COVID-19 Questions
Two Huge Covid-19 Studies Are Retracted After Scientists Sound Alarms

The reports, published in two leading journals, were retracted after authors could not verify an enormous database of medical records.


Retraction—Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis.

Notice of Retraction: Effectiveness of Surgical and Cotton Masks in Blocking SARS-CoV-2.
What’s a clinician to do?
Unprecedented Volume, PrePub, No Peer Review, Peer Review, Retractions...

What data will stand the test of time and be impactful?

Today

– a few studies concisely reviewed to help understand this virus a little better (for now)
– Presymptomatic vs asymptomatic, testing asymptomatic, viral dynamics, your questions
Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study

COVIDSurg Collaborative*

Lancet published Online May 29, 2020
Corrected version June 9, 2020

As elective procedures return, what do we know about risks?
• Intl cohort study (235 hospitals in 24 countries)
• All pts having surgery who had CoV diagnosed within 7 days before or 30 days after surgery
• Primary EP: 30-day postop mortality
• Secondary EP: pulmonary complications (pneumonia, ARDS, unexpected postop ventilation)
• 1128 pts (Jan 1-Mar 31)
  – CoV dx: 86% lab testing, 7% imaging, 6% clinical
  – 294 (26%) preop CoV, 806 (72%) postop CoV
  – 835 (74%) emergency, 280 (25%) elective
  – Wide range of benign, malignant, trauma, obstetric surgeries
• 30-day mortality 24% (268/1128)
  – Male sex, age > 70, ASA grades 3-5, malignant, emergency, major

• Pulmonary complications 51% (577/1128)
  – 30-day mortality 38% (219/577)
  – Pneumonia 40%, unexpected ventilation 21%, ARDS 14%
FINDINGS FROM INVESTIGATION AND ANALYSIS OF RE-POSITIVE CASES

Korean Centers for Disease Control and Prevention
www.cdc.go.kr

Transmission risk from those who stay PCR positive after recovery
• “Re-positive cases” are cases that test positive after recovery and removal from isolation (KCDC criteria)
  – Renamed “PCR re-detected after discharge from isolation”
• Why were these individuals retested?
  – Screening (60%), Symptoms (38%)

TIMING OF TESTING RE-POSITIVE

○ On average, it took 44.9 days (range: 8-82 days) from initial symptom onset date to testing positive after discharge. (Based on 226 cases symptomatic at the time of initial confirmation)
• 285 had epidemiologic and contact investigation
  – 790 contacts (351=family, 439=others)
  – No cases among contacts from re-positive exposure alone
  – 3 newly confirmed cases among contacts had other risks

• 108 had viral cell culture testing
  – All were culture negative
  – RT-PCR cycle threshold (Ct) values > 30 in 90%
  – 96% (23 cases with acute/convalescent serum) had neutralizing antibodies

Korean Centers for Disease Control and Prevention
www.cdc.go.kr
Munich outbreak 16 cases after exposure to single primary case in Jan 2020
Relatively young, healthy, mild illness
Hospitalized for public health purposes

Viral testing – throat, NP, sputum, stool, urine, blood
Viral load testing daily
Viral culture
Genotyping
9 individuals

Early study with important virologic correlates
Demonstrated replication in upper respiratory tract
OP and NP swab avg viral loads (copies/ml)
6.76 x 10^5 until day 5
7.11 x 10^8 peak at day 5
3.44 x 10^5 after day 5

No positive cultures after day 8 of sx
No positive culture at < 10^6 copies/ml VL
Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020

How common are presymptomatic infections? What are the implications for transmission?

Following identification of CoV in a HCW, 23/76 (30%) SNF residents tested positive.

Of the 23 positive, 10 (43%) had symptoms, 13 (57%) were asymptomatic. (symptoms were assessed from day of testing – 14 days)
7 days after testing 10/13 asymptomatic residents had developed symptoms. They were PRE-symptomatic at the time of testing.
No difference in Ct distribution among symptomatic, pre-, or asymptomatic Suggests high burden viral RNA and potential for transmission
Contact Tracing Assessment of COVID-19 Transmission Dynamics in Taiwan and Risk at Different Exposure Periods Before and After Symptom Onset

Hao-Yuan Cheng, MD, MSc; Shu-Wan Jian, DVM, MPH; Ding-Ping Liu, PhD; Ta-Chou Ng, BSc; Wan-Ting Huang, MD; Hsien-Ho Lin, MD, ScD; for the Taiwan COVID-19 Outbreak Investigation Team
• 100 lab-confirmed patients and their contacts
  – 2761 close contacts
  – Followed up until 14 days after last exposure to index
  – Symptom onset minus 4 days (period of investigation)
  – Symptoms triggered testing
  – High-risk contacts (family, hospital) tested initially regardless of symptoms and with any new symptoms

• 22 paired index-secondary cases
  – Secondary clinical attack rate 0.7%
Table 2. Secondary Clinical Attack Rate for COVID-19 Among the 2761 Close Contacts by Different Exposure Settings, Times, and Characteristics

<table>
<thead>
<tr>
<th>Time from onset to exposure, d(^b)</th>
<th>No. of secondary cases (asymptomatic case)</th>
<th>No. of contacts</th>
<th>Secondary clinical attack rate, % (95% CI)</th>
<th>Risk ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0</td>
<td>10 (3)</td>
<td>735</td>
<td>1.0 (0.5-2.0)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>0-3</td>
<td>9 (1)</td>
<td>867</td>
<td>0.9 (0.5-1.8)</td>
<td>0.97 (0.35-2.66)</td>
</tr>
<tr>
<td>4-5</td>
<td>3 (0)</td>
<td>216</td>
<td>1.4 (0.5-4.0)</td>
<td>1.46 (0.38-5.59)</td>
</tr>
<tr>
<td>6-7</td>
<td>0</td>
<td>119</td>
<td>0 (0-3.1)</td>
<td>0</td>
</tr>
<tr>
<td>8-9</td>
<td>0</td>
<td>449</td>
<td>0 (0-0.9)</td>
<td>0</td>
</tr>
<tr>
<td>&gt;9</td>
<td>0</td>
<td>284</td>
<td>0 (0-1.3)</td>
<td>0</td>
</tr>
</tbody>
</table>

| Exclusively presymptomatic exposure\(^c\) | No | 20 (4) | 2371 | 0.7 (0.4-1.1) | 1 [Reference] |
|                                         | Yes| 2 (0)  | 299  | 0.7 (0.2-2.4) | 0.99 (0.23-4.29) |

\(^b\) Elapsed time between the date at symptom onset of the index case and the first date at exposure. For example, people from the group “<0 days” had their first contact with the index case before the case had any symptoms.

- No asymptomatic (n=9) index case transmitted a secondary case
- Presymptomatic exposure led to secondary transmission (n=2)
- Secondary attack rate higher when exposed to index case within 5 days of symptom onset

JAMA Intern Med
Published online May 1, 2020
A lot of phone calls about asymptomatic testing, right?
Close contact
Being within 6 ft of confirmed or probable COVID-19 case for at least 15 mins during a single day.

Close contacts should wait at least 24 hr after exposure before testing.

A negative result should not exempt a contact from quarantine which should be continued for 14 days in all cases.

Consider repeat testing near end of quarantine period in some.

WARNING – This may not be relevant for where you live. Follow local DHS Guidance.

Table 1: COVID-19 Testing Recommendations

<table>
<thead>
<tr>
<th>Symptomatic</th>
<th>Asymptomatic</th>
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<tbody>
<tr>
<td>1. People who have recently developed any one or more of the following symptoms:</td>
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<tr>
<td>• Fever, defined as a measured temperature greater than 100.4°F</td>
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<td>• Subjective fever, for example if a person feels unusually warm to the touch, or reports sensations similar to previous experiences of fever</td>
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<tr>
<td>• Cough</td>
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<td>• Shortness of breath or difficulty breathing</td>
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<td>• Sore throat</td>
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<td>• Headache</td>
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<tr>
<td>• Chills or rigors (repetitive shaking chills)</td>
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<tr>
<td>• Myalgia (muscle aches)</td>
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<tr>
<td>• New loss of taste or smell</td>
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<tr>
<td>• Nausea, vomiting, or diarrhea</td>
<td></td>
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<tr>
<td>• Nasal congestion or runny nose</td>
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<tr>
<td>2. People who have been in close contact of a person with COVID-19, regardless of symptoms</td>
<td></td>
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<tr>
<td>3. People who have been instructed by a public health agency to get a COVID-19 test as part of a public health investigation, regardless of symptoms</td>
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<tr>
<td>Scenarios in which public health agencies may recommend testing for asymptomatic people include the following:</td>
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<tr>
<td>3.1 Investigation of outbreaks, such as multiple cases in a workplace, residential facility or correctional facility</td>
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<tr>
<td>3.2 Testing all residents and staff in high-risk congregate facilities to prevent or contain outbreaks</td>
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<tr>
<td>3.3 When testing is needed to contain an epidemic in a community with high-level transmission, and resources are sufficient for appropriate follow-up and case investigation, as determined in partnership with state and local health officials</td>
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<tr>
<td>4. People who have been instructed by a health care provider to get a COVID-19 test for the purpose of infection control, regardless of symptoms</td>
<td></td>
</tr>
<tr>
<td>Scenarios in which health care providers may recommend testing for asymptomatic people include the following:</td>
<td></td>
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<tr>
<td>4.1 As part of a test-based strategy to inform return-to-work decisions for individuals diagnosed with COVID-19</td>
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<tr>
<td>4.2 Outbreak investigations in health care settings, to understand prevalence among staff and patients</td>
<td></td>
</tr>
<tr>
<td>4.3 Screening before aerosol generating procedures, such as endoscopy, dentistry, or procedures requiring intubation</td>
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</tr>
</tbody>
</table>

https://content.govdelivery.com/accounts/WIDHS/bulletins/293c483. Wisconsin DHS July 1, 2020
Laboratory Diagnosis of COVID-19: Current Issues and Challenges

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