Navigating Coronavirus Series

COVID-19: Clinical Considerations for Primary Care
July 28, 2020
This webinar series brought to you by:
Logistics for today’s COVID-19 Forum

Question during the live webinar

Technical assistance
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Today’s Presenters

- **David Weber, MD, MPH**, Professor of Medicine, Pediatrics and Epidemiology at UNC, Associate Chief Medical Officer for UNC Health and Medical Director for UNC Hospitals’ Departments of Hospital Epidemiology

- **Michael J. Smith, MD**, Associate Professor of Pediatrics at Duke University and a member of the Duke Antimicrobial Stewardship and Evaluation Team

- **Therese Garrett, MD**, Medical Director, Behavioral Health, WellCare of North Carolina, Co-Chair of the NC Psychiatric Association’s Disaster Committee, and President of the NC Council on Child and Adolescent Psychiatry
COVID-19 (SARS Co-V-2): Focus on Issues Relevant to Primary Care Specialists

David Jay Weber, M.D., M.P.H., FSHEA, FIDSA, FRSM (London)

- Professor of Medicine, Pediatrics, Epidemiology
- Associate Chief Medical Officer, UNC Hospitals
- Medical Director, Hospital Epidemiology, University of North Carolina at Chapel Hill

Disclosures: Consultant-PDI, Germitec, Pfizer, Merck
COVID-19: New Information

- Increasing cases in US; largest increase in the 18-45 year age range
- Percent of population that has had COVID-19 (CDC): 2% TO 5% (outlier, NYC = 23%)
- Percent of asymptomatic infections: 20% to 80% (depends on study population)
- Among symptomatic persons: mild disease, 80%; severe disease, 15%; critical disease, 5%
- Data suggests that airborne (>6 feet) transmission does NOT occur
- Duration of infectiousness: Ambulatory patients, <11 days (5 studies); hospitalized patients, <20 days (2 studies)
COVID-19: New Information

- Viral mutations: Mutations with increased transmissibility reported; but similar virulence
- Likely effective therapies: Remdesivir, Dexamethasone, prone ventilation
- Vaccine: Likely not available in 2020
- Masks very effective in preventing transmission when worn by infected persons, and in preventing acquisition when worn by uninfected persons
- COVID-19 case data now sent to US DHHS: Concerns = potential time delays, lack of transparency and manipulation
- Continued challenges: Limited testing capacity
COVID-19: Worldwide Epidemiology

Source: Johns Hopkins University, national health agencies, data up to 26 July

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/
COVID-19, U.S.

Worldwide >16,264,000 cases (>648,000 deaths)
US >4,234,000 cases, 25% of world’s total (>147,000 deaths):
- deaths undercounted; a leading cause of death in the US
NC >101,000 cases (>1,670 deaths; 1,086 hospitalized)
NC >1,423,000 COVID-19 tests (~10% positive)

Source: COVID Tracking Project
COVID-19 Epidemiology: Increasing Cases in Persons 18-49 Years of Age

Transmission of SARS CoV-2

- Droplet (<6 feet) and direct contact predominant modes of transmission: Household transmission major mode of spread in China
- Indirect (via the contaminated environment) – Important
- Evidence does not support airborne transmission (>6 feet)
- Pre-symptomatic – transmission well documented
Transmission of SARS CoV-2

- Asymptomatic (infection demonstrated) – infectivity undefined
- Aerosolization of stool (viable virus occasionally demonstrated in stool) – no evidence for transmission
- Airborne – no evidence for transmission
- Transplacental/vertical – possible rare cases
- Companion animals – may develop mild symptoms (cats, dogs, tigers, minks) – possible mink-to-human transmission
A negative COVID-19 RT-PCR test does NOT exclude COVID-19 infection if the person is within the 14-day incubation period
A positive antibody test does NOT exclude infectious COVID-19 if the person is symptomatic
A positive antibody test does not necessarily indicate immunity to re-infection
The rapid point-of-care antigen test is only 80% sensitive and has NOT been validated for testing asymptomatic persons
Current turnaround time for commercial tests is 5-10 days
Concentrations of SARS-CoV-2 RNA measured in upper respiratory specimens decline after onset of symptoms (CDC, unpublished data, 2020; Midgley et al., 2020; Young et al., 2020; Zou et al., 2020; Wölfel et al., 2020; van Kampen et al., 2020).

The likelihood of recovering replication-competent virus also declines after onset of symptoms. For patients with mild to moderate COVID-19, replication-competent virus has not been recovered after 10 days following symptom onset (CDC, unpublished data, 2020; Wölfel et al., 2020; Arons et al., 2020; Bullard et al., 2020; Lu et al., 2020; personal communication with Young et al., 2020; Korea CDC, 2020). Recovery of replication-competent virus between 10 and 20 days after symptom onset has been documented in some persons with severe COVID-19 that, in some cases, was complicated by immunocompromised state (van Kampen et al., 2020). However, in this series of patients, it was estimated that 88% and 95% of their specimens no longer yielded replication-competent virus after 10 and 15 days, respectively, following symptom onset.

A large contact tracing study demonstrated that high-risk household and hospital contacts did not develop infection if their exposure to a case patient started 6 days or more after the case patient’s illness onset (Cheng et al., 2020).

Although replication-competent virus was not isolated 3 weeks after symptom onset, recovered patients can continue to have SARS-CoV-2 RNA detected in their upper respiratory specimens for up to 12 weeks (Korea CDC, 2020; Li et al., 2020; Xiao et al., 2020). Investigation of 285 “persistently positive” persons, which included 126 persons who had developed recurrent symptoms, found no secondary infections among 790 contacts attributable to contact with these case patients. Efforts to isolate replication-competent virus from 108 of these case patients were unsuccessful (Korea CDC, 2020).

Specimens from patients who recovered from an initial COVID-19 illness and subsequently developed new symptoms and retested positive by RT-PCR did not have replication-competent virus detected (Korea CDC, 2020; Lu et al., 2020). The risk of reinfection may be lower in the first 3 months after initial infection, based on limited evidence from another betacoronavirus (HCoV-OC43), the genus to which SARS-CoV-2 belongs (Kiyuka et al, 2018).

Currently, 6 months after the emergence of SARS-CoV-2, there have been no confirmed cases of SARS-CoV-2 reinfection. However, the number of areas where sustained infection pressure has been maintained, and therefore reinfections would be most likely observed, remains limited.

Serologic or other correlates of immunity have not yet been established.
Caveats:

- In a recent study of skilled nursing facility workers followed prospectively for asymptomatic infection, one of 48 infected staff had a nasopharyngeal swab which was weakly positive on a single-passage plaque assay more than 20 days after initial diagnosis; however, the specimen was not subjected to serial passage to demonstrate the presence of replication-competent virus (Quicke et al., 2020).

- In one case report, a person with mild illness provided specimens that yielded replication-competent virus for up to 18 days after symptom onset (Liu et al., 2020).

- Data currently available are derived from adults; equivalent data from children and infants are not presently available.

- More data are needed concerning viral shedding in some situations, including in immunocompromised persons.
Symptom Screening at Illness Onset; HCP with SARS-CoV-2, King County, WA

Other potential symptoms: Acute cardiovascular events, acute neurological events
Children: Skin lesions, 0.2% (erythematous rash, urticarial, vesicular lesions); toxic shock like presentation; Kawasaki disease; chilblains (acral lesions on hands/feet)

Chow EJ, et al. JAMA 2020;17 April
Symptom Screening at Illness Onset; HCP with SARS-CoV-2, King County, WA

Figure. Symptom Screening Combination for Health Care Personnel With Coronavirus Disease 2019 at Illness Onset (N = 48)

COVID-19, Timeline of Infection Course

Symptoms begin 4-5 days after exposure (range 2-14)

Based on analysis of 41 patients infected with 2019-nCoV in Wuhan, China

Number of days

0 4 5 7 8 9 10 13 14 17

Onset of symptoms (most common: fever, cough, fatigue)
41 patients, all with pneumonia

Admission to hospital
41

Shortness of breath
21

Acute respiratory distress syndrome
11

Admission to intensive care unit
16

Individuals of all ages are at risk for infection and severe disease. However, the probability of fatal disease is highest in people aged ≥ 65 years and those living in a nursing home or long-term care facility. Other high risks population are those with underlying conditions including:

- Hypertension
- Cardiovascular disease
- Diabetes
- Chronic respiratory disease
- Cancer
- Renal disease
- Obesity

Pediatric multisystem inflammatory syndrome: Syndrome characterized by persistent fever and features of Kawasaki disease and/or toxic shock syndrome in patients <21 years old with confirmed or suspected SARS-CoV-2 infection

Persistent Symptoms in Patients After Acute COVID-19

- Study goal: Post-care assessment of symptoms in patients who had had COVID-19
- Methods: Standard collection of symptoms
- Results (N=143):
  - Mean age, 56.5 (SD, 14.6); 53% female; 72.7% had evidence of interstitial pneumonia; mean LOS in hospital was 13.5 d (SD, 9.7); 21 (15%) non-invasive ventilation; 7 (5%) invasive ventilation
  - Mean time at assessment, 60.3d from first symptom; only 18 (12.6%) completely free on any COVID-related symptom
  - Common symptoms=fatigue, 53.1%; dyspnea, 43.4%; joint pain, 27.3%; chest pain, 21.7%

Persistent Symptoms in Patients After Acute COVID-19

The figure shows percentages of patients presenting with specific Coronavirus disease 2019 (COVID-19)-related symptoms during the acute phase of the disease (left) and at the time of the follow up visit (right).

Risk Factors Associated with COVID-19 Deaths

- **Goal:** Assess factors associated with COVID-19 deaths in 17 million patients
- **Methods:**
  - Primary care records of 17,278,392 adults were linked to 10,926 COVID-19 related deaths
  - Death related to: male, HR 1.59 (CI, 1.53-1.65); older age and deprivation (both with a strong gradients; diabetes; severe asthma; and various other medical conditions
  - Black and South Asian people at higher risk even after adjustment for other factors, HR 1.48 (1.30-1.69), HR 1.44 (1.32-1.58) respectively

https://doi.org/10.1038/s41586-020-2521-4
Potential Therapies for COVID-19

Therapies available at UNC:
- Remdesivir
- Convalescent plasma
- High titer mono-clonal antibodies
- Steroids
- Lopinavir-ritonavir
- Tocilizumab

Methods for providing
- FDA EUA
- IRB approved research
- Off label use

Thank you all – for what you do to support UNC during this pandemic
COVID-19 in Children

Michael J. Smith, M.D.

- Associate Professor of Pediatrics at Duke University
- Member of the Duke Antimicrobial Stewardship and Evaluation Team
COVID in Children (United States: 7/23/20)

- 288,287 cases in children
  - 8.4% of all cases
  - 380 cases per 100,000 children
- Children account for 0.8 – 2.9% of all hospitalizations
  - 0.6 – 9% of child COVID cases result in hospitalization
- Children account for 0 – 0.8% of all COVID deaths
  - 0 – 0.3% of cases result in death
## Pediatric Cases Over Time

<table>
<thead>
<tr>
<th>Date</th>
<th>Number of locations reporting age</th>
<th>Cumulative total cases (all ages)</th>
<th>Cumulative child cases</th>
<th>Percent children of total cases</th>
<th>Cases per 100,000 children</th>
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</thead>
<tbody>
<tr>
<td>7/23/20</td>
<td>49 states, NYC, DC, PR, and GU</td>
<td>3,416,630</td>
<td>288,287</td>
<td>8.4%</td>
<td>379.7</td>
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<td>7/16/20</td>
<td>49 states, NYC, DC, PR, and GU</td>
<td>3,042,413</td>
<td>241,904</td>
<td>8.0%</td>
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<td>7/9/20</td>
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<td>200,184</td>
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<td>7/2/20</td>
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<td>2,335,060</td>
<td>165,845</td>
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<td>218.4</td>
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<td>6/25/20</td>
<td>49 states, NYC, DC, PR, and GU</td>
<td>2,073,387</td>
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<td>6.7%</td>
<td>182.0</td>
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<td>6/18/20</td>
<td>49 states, NYC, DC, PR, and GU</td>
<td>1,885,905</td>
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<td>6/11/20</td>
<td>49 states, NYC, DC, PR, and GU</td>
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<td>6/4/20</td>
<td>49 states, NYC, DC, PR, and GU</td>
<td>1,623,334</td>
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<td>5.2%</td>
<td>110.7</td>
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<tr>
<td>5/28/20</td>
<td>47 states, NYC, DC, PR, and GU</td>
<td>1,425,154</td>
<td>66,513</td>
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<td>91.5</td>
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<td>5/21/20</td>
<td>47 states, NYC, DC, PR, and GU</td>
<td>1,288,305</td>
<td>54,031</td>
<td>4.2%</td>
<td>74.4</td>
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<td>5/14/20</td>
<td>47 states, NYC, DC, PR, and GU</td>
<td>1,159,407</td>
<td>42,370</td>
<td>3.7%</td>
<td>58.3</td>
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<td>5/7/230</td>
<td>46 states, NYC, DC, PR, and GU</td>
<td>1,010,112</td>
<td>32,568</td>
<td>3.2%</td>
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<td>4/30/20</td>
<td>47 states, NYC, DC, and PR</td>
<td>849,615</td>
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<td>2.7%</td>
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<td>4/23/20</td>
<td>48 states, NYC, DC, PR, and GU</td>
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<td>4/16/20</td>
<td>46 states, NYC, and DC</td>
<td>456,923</td>
<td>9,259</td>
<td>2.0%</td>
<td>13.3</td>
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</table>
COVID in Children (North Carolina: 7/23/20)

- 288,287 cases in children
  - 8.4% of all cases (11%)
  - 380 cases per 100,000 children (504)
- Children account for 0.8 – 2.9% of all hospitalizations
  - 0.6 – 9% of child COVID cases result in hospitalization
- Children account for 0 – 0.8% of all COVID deaths (0.1%)
  - 0 – 0.3% of cases result in death (0)
Multisystem Inflammatory Syndrome in Children (MISC)

- An individual aged <21 years presenting with fever*, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); AND
- No alternative plausible diagnoses; AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms
Multisystem Inflammatory Syndrome in Children (MISC)

- An individual aged <21 years presenting with fever*, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); AND
- No alternative plausible diagnoses; AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms
- *Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
MISC: Geography

Reported MIS-C Cases in the United States as of July 15, 2020
MISC: Demographics

**Race & Ethnicity**
- Hispanic or Latino: 38%
- Non Hispanic Black: 33%
- Non Hispanic White: 15%
- Other: 6%
- Multiple: 4%
- Asian: 3%
- American Indian/Alaskan Native: 0%

**Age (In years)**
- <1: 5%
- 1-4: 25%
- 5-9: 29%
- 10-14: 27%
- 15-20: 14%

**Gender**
- Male: 55%
- Female: 45%
Returning to School

If a child’s school is open for in-person learning, should they go back?

▪ Likelihood of acquiring infection
  - Local epidemiology
  - School mitigation strategies

▪ Likelihood of severe disease if they get infected
  - High-risk: Immunocompromised
  - Lower risk: Asthma, Diabetes, Obesity

▪ Family considerations
NCDHHS Outbreaks and Clusters

## Childcare Clusters in North Carolina

### Child Care or School Setting with an Ongoing Cluster:

<table>
<thead>
<tr>
<th>Setting Type</th>
<th>Setting County</th>
<th>Facility</th>
<th>Staff</th>
<th>Children</th>
<th>Total</th>
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<tr>
<td></td>
<td></td>
<td>Cases</td>
<td>Deaths</td>
<td>Cases</td>
<td>Deaths</td>
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<td>3</td>
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<td>Iredell</td>
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<td>McDowell</td>
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<tr>
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<td>0</td>
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<tr>
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<td>7</td>
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<td>Moore</td>
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<td>4</td>
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<td>New Hanover</td>
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<td>7</td>
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<td>Union</td>
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</table>
Questions from the Outpatient Setting

- Newborns with COVID+ parents/caretakers
- Reinfection
- Testing strategies for office staff/HCWs
Impact of universal masking

Interventions in Massachusetts
- March 10: Massachusetts declares state of emergency
- March 16: Massachusetts classes schools
- March 17: Massachusetts reduces public transportation
- March 24: Massachusetts issues stay-at-home orders for nonessential workers

Interventions at MGB
- March 12: MGB restricts visitors
- March 14: MGB restricts elective procedures
- March 16: MGB restricts all business travel and limits on-site working
- March 25: MGB universal masking of HCWs
- April 6: MGB universal masking of patients

No. of HCWs tested per day
- <20
- 20-100
- 101-200
- >200

SARS-CoV-2 positivity rate in MGB, HCWs, %

P < .001

Date (2020)

March 6
March 10
March 16
March 25
April 6
April 11
April 29

JAMA. Published online July 14, 2020. doi:10.1001/jama.2020.12897
Psychiatric Consequences of Coronavirus Infections

Therese Garrett, M.D.
- Behavioral Health Medical Director, WellCare of North Carolina
- Co-chair - NCPA Disaster Committee
- President - NC Council on Child and Adolescent Psychiatry
Psychiatric Consequences of Coronavirus Infections

Acute
- Delirium/confusion occurred in 27.9% of patients
- Common: depression, anxiety
- Mania/psychosis - small minority (0.7%) – likely secondary to exogenous corticosteroids
- Lability, irritability, pressured speech, euphoria common - subthreshold mania

Long-term
- Sleep disorder, fatigue
- Frequent traumatic memory recall
- Lability
- Impaired concentration/ memory

High point prevalence - anxiety, depression, PTSD
- Difficult to separate infection effects from effects on population as a whole

Positive effects in terms of personal growth during adversity

Neurological Syndromes

- UK review: neuropsychiatric symptoms: 62% were CVA, with AMS in 31%, ‘other’ neurologic problems 9%
  - Majority of CVA- ischemic stroke
  - Neurocognitive syndromes, new onset psychosis
- Case reports - Guillain-Barre, acute myelitis, encephalopathies, post-viral syndrome resembling depression,
- MIS-C- AMS, seizures in children

Possible Etiologies of Neuro-Psychiatric Consequences of Coronavirus Infections

Multifactorial

- Immunologic response
- Cerebrovascular disease
- Direct effects- including brain infection
- Degree of physiological compromise (lack of oxygenation- hypoxia)
- Medical interventions
- Social isolation, stigma, fears about infecting others
- Psychological impact of novel, severe, potentially fatal illness

Rogers et al, Lancet Psychiatry, May 18, 2020: Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic
Mental Health Impacts of Critical Illness

- 1-year prevalence
  - Depression 29%
  - Anxiety 34%
  - PTSD 34%

- Acute Respiratory Distress Syndrome
  - Common - agitation, confusion, corticospinal tract signs
  - Prolonged mechanical ventilation associated with greater reductions in QOL than ICU admissions for other reasons
  - Majority at 1 year show impaired memory, attention, concentration, mental processing speed

- Dysexecutive syndrome

- Steroid induced mania/psychosis

- Cognitive decline/acceleration of dementia

Rogers et al, Lancet Psychiatry, May 18, 2020: Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic
Impact of Pandemic and Lockdown on Pre-existing Psychiatric Illness

- Case-control study in China- pre-COVID dx of F32.x, F33.x, F41.x
- Did not include bipolar or psychotic disorder diagnoses or < age 18
- Significant PTSD symptoms - 43% of psychiatry patients, 27.5% controls
- ¼ of psychiatry patients reported moderate to severe anxiety, depression, insomnia
- Individuals with physical symptoms much more likely to report psychiatric symptoms
- Incorporation into delusional systems
- Out of proportion anxiety/obsessions

Impact on Family of COVID Patients

- Traumas related to separation and inability to be with their loved one
- Uncertainty and delays in information/updates
- Deaths - disruption of the grieving process
  - Saying goodbye
  - Altered grieving rituals
  - Increased risk of complicated grief, depressive and anxiety disorders
- Stigmatization by others
- Guilt about being vector of infection
- Challenges with COVID positive mother of newborn and separations - impact on hospital care and post-hospital newborn care
Prescriptions During Early COVID-19

- Starting 2/16, rates have climbed dramatically (2/16-3/15)
- Anti-anxiety prescriptions rose 34.1% (2/16-3/15)
- Antidepressant prescriptions filled increased 18.6%
- Anti-insomnia prescriptions increased 14.8%
- Majority of prescriptions were NEW prescriptions (78%)
- Why is this significant?
  - 2015-2019- decreased use of anti-anxiety (12%), decline in use of insomnia meds (11.3%)
  - 2015-2019- 15% increase in antidepressants

Requests from Health Care Professionals

- **Hear Me** - Listen and act on HCP expert perspective, understand/address their concerns
- **Protect Me** - Reduce the risk of HCP acquiring COVID or being a portal of the virus to their families
- **Prepare Me** - Provide training/support that allows provision of high-quality care
- **Support Me** - Provide support that acknowledges human limitations during extreme work hours, uncertainty, increased exposures
- **Care for Me** - Provide holistic support for individual and family if they require quarantine/treatment

Shanafelt, Ripp and Trockel, JAMA, April 7, 2020: Understanding and Addressing Sources of Anxiety Among Health Care Professionals during the COVID-19 Pandemic
“Hey! The experts are saying it’s safe to go out again.”