



The Impact of COVID-19 in Children – Session Two

April 2, 2020





Agenda

Introductions

Scientific and Clinical Update

Therapeutics

UNC Children's Updates

Questions





Guidelines

1. Phones will all be muted centrally
2. Questions were pre-submitted, but we will also be able to answer questions submitted in the chat
3. Please send any follow-up questions or emails to Bays Seagroves at Bays.Seagroves@unchealth.unc.edu and she will facilitate getting your answer





SCIENTIFIC AND CLINICAL UPDATE ON COVID-19

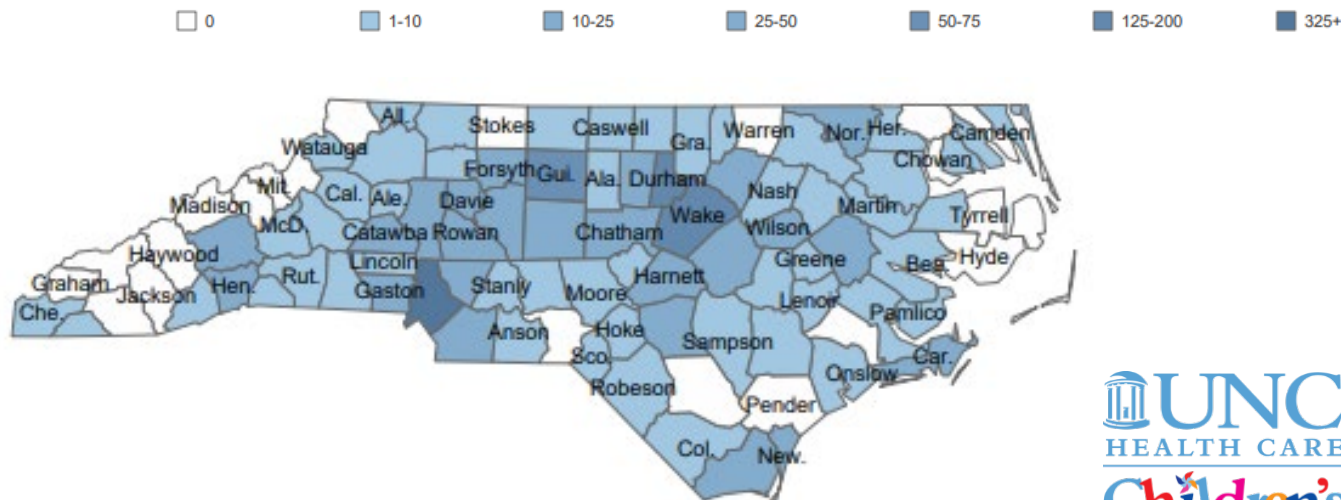


Coronavirus Disease 2019: Brief Review & Update

- COVID-19 Updates
 - » Current epidemiology
 - » Infection & clinical presentation
 - » Diagnostic tests
 - » Prevention
 - » Treatment

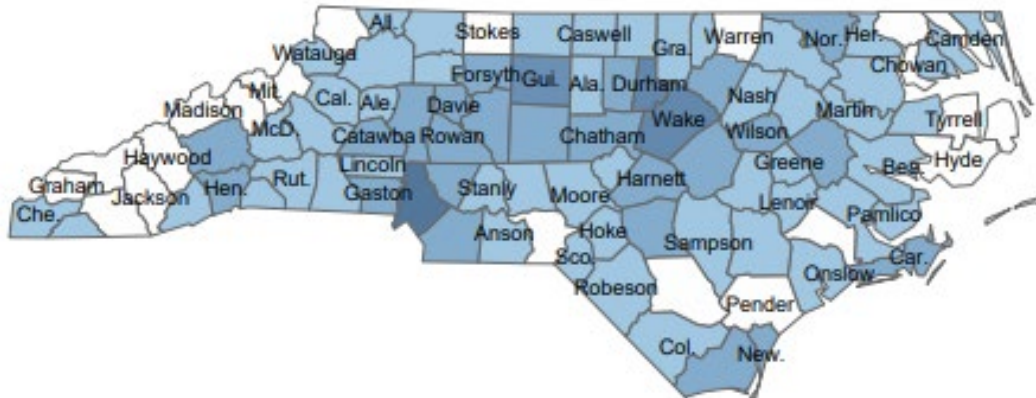
- Resources

Cases by NC County



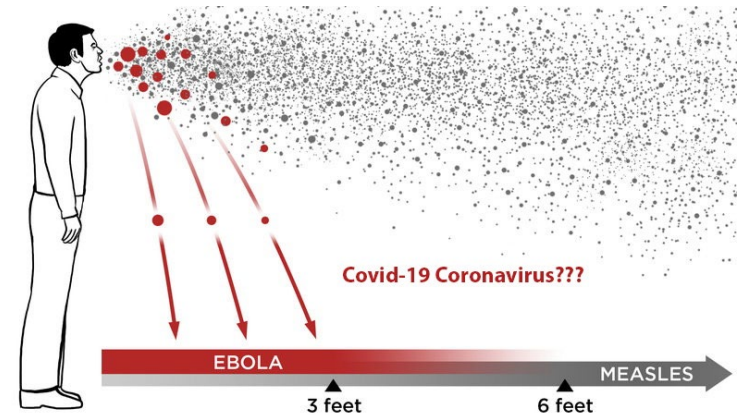
Epidemiology: COVID-19 Cases: Data as of 4/1-2/2020

- **Total confirmed world cases:** >940,000, **deaths** >47,000
- Most cases to date: US 216,722, Italy 110,574, Spain 104,118, China 82,394; Germany 77,981
- **US:** Rapidly increasing, >5,100 deaths;
- **NC** >1,584 (confirmed), 10 deaths.
 - » Mecklenburg (444), Wake (195), Durham (126) greatest number



COVID-19, Infection, Clinical Sx

- Major route of spread **droplet**
 - » Likely surface contact; possible other body fluids
 - » Most transmission from symptomatic people, early in disease
- Clinical course in adults
 - » Time to symptom onset: **average 5-6 days (2-14d)**
 - Recovery 2 wks; if severe -3-6wks, death 2-8wks (most from ARDS / secondary infx)
 - » **Fever (44-98%)*, cough (46-85%), myalgias/fatigue, short of breath (3-31%)**
 - *Fever may not be present initially
 - Symptoms / disease progressive
 - Other signs /sx: sore throat, diarrhea, other



COVID-19: Infection & Clinical Sx

- The good news!
 - » **Children have milder disease**
 - » Infants and children may be asymptomatic – mild dz
 - » Data on mortality from China:
 - Age 0-9yo: 0
 - Age 10-19: 0.2%
 - Age 20-29: 0.2%
 - Vs. 1-3% overall & >14% in highest risk groups
 - Adult high-risk groups: **elderly, co-morbidities of heart disease, HTN, diabetes, also immunocompromised**
 - » Transmission from children –unclear if community spread (usually household)
 - » But: transmission may occur prior to symptoms onset / if asymptomatic





COVID-19 in Young Infants

- Case reports of early-onset disease due to COVID-19
 - » Case reports
 - JAMA Pediatrics. Zeng, L. et al. March 26, 2020
 - » 3 infants with early-onset disease
 - Additional case reports (official, unofficial)
 - » Question of **route of transmission** (vertical or horizontal?)
 - » **Implications** for:
 - Evaluation of infants
 - Infection prevention
 - Management of exposed infants
 - » Breast feeding
 - » Disease in **older infants**





COVID-19: Focus on Select Additional Clinical Manifestations

- Full spectrum of respiratory illness
- Loss of smell or taste –so it really is a thing?!
- CNS: encephalitis (rare?)
- Role of immune system in disease process
 - » The good and the bad
 - » Cytokine storm





Diagnostic Tests

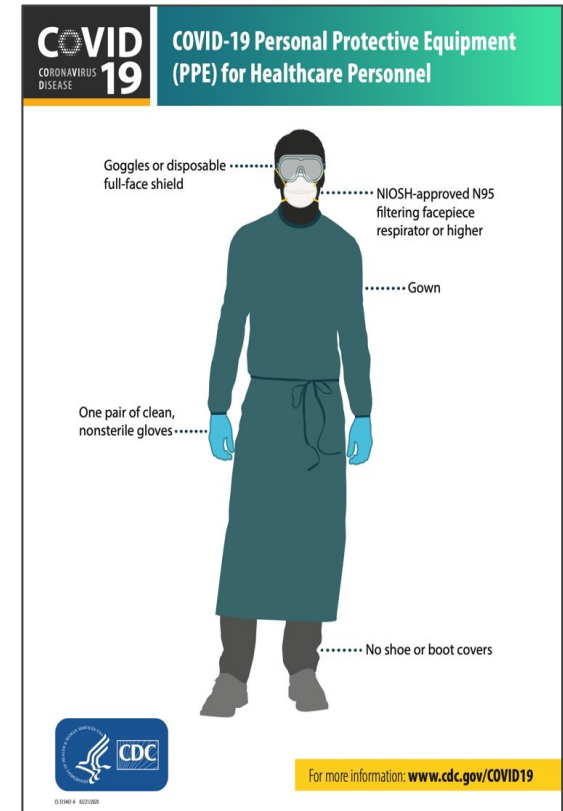
- Current: COVID-19 PCR
 - » **NP swab specimen of choice**
 - » Role of OP swab, specimen from lower respiratory secretions / BAL
- New Rapid Diagnostic Assays
- Serology
- Who to test?
 - » **Current process in NC and at UNCH**
 - » **Discussion : testing the asymptomatic?**



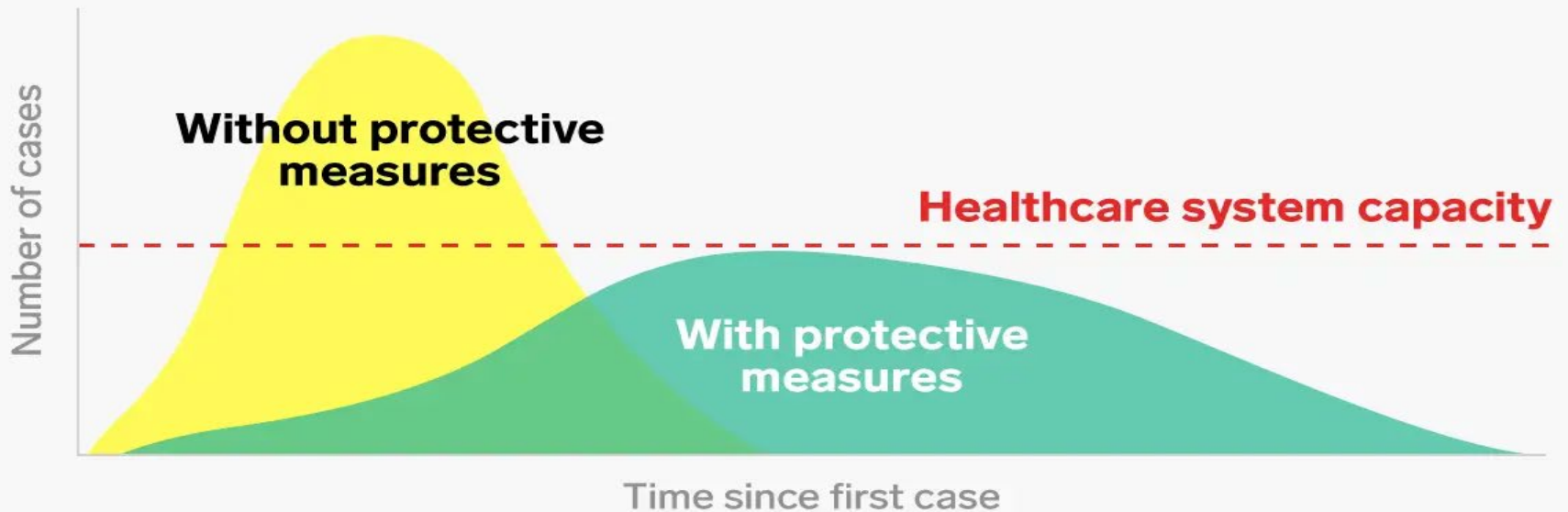


COVID-19, Prevention

- Usual precautions for respiratory viruses
- Personal:
 - » Frequent **hand washing** (20 seconds soap & water; hand sanitizer); avoid touching eyes nose mouth, avoid ill individuals, stay home if sick, cover mouth if cough / sneeze, “~~social~~ **physical distancing**” (6-foot rule), facemask if sick
 - » During Covid-19 patient contact: Gown, gloves, face mask OR respirator (N95), eye protection (goggles or face shield)
 - » **PPE Stewardship**
- Public Health measures
 - » Isolation, quarantine, avoidance of large groups, et al.



Possible spread of COVID-19 with and without protective measures





Resources for Clinicians

- <https://epi.dph.ncdhhs.gov/cd/coronavirus/providers.html>
- <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>
- [Travel Requirements Announced for UNC Health / UNC SOM](#)
- UNC Health's [COVID-19 Intranet page](#) – Visit for the latest updates.
- External [UNC COVID-19 information](#) on our website.
- Lib guides - <https://guides.lib.unc.edu/COVID19>
- Daily Briefings:
<https://unchcs.intranet.unchealthcare.org/Pages/2020/03-Mar/covid-19-brief/Daily-Briefings.aspx>





COVID-19 Therapeutics

- Hydroxychloroquine and chloroquine
- Remdesivir – clinical trials ongoing
- Anti-inflammatory drugs:
 - » Tocilizumab
- NSAIDs, ACE inhibitors, ARBs
- Others not discussed today: ribavirin, faviparivir, lopinavir-ritonavir, convalescent serum





Hydroxychloroquine/Chloroquine

- Antimalarial and anti-inflammatory drugs
- *In vitro* antiviral effects against influenza, dengue, Chikungunya, HIV, Zika
 - » HCQ failed clinical trials for influenza and dengue
 - » Chloroquine *enhances* Chikungunya in primates
- Despite *in vitro* effects, no antiviral applications for either drug
- Toxicities: cardiomyopathy, QT prolongation, retinopathy
 - » Chloroquine also multiple drug-drug interactions





International Journal of Antimicrobial Agents

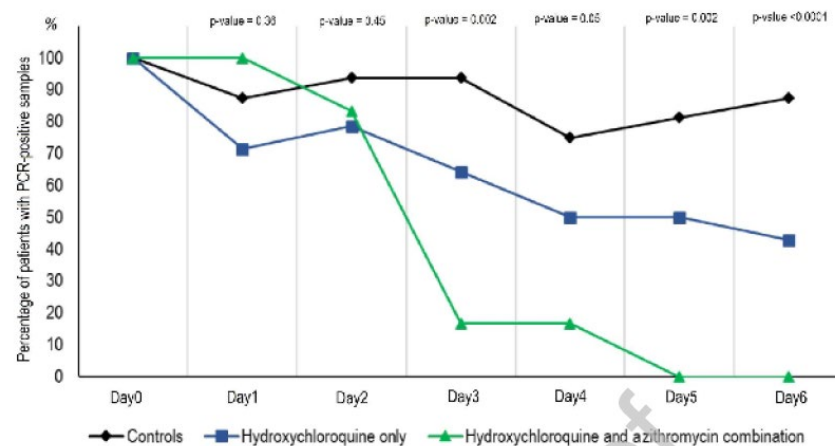
Available online 20 March 2020, 105949

In Press, Journal Pre-proof



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

Philippe Gautret ^{a, b, S}, Jean-Christophe Lagier ^{a, c, S}, Philippe Parola ^{a, b}, Van Thuan Hoang ^{a, b, d}, Line Meddeb ^a, Morgane Mailhe ^a, Barbara Doudier ^a, Johan Courjon ^{e, f, g}, Valérie Giordanengo ^h, Vera Esteves Vieira ^a, Hervé Tissot Dupont ^{a, c}, Stéphane Honoré ^{i, j}, Philippe Colson ^{a, c}, Eric Chabrière ^{a, c}, Bernard La Scola ^{a, c}, Jean-Marc Rolain ^{a, c}, Philippe Brouqui ^{a, c}, Didier Raoult ^{a, c, g, k}



- 42 patients: 26 received HCQ and 16 did not
- All HCQ recipients at one hospital, controls could be from other sites
- 6 HCQ recipients also received azithromycin



Problems with Gautret P, et al.

- HCQ recipients and controls treated at separate sites
- Significant baseline differences in groups
- Many controls had qualitative values only; all HCQ recipients had quantitative results (different assays?)
- 6 HCQ recipients excluded:
 - » 3 went to ICU; 1 died; 1 got better and left (PCR negative on Days 1 and 2); 1 quit due to nausea
- Some data changed from preprint and published versions
- Very limited peer review
 - » Accepted the day after submission
 - » Editor-in-Chief of journal is a coauthor
- Didier Raoult and lab have history of falsifying data





Letter

DOI: 10.5582/bst.2020.01047

Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies

Jianjun Gao^{1,*}, Zhenxue Tian², Xu Yang²

“Thus far, results from more than 100 patients have demonstrated that chloroquine phosphate is superior to the control treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course according to the news briefing.”

As of Feb 15, 2020: “The drug is recommended for inclusion in the next version of the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China.”

No data have been published yet.





HCQ/Chloroquine Clinical Trial Data

Chen J et al., Journal of ZheJiang University, March 3, 2020

- 30 patients randomized 1:1 to HCQ or nothing (unclear if placebo given)
- Primary outcome measure: viral clearance on Day 7
 - » HCQ: 13/15; Control: 14/15
- Time to fever resolution: no difference
- Limited data about trial design, patient characteristics, more meaningful outcomes





Remdesivir

- Adenosine analog with broad in vitro activity against RNA viruses, including SARS-CoV, MERS-CoV, and SARS-CoV-2
- No current approvals
- Multiple clinical trials ongoing; no data published
- Good safety profile in Ebola trials; pediatric dosing is available
- Compassionate use program ended except for children <18 and pregnant women



Tocilizumab

- “Cytokine storm” frequently described in severe COVID-19 cases:
 - » Elevated pro-inflammatory cytokines
 - » Persistent fever
 - » Cytopenias
 - » Elevated LDH, ferritin
- These findings appear to predict mortality
- Tocilizumab:
 - » Monoclonal antibody against IL-6 receptor; used in a variety of autoimmune and inflammatory disorders
 - » 5 COVID-19 trials registered, including a Phase II study enrolling children



NSAIDs, ACE inhibitors, ARBs

- Concern for increased susceptibility to COVID-19 or increased severity of disease
 - » Increased
- *No clinical evidence of this phenomenon*
- At this time, would not recommend:
 - » Changing blood pressure medications
 - » Routinely avoiding NSAIDs during the pandemic
- Some centers: NSAID avoidance in patients with COVID-19





Summary

- At this time, there is no proven effective therapy for COVID-19.
- Multiple clinical trials are ongoing (few in children).





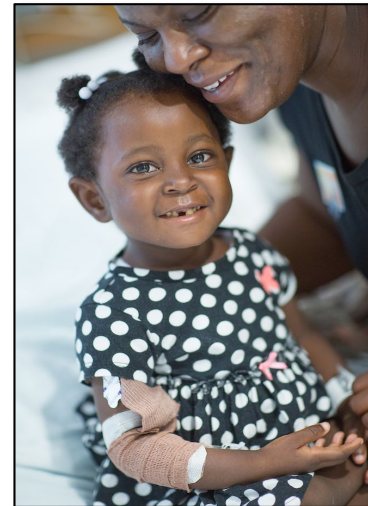
UNC CHILDREN'S UPDATES





Inpatient Updates

- No COVID-19 positive patients
- Many rule-outs
- All patients who are having a respiratory viral panel or flu swab will automatically have a COVID swab ordered





Outpatient Updates

- Moving multi-specialty clinic visits to Raleigh, where possible
- All in-person visits moving out of Chapel Hill location to UNC Children's Raleigh
- Ambulatory Care Center space for urgent patients that can only be seen in Chapel Hill
- Peds focused RDC still open in Cary

UNC Children's Raleigh



UNC COVID Hotline / HealthLink: 888-850-2684



Telehealth Updates

- Rapid increase in telephone visits with families and patients
- All UNC Children's specialty and primary care providers now have video visit capability
- Payors making dramatic changes in coverage of telehealth visits during this emergency





Health & Wellness Updates

- **Social Media**
 - » Created shared Instagram account to share uplifting and encouraging photos
- **Virtual Gatherings**
 - » Zoom parties to be held by Divisions
 - » Yoga, meditation, grief support groups in development
- **Peer Support**
 - » Developing 1:1 buddy system for internal support via Zoom
- **Collection of Wellness Tools**
 - » Creating list of tools to help with eye strain, increased screen time, etc. (e.g., Headspace)
- **Grand Rounds**
 - » Dedicate Grand Rounds or conference to focus on providers coping during COVID-19
- **Be Vocal & Transparent**
 - » Reiterate to colleagues that it is natural to have an emotional response to the situation
 - » Connect with a mental health professional





Facilitated Questions and Responses





Thank you all!

You have been compassionate, mission-focused, and selfless!

"Hope and Fear cannot occupy the same space.

Invite one to stay." Maya Angelou

