

COVID-19 update:

summary of studies from HTB

UK-CAB: 1 May 2020

Simon Collins

www.i-Base.info

ISSN 1753-8688

HIV and COVID-19 no. 2



HTB supplement 07: 17 April 2020

CONTENTS

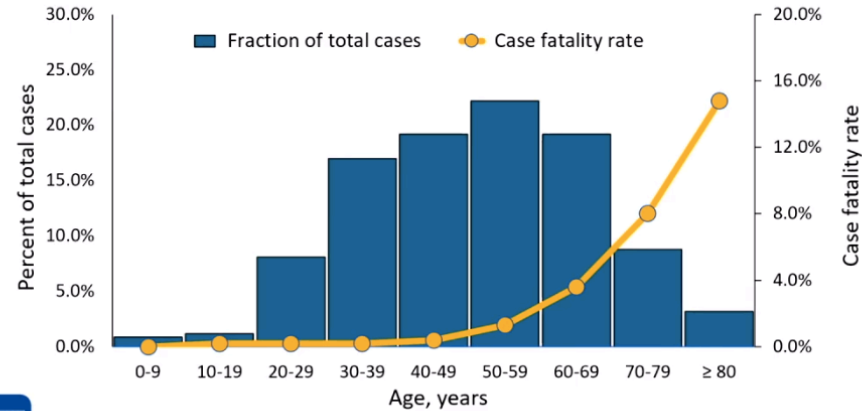
COVID-19 SUPPLEMENT ISSUE 1	3
SUMMARY	3
HTB & COVID-19 CONNECTIONS	4
<ul style="list-style-type: none">• Why it is important to include HIV status and HIV testing in managing COVID-19• COVID-19 symptoms in HIV positive people similar to general population in UK and• Case study of COVID-19 in HIV positive person with history of HIV• Case series of five HIV positive people diagnosed with COVID-19 in Spain	5
COVID-19 TREATMENTS	6
<ul style="list-style-type: none">• Evidence review for repurposed compounds: EMA guidelines for COVID-19• First results from remdesivir compassionate access programme• Treatment of hydroxychloroquine and azithromycin in people hospitalized with COVID-19• High-dose chloroquine study for COVID-19 stopped with worse outcomes	6
COVID-19 TREATMENT ACCESS	8
<ul style="list-style-type: none">• Priority review for COVID-19 could be manufactured by 11 a day or less• MEP calls for no patents or profiteering on COVID-19 drugs, tests, and vaccines in pandemic	8
COVID-19 NEW RESEARCH	10
<ul style="list-style-type: none">• Clinical research UK sites for two phase-2 studies of remdesivir to treat COVID-19• Prospective trials to study COVID-19• COVID-19 prophylaxis using TMP-PST and low-dose hydroxychloroquine in Spanish health workers• Community survey on impact of COVID-19 and themes• European rapid community assessment reports for COVID-19	10
COVID-19 INFORMATION	16
<ul style="list-style-type: none">• A clinical French-style study prepared for COVID-19	16
COVID-19 TRANSMISSION	16
<ul style="list-style-type: none">• Five papers on COVID transmission• Studies show concern about coronavirus contagion through air or speech	16
COVID-19 AND HEALTH SERVICES	17
<ul style="list-style-type: none">• BASH response to impact of COVID-19 on sexual health services	17
COVID-19 BLOOD SERVICES	20
<ul style="list-style-type: none">• FDA reduces restrictions on gay men as blood donors due to COVID-19• CoVid identified 2 blood donations in China	20

Contents continued inside...

Published by HIV i-Base

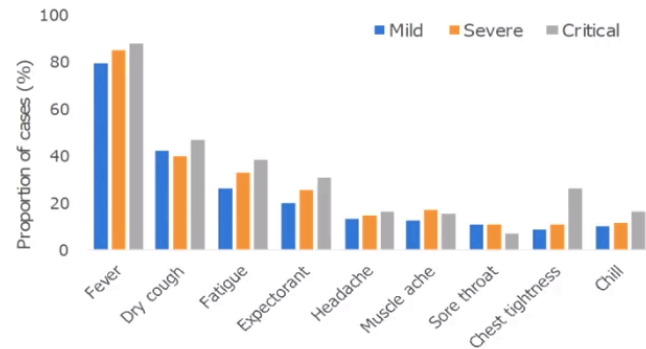
COVID-19: first information from China

Age Distribution and Case Fatality Rate COVID-19 China through 11-Feb-2020 (N = 44,672 confirmed cases)



adapted from Zhang 2020, China CDC Weekly Rep; 2(8):113-122.

Common Symptoms of COVID-19 in China



19230 Confirmed cases with detailed epidemiological investigation information

China CDC/NHC 2020

Key epi/technical insights from China (2 of 3)

2-Natural history:

- At **diagnosis**: approx. **80%** are mild/moderate; **15%** severe; **5%** critical
- **Progression**: approx. **10-15%** of mild/moderate cases become severe, and approximately **15-20%** of severe become critical
- **Average times**:
 - from exposure to symptom onset is **5-6 days**;
 - from symptom onset to recovery for mild cases is **2 weeks** and for severe cases is **3-6 weeks**;
 - from symptom onset to death is **2-8 weeks**
- Truly **asymptomatic** infection is unknown without serology, but appears to be rare using molecular testing (**<1%**)
 - an estimated **75%** of 'asymptomatic' cases at time of diagnosis soon progress to disease
- **Children** tend to have milder disease than adults

Aylward B et al, WHO-China Mission, 2020

Epidemiology links

Total tests, diagnoses, deaths, by-country, total and adjusted by population etc.

- UK data

<https://covid.joinzoe.com/data#interactive-map>

- WHO daily situation reports

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>

- Johns Hopkins:

<https://coronavirus.jhu.edu>

- Worldometers

<https://www.worldometers.info/coronavirus/#repro>

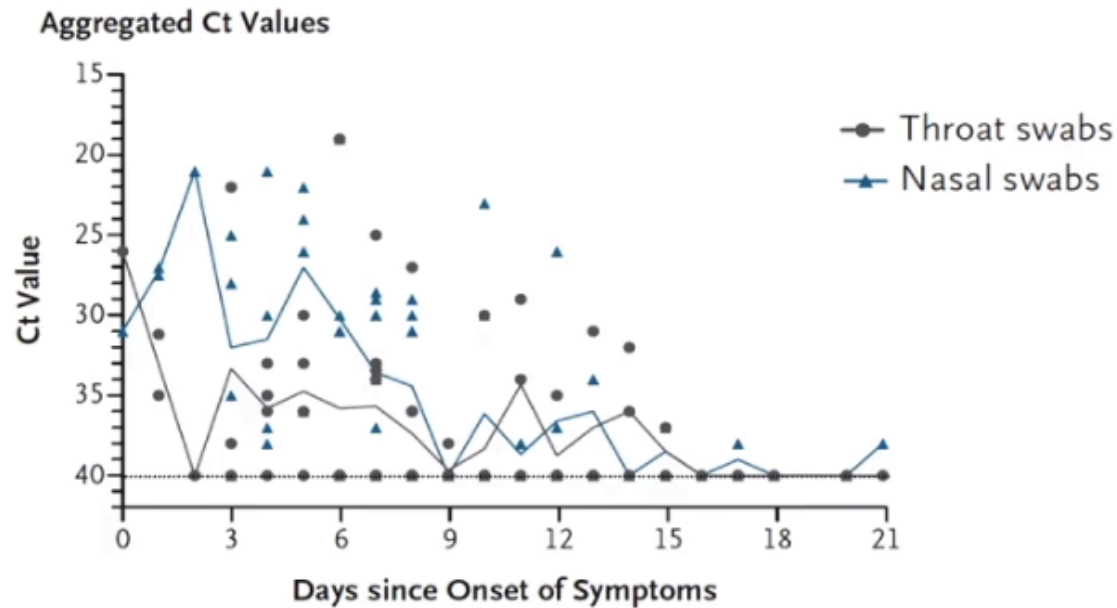
Transmission

- Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1
<http://i-base.info/htb/37421>
- Median estimated incubation period of COVID-19 is five days – but can be two weeks
<http://i-base.info/htb/37423>
- Four papers on CoV-2 transmission: sometimes easy, sometimes rare
<http://i-base.info/htb/37652>
- Studies stoke concern about coronavirus contagion through air via speech
<http://i-base.info/htb/37659>

COVID-19

Viral Shedding Greatest At Time Symptoms Start

- SARS-CoV-2 viral loads in 17 symptomatic patients
- No data regarding duration of replication-competent virus shedding (e.g., culture)



Symptoms

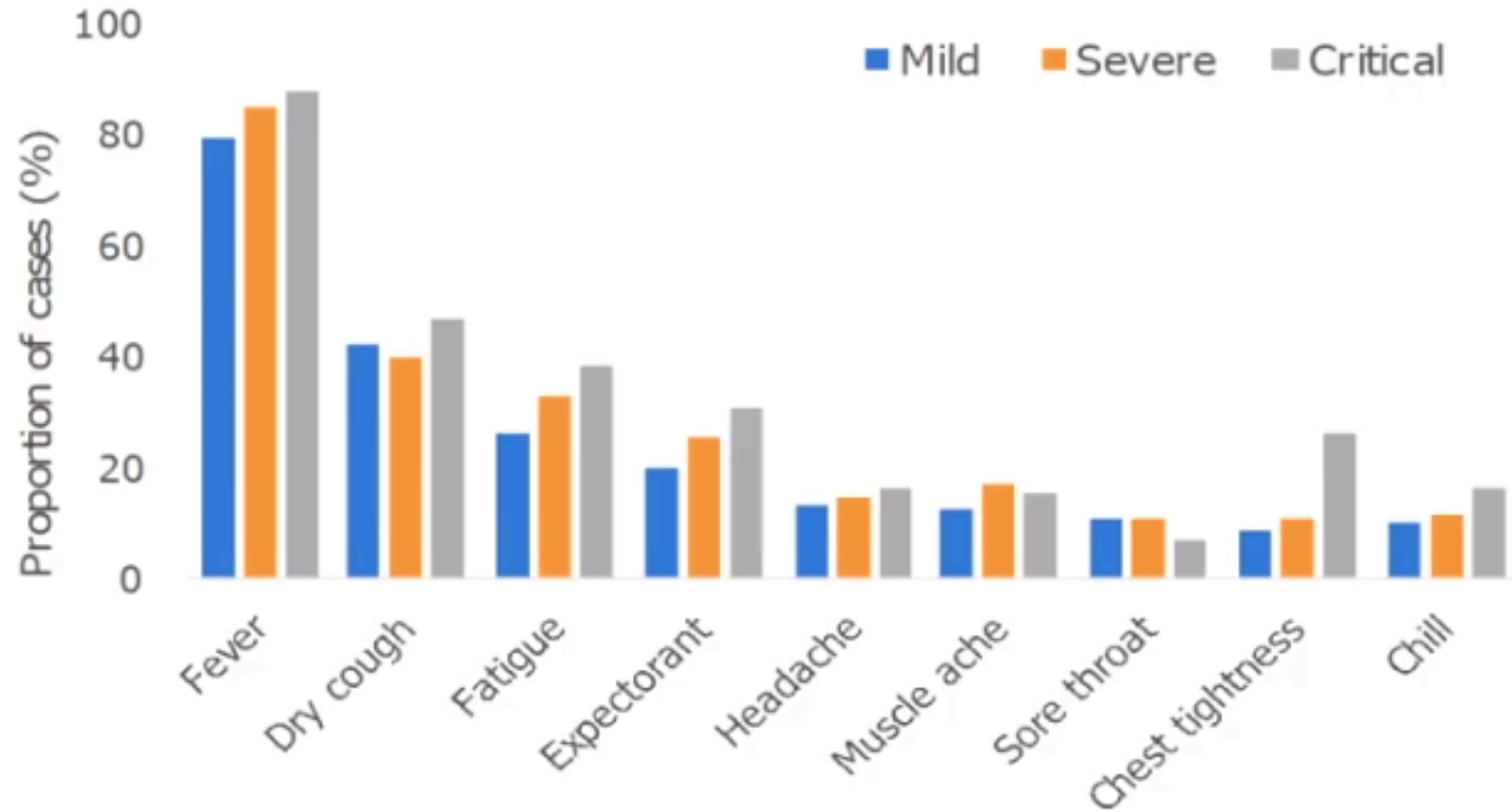
<https://www.nhs.uk>

1. **High temperature** – this means you feel hot to touch on your chest or back (you do not need to measure your temperature)

2. **New, continuous cough** – this means coughing a lot for more than an hour, or three or more coughing episodes in 24 hours (or having a worse cough than usual)

- Loss of smell or taste
- Chest pain or tightness in the chest
- New diarrhoea
- New muscle aches
- Feeling unusually tired
- An unusually hoarse voice
- Unusual stomach pain
- New headaches
- Skipped more meals than normal
- Feeling confused, disorientated or drowsy

Common Symptoms of COVID-19 in China



ACTION

<https://www.nhs.uk>

1. 999 if medical emergency
2. symptom checker : NHS 111 - you and/or people you live with
<https://111.nhs.uk/covid-19>
2. self isolation: you and people you live with
3. need for hospital care

Staging

A clinical-therapeutic staging proposal for COVID-19

<http://i-base.info/htb/37627>

STAGE I (MILD) – EARLY INFECTION

The initial stage occurs at the time of inoculation and early establishment of disease. For most people, this involves an incubation period associated with mild and often non-specific symptoms such as malaise, fever and a dry cough.

STAGE II (MODERATE) – PULMONARY INVOLVEMENT (IIA) WITHOUT AND (IIB) WITH HYPOXIA:

In the second stage of established pulmonary disease, viral multiplication and localised inflammation in the lung is the norm. During this stage, patients develop pneumonia, with cough, fever and possibly hypoxia (defined as a PaO₂/FiO₂ of <300 mmHg).

STAGE III (SEVERE) – SYSTEMIC HYPERINFLAMMATION:

A minority of COVID-19 patients will transition into the third and most severe stage of illness, which manifests as an extra-pulmonary systemic hyperinflammation syndrome. In this stage, markers of systemic inflammation appear to be elevated. COVID-19 infection results in a decrease in helper, suppressor and regulatory T cell counts.

Risk factors

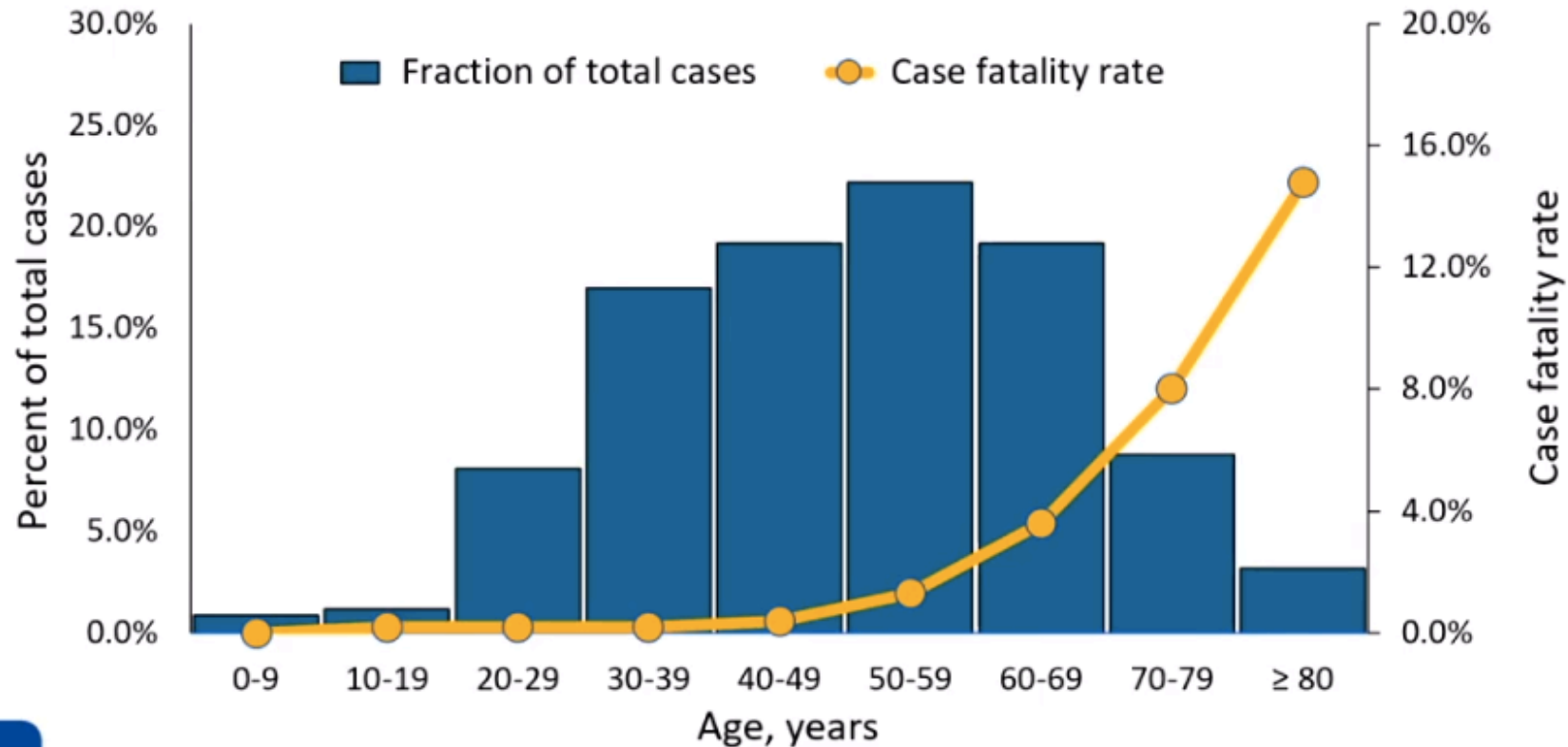
- Clinical characteristics of COVID-19 in China (NEJM)

<http://i-base.info/htb/37429>

- older age
- male sex
- other health problems (comorbidities):
 - lung and breathing problems (asthma, COPD etc)
 - diabetes
 - heart disease (current)
 - liver and kidney disease
 - cancer (and being on chemotherapy)
 - immunodeficiency (CD4 <50) – in some guidelines, organ transplant recipients

Risk factors: age

Age Distribution and Case Fatality Rate COVID-19 China through 11-Feb-2020 (N = 44,672 confirmed cases)



adapted from Zhang 2020, *China CDC Weekly Rep*; 2(8):113-122.

HIV and COVID-19 coinfection

- Why it is important to include HIV status and HIV testing in managing COVID-19
<http://i-base.info/htb/37588>
- COVID-19 symptoms in HIV positive people similar to general population in Wuhan
<http://i-base.info/htb/37542>
- Case series of five HIV positive people diagnosed with COVID-19 in Spain
<http://i-base.info/htb/37661>
- HIV is not linked to higher risk of COVID-19 in large New York cohort
<http://i-base.info/htb/37739>

HIV risk and COVID-19?



Are HIV positive people at higher risk from COVID-19?

<http://i-base.info/qa/15483>

People with CD4 above 200 and undetectable on ART: follow [general population advice](#) (ie social physical distancing).

People with CD4 that is 50 to 200, who have detectable viral load or who are not on ART: follow [social distancing advice](#) very closely.

People with a CD4 count <50 or opportunistic illness in last 6 months: follow [shielding advice](#) for extremely vulnerable. This includes avoiding face-to-face contact for 12 weeks – and you will need support to do this.

Refs: BHIVA and EACS statements

Treatment guidelines

- Evidence review for treatment: IDSA guidelines for COVID-19
<http://i-base.info/htb/date/2020/04>
- US interim guidelines on COVID-19 and HIV
<http://i-base.info/htb/37387>
- WHO guidance on severe acute respiratory infection when COVID-19 is suspected
<http://i-base.info/htb/37582>
- BMJ guidelines resources page
<https://bestpractice.bmj.com/topics/en-gb/3000168/guidelines>

Treatment

- COVID-19 treatment studies – >1200 studies, many dual
<https://clinicaltrials.gov/ct2/results?cond=&term=covid-19&cntry=&state=&city=&dist=>
- antiviral drugs (remdesivir, HIV: Kaletra)
- hydroxychloroquine – many different doses – with or without azithromycin
- anti-inflammatory drugs: NSAIDS, tocilizumab (to reduce IL-6)
- convalescent plasma
- corticosteroids (not recommended by WHO for pneumonia).

Remdesivir

- NIAIDS placebo study (n>1000) – 11 vs 15 days recovery (29 April 2020)
<https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19>
- Remdesivir for COVID-19: published paper shows no evidence of direct antiviral effect. Lancet, Chinese Study. (29 April 2020). (Also WHO early release)
<http://i-base.info/htb/37750>
- Remdesivir for COVID-19: first results from compassionate access programme. NEJM, (10 April 2020).
<http://i-base.info/htb/37593>
- Gilead: trials, EAP, drug supply etc
<https://www.gilead.com/purpose/advancing-global-health/covid-19/about-remdesivir>

Hydroxychloroquine

- No benefit of hydroxychloroquine and azithromycin in people hospitalised with COVID-19.

<http://i-base.info/htb/37524>

- High-dose chloroquine study for COVID-19 stopped with worse outcomes: high risk of cardiovascular events.

<http://i-base.info/htb/37691>

- Guatret et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102549>

- Hydroxychloroquine study (HCQ) – HIV (2011) no impact on inflammation

<http://i-base.info/hydrochloroquine-study>

PrEP for health workers

- COVID-19 prophylaxis using TDF/FTC and low-dose hydroxychloroquine in Spanish health workers

<http://i-base.info/htb/37625>

- COVID-19 prophylaxis studies – >100 studies, many dual treatment.
<https://clinicaltrials.gov/ct2/results?cond=&term=COVID-19+prophylaxis&cntry=&state=&city=&dist=>
 - Hydroxychloroquine – many different doses.
 - antibiotics (azithromycin etc).
 - anti-parasite (nitroxinide, levamisole).
 - antiviral drugs (isoprinosine, HIV: Kaletra, TDF/FTC) etc.
 - vitamins C, D, zinc.
 - BCG vaccine.

Masks ?



Why face masks to prevent COVID-19 might now be recommended...

<http://i-base.info/qa/15571>

Refs:

Greenhaulgh T et al. Face masks for the public during the COVID-19 crisis. BMJ 2020; 369:m1435. doi: 10.1136/bmj.m1435 (09 April 2020).

<https://www.bmj.com/content/369/bmj.m1442>

Gandhi M and Havlir D. The time for universal masking of the public for coronavirus disease 2019 is now. Open Forum Infect Dis. (15 April 2020).

<https://academic.oup.com/ofid/article/7/4/ofaa131/5820544>

More information: webinars and talks

- WHO
<http://i-base.info/htb/37703>
- IAS webinar
<https://www.youtube.com/watch?v=25ve6LevLpY>
- Other online talks and webinars
<http://i-base.info/htb/37455>
<http://i-base.info/htb/37707>

Thanks – and Questions

BHIVA CROI working group for help with slides

COVID-19

COVID-19 in High-Risk Groups

- **Comorbidity and advanced age increase risk for severe illness and death**
 - Cardiovascular disease, diabetes, chronic respiratory disease (CFR >5%)
- **Immunocompromised (medical, acquired) – no data at present**
 - For persons with HIV, risk likely greatest at low CD4 cell counts or if not virally suppressed
 - Nonetheless all should take precautions given this is a new virus
 - CDC estimates that $\geq 50\%$ of people with HIV are more than 50 years old
- **Pregnancy**
 - Current observational data only exist for women infected in third trimester
 - Maternal morbidity similar to that of uninfected women without COVID-19
 - No definitive evidence infection transmitted perinatally



COVID-19

Therapeutics for SARS-CoV-2 (COVID-19)

■ Antivirals, monoclonal antibodies and other agents are being tested

- **Remdesivir (nucleotide analogue)**, has shown promise against coronaviruses in animal models
- **Kaletra (lopinavir/ritonavir) (protease inhibitors) and interferon-beta** have been used investigationaly for other coronaviruses
- **Other broad-spectrum antivirals**
- **Chloroquine**
- **Drug screening and targeted drug design**
- **Monoclonal antibodies being isolated and tested**



Clinical Testing of Remdesivir for Treatment of COVID-19

- Five randomized controlled trials in hospitalized patients with diagnosed COVID-19

COVID-19 Study Design	Location	Sponsor	Study size (randomization)	First patient enrolled	Primary endpoint
Severe Double-blind Placebo-controlled	Wuhan, China	Capital Medical University, China	N = 453 (2:1) 10d RDV:Placebo	Feb 6, 2020	Time to clinical improvement by Day 28
Mild/Moderate Double-blind Placebo-controlled	Wuhan, China	Capital Medical University, China	N = 308 (1:1) 10d RDV:Placebo	Feb 13, 2020	Time to clinical recovery by Day 28
All hospitalized* Double-blind Placebo-controlled	Global	NIAID	N = 394 (1:1) 10d RDV:Placebo	Feb 21, 2020	Clinical status at Day 15 based on 7-point ordinal scale
Severe Open-label	Global	Gilead	N = 400 (1:1) 10d RDV:5d RDV	Enrollment not yet started	Normalization of fever and O ₂ saturation by Day 14
Moderate Open-label	Global	Gilead	N = 600 (1:1:1) 10d:5d RDV: Placebo	Enrollment not yet started	Hospital discharge by Day 14

* Stratified by disease severity at enrollment

Chinese response to COVID-19

Measures in Numbers

Nationwide:

≈1.4 billion people underwent 10 days of at-home isolation

Hubei:

≈59.2 million people were subjected to cordon sanitaire

>50,000 hospital beds were opened for COVID-19 patients
(including 3 new hospitals + 16 temporary module hospitals)

>40,000 healthcare workers were deployed to Hubei