CLINICAL CARE OPTIONS®
INFECTIOUS DISEASE

Comprehensive COVID-19 Slideset: Special Populations and Comorbidities

Version 17 – March 18, 2021

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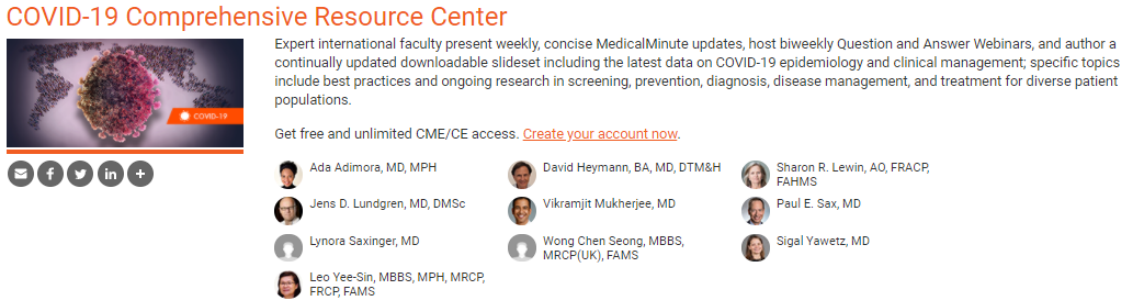
Check out more coverage on these topics in the Resource Center!



MedicalMinute	Topic/Studies Covered
1 Remdesivir EUA	ACTT-1 trial
2 SARS-CoV-2 serology	Ab: detection, neutralizing; POC testing
3 COVID-19 diagnosis	Ab, RNA, chest CT, diagnosis timeframe
4 Clinical presentation	Incubation, symptoms, disease severity
5 Mild/mod COVID-19	ACTT-1, SIMPLE-moderate, SIMPLE-severe
6 Racial disparities	Incidences, hospitalizations, deaths
7 Sev/crit COVID-19	Def, management, NIH and IDSA guidelines
8 Dexamethasone data	RECOVERY trial, recommendations, caveats
9 Immunocompromise	HIV, malig, organ tx, immunomodulators
10 COVID-19 in children	Incidence, severity, MIS-C, remdesivir EUA

MedicalMinute	Topic/Studies Covered
11 Vaccines in phase III	Moderna, Oxford, CanSino trials
12 Viral transmission	Droplets, aerosols, phys dist, air circ, masks
13 Pregnancy	Labor/delivery, transmission, remdesivir
14 Diagnostics, epi	Tests: antibody, antigen, RT-PCR for RNA
15 Coagulopathy	Anticoagulation, thromboprophylaxis
16 Adaptive immunity	IgG durability, memory T-cells, reinfection
17 Convalescent plasma	Li study in JAMA, conCOVID, FDA EUA
18 Herd Immunity	R_0, pop heterogeneity, immune duration
19 Long-term sequelae	Pulmonary and extra-pulmonary sequelae
20 Corticosteroids	RECOVERY, CoDex, REMAPCAP, CapeCOVID

https://www.clinicaloptions.com/infectious-disease/programs/covid19-resources

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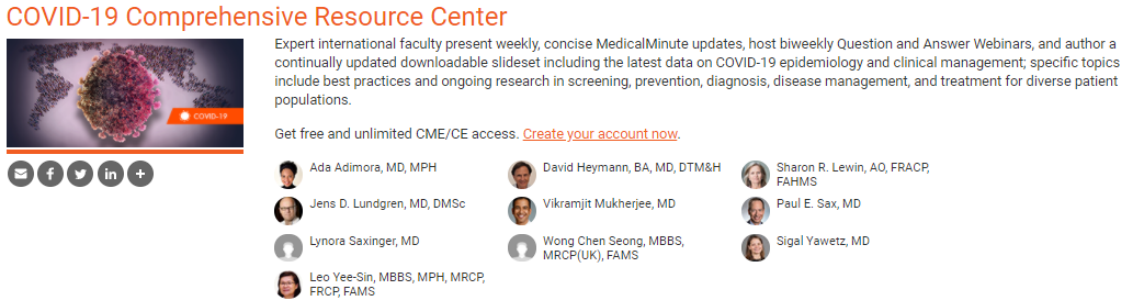

MedicalMinute	Topic/Studies Covered
21 Comorbidities	Cancer, CVD (BRACE-corona), DM, CKD
22 Immunomodulation	TESEO, COVACTA, EMPACTA, ongoing trials
23 Coinfections	Secondary infection incidence in COVID-19
24 Treatment updates	ACTT-1, SOLIDARITY, remdesivir approval
25 Reinfection	Reinfection with SARS-CoV-2, Ab kinetics
26 Epi in HCWs	Infection rates in HCWs vs gen pop
27 SARS-CoV-2 mutation	Mutations/rates, global distribution, impact
28 HIV and COVID-19	Mortality/comorbidity in larger studies, Ad5
29 Vaccine hesitancy	Factors that impact hesitancy, survey data
30 Vaccine updates	Safety and efficacy, EUAs, global concerns

MedicalMinute	Topic/Studies Covered
31 Treatment update	Baricitinib, anti-spike antibodies, ivermectin
32 Antigen testing	Antigen test algorithms, EUAs, at-home test
33 Anticoagulation	Update on thromboprophylaxis trials, data
34 Investigational agents	TMPRSS2 inhibitors, CRISPR-Cas13, IFN Λ

https://www.clinicaloptions.com/infectious-disease/programs/covid19-resources

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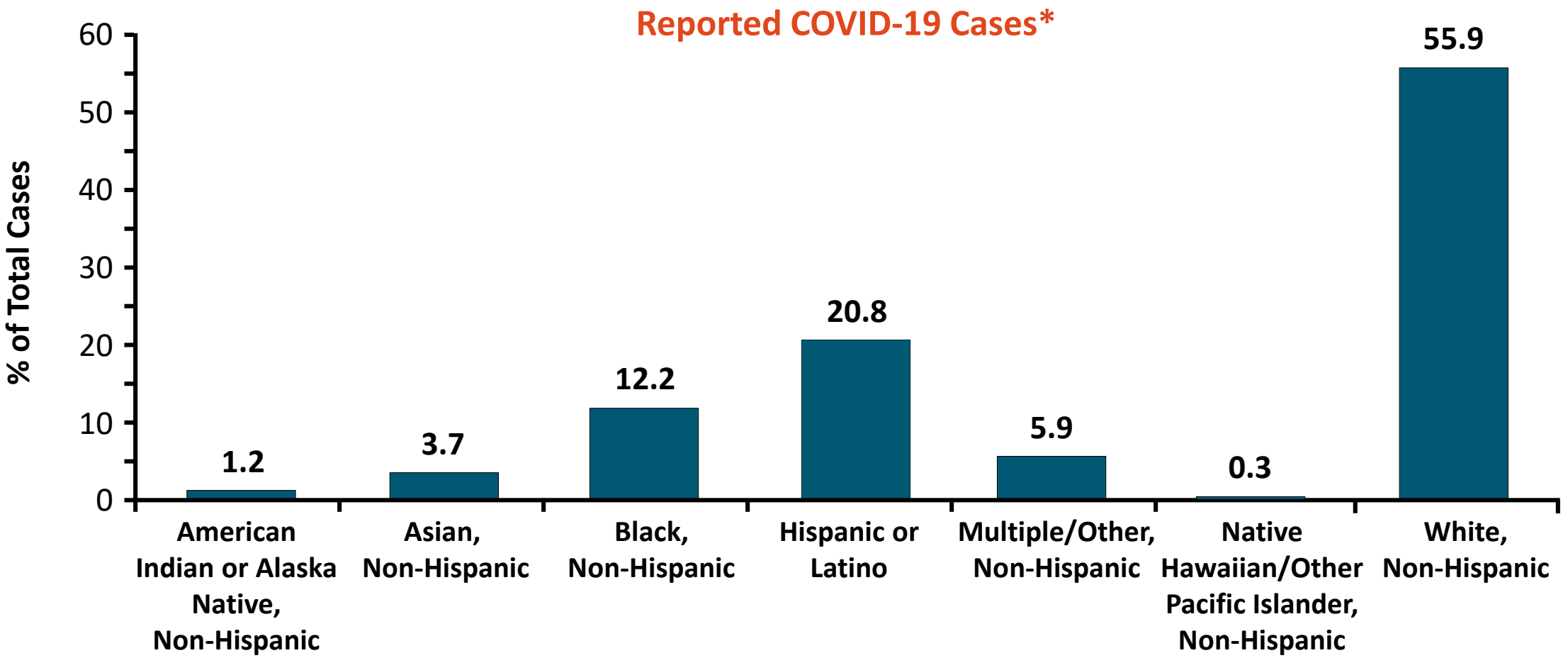
Racial/Sociodemographic Disparities

CDC COVID Data Tracker: Reported COVID-19 Cases by Race/Ethnicity

Updated



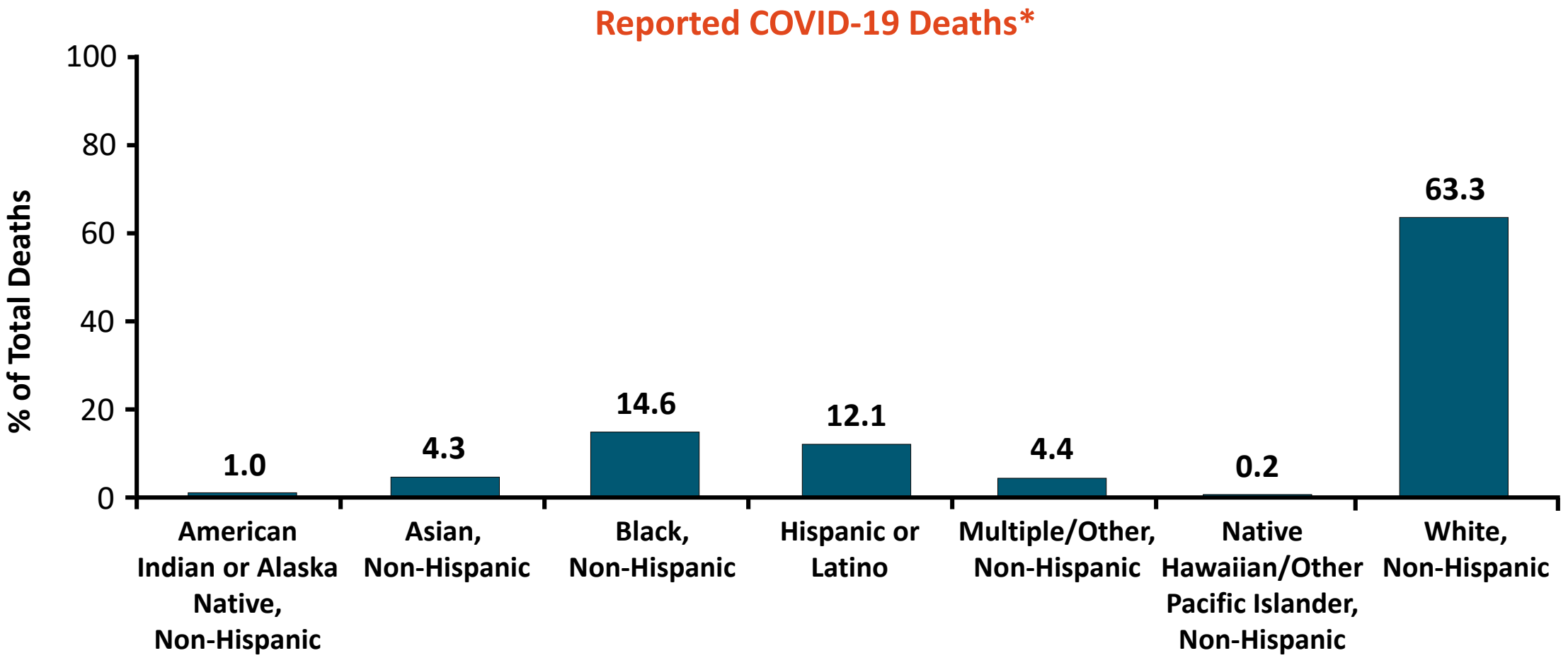
*Last updated March 17, 2021, 1:37 PM ET. Includes race/ethnicity data available for 12,007,961 cases.

https://www.cdc.gov/covid-data-tracker/index.html#demographics

Slide credit: clinicaloptions.com

CDC COVID Data Tracker: Reported COVID-19 Deaths by Race/Ethnicity

Updated



*Last updated March 17, 2021, 1:37 PM ET. Includes race/ethnicity data available for 297,119 deaths.

https://www.cdc.gov/covid-data-tracker/index.html#demographics

Slide credit: clinicaloptions.com

CDC: Risk for SARS-CoV-2 Infection, Hospitalization, or Death by Race/Ethnicity

New

Rate Ratio* vs White, Non-Hispanic Persons	Cases	Hospitalization	Death
American Indian or Alaska Native, non-Hispanic	1.7x	3.7x	2.4x
Asian, non-Hispanic	0.7x	1.0x	1.0x
Black, non-Hispanic	1.1x	2.9x	1.9x
Hispanic or Latino	1.3x	3.1x	2.3x

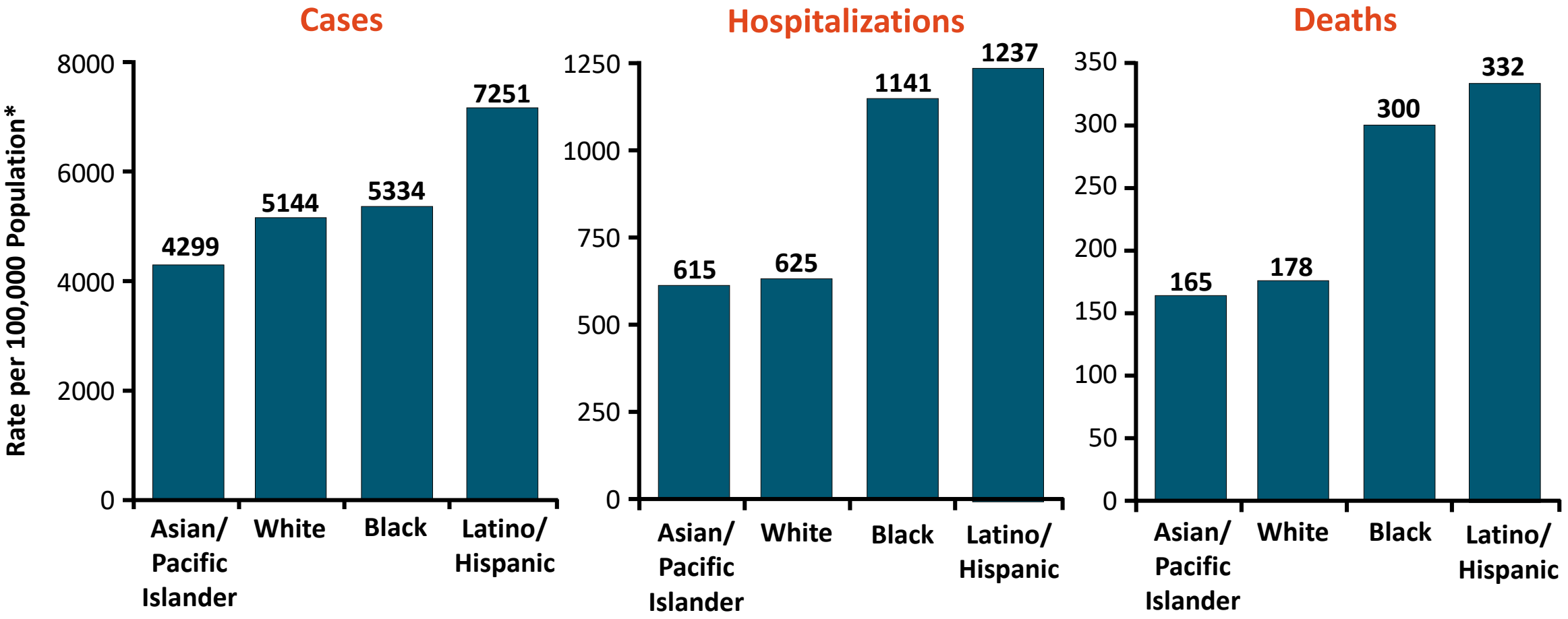
*Age-adjusted rates standardized to the 2019 US intercensal population estimate (cases/death) or the 2019 US standard COVID-NET catchment population (hospitalization).

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html

Slide credit: clinicaloptions.com

COVID-19 Cases, Hospitalizations, and Deaths by Race/Ethnicity in NYC

Updated



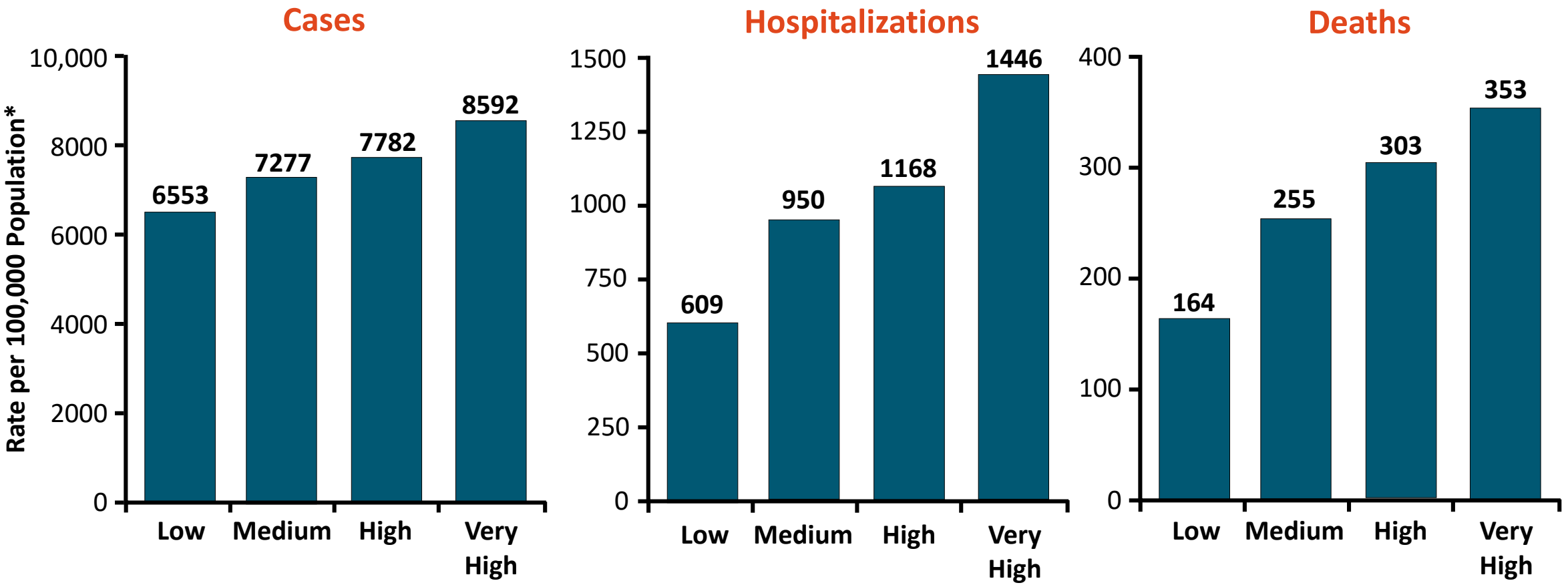
*Age-adjusted. Last updated March 17, 2021, 1:00 PM ET. Data not provided on those identified as other categories (eg, Native American/Alaska Native or multiracial). Latino/Hispanic includes people of any race. Race/ethnicity data most complete for those hospitalized or who have died.

https://www1.nyc.gov/site/doh/covid/covid-19-data-totals.page#rates.

Slide credit: clinicaloptions.com

COVID-19 Cases, Hospitalizations, and Deaths by Poverty Level in NYC

Updated



*Age-adjusted. Last updated March 17, 2021, 1:00 PM ET. Neighborhood poverty is based on the percent of a ZIP code's population living below the Federal Poverty Level. Low poverty: < 10%; medium poverty: 10% to 19.9%; high poverty: 20% to 29.9%; very high poverty: ≥ 30%.

https://www1.nyc.gov/site/doh/covid/covid-19-data-totals.page#rates

Slide credit: clinicaloptions.com

Multivariate Analysis of Predictors of COVID-19 Cases and Associated Mortality in US Counties

Covariates Assessed by County	Rate Ratio COVID-19 Cases (95% CI)	Rate Ratio COVID-19 Deaths (95% CI)
Percent black	1.23 (1.17- 1.33)	1.18 (1.00-1.40)
Percent white	1.02 (0.92-1.13)	0.93 (0.70-1.23)
Percent > 65 yrs old	1.03 (0.97-1.09)	1.25 (1.08-1.45)
Percent unemployed	0.89 (0.84-0.94)	0.95 (0.82-1.11)
Percent uninsured	1.16 (1.07-1.26)	1.13 (0.91-1.41)
Percent diabetes diagnoses	0.97 (0.92-1.03)	1.01 (0.88-1.16)
Heart disease death rate	1.01 (0.96-1.07)	1.07 (0.91-1.26)
HIV infection rate	1.00 (0.96-1.04)	1.01 (0.93- 1.10)
Cerebrovascular and HTN death rate	1.02 (0.99-1.05)	1.03 (0.91-1.11)

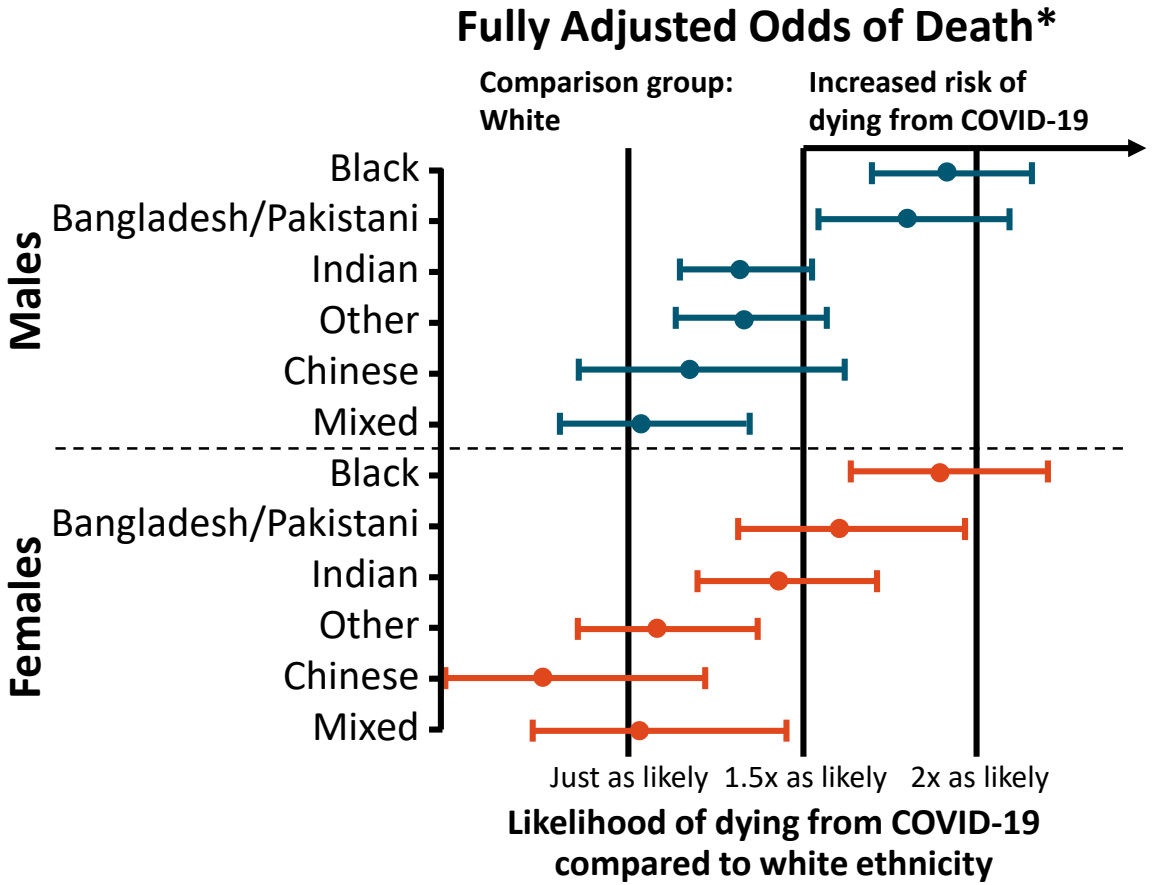
Covariates Assessed by County	Rate Ratio COVID-19 Cases (95% CI)	Rate Ratio COVID-19 Deaths (95% CI)
Urbanicity score	1.00 (0.92-1.09)	0.83 (0.66-1.04)
Air toxins ($PM_{2.5}$)	1.03 (0.93-1.14)	1.09 (0.87-1.38)
Household occupancy > 1 person/room	1.05 (1.01-1.10)	1.05 (0.93-1.19)
Social distancing score	0.88 (0.84-0.92)	0.82 (0.73-0.93)
Days since first case of diagnosis	3.10 (2.89-3.33)	3.08 (2.50-3.80)

Millett. Ann Epidemiol. 2020;47:37.

Slide credit: clinicaloptions.com

Global Outlook: COVID-19–Related Deaths by Ethnic Group in England and Wales

- In age-adjusted analysis, black males were 4.2x more likely and black females 4.3x more likely to die from COVID-19-related death compared with their white counterparts
  - Adjusting for socio-demographic characteristics substantially reduced the odds of death from COVID-19 relative to white patients



*Adjusted for age, region, rural and urban classification, area deprivation, household composition, socio-economic position, highest qualification held, household tenure, and health or disability in the 2011 Census.

Office for National Statistics. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/coronavirusrelateddeathsbyethnicgroupenglandandwales/2march2020to10april2020

Slide credit: clinicaloptions.com

Global Outlook: Additional Data on Ethnicity and COVID-19 Outcomes From the UK

- **OpenSAFELY**[1]: secure health analytics platform housing primary care EHR data for 40% of England's patients (N = 17,278,392 adults)
  - Ethnicity recorded for 74% of patients
- n = 10,926 COVID-19–related deaths
  - Death associated with male sex, older age, deprivation, and varied comorbidities (eg, severe asthma, diabetes, obesity, kidney dysfunction)
  - Black and South Asian patients at **higher risk of death** vs whites

- **ISARIC CCP-UK**[2]: prospective observational cohort study of patients with suspected/confirmed COVID-19 in 260 hospitals in England, Scotland, and Wales (N = 34,986)
  - Ethnicity recorded for 88% of patients
- Ethnic minorities were younger; more likely to: have diabetes, be admitted to critical care, and need invasive mechanical ventilation vs whites
  - **Higher adjusted mortality** for South Asians vs whites

1. Williamson. Nature. 2020;584:430. 2. Harrison. Lancet. 2020;[Preprint]. Note: This study has not been peer reviewed.

Slide credit: clinicaloptions.com

Factors Influencing Racial and Ethnic Minority Group Health

Living/Work Conditions

- Discrimination promotes **chronic and toxic stress**
- Work in **essential industries with increased exposure**, lack paid sick leave
- Reside in economically depressed areas with **high housing density** and **limited access to healthy foods**
- **Multigenerational households and limited space** may make it more difficult to follow prevention strategies

Health & Access to Care

- **High prevalence of comorbid conditions** that can increase likelihood and severity of COVID-19
- **Factors restricting access to care**: language barriers; lack of insurance, transportation, or child care; financial implications of missing work to receive care; cultural differences between patients and providers; distrust of government and healthcare systems

CDC. Health equity considerations and racial and ethnic minority groups. Last updated February 12, 2021. Yancy. JAMA. 2020;323:1891.

Healthcare Delivery Systems: What Can We Do?

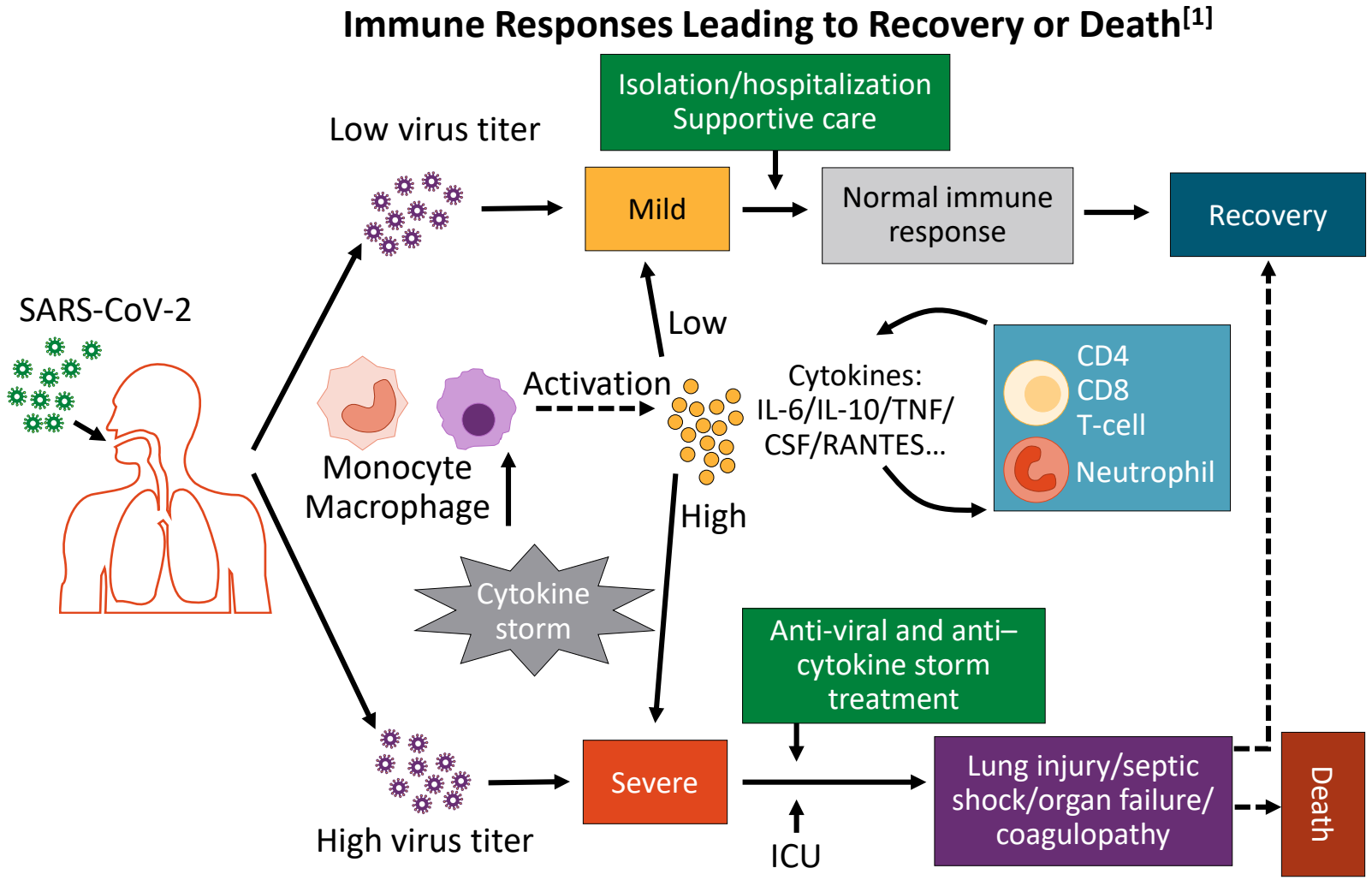
- Maintain disease prevention and management services
- Increase availability/accessibility of COVID-19 testing
- Connect community members with health resources
- Engage with organizations trusted by the community
- Provide tailored telehealth options
- Ensure HCPs are aware and respectful of culture
- Train employees to identify/interrupt discrimination and implicit bias
- Adapt public health recommendations to community circumstances

CDC. What we can do. Last updated July 24, 2020.
https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/what-we-can-do.html

Slide credit: clinicaloptions.com

Immunocompromised Patients and COVID-19

Immune Response to SARS-CoV-2



Adequate immune responses[2]

- Timely innate/adaptive responses
- Quick type 1 IFN response
- Activation of efficient antiviral response (clearance by macrophages)
- Activation of Th1 cells and B-cells for production of neutralizing antibodies

Inadequate immune responses[2]

- Delayed/limited type 1 IFN
- Endothelial cell death
- Epithelial/endothelial leakage
- Overactivation/exhaustion T-cells and NK cells
- Accumulation of activated macrophages → cytokine storm

1. Wang. J Leukoc Biol. 2020;108:17. 2. Sokolowska. Allergy. 2020;75:2445.

Slide credit: clinicaloptions.com

Immune-Related Risk Factors for Susceptibility to Severe COVID-19

- Older persons have impaired B-cell and T-cell immune responses vs younger persons (eg, blunted antibody response to vaccination, excess sepsis risk)[1-3]
- Impaired B-cell response: reduced ability to mount a neutralizing antibody response[4]
- Impaired T-cell response: role of T-cell response in control of ongoing SARS-CoV-2 uncertain[5-6]
  - Likely contributing to control but not preventive/eradicative
- Younger persons with impaired or dysregulated B-cell and T-cell immune responses may also be at risk

1. Mueller. Aging (Albany NY). 2020;12:9959. 2. Goodwin. Vaccine. 2006;24:1159.
3. Opal. Clin Infect Dis. 2005;41:S504. 4. Vabret. Immunity. 2020;52:910.
5. Diao. Front Immunol. 2020;11:827. 6. Oja. Eur J Immunol. 2020;50:1998.

CDC: COVID-19 and Immunocompromised Patients

Updated

- *"Many conditions and treatments can cause a person to be immunocompromised or have a weakened immune system"*
  - Solid organ transplantation, blood/bone marrow transplantation, immune deficiencies, HIV with a low CD4+ cell count or not on treatment, prolonged use of corticosteroids, or use of other immune weakening medicines
- Having a weakened immune system may increase the risk of severe illness from COVID-19
- Limited data suggest that persons with HIV and viral suppression have the same risk for COVID-19 as persons without HIV

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html
https://www.cdc.gov/hiv/basics/covid-19.html

Slide credit: clinicaloptions.com

COVID-19 in Immune-Mediated Inflammatory Diseases Treated With Immunomodulatory Therapies

- Prospective case series of patients with known immune-mediated inflammatory disease (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, psoriasis, IBS, etc) who were receiving anticytokine biologics, other immunomodulatory therapies, or a combination when diagnosed with confirmed or highly suspected COVID-19 (N = 86)
  - Incidence of hospitalization: 16%
- Incidence of hospitalization reported for general population in NYC: 26%
- BL use of biologics not associated with worse outcome

Variable	All Patients (N = 86)	Ambulatory (n = 72)	Hospitalized (n = 14)
Mean age, yrs (range)	46 (22-74)	46 (22-74)	50 (25-73)
Tx at BL, n (%)			
▪ Biologic/JAK inhibitor	62 (72)	55 (76)	7 (50)
▪ Oral glucocorticoid	8 (9)	4 (6)	4 (29)
▪ HCQ	8 (9)	5 (7)	3 (21)
▪ MTX	17 (20)	11 (15)	6 (43)
Use of supplementary oxygen, n (%)	--	--	7 (50)
Death, n (%)	--	--	1 (7)

Haberman. NEJM. 2020;383:85.

Slide credit: clinicaloptions.com

Potential for Severe COVID-19 Outcomes in Solid Transplant Patients

- Report of outcomes among solid organ transplant recipients with SARS-CoV-2 at 2 centers in New York City during the first 3 wks of the outbreak (N = 90)
  - Most common transplants were kidney (51%), lung (19%), liver (14%), and heart (10%)

Baseline Characteristic	All Patients (N = 90)	Mild/ Moderate Disease (n = 63)	Severe Disease (n = 27)	*P* Value
Median age, yrs (IQR)	57 (46-68)	54 (39-64)	67 (56-74)	.001
Median time from transplant to diagnosis, yrs (IQR)	6.6 (2.87-10.61)	6.25 (2.6-10.69)	6.86 (2.87-10.16)	.92
Hospital admission, n (%)	68 (76)	41 (65)	27 (100)	< .001

Outcome,* n (%)	Hospitalized Patients (N = 68)	Mild/ Moderate Disease (n = 41)	Severe Disease (n = 27)
Intubation or ECMO	24 (35)	0 (0)	23 (85)
ICU admission	23 (34)	0 (0)	23 (85)
Mortality	16 (24)	0 (0)	16 (59)

*Immunosuppressive therapy was reduced in all patients; 91% of patients were treated with hydroxychloroquine, 66% of patients were treated with azithromycin, and 3% of patients were treated with remdesivir.

Periera. Am J Transplant. 2020;20:1800.

Slide credit: clinicaloptions.com

COVID-19 in Lung Transplant Patients

- Study of lung transplant patients diagnosed with COVID-19 at a lung transplant center via PCR or consensus opinion between March 26 and April 30, 2020 (N = 8)
  - 5 patients transplanted within past yr
  - Common comorbidities: diabetes (35.7%), HTN (37.5%), CKD (37.5%), and atrial fibrillation (37.5%)
  - All patients were on 3-drug immunosuppression including calcineurin inhibitor, a nucleotide-blocking agent, and steroids

Variable, n (%)	Lung Transplant Patients (N = 8)
Treatment	
▪ Remdesivir (clinical trial)	2 (25)
▪ Methylprednisolone (> 125 mg/day)	6 (75)
▪ Anakinra	1 (12.5)
▪ IVIG	4 (50)
▪ Tocilizumab	2 (25)
▪ Nucleotide-blocking agent held	6 (75)
▪ No change to immunosuppression	2 (25)
Outcomes	
▪ Hospital admission	8 (100)
▪ ICU admission	3 (37.5)
▪ Required mechanical ventilation	2 (25)
▪ Death*	2 (25)

*1 sepsis and 1 necrotizing pancreatitis; both had received basiliximab induction and transplant within previous 2 wks.

Myers. Transpl Infect Dis. 2020;22:e13364.

Slide credit: clinicaloptions.com

COVID-19 in Kidney Transplant Patients

- Case study of 2 patients diagnosed with COVID-19 within 1 month of living donor kidney transplant with triple immunosuppression (prednisolone, tacrolimus, mycophenolate mofetil) and ATG induction

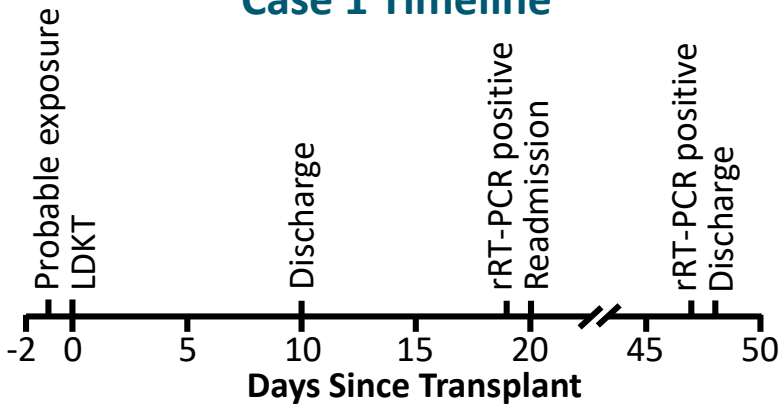
Case 1

- 35-yr-old man with CKD and HTN
- Mild COVID-19
- Tapered prednisolone and dose adjusted tacrolimus
- Stopped mycophenolate mofetil due to lymphopenia
- Received hydroxychloroquine/azithromycin

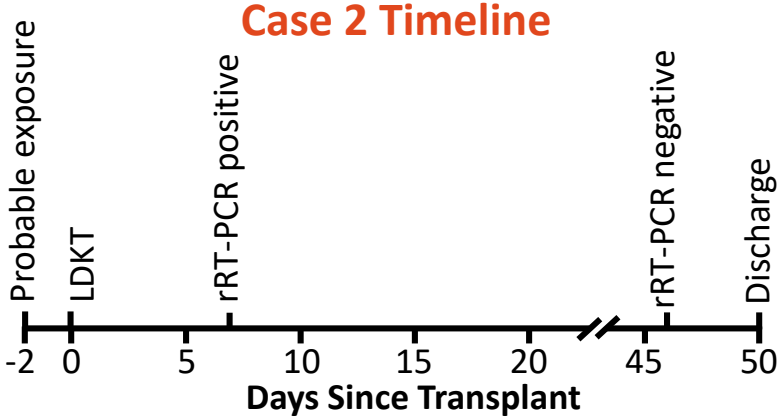
Case 2

- 45-yr-old man with HBV and CKD
- Mild COVID-19
- Tapered prednisolone and dose adjusted tacrolimus
- Mycophenolate mofetil reduced
- Received hydroxychloroquine/azithromycin

Case 1 Timeline



Case 2 Timeline



Shingare. Am J Transplant. 2020;20:3206.

Slide credit: clinicaloptions.com

COVID-19 Severity and Mortality in Patients With Chronic Lymphocytic Leukemia

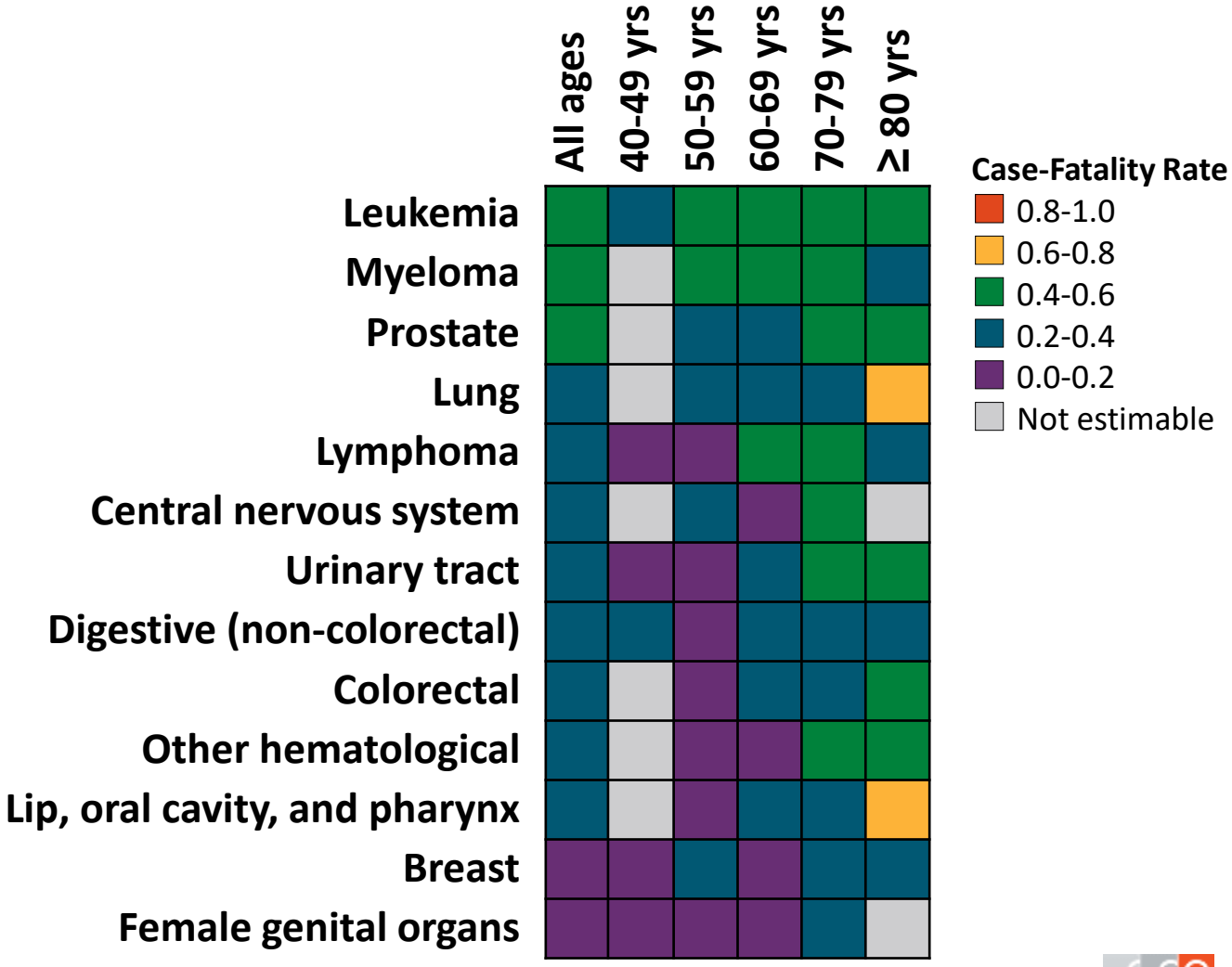
- Retrospective, international study assessing patients with CLL diagnosed with confirmed COVID-19 in Europe between March 28, 2020, and May 22, 2020 (N = 190)
  - Almost 90% of patients in cohort were in Italy and Spain
  - 151 (79%) presented with severe disease requiring oxygen and/or ICU admission
  - Severe disease associated with age ≥ 65 yrs (OR: 3.72; 95% CI: 1.79-7.71)
- 39.7% of patients with severe COVID-19 had received CLL treatment in the previous 12 mos vs 61.5% of patients with nonsevere COVID-19 ($P < .05$)
- Hospitalization rate was lower for patients on ibrutinib vs patients on other regimens or not on treatment for CLL ($P < .05$)
- 32.5% mortality among hospitalized patients in cohort vs 13.4% for general population in Italy; however ~ 75% of patients in cohort had ≥ 1 comorbidity

Scarfò. Leukemia. 2020;34:2354.

Slide credit: clinicaloptions.com

COVID-19 Mortality in Patients With Cancer

- Prospective study evaluating the effect of primary tumor subtype, age, and sex on SARS-COV-2 prevalence and CFR during hospitalization among cancer patients in the UKCCMP cohort (N = 1044)
- All-cause CFR significantly increased with age from 0.10 for subset aged 40-49 yrs vs 0.48 if ≥ 80 yrs
- COVID-19 trajectory more severe in patients with hematologic malignancies vs solid organ tumors (OR: 1.57, *P* < .0043)
  - Patients with leukemia had highest CFR



Lee. Lancet Oncol. 2020;21:1309.

Slide credit: clinicaloptions.com

HIV and COVID-19

COVID-19 and HIV: In the Beginning

- Case Report 28 Jan 2020; Wuhan, China
  - 61-yr-old man with type 2 diabetes, heavy smoker
  - Presented with fever and cough
  - Also found to have HIV infection and CD4% 4.75; HIV viral load not reported
  - Chest CT showed pneumonia; RT-PCR+ for SARS-CoV-2
  - Treated with LPV/r, steroids, and recovered
- Over the next several months, several small case series published from Asia, Europe, and US—implications unclear given small sample size

Zhu. J Med Virol. 2020;92:529.

Slide credit: clinicaloptions.com

COVID-19 and HIV: Today

- Ongoing speculations
  - Are PWH being “protected” by their antivirals?
  - Is some immunosuppression paradoxically helpful given immune-mediated aspects of severe COVID-19?
- Some larger (n > 200) studies have been published with preliminary conclusions about COVID-19 in PWH
  - Some studies also include an HIV-negative population for comparison
- Ongoing concerns about the effect of the COVID-19 pandemic on access to care and psychological well-being
- Unresolved questions about COVID-19 vaccine for PWH

Slide credit: clinicaloptions.com

Risk and Features of COVID-19 in Persons With HIV in the US

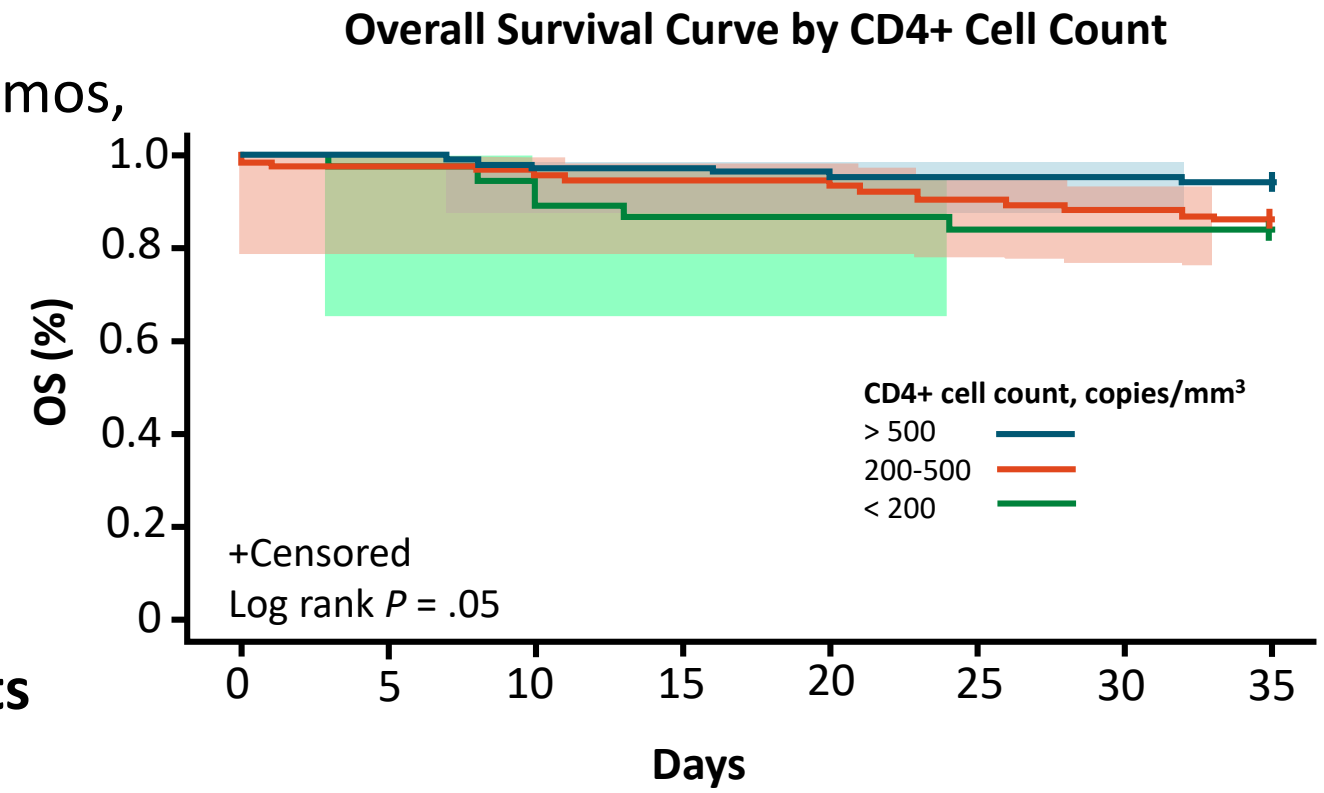
- MGH series: 36 PWH with confirmed, 11 with probable COVID-19[1]
  - 77% non-Hispanic black, Hispanic/Latinx (vs 40% black, Hispanic/Latinx in HIV clinic overall)
  - 85% had comorbidity associated with severe disease: obesity (33%), HTN (31%), DM (22%), hyperlipidemia (22%), chronic kidney disease (22%)
- Mount Sinai Hospital System: case-control study[2]
  - PWH admitted with COVID-19 (n = 88) matched to HIV-negative group by age, race/ethnicity, sex, wk of COVID-19 hospitalization admission (n = 405)
  - **No differences in disease severity on admission (*P* = .15) or adverse outcomes (mechanical ventilation or death) with vs without HIV infection**

1. Meyerowitz. AIDS. 2020;34:1781. 2. Sigel. Clin Infect Dis. 2020;71:2933.

Slide credit: clinicaloptions.com

COVID-19 and HIV: Multicenter Cohort

- 286 persons with HIV and COVID-19 from 36 institutions collected over 3 mos, mostly from US sites
  - 94.3% on ART; 88.7% with HIV virologic suppression
  - Primary outcome = ICU admission, mechanical ventilation, or death
- Older age, chronic lung disease, hypertension, and **lower CD4+ counts** associated with decreased survival
  - *No association between ART or lack of viral suppression and COVID-19 outcomes*



Dandachi. Clin Infect Dis. 2020;[Epub].

Slide credit: clinicaloptions.com

Incidence and Severity of COVID-19 in Persons With HIV Receiving ART in Spain

- Of 77,590 PWH receiving ART, 236 were diagnosed with COVID-19 in February - April 2020
- Calculated 75-day risk for COVID-19 diagnosis; hospital, ICU admission; and death
  - 151 hospitalizations, 15 admitted to the ICU, 20 deaths
- PWH did not have increased risk of COVID-19 diagnosis
- Higher age- and sex-standardized mortality from COVID-19 in PWH (3.7 per 10,000) than in the general population (2.1 per 10, 000)
  - In-line with greater all-cause mortality of PWH vs HIV-negative population in Spain
- Study unable to exclude residual confounding, but separately published sensitivity analyses did not change results

Del Amo. Ann Intern Med. 2020;173:536.

Slide credit: clinicaloptions.com

Outcomes of COVID-19 in Persons With HIV Receiving ART in Spain—Effect of ART?

- Patients receiving TDF (but not TAF) had *BETTER* outcomes: Is TDF protective or are those receiving TDF healthier?

Risk per 10,000 Persons Among PWH Receiving ART (95% CI)		PCR-Confirmed COVID-19 Diagnosis	COVID-19 Hospital Admission	COVID-19 ICU Admission	COVID-19 Death
Overall		30.4 (26.7-34.6)	19.5 (16.5-22.8)	1.9 (1.1-3.2)	2.6 (1.6-4.0)
Standardized*		30.0 (29.8-30.2)	17.8 (17.7-18.0)	2.5 (2.4-2.6)	3.7 (3.6-3.8)
NRTI	▪ FTC/TDF	16.9 (10.5-25.9)	10.5 (5.6-17.9)	0 (-2.9)†	0 (-2.9)†
	▪ FTC/TAF	39.1 (31.8-47.6)	20.3 (15.2-26.7)	2.7 (1.1-6.5)	3.9 (1.9-7.2)
	▪ ABC/3TC	28.3 (21.5-36.7)	23.4 (17.2-31.1)	3.0 (1.1-6.5)	4.0 (1.7-7.8)
	▪ Other regimens	29.7 (22.6-38.4)	20.0 (14.2-27.3)	1.0 (0.1-3.7)	1.0 (0.1-3.7)

*Standardized by age and sex of general Spanish population aged 20-79 yrs. †1-sided 97.5% CI.

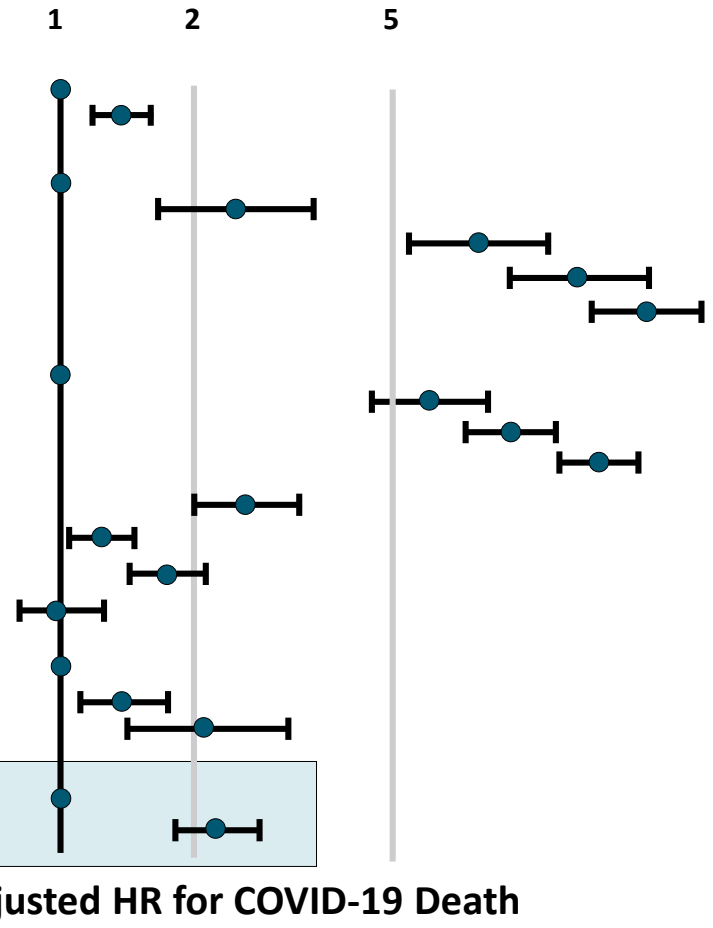
Del Amo. Ann Intern Med. 2020;173:536.

Slide credit: clinicaloptions.com

COVID-19 and HIV: Routine Public Sector Data in Western Cape, South Africa

- Evaluated factors among all adult public sector patients (N = 3,460,932)

Patient Characteristics	Adjusted HR	95% CI
Sex		
Female	1.00	
Male	1.45	1.23-1.70
Age		
20-39 yrs	1.00	
40-49 yrs	2.83*	1.92-4.15
50-59 yrs	7.78*	5.51-10.98
60-69 yrs	11.54*	8.11-16.42
≥ 70 yrs	16.79*	11.69-24.11
Noncommunicable diseases		
None	1.00	
Diabetes well controlled (A1C < 7%)	5.37*	3.96-7.27
Diabetes poorly controlled (A1C 7-8.9%)	8.53*	6.60-11.02
Diabetes uncontrolled (A1C ≥ 9%)	12.07*	9.70-15.02
Diabetes, no measure of control	2.91*	2.18-3.89
Hypertension	1.31†	1.09-1.57
Chronic kidney disease	1.86*	1.46-2.33
Chronic pulmonary disease	0.93	0.73-1.17
Tuberculosis		
Never tuberculosis	1.00	
Previous tuberculosis	1.51‡	1.18-1.93
Current tuberculosis	2.70*	1.81-4.04
HIV		
Negative	1.00	
Positive	2.14	1.70-2.70*



*$P < .001$. †$P = .004$. ‡$P = .001$.

22,308 total persons including 3978 PWH diagnosed with COVID-19

Standard mortality ratio for COVID-19 death *with* vs *without* HIV: 2.39 (95% CI: 1.96-2.86)

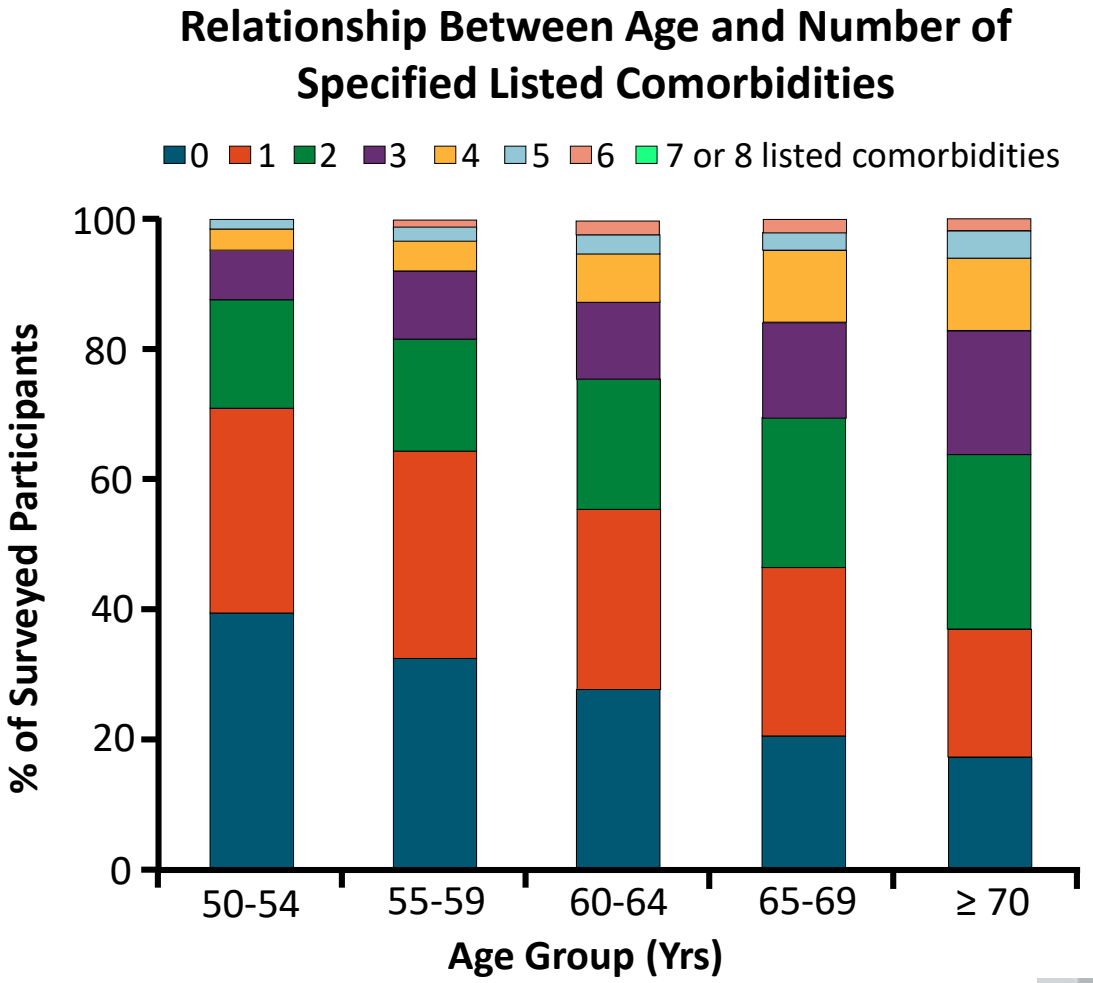
Study did not control for social determinants of care

Boulle. Clin Infect Dis. 2020;[Epub].

Slide credit: clinicaloptions.com

Comorbidities Increasingly Common as PWH Age

- National survey of PWH ≥ 50 yrs in UK (n = 4959)
- 97% on ART with viral load measured in last 9 mos
- Comorbidities: hypertension, 31%; hyperlipidemia, 31%; depression, 24%; renal impairment, 15%; CVD, 12%; obesity, 11%; type 2 diabetes, 11%; osteoporosis, 5%
- Multiple comorbidities common in older age groups

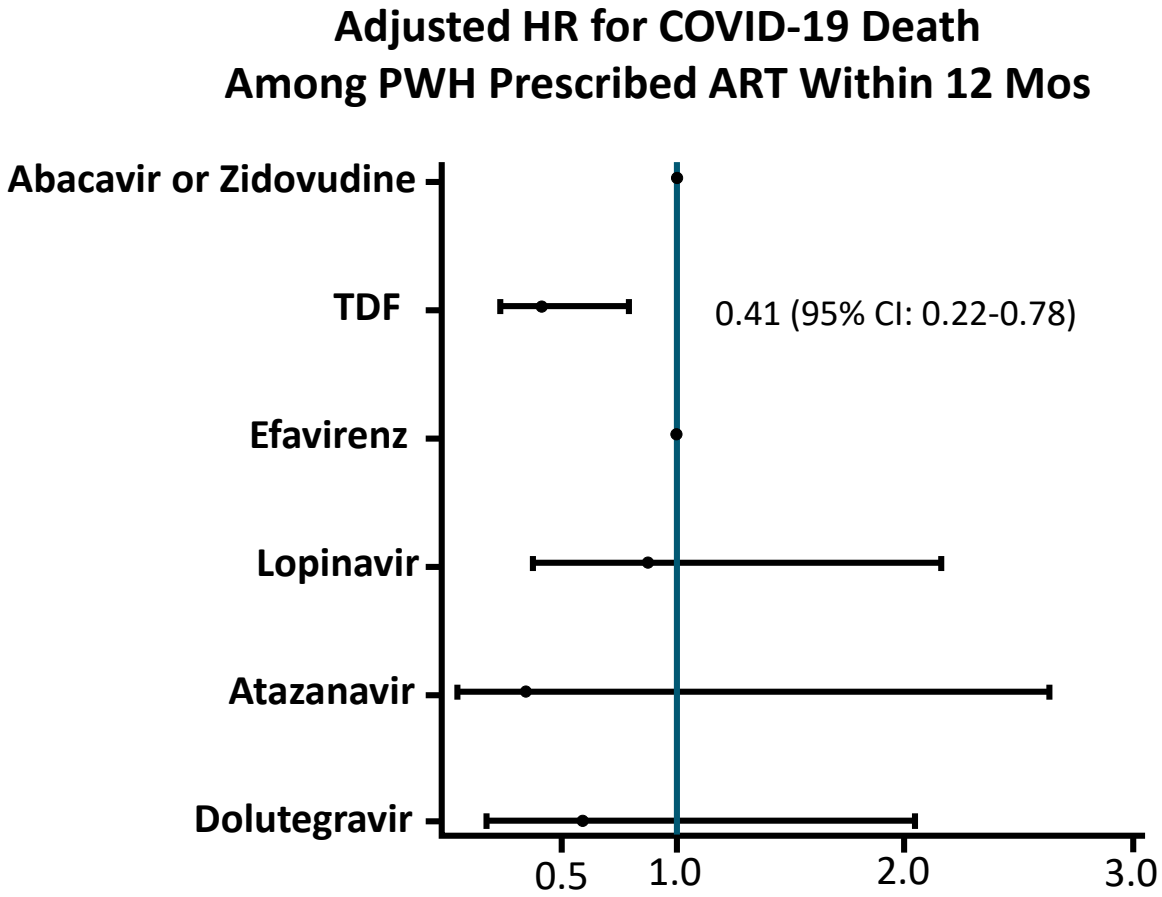


Ekong. HIV Med. 2020;21:409.

Slide credit: clinicaloptions.com

COVID-19 Mortality and HIV: Effect of Specific ART in South African Public Sector Data

- First line: TDF + XTC + EFV
- Second line: ZDV + 3TC + LPV/r
- DTG introduced January 2020 for both first- and second-line therapy
- Reduced risk of death in TDF group—group "enriched" for first-line therapy, possible confounder

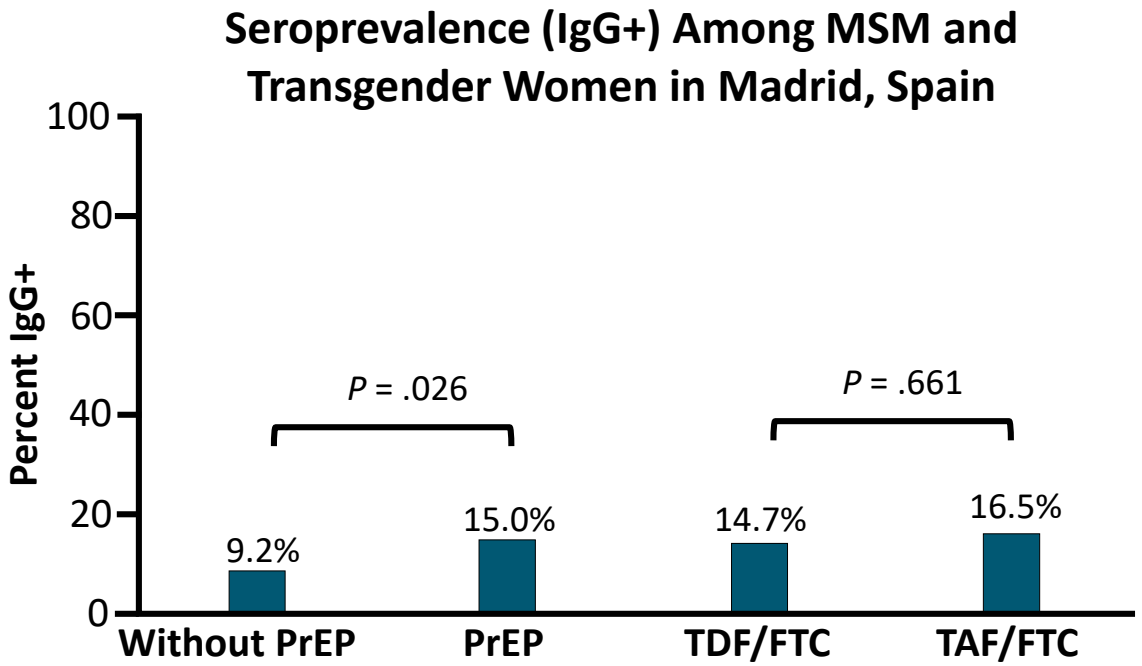


Boulle. Clin Infect Dis. 2020;[Epub]. Davies. medRxiv. 2020;[Preprint]. Note: This study has not been peer reviewed.

Slide credit: clinicaloptions.com

Preventative Efficacy of Tenofovir/Emtricitabine Against SARS-CoV-2 in PrEP Users?

- Observational study of MSM and transgender women without (n = 250) and with (n = 500) PrEP use: TDF/FTC (n = 409); TAF/FTC (n = 91)



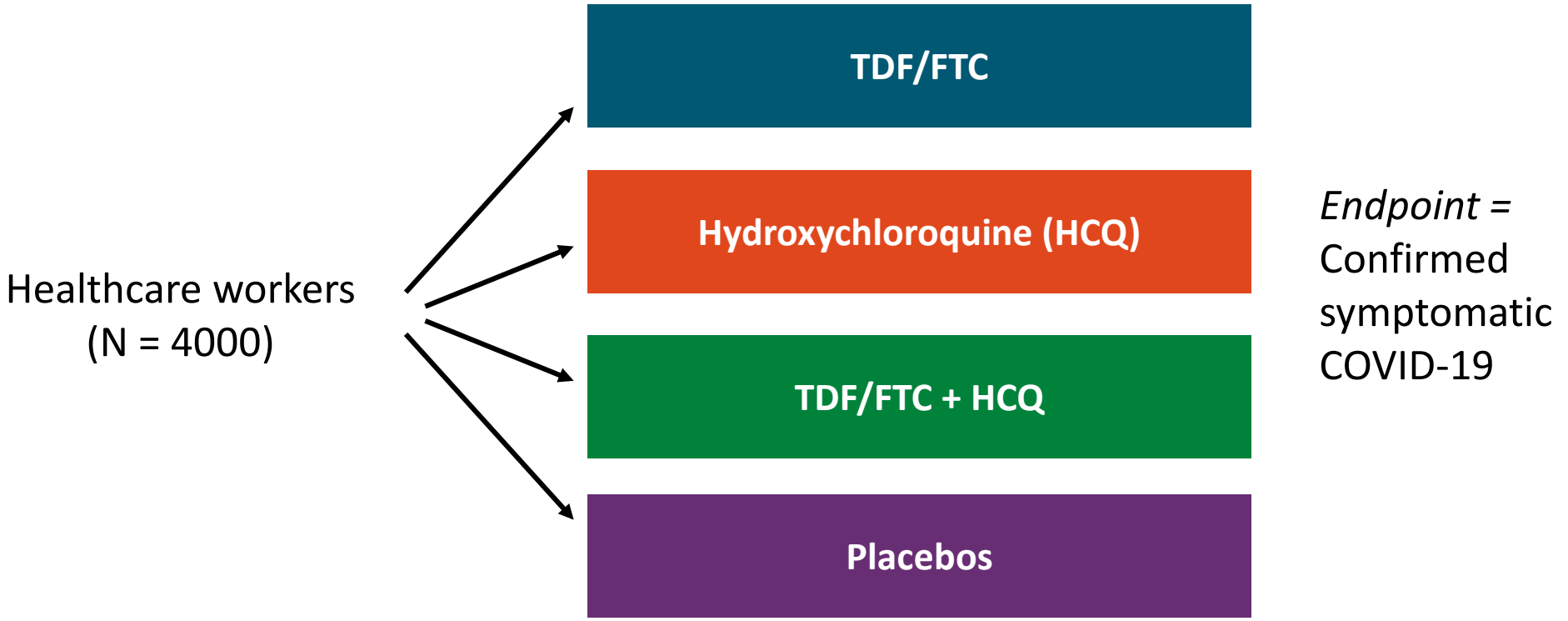
COVID-19 Outcome	PrEP Use		*P* Value	PrEP Type		*P* Value
	No	Yes		TDF/FTC	TAF/FTC	
Median symptom duration, days (IQR)	7 (4-14)	7 (4-13)	.41	7 (4-13)	10 (4-14)	.27
Required treatment, %	2	2.4	.73	2.7	1.1	.70

Ayerdi. Open Forum Infect Dis. 2020;7:ofaa455.

Slide credit: clinicaloptions.com

Ongoing Investigation: Drug Prevention of COVID-19

- EPICOS: Randomized trial for prevention of SARS-CoV-2 infection in healthcare personnel



NCT04334928.

Slide credit: clinicaloptions.com

VACS: COVID-19 Testing and Outcomes in PWH vs Persons Without HIV

- Compared PWH and COVID-19 (n = 253), PWH and no COVID-19 (n = 2346), HIV-uninfected persons with COVID-19 (n = 504), and HIV-uninfected persons without COVID-19 (n = 4473)
- Persons with HIV were more likely to be tested for COVID-19; HIV did not increase susceptibility to COVID-19, nor incidence of severe disease

COVID-19 Testing	PWH	HIV-	OR (95% CI)*
Alive in 2020, n	30,981	76,745	--
Total tested, n (%)†	2599 (8.4)	4977 (6.5)	1.36 (1.29-1.43)
Total COVID-19+, n	253	504	
▪ % of total alive	0.8	0.7	1.38 (1.18-1.61)
▪ % of those tested	9.7	10.1	1.05 (0.89-1.24)

COVID-19 Outcomes, n (%)	PWH (n = 253)	HIV- (n = 504)	HR (95% CI)‡
Hospitalization	86 (34.0)	178 (35.3)	1.09 (0.85-1.41)
ICU admission	35 (13.8)	75 (14.9)	1.08 (0.72-1.62)
Intubation	16 (6.3)	40 (7.9)	0.89 (0.49-1.59)
Death	24 (9.5)	56 (11.1)	1.08 (0.66-1.75)

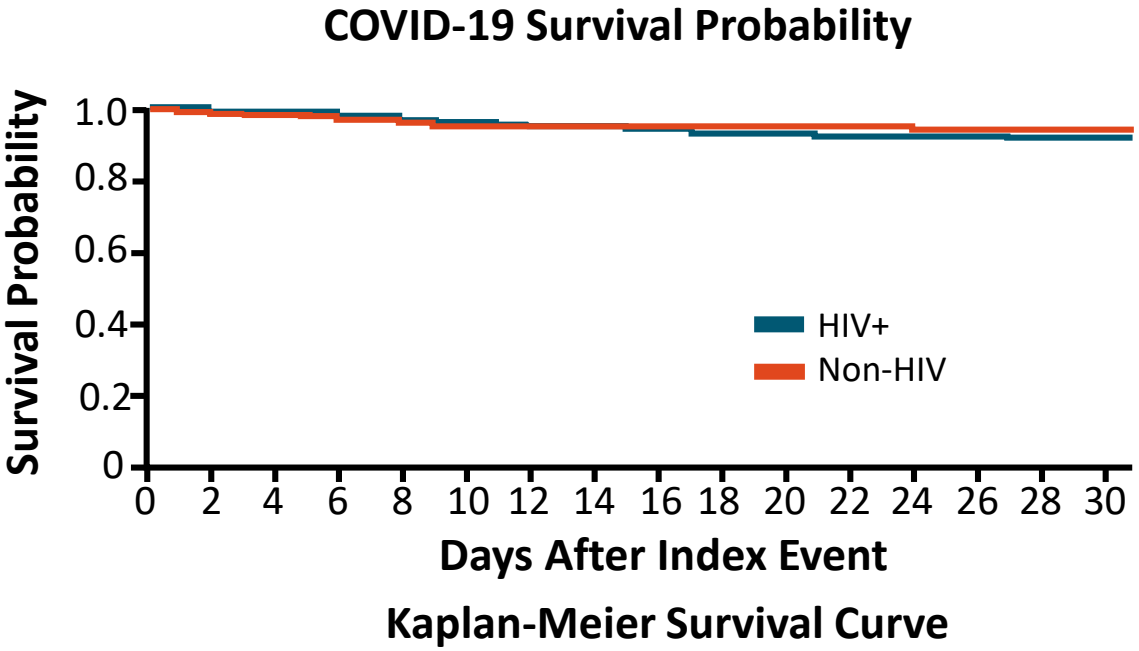
*Adjusted for age, race/ethnicity, sex, BMI, alcohol consumption, smoking. † % of total alive in 2020. ‡Adjusted for age, race/ethnicity, sex.

Park. AIDS 2020. Abstr LBPEC23.

Slide credit: clinicaloptions.com

Characteristics and Outcomes of COVID-19 in PWH: Multicenter Research Network

- Outcomes in COVID-19–positive patients with HIV (n = 404) compared with a propensity-matched cohort of patients without HIV (n = 49,763)
- In unmatched analysis, crude mortality higher for HIV
- **After 1:1 matching** (BMI, diabetes, hypertension, chronic lung diseases, chronic kidney disease, race, history of nicotine dependence and sex), **mortality no longer significantly different with vs without HIV (risk ratio: 1.33; 95% CI: 0.69-2.57)**



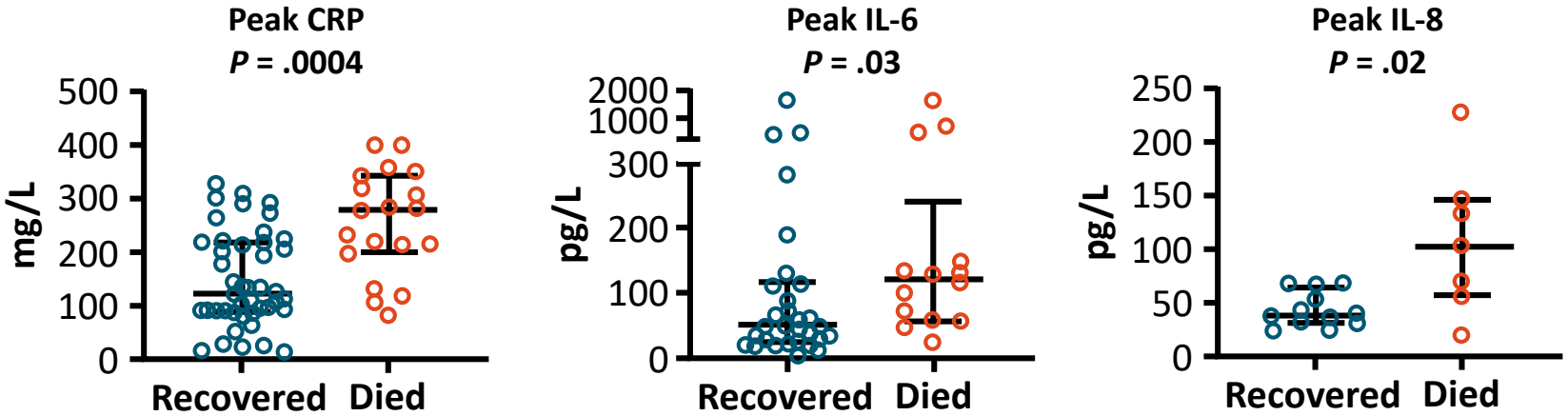
Kaplan-Meier Survival Curve

Hadi. AIDS. 2020;34:F3.

Slide credit: clinicaloptions.com

COVID-19 in PWH: Differences Between Patients Who Died and Patients Who Recovered

- 72/93 hospitalized; 26% (19/93) died; 74% (53/93) recovered
- Patients who died had lower nadir absolute lymphocyte counts (*P* = .0005) and final absolute lymphocyte counts (*P* = .002) vs patients who recovered
- Patients who died had higher CRP, IL-6, and IL-8 levels vs patients who recovered (differences in peak fibrinogen, D-dimer, TNF-α not statistically significant)



- No differences in age, sex, BMI, HIV duration, nadir/preceding/presenting CD4+ cell count, viral suppression before/during COVID-19

Ho. AIDS 2020. Abstr OAXLB01. Ho. J Infect Dis. 2021;223:403.

Slide credit: clinicaloptions.com

US Guidance on COVID-19 and HIV

Updated

CDC[1]

- Older adults and those with underlying medical conditions (eg, diabetes, heart conditions, COPD, obesity) are at highest risk of life-threatening COVID-19
- PWH not receiving effective ART or with low CD4+ cell counts may also be at increased risk for severe disease
- PWH should not switch their HIV medicine in an attempt to prevent or treat COVID-19
- In case of suppressed HIV viral load, PWH may discuss temporary postponement of routine medical and laboratory visits

NIH[2]

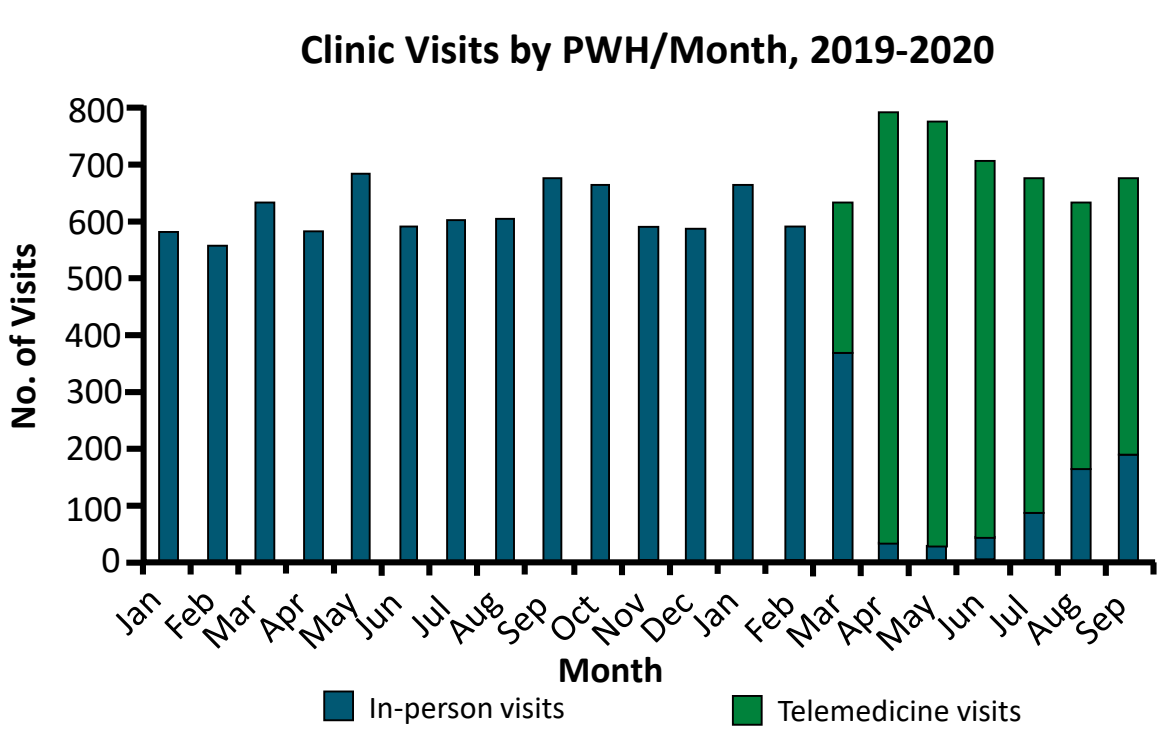
- Recommendations for treatment in PWH are the same as those for the general population
- In persons with advanced HIV and suspected or documented COVID-19, HIV-associated OIs should be considered in the differential diagnosis of febrile illness
- Pay attention to potential DDIs and overlapping toxicities among COVID-19 treatments, ARV medications, and other comedicatons
- PWH should be offered the opportunity to participate in clinical trials of vaccines and potential treatments for COVID-19

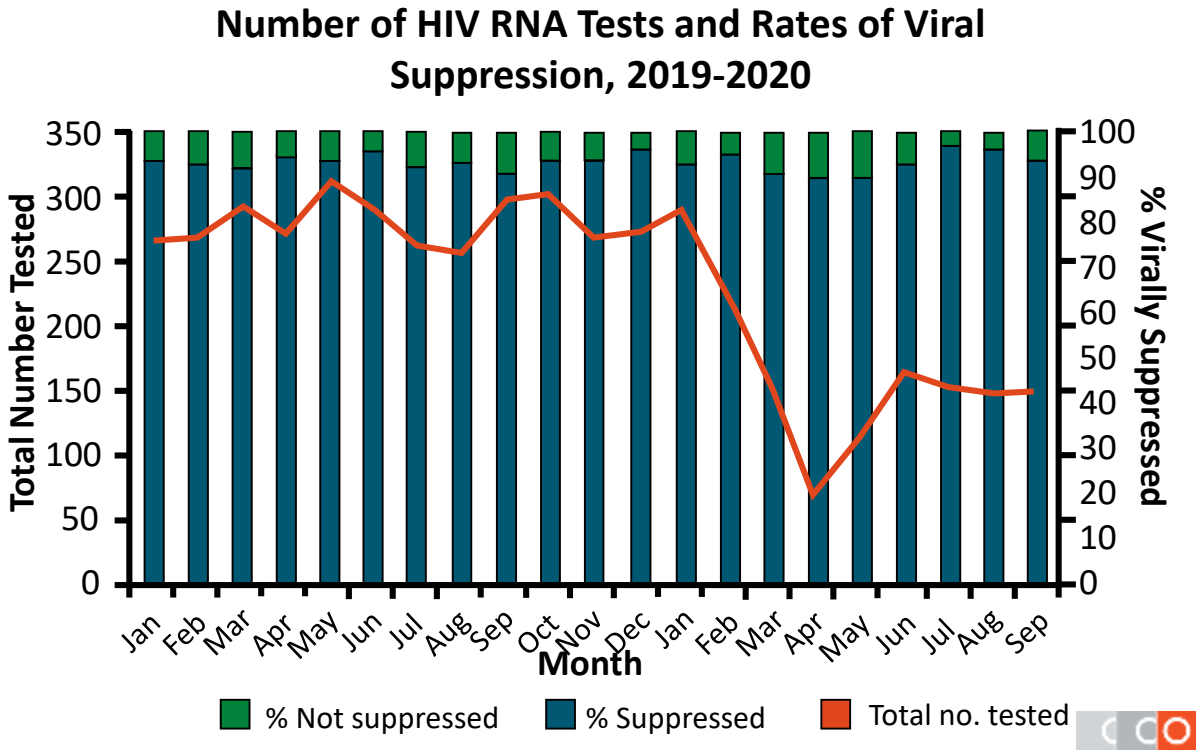
1. CDC. What to know about HIV and COVID-19. Last updated February 1, 2021.
2. NIH COVID-19 Treatment Guidelines. Special considerations in people with HIV. Last updated October 9, 2020.

Slide credit: clinicaloptions.com

COVID-19 and HIV: Impact of Telemedicine on Viral Suppression in PWH

- Analysis of in-person vs telemedicine visits at Fenway Community Health Center, Boston among 2016 PWH
- Visits overall increased despite a dramatic reduction in in-person care
- **No reduction in rate of viral suppression;** number of HIV-1 RNA tests declined sharply





Mayer. IDWeek 2020. Abstr 541.

Slide credit: clinicaloptions.com

Theoretical Risk of Adenovirus Type 5–Vectored Vaccines: Recent Expert Commentary

- In 2007, the Step and Phambili phase IIb HIV vaccine trials were halted for lack of efficacy
  - Vaccine: rAd5 viral vector without HIV-1 envelope
- Post-hoc analyses showed increased HIV infections in certain subgroups of men from both Step and Phambili
- A separate trial of DNA/rAd5 HIV-1 vaccine that *did* contain HIV envelope showed *no* increased risk of HIV acquisition
- 2013 NIH consensus conference on Ad5 vectors:
  - Warned that **non-HIV** vaccine trials using similar Ad5 viral vectors in areas of high HIV prevalence could lead to increased HIV-1 acquisition
- Buchbinder et al. recommend further safety studies for Ad5-vectored SARS-CoV-2 vaccines in development
- In some instances, HIV providers may need to counsel on mRNA and protein-based vs Ad5-vectored vaccines

Buchbinder. Lancet. 2020;396:e68.

Slide credit: clinicaloptions.com

COVID-19 in Pregnancy

Clinical Course of COVID-19 in Pregnancy

- Overall spectrum of COVID-19 symptoms similar in pregnant and nonpregnant women
- Early data from systematic review of studies to April 29, 2020, suggested pregnant women had similar COVID-19 course as nonpregnant adults[1]

Clinical Outcome, % (95% CI)	Total (N = 538*)
Severe disease	15.3 (11.1-20.8)
Critical disease	1.4 (0.5-4.1)
ICU admission	3.0 (1.6-5.9)

*China, n = 420; US, n = 76; Europe, n = 42.

- However, several recent studies demonstrated increased rate of hospitalizations, ICU care, and mechanical ventilation, but not death, in pregnant women vs age-matched nonpregnant controls[2-4]

1. Huntley. Obstet Gynecol. 2020;136:303. 2. Ellington. MMWR. 2020;69:769.
3. Badr. Am J Obstet Gynecol. 2020;223:764. 4. Blitz. Am J Obstet Gynecol. 2020;223:290.

COVID-19 and Pregnancy

- Assessment of incidence of hospitalization and ventilation among pregnant vs nonpregnant women of childbearing age with laboratory-confirmed SARS-CoV-2 infection in the US January 22 - June 7, 2020 (N = 91,412)

Characteristic, n (%)	Pregnant (n = 8207)	Nonpregnant (n = 83,205)
Age, yrs		
▪ 15-24	1921 (23.4)	19,557 (23.5)
▪ 25-34	4469 (54.4)	31,818 (38.2)
▪ 35-44	1817 (22.1)	31,830 (38.3)
Symptomatic	5199 (97.1)	72,549 (96.9)
Symptoms		
▪ Cough	1799 (51.8)	23,554 (53.7)
▪ Fever	1190 (34.3)	18,474 (42.1)
▪ Muscle aches	1323 (38.1)	20,693 (47.2)
▪ Chills	989 (28.5)	15,630 (35.6)
▪ Headache	1409 (40.6)	22,899 (52.2)
▪ Dyspnea	1045 (30.1)	13,292 (30.3)

Characteristic, n (%)	Pregnant (n = 8207)	Nonpregnant (n = 83,205)
Symptoms, cont'd		
▪ Sore throat	942 (27.1)	13,681 (31.2)
▪ Diarrhea	497 (14.3)	10,113 (23.1)
▪ Nausea/vomiting	682 (19.6)	6,795 (15.5)
▪ Loss of taste/smell	587 (16.9)	7,262 (16.6)
Underlying condition	1878 (22.9)	29,142 (35.0)
▪ Diabetes mellitus	288 (15.3)	1866 (6.4)
▪ Chronic lung disease	409 (21.8)	3006 (10.3)
▪ Cardiovascular disease	262 (14.0)	2082 (7.1)
▪ Chronic renal disease	12 (0.6)	266 (0.9)
▪ Chronic liver disease	8 (0.4)	141 (0.5)
▪ Immunocompromised	66 (3.5)	811 (2.8)

Ellington. MMWR. 2020;69:769.

Slide credit: clinicaloptions.com

COVID-19 Among Pregnant vs Nonpregnant Women

- Increased rates of hospitalization, ICU care, and mechanical ventilation, but no increase in symptomatic disease or mortality
  - Indication for hospitalization not recorded (may have tested positive during hospitalization for labor and delivery)

Outcome, n (%)	Pregnant (n = 8207)	Nonpregnant (n = 83,205)	Crude Risk Ratio (95% CI)	Adjusted Risk Ratio* (95% CI)
Hospitalization[†]	2587 (31.5)	4840 (5.8)	5.4 (5.2-5.7)	5.4 (5.1-5.6)
ICU admission[‡]	120 (1.5)	757 (0.9)	1.6 (1.3-1.9)	1.5 (1.2-1.8)
Mechanical ventilation[§]	42 (0.5)	225 (0.3)	1.9 (1.4-2.6)	1.7 (1.2-2.4)
Death[‖]	16 (0.2)	208 (0.2)	0.8 (0.5-1.3)	0.9 (0.5-1.5)

*Adjusted for age as continuous variable, yes/no for presence of underlying conditions, categorical race/ethnicity variable; nonpregnant women are the reference group. [†]Missing information for 1539 (18%) pregnant women and 9744 (12%) nonpregnant women, who were assumed to have not been hospitalized. [‡]Missing information for 6079 (74%) pregnant women and 58,888 (71%) nonpregnant women, who were assumed to have not been admitted to ICU. [§]Missing information for 6351 (77%) pregnant women and 63,893 (77%) nonpregnant women, who were assumed to have not required mechanical ventilation. [‖]Missing information for 3819 (47%) pregnant women and 17,420 (21%) nonpregnant women, who were assumed to have survived.

Ellington. MMWR. 2020;69:769.

Slide credit: clinicaloptions.com

ICU Admissions Among COVID-19–Positive Pregnant vs Nonpregnant Women: France, Belgium

- Multicenter case-control study of clinical outcomes among pregnant and nonpregnant women of reproductive age with positive SARS-CoV-2 RT-PCR test between January 1, 2020, and May 13, 2020, at 4 large university hospitals in France and Belgium (N = 200)
  - No difference in BMI or comorbidities

Clinical Outcomes, %	Pregnant (n = 83)	Nonpregnant (n = 107)	Adjusted *P* Value
ICU admission	11.08	2.38	.024
Hospital admission for COVID-19	58.21	17.4	< .001
Oxygen therapy	36.04	17.24	.006
Endotracheal intubation	10.16	1.67	.022

Badr. Am J Obstet Gynecol. 2020;223:764.

Slide credit: clinicaloptions.com

ICU Admissions Among COVID-19–Positive Pregnant vs Nonpregnant Women: NYC

- Retrospective analysis of ICU admissions among pregnant and nonpregnant women of reproductive age with positive SARS-CoV-2 RT-PCR test between March 4, 2020, and April 9, 2020, at 7 NYC hospitals (N = 414)

ICU Admissions by Age, n/N (%)	Pregnant (n = 82)	Nonpregnant (n = 332)	*P* Value
< 25 yrs	1/11 (9.1)	3/7 (42.9)	.09
25-29 yrs	0/17 (0)	5/40 (12.5)	.16
30-34 yrs	2/33 (6.1)	5/44 (11.4)	.46
35-39 yrs	3/15 (20.0)	9/55 (16.4)	.73
40-49 yrs	2/6 (33.3)	28/190 (14.7)	.28
Total	8/82 (9.8)	50/332 (15.1)	.22

Blitz. Am J Obstet Gynecol. 2020;223:290.

Slide credit: clinicaloptions.com

Preterm Labor and Nonelective Cesarean Deliveries

- Pregnant women with severe COVID-19 appear to have increased risk of preterm and CD
- Fever and hypoxemia: known risk factors for preterm labor and PPROM
- Preterm deliveries by CD may be due to interventions to improve maternal respiratory status

- Review of 538 COVID-19 cases (420 in China)[1]
  - 20% delivered before 37 wks; 85% delivered by CD
- Prospective cohort of 241 SARS-CoV-2+ women in NYC hospitals[2]
  - 61.4% asymptomatic (31% subsequently symptomatic); 14.6% preterm births
  - CD: 41.5% all comers, 52.4% severe disease, 91.7% critical disease

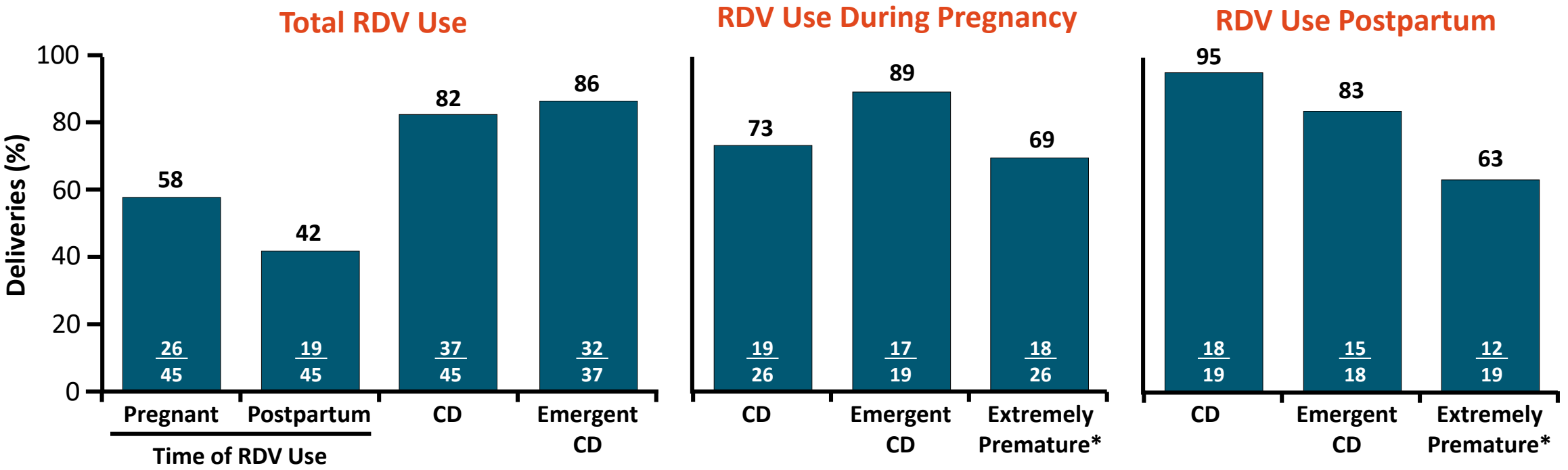
1. Huntley. Obstet Gynecol. 2020;136:303. 2. Khoury. Obstet Gynecol. 2020;136:273.

Slide credit: clinicaloptions.com

Pregnancy Outcomes in COVID-19–Positive Pregnant Women Receiving Compassionate Use Remdesivir

Updated

- Compassionate use of remdesivir among pregnant women hospitalized with COVID-19 between March 21, 2020 and June 16, 2020 (N = 86)
- Among 45 deliveries, CD rate was higher among women who received remdesivir postpartum vs during pregnancy



*24-32 wks of gestation.

Burwick. Clin Infect Dis. 2020;[Epub].

Slide credit: clinicaloptions.com

Mother-to-Child Transmission of SARS-CoV-2 and Neonatal Infections

- Need for classification based on timing of transmission (in utero or congenital, intrapartum, postpartum); several proposed classifications exist
- Congenital and intrapartum infections are rare events (limited to case reports and small case series)
- Outcome in neonates favorable; assessment may be complicated by risks of prematurity

- Prospective cohort of 245 liveborn neonates born to 241 SARS-CoV-2+ women giving birth in NYC hospitals[1]
  - 30.0% newborn resuscitation beyond standard, 25.7% admitted to NICU (mostly owing to prematurity), 62.4% hospitalized ≤ 2 days
  - 230/236 (97.5%) of documented SARS-CoV-2 RT-PCR results negative
  - Rates of spontaneous abortion, stillbirth, IUGR unknown, but 2 anecdotal case reports (0.8%) in this series

1. Khoury. Obstet Gynecol. 2020;136:273.

Slide credit: clinicaloptions.com

Case Study: Transplacental Transmission of SARS-CoV-2 Infection

- Mother with documented viremia delivered male neonate in third trimester
  - Neonatal viremia soon after birth
  - Neonate bronchoalveolar lavage positive for SARS-CoV-2 E and S genes by RT-PCR
- Histologic examination of placenta showed inflammation with intervillositis and infiltrates of neutrophil and CD68+ histiocytes
  - Perivillous trophoblastic cells stained positive for SARS-CoV-2 by immunohistochemistry
  - Very high viral load: 11.15 log copies/1 x 10^6 placental cells by RT-PCR
- On Day 3, neonate had sudden irritability, poor feeding, axial hypertonia, opisthotonos; CSF negative for SARS-CoV-2 and other pathogens; cerebral ultrasound and EEG normal
  - Symptoms improved slowly over 3 days
- Neonate had radiographic evidence of CNS involvement on MRI at Day 11: bilateral gliosis of deep white periventricular and subcortical matter, with slightly left predominance
- Neonate gradually recovered and was discharged after 18 days

Vivanti. Nat Commun. 2020;11:3572.

Management of Symptomatic COVID-19 in Pregnancy

Potential Therapy	Considerations
Remdesivir	▪ PALM study of Ebola included pregnant women (6/77 or 7.8% of remdesivir recipients)[1] ▪ Manufacturer guidance: use only if potential benefit justifies potential risk for mother/fetus[2]
Hydroxychloroquine ± azithromycin	▪ Used for other indications in pregnancy; data do not support efficacy in COVID-19
Systemic corticosteroids	▪ Limit betamethasone use to those at high risk for preterm delivery within 7 days; administer only between 23 wks and 33 wks, 6 days of gestation[3] ▪ Dexamethasone may be considered for severe COVID-19 with hypoxemia (MFM consultation) ▪ After initial dexamethasone use, prednisone or betamethasone may be favorable substitute
Other immunomodulators and convalescent plasma	▪ Should be used only in clinical trial that allows enrollment of pregnant women
Other considerations[4]	▪ Fever control (acetaminophen) and VTE prophylaxis ▪ Most clinical trials in COVID-19 exclude pregnant women

1. Mulangu. NEJM. 2019;381:2293. 2. Remdesivir PI. 3. Barbieri. NEJM Journal Watch Women's Health. COVID-19 Obstetric Practice Recommendations. 4. Favilli. J Matern Fetal Neonatal Med. 2020:1.

Compassionate Use of Remdesivir in Pregnant Women With Severe COVID-19

Updated

Patients With Lab Abnormality, n (%)	All (N = 86)	Pregnant (n = 67)	Postpartum (n = 19)
Any grade 3/4	n = 84 15 (18)	n = 67 12 (18)	n = 18 3 (17)
ALT	n = 81	n = 64	n = 17
▪ Grade 1	13 (16)	10 (16)	3 (18)
▪ Grade 2	9 (11)	8 (13)	1 (6)
▪ Grade 3	7 (9)	6 (9)	1 (6)
▪ Grade 4	0	0	0
AST	n = 79	n = 62	n = 17
▪ Grade 1	16 (20)	10 (16)	6 (35)
▪ Grade 2	14 (18)	12 (19)	2 (12)
▪ Grade 3	4 (5)	3 (5)	1 (6)
▪ Grade 4	0	0	0

Patients With Lab Abnormality, n (%)	All (N = 86)	Pregnant (n = 67)	Postpartum (n = 19)
Creatinine	n = 83	n = 65	n = 18
▪ Grade 1	4 (5)	2 (3)	2 (11)
▪ Grade 2	7 (8)	5 (8)	2 (11)
▪ Grade 3	3 (4)	1 (2)	2 (11)
▪ Grade 4	3 (4)	3 (5)	0

Burwick. Clin Infect Dis. 2020;[Epub].

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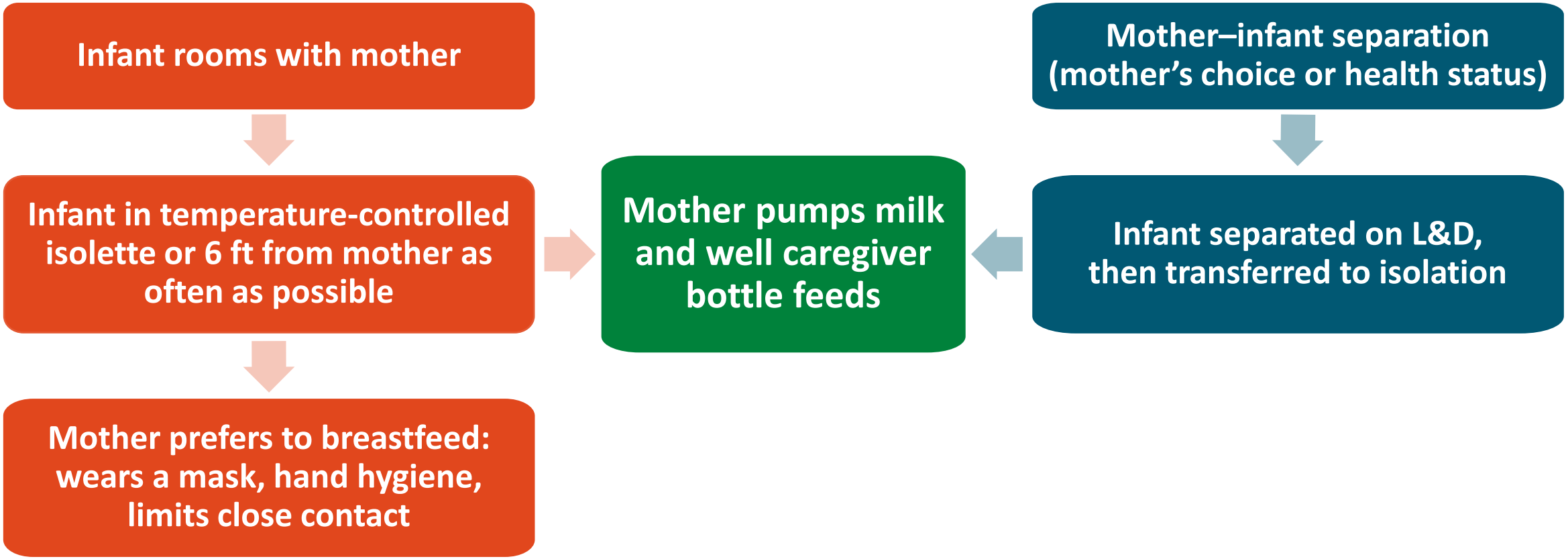
Management of Laboring Mothers: Universal Screening on Labor and Delivery

Area (N)	Prevalence of SARS-CoV-2 in Asymptomatic Patients, %	Time Frame
New York/Mount Sinai (155)[1]	15.5	April 4-15, 2020
Connecticut (770)[2]	2.9	April 2-29, 2020
Boston (757)[3]	1.5	April 18 - May 5, 2020
Chicago (614)[4]	1.6	April 8-27, 2020
Los Angeles (80)[5]	0	April 4-11, 2020

1. Bianco. Obstet Gynecol. 2020;136:283. 2. Campbell. JAMA. 2020;323:2520. 3. Goldfarb. Infect Control Hosp Epidemiol. 2020;27:1. 4. Miller. Obstet Gynecol. 2020;136:232. 5. Naqvi. Obstet Gynecol. 2020;136:235.

Postpartum Management of Mothers With Suspected or Confirmed COVID-19



https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019
https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html
https://www.cdc.gov/coronavirus/2019-ncov/hcp/caring-for-newborns.html

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COVID-19 in Children

NIH: Special Considerations for COVID-19 in Children

- Limited data available on disease severity and pathogenesis of SARS-CoV-2 infection in children
- Epidemiologic studies suggest that manifestations of acute disease are less severe in children vs adults
  - Preliminary CDC data show lower hospitalization, ICU admission rates in children vs adults
  - Severe cases in children associated with younger age and underlying conditions
- Multisystem inflammatory syndrome reported in children (MIS-C)

"Currently, remdesivir is the only drug approved by the FDA for the treatment of COVID-19 in hospitalized patients… It is approved for children with COVID-19 who are aged ≥ 12 yrs and weigh ≥ 40 kg. Remdesivir is also available for younger children (and those weighing < 40 kg and > 3.5 kg) through an FDA Emergency Use Authorization."

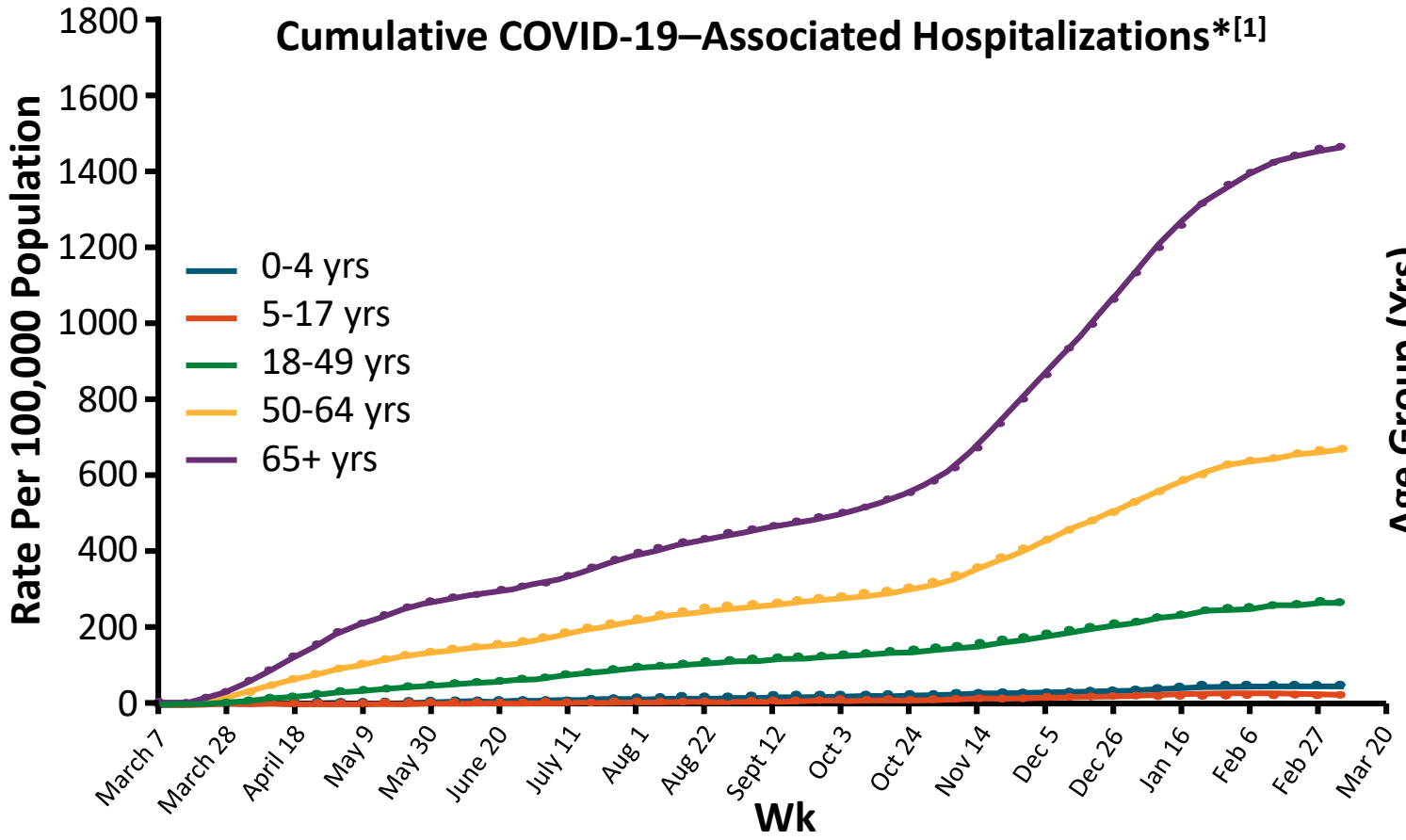
"For other agents outlined in these guidelines, there are insufficient data to recommend for or against the use of specific antivirals or immunomodulatory agents for the treatment of COVID-19 in pediatric patients."

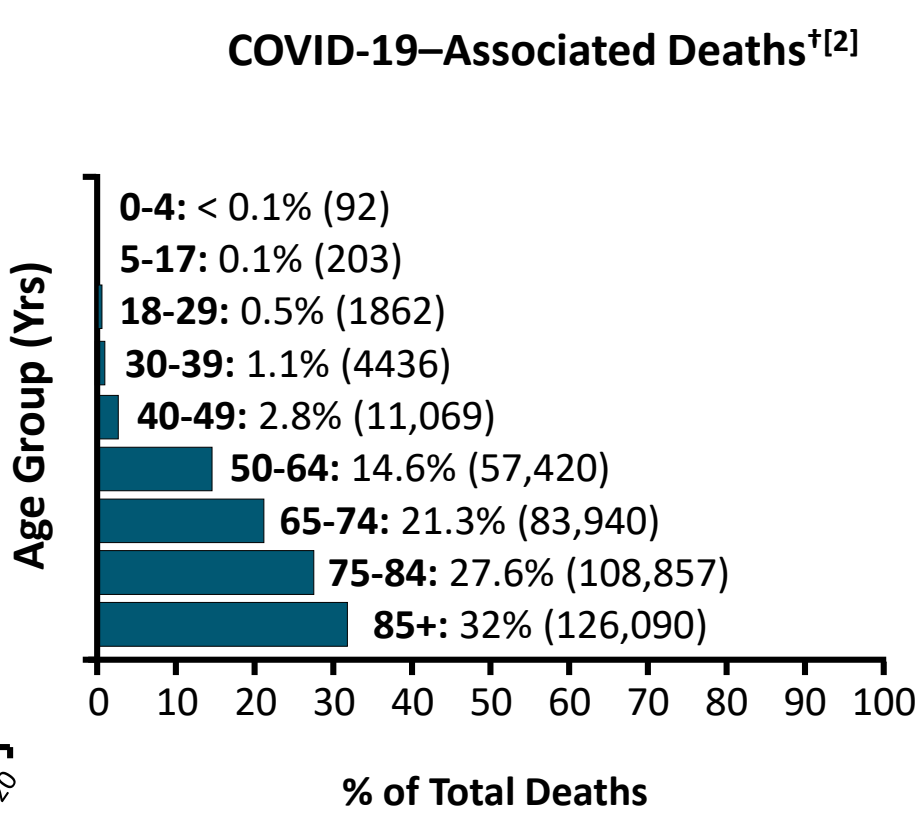
NIH COVID-19 Treatment Guidelines. Special considerations in children. Last updated November 3, 2020.

Slide credit: clinicaloptions.com

COVID-19–Associated Hospitalization and Death Rates Increase With Age in US

Updated





*Lab-confirmed COVID-19 cases; covers ~ 10% of US population: 99 counties in 14 states (CA, CO, CT, GA, IA, MD, MI, MN, NM, NY, OH, OR, TN, UT).

†Data from 394,004 deaths in confirmed and probable COVID-19 cases as reported by US states and territories; age group data available for 393,969 deaths (99%).

1. https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html
2. https://www.cdc.gov/covid-data-tracker/index.html#demographics.

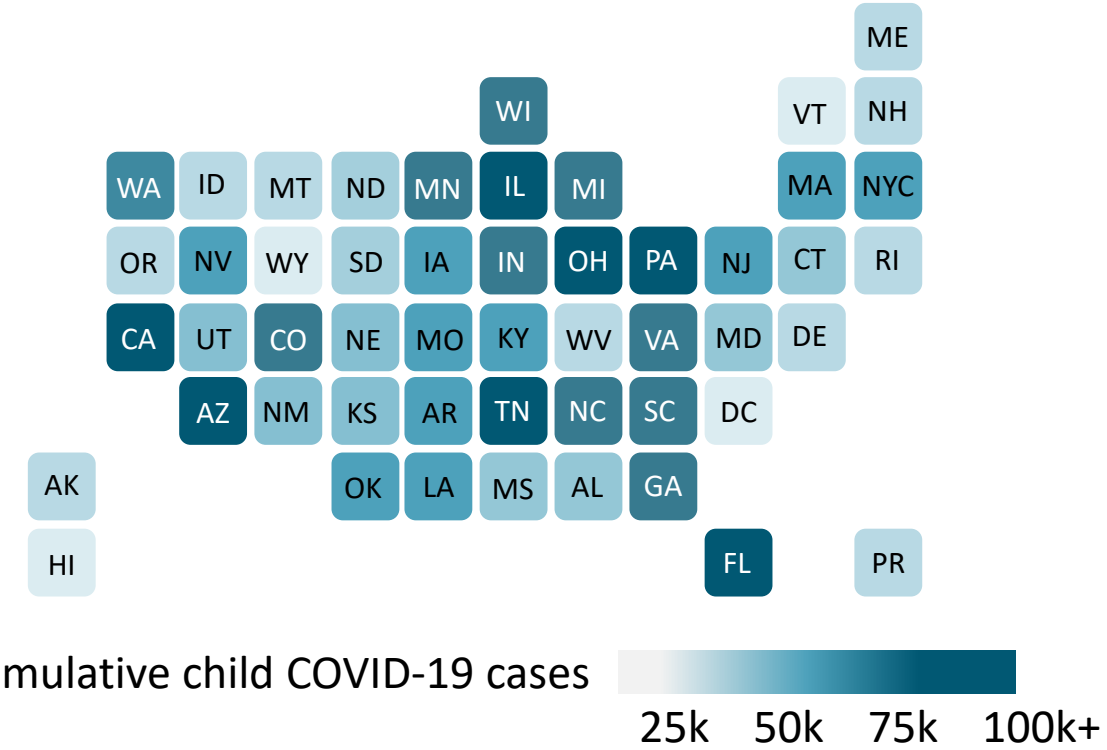
Slide credit: clinicaloptions.com

American Academy of Pediatrics: COVID-19 Cases in Children in the United States

Updated

Cumulative COVID-19 Child Cases*

8 states with 100,000+ cumulative child cases



- 3,284,531 total child COVID-19 cases reported; 13.2% of all cases
  - Rate: 4364 cases/100,000 population
- In 24 states and NYC, children were 1.3% to 3.0% of total hospitalizations
  - 0.1% to 2.1% of all child COVID-19 cases resulted in hospitalization
- In 43 states, NYC, Puerto Rico, and Guam, children were 0% to 0.19% of deaths
  - 0% to 0.03% of all child COVID-19 cases resulted in death

*Based on data from health department Web sites from 49 states, NYC, Washington DC, Puerto Rico, and Guam on March 11, 2021. Age ranges reported for children vary by state (0-14, 0-17, 0-18, 0-19, or 0-20 yrs).

AAP. Children and COVID-19: State-Level Data Report.
https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/

Systematic Review of COVID-19 in Pediatric Patients

- Systematic review of studies reporting cases of COVID-19 confirmed by RT-PCR in patients < 21 yrs of age (131 studies, N = 7880)

Characteristic	N	All Patients
Male sex, n (%)	4640	2582 (55.6)
Mean age, yrs (SD)	4517	8.9 (0.5)
Exposure from family member, n (%)	1360	1028 (75.6)
Underlying condition, n (%)	655	233 (35.6)
▪ Immunosuppression	655	71 (30.5)
▪ Respiratory	655	49 (21.0)
▪ Cardiovascular	655	32 (13.7)
Coinfection, n (%)	1183	72 (5.6)
Asymptomatic, n (%)	2367	456 (19.3)
Fever, n (%)	2445	456 (59.1)
Cough, n (%)	2445	1367 (55.9)

Outcome, n (%)	N	All Patients
Chest CT findings		
▪ Normal	1115	367 (32.9)
▪ Patchy lesions	1115	211 (18.9)
▪ Ground-glass opacity	1115	117 (10.5)
▪ Consolidation	1115	72 (6.5)
ICU admission	3564	116 (3.3)
Mechanical ventilation	7780	42 (0.54)
Complications		
▪ Shock	7780	19 (0.24)
▪ DIC	7780	9 (0.12)
▪ Kidney failure	7780	9 (0.12)
▪ Cardiac failure	7780	8 (0.10)
▪ MIS-C	7780	11 (0.14)
Death	7780	7 (0.09)

Hoang. EClinicalMedicine. 2020;24:100433.

Slide credit: clinicaloptions.com

CDC Case Definition: Multisystem Inflammatory Syndrome in Children

Individual < 21 yrs of age presenting with fever,* laboratory evidence of inflammation,† and evidence of clinically severe illness requiring hospitalization with involvement of ≥ 2 organ systems (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurologic)

And:

No alternative plausible diagnoses

And 1 of the following:

Positive current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test

Exposure to a suspected or confirmed COVID-19 case within 4 wks prior to symptom onset

*Fever ≥ 38°C for ≥ 24 hrs or report of fever lasting ≥ 24 hrs.
†Including, but not limited to, elevated CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, LDH, or IL-6; elevated neutrophils; reduced lymphocytes; and low albumin.

CDC. Information for HCPs about MIS-C. Last reviewed February 17, 2021. https://www.cdc.gov/mis-c/hcp/.

Slide credit: clinicaloptions.com

MIS-C in Children and Adolescents in United States

- Surveillance study for MIS-C from March 15 to May 20, 2020, in pediatric health centers in 26 US states (N = 186)

Clinical Characteristics, n (%)	All (N = 186)
Previously healthy	135 (73)
No. of organ systems involved	
▪ 2	18 (10)
▪ 3	36 (19)
▪ ≥ 4	132 (71)
Outcome	
▪ Still hospitalized*	52 (28)
▪ Discharged	130 (70)
▪ Died	4 (2)

Clinical Characteristics, n (%)	All (N = 186)
Organ systems involved	
▪ Gastrointestinal	171 (92)
▪ Cardiovascular	149 (80)
▪ Hematologic/thrombotic	142 (76)
▪ Mucocutaneous	137 (74)
▪ Respiratory	131 (70)
▪ Musculoskeletal	43 (23)
▪ Renal	15 (8)
▪ Neurologic	12 (6)

*As of May 20, 2020.

Feldstein. NEJM. 2020;383:334.

Slide credit: clinicaloptions.com

CDC: Evaluation and Management of Multisystem Inflammatory Syndrome in Children

- Clinical presentation varies but typically includes persistent fever, abdominal pain, vomiting, diarrhea, skin rash, mucocutaneous lesions, elevated inflammatory markers, and markers of cardiac damage

Laboratory Testing/Evaluations
▪ Inflammation testing: CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, LDH, IL-6, neutrophils, lymphocytes, albumin
▪ SARS-CoV-2 detection by RT-PCR or antigen test
▪ SARS-CoV-2 serology testing is suggested, even in the presence of a positive RT-PCR or antigen test; any serology test should be done prior to administering IVIG or exogenous antibody treatments
▪ Echocardiogram and electrocardiogram
▪ Cardiac enzyme or troponin testing
▪ B-type natriuretic peptide (BNP) or NT-proBNP

Management*
▪ Supportive measures: fluid resuscitation, inotropic support, respiratory support, and ECMO if needed
▪ IVIG and steroids
▪ Aspirin
▪ Antibiotics
▪ Thrombotic prophylaxis

*There are no studies comparing efficacy of treatment options. The AAP and ACR have published guidance on managing pediatric patients with MIS-C.

CDC. Information for HCPs about MIS-C. Last reviewed February 17, 2021. https://www.cdc.gov/mis-c/hcp/.

SARS-CoV-2 Transmission in Schools/Children

Updated

- Preliminary evidence from 14 contact-tracing studies of reduced SARS-CoV-2 susceptibility in children/adolescents vs adults (pooled OR: 0.56; 95% CI: 0.37-0.85)[1]

Location	Data on SARS-CoV-2 Transmission in Schools/Children
Italy[2]	▪ 1.8% (1212/65,104) of schools have reported SARS-CoV-2 infections ▪ Single case in 92.7% of instances; only 1 high school–based cluster of > 10 infections identified
Victoria, Australia[3]	▪ 8.2% (1635/19,901) of SARS-CoV-2 infections linked to early child education and care or schools ▪ Single case in 66% of instances; < 10 cases 91% of the time
England[4]	▪ Student-to-student transmission occurred in 9.1% of 55 school-based outbreaks during June/July 2020; most cases linked to outbreaks (73%) originated in staff vs children
Germany[5]	▪ Among 48 school outbreaks during Jan 28-Aug 31, infections less common in those 6-10 yrs of age vs older
US[6]	▪ During Mar 1-Sept 19, COVID-19 incidence ~ 2 x higher in children 12-17 yrs of age vs 5-11 yrs of age
UK[7]	▪ 50% (34/68) of children 2-15 yrs of age positive for SARS-CoV-2 antibodies reported no symptoms in multicenter observational cohort study during Apr 16-July 3

1. Viner. JAMA Pediatr. 2021;175:143. 2. Buonsenso. Front Pediatr. 2021;8:615894. 3. Russell. COVID-19 in Victorian schools. September 25, 2020. 4. Ismail. Lancet Infect Dis. 2021;21:344. 5. Otte im Kampe. Euro Surveill. 2020;25:2001645. 6. Leeb. MMWR Morb Mortal Wkly Rep. 2020;69:1410. 7. Waterfield. Arch Dis Child. 2020;[Epub].

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