Summary of Major Literature Related to COVID-19 (Week of March 30–April 5)

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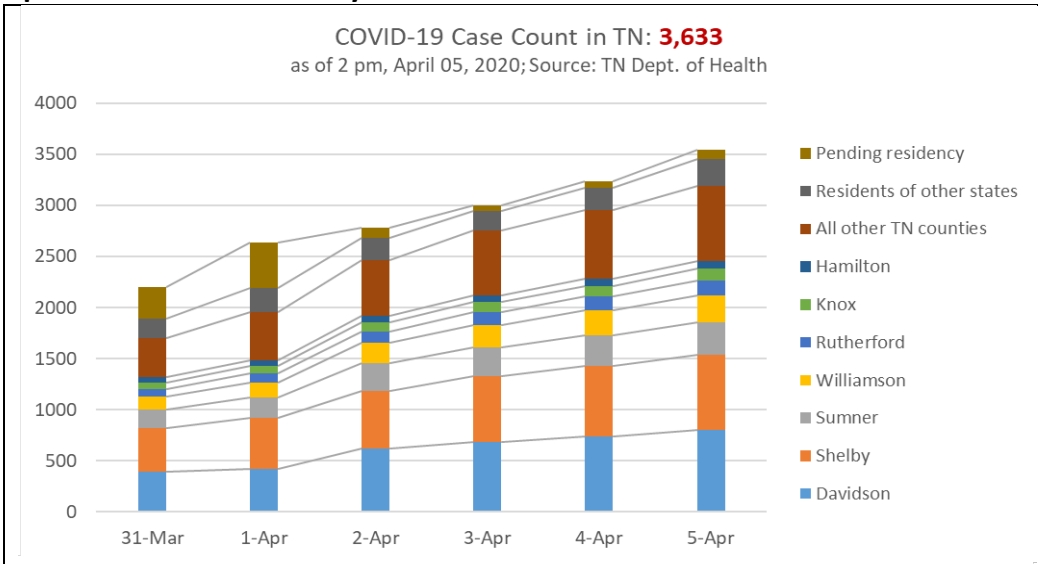
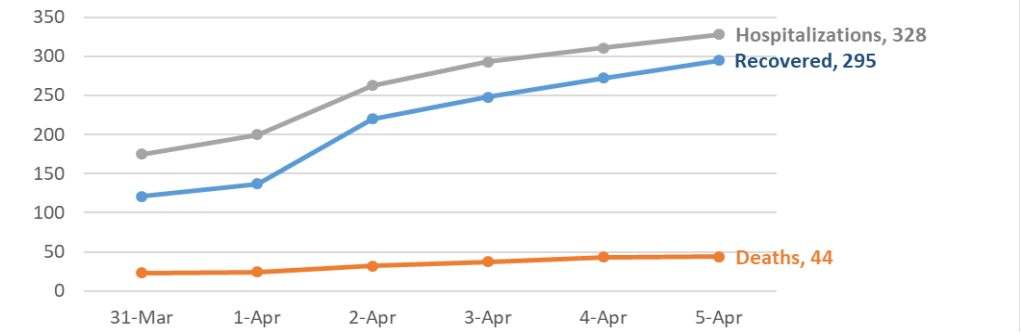
***This is informational and not intended to create variance from VUMC policies/guidance.**

EPIDEMIOLOGY

Statistics - Tennessee and Nashville

April 2: Gov Lee issues Stay at Home executive order for Tennessee





- Total TN cases = 3,633
- Total tested = 45,300
- Hospitalized = 328
- Recovered = 295
- Confirmed deaths = 44
- Top three counties:
  - Davidson = 801
  - Shelby = 736
  - Sumner = 321
- By age:

Age group	Cases	%
0–10	42	1.2%
11–20	171	4.7%
21–30	815	22.4%
31–40	608	16.7%
41–50	565	15.6%
51–60	644	17.7%
61–70	431	11.9%
71–80	215	5.9%
80+	118	3.2%

- Ages 21-50 make up 55% of cases in TN

Statistics - USA

March 27: Five congressional Democrats wrote to Health and Human Services Secretary demanding the federal government collect and release the breakdown of coronavirus cases by race and ethnicity

- IL is one of a few states to release racial data: African Americans make up 15% of IL population and 28% of confirmed cases, while whites comprise 77% of the population and 39% of confirmed cases http://www.dph.illinois.gov/news/public-health-officials-announce-488-new-cases-coronavirus-disease
- Data are needed

Case fatality/comorbidities

1. **Estimates of the severity of coronavirus disease 2019: a model-based analysis.** Verity et al. Lancet Infect Dis. March 30**.** https://www.sciencedirect.com/science/article/pii/S1473309920302437?via%3Dihub
- Mean duration from onset of symptoms to death was 17.8 days, from onset to recovery was 24.7 days

- Based on data from 70,117 laboratory-confirmed and clinically diagnosed cases from mainland China, case fatality ratio (CFR) was 1.38%
    - 6.4% for patients aged ≥60 years *vs* 0.32% for aged <60 years; 13.4% for aged ≥80 years
- Model adjusted for typical overestimation of CFR early in new epidemics due to detection of clinically severe cases, and underestimation of CFR early due to limited ascertainment of final patient outcome
- Model-based estimate of infection fatality rate (proportion of infections, including those with no symptoms or mild symptoms, who die) was 0.66%. Proportion of infected individuals likely to be hospitalized increased with age, up to 18.4% in individuals ≥80 years

2. **Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12–March 28, 2020.** CDC COVID-19 Response Team. March 31. https://www.cdc.gov/mmwr/volumes/69/wr/mm6913e2.htm

- 122,653 US laboratory-confirmed cases and 2,112 deaths reported to CDC
- Among 7,162 (5.8%) with available data, 38% have at least one underlying health condition
    - >70% among those requiring ICU admission or hospitalization vs. 27% among those not hospitalized
    - Diabetes mellitus (11%), chronic lung disease (9%), and CVD (9%) most common
- 94% of deaths were among those with at least one underlying condition
- Consistent with data from China and Italy

Pregnancy and breastfeeding

3. **Antibodies in Infants Born to Mothers With COVID-19 Pneumonia.** Zeng et al. JAMA. March 26. https://jamanetwork.com/journals/jama/fullarticle/2763854

- 6 pregnant women with confirmed COVID-19; all had cesarean deliveries, infants immediately isolated
- All neonatal throat swabs and blood specimens tested negative for SARS-CoV-2 by RT-qPCR. However, all infants had virus-specific antibodies detected in serum
    - IgG concentrations elevated in 5 infants, IgM concentrations (could have been produced by infant if the virus crossed the placenta) elevated in 2 infants
- Limitations: small sample, lack of cord blood, amniotic fluid and breast milk, no infant outcomes data

4. **Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China.** Zheng et al. JAMA Pediatrics. March 26. https://jamanetwork.com/journals/jamapediatrics/fullarticle/2763787

- 33 neonates born to mothers with COVID-19. Three (9%) tested positive for SARS-CoV-2
    - All were delivered by cesarean. No deaths were reported
    - All three with SARS-CoV-2 had clinical & radiographic pneumonia
- Vertical maternal-fetal transmission cannot be ruled out

TRANSMISSION/TESTING

April 3: CDC recommends that people wear cloth face mask when entering public places

5. **Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020.** Wei at al. CDC Morbidity and Mortality Weekly Report. April 1. https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_x

- Of 243 COVID-19 cases reported in Singapore, 157 were locally acquired
    - 10 clusters of 2-5 patients each
    - Of these, 6.4% were presumably acquired through presymptomatic transmission
- Presymptomatic transmission occurred 1–3 days before symptom onset of the source patient

- Limitation: mild symptoms may not be recognized by the source patient
- **Implication**: Social distancing is critical in preventing COVID-19 spread

6. **Virological assessment of hospitalized patients with COVID-2019.** Wolfel et al. Nature, April 1. https://www.nature.com/articles/s41586-020-2196-x
- Study subjects had mild clinical course, all young- to middle-aged without significant underlying disease
- Pharyngeal virus shedding was very high during the first week of symptoms (peak at day 4), indicating efficient transmission at a time when symptoms are still mild
- Infectious virus was isolated from throat- and lung-derived samples. The new data indicate active replication in the gastrointestinal tract. Blood and urine never yielded virus.
- Seroconversion occurred after 7 days in 50% of patients but was not followed by rapid decline in viral load; seroconversion early in week 2 coincides with slow but steady decline of sputum viral load.
- Shedding of viral RNA from sputum outlasted the end of symptoms
- **Implication**: Early discharge with ensuing home isolation could be chosen for patients who are beyond day 10 of symptoms with less than 100,000 viral RNA copies per ml of sputum

7. **SARS-CoV-2–Positive Sputum and Feces After Conversion of Pharyngeal Samples in Patients With COVID-19.** Chen et al. Ann Intern Med. March 30. https://annals.org/aim/fullarticle/2764036/sars-cov-2-positive-sputum-feces-after-conversion-pharyngeal-samples
- Among 133 COVID-19 inpatients, 22 (16.5%) had positive RT-qPCR results for SARS–CoV-2 in sputum or feces for up to 39 and 13 days, respectively, after pharyngeal swabs became negative
- **Implication**: unclear whether patients with negative pharyngeal swabs are truly virus-free, and whether sampling of additional body sites is needed
- Limitations: unknown whether positive sputum and feces results indicate continued risk for transmission; sample collection was not standardized
- Related publication: **Detectable SARS-CoV-2 Viral RNA in Feces of Three Children during Recovery Period of COVID-19 Pneumonia**. Zhang et al. J Med Virol. March 29. https://onlinelibrary.wiley.com/doi/10.1002/jmv.25795

CLINICAL MANAGEMENT/SYMPTOMS

8. **Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China**. Wu et al. JAMA Ophthalmol. March 31. https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2764083
Perspectives on Coronavirus Disease 2019 Control Measures for Ophthalmology Clinics Based on a Singapore Center Experience. Jun et al. JAMA Ophthalmol. March 31. https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2764085
- Case series (N=38 with clinically confirmed COVID-19) raises possibility of transmission through the eye
- 31.6% had ocular abnormalities consistent with conjunctivitis, including conjunctival hyperemia, chemosis, epiphora, or increased secretions
- SARS-CoV-2 tested positive by RT-PCR in conjunctival swabs of 2 of 11 patients tested (18%)
- **Important coronavirus updates for ophthalmologists**. CDC, WHO. April 2. CDC, WHO. https://www.aao.org/headline/alert-important-coronavirus-context
    - SARS-CoV-2 can cause a mild follicular conjunctivitis indistinguishable from other viral causes, and possibly be transmitted by aerosol contact with conjunctiva
    - American Academy of Ophthalmology and federal officials recommend protection for the mouth, nose and eyes when caring for patients potentially infected with SARS-CoV-2

9. **Initial Clinical Impressions of the Critical Care of COVID-19 Patients in Seattle, New York City, and Chicago.** Sommer et al. Anesthesia & Analgesia. March 25. https://journals.lww.com/anesthesia-analgesia/Abstract/publishahead/Initial_Clinical_Impressions_of_the_Critical_Care.95733.aspx

- Early clinical presentation:
  - A protean spectrum, including classic "fever, fatigue, cough" but also chest pain, headaches, altered mental status, gastrointestinal symptoms, and myocardial injury
  - Shortness of breath/severe respiratory failure occurs ~1 week after initial symptoms, when patients may feel as if symptoms are resolving. Progress is rapid for those requiring intubation.
  - Increase in % of younger patients requiring ICU care compared other countries
- Laboratory values:
  - Elevated CRP (correlates with severity), ferritin, IL-6, and D-dimer; Reduced blood lymphocytes
  - Daily tracking of metabolic and hematologic panels, CRP, ferritin, D-dimers, fibrinogen, lactate dehydrogenase, and cardiac function
  - Radiography: patchy opacities almost always present, severity of opacifications correlates with severity of disease
  - Rapid nasal PCR sensitivity only 30-60%
- Organ system effects:
  - Severe cardiomyopathy that presents when respiratory symptoms are resolving dramatically increases mortality
  - Acute kidney injury and refractory metabolic acidosis are observed
  - Non-invasive ventilation & high flow O2 via nasal cannula typically ineffective, move towards earlier intubation for disease management and to reduce risk of nosocomial spread including to providers

TREATMENT

10. **The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro.** Caly et al. Antiviral Res. April 3. https://www.sciencedirect.com/science/article/pii/S0166354220302011

- Ivermectin is an FDA-approved anti-parasitic agent**,** has an established safety profile in humans, has demonstrated broad-spectrum anti-viral activity *in* vitro, and is widely available
- In vitro study showed that ivermectin is an inhibitor of the COVID-19 causative virus (SARS-CoV-2)
- ~5000-fold reduction (99.98% reduction) in viral RNA at 48h following a single treatment in cell culture
- Clinical trials are needed to evaluate the potential to repurpose ivermectin for treating COVID-19 and to establish the dose and treatment regimen

11. **Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial.** Chen et al. medRxiv preprint, April 1. https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2.full.pdf

- 62 COVID-19 patients randomized in a parallel-group trial, 31 assigned to receive an additional 5-day hydroxychloroquine (HCQ, 400 mg/d) treatment; time to clinical recovery, clinical characteristics, and radiological results assessed at baseline and 5 days after treatment.
- Body temperature recovery time and cough remission time significantly shortened in HCQ group
- Larger proportion of patients with improved pneumonia in HCQ treatment group (80.6%, 25 of 32) vs control group (54.8%, 17 of 32) (p=0.057)
- All 4 patients who progressed to severe illness were in control group
- There were 2 patients with mild adverse reactions in the HCQ treatment group
- **See also: Use of Hydroxychloroquine and Chloroquine During the COVID-19 Pandemic: What Every Clinician Should Know.** Yazdany and Kim. Ann Intern Med. March 31, 2020**.**

https://annals.org/aim/fullarticle/2764199/use-hydroxychloroquine-chloroquine-during-covid-19-pandemic-what-every-clinician

12. **Coronavirus disease 2019 (COVID-19) and anti-rheumatic drugs.** Georgiev. Rheumatol Int. April 2**.** https://link.springer.com/article/10.1007/s00296-020-04570-z

- COVID-19 has cytokine storm syndrome similar to that seen in inflammatory rheumatic disorders, warranting consideration of using anti-rheumatic drugs
- The World Health Organization recommends avoiding routine administration of systemic corticosteroids for the treatment of viral pneumonia outside clinical trials
- Chloroquine and its less toxic derivative hydroxychloroquine are well known for their immunomodulating effects in rheumatology and are being tested for treating COVID-19
- IL-6 levels are significantly elevated in severe COVID-19 and are associated with SARS-CoV-2 viral load. Tocilizumab, which blocks IL-6 receptor, might be a promising strategy in COVID-19 management
- Tocilizumab therapy is listed in the recommendations for severe COVID-19 management by the National Institute for the Infectious Diseases 'Lazzaro Spallanzani'. https://www.pagepress.org/journals/index.php/idr/article/view/8543

MENTAL HEALTH

13. **Factors Associated with Mental Health Outcomes Among Health Care Workers Exposed to COVID-19.** Lai et al. JAMA. March 23. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2763229

- Mental health survey data collected from 1,257 health care workers in 34 hospitals in China
- 50% reported depressive symptoms, 15% reported moderate or severe depressive symptoms, 45% reported anxiety, and 34% reported insomnia.
- Women, frontline workers, and those at the center of the epidemic in Wuhan reported increased risk and more severe degrees of all mental health measurements