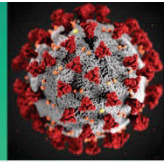# COVID-19 Science Update

**From the Office of the Chief Medical Officer, CDC COVID-19 Response, and the CDC Library, Atlanta, GA.
Intended for use by public health professionals responding to the COVID-19 pandemic.**

*** Available on-line at https://www.cdc.gov/library/covid19 ***

Epidemiology

PREPRINTS (NOT PEER-REVIEWED)

ACE2 and TMPRSS2 variants and expression as candidates to sex and country differences in COVID-19 severity in Italy. Asselta *et al*. medRxiv (April 2, 2020). Published in Aging (June 5, 2020).

Key findings:

- The transmembrane protease TMPRSS2 is critical for entry of SARS-CoV-2 into cells after it binds to the ACE-2 receptor.
- The TMPRSS gene was expressed slightly more in males than females (Figure).
   - Genetic variants in TMPRSS2 that may predispose to more severe COVID-19 were more common in East Asians and Italians than in other Europeans.
- Expression of the ACE2 gene in lung tissue did not differ by sex.
   - Genetic variant in *ACE2* that predisposes to hypertension, diabetes, and coronary artery disease was more common in East Asians than Italians.

Methods: Using exome and single nucleotide polymorphism array data from a large (>3,000 persons) population-based Italian cohort, investigators assessed the frequency of genetic variants in the Italian, other European, and East Asian populations. *Limitations:* Only examined two genes; did not account for non-genetic factors affecting differences in disease severity (e.g., smoking, population age distributions, environmental factors).

Implications: These preliminary data suggest host genetic factors may alter COVID-19 disease severity.

Figure:
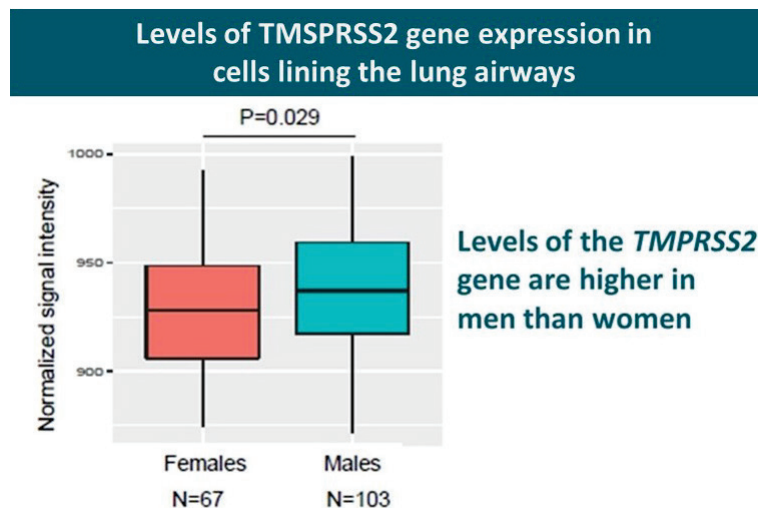
Note: Adapted from Asselta *et al*. Figure shows TMPRSS2 mRNA expression levels in cells lining the lung airways from **men** and **women**. Licensed under CC-BY-3.0.

A territory-wide study of COVID-19 cases and clusters with unknown source in Hong Kong community: a clinical, epidemiological and phylogenomic investigation. Leung e*t al.* medRxiv (April 7, 2020).
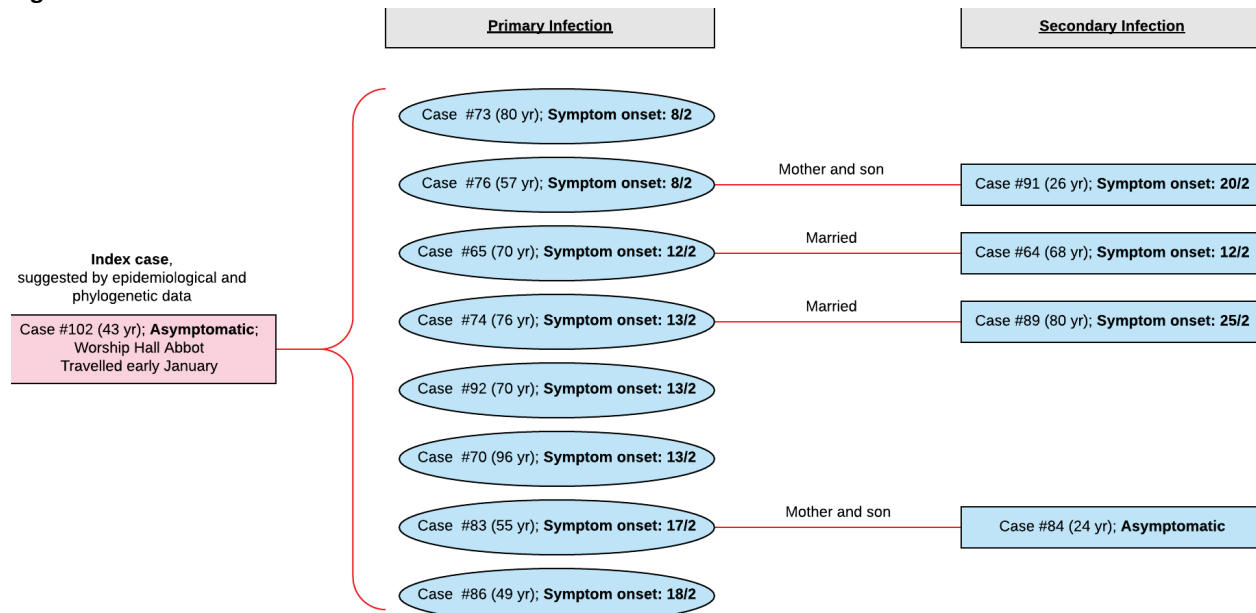
Key findings:

- Among 6 COVID-19 clusters described, 3 included people who had travelled outside Hong Kong within 14 days before symptom onset.
- The largest cluster (n = 13) occurred within a Buddhist worship hall. Likely source was the abbot, who was infected during travel to mainland China but was consistently asymptomatic (Figure).
- Phylogenetic data (i.e., molecular fingerprinting) showed links between this cluster and another.

Methods: Investigators used whole genome sequencing and epidemiological data to identify transmission links between 53% (50/93) of diagnosed cases in Hong Kong through February 28, 2020.

Implications: Phylogenetic analyses (i.e., molecular fingerprinting) can identify how COVID-19 transmission clusters are related in ways that would otherwise be inapparent. These analyses may be especially useful in evaluating clusters and networks that include asymptomatically infected persons.

Figure:

	Primary Infection		Secondary Infection
	Case #73 (80 yr); **Symptom onset: 8/2**		
	Case #76 (57 yr); **Symptom onset: 8/2**	Mother and son	Case #91 (26 yr); **Symptom onset: 20/2**
Index case, suggested by epidemiological and phylogenetic data	Case #65 (70 yr); **Symptom onset: 12/2**	Married	Case #64 (68 yr); **Symptom onset: 12/2**
Case #102 (43 yr); **Asymptomatic**; Worship Hall Abbot Travelled early January	Case #74 (76 yr); **Symptom onset: 13/2**	Married	Case #89 (80 yr); **Symptom onset: 25/2**
	Case #92 (70 yr); **Symptom onset: 13/2**		
	Case #70 (96 yr); **Symptom onset: 13/2**		
	Case #83 (55 yr); **Symptom onset: 17/2**	Mother and son	Case #84 (24 yr); **Asymptomatic**
	Case #86 (49 yr); **Symptom onset: 18/2**		

Note: Adapted from Leung *et al*. Epidemiological investigation of 'cluster 6'. Rectangular box-male; oval-female. The **pink** box corresponds to the abbot, who travel to Wuhan within the 14-day period prior to symptom onset. Used by permission from author.

Modeling & Transmission

PEER-REVIEWED

Quantifying SARS-CoV-2 transmission suggest epidemic control with digital contact tracing. Ferretti *et al*. Science (March 31, 2020).

Key Findings:

- Modelers estimated the contributions to new infections from persons during various phases of infection, as well as from asymptomatically infected persons and environmental contact (Figure 1).
- Contact tracing delays of even one day substantially limited the estimated effectiveness of case isolation, contact tracing, and quarantine efforts (Figure 2).

Methods: A probabilistic mathematical model examined the effectiveness of non-pharmaceutical interventions combined with traditional "shoe-leather" contact tracing (versus instant digital contact tracing with a smartphone app) to durably suppress a COVID-19 epidemic. *Limitations:* Model parameters derived from China's early stages may not apply to countries where the epidemic spread quicker; the relative infectiousness of asymptomatic people, potentially under-estimated the contribution of asymptomatic transmission.

Implications: Rapid and immediate digital contact tracing after diagnosis may better control COVID-19, but there are barriers to feasibility. Substantial levels of pre-symptomatic transmission reinforce the importance of prevention measures, including social distancing and cloth face coverings.

Figure 1
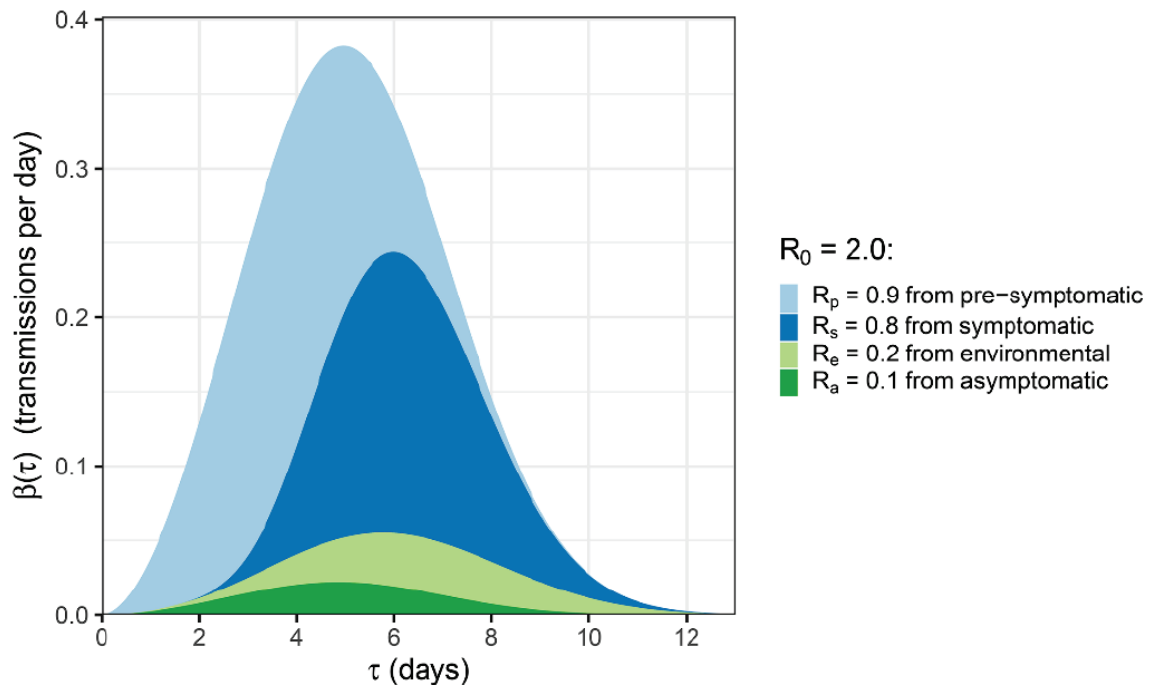
Note: Adapted from Ferretti *et al*. Figure displays relative infectiousness of the four transmission types considered in the model. **Pre-symptomatic persons** contribute relatively more to viral transmission than **symptomatic persons**, **environmental transmission**, and **asymptomatic persons**. R_0 is a mathematical indicator of contagiousness and indicates the average number of people who will catch a disease from one contagious person (e.g. $R_0 = 2$ means that one infected person will infect two other people). Licensed under CC-BY 4.0.

Figure 2
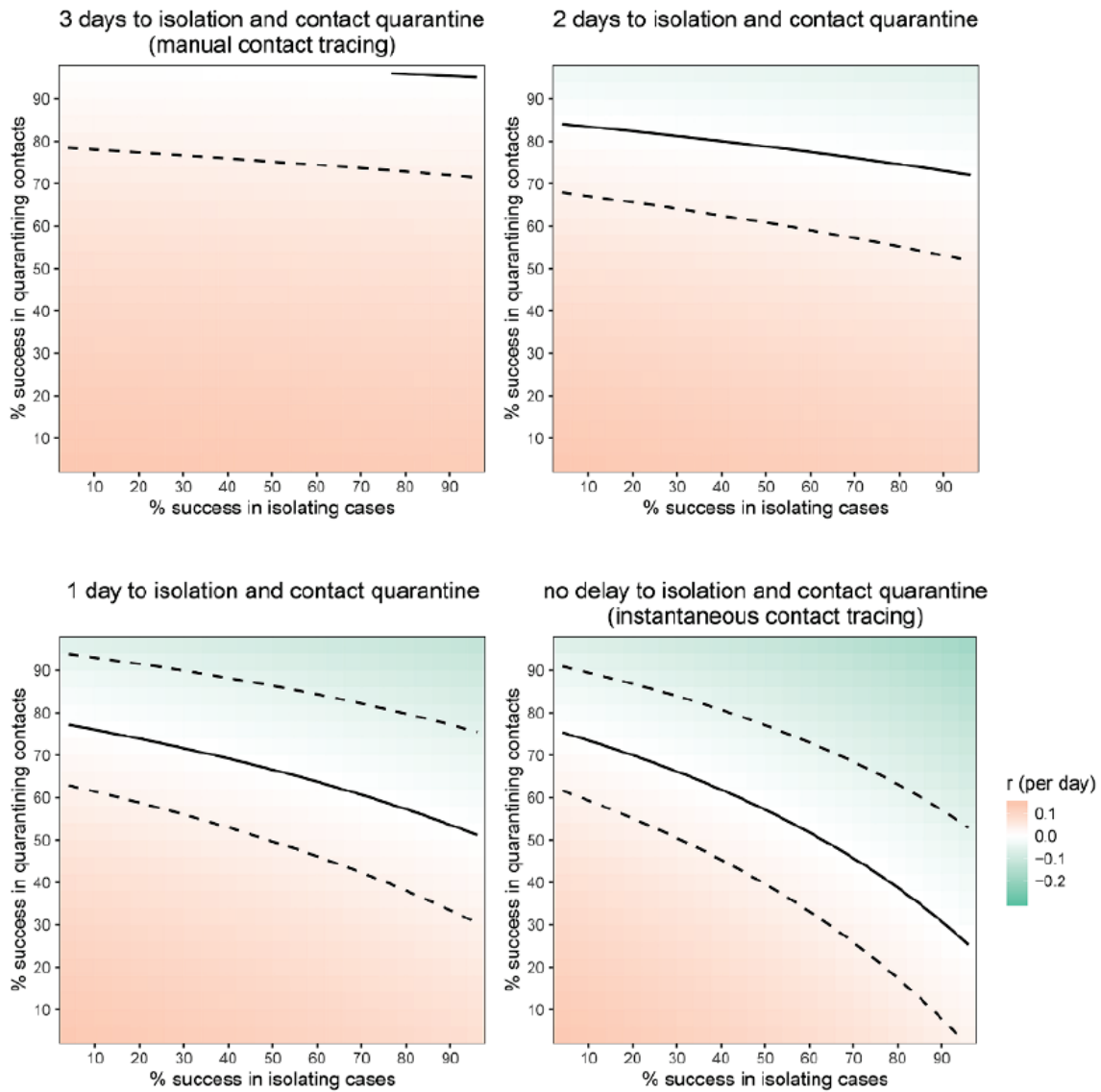
Note: Adapted from Ferretti *et al*. Figure displays the exponential growth rate of the epidemic (*r*) at differing levels of success with quarantine of contacts (vertical axis) and isolating cases (horizontal axis). The **top left figure** assumes it takes three days to isolate a case and quarantine contacts. The **bottom right figure** assumes case isolation and contact quarantine immediately after diagnosis of the case (i.e., no delay). Licensed under CC-BY 4.0.

Clinical Treatment & Management

PEER-REVIEWED

Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. Shen *et al.* JAMA (March 27, 2020).

Key Findings:
- 5 critically ill COVID-19 patients appeared to stabilize or improve after receiving a transfusion of plasma containing anti-SARS-CoV-2 antibodies from recovered patients (i.e., convalescent plasma therapy); their improvement was assessed by reductions in Sequential Organ Failure Assessment (SOFA) scores (Figure).
- Three patients were weaned from mechanical ventilation 2–9 days post-transfusion and later discharged; two remained intubated but cleared detectable virus within 2 weeks post-transfusion.

Methods: Clinical case series of 5 critically ill and intubated COVID-19 patients in Shenzhen, China with severe acute respiratory distress syndrome, one with multiorgan system failure. During days 10–22 of hospitalization, patients received transfusions of convalescent plasma from 5 recovered COVID-19 patients. *Limitations*: Sample size; lack of control group; not possible to distinguish effect of convalescent plasma from antiviral and corticosteroid treatment; no information on adverse events.

Implications: Findings from this small clinical case series suggest convalescent plasma therapy might be beneficial for treating COVID-19. Clinical trials are planned to investigate the safety and efficacy of this potential COVID-19 treatment.

Figure:
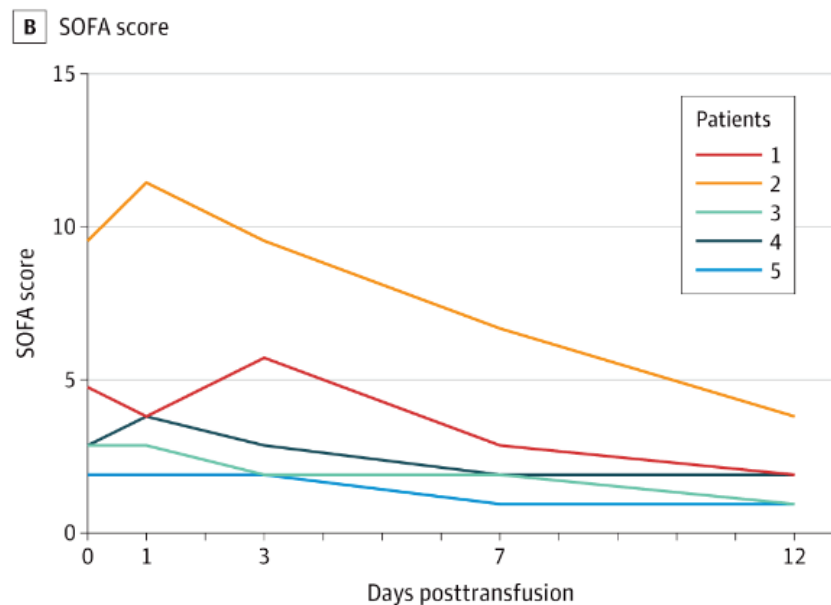
Note: From Shen *et al*. Figure displays Sequential Organ Failure Assessment (SOFA) scores of each patient for 12 days post convalescent plasma transfusion. SOFA scores range from 0–24, with higher scores indicating more severe illness. The SOFA score is calculated using 6 systems: respiratory, coagulation, hepatic, cardiovascular, central nervous system, and kidney. Decreasing SOFA scores = clinical benefit. Reproduced with permission from JAMA. doi:10.1001/jama.2020.4783. Copyright©2020 American Medical Association. All rights reserved.

PREPRINTS (NOT PEER-REVIEWED)

Assessing SARS-CoV-2 RNA levels and lymphocyte/T cell counts in COVID-19 patients revealed initial immune status of patients as a major determinant of disease severity. Han *et al*. SSRN (March 31, 2020). Published in Medical Microbiology and Immunology (August 28, 2020).

Key findings:
- On admission, patients with severe COVID-19 had more comorbidities; lower absolute serum lymphocyte counts (especially T cell counts: Figures 1 and 2); and higher immune markers (C-reactive protein, interleukin-6, serum amyloid A protein, procalcitonin).
- At 3–5 days after admission, SARS-Cov-2 RNA viral loads were highest among the most severely ill patients.
- Total lymphocyte and T cell count levels were most predictive of disease severity.

Methods: Retrospective study of 154 COVID-19 patients from China. Researchers estimated viral RNA levels with cycle threshold values, as well as lymphocyte and cytokine profiles, with flow cytometry and immunoassays. Principal component analyses were used to identify most relevant immunological markers for predicting mild vs severe cases. *Limitation*: Single center study.

Implications: Severe COVID-19 was more common among persons with lower total lymphocyte and T cell counts, regardless of SARS-CoV-2 viral loads at admission. Weakened immunity might lead to higher viral loads, and early antiviral treatments may be particularly beneficial for such persons.

Figure 1
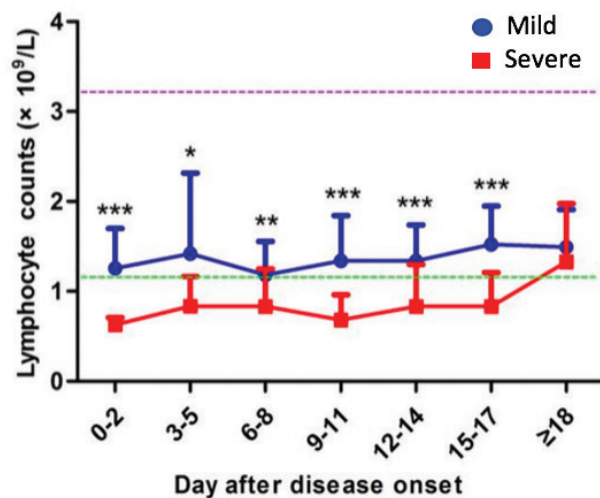
Figure 2
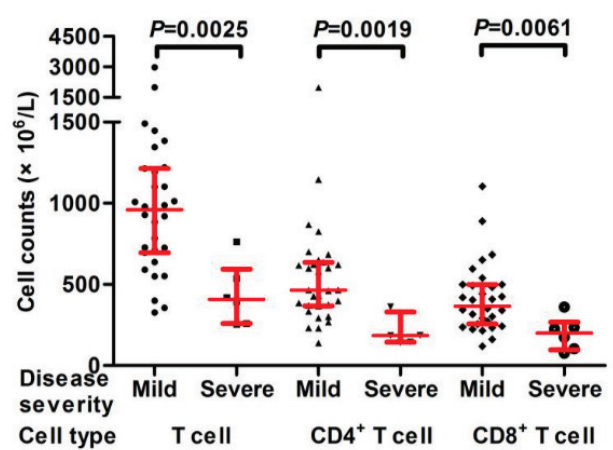
Note: Adapted from Han *et al*. **Figure 1** displays lymphocyte cell counts in blood of **mild (blue)** and **severe (red)** COVID-19 patients shown by day after disease onset. Limits of normal values indicated by the **purple line (upper limit)** and **green line (lower limit).** Patients with severe COVID-19 had lower lymphocyte counts. * p <0.05, ** p <0.01, *** p <0.001. **Figure 2**: T cell counts in mild vs severe COVID-19 patients' blood specimens at 3-5 days after disease onset. Patients with severe COVID-19 had lower T cell counts than those with mild COVID-19. Available via Nature Public Health Emergency Collection through PubMed Central.

In Brief

Incarcerated Populations

- Rubin R. **The challenge of preventing COVID-19 spread in correctional facilities**. JAMA. Provides a summary of the challenges in preventing COVID-19 spread in correctional facilities.

Mental Health

- Ayanian J. **Mental health needs of health care workers providing frontline COVID-19 care**. JAMA Health Forum. Factors including emotional strain, physical exhaustion, caring for coworkers, shortages of PPE and medical equipment, and concerns about infecting family contribute to the psychological distress of health care workers providing direct frontline care to patients with COVID-19.
- Shanafelt *et al*. **Understanding and addressing sources of anxiety among health care professionals during the COVID-19 pandemic**. JAMA. Sources of anxiety are organized into 5 requests from health care professionals to their organization: hear me, protect me, prepare me, support me, and care for me.
- Druss B. **Addressing the COVID-19 pandemic in populations with serious mental illness**. JAMA Psychiatry. Describes strategies to mitigate the outcome of this epidemic among patients with serious mental illness.

cdc.gov/coronavirus