

Supplemental Online Content

Lang R, Humes E, Coburn SB, et al; Corona-Infectious-Virus Epidemiology Team (CIVETs) of the NA-ACCORD of IeDEA. Analysis of severe illness after postvaccination COVID-19 breakthrough among adults with and without HIV in the US. *JAMA Netw Open*. 2022;5(10):e2236397. doi:10.1001/jamanetworkopen.2022.36397

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1: Definitions of In-Care and Criteria Used to Identify People With (PWH) and Without HIV (PWoH)

Cohort	Description	“In care” or “in cohort”	PWH
^a Kaiser Permanente Mid-Atlantic States (KPMAS)	Integrated Health system	In Care – KPMAS membership for ≥1 month in 2020	HIV registry*
Kaiser Permanente Northern California (KPNC)	Integrated Health system	In Care – KPNC membership for ≥1 month between 3/1/20 and 12/31/20	HIV registry*
University of North Carolina Chapel Hill (UNC)	Medical center cohort	≥1 encounter with UNC Health in 2019 and alive as of 03/01/2020	HIV diagnosis (by ICD diagnosis code)
Veterans Aging Cohort Study (VACS)	National cohort of all PWH and 1:2 demographically-matched PWoH in care in the Veterans Health Administration (VA) system	Enrolled in VACS from 1996-2017 and alive in 2020	HIV diagnosis (presence of 1 inpatient or 2 outpatient ICD codes for HIV)

^a The Kaiser Permanente Mid-Atlantic States and Northern California HIV Registries are databases of members diagnosed with HIV since 1998 and 1980, respectively. Primary sources used to identify HIV patients are HIV-specific laboratory tests, antiretroviral therapy, hospital-based HIV diagnosis, and diagnosis.

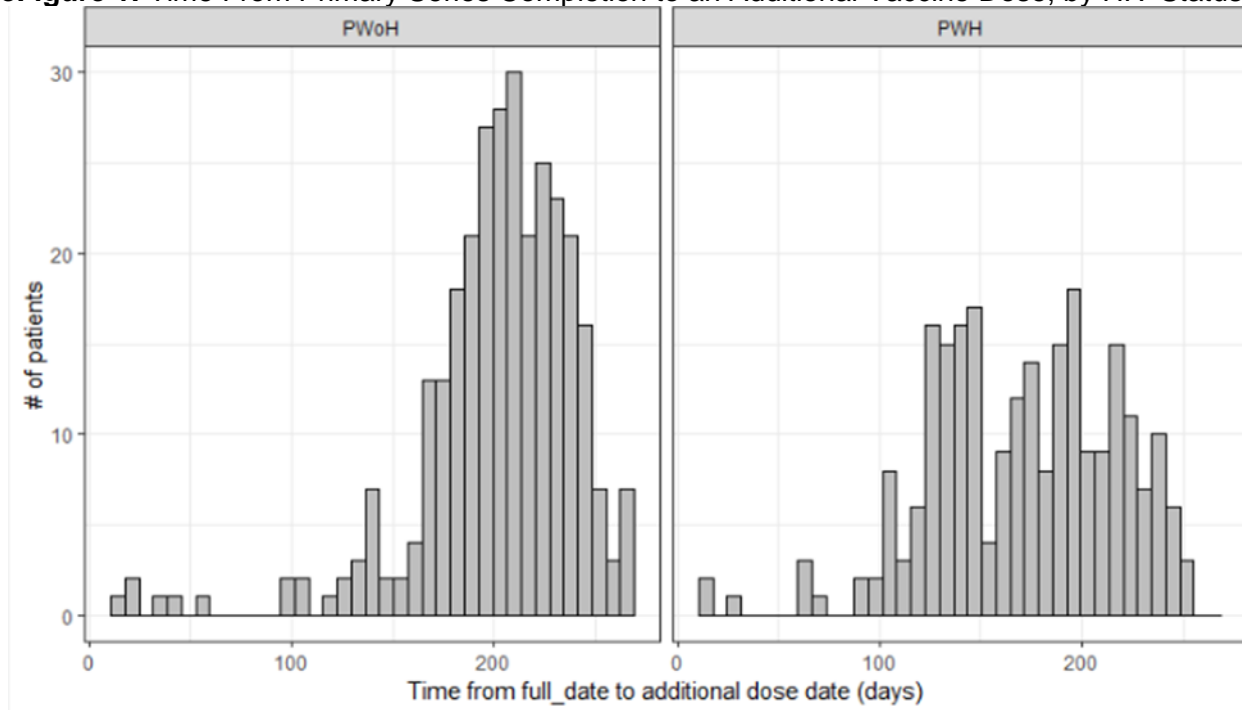
eTable 2: Diagnosis and Procedure Codes Used to Ascertain Comorbidities and Outcomes

Condition	ICD-10 Diagnosis Codes
COVID-19 breakthrough infection Between Jan 1, 2020 -Dec 31, 2021	U07.1 (specific to COVID), B34.2 (Coronavirus infection, unspecified), B97.21 (SARS-associated coronavirus causing disease classified elsewhere), B97.29 (other coronavirus as the cause of diseases classified elsewhere, J12.81 (pneumonia due to SARS-associated coronavirus, or O98.5 COVID in pregnancy, child-birth or postpartum
Immune suppressive Conditions	
Organ or tissue transplantation	Z94.x
Rheumatoid Arthritis	M05, M06
Lupus	M32
Cancer	C00-C14, C15-C26, C30-C39, C40-C41, C43-C44, C45-C49, C50, C51-C58, C60-C63, C64-C68, C69-C72, C73-C75, C76-C80, C81-C96, C7A, C7B, D45
Pregnancy	Z3A, O00-O16, O20-O48, O60-O77, O80-O82, O94-O9A
Comorbidities	
Diabetes	E11.x
End stage renal disease	N18.5 CKD stage 5, N18.6 ESRD
Hypertension	I10-I15.9, I67.4)
Obesity	E66.x, O99.21x
Outcomes of COVID-19 Hospitalization	
Mechanical Ventilation	<p>ICD-10 procedure codes: 0BH17EZ: Intubation 5A1945Z: Respiratory Ventilation, 24-96 Consecutive Hours 5A1955Z: Respiratory Ventilation, Greater than 96 Consecutive Hours 5A1935Z: Respiratory Ventilation, Less than 24 Consecutive Hours 5A1522G: Extracorporeal Oxygenation, Perph VA ECMO 5A15A2G: Extracorporeal Oxygenation, Perph VA ECMO, Intraop 5A15A2H: Extracorporeal Oxygenation, Perph VV ECMO, Intraop</p> <p>CPT codes: 94002: HC Ventilation Assist & Mgmt Inpatient 1st day 94003: HC Ventilation Assist & Mgmt Inpatient subsequent days</p>

eTable 3: Proportion of PWH Who Received Additional Vaccine Doses by CD4 Count at Fully Vaccinated (N=1,241).

CD4 at fully vaccinated (cells/mm³)	# of COVID-19 breakthroughs in PWH	# who received an additional COVID-19 vaccine, n (%)
<200	54	9 (17)
200-349	109	17 (16)
350-499	182	41 (23)
≥500	707	141 (20)
Unknown	189	34 (18)

eFigure 1: Time From Primary Series Completion to an Additional Vaccine Dose, by HIV Status



Footnotes:
PWH=People with HIV
PWoH=People without HIV

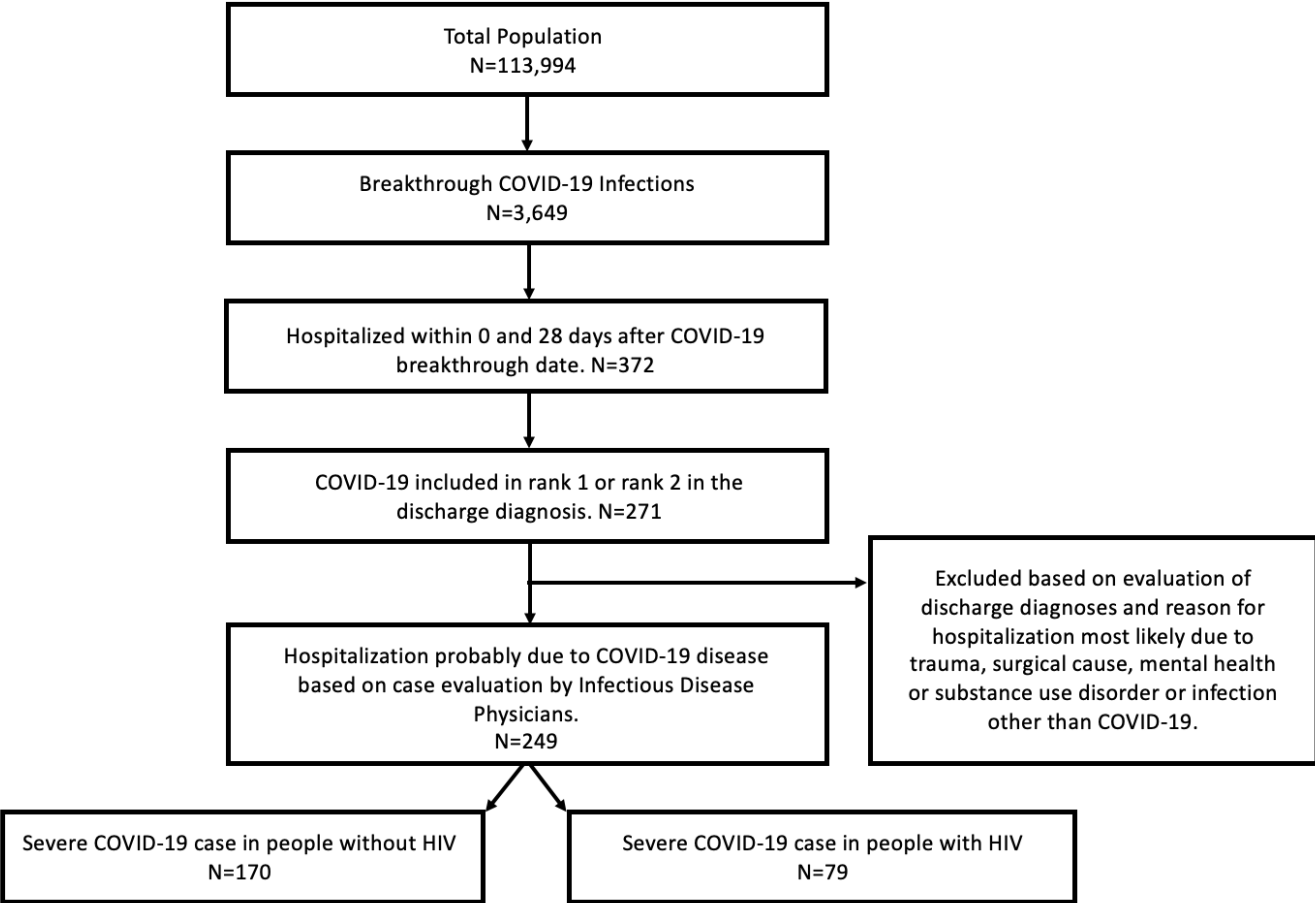
eTable 4: Characteristics of SARS-CoV-2 Breakthrough Infection, Both Severe and Nonsevere by HIV Status (N=3,649)

Characteristic	Patients, No. (%)			
	PWOH N=2,408		PWH N=1,241	
	No Severe Breakthrough N = 2,238	Severe Breakthrough N = 170	No Severe Breakthrough N = 1,162	Severe Breakthrough N = 79
^a Age (years)				
<55	907 (40.5)	10 (5.8)	534 (46.0)	16 (20.3)
55-64	436 (19.5)	56 (32.9)	333 (28.6)	26 (32.9)
65-74	726 (32.4)	71 (41.8)	240 (20.7)	24 (30.4)
75+	506 (22.6)	33 (19.4)	55 (4.7)	13 (16.5)
Sex				
Male	1944 (86.9)	164 (96.5)	1,065 (91.7)	71 (89.9)
Female	294 (13.1)	6 (3.5)	97 (8.3)	8 (10.1)
Ethnicity and Race				
Hispanic	342 (15.3)	24 (14.1)	173 (14.9)	10 (12.7)
Non-Hispanic Black/ African American	1,060 (47.4)	91 (53.5)	515 (44.3)	40 (50.6)
Non-Hispanic White	694 (31.0)	50 (29.4)	397 (34.2)	24 (30.4)
Other	127 (5.7)	4 (2.3)	66 (5.7)	5 (6.3)
Unknown	15 (0.7)	1 (0.6)	11 (0.9)	0 (0.0)
Month of breakthrough				
Jan-June	231 (10.3)	16 (9.4)	129 (11.1)	5 (6.3)
July-Oct	1,024 (45.8)	108 (63.5)	585 (50.3)	54 (68.4)
Nov-Dec	983 (43.9)	46 (27.0)	448 (38.6)	20 (25.3)
Vaccine series				
Pfizer	1,103 (49.3)	91 (53.5)	559 (48.1)	46 (58.2)
Pfizer + 3rd dose	187 (8.4)	7 (4.1)	160 (13.8)	5 (6.3)
Moderna	629 (28.1)	47 (27.6)	285 (24.5)	16 (20.3)
Moderna + 3rd dose	90 (4.0)	5 (2.9)	67 (5.8)	1 (1.3)
J&J	215 (9.6)	20 (11.8)	82 (7.1)	11 (13.9)
J&J + 2 nd dose	14 (0.6)	1 (0.6)	9 (0.8)	0 (0.0)
COVID prior to full vaccination date	283 (12.6)	9 (5.2)	170 (14.6)	6 (7.6)
Comorbidities before fully vaccinated				

Obese BMI (>=30 kg/m ²)	1,132 (50.6)	86 (50.6)	402 (34.3)	32 (40.5)
Diabetes	718 (32.1)	99 (58.2)	276 (23.8)	32 (40.5)
Hypertension	1,287 (57.5)	156 (91.8)	577 (49.7)	56 (70.9)
End-stage kidney disease	41 (1.8)	22 (12.9)	34 (2.9)	4 (5.1)
Organ or tissue transplantation	27 (1.2)	16 (9.4)	17 (1.5)	1 (1.3)
Rheumatoid arthritis	38 (2.8)	6 (3.5)	13 (1.1)	1 (1.3)
Systemic lupus erythematosus	8 (0.4)	2 (1.2)	3 (0.3)	0 (0.0)
Cancer diagnosis	157 (7.0)	30 (17.6)	111 (9.5)	18 (22.8)
Pregnancy	4 (0.2)	0 (0.0)	3 (0.3)	0 (0.0)

^a Age was categorized into a 4-level group to assess a dose response relationship among older people (i.e., 55+) that are known to be at greater risk.

eFigure 2: Identification of Severe COVID-19 Breakthrough Infections



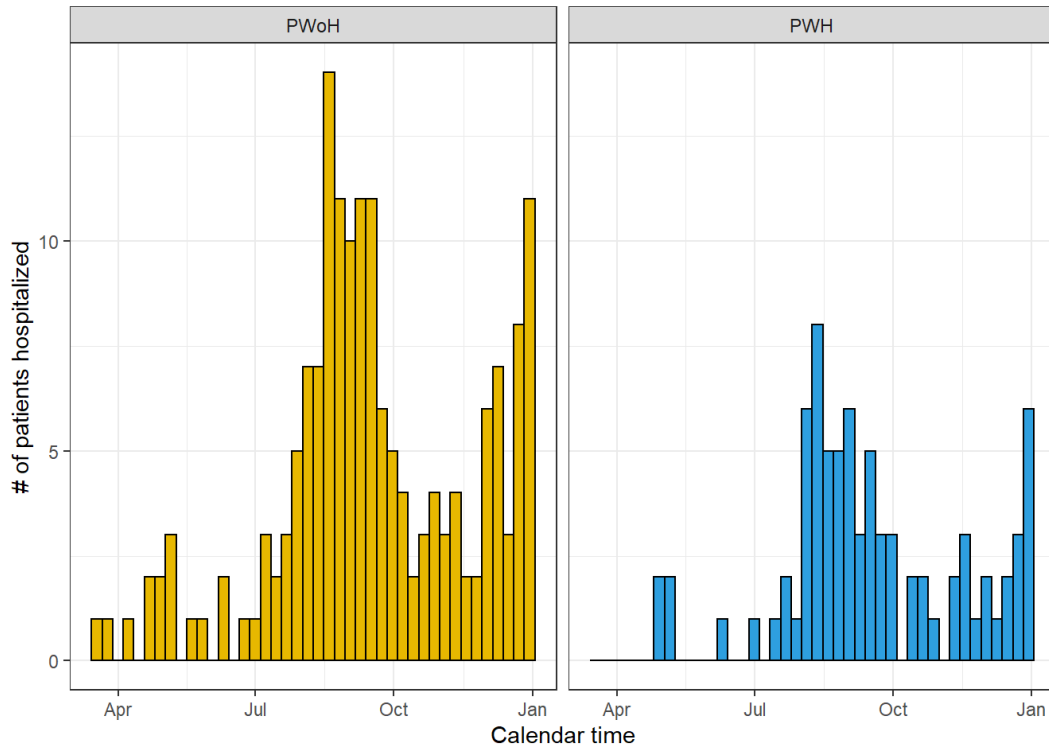
eTable 5: Severe COVID-19 Breakthrough Illness Incidence Rates and 95% Confidence Intervals, by Month and HIV Status

		# of severe COVID-19 breakthroughs	# of person-years	IR (95% CI) per 100 person years
Total				
	Overall	249	191.3	137.5 (117.6-159.8)
	PWH	79	67.7	116.7 (92.4-145.4)
	PWoH	170	123.6	130.2 (114.5-147.4)
Moderna				
	Overall	69	61.9	111.5 (86.8-141.2)
	PWH	17	21.0	81.1 (47.3-129.9)
	PWoH	52	40.9	127.1 (94.9-166.7)
Pfizer				
	Overall	149	110.3	135.1 (114.3-158.7)
	PWH	51	41.1	124.1 (92.4-163.2)
	PWoH	98	69.2	141.7 (115.0-172.7)
J&J				
	Overall	31	19.2	161.5 (109.7-229.2)
	PWH	11	5.7	194.4 (97.0-347.8)
	PWoH	20	13.5	147.8 (90.2-228.2)

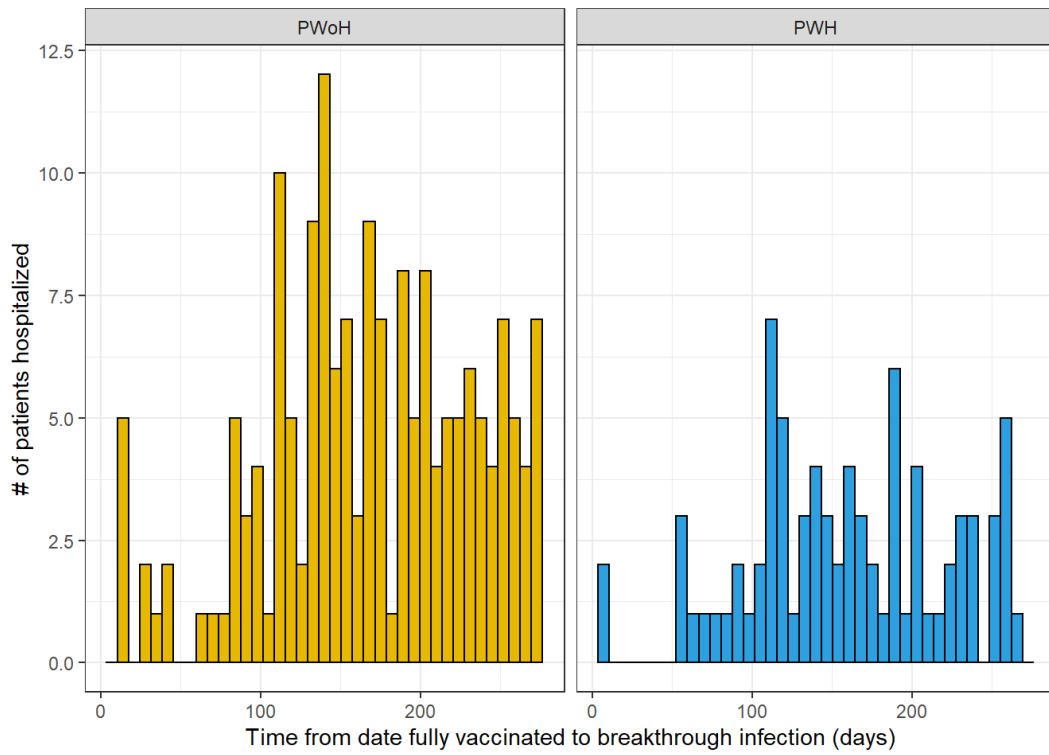
By calendar month				
Jan	Overall	0	0.02	0.0 (0.0-19248.5)
	PWH	0	0	NA
	PWoH	0	0.02	0.0 (0.0-19248.1)
Feb	Overall	0	0.35	0.00 (0.00-1052.6)
	PWH	0	0.14	0.0 (0.0-2641.9)
	PWoH	0	0.21	0.0 (0.0-1749.8)
Mar	Overall	2	2.56	78.2 (9.5-282.5)
	PWH	0	0.90	0.0 (0.0-409.5)
	PWoH	2	1.66	120.7 (14.6-436.2)
Apr	Overall	6	6.06	99.0 (36.3-215.5)
	PWH	1	2.13	47.0 (1.2-261.6)
	PWoH	5	3.93	127.2 (41.3-296.8)
May	Overall	8	9.07	88.2 (38.1-173.8)
	PWH	3	3.13	95.8 (19.8-272.9)
	PWoH	5	5.94	84.2 (27.3-196.5)
June	Overall	3	7.33	41.0 (8.4-119.7)
	PWH	1	2.52	39.7 (1.0-221.2)
	PWoH	2	4.81	41.6 (5.0-150.3)
Jul	Overall	16	13.25	120.7 (69.0-196.1)
	PWH	4	5.60	71.4 (19.5-182.7)
	PWoH	12	7.65	156.9 (81.1-274.1)
Aug	Overall	69	44.68	154.4 (120.2-195.4)
	PWH	25	19.2	130.2 (84.3-192.2)
	PWoH	44	25.5	172.7 (125.5-231.8)
Sept	Overall	57	42.40	134.5 (101.8-174.2)
	PWH	18	13.9	129.9 (77.0-205.3)
	PWoH	39	28.5	136.7 (97.2-186.8)
Oct	Overall	20	29.25	68.4 (41.8-105.6)
	PWH	7	9.5	74.1 (29.8-152.7)
	PWoH	13	19.8	65.7 (35.0-112.3)

Nov	Overall	24	19.15	125.3 (80.3-186.5)
	PWH	7	6.0	117.3 (47.2-241.8)
	PWoH	17	13.2	128.9 (75.1-206.4)
Dec	Overall	44	36.67	120.0 (87.2-161.1)
	PWH	13	11.4	114.4 (60.9-195.7)
	PWoH	31	25.3	122.5 (83.2-173.8)

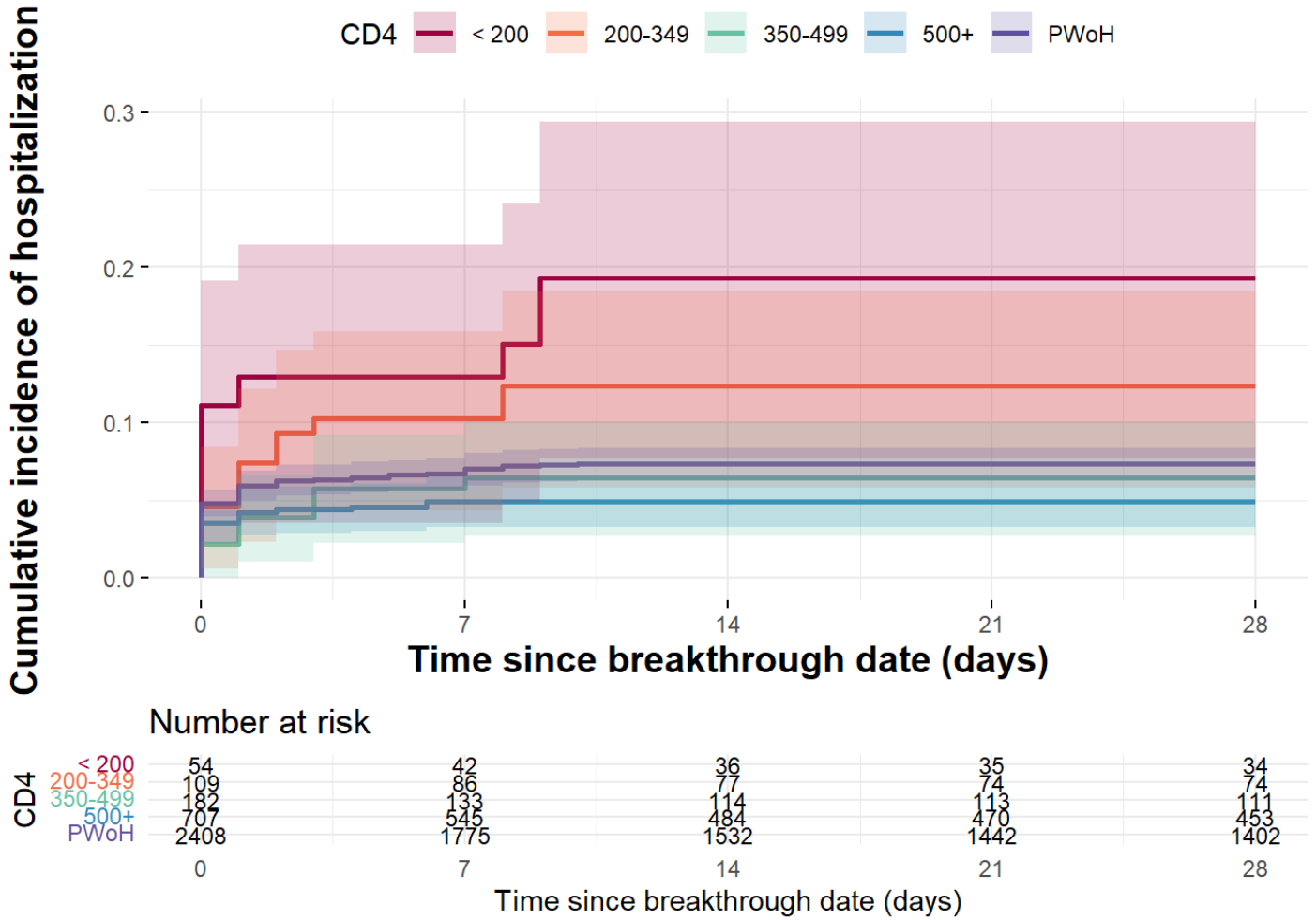
eFigure 3: Histograms of the Date of Severe SARS-CoV-2 Breakthrough Infection, by HIV Status
a) Calendar time



b) Time from date fully vaccinated to breakthrough



eFigure 4: Cumulative Incidence of Severe COVID-19 Breakthrough Illness (and 95% Confidence Intervals Represented by the Shading) Stratified by CD4 Count and HIV Status



Log-rank test: $p < 0.001$

eTable 6: Characteristics of Participants With Breakthrough COVID-19 Illness Requiring Hospitalization, Mechanical Ventilation or in Those Who Died

Characteristic	Patients, No. (%)		
	Hospitalized (Severe COVID-19)	Mechanical ventilation	Death
	N = 249	N = 24	N = 20
HIV Status			
PWoH	170 (68.3)	16 (66.7)	14 (70.0)
PWH	79 (31.7)	8 (33.3)	6 (30.0)
Age (years)			
<55	26 (10.4)	3 (12.5)	2 (10.0)
55-64	82 (32.9)	9 (37.5)	4 (20.0)
65-74	95 (38.2)	6 (25.0)	5 (25.0)
75+	46 (18.5)	6 (25.0)	9 (45.0)
Sex			
Male	235 (94.4)	20 (83.3)	18 (90.0)
Female	14 (5.6)	4 (16.7)	2 (10.0)
Ethnicity and Race			
Hispanic	34 (13.7)	4 (16.7)	4 (20.0)
Non-Hispanic Black/African American	131 (52.6)	18 (75.0)	11 (55.0)
Non-Hispanic White	74 (29.7)	2 (8.3)	5 (25.0)
Other	9 (3.6)	0 (0.0)	0 (0.0)
Unknown	1 (0.4)	0 (0.0)	0 (0.0)
Month of breakthrough			
Jan-June	21 (8.4)	3 (12.5)	3 (15.0)
July-Oct	162 (65.1)	16 (66.7)	13 (65.0)
Nov-Dec	66 (26.5)	5 (20.8)	4 (20.0)
COVID prior to vaccination	15 (6.0)	0 (0.0)	0 (0.0)
Vaccine Series			
Primary Series Only	230 (92.4)	21 (87.5)	18 (90.0)
Primary Series + additional dose	19 (7.6)	3 (12.5)	2 (10.0)
Obese BMI (≥ 30 kg/m²)	118 (50.0)	20 (87.0)	13 (65.0)
Unknown	13 (5.2)	1 (4.2)	1 (5.0)
Diabetes	131 (52.6)	15 (62.5)	13 (65.0)
Hypertension	212 (85.1)	23 (95.8)	19 (95.0)
End-stage kidney disease	26 (10.4)	5 (20.8)	6 (30.0)
Organ or tissue transplantation	17 (6.8)	5 (20.8)	4 (20.0)
Rheumatoid arthritis	7 (2.8)	3 (12.5)	2 (10.0)
Systemic lupus erythematosus	2 (0.8)	0 (0.0)	0 (0.0)
Cancer diagnosis	48 (19.3)	5 (20.8)	5 (25.0)
CD4 at ART initiation, median (IQR)	399 (212,546)	376 (324,417)	398 (354,855)
Unknown	210 (84.3)	20 (83.3)	1 (16.7)
AIDS before fully vaccinated	29 (36.7)	3 (37.5)	3 (50.0)
Unknown	170 (68.3)	16 (66.7)	0 (0.0)

CD4 at fully vaccinated, median (IQR)	498 (305,746)	352 (172,542)	352 (291,423)
Unknown	181 (72.7)	18 (75.0)	0 (0.0)
Supressed HIV RNA at fully vaccinated	59 (86.8)	5 (83.3)	4 (100.0)
Unknown	181 (72.7)	18 (75.0)	0 (0.0)

eFigure 5: Outcomes of Breakthrough Illness Among Those Hospitalized After Fully Vaccinated to Dec 31, 2021, by HIV Status (n=170 PWoH) and CD4 Count (n=23 <350 Cells/mm³ and n=45 ≥350 Cells/mm³) Among PWH

