

COVID 19

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March 30, 2020



Faculty/Presenter Disclosure

- Faculty: Dr M John Gill
Financial affiliations:
 - HIV Advisory boards: ViiV, Gilead, Merck .
 - Grants, clinical trials: Amgen ,Merck, CIHR, NIH
 - Patents, royalties: Nil
 - Investments in health organizations: Nil
 - Other influential affiliations: Nil

Disentangling the message

- Lots of “papers” now published online before even reviewed
- Science may be correct but may jump to conclusions or clearly be incorrect or incomprehensible and will/would never be published
- Even in top quality peer-viewed journals the articles may be premature / over interpreted / incomplete or without necessary caveats
- Authors, reviewers and journals are under immense pressure to be fast and first
- Be careful

Diagnostic Clinical Challenges unchanged

Influenza-like-illness (ILI)

- **New or changed cough**

AND one or more of the following:

- **Fever** (or history of fever in the last 24 hours)
- **Muscle aches**
- **Severe exhaustion/weakness**
- Sore throat
- Joint pain

COVID-19

- **Fever** (98%)
- **Cough** (76%)
- **Myalgia or fatigue** (44%)
- Sputum production (28%)
- Headache (8%)
- Hemoptysis (5%)
- Diarrhea (3%)
- **Anosmia/hyposmia/dysgeusia ?**
- Contact /travel

Diagnosis of COVID 19 Infection

- A nasopharyngeal swab (NP) on good respiratory samples looking for viral genetic sequences (molecular testing) is only current diagnostic test. N95 not required for NP swab. BAL seldom indicated
- Two step process now identifies “e gene” coronavirus sequence then confirmed by SARS-CoV-2 “polymerase gene” sequence
- As with other tests, sampling and timing issues: Too early/bad sample limits sensitivity and do virus sequences found post-recovery mean active infectious virus?
- Severe global “reagent” shortage. Do not test asymptomatic!
- No serology testing yet, meaning we are unable to determine past asymptomatic exposures

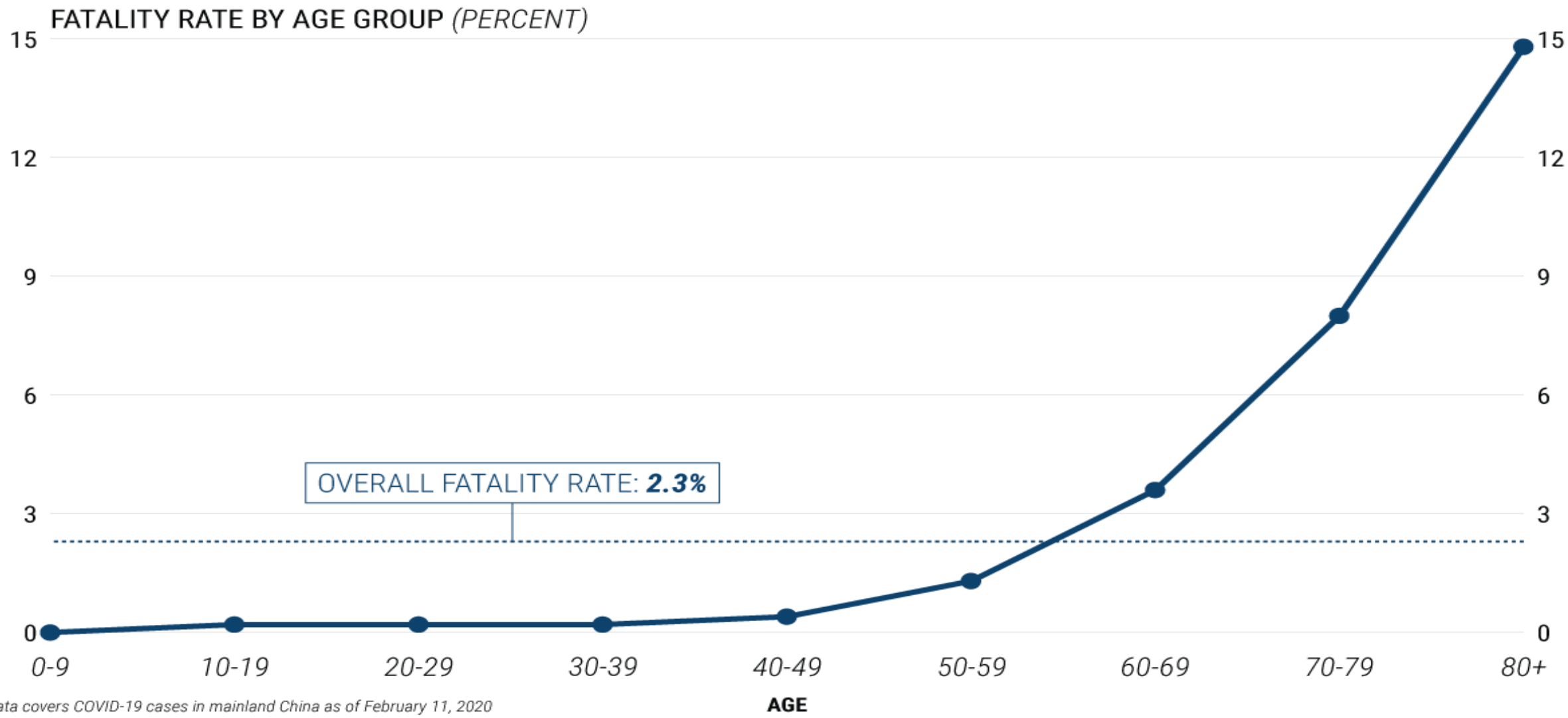
Natural History in Humans

- Incubation period likely 2-14 days (median ~5 days)
- 97.5% develop symptoms within 11 days
- Proportion of asymptomatic infections unknown. May be low but critical for understanding possible transmission and HCW immunity
- Currently we believe of those diagnosed, 80% have self-limited mainly respiratory illness probably of ~ 14 Days duration
- 20% have more severe illness requiring medical care +/- hospitalization
- Risk in hospitalized is mainly respiratory then multi organ failure requiring ventilation and high risk of death
- Progression risk and rate down pathway below is unclear

Fatality rate

- Is it 0.5% or 10%?
- Difference driven in part by age of population and comorbidities (Korea v Lombardy)
- Stage of presentation
- Medical care available at time (i.e. overwhelmed)
- Duration of local epidemic (recent infections do not have endpoints)

COVID-19: *Fatality Rate*



Note: Data covers COVID-19 cases in mainland China as of February 11, 2020
Source: Chinese Center for Disease Control and Prevention

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COVID 19 Infection treatment

- Supportive care
- Kaletra disappointing in a NEJM study published 10 days ago despite benefit in SARS
- Hydrochloroquine / azithromycin / chloroquine value unclear
- Awaiting many trial results (>500 listed as in progress)
- Until then <https://www.albertahealthservices.ca/assets/info/ppih/if-ppih-covid-19-recommendations.pdf>
- My main hope/interest is Remdesivir (unavailable in Canada)

Americans Reportedly Turning To Mexico To Obtain Drug Trump Touts As Potential Coronavirus Cure.

The [Dallas Morning News](#) (3/23, Branham) reports that “Americans are making a mad dash south of the border in search of” hydroxychloroquine, a drug President Trump “calls a potential cure for the coronavirus, even as some health experts cast doubt on its effectiveness.” The drug, an “anti-malaria medication known as Plaquenil, is a hot drug here, with more than a dozen pharmacies saying they’ve run out.” Due to the high demand, pharmacists “said Monday and over the weekend that they’re now requiring written prescriptions from doctors who must state the medicine is for patients with conditions that include lupus and malaria, conditions for which the drug is normally used.”

Scientific topics generating noise

- **Sex:** Why is COVID 19 infection mortality in men across many studies/countries twice that of women? Is it related to other factors -- smoking, hand washing or that immune genes reside on X chromosome?
- **Blood type A:** Are they more vulnerable? Some viruses do not infect people. Unclear here if that may be factor
- **NSAIDS ??**
- **Pregnancy:** Unclear if risk to fetus but viremia not common in COVID 19
- Does presence of viral genetic material match infectious virus?

The role of Angiotensin converting enzyme 2

- Increased rate of non-survival in ICU seen in CVD DM and high BP. Often these patients were on ACE inhibitors
- SARS-COV-2 enters cell by ACE 2 receptor which is expressed on epithelial cells in lung intestine kidney and blood vessels
- ACE 2 expression is increased in DM T 1 and 2 who are treated with ACE inhibitors and angiotensin II type 1 receptor blockers
- Calcium channel blockers do not increase ACE 2 expression

The “Love Boat” saga 2020

- The Diamond Princess, hosted 3,711 passengers/crew who underwent a two-week quarantine after a disembarked passenger was diagnosed with COVID-19
- Over 16 days, a total of 3,063 tests were conducted and **634 persons tested positive**. Of these, 476 (75.1%) of cases were ≥ 60 years old and 313 (49.3%) were female
- Of the 634 positive passengers, 306 (48.3%) were symptomatic and 328 (51.7%) were reported as asymptomatic at testing
- Using modeling it was estimated that 197 of the 328 (60.6%) asymptomatic cases would become symptomatic. As such, they estimate that **17.9% of infected cases would be truly asymptomatic** throughout their infection

Therapeutic Trials

- CATCO
- Solidarity
- HOPE (outpatient early therapy)
- Post-exposure prophylaxis study for HCW
- Anti inflammatory studies in hospitalized patients: Colchicine
Tocilizumab (binds IL-6)

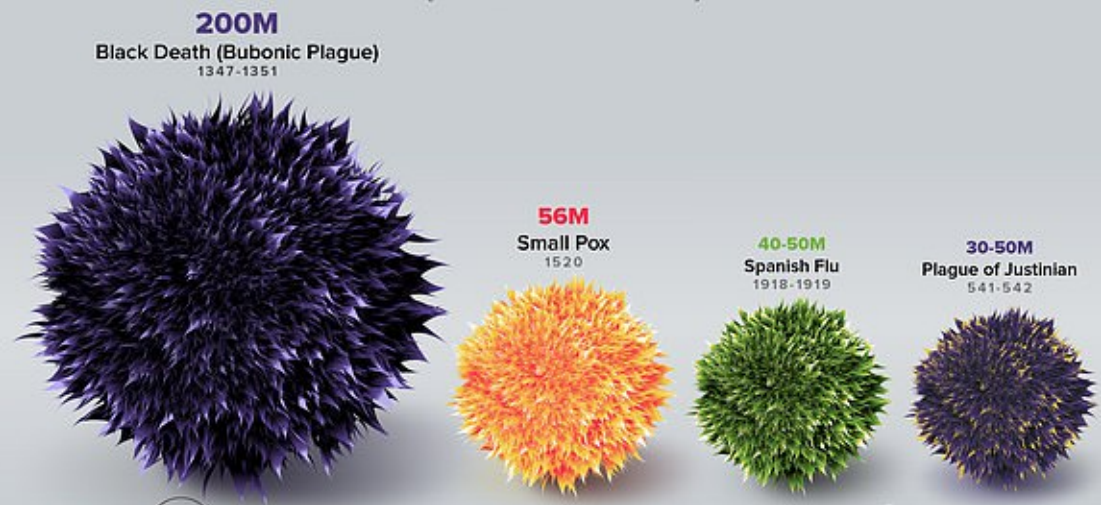
Encouraging News

- Virus not mutating significantly. So vaccine more possible but virus less likely to “flame out” or become less pathogenic
- Variation is, however, enough for phylogenetic studies to track networking
- IGG and IGM Antibody tests are close: Will be very useful for determining natural history and possible health care staffing

Until then science matures



Questions?

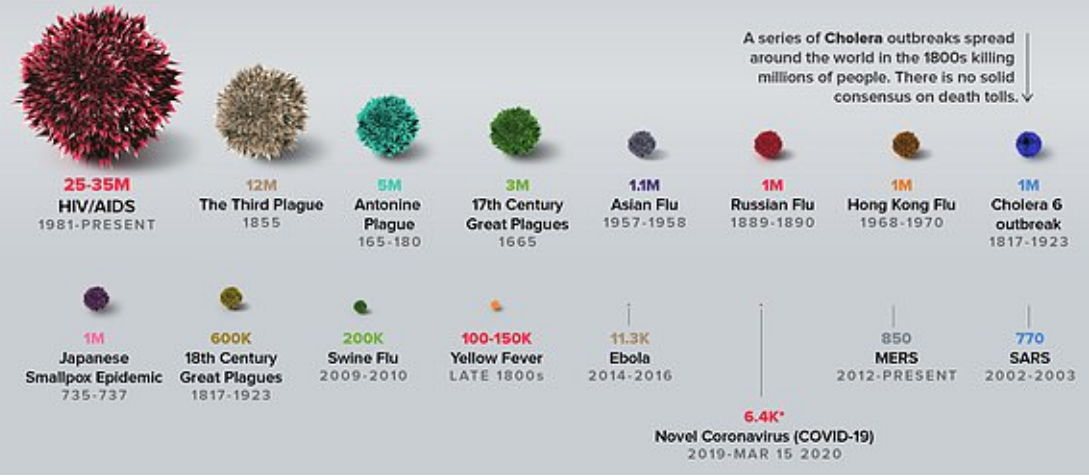


The plague originated in rats and spread to humans via infected fleas.

The outbreak wiped out 30-50% of Europe's population. It took more than 200 years for the continent's population to recover.

Smallpox killed an estimated 90% of Native Americans. In Europe during the 1800s, an estimated 400,000 people were being killed by smallpox annually. The first ever vaccine was created to ward off smallpox.

The death toll of this plague is still under debate as new evidence is uncovered, but many think it may have helped hasten the fall of the Roman Empire.



The Grocery Delivery

- Wipe down any soiled or dirty packages
- Wash all veggies and fruits regardless if triple washed
- Wipe milk and refrigerated containers to remove condensation dirt or spots
- Hands below the T region of the face
- Then appropriate 20-30 sec hand hygiene
- Pack away the groceries

Labs

- Lymphopenia
- D Dimer elevated
- IL-6 elevated (target for monoclonals)

Questions

- Inoculum effect?
- Kaletra is aspartic Protease inhibitor: SARS-COV2 has a cysteine protease
- Pregnancy

Pre-submission paper

- Viral titers very high 7×10^8 first week THEN DECLINE
- No virus in blood, stool or in urine
- T cell depletion and exhaustion