New Hampshire Coronavirus Disease 2019 Weekly Call for Healthcare Providers and Public Health Partners

January 28, 2021

Ben Chan
Elizabeth Talbot
Beth Daly
Lindsay Pierce

Thursday noon-time partner calls will focus on science, medical, and vaccine updates geared towards our healthcare partners
Agenda

• Epidemiology Update

• **Lancet Publication**: 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study

• **medRxiv Study**: Efficacy of Colchicine in Non-Hospitalized Patients with COVID-19

• Questions & Answers (Q&A)
CDC COCA Webinar (2-3 pm today)

Treating Long COVID: Clinician Experience with Post-Acute COVID-19 Care

Presenters
Alfonso C Hernandez-Romieu, MD, MPH
LCDR, U.S. Public Health Service
Late Sequelae Unit, Clinical Team
COVID-19 Response
Centers for Disease Control and Prevention

Jennifer Possick, MD
Associate Professor, Section of Pulmonary, Critical Care and Sleep Medicine
Department of Internal Medicine
Yale University School of Medicine

Allison Navis, MD
Assistant Professor, Division Neuro-Infectious Diseases
Icahn School of Medicine at Mount Sinai
Mount Sinai Health System

https://emergency.cdc.gov/coca/calls/2021/index.asp
More than 25.6 million cumulative cases in the U.S. (25% of all global infections)
More than 429,000 deaths in the U.S. from COVID-19 (20% of all global deaths)
Number of New COVID-19 Cases per Day in NH

https://www.nh.gov/covid19/dashboard/overview.htm#dash
% of Tests (Antigen and PCR) Positive for COVID-19 (7-Day Average)

Date Laboratory Test Completed

% of Specimens Positive

Mar 1, 20  May 1, 20  Jul 1, 20  Sep 1, 20  Nov 1, 20  Jan 1, 21

0.0%  5.5%  11.8%
Number of COVID-19 Deaths in NH by Report Date

In the last 7 days:
• 60 people have died
• 26 (43%) are NOT associated with a LTCF
• 34 (57%) associated with a LTCF
Long COVID
Potential Long-Term Health Consequences of COVID-19 (Long COVID)

- Fatigue and malaise
- Shortness of breath
- Joint pains
- Chest pains
- Myocardial injury (myocarditis, arrhythmias)
- Thromboembolic disease

- Pulmonary dysfunction
- Headache
- Vertigo
- Loss of taste/smell
- Encephalitis & seizures
- mood swings, brain fog
- Emotional health

https://jamanetwork.com/journals/jama/fullarticle/2771581
6-month consequences of COVID-19 in patients discharged from hospital: a cohort study

Chaolin Huang*, Lixue Huang*, Yeming Wang*, Xia Li*, Lili Ren*, Xiaoying Gu*, Liang Kang*, Li Guo*, Min Liu*, Xing Zhou, Jianfeng Luo, Zhenghui Huang, Shengjin Tu, Yue Zhao, Li Chen, Decui Xu, Yanping Li, Caichong Li, Lu Peng, Yong Li, Wuxiang Xie, Dan Cui, Lianhan Shang, Guohui Fan, Jiuyang Xu, Geng Wang, Ying Wang, Jingchuan Zhong, Chen Wang, Jianwei Wang†, Dingyu Zhang†, Bin Cao†

- Cohort study of patients hospitalized with confirmed COVID-19 at Jin Yin-tan Hospital (first designated hospital for patients with COVID-19 in Wuhan, China)
  - Discharged: 1/7/20 – 5/29/20
  - Follow-up: 6/16/20 – 9/3/20
- 1,733 participated
- 736 excluded

736 patients excluded
- 347 subjective rejection
- 65 living in a nursing or welfare home
- 63 osteoarticular disease
- 62 unable to be contacted
- 56 dementia or psychotic disease
- 51 living outside Wuhan city
- 33 died
- 30 immobile before discharge
- 25 readmitted to hospitals
- 4 immobile after discharge (3 with ischaemic stroke and 1 with pulmonary embolism)

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32656-8/fulltext
Assessment of Participants (N=1,733)

- Self-reported symptom questionnaire
- modified British Medical Research Council (mMRC) scale: scale to characterize level of dyspnea with physical activity
- EQ-5D-5L questionnaire: evaluate patient quality of life
- EQ-VAS scale: subjective assessment of generic health
- Ischemic stroke and cardiovascular event registration form
- Physical examination
- 6-minute walking test
- Laboratory tests: CBC, creatinine, HgA1c
- A subset (N=390) underwent PFTs, ultrasound of the Les, ultrasound of the abdomen, high-res chest CT
Outcomes

• Primary Outcomes:
  – Symptoms
  – Exercise capacity
  – Health-related quality of life
  – Lung function and chest CT pattern

• Secondary Outcomes:
  – Extra-pulmonary organ function (renal function, HgA1c, DVTs, ultrasonography of abdominal organs)
  – Antibody titers and seropositivity (checked in a subset)

• Stratify outcomes by disease severity
Participant Characteristics

- Median length of hospital stay: 14 days
- # Requiring ICU admission: 76 (4%)
- Median time from symptom onset to follow-up: 186 days (~6 months)
- Median time from discharge to follow-up: 153 days (~5 months)
Findings after a Median 6 Months of F/U

- 76% of patients reported at least one persistent symptom (symptom questionnaire):
  - Fatigue or muscle weakness (63%)
  - Sleep difficulties (26%)
- Quality of life assessment (EQ-5D-5L questionnaire):
  - Pain or discomfort (27%)
  - Anxiety or depression (23%)
- >50% had residual CT abnormalities (in all severity groups)
  - Ground-glass opacities in 40-50% of participants
- Impairment in pulmonary diffusion capacity (on PFTs)
  - 22% of people hospitalized but NOT requiring oxygen therapy
  - 56% of patients requiring high-flow oxygen, non-invasive ventilation or IMV
- No DVTs; abdominal ultrasounds were normal
## Study Findings

<table>
<thead>
<tr>
<th>EQ-5D-5L questionnaire†</th>
<th>113/1622 (7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility: problems with walking around</td>
<td>11/1622 (1%)</td>
</tr>
<tr>
<td>Personal care: problems with washing or dishing</td>
<td>25/1611 (2%)</td>
</tr>
<tr>
<td>Usual activity: problems with usual activity</td>
<td>431/1616 (27%)</td>
</tr>
<tr>
<td>Pain or discomfort</td>
<td>367/1617 (23%)</td>
</tr>
</tbody>
</table>

### Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Count/Population (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any one of the following symptoms</td>
<td>1265/1655 (76%)</td>
</tr>
<tr>
<td>Fatigue or muscle weakness</td>
<td>1038/1655 (63%)</td>
</tr>
<tr>
<td>Sleep difficulties</td>
<td>437/1655 (26%)</td>
</tr>
<tr>
<td>Hair loss</td>
<td>359/1655 (22%)</td>
</tr>
<tr>
<td>Smell disorder</td>
<td>176/1655 (11%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>154/1655 (9%)</td>
</tr>
<tr>
<td>Joint pain</td>
<td>154/1655 (9%)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>138/1655 (8%)</td>
</tr>
<tr>
<td>Taste disorder</td>
<td>120/1655 (7%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>101/1655 (6%)</td>
</tr>
<tr>
<td>Diarrhoea or vomiting</td>
<td>80/1655 (5%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>75/1655 (5%)</td>
</tr>
<tr>
<td>Sore throat or difficult to swallow</td>
<td>69/1655 (4%)</td>
</tr>
<tr>
<td>Skin rash</td>
<td>47/1655 (3%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>39/1655 (2%)</td>
</tr>
<tr>
<td>Headache</td>
<td>33/1655 (2%)</td>
</tr>
<tr>
<td>Low grade fever</td>
<td>2/1655 (&lt;1%)</td>
</tr>
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[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32656-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32656-8/fulltext)
Limitations

- Study limited to hospitalized patients – excluded outpatients with more mild illness
- Limited to one hospital in one city/country
- No baseline (pre-COVID) assessment of pulmonary function and patient signs/symptoms
- No assessment of trajectory of symptoms
- Impaired pulmonary function and exercise capacity cannot be directly attributed to COVID-19
- Lack of thorough cardiac function or neurologic evaluation
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Clinical Course of COVID-19

- Dexamethasone for hospitalized on mechanical ventilation or supplemental oxygen
- Anti-IL-6 receptor antibody tocilizumab for hospitalized to reduce progression to mechanical ventilation

**Clinical Symptoms**
- Mild constitutional symptoms
  - Fever >99.6°F
  - Dry Cough, diarrhea, headache

**Clinical Signs**
- Lymphopenia, increased prothrombin time, increased D-Dimer and LDH (mild)
- Shortness of Breath
- Hypoxia (PaO2/FiO2 ≤ 300 mmHg)
- Abnormal chest imaging
- Transaminitis
- Low-normal procalcitonin

**Complications**
- ARDS
- SIRS/Shock
- Cardiac Failure
- Elevated inflammatory markers (CRP, LDH, IL-6, D-dimer, ferritin)
- Troponin, NT-proBNP elevation

~81% mild/mod

14% Severe

5% Critical

Siddiqi et al. 2020 Yang, Lancet Resp Med 2020
CQ/HCQ – increase pH, compromise endosome and subsequent virus release

Anti-inflammatories
- CQ/HCQ – TNF, IL-6
- Steroids
- Tocilizumab (anti-IL-6)

COLCORONA Trial
- Colchicine orally administered, anti-inflammatory medication beneficial in gout, pericarditis
  - Inhibits tubulin polymerization
  - Studied for ARDs

Plasma – neutralizing Ab’s

Camostat mesylate – inhibits TMPRSS2 (primes S protein)

HIV PI (Kaletra) – protease inhibitor (weak)

Ribavirin - mRNA

CQ/HCQ – alters glycosylation of receptors

Remdesivir – nucleotide analog

Favipiravir – nucleoside analog
Phase 3 RCT in PCR+ outpatients
>40yo with >1 high-risk criterion*  
colchicine 0.5 mg BID 3d and QD or placebo for 30d

>70y, BMI >30 kg/m2, DM, SBP ≥150 mm Hg, respiratory disease, heart failure, CAD; F≥ 38.4°C within 48h, dyspnea at presentation, bicytopenia, pancytopenia, or high PMN and low lymphs
## Trial Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Colchicine (N=2235)</th>
<th>Placebo (N=2253)</th>
</tr>
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<tbody>
<tr>
<td>Age - years</td>
<td>54.4±9.7</td>
<td>54.9±9.9</td>
</tr>
<tr>
<td>Female sex - no. (%)</td>
<td>1238 (55.4%)</td>
<td>1183 (52.5%)</td>
</tr>
<tr>
<td>Caucasian - no. (%)</td>
<td>2086 (93.3%)</td>
<td>2096 (93.2%)</td>
</tr>
<tr>
<td>Body-mass index (kg/m²)</td>
<td>30.0±6.2</td>
<td>30.0±6.3</td>
</tr>
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<td>Smoking - no. (%)</td>
<td>217 (9.7%)</td>
<td>212 (9.4%)</td>
</tr>
<tr>
<td>Hypertension - no. (%)</td>
<td>781 (34.9%)</td>
<td>848 (37.6%)</td>
</tr>
<tr>
<td>Diabetes - no. (%)</td>
<td>444 (19.9%)</td>
<td>450 (20.0%)</td>
</tr>
<tr>
<td>Respiratory disease - no. (%)</td>
<td>583 (26.1%)</td>
<td>605 (26.9%)</td>
</tr>
<tr>
<td>Prior MI - no. (%)</td>
<td>65 (2.9%)</td>
<td>72 (3.2%)</td>
</tr>
<tr>
<td>Prior heart failure - no. (%)</td>
<td>24 (1.1%)</td>
<td>18 (0.8%)</td>
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MI denotes myocardial infarction.
## COLCORONA Results

<table>
<thead>
<tr>
<th>Clinical Outcome</th>
<th>Colchicine</th>
<th>Placebo</th>
<th>Odds Ratio (95% CI)</th>
<th>P Valu</th>
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<tr>
<td>ITT population</td>
<td>N=2235</td>
<td>N=2253</td>
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<td>Primary composite endpoint - no. (%)</td>
<td>104 (4.7%)</td>
<td>131 (5.8%)</td>
<td>0.79 (0.61-1.03)</td>
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Components of primary endpoint:

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<td>Death - no. (%)</td>
<td>5 (0.2%)</td>
<td>9 (0.4%)</td>
<td>0.56 (0.19-1.67)</td>
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<td>Hospitalization for COVID-19 no. (%)</td>
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<td><strong>Patients with PCR-proven COVID-19</strong></td>
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<td>10 (0.5%)</td>
<td>20 (1.0%)</td>
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