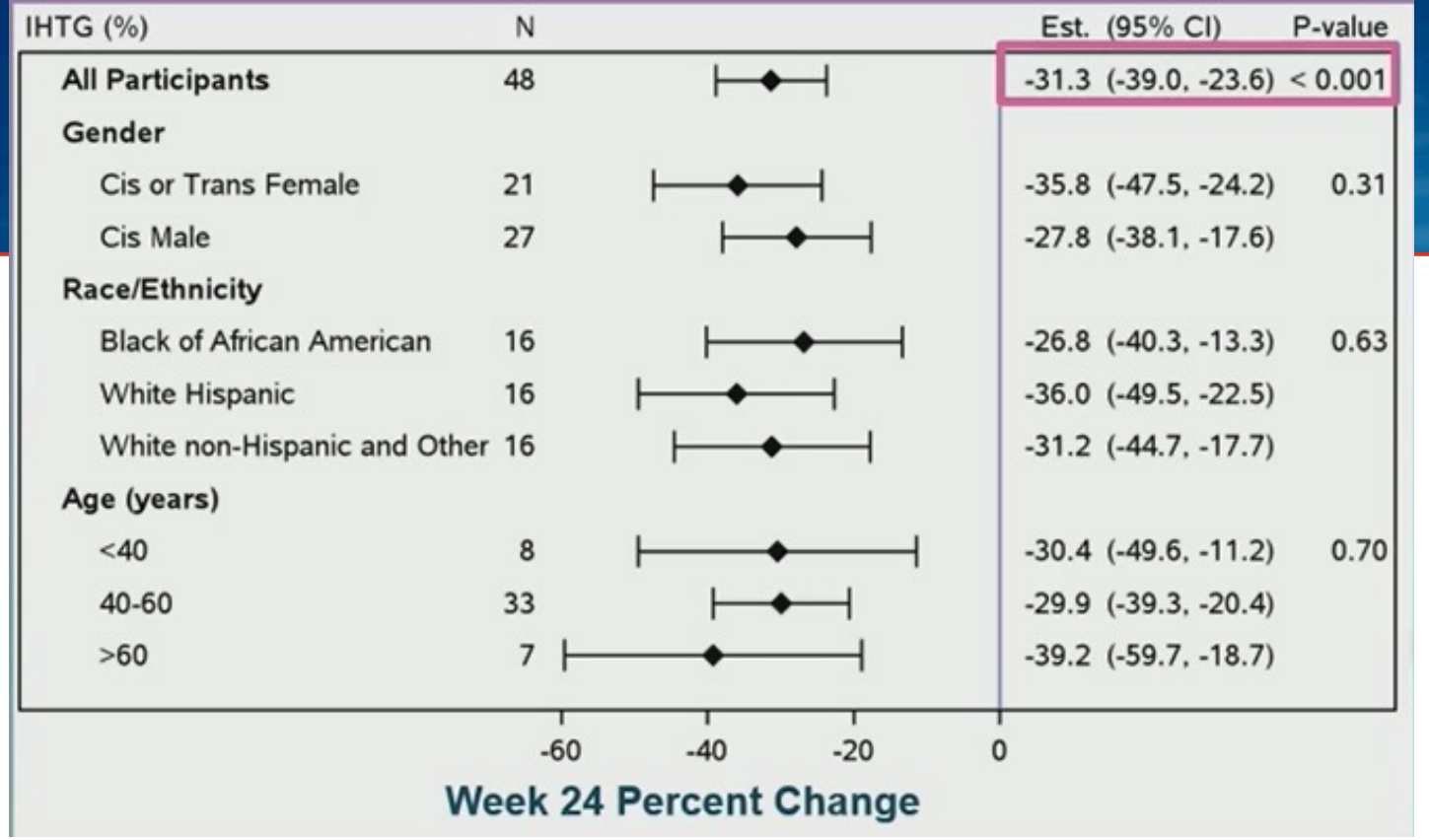
Lake et al. Clin Gastroenterol Hepatol 2022; Lake et al. CROI 2024

MWAETC

SLIM LIVER

Demographics:

- 37% cis-women, 6% transwomen, 57% cis-men
- 27% white non-Hispanic, 33% Black or African American, 39% Hispanic
- Median BMI 35 kg/m2, Median waist circumference 114 cm
- Median CD4 701 (IQR 586,869)
- 82% on INSTI, 22% on NNRTI, 4% on PI



Overall clinically significant reductions in IHTG

- 1/3 of participants with complete MASLD resolution
- IHTG improvements correlated with weight loss (mean 7.8 kg loss over 24 weeks) along with waist circumference, fasting plasma glucose, A1c, and serum triglycerides

Lake et al. CROI 2024

MWAETC

Semaglutide in HIV

- Effects of Semaglutide on Muscle Structure and Function in the SLIM Liver Study (Ditzenberger et al.)
  - Use of semaglutide associated with loss of psoas muscle volume (without change in physical function) but no change in muscle fat among SLIM Liver participants

- Impact of Semaglutide on Weight Change Among People with HIV: A Stratified Analysis by Baseline BMI (Crane et al.)
  - Among PWH, semaglutide a/w significant weight loss (6.5 kg, 5.7% of body weight)
  - Sensitivity analysis: weight loss was the same regardless of INSTI use

Ditzengerger et al CROI 2024
Crane et al CROI 2024

MWAETC

Takeaways

- Use of semaglutide in PWH:
  - Associated with significant weight loss
  - Can be used for successful treatment of MASLD
  - May impact muscle volume without impact in physical function (in short term)

- Needs:
  - Longer term data
  - Access to medication!

MWAETC

Hepatitis B Vaccination in PWH

MWAETC

Background

- HBV vaccine seroprotection rates (SPR) in persons with HIV (PWH) are lower (range 18-71%) than in adults without HIV (range 60-80%) with conventional HBV vaccine (HepB-alum)[1]

- ACTG 5379 (BEe-HIVe):

<u>Arm B (vaccine naïve)</u>[2]

  - 100% of PWH receiving 3-dose series HepB-CpG (Heplisav-B) vaccine achieved seroprotection response (SPR, HBsAb ≥ 10 mIU/mL), 84% HBsAb ≥ 1000 mIU/mL
  - 98.5% achieved SPR after two doses, though at lower titers (28% HBsAb ≥ 1000 mIU/mL)

[1] Kim NH, et al. Int J STD AIDS. 2009
[2] Marks KM, et al. Clin Infect Dis 2023

MWAETC

B-Enhancement of HBV Vaccination in Persons Living With HIV (BEe-HIVe): Study Design

- **Entry Criteria Arm A and B**
  - PWH and age 18-70 years
  - On ART & HIV-1 RNA <1,000 copies/mL
  - CD4 >100 cells/mm^3
  - Negative HBV surface Ab (sAb)
  - No history of hepatitis B
  - Not pregnant
- **Arm A (Vaccine Non-Responders)**
  - Serum Hep B sAb <10 mIU/mL
  - HBV vaccination (>168 days prior)
- **Arm B (Vaccine Naïve)**
  - Hep B sAb negative (<45 days)

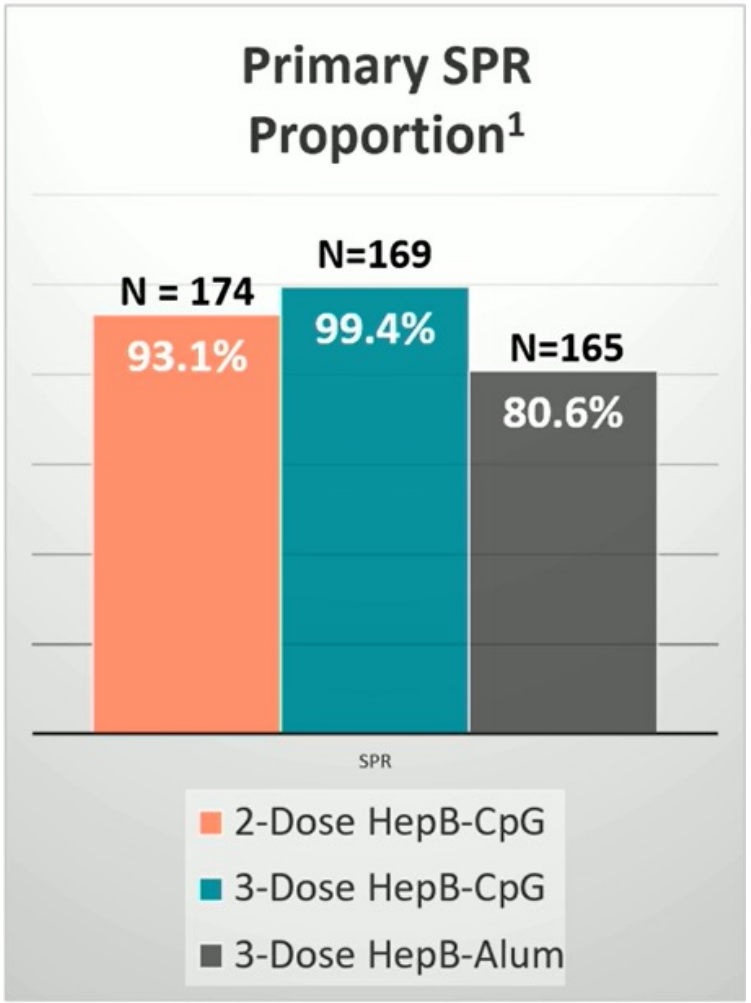
Arm A: HBV Vaccine Non-Responders	
HepB (CpG)	2 doses: 0, 4 weeks
HepB (CpG)	3 doses: 0, 4, and 24 weeks
HepB (Eng-B)	3 doses: 0, 4, and 24 weeks

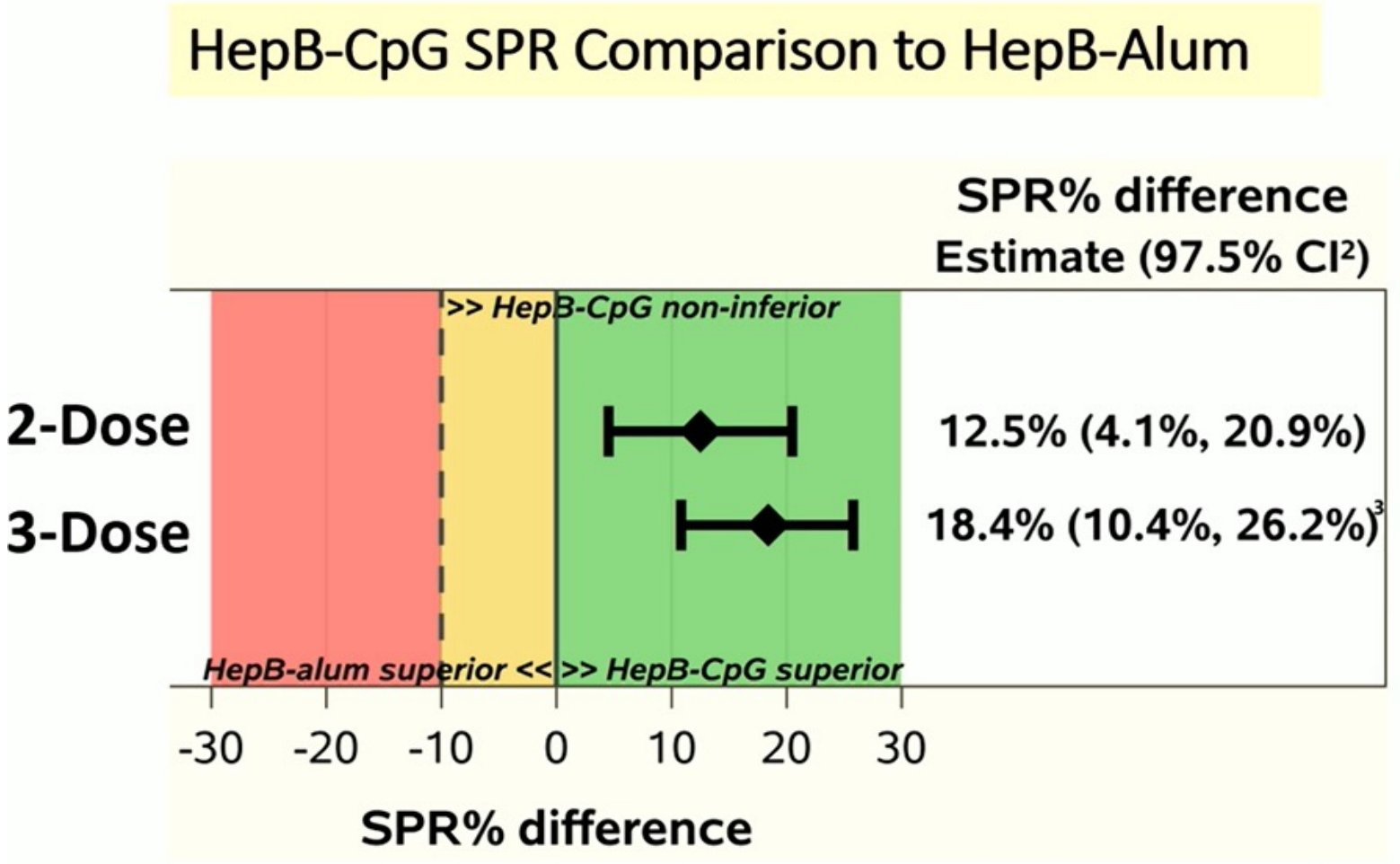
Arm B: HBV Vaccine Naïve	
HepB (CpG)	3 doses: 0, 4, and 24 weeks

Source: Marks K, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster LB749.; National HIV Curriculum

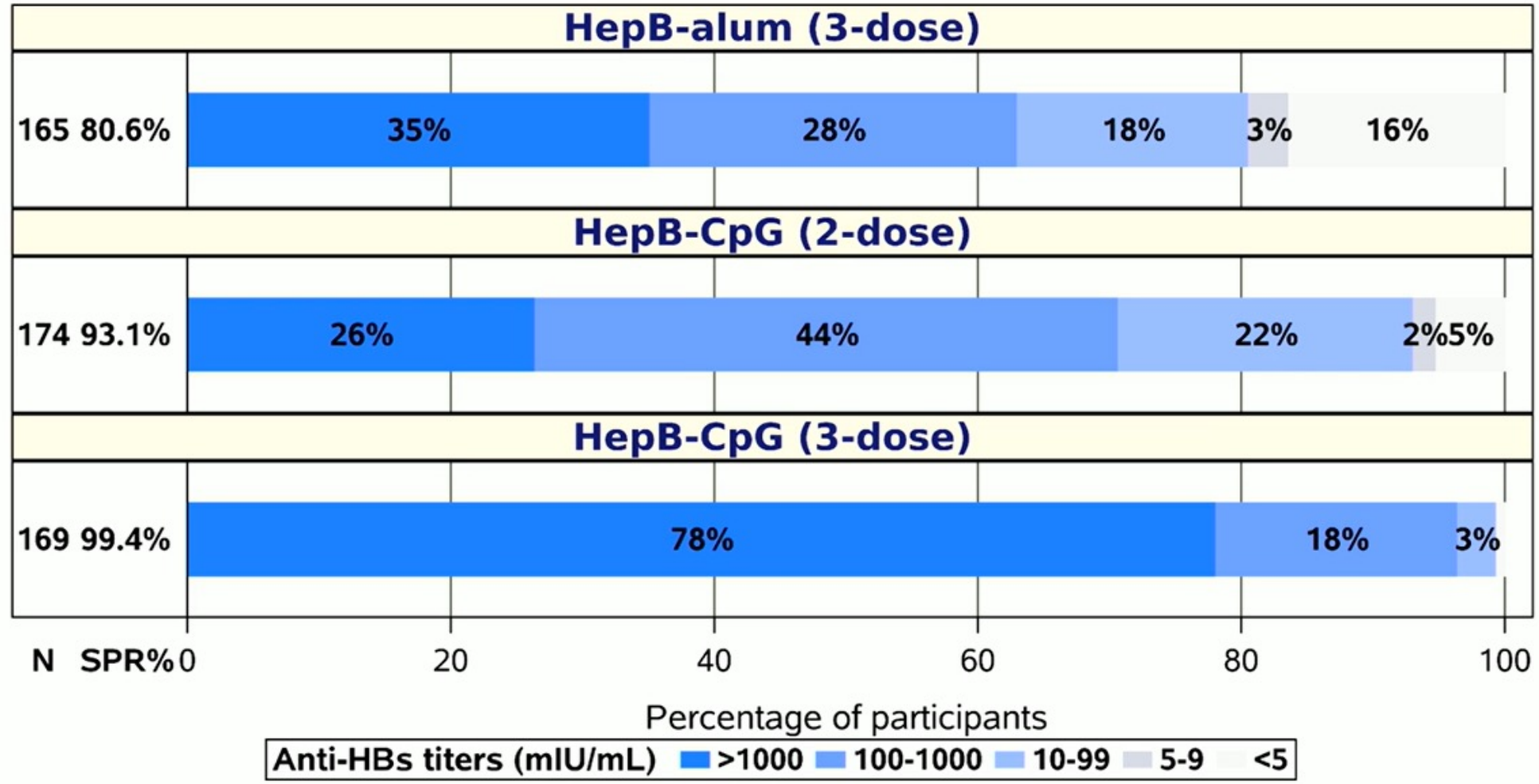
MWAETC

BEe-HIVe: Arm A (Vaccine Non-Responder) Results





Distribution of Anti-HBs titers at respective endpoints



Takeaways

- PWH with non-response to conventional HBV vaccine achieved superior SPR as compared to 3 doses of HepB-alum

- Three doses of HepB-CpG achieved high proportion of SPR with HBsAb titers > 1000 mIU/mL (78%)
  - Do we need titers this high?
  - Underrepresentation of factors associated with poor response (low CD4 cell count, HIV viremia, HCV, older age)

- No unexpected safety issues or deaths

MWAETC

Co-Occurring Conditions: Take Home Points

- A triaged referral process including CD4 nadir, age, MSM, and HR-HPV (including self-testing) for anal cancer screening in PWH may help tailor population who will benefit most

- Semaglutide leads to significant weight loss and improvement of MASLD in PWH

- HepB-CpG (Heplisav-B) is superior to conventional HBV vaccination in PWH who are prior vaccine non-responders

MWAETC

Questions?

raaka@uw.edu

Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $3,333,289 with 0% financed with non-governmental sources.

AETC AIDS Education & Training Center Program Mountain West