Virtual Pre-Conference

Continuity of HIV Care in the Presence of COVID-19

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What to Know about COVID-19, HIV, and Antiretrovirals

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INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

Outline

- Evolution and epidemiology of COVID-19 pandemic
- Clinical presentation and diagnostic approaches
- Antiretrovirals as treatment for COVID-19
- COVID-19 infection among PWH
- Synergies and lessons learned from HIV
- Conclusions and Recommendations

Evolution and Epidemiology of COVID-19 Pandemic

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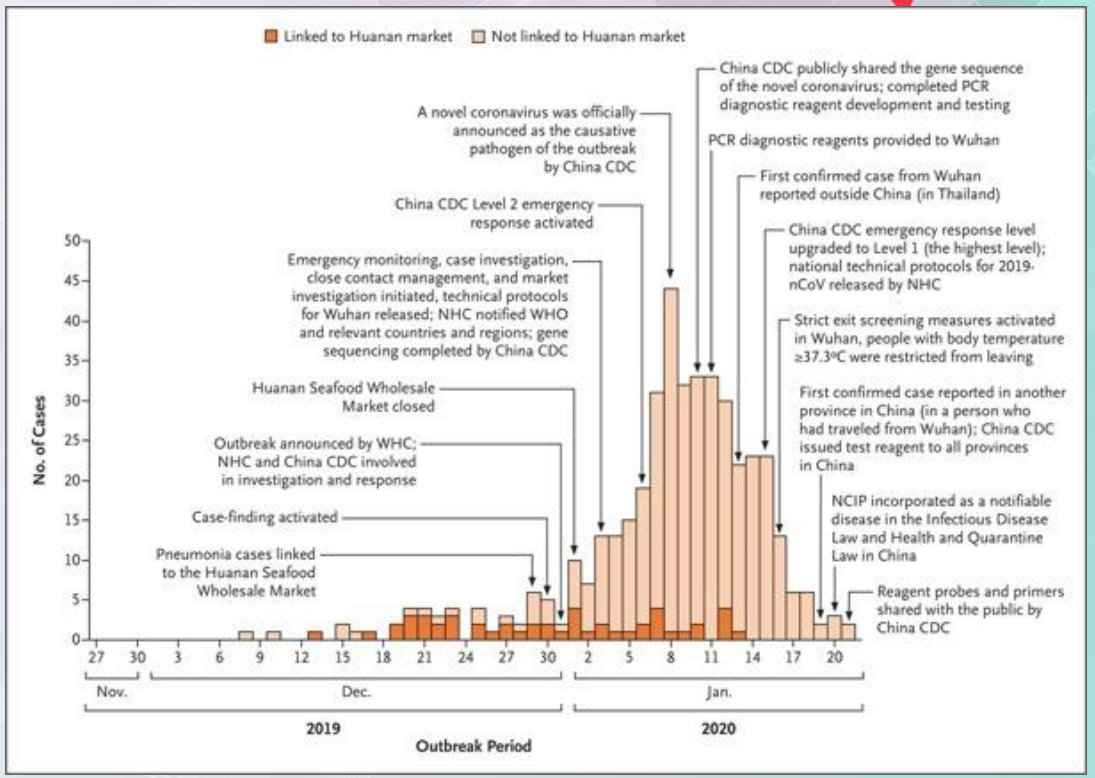
Identification and Evolution of COVID-19 Pandemic

- **December 2019**: A pneumonia of unknown origin was detected in Wuhan, China
- **January 2020**: WHO declared a Public Health Emergency of International Concern
- **February 2020**: New coronavirus disease identified as COVID-19 (SARS-CoV-2)
- **March 2020**: WHO declared a Global Pandemic
- **May 2020**: More than 3,650,000 cases of COVID-19 reported globally



Source: N Engl J Med 2020; 382:1199-1207
DOI: 10.1056/NEJMoa2001316

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Rapid Expansion from Hubei to Global Spread

Figure 1. Countries, territories or areas with reported confirmed cases of 2019-nCoV, 23 January 2020

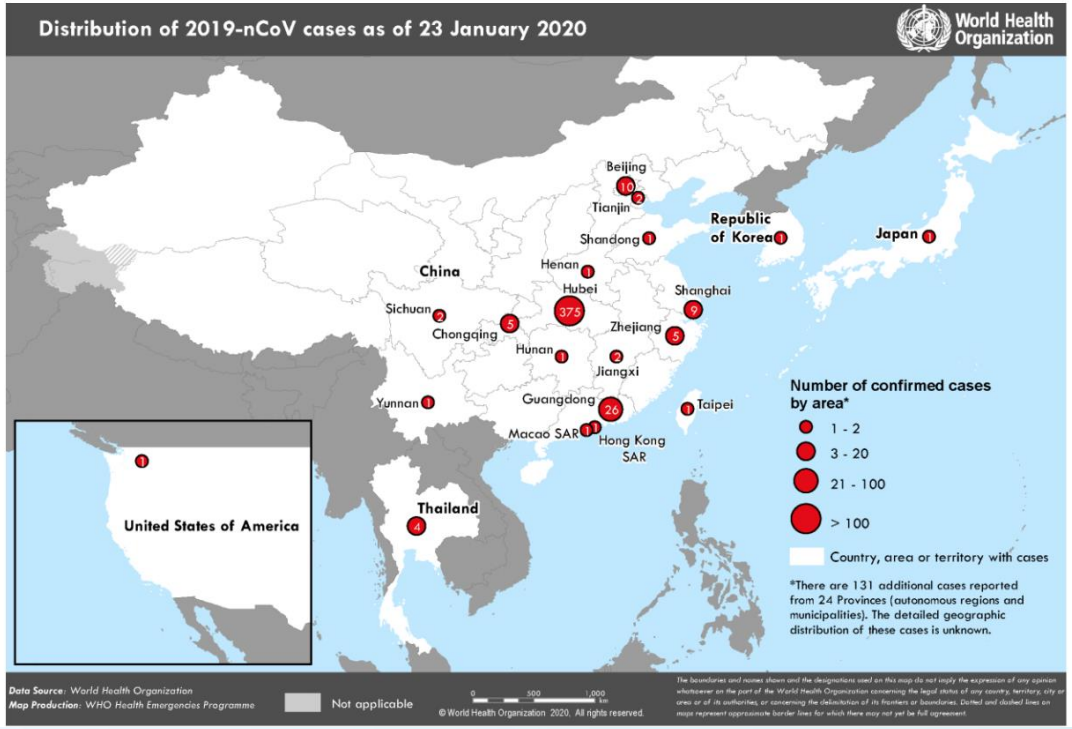
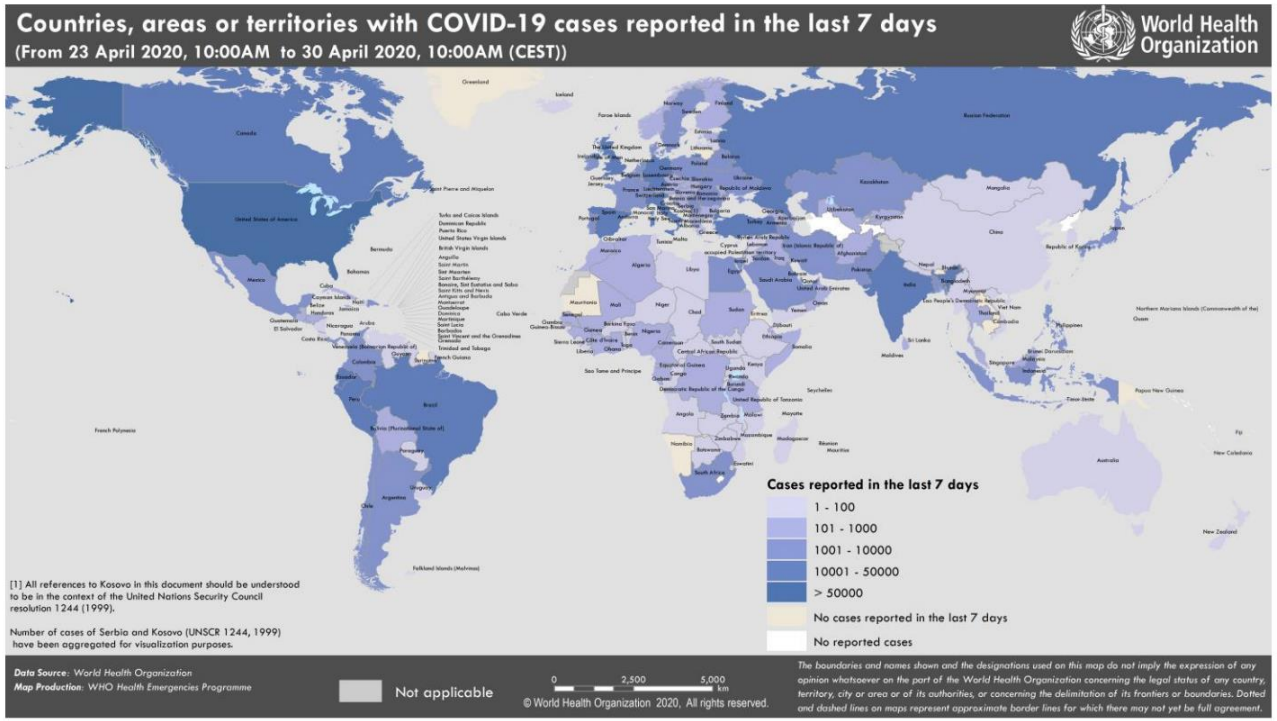


Figure 1. Countries, territories or areas with reported confirmed cases of COVID-19, 30 April 2020



Source: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200123-sitrep-3-2019-ncov.pdf?sfvrsn=d6d23643_8

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Source: https://coronavirus.jhu.edu/map.html

Global Impact of COVID-19

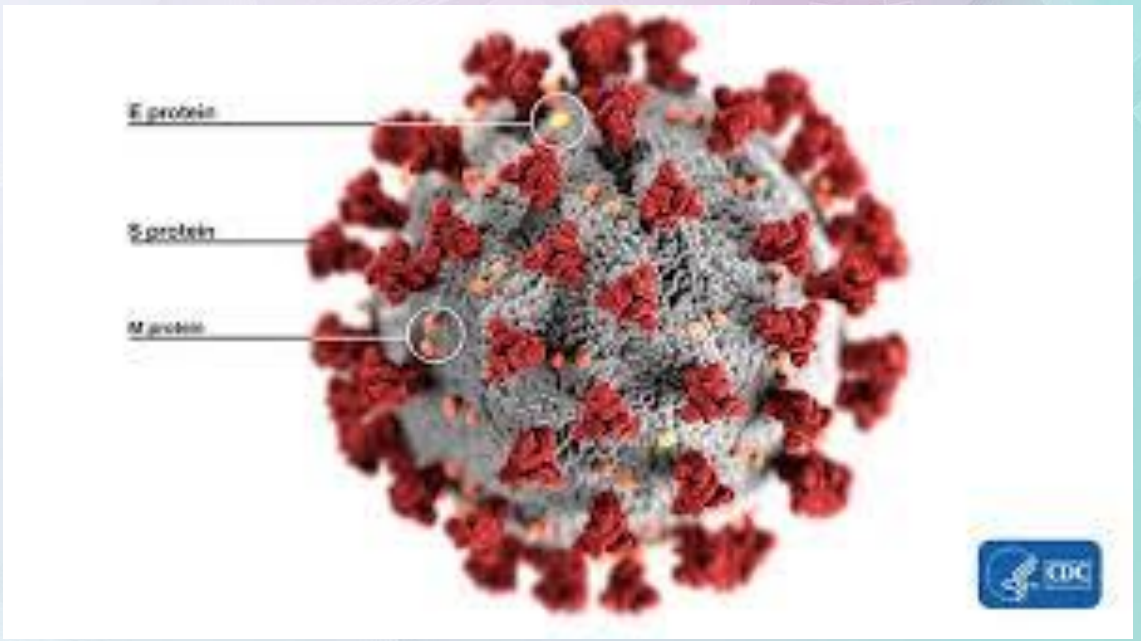
History of Viral Pandemics

Year	Virus	Geographic Spread	Estimated Deaths
1918	Spanish Influenza	Global	20-100 million
1957	Asian Influenza	Global	0.7-1.5 million
1968	Hong Kong Influenza	Global	1 million
1981	HIV/AIDS	Global	36.7 million
2003	Severe Acute Respiratory Syndrome (SARS)	4 continents; 37 countries	744
2009	H1N1 Swine Influenza	Global	151,000-575,000
2015	Zika	76 countries	4 million infections

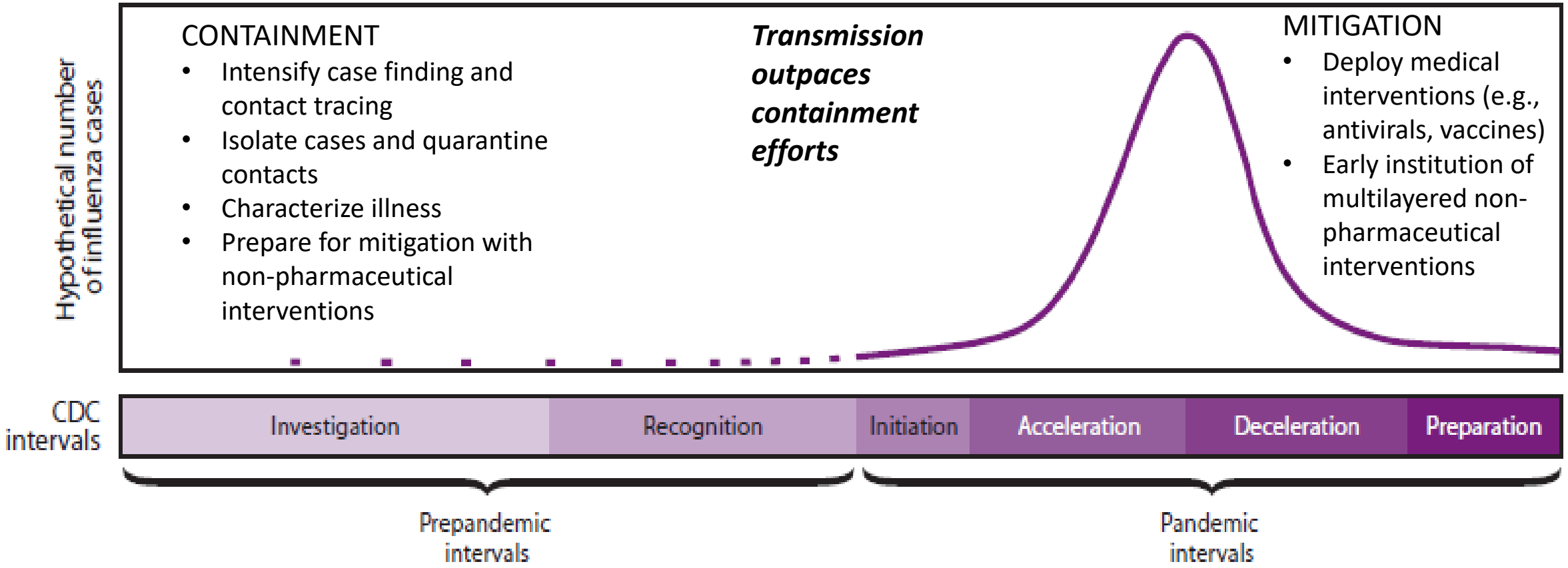
Source: Adapted from COVID-19 and HIV, IAS Webinar, Dr. Anton Pozniak; available at https://www.iasociety.org/HIV-Programmes/Cross-cutting-issues/COVID-19-and-HIV-Webinars

SARS CoV-2

- Member of the *Coronaviridae* family
  - Severe Acute Respiratory Virus (SARS-CoV), 2003
  - Middle East Respiratory Syndrome (MERS-CoV), 2012
- Natural reservoir in bats; spillover into humans at wet markets
- Illness that it causes is COVID-19

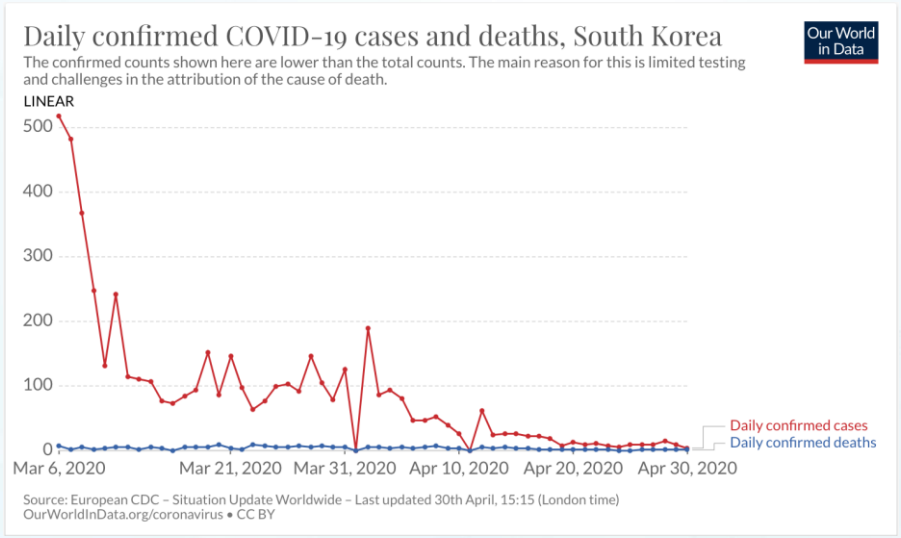


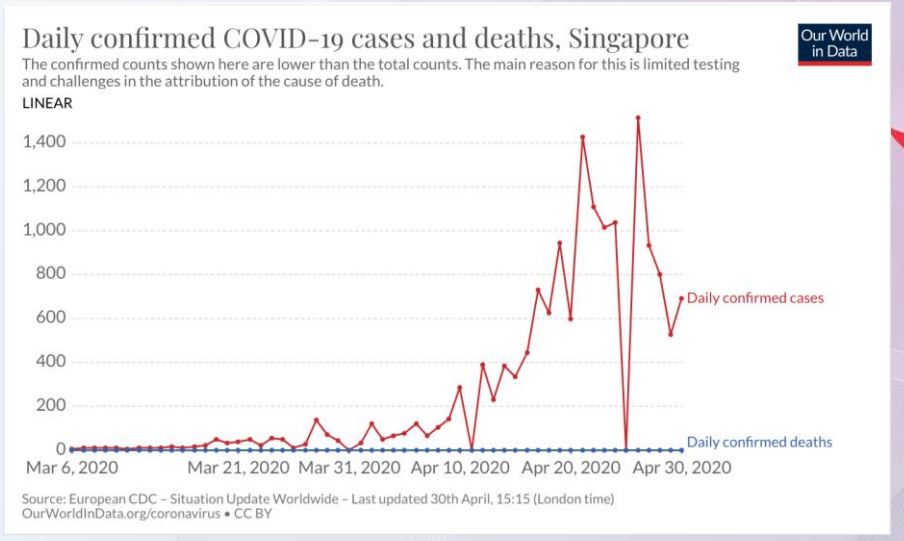
Response: Containment, Contact Tracing and Mitigation

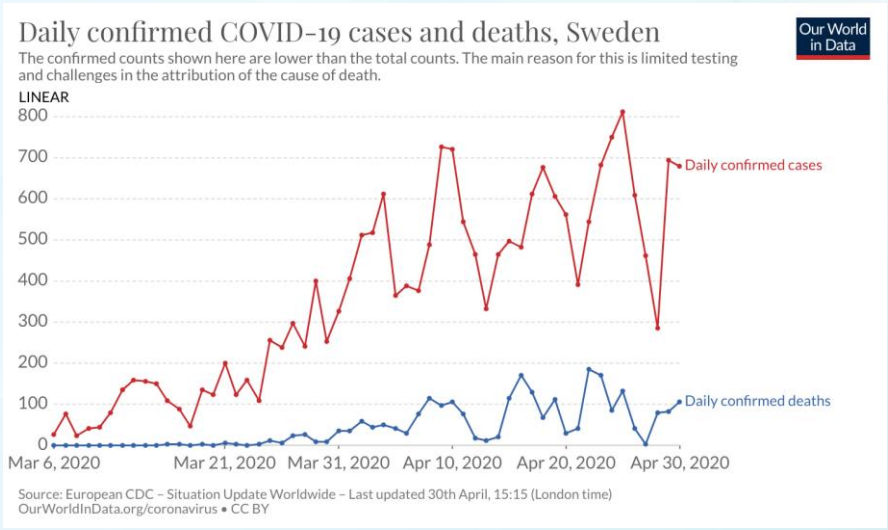


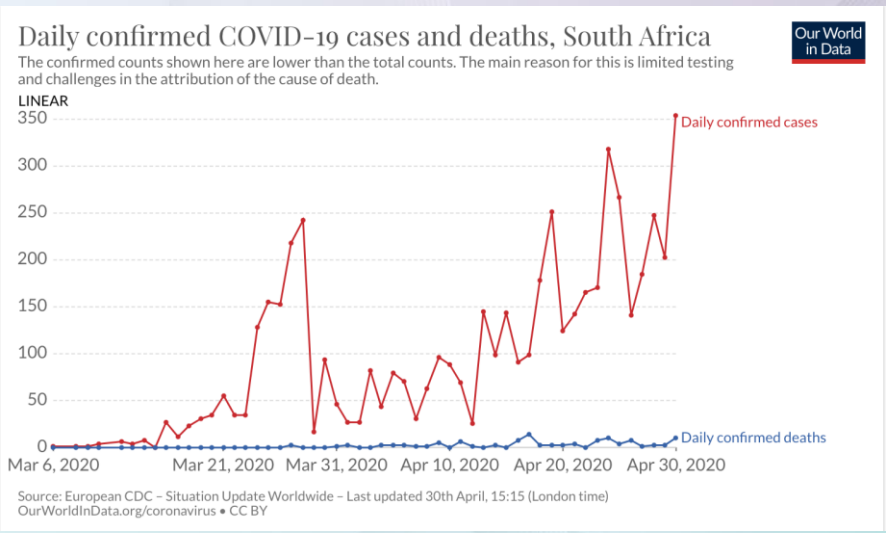
Adapted from Dr. John Brooks, CDC, March 10, 2020 CROI presentation
Sources: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6306a1.htm, https://www.cdc.gov/nonpharmaceutical-interventions/index.html

Differing Responses to COVID-19









Source: https://ourworldindata.org/grapher/daily-covid-cases-deaths?year=2020-04-30&time=2020-03-06..&country=KOR

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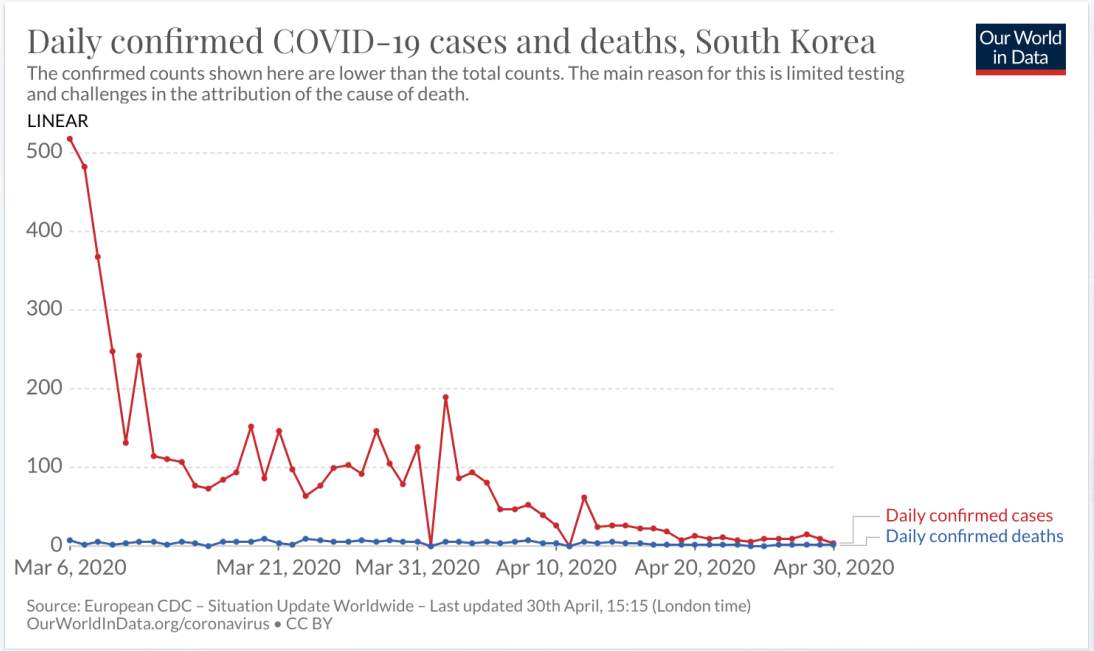
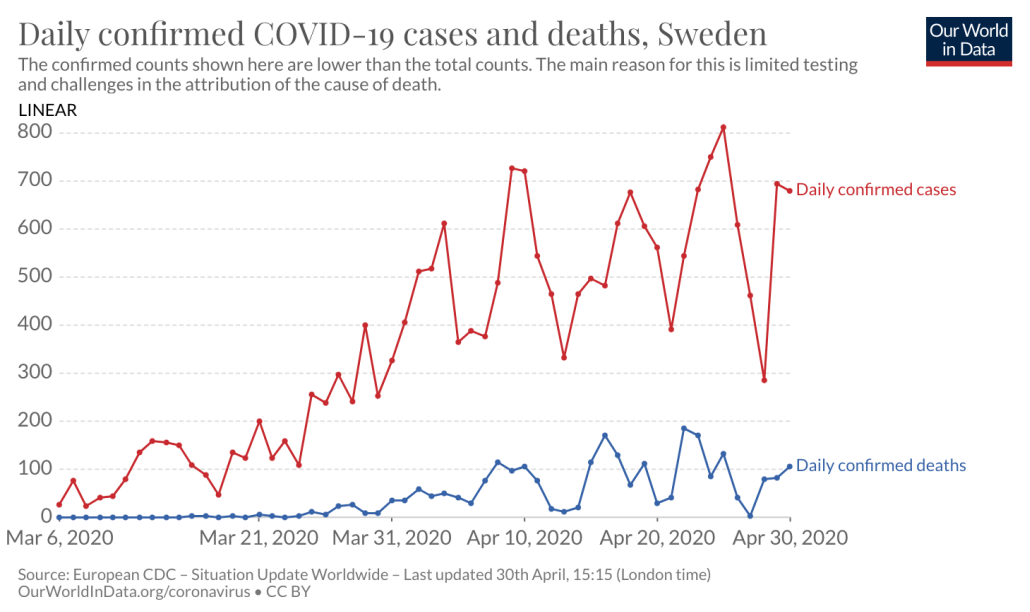
Differing Responses to COVID-19- South Korea



- Widespread testing available ~10,000s of people/day
- In late February had an outbreak among a religious group which was rapidly contained
- Since then decrease in daily number of confirmed cases to less than 10 per day

Source: https://ourworldindata.org/grapher/daily-covid-cases-deaths?year=2020-04-30&time=2020-03-06..&country=KOR

Differing Responses to COVID-19- Sweden

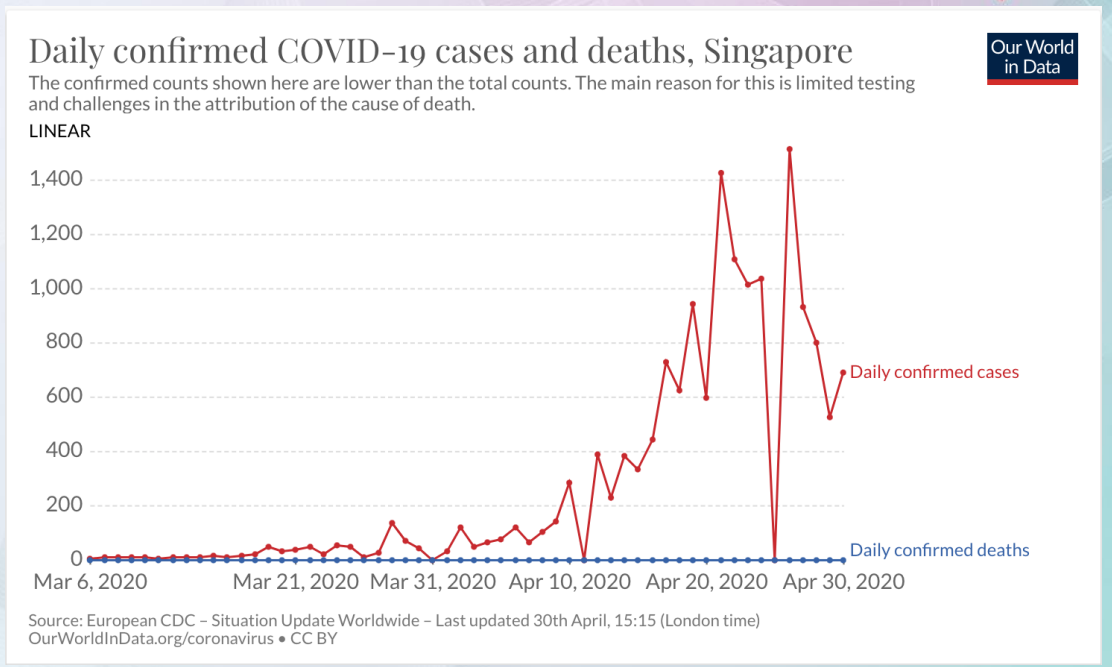


- No stay at home orders issued
- Prohibited public gatherings of >50 and visits to nursing homes
- Social distancing in restaurants
- Online secondary schools and universities; primary schools and daycares remain open
- High numbers of deaths
- Likely high levels of herd immunity

Source: https://ourworldindata.org/grapher/daily-covid-cases-deaths?year=2020-04-30&time=2020-03-06..&country=KOR

Differing Responses to COVID-19- Singapore

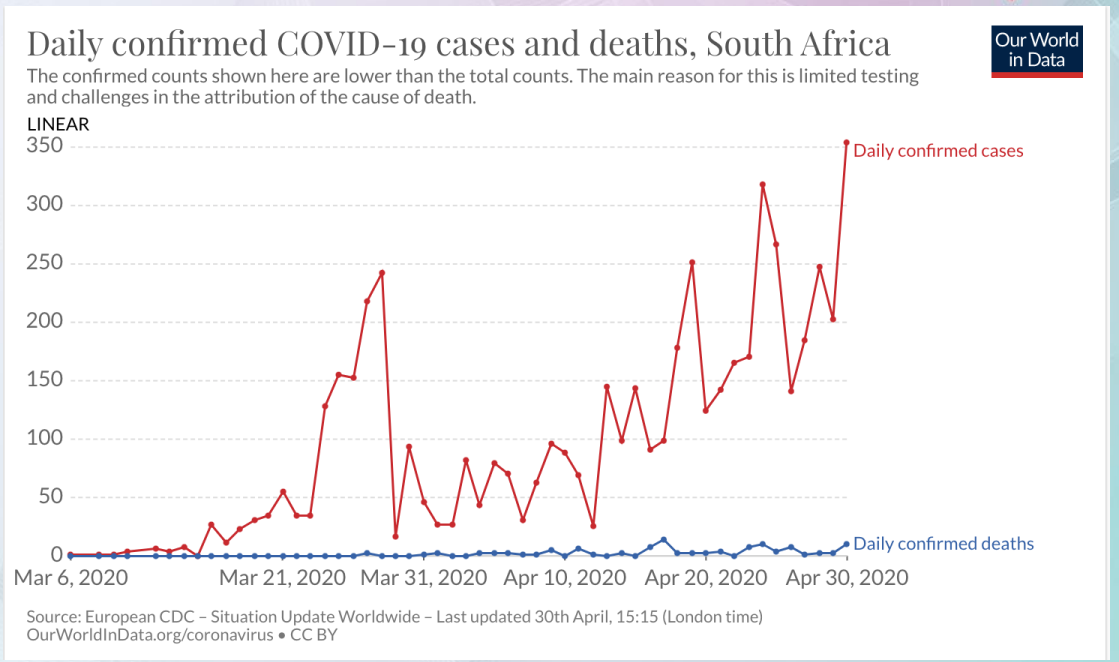
- Instituted a “circuit breaker”- i.e., package of restrictions
- Activated Pandemic Preparedness Plan
- Conducted enhanced surveillance for pneumonia and ILI
- Instituted quarantines and contact tracing
- All persons testing positive were hospitalized in a dedicated ID facility
- Developed extensive public awareness campaigns
- Cluster of cases associated with migrant worker population



Source: https://ourworldindata.org/grapher/daily-covid-cases-deaths?year=2020-04-30&time=2020-03-06..&country=KOR

Differing Responses to COVID-19- South Africa

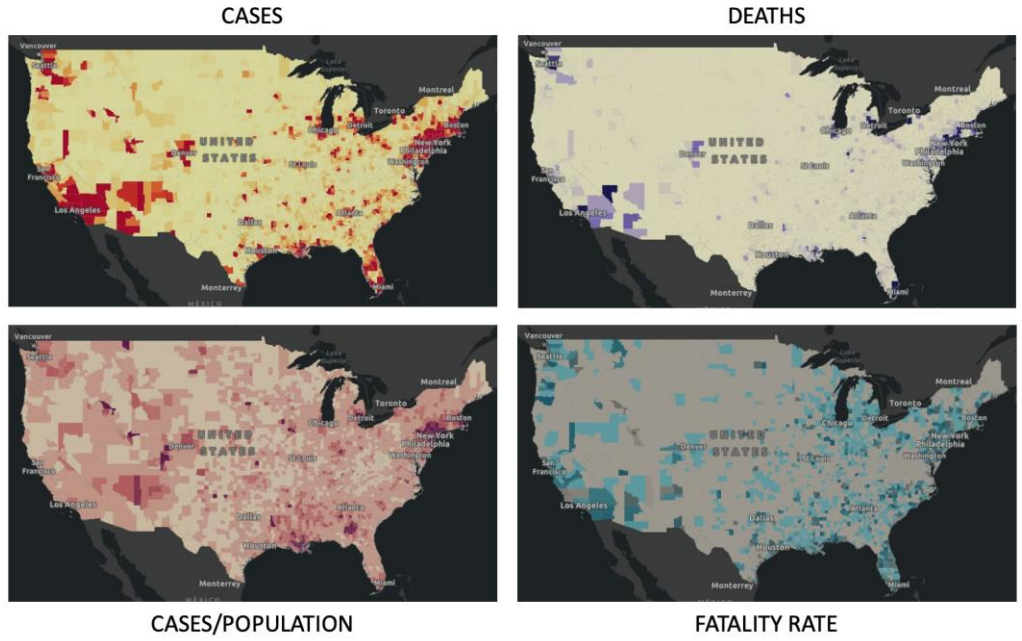
- Early March- 1st case detected
- Mid-March- Declared National State of Emergency
- Late March- Instituted 21-day lockdown which was extended
- Deployed 28,000 CHWs to conduct screening and testing
- Began a phased re-opening in May



Source: https://ourworldindata.org/grapher/daily-covid-cases-deaths?year=2020-04-30&time=2020-03-06..&country=KOR; https://www.sciencemag.org/news/2020/04/south-africa-flattens-its-coronavirus-curve-and-considers-how-ease-restrictions

COVID-19 in the U.S.

- January 2020
  - First case reported in Seattle, WA
  - CDC testing rollout
  - White House Coronavirus Task Force formed
- February 2020
  - First US death reported
- March 2020
  - Social distancing encouraged
  - Most states instituted stay-at-home orders
- April 2020
  - Plan to Reopen America proposed
- May 5, 2020
  - 1,201,337 cases and 70,847 deaths



Slide image courtesy of H. Akselrod

Clinical Presentation and Diagnostic Approaches to COVID-19

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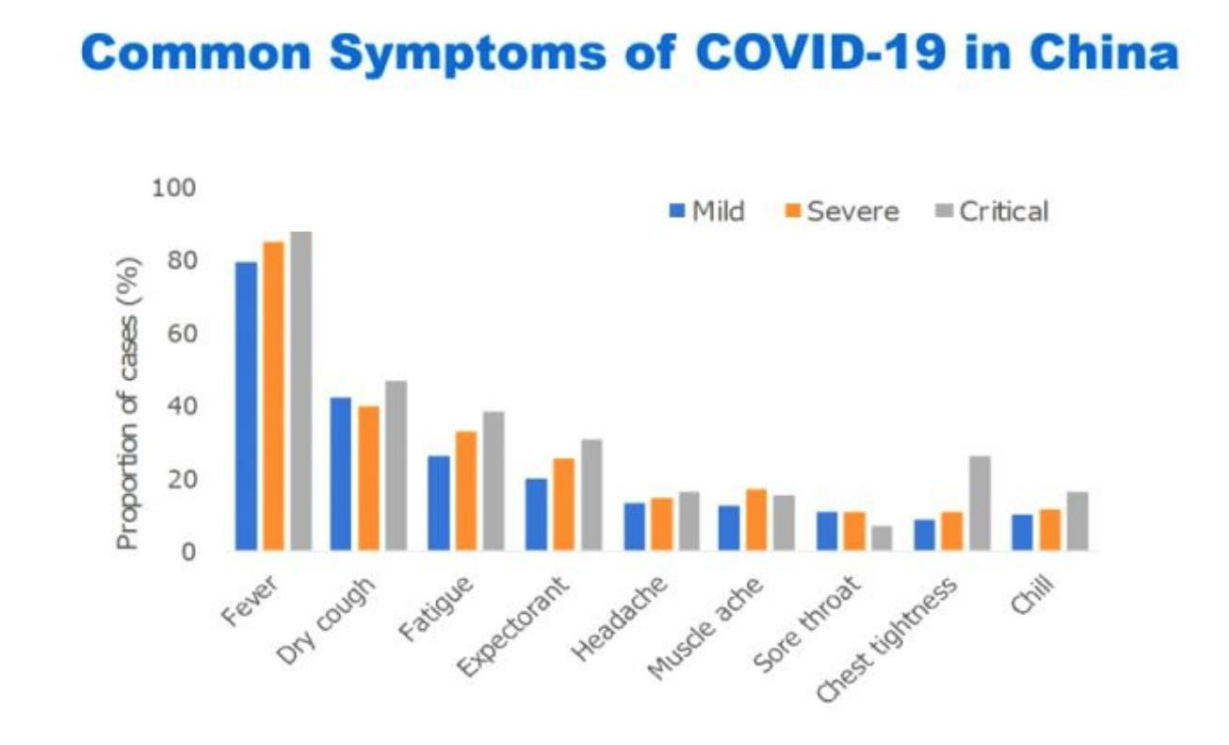
Source: CROI 2020, NIH treatment guidelines

COVID-19 Clinical Features

- **Incubation Period**: Average time from exposure to onset of symptoms: median 4-5 days (range 2-14)
- **Symptom** severity at diagnosis (25% asymptomatic)
  - 80% mild-moderate
  - 15% severe (hospitalized)
  - 5% critical (acute respiratory distress syndrome, death)
- **Duration of illness**: 1-2 weeks if mild, 4-6 if severe
- **Viral shedding** is highest in early days of illness
  - Continues for 7-12 days
  - Can occur 24-48 hours prior to onset of symptoms
- **Attack rate** among close contacts: 10%

Signs and Symptoms of COVID-19



Other common symptoms:

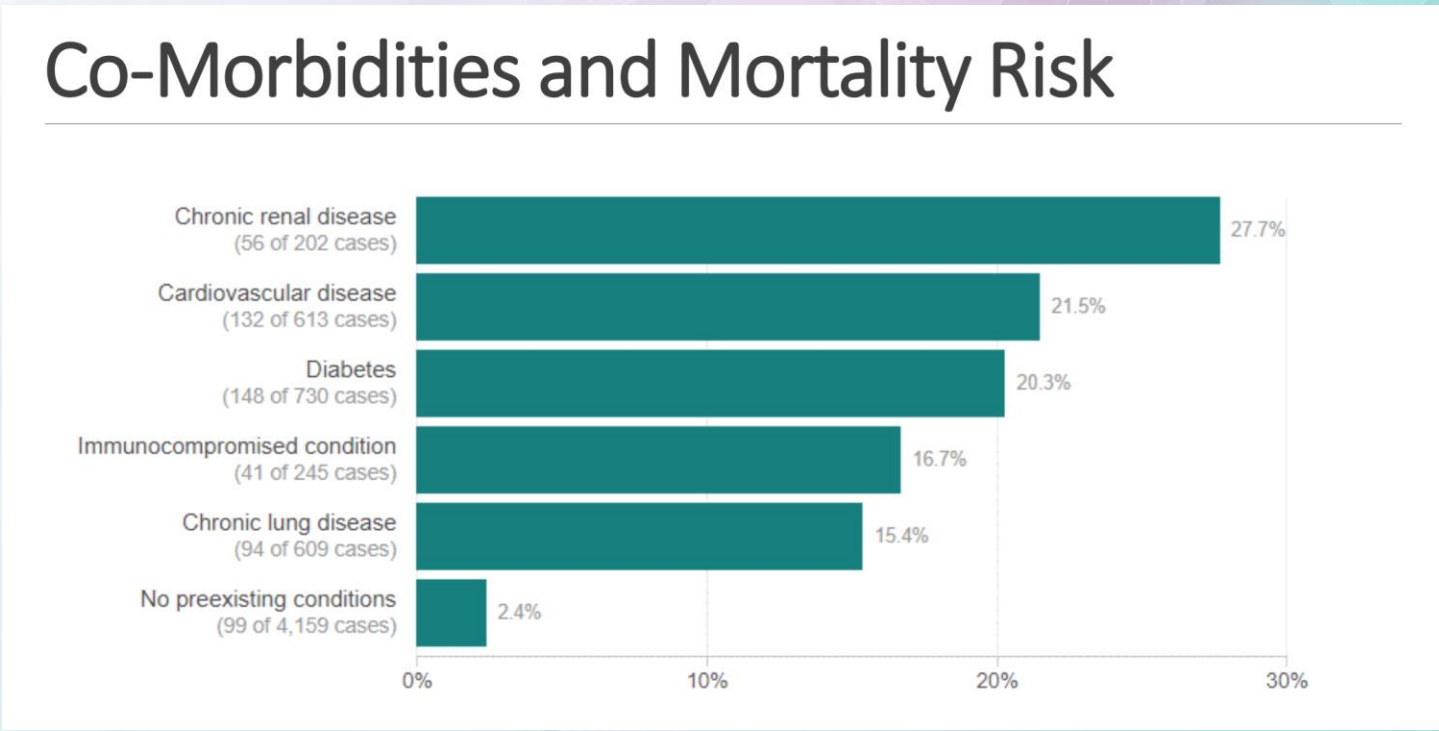
- GI symptoms (diarrhea, nausea, vomiting, anorexia, abdominal pain)
- Myalgias
- Sore throat
- Dysgeusia (loss of taste)
- Anosmia (loss of smell)
- Dizziness
- Rhinorrhea

Sources: CROI 2020 -China CDC presentation, CDC MMWR, NIH treatment guidelines

Co-Morbidities and Mortality

Persons Most at Risk

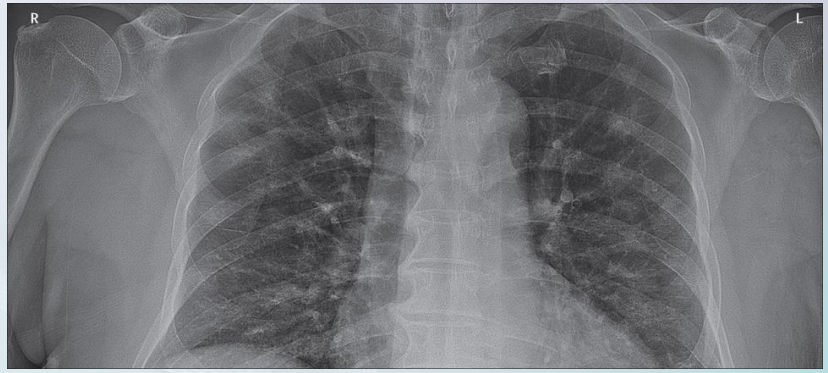
- Aged 65 and older
- Residents of LTCF and nursing homes
- Hypertension
- Cardiovascular disease
- Diabetes
- Chronic respiratory disease
- Cancer
- Renal disease
- Obesity
- Immunocompromised



Source: CDC MMWR, https://www.cdc.gov/mmwr/volumes/69/wr/mm6915e3.htm?s_cid=mm6915e3_w

Diagnosis

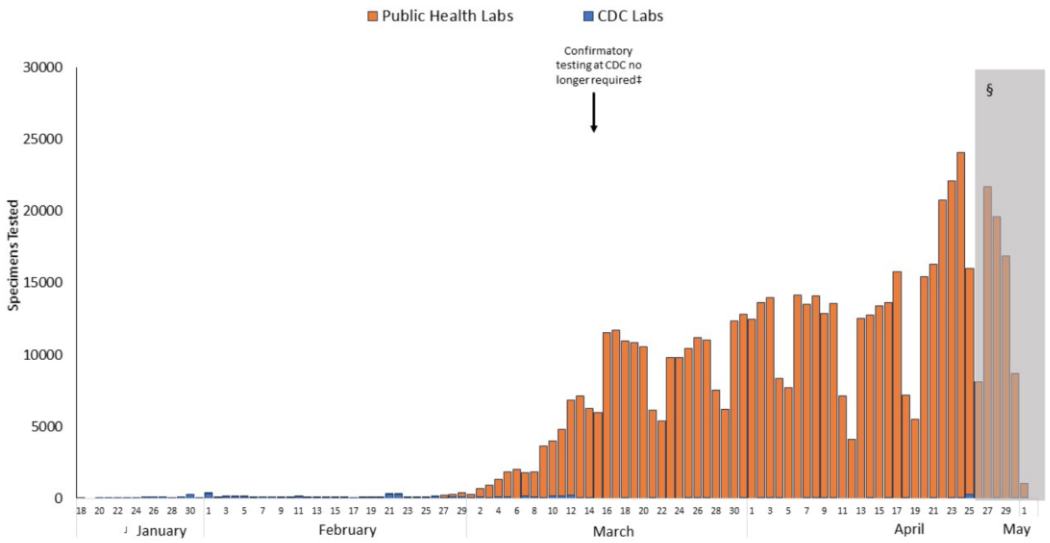
- Common laboratory findings
  - Leukopenia and lymphopenia
  - Elevated aminotransferase levels, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase
- Common radiologic findings
  - Chest X-ray: Bilateral multi-focal opacities
  - Chest CT: Bilateral peripheral ground-glass opacities with areas of consolidation
  - Imaging may be normal early in infection and can be abnormal in the absence of symptoms



Source: NIH treatment guidelines available at https://covid19treatmentguidelines.nih.gov/overview/; https://www.itnonline.com/content/coronavirus-ct-findings-linked-disease-time-course; https://www.thelancet.com/article/S0140-6736(20)30370-6/fulltext

Testing for COVID-19

Number of specimens tested for SARS CoV-2 by CDC labs (N= 5,642) and U.S. public health laboratories* (N= 613,041)†



- Viral RNA detection for acute infection
  - Higher accuracy during peak symptoms
  - Sensitivity of the test may vary in different settings
  - CDC RT-PCR to Public health labs
  - Cepheid Xpert Xpress SARS-CoV-2 real time rapid PCR
- Serologic testing (IgG and IgM for immunity)
  - Abbott's ARCHITECT detects IgG for SARS-CoV-2
  - Various others being approved for use
- Emergency Use Authorizations have allowed for expanded testing (US FDA)
- *Does Ab detection imply immunity?*
- Innovations:
  - Self-testing, rapid testing, home-based testing

ARVs as Treatment for COVID-19

WHO SOLIDARITY Clinical Trial

- International clinical trial launched by WHO to find effective treatment for COVID-19
- Goal is to more rapidly identify effective treatments than traditional clinical trials approaches
- Compare 4 treatment options to standard of care in multiple countries
  - Chloroquine and hydroxychloroquine
  - Lopinavir/Ritonavir
  - Interferon beta-1a
  - Remdesivir

Source: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

Lopinavir/Ritonavir and COVID-19

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

Bin Cao, M.D., Yeming Wang, M.D., Danning Wen, M.D., Wen Liu, M.S., Jingli Wang, M.D., Guohui Fan, M.S., Lianguo Ruan, M.D., Bin Song, M.D., Yanping Cai, M.D., Ming Wei, M.D., Xingwang Li, M.D., Jiaan Xia, M.D., et al.

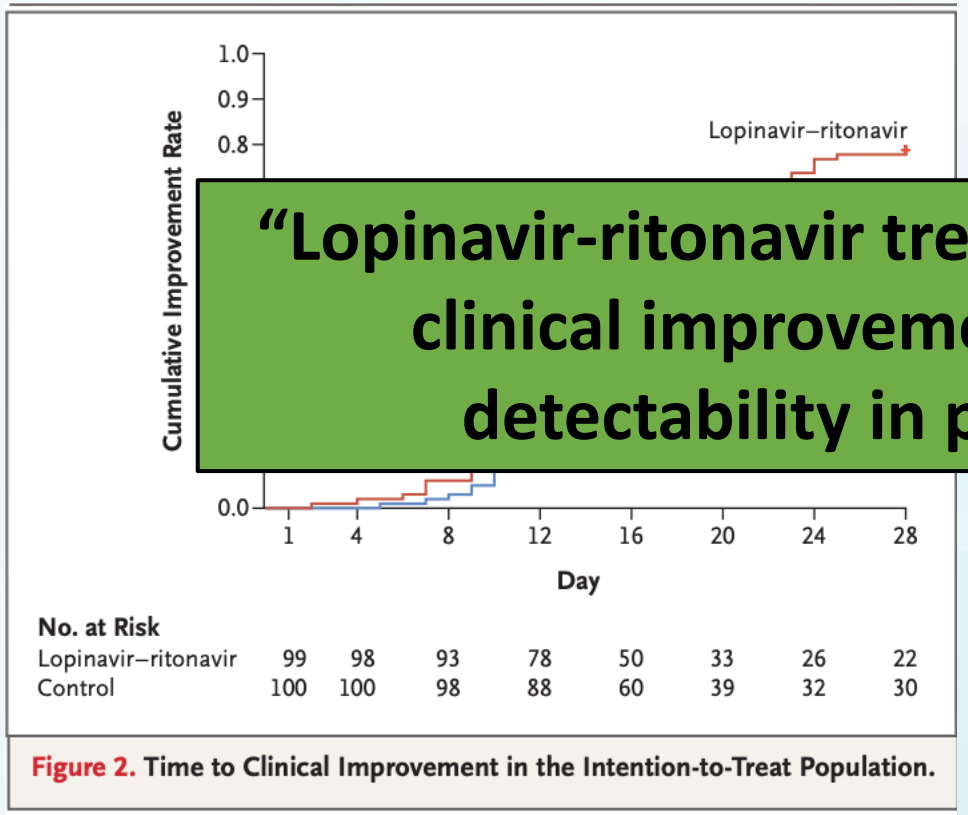


Figure 2. Time to Clinical Improvement in the Intention-to-Treat Population.

"Lopinavir-ritonavir treatment did not significantly accelerate clinical improvement, reduce mortality or viral RNA detectability in patients with serious Covid-19. "

Table 3. Outcomes in the Intention-to-Treat Population.*

Characteristic	Total (N=199)	Lopinavir–Ritonavir (N=99)	Standard Care (N=100)	Difference†
Time to clinical improvement — median no. of days (IQR)	16.0 (15.0 to 17.0)	16.0 (13.0 to 17.0)	16.0 (15.0 to 18.0)	1.31 (0.95 to 1.80)‡
				8 (–17.3 to 5.7)
				0 (–25.3 to 9.3)
				8 (–19.1 to 11.6)
				1 (–1.4 to 9.5)
				5 (2.2 to 28.8)
				8 (–3.3 to 20.9)
				–5 (–9 to 0)
(IQR)				
Of survivors	10 (8 to 17)	9 (5 to 44)	11 (9 to 14)	–1 (–16 to 38)
Of nonsurvivors	10 (4 to 14)	6 (2 to 11)	12 (7 to 17)	–6 (–11 to 0)
Duration of invasive mechanical ventilation — median no. of days (IQR)	5 (3 to 9)	4 (3 to 7)	5 (3 to 9)	–1 (–4 to 2)
Oxygen support — days (IQR)	13 (8 to 16)	12 (9 to 16)	13 (6 to 16)	0 (–2 to 2)
Hospital stay — median no. of days (IQR)	15 (12 to 17)	14 (12 to 17)	16 (13 to 18)	1 (0 to 2)
Time from randomization to discharge — median no. of days (IQR)	13 (10 to 16)	12 (10 to 16)	14 (11 to 16)	1 (0 to 3)
Time from randomization to death — median no. of days (IQR)	10 (6 to 15)	9 (6 to 13)	12 (6 to 15)	–3 (–6 to 2)

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2001282

Remdesivir

- Originally developed as an Ebola treatment
- Blocks viral enzymes used to replicate
- Given intravenously
- Recent
  patients
  placebo
  - 31% faster recovery (11 vs. 15 days)
  - Mortality rate: 8% vs. 11%
- 5-day vs. 10 –day course had similar efficacy

"Remdesivir accelerates recovery from advanced COVID-19."

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

J. Grein, N. Ohmagari, D. Shin, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green, M.L. Green, F.-X. Lescure, E. Nicastri, R. Oda, K. Yo, E. Quiros-Roldan, A. Studemeister, J. Redinski, S. Ahmed, J. Bernett, D. Chelliah, D. Chen

		10-Day RDV n=197	Baseline adjusted p-value[1]
scale	129 (65)	107 (54)	0.16
Clinical recovery	129 (65)	106 (54)	0.17
Discharge	120 (60)	103 (52)	0.44
Death	16 (8)	21 (11)	0.70
Safety			
Any adverse event (AE)	141 (71)	145 (74)	0.86
Grade ≥3 study drug-related AE	8 (4)	10 (5)	0.65
Study drug-related serious adverse event (SAE)	3 (2)	4 (2)	0.73
AE leading to discontinuation	9 (5)	20 (10)	0.07

[1]Adjusted for baseline clinical status

Sources: https://www.nejm.org/doi/full/10.1056/NEJMoa2007016; https://www.gilead.com/news-and-press/press-room/press-releases/2020/4/gilead-announces-results-from-phase-3-trial-of-investigational-antiviral-remdesivir-in-patients-with-severe-covid-19; https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19

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COVID-19 Infection among PWH

Limited Knowledge Regarding HIV and COVID-19

- Reports of mild disease among PWH with SARS and MERS
- Limited data to date on PWH and COVID-19 (Zhu, 2020; Joob, 2020; Blanco, 2020, Feng 2020)
  - Incidence of COVID-19 ranging from 0-<1%
  - Potential for mild or moderate disease with good recovery
  - Despite low CD4 counts, patients still have outcomes similar to HIV negative persons
  - Older age as a risk factor
- Are immunosuppressives/ARVs protective?
- However, many PWH are aging and have multiple co-morbidities

Source: Zhu, https://doi.org/10.1002/jmv.25732 Joob, https://doi.org/10.1002/jmv.25782; Blanco https://doi.org/10.1016/S2352-3018(20)30111-9; Feng http://www.natap.org/2020/COVID/SSRN-id35500292.pdf

Interim Guidance for PWH

World Health Organization

Q&A on COVID-19, HIV and antiretrovirals

24 March 2020 | Q&A

Are people living with HIV at increased risk of being infected with the virus that causes

Can antiretrovirals be used to treat COVID-19?

Can antiretrovirals be used to prevent COVID-19 infection?

What studies on treatment and prevention of COVID-19 with antiretrovirals are being p

What is WHO's position on the use of antiretrovirals for the treatment of COVID-19?

U.S. Department of Health and Human Services

AIDSinfo

OFFERING INFORMATION C
TREATMENT, PREVENTION,

Interim Guidance for COVID-19 and Pe with HIV

Last Updated: April 21, 2020; Last Reviewed: April 21, 2020

This interim guidance reviews special considerations for persons with HIV and thei providers in the United States regarding COVID-19. Information and data on COVID- evolving. This guidance includes general information to consider. People with HIV have an excellent prognosis, and they should be clinically managed the same as pe general population with COVID-19, including when making medical care triage dete

CROI 2020

Recommendations for People with HIV

- Ensure ample medication supply
  - 30-days supply at all times
- Keep vaccinations up to date
  - influenza, pneumococcal
- Establish plan for clinical care if isolated/quarantined
  - telemedicine options
  - physician on-line portals
- Maintain a social network but remotely
  - Social contact helps us stay mentally healthy and fights boredom

CDC

Source: https://www.who.int/news-room/q-a-detail/q-a-on-covid-19-hiv-and-antiretrovirals; https://aidsinfo.nih.gov/guidelines/html/8/covid-19-and-persons-with-hiv--interim-guidance-/554/interim-guidance-for-covid-19-and-persons-with-hiv

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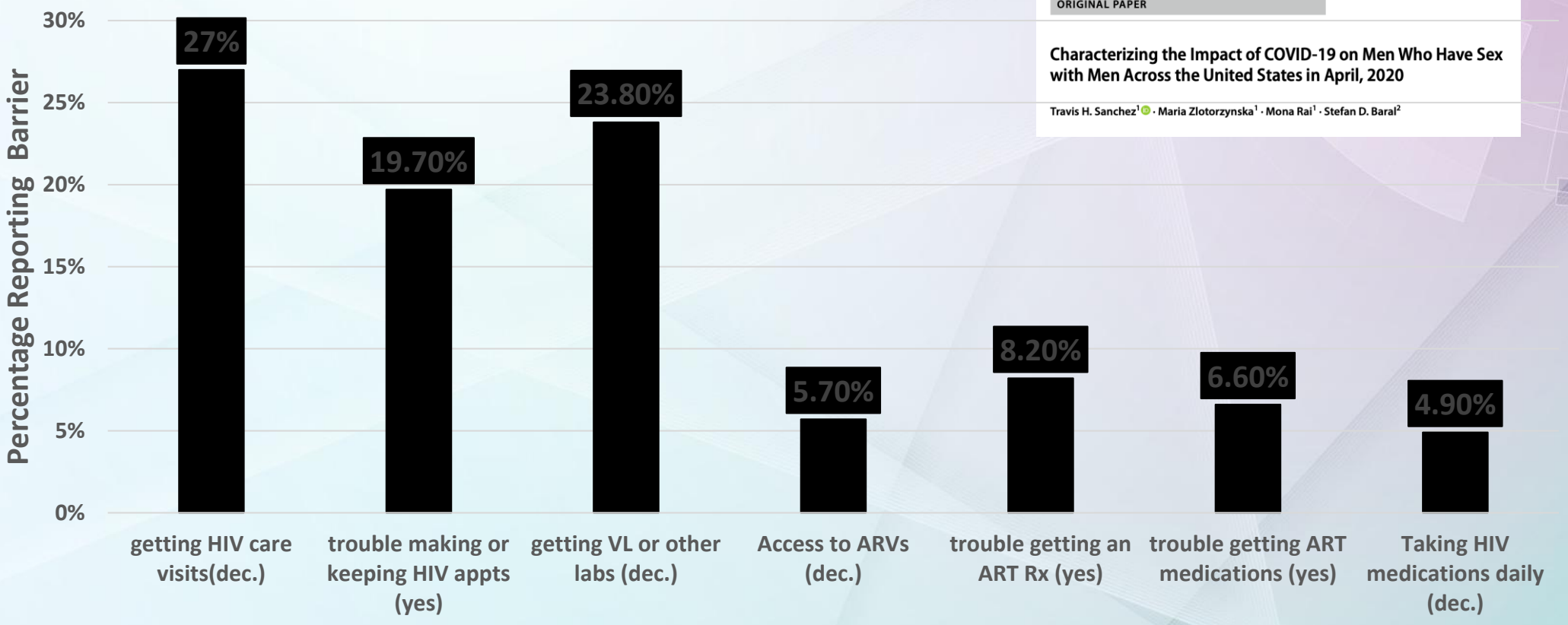
COVID-19 Disruptions in Care among MSM Living with HIV



AIDS and Behavior
https://doi.org/10.1007/s10461-020-02894-2

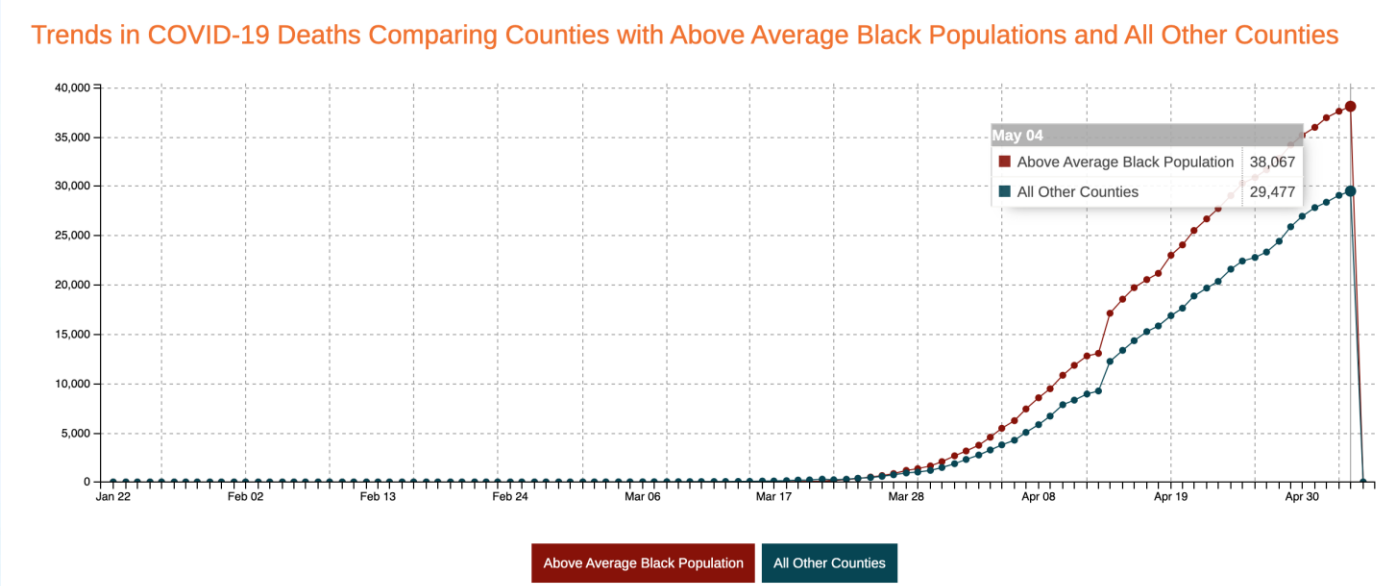
ORIGINAL PAPER

Characterizing the Impact of COVID-19 on Men Who Have Sex with Men Across the United States in April, 2020

Travis H. Sanchez[1] · Maria Zlotorzynska[1] · Mona Rai[1] · Stefan D. Baral[2]

Source: Sanchez, Travis H. et al. "Characterizing the Impact of COVID-19 on Men Who Have Sex with Men Across the United States in April, 2020." *AIDS and Behavior*, 1–9. 29 Apr. 2020, doi:10.1007/s10461-020-02894-2

Health Disparities and COVID-19



PWH in Washington, DC, N=10,614

- Median age 47.8 (43% >50 yrs old)
- 77% Black; 6% Hispanic
- 7% homeless/unstably housed
- 25% unemployed/disabled
- 49% ever smoked
- 25-44% obese
- 30% HTN
- 10% asthma
- 5% with chronic renal failure

Source: https://ehe.amfar.org/inequity?_ga=2.135282481.1294687472.1588698565-1927484729.1588161773

Synergies and Lessons Learned from HIV

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Synergies between HIV and COVID-19

Maintaining HIV care during the COVID-19 pandemic

Coronaviru
around th
in China
characteris
Approxima
are at risk

When pandemics collide

One pandemic virus ha
health for almost 40 y
just 4 months ago, but,
now been reported in n
COVID-19 are on a colli
learned a remarkable ar
short time, its potentia

AIDS and Behavior
https://doi.org/10.1007/s10461-020-02871-9

NOTES FROM THE FIELD

The Burden of COVID-19 in People Living with HIV: A Syndemic Perspective

Stephanie Shiau[1] · Kristen D. Kr

African Journal of AIDS Research

EDITORIAL: Managing the march of COVID-19: lessons from the HIV and AIDS epidemic

Alan Whiteside[1], Warren Parker[2]

[1]Global Health Policy, Balsillie School
[2]Independent public health and comm
[3]NISC (Pty) Ltd, Makhanda, South Afr

AIDS and Behavior
https://doi.org/10.1007/s10461-020-02856-8

NOTES FROM THE FIELD

How Do We Balance Tensions Between COVID-19 Public Health Responses and Stigma Mitigation? Learning from HIV Research

Carmen I

Three lessons for the COVID-19 response from pandemic HIV

The HIV pandemic provides lessons for the response to the novel coronavirus disease 2019 (COVID-19) pandemic: no vaccine is available for either and there are no licensed pharmaceuticals for COVID-19, just as there of less well-off people died because of inequitable access to life-saving antiretrovirals, and the same trend might occur with COVID-19.[7] Global policy must prioritise access to innovations for those individuals in greatest need.

Lancet HIV 2020
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S2352-3018(20)30110-7

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Characteristics of COVID-19 vs. HIV

	COVID-19	HIV
Animal source	Bat	Primates
Transmission	Aerosols, respiratory droplets, contacts and surface contamination	Bodily fluids
Asymptomatic spread	yes	yes
Reproductive rate	1.4-5.5	2-4
Case fatality rate	3	80 (w/out treatment)
Number of people infected	3 million	38 million

Source: Chen, Pathogenicity and transmissibility of 2019-nCoV, *Microb Inf*, 2020

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COVID-19 and HIV: Similarities in Response

- Essential role of testing and diagnostics
- Implementation of surveillance systems and use of contact tracing
- Development of therapeutics and vaccines
- Addressing the social and economic consequences
- Fighting fear, stigma, and criminalization

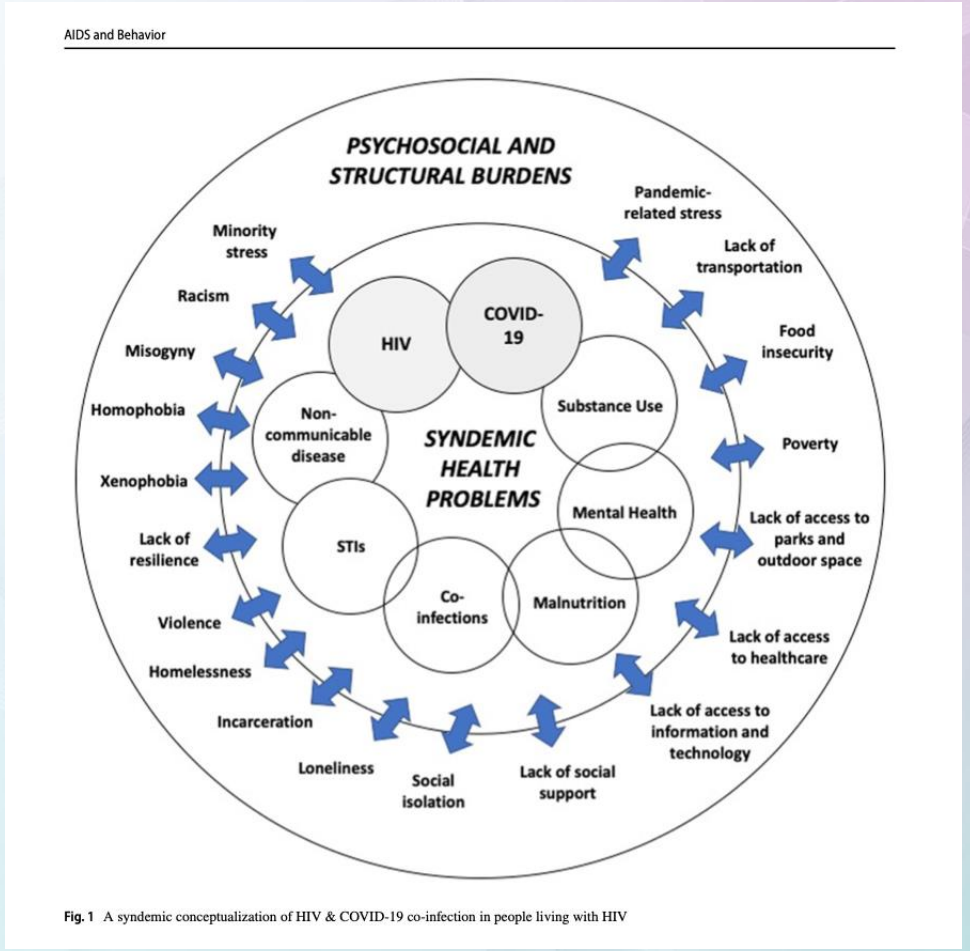

Fig. 1 A syndemic conceptualization of HIV & COVID-19 co-infection in people living with HIV

Sources: Logie & Turan; Whiteside et al; Shiau; Relf et al

Challenges and Unknowns

COVID-19

- Impact on low and middle income countries
- Levels of herd immunity
- How best to re-open
- Risk of second wave
- Seasonality
- Treatments and vaccines

HIV and COVID-19

- Course of infection among PWH
  - Age, VS, ARVs, co-morbidities, complications
  - Pregnancy and pediatric impact
- Impact on ability to achieve 90-90-90
- Disruptions in care
  - ARV access
  - Mental health services
  - Substance use services
  - STIs and HIV prevention
- Role of telehealth

Conclusions and Recommendations

- Evolving situation with unprecedented global impact
- Capitalize on knowledge from prior pandemics and epidemics
- Protect the most vulnerable including minorities and PWH
- Conduct sound scientific research on COVID-19 prevention, treatment and vaccine development
- Advocate for structural and policy level changes to address racial disparities, stigma, and discrimination
- Begin to adequately plan for the next pandemic

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