2019-nCoV Literature Situation Report (Lit Rep)
February 6, 2020

Key Takeaways

- **Persons testing positive for 2019-nCoV with mild or no symptoms have been found through investigation of family clusters in multiple countries.**
- **Current epidemiologic parameters identified for 2019-nCoV appear to fall within the ranges identified in the literature for other human coronaviruses.**
- **Home isolation of sick persons may be the most effective way to limit transmission of a pandemic respiratory viral illness, based on findings from pandemic influenza.**

Transmission and Global Spread

- Based on a review of 188 confirmed cases from Guangdong Province (China), Kang, et al. describe characteristics of human-to-human transmission.
    - Average age was 49 years; half male. 158 cases (84%) had traveled to Hubei Province within 14 days of onset. Average duration of symptom onset to diagnosis was 5.4 days.
    - 31 clusters accounting for 84 cases (45%). Among the 31 clusters, 13 were in families [not necessarily in same household], and these families accounted for 37 cases. Detailed descriptions of five family clusters are provided.
    - Of 30 secondary cases (16%), nine occurred in five of the 13 family clusters. In these five, the secondary cases shared a household with at least one family member in that cluster. It appeared that cases among family members with no travel history occurred 2-7 days after the onset date of the family member who traveled.

  Kang, et al. (Feb 5, 2020). Evidence and characteristics of human-to-human transmission of 2019-nCoV. Pre-Print downloaded on 6 Feb, 2020 from, https://www.medrxiv.org/content/10.1101/2020.02.03.20019141v2

Modelling and Prediction

- Spencer, et al. examine five virus groups (influenza, respiratory syncytial virus (RSV), rhinovirus, adenovirus, and human coronaviruses) that often contribute to the total category of "influenza-like-illness" (ILI). They estimate human coronaviruses account for around 8.8% of ILI cases annually. Epidemiologic characteristics are compared between human coronaviruses and the other four virus groups assessed.
    - *Incubation period, 1.9-14.7 days*. This is potentially longer then influenza (1-6.3 days) or rhinovirus (0.4-5.5 days); inclusive of RSV (3-8 days); and potentially less than adenovirus (1-30 days)
    - *Infectious period, 7-35 days*. This is potentially longer than any of the other viruses (influenza, 1-9 days; rhinovirus, 7-16 days; RSV, 1-21 days; and adenovirus, 7-17 days)

- *Hospitalization period, 1.5-11 days*. Rhinovirus is the narrowest range (0.4-1.7 days); RSV, the widest (2-17.5 days). Influenza (3.5-11.3) and adenovirus (3.1-7 days) are mostly within range.
- *Hospitalization proportion, 0.2% to 52%*. By comparison adenovirus is 1.4% to 95%; RSV, <<0.1% to 29%; influenza, <<0.1% to 6.2%; and rhinovirus, 0.9% to 2.4%.
- *Case fatality proportion, 0-34%.* At the upper end, this value is higher than any of the other viruses considered (upper ranges: adenovirus, 16%; RSV, 16.5%; influenza, 8.3%; and rhinovirus, 12.5%)
- *R_0 range, 2.7 to 8*. Rhinovirus (1.2-1.8) and influenza (1.1-3.4) have narrower ranges; RSV, a wide range (1.2-9.1). Adenovirus has a single value (2.3)

Spencer, et al. (Feb 5, 2020). Epidemiological parameter review and comparative dynamics of influenza, respiratory syncytial virus, rhinovirus, human coronavirus, and adenovirus. Pre-Print downloaded on 6 Feb, 2020 from, https://www.medrxiv.org/content/10.1101/2020.02.04.20020404v1

- Chowell, et al. model the effects of potential control measures. With a 100% effective vaccine, 80% coverage could end the epidemic in 6 months. Absent a vaccine, testing and isolation could end the epidemic in a similar timeframe if 90% of symptomatic cases could be reached within 24 hours of symptom onset. Other scenarios are also provided.

  Chowell, et al. (Feb 5, 2020). Getting to zero quickly in the 2019-nCov epidemic with vaccines or rapid testing. Pre-Print downloaded on 6 Feb, 2020 from, https://www.medrxiv.org/content/10.1101/2020.02.03.20020271v1

Virology

- Based on a phylogenetic analysis (FastTree), Zhang, et al. report finding six 2019-nCoV genotypes based on 27 isolates collected from Wuhan, two other Chinese cities, and one Thai city. They suggest infections outside Wuhan originating from different places in Wuhan.

  Zhang L, et al. (Feb 3, 2020). Origin and evolution of the 2019 novel coronavirus. Clinical Infectious Diseases, ciaa112, https://doi.org/10.1093/cid/ciaa112

Clinical Characteristics and Care Seeking

- Kanne reviews the current literature on chest image findings for patients with 2019-nCoV lung infections. Overall, the current review finds similarities in chest imaging among 2019-nCoV, SARS-CoV, and MERS-CoV patients
- The review supports the common radiograph finding of bilateral lung consolidation. Small pleural effusions may be a sign of worsening clinical condition.
- From a case series of CT scans, "Patients admitted to the [ICU] were more likely to have larger areas of bilateral consolidation…whereas patients…with milder illness were more likely to have ground-glass opacity and small areas of consolidation..." A handful of patients had normal scans.

  Kanne JP (In press). Chest CT Findings in 2019 Novel Coronavirus (2019-nCoV) Infections from Wuhan, China: Key Points for the Radiologist. Radiology. https://doi.org/10.1148/radiol.2020200241

Testing and Treatment

- Russell, *et al.* review reasons not to use corticosteroids for treatment of 2019-nCoV, following WHO advice against their use in cases of novel coronavirus. Reasons are based on similarities in the biology and clinical presentation of 2019-nCoV, SARS, and MERS.
- An addition to other negative clinical outcomes described based on earlier studies, use of corticosteroid therapy in novel coronavirus patients likely delays clearance of viral RNA from respiratory secretions; and patients treated with corticosteroids were more likely to be viremic 2-3 weeks after treatment than persons given a saline control.

  Russell, et al. (Feb 6, 2020). Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. The Lancet. https://doi.org/10.1016/S0140-6736(20)30317-2

- *In vitro* assessments of existing antivirals and selected other drugs found that remdesivir and chloroquine could be effective against 2019-nCoV. Remdeivir is noted as an inhibitor of viral reproduction that is already in clinical development for other severe viral illnesses (e.g., ebola and SARS), whereas chloroquine – a well-established antimalarial – might act by preventing viral entry into the host cell.

  Wang M, et al. (Feb 4, 2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research. https://doi.org/10.1038/s41422-020-0282-0

Policy and Prevention

The CDC published three early release articles in Emerging Infectious Diseases on nonpharmaceutical measures for pandemic influenza in nonhealthcare settings. Given similarities in modes of transmission and potentially effective prevention strategies, these articles may inform current 2019-nCoV policies.

- Contact tracing was deemed useful early in an epidemic, or for specific, vulnerable populations, decreasing in utility as disease becomes more widespread.
- Various social distancing measures were assessed across observational studies.
  - Isolation practices focused on home isolation based on feasibility constraints with using medical settings. Isolation in the home is considered a useful strategy, though the degree of potential asymptomatic transmission influences this observation.
  - Workplace measures (e.g., teleworking) and school closures were generally found to be weak or ineffective measures in the context of existing spread (preemptive school closures being a possible exception). School closures may also inequitably impact vulnerable populations.
  - Avoiding crowding through bans on public gatherings were considered difficult to implement and assess.

  Fong MW, et al. (Feb 6, 2020). Nonpharmaceutical measures for pandemic influenza in nonhealthcare settings—social distancing measures. Emerg Infect Dis. *https://doi.org/10.3201/eid2605.190995*

- International travel measures:
  - No evidence was found that **traveler screening** was an effective method to prevent spread of pandemic influenza.

- **Travel restrictions** limiting the overall movement of people between locations (e.g., strict restrictions on all airline travel) may delay the arrival to a new locale, but does not ultimately prevent it.
- Complete **boarder closure** was found to be unfeasible, with the possible exception of small island countries. However, even for the latter, potentially substantial economic and social disruption would result in other challenges.

Ryu S, et al. (Feb 6, 2020). Nonpharmaceutical measures for pandemic influenza in nonhealthcare settings—international travel–related measures. Emerg Infect Dis. https://doi.org/10.3201/eid2605.190993

- Personal protective measures assessed were hand hygiene, respiratory etiquette, and face masks. Environmental hygiene measure assessed was surface and object cleaning with viral disinfectants.
- While hypothetically promising, in practice, none of the personal protection measures (as used by the general public) appeared to affect influenza spread. Hand hygiene was noted as still effective for other infectious diseases, and has few negative consequences.
- As with hand hygiene, surface and object cleaning did not appear to, in practice, affect transmission of influenza, though its utility in controlling spread of other agents was noted.

Xiao J et al. (Feb 6, 2020). Nonpharmaceutical measures for pandemic influenza in nonhealthcare settings—personal protective and environmental measures. Emerg Infect Dis. *https://doi.org/10.3201/eid2605.190994*

Other Resources

Need to get caught up? JAMA has a quick read for clinicians.

- Del Rio and Malani provide a useful overview of 2019-nCoV for healthcare providers in the US. They review key features of 2019-nCoV epidemiology, molecular biology, and clinical presentation, along with a good description of how to identify and follow up with a person under investigation (PUI; when to collect travel history, reporting and testing, etc.) and current treatment options.

del Rio C and Malani PN. (Feb 5, 2020). 2019 Novel Coronavirus—Important Information for Clinicians. JAMA doi:10.1001/jama.2020.1490
Available from: https://jamanetwork.com/journals/jama/fullarticle/2760782

- Elsevier coronavirus information center is also a useful resource curated by clinical experts: https://www.elsevier.com/connect/coronavirus-information-center

In addition to the articles described here, there are several editorials, commentaries, and technical (e.g., drug trial) papers available to view via the 2019-nCoV SharePoint site along with previous Lit Reps.