In Case You Missed It: The Latest in HIV Literature and Monkeypox

Roger J. Bedimo, MD, MS
Professor of Medicine
University of Texas Southwestern Medical Center
VA North Texas Health Care System
Dallas, Texas

Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Bedimo has received research funding from ViiV Healthcare and Merck & Co. Inc, and serves on the Scientific Advisory Board for Merck & Co, Inc, ViiV Healthcare, Gilead Sciences, Inc, and Theratechnologies. (Updated 9/6/22)

Slide 2

Learning Objectives

After attending this presentation, learners will be able to:

- Describe the clinical presentation of Monkeypox virus infection.
- Outline new finding on complications of antiretroviral therapy.
- Describe new data on management of co-infections and opportunistic infections.
- Discuss key new findings on COVID prevention in HIV

Slide 3

Outline

1. Monkeypox Overview:
   a. Update on clinical presentation
   b. Management Considerations in PWH
2. Non-AIDS Complications:
   a. Trends in 2022; Incidence in individuals with spontaneous control of HIV
   b. INSTIs and cardiometabolic outcomes.
3. Cure agenda:
   a. Exceptional Post-Treatment HIV Control in acute HIV-infected woman
   b. Disappointing results of VRC-01?
4. Opportunistic Infections:
   a. TDF vs. TAF in HBV/HIV Co-infected. .
   b. PrEP and PEP: Disparities, STIs and Doxycycline PEP
   c. Crypto Meningitis
5. COVID-19
   a. Efficacy of home testing.
   b. Vaccine effectiveness during Omicron
   c. Impact of HIV on survival.

Slide 4

Monkeypox: Clinical Presentation Update

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Monkeypox Virus Infection in Humans

ac

Morbidity and Mortality Weekly Report

Epidemiologic and Clinical Characteristics of Monkeypox Cases — United States, May 17–July 22, 2022

- Concomitan

- Three people epiglottitis in person living

https://www.nejm.or

tinents:
6% on ART, 95% with
nm3).
those with and without

Clinical features and management of human monkeypox: a retrospective observational study in the UK

Hugh Adler, Susan Gould, Paul Hine, Luke B Snell, Waison Wong, Catherine F Houlihan, Jane C Osborne, Tommy Rampling, Mike EJ Beadsworth, Christopher JA Duncan, Jake Dunning, Tom E Fletcher, Ewan R Hunter, Michael Jacobs, Saye H Khoo, William Newsholme, David Porter, Robert J Porter, Libuse Ratcliffe, Matthias L Schmid, Malcolm G Semple, Anne J Tonbridge, Tom Wingfield*, Nicholas M Price* on behalf of the NIHR England High Consequence Infectious Diseases (Airborne) Network†

Slide 5

Monkeypox: How Common is Asymptomatic Infection?

- Sexual health clinic in Paris, France: PWH and on PrEP (June-July 2022)
- Anal swabs routinely collected for STI surveillance and negative for *Neisseria gonorrhea* and *Chlamydia trachomatis* were tested for

Table. Screening for Sexually Transmitted Infections and MPXV Infection in 706 MSM Visiting the Sexual Health Clinic Between 5 June and 11 July 2022

Variable	MSM With No Symptoms of MPXV Infection	MSM With Symptoms Suggesting MPXV Infection
Total number of MSM visiting between 5 June and 11 July 2022	323	383
C trachomatis infections detected on anal swab, *n/N (%)*	32/323 (9.9)	Not tested
N gonorrhoeae infections detected on anal swab, *n/N (%)*	24/323 (7.4)	Not tested
C trachomatis and *N gonorrhoeae* co-infection detected on anal swab, *n/N (%)*	8/323 (2.5)	Not tested
C trachomatis infections detected on first-void urine sample or urethral swab, *n/N (%)*	6/323 (1.9)	Not tested
N gonorrhoeae infections detected on first-void urine sample or urethral swab, *n/N (%)*	3/323 (0.9)	Not tested
C trachomatis and *N gonorrhoeae* co-infection detected on first-void urine sample or urethral swab, *n/N (%)*	1/323 (0.3)	Not tested
MPXV-positive test result, *n/N (%)*	13/200* (6.5)	271/383 (71)

C trachomatis = *Chlamydia trachomatis*; MPXV = monkeypox virus; MSM = men who have sex with men; *N gonorrhoeae* = *Neisseria gonorrhoeae*.
* All 200 of the asymptomatic participants who were tested for MPXV were negative for both *C trachomatis* and *N gonorrhoeae* on anal swab.

Slide 6 Ferré VM et al. Ann Intern Med 2022 Aug 16

Monkeypox: Clinical Presentation Update

- During the current global outbreak:
  - Lesions often occur in the genital and anorectal areas or mouth.
  - Rash is not always disseminated across many sites on the body.
  - Rash may be confined to only a few lesions or a single lesion.
  - Rash does not always appear on palms and soles.
- Rectal symptoms (e.g., purulent or bloody stools, rectal pain, or rectal bleeding) have been frequently reported in current outbreak.
- Lesions are often described as painful until the healing phase when they become itchy (crusts).
- Fever and other prodromal symptoms (e.g., chills, lymphadenopathy, malaise, myalgias, or headache) can occur before rash but may occur after rash or not be present at all.
- Respiratory symptoms (e.g. sore throat, nasal congestion, or cough) can occur.

Slide 7

Clinical Recognition | Monkeypox | Poxvirus | CDC

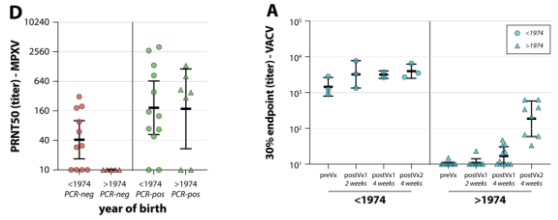
Management Considerations in PWH

- People with advanced HIV or who are not virologically suppressed with antiretroviral therapy can be at increased risk of severe disease with monkeypox.
- Post-exposure prophylaxis and antiviral treatments are available for people exposed to monkeypox or with monkeypox virus infection.
- Tecovirimat may result in a reduction in levels of NNRTIs doravirine and rilpivirine, and the CCR5 antagonist maraviroc.
  - No evidence that dose adjustment is necessary
  - Avoid initiating CAB/RPV during TPOXX therapy
- Vaccination with JYNNEOS is considered safe for people with HIV.
- ACAM2000 should not be given to people with HIV (regardless of immune status).

Slide 8

Https://www.cdc.gov/poxvirus/monkeypox/clinicians/people-with-HIV.html
Liverpool HIV Interactions (hiv-druginteractions.org)

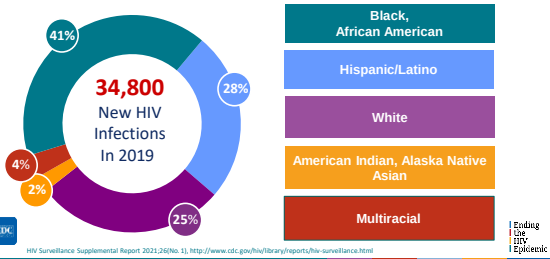
Low levels of monkeypox virus neutralizing antibodies after MVA-BN 2



Slide 9

Zaeck. https://www.medrxiv.org/content/10.1101/2022.08.31.22279414v1

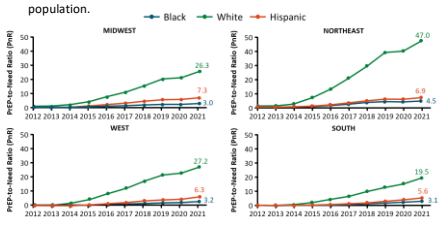
Black/African American and Hispanic/Latino Account for Majority of New HIV Infections



HIV Surveillance Supplemental Report 2021;26(No. 1), http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html

Unmet Needs in PrEP and PEP: Inequity…

The PrEP-to-Need Ratio (PnR) is the number of PrEP users divided by the number of new diagnoses in a given year. PnR serves as measurement of how PrEP use compares to the need for PrEP in a population.



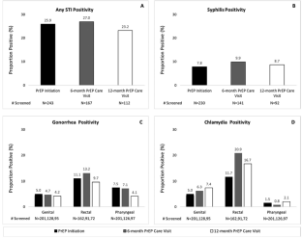
PnR gap increased over time in all regions, but was highest for White and lowest for Black people

So, racial gap continues to widen…

Slide 11 Sullivan. AIDS 2022. Abstr OALBX0106

Unmet Needs in PrEP and PEP: What about STIs?:

- High incidence of STIs in PrEP recipients. Effectiveness of screening has been limited. IMPACT Partner Collaborative.
- Among 290 MSM initiating PrEP, 43.1% (n = 125) were screened per guidelines at PrEP initiation
- 25% with at least one STI



Slide 12 Schumacher. Clin Infect Dis. 2020 Dec 17;71(10):2637-2644.

Unmet Needs in PrEP and PEP: What about STIs?:

- MSM/TGW with HIV or on PrEP. Had STI in past year.
- Randomized 2:1 to 200 mg doxycycline within 72 hours of condomless sex or no doxycycline with STI testing at enrollment, quarterly, and when symptomatic
- Quarterly STI incidence by HIV Status:

	HIV uninfected MSM/TGW on PrEP		MSM/TGW living with HIV	
	Doxy arm N=240	Control arm N=120	Doxy arm N=134	Control arm N=60
Follow up quarters	491	220	266	108
Participants with an incident STI (GC, CT or syphilis)	41	42	24	18
Primary STI endpoints	47 (9.6%)	65 (29.5%)	31 (11.7%)	30 (27.8%)
Gonorrhea	40 (8.1%)	45 (20.5%)	21 (7.9%)	20 (18.5%)
Chlamydia	7 (1.4%)	23 (10.5%)	12 (4.5%)	16 (14.8%)
Syphilis	1 (0.2%)	5 (2.3%)	3 (1.1%)	2 (1.9%)

Risk Reduction in STI Incidence per Quarter (95% CI)	Doxy PEP*
PrEP	0.34 (0.24-0.46)
PWH	0.38 (0.24-0.60)
Total	0.35 (0.27-0.46)

*All *P* <.0001

Risk Reduction per Quarter (95% CI)	PrEP	PWH
Gonorrhea	0.45 (0.32-0.65) *P* <.0001	0.43 (0.26-0.71) *P* = .001
Chlamydia	0.12 (0.05-0.25) *P* <.0001	0.26 (0.12-0.57) *P* = .0007
Syphilis	0.13 (0.03-0.59) *P* = .0084	0.23 (0.04-1.29) *P* = .095

Slide 13 Luetkemeyer A et al. AIDS 2022. Abstract OALBX0103

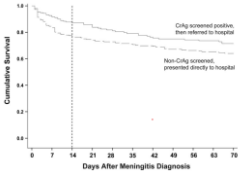
Unmet Needs in Opportunistic Infections? Benefits of sCrAg Screening

- 489 PWH with CM who had been prospectively enrolled in Uganda between 2018 and 2021 (after implementation of a serum CrAg screening program).
  - 194 (40%) had undergone outpatient CrAg screening and 295 (60%) had not. Median time from screening to CM diagnosis was 2 days.
- Ninety-five screened subjects compared with 32 unscreened subjects received fluconazole prior to the CM diagnosis (49% vs. 11%; *P*<0.001).
- Median CD4 cell counts were <30/µL in both groups.
- Lower CSP opening pressure (190 vs. 225 mm H_2O) and lower 14-day mortality (12% vs. 21%) (*P*≤0.005 for both comparisons).

Slide 14 Levin. *Clin Infect Dis* 2022 Jul 21; [e-pub].

Unmet Needs in Opportunistic Infections? Benefits of sCrAg Screening

- CrAg screening likely detects cryptococcal meningitis at an earlier stage
- DHHS Guidelines:
  - Serum CrAg screening in those with CD4 ≤100/µL (especially those with CD4 ≤50/µL).
  - In screen-positive patients, a CSF evaluation should be performed to rule out CM.



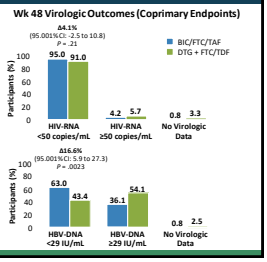
https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cryptococcosis, opens in new tab)

Slide 15 Levin. *Clin Infect Dis* 2022 Jul 21; [e-pub].

ALLIANCE: BIC/FTC/TAF vs. DTG + FTC/TDF in HIV/HBV

- Adults with HIV/HBV coinfection, Rx-naive for both, with HIV-1 RNA ≥500 copies/mL, HBV DNA ≥2000 IU/mL; HIV genotypic sensitivity to FTC and TFV; $eGFR_{CG}$ ≥50 mL/min (N = 243)
- Secondary endpoints at Week 48:

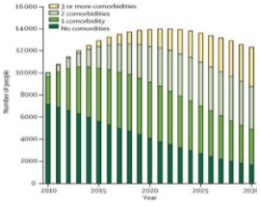
	BIC/FTC/TAF	DTG + FTC/TDF
ALT Normalization	73.3%	55.3%
HBsAg loss	12.6%	5.8%
HBeAg loss	25.6%	14.4%



Slide 16 Avihingsanon. AIDS 2022. Abstr OALBX0105.

Unmet Needs?: Improving Survival in PWH on ART → Prevention of NCDs

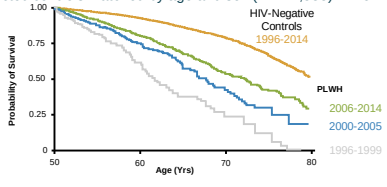
- Predicted burden of non-communicable diseases (NCDs) in HIV patients modeled for 2010-2030
- Increasing proportion with more NCDs over time
- NCDs include
  - Cardiovascular disease (hypertension, hypercholesterolemia, myocardial infarction, stroke)
  - Diabetes
  - Chronic kidney disease
  - Osteoporosis
  - Non-AIDS malignancies



Slide 17 Smit Lancet ID 2015.

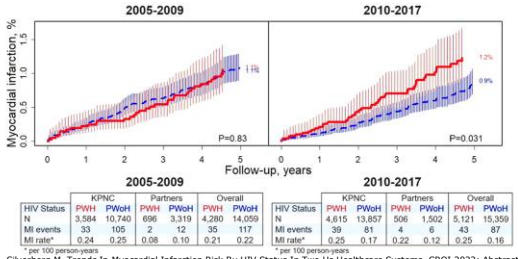
Decreased Life Expectancy in Older Adults with HIV in Modern ART Era

- Population-based cohort study of survival in HIV-infected pts (n = 2440) and uninfected controls matched by age and sex (n = 14,588) in Denmark



Slide 18 Legarth RA, et al. J Acquir Immune Defic Syndr. 2016;71:213-218.

Cummulative incidence of MI by HIV status:



2005-2009	KPNC		Partners		Overall	
HIV Status	PWH	PWoH	PWH	PWoH	PWH	PWoH
N	3,584	10,740	696	3,319	4,280	14,059
MI events	33	105	2	12	35	117
MI rate*	0.24	0.25	0.08	0.10	0.21	0.22

2010-2017	KPNC		Partners		Overall	
HIV Status	PWH	PWoH	PWH	PWoH	PWH	PWoH
N	4,615	13,857	506	1,502	5,121	15,359
MI events	39	81	4	6	43	87
MI rate*	0.25	0.17	0.22	0.12	0.25	0.16

* per 100 person-years

Silverberg M. Trends In Myocardial Infarction Risk By HIV Status In Two Us Healthcare Systems. CROI 2022; Abstract 39)

Slide 19

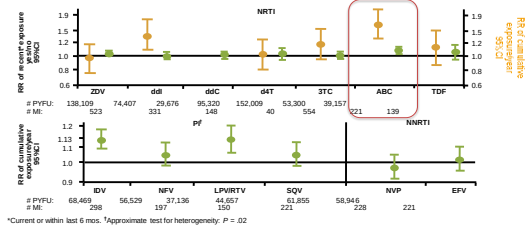
Non-AIDS-events in individuals with spontaneous control of HIV-1

- Systematic Review: 12 studies were included: Five cohorts, two cross-sectional prevalence studies, four cross-sectional imaging studies and one case series.
- Four of five cohort studies showed that spontaneous controllers have a similar risk to develop nADEs compared with PLHIV on suppressive ART:
  - Specifically cardiovascular events, non-AIDS-malignancies, hepatic disease and bacterial pneumonia.
- Cross-sectional imaging studies showed a higher presence of subclinical cardiovascular disease in spontaneous controllers, like in PLHIV on ART, than in people without HIV.

Slide 20

Groenendijk AL. J Acquir Immune Defic Syndr. 2022 Aug 15.

D:A:D: Recent and/or Cumulative ARV Exposure and Risk of MI

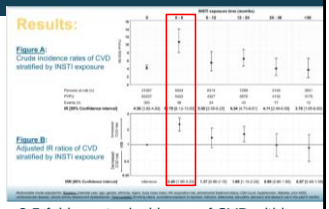


*Current or within last 6 mos. †Approximate test for heterogeneity: $P = .02$

Slide 21 Lundgren JD, et al. CROI 2009. Abstract 44LB.

RESPOND: INSTIs and CVD Risk:

- International collaboration of 17 cohorts
- Composite endpoint of MI, stroke and invasive cardiovascular procedure; adjudicated events
- N=21267 (46% exposed to INSTI)
- 517 CVD events, 4.9/1000 PY
- Could not specifically examine ART-naive



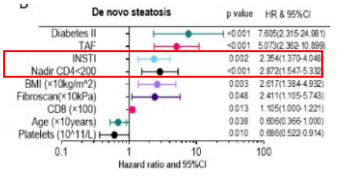
- INSTI exposure associated with a 2.5-fold greater incidence of CVD within first 6 months of exposure compared to no exposure in adjusted analyses

Slide 22 Neesgaard et al. vCROI 2021, abstract 488; *Lancet HIV* 2022 Jun 7; [e-pub].

De-Novo Hepatic Steatosis with Weight Gain After ART Initiation

- Exposure to TAF and INSTIs associated with de-novo steatosis.

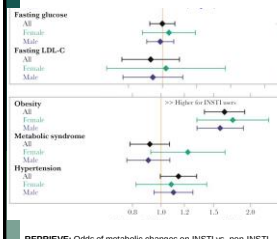
- Prospective cohort of 319 HIV mono-infected on ART;
  - 155 (52%) with no b/l steatosis → 69 (45%) developed steatosis on f/u
- BMI of >23 kg/m² for males is significantly associated with development of de novo steatosis (68% risk vs. 25% for females)
- TDF associated with lower risk of de-novo steatosis.



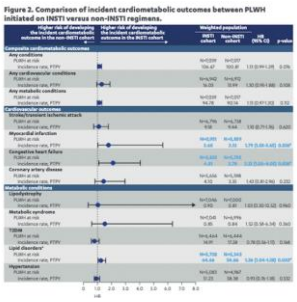
Bischoff. EClinicalMedicine 2021 Sept 5;40:101116

Slide 23

Metabolic Risks of INSTI?



REPRIEVE: Odds of metabolic changes on INSTI vs. non-INSTI



Rebeiro. AIDS 2022, Abstract EPB108.

Slide 24 Kileel. OFID; 2021 Nov 20;8(12):ofab537

IMPAACT 2008: Safety and Efficacy of VRC01

- Infants with HIV aged 72 hr to ≤84 days who started ART ≤14 days prior to study entry (n=61).
- Randomized to VRC01 + ART vs. ART alone
  - VRC01 dosed 40 mg/kg SC at Wk 0, 2, 6, and 10
- VRC01 was well tolerated, but had no apparent effect on HIV-1 RNA or HIV-1 DNA levels at Wk 14
- Pretreatment VRC01 resistance was common
- VRC01 plasma levels were lower and more variable than predicted by previous studies of HIV-exposed uninfected infants

HIV-1 DNA Level	VRC01 + ART	ART Only	*P* Value
Median change at Wk 14 vs Wk 0, log_{10} copies/million PBMCs (IQR)	-0.41 (-0.94 to -0.30)	-0.53 (-0.70 to -0.33)	.42

Khaitan. AIDS 2022. Abstr OALBB0102.

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IMPAACT 2008: Efficacy

- Infants with HIV aged 72 hr to ≤84 days who started ART ≤14 days prior to study entry (n=61).
- Randomized to VRC01 + ART vs. ART alone
  - VRC01 dosed 40 mg/kg SC at Wk 0, 2, 6, and 10
- Similar decline in HIV-1 RNA in VRC01 + ART and ART-only groups during 14-wk treatment period
- HIV-1 RNA decline did not differ by presence of baseline VRC01 resistance
- In a post hoc analysis, higher VRC01 concentrations correlated with larger reductions in HIV-1 DNA from Wk 0-14 (Spearman correlation -0.42; *P* = .03)

HIV-1 DNA Level	VRC01 + ART	ART Only	*P* Value
Median change at Wk 14 vs Wk 0, log_{10} copies/million PBMCs (IQR)	-0.41 (-0.94 to -0.30)	-0.53 (-0.70 to -0.33)	.42

Khaitan. AIDS 2022. Abstr OALBB0102.

Slide 26

"City of Hope" Patient Case: Prolonged HIV-1 Remission Without ART After Allogeneic Stem Cell Transplant

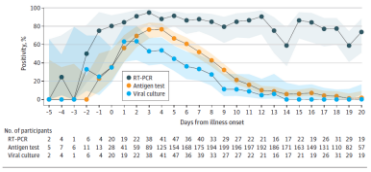
- Fourth reported person with long-term HIV-1 remission: 42 mo post allogeneic HCT and 17 mo post ART
- 63-yr-old White male diagnosed with HIV-1 in 1988; has had undetectable HIV-1 RNA on ART for many years
- Received transplant of CCR5-Δ32/Δ32 donor cells for high-risk AML
  - Donor: HLA homozygous CCR5Δ (nonfunctional CCR5 receptor)
  - Patient pre HCT: HLA wild-type homozygous CCR5 receptors, HIV-1 coreceptors majority R5, X4, false
- Received 3 courses of chemotherapy and achieved remission

Slide 27 Dickter. AIDS 2022. Abstr OALBB0104.

How Good is Home COVID-19 Antigen Testing?

- San Diego and Denver in early 2021, 225 individuals with positive SARS-CoV-2 RT-PCR results performed daily antigen self-testing for 14 days.
- Antigen test sensitivity was 50% during the infectious period, 64% compared with same-day RT-PCR, and 84% compared with same-day cultures
- Antigen test sensitivity improved with a second antigen test 1 to 2 d. later
- Caveat: Done pre-Omicron circulation…

Figure 1. Daily Percentage of Positive SARS-CoV-2 Tests in Participants With Reverse Transcription–Polymerase Chain Reaction (RT-PCR)–Confirmed Infection

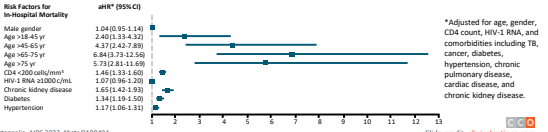


No. of participants																													
RT-PCR	2	4	1	6	4	20	19	22	38	41	47	36	40	33	29	27	22	21	16	17	22	19	26	31	29	19			
Antigen test	5	7	6	11	13	28	41	59	89	125	154	168	175	194	199	196	197	192	186	171	163	149	131	110	82	57			
Viral culture	2	4	1	6	4	20	19	22	38	41	47	36	39	33	27	27	22	21	16	17	21	19	26	31	29	19			

Slide 28 Chu. *JAMA Intern Med*. 2022;182(7):701-709.

In-Hospital Mortality From COVID-19 Among PWH: Study Population, Methods, and Risk Factors

- WHO online platform for HCP-submitted electronic reports of hospitalized COVID-19 cases
  - 362,941 patient reports from 42 countries (96.8% in Africa); 8.2% (29,530) PWH
- Multivariable regression to determine risk of 21-day in-hospital mortality from COVID-19
- 59% PWH had ≥1 underlying condition vs 45% without HIV (*P* <.0001)
  - Among PWH: 52% had 1-2 underlying conditions; 7.1% had ≥3 underlying conditions



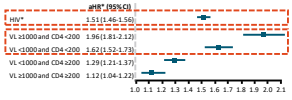
*Adjusted for age, gender, CD4 count, HIV-1 RNA, and comorbidities including TB, cancer, diabetes, hypertension, chronic pulmonary disease, cardiac disease, and chronic kidney disease.

Bertagnolio. AIDS 2022. Abstr OAB0404.

Slide credit: clinicaloptions.com

Risk of In-Hospital Mortality by HIV Factors and Differential Impact of COVID-19 Variant on Mortality

Association of HIV and HIV Parameters With In-Hospital Mortality



*Adjusted for patient age, gender, and comorbidities.

Mortality	Delta (Aug 2 - Oct 3, 2021)	Omicron (Nov 15, 2021 - May 26, 2022)	Absolute Difference With Delta vs Omicron, % (95% CI)	*P* Value
Without HIV	19.4%	8.1%	**13.0 (12.5-13.6)**	**<.0001**
With HIV	21.8%	17.6%	**4.8 (3.1-6.5)**	**<.0001**
Adjusted HR With vs Without HIV (95% CI)	**1.55 (1.43-1.674)**	**2.47 (2.27-2.68)**		

- Analysis did not account for COVID-19 vaccination status, prior COVID-19, BMI, or patient-level variant data

Bertagnolio. AIDS 2022. Abstr OAB0404.

Slide credit: clinicaloptions.com

COVID Vaccine Effectiveness during Omicron

- VE during the BA.2/BA.2.12.2 period was lower than that during the BA.1 period. A third vaccine dose provided additional protection against moderate and severe COVID-19–associated illness in all age groups, and a fourth dose provided additional protection in eligible adults aged ≥50 years.

TABLE 2. mRNA COVID-19 vaccine effectiveness* against laboratory-confirmed COVID-19–associated† emergency department and urgent care encounters and hospitalizations among adults aged ≥18 years, by Omicron–predominant period, age group, number and timing of vaccine doses,§ and median interval since last dose — VISION Network, 10 states, December 2021–June 2022

	Omicron BA.1–predominant period¶				Omicron BA.2/BA.2.12.1–predominant period**			
Encounter type	Total	No. (%) of positive test results†	Median interval since last dose, days (IQR)	VE %* (95% CI)	Total	No. (%) of positive test results†	Median interval since last dose, days (IQR)	VE %* (95% CI)
ED or UC, age group (days since last dose)								
All ages, yrs								
Unvaccinated (Ref)	51,359	23,175 (45.1)	—	—	27,907	3,501 (12.6)	—	—
2 doses (14–149)	7,286	2,377 (32.6)	107 (76–129)	47 (44–50)	1,774	110 (6.2)	104 (71–128)	51 (38–60)
2 doses (≥150)	32,740	11,365 (34.7)	267 (232–306)	39 (37–41)	20,883	2,584 (12.4)	352 (278–398)	12 (7–17)
3 doses (7–119)	29,333	3,667 (12.5)	66 (41–89)	84 (83–85)	9,142	441 (4.8)	94 (72–108)	56 (51–61)
3 doses (≥120)	3,315	217 (6.5)	132 (125–142)	73 (68–77)	26,654	3,186 (11.9)	166 (145–190)	26 (21–30)

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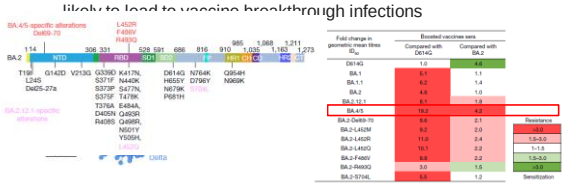
Link-Gelles. MMWR / July 22, 2022 / Vol. 71 / No. 29

COVID Vaccine Effectiveness during Omicron

- **Antibody evasion by Omicron subvariants BA.2.12.1, BA.4 and BA.5**
  - BA.4/5 is substantially (4.2-fold) more resistant and thus more likely to lead to vaccine breakthrough infections



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Wang, Q., Guo, Y., Iketani, S. *et al. . Nature* **608**, 603–608 (2022)

Bivalent mRNA Vaccines Are Here…

- CDC Guidance Issued On September 1, 2022 (following FDA's EUA):
  - A single dose of bivalent Pfizer-BioNTech COVID-19 vaccine is recommended for individuals ages 12 years and older at least 2 months after receipt of a primary series or prior monovalent booster dose.
  - A single dose of bivalent Moderna COVID-19 vaccine is recommended for individuals ages 18 years and older at least 2 months after receipt of a primary series or prior monovalent booster dose.
  - CDC repeals its previous recommendations for administration of monovalent Pfizer-BioNTech and Moderna COVID-19 vaccine boosters for persons 12 years and old

CDC Recommends the First Updated COVID-19 Booster | CDC Online Newsroom | CDC

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Question-and-Answer Session
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IAS–USA