In Case You Missed It: Updates from Recent Publications and Meetings

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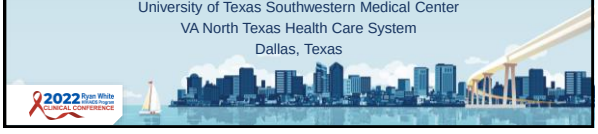


Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Bedimo has served on scientific advisory boards for ViiV Healthcare, Gilead Sciences, Theratechnologies, and Merck & Co, Inc. He has received research funding from ViiV Healthcare and Merck & Co, Inc. (Updated 10/5/22)

Slide 2

Learning Objectives

After attending this presentation, learners will be able to:

- Describe the clinical presentation of human Monkeypox virus infection
- Outline new findings on complications of antiretroviral therapy
- Describe new data on management of co-infections and prevention of sexually transmitted infections
- Discuss key new findings on COVID-19 prevention in HIV

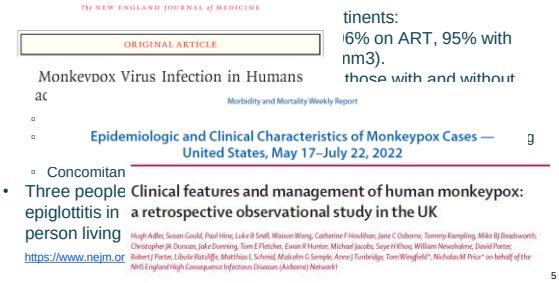
Slide 3

Outline

1. Monkeypox Overview:
   a. Update on clinical presentation
   b. Vaccine Effectiveness
   c. 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. Co-Infections:
   a. TDF vs. TAF in HBV/HIV Co-infected. .
   b. PrEP and PEP: Disparities, STIs and Doxycycline PEP
5. COVID-19
   a. Efficacy of home testing.
   b. Monoclonal antibodies and vaccine effectiveness during Omicron

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

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

Hugh Adler, Susan Gould, Paul Hine, Luke B Snell, Watson 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 NHS England High Consequence Infectious Diseases (Airborne) Network†

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

g

- Concomitan

- Three people epiglottitis in person living

https://www.nejm.or

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 MPX.

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

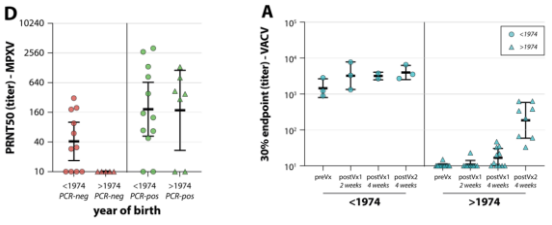
Variable	MSM With No Symptoms of MPXV Infection	MSM With Symptoms Suggesting MPXV Infection
Total number of MSM visiting between 5 June and 11 July 2022	323	383
C trachomatis infections detected on anal swab, n/N (%)	32/323 (9.9)	Not tested
N gonorrhoeae infections detected on anal swab, n/N (%)	24/323 (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.

Ferre VM et al. Ann Intern Med 2022 Aug 16

Slide 6

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

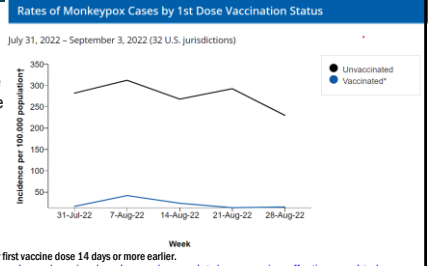


Zaeck. https://www.medrxiv.org/content/10.1101/2022.08.31.22279414v1

Slide 7

Monkeypox Vaccine Effectiveness

- **Unvaccinated people had 14** times the risk of monkeypox disease compared to people who were vaccinated*

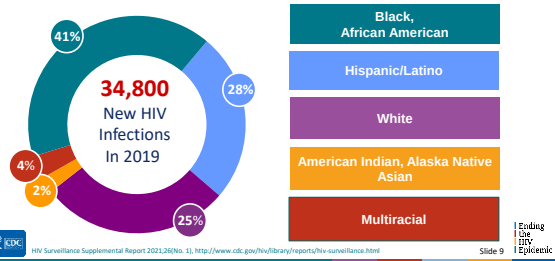


*Those who had received their first vaccine dose 14 days or more earlier.

. https://www.cdc.gov/poxvirus/monkeypox/cases-data/mpx-vaccine-effectiveness.html

Slide 8

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

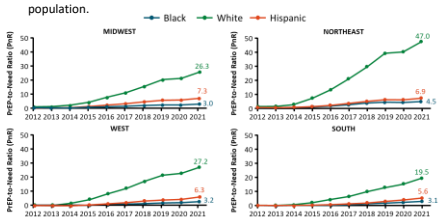


HIV Surveillance Supplemental Report 2021;26(No. 1). http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html

Slide 9

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

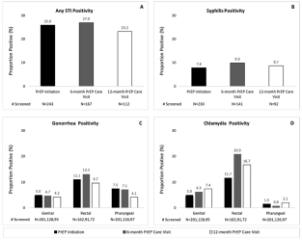
So, racial gap continues to widen…

Sullivan. AIDS 2022. Abstr OALBX0106

Slide 10

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



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

Slide 11

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

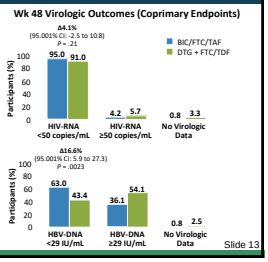
Luetkemeyer A et al. AIDS 2022. Abstract OALBX0103

Slide 12

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%

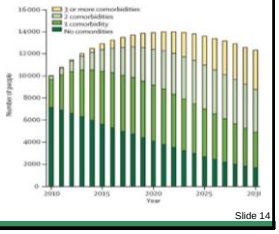


Avihingsanon. AIDS 2022. Abstr OALBX0105.

Slide 13

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

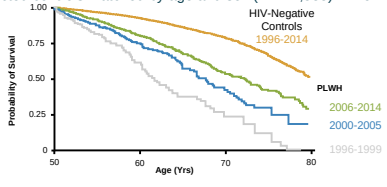


Smit Lancet ID 2015.

Slide 14

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

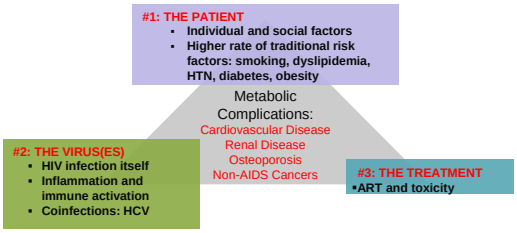
- Population-based cohort study of survival in HIV-infected pts (n = 2440) and uninfected controls matched by age and sex (n = 14,588) in Denmark



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

Slide 15

Pathogenesis of Chronic Complications of HIV Infection



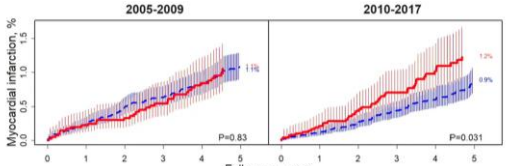
Slide 16

#2: THE VIRUS(ES): 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.

Groenendijk AL. J Acquir Immune Defic Syndr. 2022 Aug 15. Slide 17

Cumulative 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

* per 100 person-years

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 18

#2: THE VIRUS(ES)

CVD Risk with HIV/HCV Co-Infection

- Data from NA-ACCORD: January 1, 2000, to December 31, 2017, PWH (aged 40–79years) who had initiated antiretroviral therapy.
- The primary outcome was an adjudicated T1MI event.
- Among 23361 PWH, 4677 (20%) had HCV.
- No association b/w HCV coinfection with increased T1MI risk
- However, greater increase in T1MI with age in co-infected. Adjusted hazard ratio per 10-year increase in age :
  - Without HCV co-infection: 1.30 (95% CI, 1.13–1.50
  - With HCV Co-infection: 1.85 (95% CI, 1.38–2.48)
  - P<0.001, test of interaction

Lang. J Am Heart Assoc. 2022;11:e026473

Slide 19

CVD Risk with HIV/HCV Co-Infection

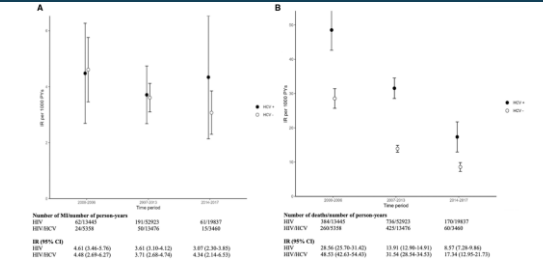
Table 2. Crude and Adjusted Hazard Ratios of Risk Factors Associated With Myocardial Infarction Among People With HIV in NA-ACCORD (N=23 361)

	cHR		aHR with no interaction term		aHR with interaction term b/w age and HCV	
Characteristic	cHR	95% CI	*aHR	95% CI	†aHR	95% CI
Age (per 10-y increase)	1.71	1.52–1.92	1.38	1.21–1.57	…	…
Per 10-y increase in age among HCV negative	…	…	…	…	1.30	1.13–1.50
Per 10-y increase in age among HCV positive	…	…	…	…	1.85	1.38–2.48
Hepatitis C infection	1.09	0.86–1.38	0.98	0.74–1.30	…	…

Lang. J Am Heart Assoc. 2022;11:e026473

Slide 20

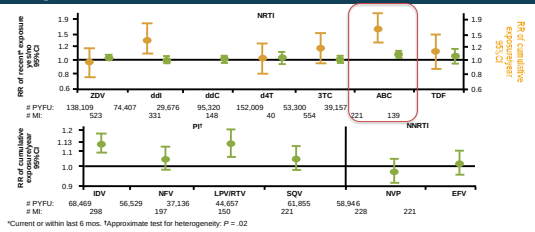
CVD Risk with HIV/HCV Co-Infection



Lang. J Am Heart Assoc. 2022;11:e026473

Slide 21

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



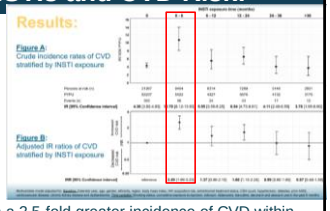
*Current or within last 6 mos. †Approximate test for heterogeneity: *P* = .02

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

Slide 22

#3: THE TREATMENT
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

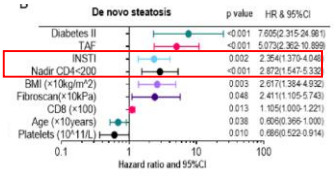
Neesgaard et al. vCROI 2021, abstract 488; *Lancet HIV* 2022 Jun 7; [e-pub].

Slide 23

De-Novo Hepatic Steatosis with Weight Gain After ART Initiation

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

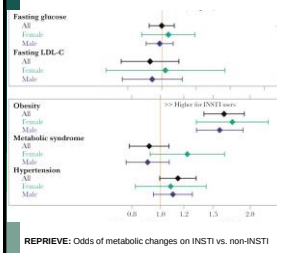
- Prospective cohort of 319 HIV mono-infected on ART;
  - 155 (52%) with no b/l steatosis → 69 (45%) developed steatosis on f/u
- BMI of >23 kg/m^2 for males is significantly associated with development of de novo steatosis (68% risk vs. 25% for females)
- TDF associated with lower risk of de-novo steatosis.



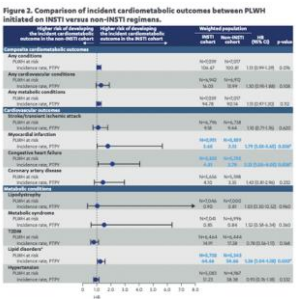
Bischoff. EClinicalMedicine 2021 Sept 5;40:101116

Slide 24

Metabolic Risks of INSTI?



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



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

Rebeiro. AIDS 2022, Abstract EPB108.

Slide 25

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
- Post- hoc analysis: higher VRC01 concentrations correlated with larger reductions in HIV-1 DNA from Wk 0-14 (Spearman correlation -0.42)

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

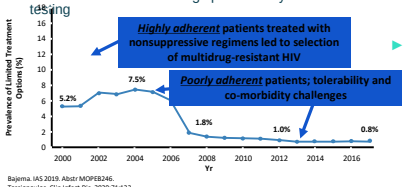
- Fourth reported person with long-term HIV-1 remission: 42 mo post allogeneic HCT and 17 mo post ART
- 63-yr-old White male diagnosed with HIV-1 in 1988; has had undetectable HIV-1 RNA on ART for many years
- Received transplant of CCR5-Δ32/Δ32 donor cells for high-risk AML
  - Donor: HLA homozygous 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

Dickter. AIDS 2022. Abstr OALBB0104.

Slide 27

Heavily Treatment–Experienced Patients With Multiclass Resistance/Limited Treatment Options

- CNICS cohort of > 26,000 ART-experienced people with HIV receiving care in the US
- Limited treatment options defined as ≤ 2 available classes with ≤ 2 active drugs per class by resistance testing



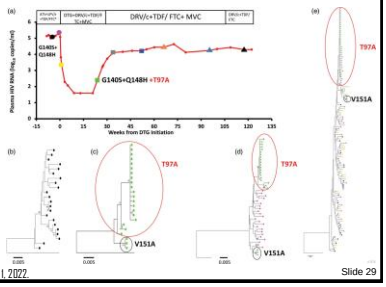
Bajema. IAS 2019. Abstr MOPEB246.
Tasiopoulos. Clin Infect Dis. 2020;71:133.

- Caution about partial sensitivity to DTG at baseline; e.g. prior exposure to RAL
  - (BRIGHTE. Gartland, 18th EACS. 2021)
- Addition of the secondary mutation T97A can result in rapid treatment failure in individuals with INSTI mutations at positions 140 and 148.

Slide 28

Emergence of High Level DTG Resistance

- Case report of emergence of T97A-containing HIV from a large replicating population.
- T97A-containing variants spread by replication and recombination, and persisted for months after discontinuing DTG

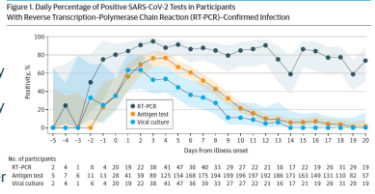


AIDS. 36(13):1835-1840. November 1, 2022.

Slide 29

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…



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

Slide 30

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

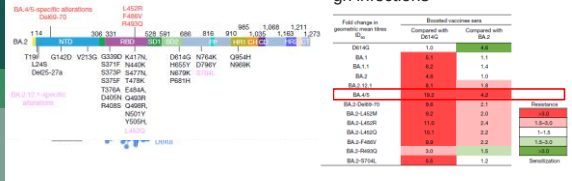
	Omicron BA.1–predominant period¶				Omicron BA.2/BA.2.12.1–predominant period**			
Encounter type	Total	No. (%) of positive test results†	Median interval since last dose, days (IQR)	VE %* (95% CI)	Total	No. (%) of positive test results†	Median interval since last dose, days (IQR)	VE %* (95% CI)
ED or 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)

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

Slide 31

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



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

Slide 32

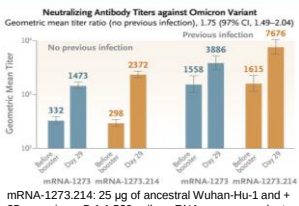
The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

A Bivalent Omicron-Containing Booster Vaccine against Covid-19

Chalkias S et al. DOI: 10.1056/NEJMoa2208343

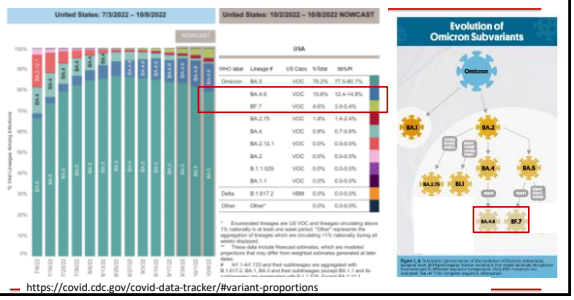
- 819 participants s/p 2-dose mRNA-1273 primary series + booster ≥ 3 mo. earlier.
- Second booster with either the bivalent mRNA-1273.214 vaccine or the monovalent 50-µg mRNA-1273 booster.
- Study suggests that a bivalent booster can retain the safety and serologic efficacy of the original monovalent booster, while broadening the spectrum of antibody response.



mRNA-1273.214: 25 µg of ancestral Wuhan-Hu-1 and + 25 µg omicron B.1.1.529 spike mRNAs vs. monovalent 50-µg mRNA-1273 booster (only Wuhan-Hu-1).

Chalkias S et al. *N Engl J Med* 2022 Sep 16; [e-pub].

Current Omicron situation in US as of 10/08/22



https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Neutralization Potential of mAbs against Omicron Subvariants

IC50 (ng/ml)	B.1	BA.5	BA.4.6	BA.2.10.4	BA.2.75.2
S309 (sotrovimab)	119	559	925	560	442
Cilgavimab	12	71	>1000	168	>1000
Tixagevimab	4	>1000	>1000	>1000	>1000
Evusheld	6	120	>1000	816	>1000
LY-CoV1404 (bebtelovimab)	4	1	2	3	2
REGN10933 (casivirimab)	14	>1000	>1000	>1000	>1000
REGN10987 (imdevimab)	10	>1000	>1000	>1000	>1000
LY-CoV016 (etesevimab)	29	>1000	>1000	>1000	>1000
LY-CoV555 (bamlanivimab)	9	>1000	>1000	>1000	>1000
ADG-20	56	>1000	>1000	>1000	>1000
S2E12	4	>1000	>1000	>1000	>1000
S2K146	18	118	78	207	62
A23-58.1	6	>1000	>1000	>1000	>1000

Sheward. //www.biorxiv.org/content/10.1101/2022.09.16.508299v1.full.pdf

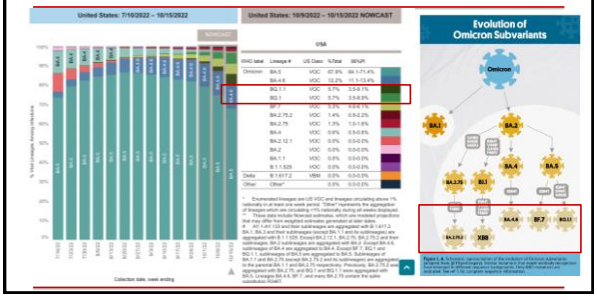
Slide 35

Efficacy of Monoclonal Antibodies vs Variants

Omicron	Bamlanivimab/ Etesevimab	Casirivimab/ Imdevimab	Sotrovimab	Bebtelovimab	Tixagevimab + cilgavimab
BA.1, BA.1.1	✗	✗	✓	✓	?
BA.2	✗	✗	✗	✓	✓
BA.5	✗	✗	✗	✓	✓
BA.4.6	✗	✗	✗	✓	✗
BA.2.75	✗	✗	✓?	✓	✓

Concerns for loss of efficacy of Tixagevimab/Cilgavimab (Evusheld) for prophylaxis…

Current Omicron situation in US as of TODAY



Efficacy of Monoclonal Antibodies vs Variants

Omicron	Bamlanivimab/ Etesevimab	Casirivimab/ Imdevimab	Sotrovimab	Bebtelovimab	Tixagevimab + cilgavimab
BA.1, BA.1.1	✗	✗	✓	✓	?
BA.2	✗	✗	✗	✓	✓
BA.5	✗	✗	✗	✓	✓
BA.4.6	✗	✗	✗	✓	✗
BA.2.75	✗	✗	✓?	✓	✓
BQ.1.1	✗	✗	✗	✗	✗
XBB	✗	✗	✗	✗	✗

Concerns for loss of efficacy of ALL monoclonal antibodies for treatment or prevention…

Q and A Session