COVID and HIV:
Dual Level Interactions

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

Dr Schooley has served as a consultant to LysNtech and Merck and serves on Data Monitoring Committees for Merck and VIR Biotechnology. He has stock options from Antiva Biosciences and CytoDyn. (Updated 11/3/21)

Slide 2

Learning Objectives

After attending this presentation, learners will be able to:

- Describe the potential biological and clinical interactions between SARS CoV-2 and HIV.
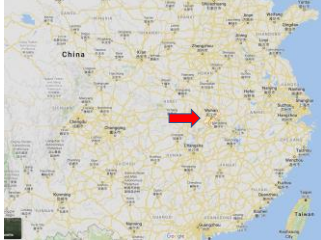- Describe appropriate use of COVID drugs and vaccines for the HIV-1 infected population

Slide 3

Wuhan China: Fall 2019

Clinical Infectious Diseases

EDITORIAL COMMENTARY

IDSA — Infectious Diseases Society of America   hivma — hiv medicine association   OXFORD

When Epidemics Collide: Why People With Human Immunodeficiency Virus May Have Worse Coronavirus Disease 2019 Outcomes and Implications for Vaccination

Virginia A. Triant,[1,2,3] and Rajesh T. Gandhi[1,3]

[1]Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts, USA, [2]Division of General Internal Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA, and [3]Harvard Medical School, Boston, Massachusetts, USA

Triant and Gandhi, Clin Infect Dis. 2021 Jun 15;72(12):e1030-e1034. doi: 10.1093/cid/ciaa1946.

COVID and HIV: Dual Level Interactions

Individual   **Society**

COVID Interactions with HIV at the Individual and Societal Levels

- Biological Interactions at the Individual Level
  - Host defense from SARS CoV-2 requires an intact immune response
    - Implications for disease
    - Implications for prophylaxis and therapy
  - Substantial components of morbidity and mortality from COVID relate to immunoregulatory dysfunction and excessive activation
- Interactions at the Societal Level
  - Disruption of health care systems
  - Food insecurity
  - Stigmatized populations

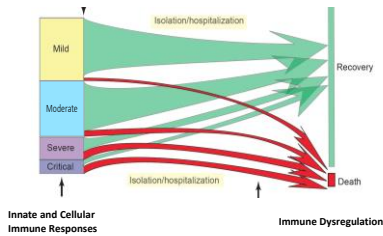## SARS CoV-2: Pathogenesis

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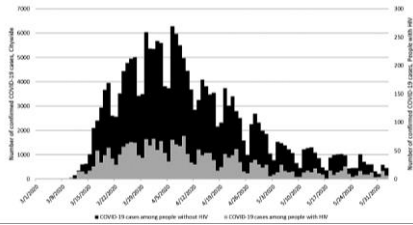## Are People with HIV at Risk for More Severe Outcome if they Become Infected with SARS CoV-2?

Coronavirus Disease 2019 (COVID-19) Infection Among People With Human Immunodeficiency Virus in New York City: A Population-Level Analysis of Linked Surveillance Data

Braunstein SL. *Clin Infect Dis* 2021;72(12):e1021–9

Coronavirus and HIV-1 in New York: NYC Wave 1

- Linkage of the NYC Department of Health and Mental Hygiene's (DOHMH) HIV surveillance registry with the NYC DOHMH COVID-19 surveillance system through June of 2020
- 204,583 COVID-19 cases of which 2410 were PLWHIV

	HIV with COVID	HIV without COVID	COVID without HIV
Subjects, n	2410	113,907	202,012
Male, %	71.4	73.4	51.1
Black,%	45	44	16
Hispanic,%	41	34	17
≥ Underlying condition, %	64		35

Braunstein SL. *Clin Infect Dis* 2021;72(12):e1021–9

Coronavirus and HIV-1 in New York: Outcomes
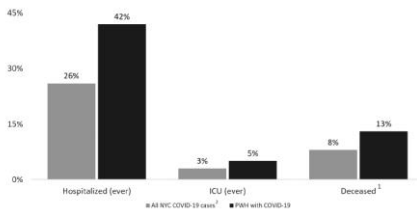
Braunstein SL. *Clin Infect Dis* 2021;72(12):e1021–9

Coronavirus and HIV-1 in New York: Conclusions

- No overrepresentation of COVID cases among PLWHIV in New York
  - 1.06% of COVID patients in NYC were PLWHIV
  - 1.5% of New Yorkers are PLWHIV
- A higher proportion of NYC PWH with COVID-19 were hospitalized for COVID-19, admitted to the ICU, and died due to COVID-19.
- NYC PWH have characteristics in common with people who have been diagnosed with COVID-19 and had poor outcomes.
- Compared with PWH without COVID, PWH with COVID-19 were more likely to be Latino and less likely to be White

Braunstein SL, *Clin Infect Dis* 2021;72(12):e1021–9

Multicenter Registry of Patients With HIV and COVID-19

- COVID-19 in PWH Registry sponsored by the University of Missouri, Columbia
- Multicenter registry for PWH who had COVID-19 and received care between 1 April and 1 July 2020.
- Promoted in the IDSA and HIV Medical Association discussion forums
- 18 years and older inpatients or outpatients with a diagnosis of HIV and laboratory-confirmed COVID-19
- 286 unique PWH and laboratory-confirmed COVID-19

Dandachi D, Clin Infect Dis 2020 DOI: 10.1093/cid/ciaa1339

Multicenter Registry of Patients With HIV and COVID-19

TABLE 1: Patient Demographics and Baseline Characteristics, stratified by hospitalization (n=286)

Variables	n (%)	Non-hospitalized	Hospitalized	p-value
Mean age, years (N=286)	51.4 (SD 14.4)	45.4 (SD 12.7)	55.8 (SD 14.0)	< 0.01
Age in years				< 0.01
<40	66 (23.1%)	42 (34.4%)	24 (14.6%)	
40-60	146 (51.0%)	64 (52.5%)	82 (50.0%)	
>60	74 (25.9%)	16 (13.1%)	58 (35.4%)	
Sex (N=286)				0.23
Female	74 (25.9%)	36 (29.5%)	38 (23.2%)	
Male	212 (74.1%)	86 (70.5%)	126 (76.8%)	
Years with HIV (N=231)				< 0.01
< 1 year	14 (6.1%)	5 (4.6%)	9 (7.3%)	
1 - 5 years	37 (16.0%)	26 (24.1%)	11 (8.9%)	
> 5 years	180 (77.9%)	77 (71.3%)	103 (83.7%)	
CD4 Count (N=268)				< 0.01
< 200 cells/mm3	41 (15.3%)	5 (4.5%)	36 (23.1%)	
200 – 500 cells/mm3	98 (36.6%)	33 (29.5%)	65 (41.7%)	
> 500 cells/mm3	129 (48.1%)	74 (66.1%)	55 (35.3%)	
Viral Load suppression * (N=265)	235 (88.7%)	107 (93.9%)	128 (84.8%)	0.02

Dandachi D, Clin Infect Dis 2020 DOI: 10.1093/cid/ciaa1339

Multicenter Registry of Patients With HIV and COVID-19

TABLE 4. Multivariable analysis examining the association between hospitalization, severe outcome, and clinical characteristics of patients with HIV and COVID-19 (n=286)

Outcome		Logistic regression analysis		Generalized Estimating Equation (GEE)	
		Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
	Age, years	1.04 (1.01- 1.08)	0.01	1.08 (1.04 -1.07)	0.03
	CD4 count				
	< 200 cells/mm3	5.22 (1.28 - 21.35)	0.02	3.67 (1.64 – 17.1)	<0.01
	200 – 500 cells/mm3	1.47 (0.7-3.08)	0.30	1.12 (1.1-12.22)	0.05
Hospitalization	> 500 cells/mm3	1.00 (reference)			
	Chronic kidney disease	5.12 (1.60-16.85)	<0.01	4.08 (1.45 – 11.52)	<0.01
		1.00 (reference)			
	Chronic lung disease	4.54 (1.58-13.01)	<0.01	4.06 (1.87 – 8.81)	<0.01
		1.00 (reference)			
	Comorbidity burden				
	HIV disease with no other known comorbidity	1.00 (reference)			
	HIV with 1 or 2 comorbidities	1.19 (0.56-2.55)	0.65	1.13 (0.49- 2.6)	0.78
	HIV with 3 or more comorbidities	4.56 (1.81-11.48)	<0.01	3.57 (1.29 -9.9)	0.01

Dandachi D, Clin Infect Dis 2020 DOI: 10.1093/cid/ciaa1339

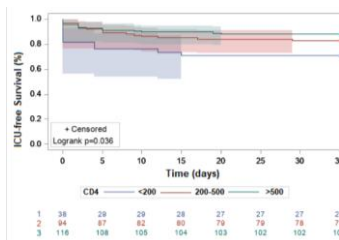## Multicenter Registry of Patients With HIV and COVID-19

TABLE 4. Multivariable analysis examining the association between hospitalization, severe outcome, and clinical characteristics of patients with HIV and COVID-19 (n=286)

Outcome		Logistic regression analysis		Generalized Estimating Equation (GEE)	
	Age, years	1.04 (1.01- 1.07)	0.02	1.04 (1.0 -1.07)	0.02
	CD4 count				
	< 200 cells/mm3	3.32 (1.11-9.93)	0.03	2.8 (1.02-7.67)	0.05
	200 – 500 cells/mm3	1.75 (0.76-4.02)	0.19	1.93 (0.73-5.06)	0.18
†Severe outcome	> 500 cells/mm3	1.00 (reference)			
	Hypertension	2.44 (1.01-5.55)	0.03	2.43 (1.2- 4.93)	0.01
		1.00 (reference)			
	Chronic lung disease	3.65 (1.56-8.56)	<0.01	3.37 (1.63- 6.97)	<0.01
		1.00 (reference)			
	Comorbidity burden				
	HIV disease with no other known comorbidity	1.00 (reference)			
	HIV with 1 or 2 comorbidities	2.58 (0.56-11.91)	0.23	2.21 (0.42-11.7)	0.35
	HIV with 3 or more comorbidities	5.09 (1.05-24.76)	0.04	5.40 (1.02-28.54)	0.05

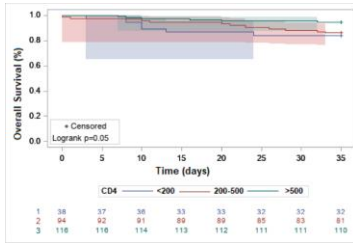Severe outcome: intensive care admission, invasive mechanical ventilation, or death

Dandachi D, Clin Infect Dis 2020 DOI: 10.1093/cid/ciaa1339

Multicenter Registry of Patients With HIV and COVID-19

Dandachi D, Clin Infect Dis 2020 DOI: 10.1093/cid/ciaa1339

Multicenter Registry of Patients With HIV and COVID-19

Dandachi D, Clin Infect Dis 2020 DOI: 10.1093/cid/ciaa1339

HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data

- Retrospective cohort study that analyzed electronic primary care data and death registry data
- >18 in a primary care database on February 1, 2020
  - Separated into those with and without HIV
  - Primary endpoint: COVID death based on ICD-10 codes on death certificate
- 17,282,905 adults of whom 27,480 were recorded to be HIV infected
- Adjusted for age, sex, index of multiple deprivation, ethnicity, co-morbidities

Bhaskaran K, Lancet HIV doi: 10.1016/S2352-3018(20)30305-2
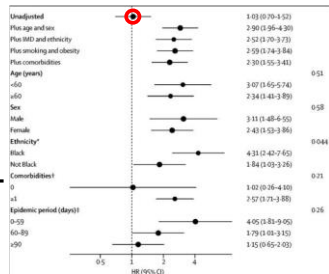

Crude risk of COVID-19 death was similar in people with and without HIV (hazard ratio [HR] 1.03, 95% CI 0.70–1.52)

Bhaskaran K, Lancet HIV doi: 10.1016/S2352-3018(20)30305-2
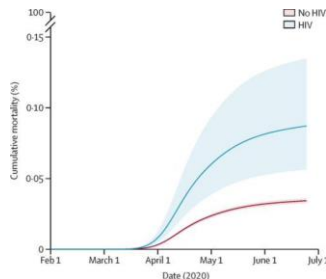
After adjusting for age and sex, HIV was associated with a 2.9-fold higher risk of COVID-19 death (HR 1.96–4.30; p<0.0001)

Bhaskaran K, Lancet HIV doi: 10.1016/S2352-3018(20)30305-2

Risk Factors for COVID-19 Death in South Africa

- Population cohort study using linked data from adults attending public-sector health facilities in the Western Cape, South Africa
- Cox proportional hazards models, adjusted for age, sex, location, and comorbidities, to examine the associations between HIV, tuberculosis, and COVID-19 death from 1 March to 9 June 2020
  - public-sector "active patients" (≥1 visit in the 3 years before March 2020)
  - laboratory-diagnosed COVID-19 cases
  - hospitalized COVID-19 cases.
- Standardized mortality ratio (SMR) for COVID-19, comparing adults living with and without HIV using modeled population estimates

Boulle, Clin Infect Dis. 2021 Oct 5;73(7):e2005-e2015. doi: 10.1093/cid/ciaa1198.

Risk Factors for COVID-19 Death in South Africa

- 3 460 932 patients (16% living with HIV)
  - 22 308 were diagnosed with COVID-19, of whom 625 died
- HIV was associated with COVID-19 mortality (adjusted hazard ratio [aHR], 2.14; [CI], 1.70–2.70)
- Similar risks across strata of viral loads and immunosuppression.
- Current and previous diagnoses of tuberculosis were associated with COVID-19 death (aHR, 2.70 [CI, 1.81–4.04] and 1.51 [CI, 1.18–1.93], respectively).
- The SMR for COVID-19 death associated with HIV was 2.39 (CI, 1.96–2.86); population attributable fraction 8.5% (95% CI, 6.1–11.1).

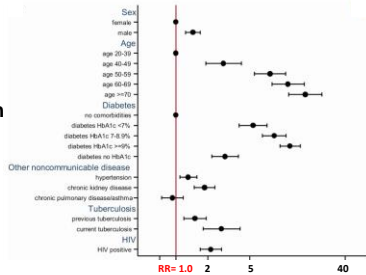Boulle, Clin Infect Dis. 2021 Oct 5;73(7):e2005-e2015. doi: 10.1093/cid/ciaa1198.

Risk Factors for COVID-19 Death in South Africa

Boulle, Clin Infect Dis. 2021 Oct 5;73(7):e2005-e2015. doi: 10.1093/cid/ciaa1198.

Risks by HIV Condition among Hospitalized Patients

Status	RR	95% CI	"p"
HIV uninfected (ref)	1.0		
HIV infected	1.45	1.14-1.84	0.002
CD4$\geq$350 cells/mm^3	1.24	.95-1.63	.112
CD4 200 – 234 cells/mm^3	1.65	.94-2.88	.08
CD4$\leq$200 cells/mm^3	2.36	1.47-3.78	<.001

Boulle, Clin Infect Dis. 2021 Oct 5;73(7):e2005-e2015. doi: 10.1093/cid/ciaa1198.

HIV and COVID: Conclusions

- No current evidence that people with HIV-1 infection are more likely to contract COVID than the non-HIV infected population given similar levels of exposure
  - PLWHIV are more likely to disproportionately share societal risks that place them at higher risk of becoming COVID exposed
- There is some evidence that after adjusting for underlying risk factors that people with HIV may be at a greater risk of dying from COVID
- Risks driving more severe COVID in those with HIV are similar to those without HIV
- People with HIV who have lower CD4 cell counts do appear to be a higher risk of death

Do People with HIV Respond Similarly to COVID-19 Vaccines?

Humoral immune responses to COVID-19 vaccination in PLWHIV receiving suppressive antiretroviral therapy

- 100 PLWH and 152 controls on ARV
  - Most recent plasma HIV RNA measurement
    - <50 copies/ml for 95 PLWH
    - 71-162 for the rest
  - Most recent CD4 cell count: 710 (IQR 525-935; range 130-1800) cells/mm^3
- 97% of controls received an mRNA vaccine for their first dose compared to 83% of PLWH; most received mRNA second doses

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Humoral immune responses to COVID-19 vaccination in PLWHIV receiving suppressive antiretroviral therapy

Time	Estimate	95% CI.	p	Estimate	95% CI	p
log$_2$ viral neutralization*						
HIV	-0.28	-0.62 to 0.056	0.10	0.17	-0.51 to 0.84	0.63
Age (per decade increment)	-0.047	-0.11 to 0.017	0.15	-0.18	-0.31 to -0.054	0.0055
Male sex	-0.1	-0.33 to 0.12	0.38	-0.37	-0.82 to 0.077	0.10
White Ethnicity	0.057	-0.14 to 0.25	0.57	-0.16	-0.56 to 0.24	0.42
# Chronic conditions (per # increment)	0.046	-0.078 to 0.17	0.47	-0.29	-0.54 to -0.047	0.02
ChAdOx1 as first vaccine	-0.14	-0.48 to 0.21	0.44	-	-	-
Dual ChAdOx1 regimen	-	-	-	-1.37	-2.40 to -0.35	0.0088
Dose interval (per week increment)	-	-	-	0.049	-0.028 to 0.13	0.21
Days since vaccine	0.024	-0.061 to 0.55	0.12	-0.0092	-0.076 to 0.058	0.79
EDTA as anticoagulant*	0.3	-0.061 to 0.66	0.1	0.83	0.061 to 1.60	0.035
COVID-19 convalescent	3.9	3.60 to 4.22	<0.0001	1.07	0.43 to 1.70	0.0011

Brumme Z medRxiv preprint doi: https://doi.org/10.1101/2021.10.03.21264320

Humoral immune responses to COVID-19 vaccination in PLWHIV receiving suppressive antiretroviral therapy

Brumme Z medRxiv preprint doi: https://doi.org/10.1101/2021.10.03.21264320
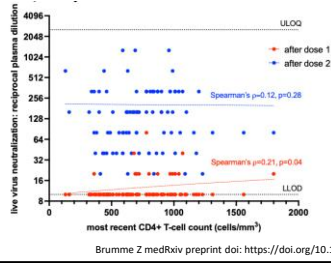
BNT162b2 mRNA Vaccine in People Living With HIV

- Twelve HIV-1 infected and 17 uninfected controls
  - PWH were on suppressive ART (3 with low level viremia)
  - Median CD4 cell count 913 cells/mm³ (range 649-1678)
- Blood drawn 7 – 17 days after the second dose of BNT162b2 vaccine
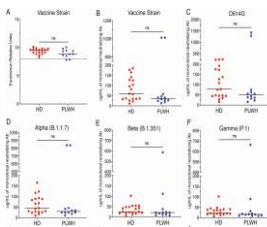
Woldemeskel BA, Clin Infect Dis, ciab648, https://doi.org/10.1093/cid/ciab648

Humoral Immune Response to COVID Vaccination in HIV-1 Infected Persons

Woldemeskel BA, Clin Infect Dis, ciab648, https://doi.org/10.1093/cid/ciab648

Cellular Immune Response to COVID Vaccination in HIV-1 Infected Persons

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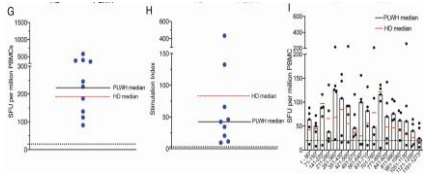
HIV and COVID: Implications for Prevention and Treatment

- Prevention
  - COVID vaccination is as essential for PLWHIV as in the non-HIV-1 infected population
  - PLWHIV generally have excellent humoral and cellular immune responses to mRNA and Ad-based COVID vaccination
    - Very modest reduction in humoral responses after a single vaccination
- Treatment
  - PLWHIV moderately more likely to get into trouble with COVID than non-HIV infected population (comorbidities and health disparities are important issues)
  - Therapeutic interventions should mirror approaches in the non-HIV-1 infected population for similar levels of risk and COVID disease

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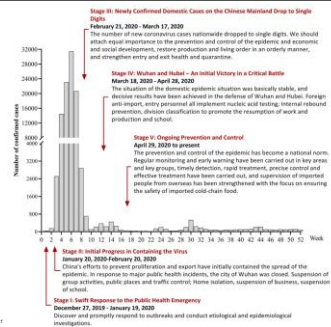## COVID and HIV: Dual Level Interactions
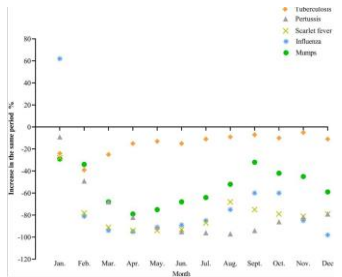

Individual   **Society**

Changes in Incidence of Notifiable Infectious Diseases in China Under the Prevention and Control Measures of COVID-19

Chen B, Front. Public Health 9:726768. doi: 10.3389/fpubh.2021.726768 October 2021

Changes in Incidence of Respiratory Diseases in China Under the Prevention and Control Measures of COVID-19
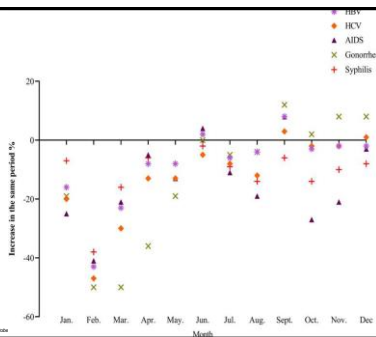

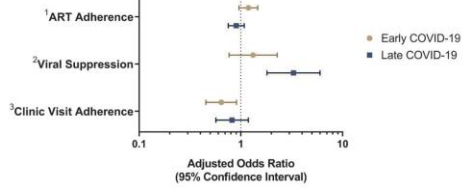Chen B, Front. Public Health 9:726768. doi: 10.3389/fpubh.2021.726768 October 2021

Changes in Incidence of Blood Diseases and STDs in China Under the Prevention and Control Measures of COVID-19

Chen B, Front. Public Health 9:726768. doi: 10.3389/fpubh.2021.726768 October 2021

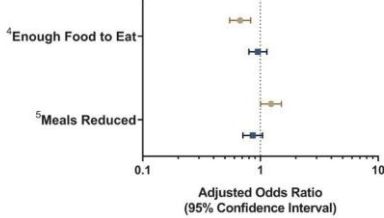**AFRICOS Cohort: Effect of COVID on HIV Care**

A) HIV care among PLWH

[1]ART Adherence
[2]Viral Suppression
[3]Clinic Visit Adherence

- Early COVID-19
- Late COVID-19

Adjusted Odds Ratio
(95% Confidence Interval)

Dear N, et. al. Clin Infect Dis 2021 DOI: 10.1093/cid/ciab979

Food Security Reduced in PLHIV in Early COVID Period

B) Food security among PLWH

[4]Enough Food to Eat
[5]Meals Reduced

Adjusted Odds Ratio
(95% Confidence Interval)

Dear N, et. al. Clin Infect Dis 2021 DOI: 10.1093/cid/ciab979

Reasons for Service Disruptions

Percent of countries

Reason	Percent
Insufficient staff availability (due to deployment to provide COVID-19 relief or other) (n=112)	66%
Community fear/mistrust in seeking health care (n=112)	57%
Decrease in outpatient volume due to patients not presenting (n=111)	57%
Decrease in inpatient volume due to cancellation of elective care (n=112)	47%
Financial difficulties during outbreak/lock down (n=112)	43%
Travel restrictions hindering access to the health facilities (n=112)	36%
Changes in treatment policies for care seeking behaviour (n=111)	35%
Insufficient Personal Protective Equipment (PPE) available (n=111)	26%
Unavailability/Stock out of essential medicines (n=111)	22%
Inpatient services/hospital beds not available (n=111)	19%
Closure of outpatient clinics (n=112)	16%
Closure of population level screening programmes (n=111)	14%
Closure of outpatient services as per government directive (n=112)	12%

Demand side factor   Supply side factor

WHO 2021: https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS-continuitysurvey-2021.1.
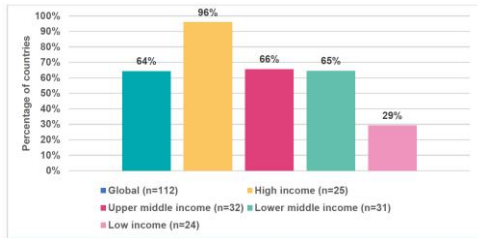
Use of Telehealth was Greatest in HICs

WHO 2021: https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS-continuitysurvey-2021.1.

Summary and Conclusions (1)

- COVID-19 had a substantial impact on the PLWHIV throughout the world
- HIV infection *per se* does not increase the risk of becoming infected with SARS CoV-2
- HIV-1 infected persons who do get infected with SARS CoV-2, morbidity and mortality directly directly by COVID is generally not substantially greater than in the uninfected population (except for those with very advanced HIV-1 infection).
  - PLWHIV experience increased COVID-related morbidity from the same risk factors as in the uninfected population but they may have more of these co-morbidities

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Summary and Conclusions (2)

- The approach to using COVID vaccines and therapeutics in the HIV-1 infected population should parallel that in the uninfected population.
- Lockdowns, isolation and quarantine reduced the number of non-COVID infections of several key types
- In some settings COVID-related disruptions to the health care systems complicated care for HIV and other diseases but, in general, the global health care work force responded incredibly well
- Disadvantaged populations are disproportionately represented in both the HIV-1 and the SARS CoV-2 infected populations.
- Health equity remains an essential but elusive goal

Thank You!

Question-and-Answer Session