

EVIDENCE SEARCH REPORT

RESEARCH QUESTION: What is the period of communicability of symptomatic SARS-CoV-2?		UNIQUE IDENTIFIER: INF042401-01 ESR
RESOURCES USED:		
<ul style="list-style-type: none"> • CDC website and database • CINAHL • Embase • European Centre for Disease Control • Google • Google Advanced Search • Google Scholar • Health Canada • LitCovid • Medline • medRxiv • PHAC website and database • PubMed • Reference/Citation Lists • WHO website and database 		
LIMITS/EXCLUSIONS/INCLUSIONS: English		REFERENCE INTERVIEW COMPLETED: April 23, 2020
DATE: April 25, 2020		
LIBRARIAN: Catherine Young, Michelle Dalidowicz & Mark Mueller		REQUESTOR: Ross Findlater
TEAM: Infectious Disease		
ALERTS: N/A		
CITE AS: Young, C; Dalidowicz, M; Mueller, M. What is the period of communicability of symptomatic SARS-CoV-2? 2020 Apr 25; Document no.: INF042401-01 ESR. In: COVID-19 Rapid Evidence Reviews [Internet]. SK: SK COVID Evidence Support Team, c2020. 35 p. (CEST evidence search report)		

LIBRARIAN NOTES/COMMENTS

Hello Dr. Findlater,

We completed a search for potentially relevant resources for determining period of communicability and did not limit the search to resources that specifically identified this as a finding.

Thanks,
Catherine, Michelle, and Mark

DISCLAIMER

This information is provided as a service by the Saskatchewan Health Authority and University of Saskatchewan Libraries. Professional librarians conduct searches of the literature. Results are subject to the limitations of the databases and the specificity, broadness and appropriateness of the search parameters presented by the requester. The Libraries do not represent in any matter that retrieved citations are complete, accurate or otherwise to be relied upon. The search results are only valid as of the date and time at which the search is conducted. The Libraries do not accept responsibility for any loss or damage arising from the use of, or reliance on, search results.

SEARCH RESULTS

To obtain the full-text articles or to request offsite access, email library@saskhealthauthority.ca.

SUMMARIES, GUIDELINES & OTHER RESOURCES

Government of Canada

- “Period of Communicability.” In: Coronavirus disease (COVID-19): Summary of assumptions. [Updated April 13, 2020] available from <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals/assumptions.html#a4>

Public Health Ontario

- What we know so far about...the period of communicability. [Updated March 30, 2020] available from <https://www.publichealthontario.ca/-/media/documents/ncov/covid-wwksf/what-we-know-communicable-period-mar-27-2020.pdf?la=en>

European Centre for Disease Prevention and Control

- Technical Report: Guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19 – first update. [Updated April 8, 2020] available from <https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-guidance-discharge-and-ending-isolation-first%20update.pdf>
- Novel coronavirus (SARS-CoV-2) - Discharge criteria for confirmed COVID-19 cases. [Updated March 10, 2020] available from <https://www.ecdc.europa.eu/en/publications-data/novel-coronavirus-sars-cov-2-discharge-criteria-confirmed-covid-19-cases>

LIBRARIAN'S NOTE: These two aforementioned reports contain answer to the following working question: What is the duration of SARS-CoV-2 virus shedding in bodily fluids of symptomatic patients after remission of symptoms?

World Health Organization

- Coronavirus disease 2019 (COVID-19) - Situation Report - 73 [Updated April 2, 2020] available from https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200402-sitrep-73-covid-19.pdf?sfvrsn=5ae25bc7_6

LIBRARIAN'S NOTE: Report summaries a brief overview of available evidence on COVID-19 transmission from symptomatic, pre-symptomatic and asymptomatic people infected with COVID-19.

ARTICLES FROM THE LIBRARY DATABASES

Note: References are sorted by year (newest to oldest)

1. **Burke RM, Midgley CM, Dratch A, et al. Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 - United States, January-February 2020. MMWR Morb Mortal Wkly Rep. 2020;69(9):245-6. DOI: 10.15585/mmwr.mm6909e1**

ABSTRACT: In December 2019, an outbreak of coronavirus disease 2019 (COVID-19), caused by the virus SARS-CoV-2, began in Wuhan, China (1). The disease spread widely in China, and, as of February 26, 2020, COVID-19 cases had been identified in 36 other countries and territories, including the United States. Person-to-person transmission has been widely documented, and a limited number of countries have reported sustained person-to-person spread.* On January 20, state and local health departments in the United States, in collaboration with teams deployed from CDC, began identifying and monitoring all persons considered to have had close contact (dagger) with patients with confirmed COVID-19 (2). The aims of these efforts were to ensure rapid evaluation and care of patients, limit further transmission, and better understand risk factors for transmission.

URL: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6909e1.htm>

DOI: 10.15585/mmwr.mm6909e1

2. **Cai J, Xu J, Lin D, et al. A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020:ciaa198. DOI: 10.1093/cid/ciaa198**

ABSTRACT: We first described the 2019 novel coronavirus infection in 10 children occurring in areas other than Wuhan. The coronavirus diseases in children are usually mild and epidemiological exposure is a key clue to recognize pediatric case. Prolonged virus shedding is observed in respiratory tract and feces at the convalescent stage.

URL: <https://pubmed.ncbi.nlm.nih.gov/32112072>

DOI: 10.1093/cid/ciaa198

3. **Chan JF-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet. 2020;395(10223):514-23. DOI: 10.1016/S0140-6736(20)30154-9**

Background: An ongoing outbreak of pneumonia associated with a novel coronavirus was reported in Wuhan city, Hubei province, China. Affected patients were geographically linked with a local wet market as a potential source. No data on person-to-person or nosocomial transmission have been published to date.

Methods: In this study, we report the epidemiological, clinical, laboratory, radiological, and microbiological findings of five patients in a family cluster who presented with unexplained pneumonia after returning to Shenzhen, Guangdong province, China, after a visit to Wuhan, and an additional family member who did not travel to Wuhan. Phylogenetic analysis of genetic sequences from these patients were done.

Findings: From Jan 10, 2020, we enrolled a family of six patients who travelled to Wuhan from Shenzhen between Dec 29, 2019 and Jan 4, 2020. Of six family members who travelled to Wuhan, five were identified as infected with the novel coronavirus. Additionally, one family member, who did not travel to Wuhan, became infected with the virus after several days of contact with four of the family members. None of the family members had contacts with Wuhan markets or animals, although two had visited a Wuhan hospital. Five family members (aged 36–66 years) presented with fever, upper or lower respiratory tract symptoms, or diarrhoea, or a combination of these 3–6 days after exposure. They presented to our hospital (The University of Hong Kong-Shenzhen Hospital, Shenzhen) 6–10 days after symptom onset. They and one asymptomatic child (aged 10 years) had radiological ground-glass lung

opacities. Older patients (aged >60 years) had more systemic symptoms, extensive radiological ground-glass lung changes, lymphopenia, thrombocytopenia, and increased C-reactive protein and lactate dehydrogenase levels. The nasopharyngeal or throat swabs of these six patients were negative for known respiratory microbes by point-of-care multiplex RT-PCR, but five patients (four adults and the child) were RT-PCR positive for genes encoding the internal RNA-dependent RNA polymerase and surface Spike protein of this novel coronavirus, which were confirmed by Sanger sequencing. Phylogenetic analysis of these five patients' RT-PCR amplicons and two full genomes by next-generation sequencing showed that this is a novel coronavirus, which is closest to the bat severe acute respiratory syndrome (SARS)-related coronaviruses found in Chinese horseshoe bats.

Interpretation: Our findings are consistent with person-to-person transmission of this novel coronavirus in hospital and family settings, and the reports of infected travellers in other geographical regions.

URL: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30154-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30154-9/fulltext)

DOI: 10.1016/S0140-6736(20)30154-9

4. Chen TM, Rui J, Wang QP, et al. A mathematical model for simulating the phase-based transmissibility of a novel coronavirus. Infect Dis Poverty. 2020;9(1):24. DOI: 10.1186/s40249-020-00640-3

ABSTRACT: BACKGROUND: As reported by the World Health Organization, a novel coronavirus (2019-nCoV) was identified as the causative virus of Wuhan pneumonia of unknown etiology by Chinese authorities on 7 January, 2020. The virus was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by International Committee on Taxonomy of Viruses on 11 February, 2020. This study aimed to develop a mathematical model for calculating the transmissibility of the virus. METHODS: In this study, we developed a Bats-Hosts-Reservoir-People transmission network model for simulating the potential transmission from the infection source (probably be bats) to the human infection. Since the Bats-Hosts-Reservoir network was hard to explore clearly and public concerns were focusing on the transmission from Huanan Seafood Wholesale Market (reservoir) to people, we simplified the model as Reservoir-People (RP) transmission network model. The next generation matrix approach was adopted to calculate the basic reproduction number (R0) from the RP model to assess the transmissibility of the SARS-CoV-2. RESULTS: The value of R0 was estimated of 2.30 from reservoir to person and 3.58 from person to person which means that the expected number of secondary infections that result from introducing a single infected individual into an otherwise susceptible population was 3.58.

CONCLUSIONS: Our model showed that the transmissibility of SARS-CoV-2 was higher than the Middle East respiratory syndrome in the Middle East countries, similar to severe acute respiratory syndrome, but lower than MERS in the Republic of Korea.

URL: <https://idpjournal.biomedcentral.com/articles/10.1186/s40249-020-00640-3>

DOI: 10.1186/s40249-020-00640-3

5. Chen W, Lan Y, Yuan X, et al. Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity. Emerging microbes & infections. 2020;9(1):469-73. DOI: 10.1080/22221751.2020.1732837

ABSTRACT: The novel coronavirus (2019-nCoV) infection caused pneumonia. we retrospectively analyzed the virus presence in the pharyngeal swab, blood, and the anal swab detected by real-time PCR in the clinical lab. Unexpectedly, the 2109-nCoV RNA was readily detected in the blood (6 of 57 patients) and the anal swabs (11 of 28 patients). Importantly, all of the 6 patients with detectable viral RNA in the blood cohort progressed to severe symptom stage, indicating a strong correlation of serum viral RNA with the disease severity (p-value=0.0001). Meanwhile, 8 of the 11 patients with anal swab virus-positive was in severe clinical stage. However, the concentration of viral RNA in the anal swab (Ct value=24±39) was higher than in the blood (Ct value=34±39) from patient 2, suggesting that the virus might replicate in the digestive tract. Altogether, our results confirmed the presence of virus RNA in extra-pulmonary sites.

URL: <https://pubmed.ncbi.nlm.nih.gov/32102625>

DOI: 10.1080/22221751.2020.1732837

6. Chen Y, Chen L, Deng Q, et al. The Presence of SARS-CoV-2 RNA in Feces of COVID-19 Patients. Journal of Medical Virology. 2020;n/a(n/a). DOI: 10.1002/jmv.25825

ABSTRACT: Abstract Background In December 2019, Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), emerged in Wuhan, China, and has spread globally. However, the transmission route of SARS-CoV-2 has not been fully understood. In this study, we aimed to investigate the SARS-CoV-2 shedding in excreta of COVID-19 patients. Methods Electronical medical records, including demographics, clinical characteristics, laboratory and radiological findings, of enrolled patients were extracted and analyzed. Pharyngeal swab, stool and urine specimens were collected and tested for SARS-CoV-2 RNA by RT-PCR. Viral shedding at multiple time points in specimens was recorded, and analyzed its correlation with clinical manifestations and the severity of illness. Results A total of 42 laboratory-confirmed patients were enrolled, 8 (19.05%) of whom had gastrointestinal symptoms. 28 (66.67%) patients tested positive for SARS-CoV-2 RNA in stool specimens, which was not associated with the presence of gastrointestinal symptoms and the severity of illness. Among them, 18 (64.29%) patients remained positive for viral RNA in feces after pharyngeal swabs turned negative. The duration of viral shedding from feces after negative conversion in pharyngeal swabs was 7 (6-10) days, regardless of COVID-19 severity. The demographics, clinical characteristics, laboratory and radiologic findings did no differ between patients tested positive and negative for SARS-CoV-2 RNA in feces. Viral RNA was not detectable in urine specimens from 10 patients. Conclusions Our results demonstrated the presence of SARS-CoV-2 RNA in feces of COVID-19 patients, and suggested the possibility of SARS-CoV-2 transmission via the fecal-oral route. This article is protected by copyright. All rights reserved.

URL: <https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25825>

DOI: 10.1002/jmv.25825

7. Cheng H-Y, Jian S-W, Liu D-P, et al. High transmissibility of COVID-19 near symptom onset. medRxiv. 2020:2020.03.18.20034561. DOI: 10.1101/2020.03.18.20034561

ABSTRACT: Background The dynamics of coronavirus disease 2019 (COVID-19) transmissibility after symptom onset remains unknown. Methods We conducted a prospective case-ascertained study on laboratory-confirmed COVID-19 cases and their contacts. Secondary clinical attack rate (considering symptomatic cases only) was analyzed for different exposure windows after symptom onset of index cases and for different exposure settings. Results Thirty-two confirmed patients were enrolled and 12 paired data (index-secondary cases) were identified among the 1,043 contacts. The secondary clinical attack rate was 0.9% (95% CI 0.5-1.7%). The attack rate was higher among those whose exposure to index cases started within five days of symptom onset (2.4%, 95% CI 1.1-4.5%) than those who were exposed later (zero case from 605 close contacts, 95% CI 0-0.61%). The attack rate was also higher among household contacts (13.6%, 95% CI 4.7-29.5%) and non-household family contacts (8.5%, 95% CI 2.4-20.3%) than that in healthcare or other settings. The higher secondary clinical attack rate for contacts near symptom onset remained when the analysis was restricted to household and family contacts. There was a trend of increasing attack rate with the age of contacts (p for trend < 0.001). Conclusions High transmissibility of COVID-19 near symptom onset suggests that finding and isolating symptomatic patients alone may not suffice to contain the epidemic, and more generalized social distancing measures are required. Rapid reduction of transmissibility over time implies that prolonged hospitalization of mild cases might not be necessary in large epidemics.

URL: <http://medrxiv.org/content/early/2020/03/19/2020.03.18.20034561.abstract>

DOI: 10.1101/2020.03.18.20034561

8. **Chong KC, Cheng W, Zhao S, et al. Transmissibility of coronavirus disease 2019 (COVID-19) in Chinese cities with different transmission dynamics of imported cases. medRxiv. 2020:2020.03.15.20036541. DOI: 10.1101/2020.03.15.20036541**

ABSTRACT: Background: Monitoring the time-varying reproduction number (R_t) of the disease is useful in determining whether there is sustained transmission in a population. In this study, we examined R_t of COVID-19 and compared its transmissibility between different intervention periods in Hangzhou and Shenzhen. Methods: Daily aggregated counts of confirmed imported and local cases between January 1, 2020 and March 13, 2020 were analysed. A likelihood function was constructed to estimate R_t , accounting for imported cases. Results: Although Hangzhou had fewer number of cases than Shenzhen, Shenzhen had higher proportion of imported cases than Hangzhou (83% vs 29%). Since the epidemic of COVID-19 in Shenzhen was dominated by imported cases, R_t was kept below unity through time. On the contrary, R_t was greater than unity in Hangzhou from 16 January to 7 February due to the surge in local cases. Credits to the Wuhan lockdown and outbreak response measures following the local lockdown, R_t decreased steadily and dropped below unity in mid-February. Conclusion: The lockdown measures and local outbreak responses helped reduce the potential of local transmission in Hangzhou and Shenzhen. Meanwhile, cities with similar epidemic trend could have different transmission dynamics given the variation in imported cases.

URL: <http://medrxiv.org/content/early/2020/03/18/2020.03.15.20036541.abstract>

DOI: 10.1101/2020.03.15.20036541

9. **Covid-19 National Emergency Response Center E, Case Management Team Kcfdc, Prevention. Early Epidemiological and Clinical Characteristics of 28 Cases of Coronavirus Disease in South Korea. Osong public health and research perspectives. 2020;11:8-14. DOI: 10.24171/j.phrp.2020.11.1.03**

ABSTRACT: OBJECTIVES: The first confirmed case of coronavirus disease 2019 (COVID-19) in South Korea was reported in January 2020, with 28 confirmed cases reported as of February 14(th), 2020. The epidemiological and clinical characteristics of all 28 cases were analyzed in response to this disease. METHODS: The epidemiological characteristics and early clinical features of the 28 patients from Korea with confirmed COVID-19 were analyzed using COVID-19 reporting and surveillance data and the epidemiological investigation reports prepared by the rapid response team. RESULTS: There were 16 patients that entered Korea from foreign countries: Wuhan, China (11 patients), Zhuhai, China, (1 patient), Singapore (2 patients), Japan (1 patient), and Thailand (1 patient). The early symptoms were fever, sore throat, cough or sputum production, chills, and muscle ache. Three patients were asymptomatic, however, 18 developed pneumonia. Of the 28 cases, 16 were index cases imported from abroad, with 10 cases of secondary infection originating in Korea, and the route of transmission still under investigation for 2 patients. The 10 patients with secondary infection were infected from contact with family members or acquaintances of primary patients, and the suspected sites of transmission were mostly at home. CONCLUSION: COVID-19 in Korea was spread by 16 infected individuals traveling from other countries, leading to second-generation cases. The initial symptoms were mostly minor, but the disease was infectious at this stage, resulting from close contact, particularly at home. Establishing an early detection strategy for COVID-19 is crucial for managing the transmission of the disease.

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7045878/>

DOI: 10.24171/j.phrp.2020.11.1.03

10. **Diaz-Quijano FA, Rodriguez-Morales AJ, Waldman EA. Translating transmissibility measures into recommendations for coronavirus prevention. Rev Saude Publica. 2020;54:43. DOI: 10.11606/s1518-8787.2020054002471**

ABSTRACT: The rapid increase in clinical cases of the new coronavirus disease, COVID-19, suggests high transmissibility. However, the estimates of the basic reproductive number reported in the literature vary widely. Considering this, we drew the function of contact-rate reduction required to control the

transmission from both detectable and undetectable sources. Based on this, we offer a set of recommendations for symptomatic and asymptomatic populations during the current pandemic. Understanding the dynamics of transmission is essential to support government decisions and improve the community's adherence to preventive measures.

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7135119/>

DOI: 10.11606/s1518-8787.2020054002471

11. Ding Y, Luo S, Zheng X, et al. Association of Population Migration and Coronavirus Disease 2019 Epidemic Control. medRxiv. 2020:2020.02.18.20024661. DOI: 10.1101/2020.02.18.20024661

ABSTRACT: Background and Objective To analyze the impact of different patterns of migration flow in two cities, Hefei and Shenzhen, on the epidemic and disease control of Coronavirus Disease 2019 (COVID-19), in order to provide insight for making differentiated controlling policies. Methods We collected demographic and epidemiological information of confirmed COVID-19 cases in Hefei and Shenzhen between January 19 and February 11, 2020, from data officially published by the provincial and municipal Centers for Disease Control and Prevention (CDC). From these data we calculated basic reproduction number R_0 to reflect the rate of spread of COVID-19 in these cities. Aggregated data of population migration during the same period was extracted from Baidu Migration. The change of R_0 in the two cities were analyzed and compared. Spearman correlation analysis between R_0 and population inflow from epidemic focus were performed. Results A total of 157 confirmed cases was identified in Hefei by 24:00 February 11, 2020, with an average age of 44.4 ± 15.6 years, 74 female (47.1%) and 386 confirmed cases were identified in Shenzhen, with an average age of 45.15 ± 17.99 years, 202 female (52.3%). Significant difference in the proportion of imported cases between the two cities was observed (Hefei vs Shenzhen, 24.2% vs 74.9%, $p=0.000$). Before January 31 2020, during the initial stage of the Level 1 Response to Major Public Health Emergencies, there was no significant association observed in Shenzhen between R_0 and the proportion of population inflow from the epidemic focus ($P=0.260$, $r=-0.452$); meanwhile in Hefei, such association was strong ($P=0.000$, $r=1.0$). However, after the initial stage of response, the situation reversed. A weak association was observed in Shenzhen between R_0 and the proportion of population inflow from the epidemic focus ($P=0.073$, $r=0.536$) but not in Hefei ($P=0.498$, $r=0.217$). Conclusion Following Level 1 Response, consistent decline of R_0 of COVID-19 was observed in both Hefei and Shenzhen. Different patterns of disease spread were observed in the two cities, driven by different patterns of population migration. This indicated that population migration should be taken into consideration when we set controlling policy of a novel infectious disease.

URL: <http://medrxiv.org/content/early/2020/02/20/2020.02.18.20024661.abstract>

DOI: 10.1101/2020.02.18.20024661

12. Fang Z, Zhang Y, Hang C, et al. Comparisons of viral shedding time of SARS-CoV-2 of different samples in ICU and non-ICU patients. J Infect. 2020. DOI: 10.1016/j.jinf.2020.03.013

ABSTRACT: Highlights: Dynamic RT-PCR test samples of nasal swabs, blood, fecal, urine, saliva and tears, Nasal swab had a longer viral shedding time of SARS-CoV-2 than blood and saliva, **Viral shedding time of SARS-CoV-2 in ICU was longer than non-ICU patients.**

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7118636/>

DOI: 10.1016/j.jinf.2020.03.013

13. Fu Y, Han P, Zhu R, et al. Impact Factors of Viral Shedding in Patients with SARS-CoV-2 Infected Pneumonia. SSRN. 2020. DOI: 10.2139/ssrn.3566168

ABSTRACT: Background: Severe acute respiratory coronavirus 2 (SARS-CoV-2) infected pneumonia suddenly outbreak in 2020 in Wuhan, China. The duration of viral RNA shedding is unclear. We aimed to analyze the duration of viral RNA shedding and risk factors for prolonged shedding time in a large cohort.

Methods: In this multicenter, retrospective, observational study, we enrolled 410 patients with SARS-CoV-2 pneumonia discharged from Wuhan Union hospital, Tongji hospital and Jin Yin-tan hospital between February 1 and February 20, 2020. Demographic characteristics, symptoms, laboratory tests, radiological examination, comorbidities, and treatments were all collected. The clinical characteristics were compared between patients with different duration of viral shedding, and factors impacting the duration of viral shedding were also analyzed.

Findings: Of these 410 patients, the viral RNA of most patients (89%) turned negative within 26 days after symptom onset, and the median time was 19 days. The median time from the date of normalized temperature to the date of negative SARS-CoV-2 RNA test was 7 days (IQR 4·0-10·0). Age ($p=0\cdot055$), gender ($p=0\cdot594$), disease severity status ($p=0\cdot742$), corticosteroid ($p=0\cdot656$), and antibacterial therapy ($p=0\cdot927$) were not associated with the duration of viral RNA shedding. Coronary heart disease (HR,0·619[95%CI,0·411-0·933], $p=0\cdot022$), the level of albumin extremum (HR,1·027[95%CI,1·005-1·049], $p=0\cdot014$), and the initial time for antiviral treatment after illness onset (HR,1·467[95%CI,1·187-1·815], $p<0\cdot001$) were independent factors of the duration of SARS-CoV-2 RNA shedding.

Interpretation: Most patients may need follow up for about 26 days after symptom onset. It is more likely to achieve negative nucleic acid test results when reexamined 7 days after body temperature recovered. Low serum albumin levels, concomitant coronary heart disease, and starting antiviral therapy more than 7 days after symptom onset may prolong the duration of SARS-CoV-2 RNA shedding.

URL: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3566168

DOI: 10.2139/ssrn.3566168

14. Ghinai I, Woods S, Ritger KA, et al. Community Transmission of SARS-CoV-2 at Two Family Gatherings - Chicago, Illinois, February-March 2020. MMWR Morb Mortal Wkly Rep. 2020;69:446-50. DOI: 10.15585/mmwr.mm6915e1.

ABSTRACT: SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), has spread rapidly around the world since it was first recognized in late 2019. Most early reports of person-to-person SARS-CoV-2 transmission have been among household contacts, where the secondary attack rate has been estimated to exceed 10% (1), in health care facilities (2), and in congregate settings (3). However, widespread community transmission, as is currently being observed in the United States, requires more expansive transmission events between nonhousehold contacts. In February and March 2020, the Chicago Department of Public Health (CDPH) investigated a large, multifamily cluster of COVID-19. Patients with confirmed COVID-19 and their close contacts were interviewed to better understand nonhousehold, community transmission of SARS-CoV-2. This report describes the cluster of 16 cases of confirmed or probable COVID-19, including three deaths, likely resulting from transmission of SARS-CoV-2 at two family gatherings (a funeral and a birthday party). These data support current CDC social distancing recommendations intended to reduce SARS-CoV-2 transmission. U.S residents should follow stay-at-home orders when required by state or local authorities.

URL: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6915e1.htm>

DOI: 10.15585/mmwr.mm6915e1

15. Gupta S, Parker J, Dolwani S, et al. Persistent viral shedding of SARS-CoV-2 in faeces - a rapid review. medRxiv. 2020:2020.04.17.20069526. DOI: 10.1101/2020.04.17.20069526

ABSTRACT: Background and aims In addition to respiratory symptoms, patients with COVID-19 can present with gastrointestinal complaints suggesting a possible faeco-oral transmission route. The primary aim of this review is to establish the incidence and timing of positive faecal samples for the SARS-CoV-2 virus in patients with COVID-19. Methods A systematic literature review was performed to identify studies describing COVID-19 patients tested for the virus in their stool. Data were extracted concerning the nature of the test, number and timing of positive samples, incidence of positive faecal tests after negative nasopharyngeal swabs and any evidence of viable faecal virus or faeco-oral

transmission of the virus. Results There were 26 relevant articles identified. Combining these results demonstrated that 53.9% of those tested for faecal RNA in these studies were positive. Duration of faecal viral shedding ranged from 1 to 33 days after nasopharyngeal swab turned negative with one result remaining positive after 47 days of onset of symptoms. There was insufficient evidence to draw firm conclusions about the proportion of cases potentially transmitted through infection via faecally shed virus. Conclusions There is a relatively high rate of positive tests and persistence of the SARS-CoV-2 virus in faecal samples of selected patients with COVID-19. Further research is needed to demonstrate how much these positive tests correlate with viable virus and transmission through the faeco-oral route. This may have important implications for duration of isolation, precautions recommended in individuals undertaking a period of isolation, protective equipment for health professionals and interventional procedures involving the gastrointestinal tract.

URL: <http://medrxiv.org/content/early/2020/04/22/2020.04.17.20069526.abstract>

DOI: 10.1101/2020.04.17.20069526

16. Han C, Duan C, Zhang S, et al. Digestive Symptoms in COVID-19 Patients With Mild Disease Severity: Clinical Presentation, Stool Viral RNA Testing, and Outcomes. Am J Gastroenterol. 2020. DOI: 10.14309/ajg.0000000000000664

ABSTRACT: OBJECTIVES: Coronavirus disease 2019 (COVID-19) most commonly presents with respiratory symptoms, including cough, shortness of breath, and sore throat. However, digestive symptoms also occur in patients with COVID-19 and are often described in outpatients with less severe disease. In this study, we sought to describe the clinical characteristics of COVID-19 patients with digestive symptoms and mild disease severity. METHODS: We identified COVID-19 patients with mild disease and one or more digestive symptoms (diarrhea, nausea, and vomiting), with or without respiratory symptoms, and compared them with a group presenting solely with respiratory symptoms. We followed up patients clinically until they tested negative for COVID-19 on at least 2 sequential respiratory tract specimens collected ≥ 24 hours apart. We then compared the clinical features between those with digestive symptoms and those with respiratory symptoms. RESULTS: There were 206 patients with low severity COVID-19, including 48 presenting with a digestive symptom alone, 69 with both digestive and respiratory symptoms, and 89 with respiratory symptoms alone. Between the 2 groups with digestive symptoms, 67 presented with diarrhea, of whom 19.4% experienced diarrhea as the first symptom in their illness course. The diarrhea lasted from 1 to 14 days, with an average duration of 5.4 \pm 3.1 days and a frequency of 4.3 \pm 2.2 bowel movements per day. Concurrent fever was found in 62.4% of patients with a digestive symptom. Patients with digestive symptoms presented for care later than those with respiratory symptoms (16.0 \pm 7.7 vs 11.6 \pm 5.1 days, $P < 0.001$). Nevertheless, patients with digestive symptoms had a longer duration between symptom onset and viral clearance ($P < 0.001$) and were more likely to be fecal virus positive (73.3% vs 14.3%, $P = 0.033$) than those with respiratory symptoms. DISCUSSION: We describe a unique subgroup of COVID-19 patients with mild disease severity marked by the presence of digestive symptoms. These patients are more likely to test positive for viral RNA in stool, to have a longer delay before viral clearance, and to experience delayed diagnosis compared with patients with only respiratory symptoms.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/32301761>

DOI: 10.14309/ajg.0000000000000664

17. Han Y, Yang H. The transmission and diagnosis of 2019 novel coronavirus infection disease (COVID-19): A Chinese perspective. Journal of medical virology. 2020:10.1002/jmv.25749. DOI: 10.1002/jmv.25749

ABSTRACT: 2019 novel coronavirus (SARS-CoV-2), which originated in Wuhan, China, has attracted the world's attention over the last month. The Chinese government has taken emergency measures to control the outbreak and has undertaken initial steps in the diagnosis and treatment of 2019 novel

coronavirus infection disease (COVID-19). However, SARS-CoV-2 possesses powerful pathogenicity as well as transmissibility and still holds many mysteries that are yet to be solved, such as whether the virus can be transmitted by asymptomatic patients or by mothers to their infants. Our research presents selected available cases of COVID-19 in China to better understand the transmission and diagnosis regarding this infectious disease.

URL: <https://pubmed.ncbi.nlm.nih.gov/32141619>

DOI: 10.1002/jmv.25749

18. He D, Zhao S, Zhuang Z, et al. Individual Variation in Infectiousness of Coronavirus 2019 Implies Difficulty in Control. SSRN- Lancet prepublication. 2020.

ABSTRACT: We showed that the individual variation in infectiousness (the number of secondary cases of a typical index case) of COVID probably follows a Poisson distribution. This reflects in a large dispersion parameter k in a more general negative-binomial distribution. This means the mitigation is relatively difficult than the severe acute respiratory syndrome which has a k of 0.16. Keywords: COVID-19, basic reproductive number, dispersion, negative binomial, mitigation

URL: <https://ssrn.com/abstract=3559370>

19. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med. 2020. DOI: 10.1038/s41591-020-0869-5

ABSTRACT: We report temporal patterns of viral shedding in 94 patients with laboratory-confirmed COVID-19 and modeled COVID-19 infectiousness profiles from a separate sample of 77 infector-infectee transmission pairs. We observed the highest viral load in throat swabs at the time of symptom onset, and inferred that infectiousness peaked on or before symptom onset. We estimated that 44% (95% confidence interval, 25-69%) of secondary cases were infected during the index cases' presymptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home. Disease control measures should be adjusted to account for probable substantial presymptomatic transmission.

URL: <https://www.nature.com/articles/s41591-020-0869-5>

DOI: 10.1038/s41591-020-0869-5

20. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. The New England journal of medicine. 2020. DOI: 10.1056/NEJMoa2001191

ABSTRACT: An outbreak of novel coronavirus (2019-nCoV) that began in Wuhan, China, has spread rapidly, with cases now confirmed in multiple countries. We report the first case of 2019-nCoV infection confirmed in the United States and describe the identification, diagnosis, clinical course, and management of the case, including the patient's initial mild symptoms at presentation with progression to pneumonia on day 9 of illness. This case highlights the importance of close coordination between clinicians and public health authorities at the local, state, and federal levels, as well as the need for rapid dissemination of clinical information related to the care of patients with this emerging infection.

URL: <https://www.nejm.org/doi/10.1056/NEJMoa2001191>

DOI: 10.1056/NEJMoa2001191

21. Huang C, Wang Y, Li X. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):496-. DOI: 10.1016/s0140-6736(20)30252-x

Background: A recent cluster of pneumonia cases in Wuhan, China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV). We report the epidemiological, clinical, laboratory, and radiological characteristics and treatment and clinical outcomes of these patients. Methods: All patients with suspected 2019-nCoV were admitted to a designated hospital in Wuhan. We prospectively collected and analysed data on patients with laboratory-confirmed 2019-nCoV infection by

real-time RT-PCR and next-generation sequencing. Data were obtained with standardised data collection forms shared by WHO and the International Severe Acute Respiratory and Emerging Infection Consortium from electronic medical records. Researchers also directly communicated with patients or their families to ascertain epidemiological and symptom data. Outcomes were also compared between patients who had been admitted to the intensive care unit (ICU) and those who had not.

Findings: By Jan 2, 2020, 41 admitted hospital patients had been identified as having laboratory-confirmed 2019-nCoV infection. Most of the infected patients were men (30 [73%] of 41); less than half had underlying diseases (13 [32%]), including diabetes (eight [20%]), hypertension (six [15%]), and cardiovascular disease (six [15%]). Median age was 49·0 years (IQR 41·0–58·0). 27 (66%) of 41 patients had been exposed to Huanan seafood market. One family cluster was found. Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), haemoptysis (two [5%] of 39), and diarrhoea (one [3%] of 38). Dyspnoea developed in 22 (55%) of 40 patients (median time from illness onset to dyspnoea 8·0 days [IQR 5·0–13·0]). 26 (63%) of 41 patients had lymphopenia. All 41 patients had pneumonia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome (12 [29%]), RNAemia (six [15%]), acute cardiac injury (five [12%]) and secondary infection (four [10%]). 13 (32%) patients were admitted to an ICU and six (15%) died. Compared with non-ICU patients, ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNF α .

Interpretation: The 2019-nCoV infection caused clusters of severe respiratory illness similar to severe acute respiratory syndrome coronavirus and was associated with ICU admission and high mortality. Major gaps in our knowledge of the origin, epidemiology, duration of human transmission, and clinical spectrum of disease need fulfilment by future studies.

URL: [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(20\)30183-5.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)30183-5.pdf)

DOI: 10.1016/s0140-6736(20)30252-x

22. Huang L, Zhang X, Zhang X, et al. Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: a prospective contact-tracing study. Journal of Infection. 2020. DOI: 10.1016/j.jinf.2020.03.006

ABSTRACT: **BACKGROUND:** The outbreak of coronavirus-disease-2019 (COVID-19) has rapidly spread to many places outside Wuhan. Previous studies on COVID-19 mostly included older hospitalized-adults. Little information on infectivity among and characteristics of youngsters with COVID-19 is available. **METHODS:** A cluster of 22 close-contacts of a 22-year-old male (Patient-Index) including youngsters with laboratory-confirmed COVID-19 and hospitalized close-contacts testing negative for severe-acute-respiratory-syndrome-coronavirus-2 (SARS-CoV-2) in Anhui Province, China was prospectively-traced. **RESULTS:** Since January 23, 2020, we enrolled a cluster of eight youngsters with COVID-19 (median age [range], 22 [16-23] years; six males) originating from Patient-Index returning from Wuhan to Hefei on January 19. Patient-Index visited his 16-year-old female cousin in the evening on his return, and met 15 previous classmates in a get-together on January 21. He reported being totally asymptomatic and were described by all his contacts as healthy on January 19-21. His very first symptoms were itchy eyes and fever developed at noon and in the afternoon on January 22, respectively. Seven youngsters (his cousin and six classmates) became infected with COVID-19 after a-few-hour-contact with Patient-Index. None of the patients and contacts had visited Wuhan (except Patient-Index), or had any exposure to wet-markets, wild-animals, or medical-institutes within three months. For affected youngsters, the median incubation-period was 2 days (range, 1-4). The median serial-interval was 1 day (range, 0-4). Half or more of the eight COVID-19-infected youngsters had fever, cough, sputum production, nasal congestion, and fatigue on admission. All patients had mild conditions. Six patients developed pneumonia (all mild; one bilateral) on admission. As of February 20, four patients were discharged. **CONCLUSIONS:** SARS-CoV-

2-infection presented strong infectivity during the incubation-period with rapid transmission in this cluster of youngsters outside Wuhan. COVID-19 developed in these youngsters had fast onset and various nonspecific atypical manifestations, and were much milder than in older patients as previously reported.

URL: [https://www.journalofinfection.com/article/S0163-4453\(20\)30117-1/pdf](https://www.journalofinfection.com/article/S0163-4453(20)30117-1/pdf)

DOI: 10.1016/j.jinf.2020.03.006

23. Huang R, Xia J, Chen Y, et al. A family cluster of SARS-CoV-2 infection involving 11 patients in Nanjing, China. The Lancet Infectious Diseases. 2020. DOI: [https://doi.org/10.1016/S1473-3099\(20\)30147-X](https://doi.org/10.1016/S1473-3099(20)30147-X)

Human infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global health concern.^{1, 2} Currently, human-to-human transmission of the virus accounts for most infections worldwide.³ We report a family cluster of SARS-CoV-2 infection involving 11 patients in Nanjing, China.

The detailed timeline of exposure for the 11 confirmed patients is presented in the appendix 2. The index patient travelled to Nanjing on Jan 21, 2020, from Xiaogan (about 70 km from Wuhan), and switched trains in Wuhan. After arriving in Nanjing, she stayed with two of her sisters (patients 1 and 2) and her mother (patient 3) at their family home. She had a family dinner with her mother, two sisters, and her brother (patient 4) on Jan 21. The index patient had another family dinner with eight relatives on Jan 23. She had been well without any symptoms of infection but started to have a fever and cough on Jan 28. She went to Zhejiang on Jan 24, where she tested positive for SARS-CoV-2 infection on Jan 29. No one in the family cluster had travelled to Wuhan in the previous 2 weeks except for the index patient. Three patients (patients 1–3) who lived together with the index patient and three relatives (patients 4, 6, and 7) who attended the dinner with the index patient on Jan 23 were positive for SARS-CoV-2 infection thereafter. Furthermore, patient 5 who lived with patient 4 and had no direct contact with the index patient was diagnosed with SARS-CoV-2 infection on Jan 30. On Jan 24, two patients (patients 6 and 7) who had been well without any symptoms attended another family dinner with 13 relatives. Three of the relatives (patients 8–10) were diagnosed with SARS-CoV-2 infection within 2 weeks.

Human-to-human transmission can occur among close contacts of SARS-CoV-2.³ However, the family cluster of patients we describe provides evidence that asymptomatic people can be potential sources of SARS-CoV-2 infection.

URL: <http://www.sciencedirect.com/science/article/pii/S147330992030147X>

DOI: [https://doi.org/10.1016/S1473-3099\(20\)30147-X](https://doi.org/10.1016/S1473-3099(20)30147-X)

24. Jiang DM. Recurrent PCR positivity after hospital discharge of people with coronavirus disease 2019 (COVID-19). Journal of Infection. 2020. DOI: 10.1016/j.jinf.2020.03.024

Dear Editor, The outbreak of coronavirus disease 2019 (COVID-19) was reported by Tang and colleagues in late December 2019 in Wuhan, China, in this journal, with a series of respiratory infected by a novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ By March 3, 2020, 105,586 cases of COVID-19 pneumonia were laboratory-confirmed in over 100 countries worldwide. Infection caused by SARS-CoV-2 can result in acute respiratory distress syndrome (ARDS), which is similar to the symptoms induced by the Middle East respiratory syndrome coronavirus. With deeper understanding of the biological characteristic of SARSCoV-2, great successful progress has been made in COVID-19 treatment. A total of 79,251 confirmed cases were reported in China by February 28, and 39,002 cases out of them have been cured and discharged from hospitals.

URL: [https://www.journalofinfection.com/article/S0163-4453\(20\)30152-3/pdf](https://www.journalofinfection.com/article/S0163-4453(20)30152-3/pdf)

DOI: 10.1016/j.jinf.2020.03.024

- 25. Jiang XL, Zhang XL, Zhao XN, et al. Transmission potential of asymptomatic and paucisymptomatic SARS-CoV-2 infections: a three-family cluster study in China. Journal of Infectious Diseases. 2020;22:22. DOI: <https://dx.doi.org/10.1093/infdis/jiaa206>**
ABSTRACT: Data concerning the transmission of SARS-CoV-2 in asymptomatic and paucisymptomatic patients are lacking. We report a three-family cluster of infections involving asymptomatic and paucisymptomatic transmission. Eight (53%) of 15 members from three families were confirmed with SARS-CoV-2 infection. Of eight patients, three were asymptomatic and one was paucisymptomatic. An asymptomatic mother transmitted the virus to her son, and a paucisymptomatic father transmitted the virus to his three-month-old daughter. SARS-CoV-2 was detected in the environment of one household. The complete genomes of SARS-CoV-2 from the patients were 99.9% identical and were clustered with other SARS-CoV-2 sequences reported from China and other countries.
URL: <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa206/5823691>
DOI: <https://dx.doi.org/10.1093/infdis/jiaa206>
- 26. Kam K-q, Yung CF, Cui L, et al. A Well Infant With Coronavirus Disease 2019 With High Viral Load. Clinical Infectious Diseases. 2020. DOI: 10.1093/cid/ciaa201**
ABSTRACT: A well 6-month-old infant with coronavirus disease 2019 (COVID-19) had persistently positive nasopharyngeal swabs up to day 16 of admission. This case highlights the difficulties in establishing the true incidence of COVID-19, as asymptomatic individuals can excrete the virus. These patients may play important roles in human-to-human transmission in the community.
URL: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa201/5766416>
DOI: 10.1093/cid/ciaa201
- 27. Kluytmans M, Buiting A, Pas S, et al. SARS-CoV-2 infection in 86 healthcare workers in two Dutch hospitals in March 2020. medRxiv. 2020:2020.03.23.20041913. DOI: 10.1101/2020.03.23.20041913**
ABSTRACT: COVID-19 is spreading rapidly over the world. On February 27, 2020, the first patient with COVID-19 was reported in the Netherlands, linked to a trip to Northern Italy. In the following weeks, we identified nine Health Care Workers (HCW) of whom eight had no epidemiological link to countries with a high incidence of COVID-19 at that time. This suggested local spread of SARS-CoV-2 in the community and prompted a low-threshold screening in HCWs. Screening was performed in two large teaching hospitals in the southern part of the Netherlands. HCWs who suffered from fever or mild respiratory symptoms were tested for SARS-CoV-2 by RT-PCR on oropharyngeal samples. Structured interviews were conducted to document symptoms. Eighty-six (6.4%) out of 1,353 HCWs were infected with SARS-Cov-2. The median age was 49 years and 15 (17.4%) were male. Most suffered from relatively mild disease. Only 46 (53.5%) HCWs had fever during the course of illness. Seventy-nine (91.9%) HCWs met a case definition of fever and/or coughing and/or shortness of breath. The majority (n=54, 62.8%) reported to have worked while being symptomatic. Within one week after the first case was reported, a substantial proportion of HCWs with fever or respiratory symptoms were proven to be infected with SARS-Cov-2. This observation suggests that there is a relatively high prevalence of mild clinical presentations that may go undetected. The spectrum of symptoms present in HCWs with COVID-19, frequently not including fever, asks for less stringent use of the currently recommended case-definition for suspected COVID-19.
URL: <http://medrxiv.org/content/early/2020/03/27/2020.03.23.20041913.abstract>
DOI: 10.1101/2020.03.23.20041913
- 28. Kolifarhood G, Aghaali M, Mozafar Saadati H, et al. Epidemiological and Clinical Aspects of COVID-19; a Narrative Review. Archives of Academic Emergency Medicine. 2020;8(1):e41.**
ABSTRACT: There are significant misconceptions and many obstacles in the way of illuminating the epidemiological and clinical aspects of COVID-19 as a new emerging epidemic. In addition, usefulness of

some evidence published in the context of the recent epidemic for decision making in clinic as well as public health is questionable. However, misinterpreting or ignoring strong evidence in clinical practice and public health probably results in less effective and somehow more harmful decisions for individuals as well as subgroups in general populations of countries in the initial stages of this epidemic.

Accordingly, our narrative review appraised epidemiological and clinical aspects of the disease including genetic diversity of coronavirus genus, mode of transmission, incubation period, infectivity, pathogenicity, virulence, immunogenicity, diagnosis, surveillance, clinical case management and also successful measures for preventing its spread in some communities.

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7117787/>

29. Lan L, Xu D, Ye G, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. JAMA. 2020;10.1001/jama.2020.783. DOI: 10.1001/jama.2020.2783

Methods: One hospitalized patient and 3 patients (all medical personnel) quarantined at home with COVID-19 were treated at Zhongnan Hospital of Wuhan University, Wuhan, China, from January 1, 2020, to February 15, 2020, and evaluated with real-time reverse transcriptase–polymerase chain reaction (RT-PCR) tests for COVID-19 nucleic acid to determine if they could return to work. All the following criteria had to be met for hospital discharge or discontinuation of quarantine: (1) normal temperature lasting longer than 3 days, (2) resolved respiratory symptoms, (3) substantially improved acute exudative lesions on chest computed tomography (CT) images, and (4) 2 consecutively negative RT-PCR test results separated by at least 1 day.

The RT-PCR tests were performed on throat swabs following a previously described method.¹ The RT-PCR test kits (BioGerm) were recommended by the Chinese Center for Disease Control and Prevention. The same technician and brand of test kit was used for all RT-PCR testing reported; both internal controls and negative controls were routinely performed with each batch of tests.

Demographic information, laboratory findings, and radiological features were collected from electronic medical records. After recovery, patients and their families were contacted directly, and patients were asked to visit the hospital to collect throat swabs for the RT-PCR tests.

This study was approved by the Zhongnan Hospital of Wuhan University institutional review board and the need for informed consent was waived.

Results: All 4 patients were exposed to the novel 2019 coronavirus through work as medical professionals. Two were male and the age range was 30 to 36 years. Among 3 of the patients, fever, cough, or both occurred at onset. One patient was initially asymptomatic and underwent thin-section CT due to exposure to infected patients. All patients had positive RT-PCR test results and CT imaging showed ground-glass opacification or mixed ground-glass opacification and consolidation. The severity of disease was mild to moderate.

Antiviral treatment (75 mg of oseltamivir taken orally every 12 hours) was provided for the 4 patients. For 3 of the patients, all clinical symptoms and CT imaging abnormalities had resolved. The CT imaging for the fourth patient showed delicate patches of ground-glass opacity. All 4 patients had 2 consecutive negative RT-PCR test results. The time from symptom onset to recovery ranged from 12 to 32 days. After hospital discharge or discontinuation of quarantine, the patients were asked to continue the quarantine protocol at home for 5 days. The RT-PCR tests were repeated 5 to 13 days later and all were positive. All patients had 3 repeat RT-PCR tests performed over the next 4 to 5 days and all were positive. An additional RT-PCR test was performed using a kit from a different manufacturer and the results were also positive for all patients. The patients continued to be asymptomatic by clinician examination and chest CT findings showed no change from previous images. They did not report contact with any person with respiratory symptoms. No family member was infected.

Discussion: Four patients with COVID-19 who met criteria for hospital discharge or discontinuation of quarantine in China (absence of clinical symptoms and radiological abnormalities and 2 negative RT-PCR test results) had positive RT-PCR test results 5 to 13 days later. These findings suggest that at least a

proportion of recovered patients still may be virus carriers. Although no family members were infected, all reported patients were medical professionals and took special care during home quarantine. Current criteria for hospital discharge or discontinuation of quarantine and continued patient management may need to be reevaluated. Although false-negative RT-PCR test results could have occurred as suggested by a previous study, 6/2 consecutively negative RT-PCR test results plus evidence from clinical characteristics and chest CT findings suggested that the 4 patients qualified for hospital discharge or discontinuation of quarantine.

The study was limited to a small number of patients with mild or moderate infection. Further studies should follow up patients who are not health care professionals and who have more severe infection after hospital discharge or discontinuation of quarantine. Longitudinal studies on a larger cohort would help to understand the prognosis of the disease.

URL: <https://jamanetwork.com/journals/jama/fullarticle/2762452>

DOI: 10.1001/jama.2020.2783

30. Lei Z, Cao H, Jie Y, et al. A cross-sectional comparison of epidemiological and clinical features of patients with coronavirus disease (COVID-19) in Wuhan and outside Wuhan, China. *Travel Medicine & Infectious Disease*. 2020:101664. DOI: <https://dx.doi.org/10.1016/j.tmaid.2020.101664>

ABSTRACT: BACKGROUND: Coronavirus disease 2019 (COVID-19) has spread outside the initial epicenter of Wuhan. We compared cases in Guangzhou and Wuhan to illustrate potential changes in pathogenicity and epidemiological characteristics as the epidemic has progressed. METHODS: We studied 20 patients admitted to the Third Affiliated Hospital of Sun Yat-Sen University in Guangzhou, China from January 22 to February 12, 2020. Data were extracted from medical records. These cases were compared with the 99 cases, previously published in *Lancet*, from Wuhan Jinyintan Hospital from January 1 to January 20, 2020. RESULTS: Guangzhou patients were younger and had better prognosis than Wuhan patients. The Wuhan patients were more likely to be admitted to the ICU (23% vs 5%) and had a higher mortality rate (11% vs 0%). Cases in Guangzhou tended to be more clustered. Diarrhea and vomiting were more common among Guangzhou patients and SARS-CoV-2 RNA was found in feces. Fecal SARA-CoV-2 RNA remained positive when nasopharyngeal swabs turned negative in some patients. CONCLUSIONS: This study indicates possible diminishing virulence of the virus in the process of transmission. Yet persistent positive RNA in feces after negative nasopharyngeal swabs suggests a possible prolonged transmission period that challenges current quarantine practices.

URL: <https://www.sciencedirect.com/science/article/pii/S1477893920301320>

DOI: <https://dx.doi.org/10.1016/j.tmaid.2020.101664>

31. Lescure F-X, Bouadma L, Nguyen D, et al. Clinical and virological data of the first cases of COVID-19 in Europe: a case series. *Lancet Infectious Diseases*. 2020. DOI: 10.1016/S1473-3099(20)30200-0

ABSTRACT: Background On Dec 31, 2019, China reported a cluster of cases of pneumonia in people at Wuhan, Hubei Province. The responsible pathogen is a novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We report the relevant features of the first cases in Europe of confirmed infection, named coronavirus disease 2019 (COVID-19), with the first patient diagnosed with the disease on Jan 24, 2020.

URL: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30200-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30200-0/fulltext)

DOI: 10.1016/S1473-3099(20)30200-0

32. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. *New England Journal of Medicine*. 2020. DOI: 10.1056/NEJMoa2001316

BACKGROUND: The initial cases of novel coronavirus (2019-nCoV)–infected pneumonia (NCIP) occurred in Wuhan, Hubei Province, China, in December 2019 and January 2020. We analyzed data on the first 425 confirmed cases in Wuhan to determine the epidemiologic characteristics of NCIP.

METHODS: We collected information on demographic characteristics, exposure history, and illness timelines of laboratory-confirmed cases of NCIP that had been reported by January 22, 2020. We described characteristics of the cases and estimated the key epidemiologic time-delay distributions. In the early period of exponential growth, we estimated the epidemic doubling time and the basic reproductive number.

RESULTS: Among the first 425 patients with confirmed NCIP, the median age was 59 years and 56% were male. The majority of cases (55%) with onset before January 1, 2020, were linked to the Huanan Seafood Wholesale Market, as compared with 8.6% of the subsequent cases. The mean incubation period was 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days. In its early stages, the epidemic doubled in size every 7.4 days. With a mean serial interval of 7.5 days (95% CI, 5.3 to 19), the basic reproductive number was estimated to be 2.2 (95% CI, 1.4 to 3.9).

CONCLUSIONS: On the basis of this information, there is evidence that human-to-human transmission has occurred among close contacts since the middle of December 2019. Considerable efforts to reduce transmission will be required to control outbreaks if similar dynamics apply elsewhere. Measures to prevent or reduce transmission should be implemented in populations at risk.

URL: <https://www.nejm.org/doi/10.1056/NEJMoa2001316>

DOI: 10.1056/NEJMoa2001316

33. Li Y, Hu Y, Yu Y, et al. Positive result of Sars-Cov-2 in faeces and sputum from discharged patient with COVID-19 in Yiwu, China. Journal of medical virology. 2020. DOI: 10.1002/jmv.25905

ABSTRACT: BACKGROUND: With the effective prevention and control of COVID - 19 in China, the number of cured cases increased significantly. Further monitoring of the disease prognosis and effective control of the "relapse" of the epidemic become the next focus of work. To analyse the clinical prognosis of discharged COVID-19 patients by monitoring their SAR-CoV-2 nucleic acid status, which may provide evidence to establish discharge standards and follow-up management for COVID-19 patients. **METHODS:** We included 13 discharged COVID-19 patients who were quarantined for 4-week at home. The patient's daily clinical signs were recorded and sputum and faecal specimens were regularly sent for the detection of SARS-CoV-2 nucleic acid. **RESULTS:** The time between initial symptoms and meeting discharge criteria was 18 - 44 days with an average of 25 +/- 6 days. The faecal samples of two patients still tested positive after meeting discharge criteria and the sputum samples of four patients returned positive 5 - 14 days after discharge. The rate of a recurring positive test result in samples from the respiratory system was 31%(4/13). **CONCLUSION:** Under the present discharge criteria, the high presence of SARS-CoV-2 nucleic acid in faecal and respiratory samples of discharged COVID-19 patients indicate potential infectivity. Therefore, we suggest that faecal virus nucleic acid should be tested as a routine monitoring index for COVID-19 and a negative result be added to the criteria. Simultaneously, we should strengthen the regular follow-up of discharged patients with continuous monitoring of the recurrence of viral nucleic acid.

URL: <https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25905>

DOI: 10.1002/jmv.25905

34. Ling Y, Xu S-B, Lin Y-X, et al. Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients. Chinese medical journal. 2020:10.1097/CM9.0000000000000774. DOI: 10.1097/CM9.0000000000000774

ABSTRACT: BACKGROUND: A patient's infectivity is determined by the presence of the virus in different body fluids, secretions, and excreta. The persistence and clearance of viral RNA from different specimens of patients with 2019 novel coronavirus disease (COVID-19) remain unclear. This study analyzed the clearance time and factors influencing 2019 novel coronavirus (2019-nCoV) RNA in different samples from patients with COVID-19, providing further evidence to improve the management of patients during convalescence. **METHODS:** The clinical data and laboratory test results of

convalescent patients with COVID-19 who were admitted to from January 20, 2020 to February 10, 2020 were collected retrospectively. The reverse transcription polymerase chain reaction (RT-PCR) results for patients' oropharyngeal swab, stool, urine, and serum samples were collected and analyzed. Convalescent patients refer to recovered non-febrile patients without respiratory symptoms who had two successive (minimum 24 h sampling interval) negative RT-PCR results for viral RNA from oropharyngeal swabs. The effects of cluster of differentiation 4 (CD4)+ T lymphocytes, inflammatory indicators, and glucocorticoid treatment on viral nucleic acid clearance were analyzed. RESULTS: In the 292 confirmed cases, 66 patients recovered after treatment and were included in our study. In total, 28 (42.4%) women and 38 men (57.6%) with a median age of 44.0 (34.0-62.0) years were analyzed. After in-hospital treatment, patients' inflammatory indicators decreased with improved clinical condition. The median time from the onset of symptoms to first negative RT-PCR results for oropharyngeal swabs in convalescent patients was 9.5 (6.0-11.0) days. By February 10, 2020, 11 convalescent patients (16.7%) still tested positive for viral RNA from stool specimens and the other 55 patients' stool specimens were negative for 2019-nCoV following a median duration of 11.0 (9.0-16.0) days after symptom onset. Among these 55 patients, 43 had a longer duration until stool specimens were negative for viral RNA than for throat swabs, with a median delay of 2.0 (1.0-4.0) days. Results for only four (6.9%) urine samples were positive for viral nucleic acid out of 58 cases; viral RNA was still present in three patients' urine specimens after throat swabs were negative. Using a multiple linear regression model ($F=2.669$, $P=0.044$, and adjusted $R^2=0.122$), the analysis showed that the CD4+ T lymphocyte count may help predict the duration of viral RNA detection in patients' stools ($t=2.699$, $P=0.010$). The duration of viral RNA detection from oropharyngeal swabs and fecal samples in the glucocorticoid treatment group was longer than that in the non-glucocorticoid treatment group (15 days vs. 8.0 days, respectively; $t=2.550$, $P=0.013$) and the duration of viral RNA detection in fecal samples in the glucocorticoid treatment group was longer than that in the non-glucocorticoid treatment group (20 days vs. 11 days, respectively; $t=4.631$, $P=0.05$). CONCLUSIONS: In brief, as the clearance of viral RNA in patients' stools was delayed compared to that in oropharyngeal swabs, it is important to identify viral RNA in feces during convalescence. Because of the delayed clearance of viral RNA in the glucocorticoid treatment group, glucocorticoids are not recommended in the treatment of COVID-19, especially for mild disease. The duration of RNA detection may relate to host cell immunity.

URL: <https://pubmed.ncbi.nlm.nih.gov/32118639>

DOI: 10.1097/CM9.0000000000000774

35. Liu J, Liao X, Qian S, et al. Community Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, Shenzhen, China, 2020. Emerg Infect Dis. 2020;26(6). DOI: 10.3201/eid2606.200239

ABSTRACT: Since early January 2020, after the outbreak of 2019 novel coronavirus infection in Wuhan, China, approximately 365 confirmed cases have been reported in Shenzhen, China. The mode of community and intrafamily transmission is threatening residents in Shenzhen. Strategies to strengthen prevention and interruption of these transmissions should be urgently addressed.

URL: https://wwwnc.cdc.gov/eid/article/26/6/20-0239_article

DOI: 10.3201/eid2606.200239

36. Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. Lancet Infect Dis. 2020. DOI: 10.1016/s1473-3099(20)30232-2

URL: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30232-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30232-2/fulltext)

DOI: 10.1016/s1473-3099(20)30232-2

- 37. Lo IL, Lio CF, Cheong HH, et al. Evaluation of SARS-CoV-2 RNA shedding in clinical specimens and clinical characteristics of 10 patients with COVID-19 in Macau. Int J Biol Sci. 2020. DOI: 10.7150/ijbs.45357**

ABSTRACT: As a city famous for tourism, the public healthcare system of Macau SAR has been under great pressure during the outbreak of the Coronavirus Disease 2019 (COVID-19). In this study, we report clinical and microbiological features of ten COVID-19 patients enrolled in the Centro Hospitalar Conde de Sao Januario (CHCSJ) between January 21 to February 16, 2020. Clinical samples from all patients including nasopharyngeal swab (NPS)/sputum, urine, and feces were collected for serial virus RNA testing by standard qRT-PCR assay. In total, seven were imported cases and three were local cases. The median duration from Macau arrival to admission in imported cases was 3 days. Four patients required oxygen therapy but none of them needed machinal ventilation. No fatal cases were noted. The most common symptoms were fever (80%) and diarrhea (80%). In the "Severe" group, there was significantly more elderly patients ($p=0.045$), higher lactate dehydrogenase levels ($p=0.002$), and elevated C-Reactive protein levels compared to the "Mild to Moderate" group ($p<0.001$). There were positive SARS-CoV-2 RNA signals in all patients' NPS and stool specimens but negative in all urine specimens. Based on our data on SARS-CoV-2 RNA shedding in stool and the possibility of a lag in viral detection in NPS specimens, the assessment of both fecal and respiratory specimen is recommended to enhance diagnostic sensitivity, and also to aid discharge decision before the role of viral RNA shedding in stool is clarified.

URL: <https://www.ijbs.com/v16p1698.htm>

DOI: 10.7150/ijbs.45357

- 38. Luo A. Positive SARS-Cov-2 test in a woman with COVID-19 at 22 days after hospital discharge: A case report. Journal of Traditional Chinese Medical Sciences. 2020. DOI: <https://doi.org/10.1016/j.jtcms.2020.04.001>**

ABSTRACT: Background In a few discharged patients with coronavirus disease 2019 (COVID-19), the nucleic acid test shows positive results again. Whether this is due to relapse of the disease, reinfection by the virus, or a false-positive result at hospital discharge is worth exploring. Case presentation A woman with COVID-19 was discharged from the hospital after integrative treatment with traditional Chinese and Western medicine because she met the discharge standards. However, she obtained positive results on a nucleic acid test 22 days later. Conclusion Based on this positive test result in a discharged patient with COVID-19, anal tests and coronavirus antibody tests should be combined with throat swab tests to further develop the diagnosis and discharge standards for patients with COVID-19.

URL: <http://www.sciencedirect.com/science/article/pii/S2095754820300247>

DOI: <https://doi.org/10.1016/j.jtcms.2020.04.001>

- 39. Ma X, Su L, Zhang Y, et al. Do children need a longer time to shed SARS-CoV-2 in stool than adults? Journal of Microbiology, Immunology and Infection. 2020. DOI: 10.1016/j.jmii.2020.03.010**

ABSTRACT: SARS-CoV-2 can be shed in the stool of patients in the recovery phase. Children show a longer shedding time than adults. We analyzed the possible causes of this finding and recommend that a negative stool sample be included in a patient's discharge criteria.

URL: <https://www.sciencedirect.com/science/article/pii/S1684118220300700>

DOI: 10.1016/j.jmii.2020.03.010

- 40. Miri SM, Roozbeh F, Omranirad A, et al. Panic of Buying Toilet Papers: A Historical Memory or a Horrible Truth? Systematic Review of Gastrointestinal Manifestations of COVID-19. Hepatitis Monthly. 2020;20(3):1-4. DOI: 10.5812/hepatmon.102729**

ABSTRACT: Context: Within only 30 days after the first announcement of infection with "SARS-CoV-2" in Wuhan, it spread to more than 20 countries and become a pandemic by WHO as a "high alarming level

of infection" with 136,343 involved cases all over the world. Methods: To uncover more about the probable gastrointestinal transmission and its clinical manifestations, we reviewed all research publications with keywords including: "COVID-19", "SARS-CoV-2", "Coronavirus", "outbreak", "ARAS-CoV" in Medline, Scopus, Google Scholar as well as all news in social media about "novel COVID-19 pandemic". Out of 40 recent publications, 10 articles were studied by 2 authors. Results: Although the SARS-CoV-2 tends to infect respiratory epithelial cells through the respiratory tracts, recent investigations detected the virus in the stool specimen, raising the question of the fecal-oral transmission route. Different studies showed that almost all gastrointestinal signs and symptoms were seen in elderly patients (more than 65 years old). including anorexia (40%), nonspecific abdominal pains (8%), diarrhea (10%) and nausea and Vomiting in about 8% of patients. Anorexia and generalized abdominal pain suffer many treated cases even 10-20 days after negative blood tests (like CRP, lymphopenia) and negative PCR of respiratory samples. The main reason for this prolonged anorexia and abdominal pain may be due to the long persistence of COVID-19 in the gastrointestinal tracts after primary treatment. Conclusions: Comparing to SARS, patients with COVID-19 showed less diarrhea, nausea, vomiting and/or abdominal discomfort before respiratory symptoms. Feces as a potential contagious source of Viral RNA can last even after viral clearance in the respiratory tract. We strongly recommend all cured patients of COVID-19 to disinfect and clean their toilets until 17-20 days after negative blood tests and solving their respiratory disorders. Gastrointestinal manifestations have been seen in all men while no women referred with GI signs.

URL: <http://hepatmon.com/articles/102729.html>

DOI: 10.5812/hepatmon.102729

41. Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. International Journal of Infectious Diseases. 2020;93:284-6. DOI: 10.1016/j.ijid.2020.02.060

ABSTRACT: Objective: To estimate the serial interval of novel coronavirus (COVID-19) from information on 28 infector-infectee pairs. Methods: We collected dates of illness onset for primary cases (infectors) and secondary cases (infectees) from published research articles and case investigation reports. We subjectively ranked the credibility of the data and performed analyses on both the full dataset (n = 28) and a subset of pairs with highest certainty in reporting (n = 18). In addition, we adjust for right truncation of the data as the epidemic is still in its growth phase. Results: Accounting for right truncation and analyzing all pairs, we estimated the median serial interval at 4.0 days (95% credible interval CrI]: 3.1, 4.9). Limiting our data to only the most certain pairs, the median serial interval was estimated at 4.6 days (95% CrI: 3.5, 5.9). Conclusions: The serial interval of COVID-19 is close to or shorter than its median incubation period. This suggests that a substantial proportion of secondary transmission may occur prior to illness onset. The COVID-19 serial interval is also shorter than the serial interval of severe acute respiratory syndrome (SARS), indicating that calculations made using the SARS serial interval may introduce bias.

URL: [https://www.ijidonline.com/article/S1201-9712\(20\)30119-3/pdf](https://www.ijidonline.com/article/S1201-9712(20)30119-3/pdf)

DOI: 10.1016/j.ijid.2020.02.060

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URL: <https://pubmed.ncbi.nlm.nih.gov/32129805>

DOI: 10.1001/jama.2020.3227

43. Pan Y, Zhang D, Yang P, et al. Viral load of SARS-CoV-2 in clinical samples. The Lancet Infectious Diseases. 2020. DOI: 10.1016/S1473-3099(20)30113-4; 25

URL: [https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099\(20\)30113-4.pdf](https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30113-4.pdf)

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URL: <https://www.tandfonline.com/doi/full/10.1080/23744235.2020.1748705>
DOI: <https://dx.doi.org/10.1080/23744235.2020.1748705>**
- 45. Su Z, Wu Y. A Multiscale and Comparative Model for Receptor Binding of 2019 Novel Coronavirus and the Implication of its Life Cycle in Host Cells. bioRxiv. 2020:2020.02.20.958272. DOI: 10.1101/2020.02.20.958272**
ABSTRACT: The respiratory syndrome caused by a new type of coronavirus has been emerging from China and caused more than 1000 death globally since December 2019. This new virus, called 2019 novel coronavirus (2019-nCoV) uses the same receptor called Angiotensin-converting enzyme 2 (ACE2) to attack humans as the coronavirus that caused the severe acute respiratory syndrome (SARS) seventeen years ago. Both viruses recognize ACE2 through the spike proteins (S-protein) on their surfaces. It was found that the S-protein from the SARS coronavirus (SARS-CoV) bind stronger to ACE2 than 2019-nCoV. However, function of a bio-system is often under kinetic, rather than thermodynamic, control. To address this issue, we constructed a structural model for complex formed between ACE2 and the S-protein from 2019-nCoV, so that the rate of their association can be estimated and compared with the binding of S-protein from SARS-CoV by a multiscale simulation method. Our simulation results suggest that the association of new virus to the receptor is slower than SARS, which is consistent with the experimental data obtained very recently. We further integrated this difference of association rate between virus and receptor into a mathematical model which describes the life cycle of virus in host cells and its interplay with the innate immune system. Interestingly, we found that the slower association between virus and receptor can result in longer incubation period, while still maintaining a relatively higher level of viral concentration in human body. Our computational study therefore provides, from the molecular level, one possible explanation that the new disease by far spread much faster than SARS.
URL: <http://biorxiv.org/content/early/2020/02/21/2020.02.20.958272.abstract>
DOI: 10.1101/2020.02.20.958272
- 46. Tan L, Kang X, Zhang B, et al. A special case of COVID-19 with long duration of viral shedding for 49 days. medRxiv. 2020:2020.03.22.20040071. DOI: 10.1101/2020.03.22.20040071**
ABSTRACT: Prolonged viral shedding is associated with severe status and poor prognosis of COVID-19 patients. Unexpectedly, here we report a non-severe patient with the longest duration of viral shedding. According to the investigation on the clinical and epidemiological information of this case, we concluded that this type of virus might have a low toxicity and transmissibility, but have a prolonged infective ability and was hardly to be eliminated in the body with regular therapy. However, infusion of plasma from recovered patients showed high efficiency in elimination of this virus. Our findings might shed light on the management of COVID-19.
URL: <http://medrxiv.org/content/early/2020/03/27/2020.03.22.20040071.abstrac>
DOI: 10.1101/2020.03.22.20040071
- 47. Thompson RN. Novel Coronavirus Outbreak in Wuhan, China, 2020: Intense Surveillance Is Vital for Preventing Sustained Transmission in New Locations. Journal of Clinical Medicine. 2020;9:498.**
ABSTRACT: The outbreak of pneumonia originating in Wuhan, China, has generated 24,500 confirmed cases, including 492 deaths, as of 5 February 2020. The virus (2019-nCoV) has spread elsewhere in China and to 24 countries, including South Korea, Thailand, Japan and USA. Fortunately, there has only been limited human-to-human transmission outside of China. Here, we assess the risk of sustained

transmission whenever the coronavirus arrives in other countries. Data describing the times from symptom onset to hospitalisation for 47 patients infected early in the current outbreak are used to generate an estimate for the probability that an imported case is followed by sustained human-to-human transmission. Under the assumptions that the imported case is representative of the patients in China, and that the 2019-nCoV is similarly transmissible to the SARS coronavirus, the probability that an imported case is followed by sustained human-to-human transmission is 0.41 (credible interval 0.27, 0.55)]. However, if the mean time from symptom onset to hospitalisation can be halved by intense surveillance, then the probability that an imported case leads to sustained transmission is only 0.012 (credible interval 0, 0.099)]. This emphasises the importance of current surveillance efforts in countries around the world, to ensure that the ongoing outbreak will not become a global pandemic.

URL: <https://www.mdpi.com/2077-0383/9/2/498>

48. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis.* 2020. DOI: 10.1016/S1473-3099(20)30196-1

ABSTRACT: BACKGROUND: Coronavirus disease 2019 (COVID-19) causes severe community and nosocomial outbreaks. Comprehensive data for serial respiratory viral load and serum antibody responses from patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are not yet available. Nasopharyngeal and throat swabs are usually obtained for serial viral load monitoring of respiratory infections but gathering these specimens can cause discomfort for patients and put health-care workers at risk. We aimed to ascertain the serial respiratory viral load of SARS-CoV-2 in posterior oropharyngeal (deep throat) saliva samples from patients with COVID-19, and serum antibody responses. METHODS: We did a cohort study at two hospitals in Hong Kong. We included patients with laboratory-confirmed COVID-19. We obtained samples of blood, urine, posterior oropharyngeal saliva, and rectal swabs. Serial viral load was ascertained by reverse transcriptase quantitative PCR (RT-qPCR). Antibody levels against the SARS-CoV-2 internal nucleoprotein (NP) and surface spike protein receptor binding domain (RBD) were measured using EIA. Whole-genome sequencing was done to identify possible mutations arising during infection. FINDINGS: Between Jan 22, 2020, and Feb 12, 2020, 30 patients were screened for inclusion, of whom 23 were included (median age 62 years range 37-75]). The median viral load in posterior oropharyngeal saliva or other respiratory specimens at presentation was 5.2 log(10) copies per mL (IQR 4.1-7.0). Salivary viral load was highest during the first week after symptom onset and subsequently declined with time (slope -0.15, 95% CI -0.19 to -0.11; R(2)=0.71). In one patient, viral RNA was detected 25 days after symptom onset. Older age was correlated with higher viral load (Spearman's $\rho=0.48$, 95% CI 0.074-0.75; $p=0.020$). For 16 patients with serum samples available 14 days or longer after symptom onset, rates of seropositivity were 94% for anti-NP IgG (n=15), 88% for anti-NP IgM (n=14), 100% for anti-RBD IgG (n=16), and 94% for anti-RBD IgM (n=15). Anti-SARS-CoV-2-NP or anti-SARS-CoV-2-RBD IgG levels correlated with virus neutralisation titre (R(2)>0.9). No genome mutations were detected on serial samples. INTERPRETATION: Posterior oropharyngeal saliva samples are a non-invasive specimen more acceptable to patients and health-care workers. Unlike severe acute respiratory syndrome, patients with COVID-19 had the highest viral load near presentation, which could account for the fast-spreading nature of this epidemic. This finding emphasises the importance of stringent infection control and early use of potent antiviral agents, alone or in combination, for high-risk individuals. Serological assay can complement RT-qPCR for diagnosis.

URL: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30196-1/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30196-1/fulltext)

DOI: 10.1016/S1473-3099(20)30196-1

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This Research Letter reports on detection of SARS-CoV-2 in human specimens, including bronchoalveolar fluid, sputum, feces, blood, and urine, to determine means of transmission besides respiratory droplets.
URL: <https://pubmed.ncbi.nlm.nih.gov/32159775>
DOI: 10.1001/jama.2020.3786

50. Woelfel R, Corman VM, Guggemos W, et al. Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. medRxiv. 2020:2020.03.05.20030502. DOI: 10.1101/2020.03.05.20030502

ABSTRACT: Background: In coronavirus disease 2019 (COVID-19), current case definitions presume mainly lower respiratory tract infection. However, cases seen outside the epicenter of the epidemic may differ in their overall clinical appearance due to more sensitive case finding. Methods: We studied viral load courses by RT-PCR in oro- and nasopharyngeal swabs, sputum, stool, blood, and urine in nine hospitalized cases. Infectious virus was detected by cell culture. Active replication was demonstrated by analysis of viral subgenomic replicative intermediates. Serology including neutralization testing was done to characterize immune response. Results: Seven cases had upper respiratory tract disease. Lower respiratory tract symptoms seen in two cases were limited. Clinical sensitivity of RT-PCR on swabs taken on days 1-5 of symptoms was 100%, with no differences comparing swab and sputum samples taken simultaneously. Average viral load was 6.76×10^5 copies per swab during the first 5 days. Live virus isolates were obtained from swabs during the first week of illness. Proof of active viral replication in upper respiratory tract tissues was obtained by detection of subgenomic viral RNA. Shedding of viral RNA from sputum outlasted the end of symptoms. Seroconversion occurred after about one week. Conclusions: The present study shows that COVID-19 can often present as a common cold-like illness. SARS-CoV-2 can actively replicate in the upper respiratory tract, and is shed for a prolonged time after symptoms end, including in stool. These findings suggest adjustments of current case definitions and re-evaluation of the prospects of outbreak containment.

URL: <http://medrxiv.org/content/early/2020/03/08/2020.03.05.20030502.abstract>

DOI: 10.1101/2020.03.05.20030502

51. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020. DOI: 10.1038/s41586-020-2196-x

ABSTRACT: Coronavirus disease 2019 (COVID-19) is an acute respiratory tract infection that emerged in late 2019(1,2). Initial outbreaks in China involved 13.8% cases with severe, and 6.1% with critical courses(3). This severe presentation corresponds to the usage of a virus receptor that is expressed predominantly in the lung(2,4). By causing an early onset of severe symptoms, this same receptor tropism is thought to have determined pathogenicity, but also aided the control, of severe acute respiratory syndrome (SARS) in 2003(5). However, there are reports of COVID-19 cases with mild upper respiratory tract symptoms, suggesting the potential for pre- or oligosymptomatic transmission(6-8). There is an urgent need for information on body site-specific virus replication, immunity, and infectivity. Here we provide a detailed virological analysis of nine cases, providing proof of active virus replication in upper respiratory tract tissues. Pharyngeal virus shedding was very high during the first week of symptoms (peak at 7.11×10^8 RNA copies per throat swab, day 4). Infectious virus was readily isolated from throat- and lung-derived samples, but not from stool samples, in spite of high virus RNA concentration. Blood and urine never yielded virus. Active replication in the throat was confirmed by viral replicative RNA intermediates in throat samples. Sequence-distinct virus populations were consistently detected in throat and lung samples from the same patient, proving independent replication. Shedding of viral RNA from sputum outlasted the end of symptoms. Seroconversion occurred after 7 days in 50% of patients (14 days in all), but was not followed by a rapid decline in viral load. COVID-19 can present as a mild upper respiratory tract illness. Active virus replication in the upper respiratory tract puts the prospects of COVID-19 containment in perspective.

URL: <https://www.nature.com/articles/s41586-020-2196-x>

DOI: 10.1038/s41586-020-2196-x

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ABSTRACT: Since December 2019, 62 medical staff of Zhongnan Hospital in Wuhan, China have been hospitalised with coronavirus disease 2019. During the post-discharge surveillance after clinical recovery, swabs were positive in two asymptomatic cases (3.23%). Case 1 had presented typical clinical and radiological manifestations on admission, while manifestation in Case 2 was very mild. In conclusion, a small proportion of recovered patients may test positive after discharge, and post-discharge surveillance and isolation need to be strengthened.

URL: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000191>

DOI: 10.2807/1560-7917.ES.2020.25.10.2000191

- 53. Xing Y-H, Ni W, Wu Q, et al. Prolonged Viral Shedding in Feces of Pediatric Patients with Coronavirus Disease 2019. Journal of Microbiology, Immunology and Infection. 2020. DOI: <https://doi.org/10.1016/j.jmii.2020.03.021>**

ABSTRACT: Objective To determine the dynamic changes of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in respiratory and fecal specimens in children with coronavirus disease 2019 (COVID-19). Methods From January 17, 2020 to February 23, 2020, three paediatric cases of COVID-19 were reported in Qingdao, Shandong Province, China. Epidemiological, clinical, laboratory, and radiological characteristics and treatment data were collected. Patients were followed up to March 10, 2020, and dynamic profiles of nucleic acid testing results in throat swabs and fecal specimens were closely monitored. Results Clearance of SARS-CoV-2 in respiratory tract occurred within two weeks after abatement of fever, whereas viral RNA remained detectable in stools of pediatric patients for longer than 4 weeks. Two children had fecal SARS-CoV-2 undetectable 20 days after throat swabs showing negative, while that of another child lagged behind for 8 days. Conclusions SARS-CoV-2 may exist in children's gastrointestinal tract for a longer time than respiratory system. Persistent shedding of SARS-CoV-2 in stools of infected children raises the possibility that the virus might be transmitted through contaminated fomites. Massive efforts should be made at all levels to prevent spreading of the infection among children after reopening of kindergartens and schools.

URL: <http://www.sciencedirect.com/science/article/pii/S1684118220300815>

DOI: <https://doi.org/10.1016/j.jmii.2020.03.021>

- 54. Xu K, Chen Y, Yuan J, et al. Factors associated with prolonged viral RNA shedding in patients with COVID-19. Clinical Infectious Diseases. 2020;09:09. DOI: <https://dx.doi.org/10.1093/cid/ciaa351>**

ABSTRACT: BACKGROUND: An outbreak of coronavirus disease 2019 (COVID-19) is becoming a public health emergency. Data are limited on the duration and host factors related to viral shedding.

METHODS: In this retrospective study, risk factors associated with severe acute respiratory coronavirus 2 (SARS-CoV-2) RNA shedding were evaluated in a cohort of 113 symptomatic patients from two hospitals outside Wuhan. RESULTS: The median duration of SARS-CoV-2 RNA detection was 17 days (Interquartile Range [IQR], 13-22 days) as measured from illness onset. When comparing patients with early (15 days) and late viral RNA clearance (=15 days after illness onset), prolonged SARS-CoV-2 RNA shedding was associated with male sex ($p=0.009$), old age ($p=0.033$), concomitant with hypertension ($p=0.009$), delayed admission to hospital after illness onset ($p=0.001$), severe illness at admission ($p=0.049$), invasive mechanical ventilation ($p=0.006$), and corticosteroid treatment ($p=0.025$). Patients with longer SARS-CoV-2 RNA shedding duration had slower recovery of body temperature ($p=0.001$) and focal absorption on radiograph images ($p=0.001$) than patients with early SARS-CoV-2 RNA clearance.

Male sex (odds ratio [OR], 3.24 [95% CI, 1.31-8.02]), delayed hospital admission (OR, 1.30 [95% CI, 1.10-1.54]), and invasive mechanical ventilation (OR, 9.88 [95% CI, 1.11-88.02]) were independent risk factors for prolonged SARS-CoV-2 RNA shedding. CONCLUSIONS: Male sex, delayed admission to hospital after illness onset, and invasive mechanical ventilation were associated with prolonged SARS-CoV-2 RNA shedding. Hospital admission and general treatments should be started as soon as possible in symptomatic COVID-19 patients, especially male patients.

URL: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa351/5818308>

DOI: <https://dx.doi.org/10.1093/cid/ciaa351>

55. Xu K, Chen Y, Yuan J, et al. Factors associated with prolonged viral RNA shedding in patients with COVID-19. Clin Infect Dis. 2020. DOI: 10.1093/cid/ciaa351

ABSTRACT: BACKGROUND: An outbreak of coronavirus disease 2019 (COVID-19) is becoming a public health emergency. Data are limited on the duration and host factors related to viral shedding.

METHODS: In this retrospective study, risk factors associated with severe acute respiratory coronavirus 2 (SARS-CoV-2) RNA shedding were evaluated in a cohort of 113 symptomatic patients from two hospitals outside Wuhan. RESULTS: The median duration of SARS-CoV-2 RNA detection was 17 days (Interquartile Range [IQR], 13-22 days) as measured from illness onset. When comparing patients with early (<15 days) and late viral RNA clearance (>=15 days after illness onset), prolonged SARS-CoV-2 RNA shedding was associated with male sex (p=0.009), old age (p=0.033), concomitantly with hypertension (p=0.009), delayed admission to hospital after illness onset (p=0.001), severe illness at admission (p=0.049), invasive mechanical ventilation (p=0.006), and corticosteroid treatment (p=0.025). Patients with longer SARS-CoV-2 RNA shedding duration had slower recovery of body temperature (p<0.001) and focal absorption on radiograph images (p<0.001) than patients with early SARS-CoV-2 RNA clearance. Male sex (odds ratio [OR], 3.24 [95% CI, 1.31-8.02]), delayed hospital admission (OR, 1.30 [95% CI, 1.10-1.54]), and invasive mechanical ventilation (OR, 9.88 [95% CI, 1.11-88.02]) were independent risk factors for prolonged SARS-CoV-2 RNA shedding. CONCLUSIONS: Male sex, delayed admission to hospital after illness onset, and invasive mechanical ventilation were associated with prolonged SARS-CoV-2 RNA shedding. Hospital admission and general treatments should be started as soon as possible in symptomatic COVID-19 patients, especially male patients.

URL: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa351/5818308>

DOI: 10.1093/cid/ciaa351

56. Xu T, Chen C, Zhu Z, et al. Clinical features and dynamics of viral load in imported and non-imported patients with COVID-19. International Journal of Infectious Diseases. 2020. DOI: <https://doi.org/10.1016/j.ijid.2020.03.022>

ABSTRACT: Objectives To compare the clinical characteristics and the dynamics of viral load between the imported and non-imported patients with COVID-19. Design and methods Data from 51 laboratory-confirmed patients were retrospectively analyzed. Results The incubation period in the tertiary group was longer than that in the imported and secondary groups (both P < 0.05). Fever was the most common symptom at the onset of illness (73.33%, 58.82%, and 68.42%, respectively), and half of the patients had a low-grade temperature (<38.0°C) with a short duration of fever (<7 days). The CT scan showed that most patients had bilateral pneumonia in the three groups (80.00%, 76.47%, and 73.68%, respectively). Ct values detected from the tertiary patients were similar to those from the imported and secondary groups at the time of admission (both P > 0.05). For the tertiary group, the viral load was undetectable for half of the patients (52.63%) on day 7, and all patients on day 14. For 1/3rd of the patients in the imported and secondary groups, the viral load remained positive on day 14 after the admission. Conclusions COVID-19 can present as pneumonia with less onset of symptoms, and the infectivity of SARS-CoV2 may gradually decrease in the tertiary patients.

URL: <http://www.sciencedirect.com/science/article/pii/S1201971220301417>

57. Yang JR, Deng DT, Wu N, et al. Persistent viral RNA positivity during recovery period of a patient with SARS-CoV-2 infection. J Med Virol. 2020. DOI: 10.1002/jmv.25940

ABSTRACT: As an emerging infectious disease, the clinical course and virological course of SARS-CoV-2 infection remain to be further investigated. In this case report, we described a case of SARS-CoV-2 infection with clinical course more than two months. This patient had recovered from the pneumonia after treatment. The viral RNA of throat swabs became negative and the viral specific antibodies were produced during recovery period. However, the viral RNA reappeared and additionally persisted in throat swabs for more than 40 days. In addition, the viral RNA was detected in multiple types of specimens with extremely high titers in the saliva. In conclusion, these findings indicate that SARS-CoV-2 can cause a long clinical course. The coexistence of viral RNA and viral specific antibodies may imply an immune evasion of SARS-CoV-2 from host's immune system. This article is protected by copyright. All rights reserved.

URL: <https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25940>

DOI: 10.1002/jmv.25940

58. Yang Y, Yang M, Shen C, et al. Laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. medRxiv. 2020:2020.02.11.20021493. DOI: 10.1101/2020.02.11.20021493

ABSTRACT: Background: The outbreak of novel coronavirus pneumonia (NCP) caused by 2019-nCoV spread rapidly, and elucidation the diagnostic accuracy of different respiratory specimens is crucial for the control and treatment of this diseases. Methods: Respiratory samples including nasal swabs, throat swabs, sputum and bronchoalveolar lavage fluid (BALF) were collected from Guangdong CDC confirmed NCP patients, and viral RNAs were detected using a CFDA approved detection kit. Results were analyzed in combination with sample collection date and clinical information. Finding: Except for BALF, the sputum possessed the highest positive rate (74.4%~88.9%), followed by nasal swabs (53.6%~73.3%) for both severe and mild cases during the first 14 days after illness onset (d.a.o). For samples collected ≥ 15 d.a.o, sputum and nasal swabs still possessed a high positive rate ranging from 42.9%~61.1%. The positive rate of throat swabs collected ≥ 8 d.a.o was low, especially in samples from mild cases. Viral RNAs could be detected in all the lower respiratory tract of severe cases, but not the mild cases. CT scan of cases 02, 07 and 13 showed typical viral pneumonia with ground glass opacity, while no viral RNAs were detected in first three or all the upper respiratory samples. Interpretation: Sputum is most accurate for laboratory diagnosis of NCP, followed by nasal swabs. Detection of viral RNAs in BLAF is necessary for diagnosis and monitoring of viruses in severe cases. CT scan could serve as an important make up for the diagnosis of NCP. Funding National Science and Technology Major Project, Sanming Project of Medicine and China Postdoctoral Science Foundation.

URL: <http://medrxiv.org/content/early/2020/02/12/2020.02.11.20021493.abstract>

DOI: 10.1101/2020.02.11.20021493

59. Yin G, Jin H. Comparison of transmissibility of coronavirus between symptomatic and asymptomatic patients: Reanalysis of the Ningbo Covid-19 data. medRxiv. 2020:2020.04.02.20050740. DOI: 10.1101/2020.04.02.20050740

ABSTRACT: We investigate the transmissibility of coronavirus for symptomatic and asymptomatic patients using the Ningbo Covid-19 data¹. Through more in-depth and comprehensive statistical analysis, we conclude that there is no difference in the transmission rates of coronavirus between the symptomatic and asymptomatic patients, which is consistent with the original findings in Chen et al.

URL: <http://medrxiv.org/content/early/2020/04/07/2020.04.02.20050740.abstract>

DOI: 10.1101/2020.04.02.20050740

- 60. Yongchen Z, Shen H, Wang X, et al. Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients. Emerg Microbes Infect. 2020:1-14. DOI: 10.1080/22221751.2020.1756699**

ABSTRACT: Effective strategy to mitigate the ongoing pandemic of 2019 novel coronavirus (COVID-19) require a comprehensive understanding of humoral responses against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the emerging virus causing COVID-19. The dynamic profile of viral replication and shedding along with viral antigen specific antibody responses among COVID-19 patients started to be reported but there is no consensus on their patterns. Here, we conducted a serial investigation on 21 individuals infected with SARS-CoV-2 in two medical centers from Jiangsu Province, including 11 non-severe COVID-19 patients, and 5 severe COVID-19 patients and 5 asymptomatic carriers based on nucleic acid test and clinical symptoms. The longitudinal swab samples and sera were collected from these people for viral RNA testing and antibody responses, respectively. Our data revealed different pattern of seroconversion among these groups. All 11 non-severe COVID-19 patients and 5 severe COVID-19 patients were seroconverted during hospitalization or follow-up period, suggesting that serological testing is a complementary assay to nucleic acid test for those symptomatic COVID-19 patients. Of note, immediate antibody responses were identified among severe cases, compared to non-severe cases. On the other hand, only one were seroconverted for asymptomatic carriers. The SARS-CoV-2 specific antibody responses were well-maintained during the observation period. Such information is of immediate relevance and would assist COVID-19 clinical diagnosis, prognosis and vaccine design.

URL: <https://www.ncbi.nlm.nih.gov/pubmed/32306864>

DOI: 10.1080/22221751.2020.1756699

- 61. You C, Deng Y, Hu W, et al. Estimation of the Time-Varying Reproduction Number of COVID-19 Outbreak in China SSRN- Lancet prepublication. 2020.**

ABSTRACT: Methods: Three approaches, namely Poisson likelihood-based method (ML), exponential growth rate-based method (EGR) and stochastic Susceptible-Infected-Removed dynamic model-based method (SIR), were implemented to estimate the basic and controlled reproduction numbers. Results: A total of 71 chains of transmission together with dates of symptoms onset and 67 dates of infections were identified among 5,405 confirmed cases outside Hubei as reported by February 2, 2020. Based on this information, we find the serial interval having an average of 4.27 days with a standard deviation of 3.44 days, the incubation period having an average of 5.33 days with a standard deviation of 3.36 days and the infectious period having an average of 10.91 days with a standard deviation of 3.95 days. The estimated controlled reproduction numbers,

URL: <https://www.medrxiv.org/content/10.1101/2020.02.08.20021253v2>

- 62. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. JAMA. 2020:10.1001/jama.2020.3204. DOI: 10.1001/jama.2020.3204**

ABSTRACT: IMPORTANCE: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, in December 2019 and has spread globally with sustained human-to-human transmission outside China. OBJECTIVE: To report the initial experience in Singapore with the epidemiologic investigation of this outbreak, clinical features, and management. DESIGN, SETTING, AND PARTICIPANTS: Descriptive case series of the first 18 patients diagnosed with polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection at 4 hospitals in Singapore from January 23 to February 3, 2020; final follow-up date was February 25, 2020. EXPOSURES: Confirmed SARS-CoV-2 infection. MAIN OUTCOMES AND MEASURES: Clinical, laboratory, and radiologic data were collected, including PCR cycle threshold values from nasopharyngeal swabs and viral shedding in blood, urine, and stool. Clinical course was summarized, including requirement for supplemental oxygen and intensive care and use of

empirical treatment with lopinavir-ritonavir. RESULTS: Among the 18 hospitalized patients with PCR-confirmed SARS-CoV-2 infection (median age, 47 years; 9 50%] women), clinical presentation was an upper respiratory tract infection in 12 (67%), and viral shedding from the nasopharynx was prolonged for 7 days or longer among 15 (83%). Six individuals (33%) required supplemental oxygen; of these, 2 required intensive care. There were no deaths. Virus was detectable in the stool (4/8 50%]) and blood (1/12 8%]) by PCR but not in urine. Five individuals requiring supplemental oxygen were treated with lopinavir-ritonavir. For 3 of the 5 patients, fever resolved and supplemental oxygen requirement was reduced within 3 days, whereas 2 deteriorated with progressive respiratory failure. Four of the 5 patients treated with lopinavir-ritonavir developed nausea, vomiting, and/or diarrhea, and 3 developed abnormal liver function test results. CONCLUSIONS AND RELEVANCE: Among the first 18 patients diagnosed with SARS-CoV-2 infection in Singapore, clinical presentation was frequently a mild respiratory tract infection. Some patients required supplemental oxygen and had variable clinical outcomes following treatment with an antiretroviral agent.

URL: <https://pubmed.ncbi.nlm.nih.gov/32125362>

DOI: 10.1001/jama.2020.3204

63. Zhang T, Cui X, Zhao X, et al. Detectable SARS-CoV-2 Viral RNA in Feces of Three Children during Recovery Period of COVID-19 Pneumonia. J Med Virol. 2020. DOI: 10.1002/jmv.25795

ABSTRACT: Coronavirus Disease 2019 (COVID-19) is a newly emerging infectious disease caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). After its first occurrence in Wuhan of China from December 2019, COVID-19 rapidly spread around the world. According to the World Health Organization (WHO) statement on March 13, 2020, there had been over 132,500 confirmed cases globally. Nevertheless, the case reports of children are rare, which result in the lack of evidence for preventing and controlling of children's infection. Here, we report 3 cases of SARS-CoV-2 infected children diagnosed from February 3 to February 17, 2020 in Tianjin, China. All of these three cases experienced mild illness and recovered soon after treatment, with the nucleic acid of throat swab turning negative within 14, 11, 7 days after diagnosis respectively. However, after been discharged, all the three cases were tested SARS-CoV-2 positive in the stool samples within 10 days, in spite of their remained negative nucleic acid in throat swab specimens. Therefore, it is necessary to be aware of the possibility of fecal-oral transmission of SARS-CoV-2 infection, especially for children cases.

URL: <https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25795>

DOI: 10.1002/jmv.25795

64. Zhang W, Du R-H, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerging microbes & infections. 2020;9(1):386-9. DOI: 10.1080/22221751.2020.1729071

ABSTRACT: In December 2019, a novel coronavirus (2019-nCoV) caused an outbreak in Wuhan, China, and soon spread to other parts of the world. It was believed that 2019-nCoV was transmitted through respiratory tract and then induced pneumonia, thus molecular diagnosis based on oral swabs was used for confirmation of this disease. Likewise, patient will be released upon two times of negative detection from oral swabs. However, many coronaviruses can also be transmitted through oral-fecal route by infecting intestines. Whether 2019-nCoV infected patients also carry virus in other organs like intestine need to be tested. We conducted investigation on patients in a local hospital who were infected with this virus. We found the presence of 2019-nCoV in anal swabs and blood as well, and more anal swab positives than oral swab positives in a later stage of infection, suggesting shedding and thereby transmitted through oral-fecal route. We also showed serology test can improve detection positive rate thus should be used in future epidemiology. Our report provides a cautionary warning that 2019-nCoV may be shed through multiple routes.

URL: <https://pubmed.ncbi.nlm.nih.gov/32065057>

65. Zhang Y, Chen C, Zhu S, et al. Isolation of 2019-nCoV from a Stool Specimen of a Laboratory-Confirmed Case of the Coronavirus Disease 2019 (COVID-19) (Chinese). *China CDC Weekly*. 2020;2(8):123–4.

The novel coronavirus (2019-nCoV) is spreading very fast in Hubei Province of China. As of February 14, 2020, 51,986 confirmed cases (including laboratory-confirmed cases and clinically-confirmed cases) were reported in Hubei Province, and 1,318 of them died. Respiratory droplets and contact transmission are considered to be the most important routes of transmission of 2019-nCoV, but do not fully account for the occurrence of all coronavirus disease 2019 (COVID-19) cases, previously known as novel coronavirus pneumonia (NCP), and the reasons for the rapid spread of this virus (1).

In Biosafety Level 3 (BSL-3) Laboratory of the National Institute for Viral Disease Control and Prevention, Vero cells were used for viral isolation from stool samples of COVID-19 patients sent by Heilongjiang CDC. A 2019-nCoV strain was isolated from a stool specimen of a laboratory-confirmed COVID-19 severe pneumonia case, who experienced onset on January 16, 2020 and was sampled on February 1, 2020. The interval between sampling and onset was 15 days. The full-length genome sequence indicated that the virus had high-nucleotide similarity (99.98%) to that of the first isolated novel coronavirus isolated from Wuhan, China (Figure 1). In the Vero cells, viral particles with typical morphology of a coronavirus could be observed under the electron microscope (Figure 2).

URL: <http://weekly.chinacdc.cn//article/id/ffa97a96-db2a-4715-9dfb-ef662660e89d>

66. Zhao S, Cao P, Chong MK, et al. The time-varying serial interval of the coronavirus disease (COVID-19) and its gender-specific difference: A data-driven analysis using public surveillance data in Hong Kong and Shenzhen, China from January 10 to February 15, 2020. *Infection control and hospital epidemiology*. 2020:1-8. DOI: 10.1017/ice.2020.64

To the Editor—An outbreak of coronavirus disease (COVID-19), which began in Wuhan, China in the end of 2019,¹ has now reached over 100 countries and poses a huge threat to the global public health and economy.² Given the risk of human-to-human transmission, the serial interval, which refers to the time interval from symptom onset of a primary case (ie, the infector) to that of a secondary case (ie, the infectee),³ is an essential quantity, in addition to the basic reproduction number, that drives the speed of spread.

We examined the publicly available materials and collected the records of COVID-19 transmission events in 2 neighboring large cities, Hong Kong⁴ and Shenzhen,⁵ in south China from January 10 to February 15, 2020, and we extracted the serial interval data. We identified 48 transmission events (21 in Hong Kong and 27 in Shenzhen), among which 40 events contained the gender information of the primary cases. The last onset date of the primary cases among all collected transmission events was February 2, 2020. The data were collected via public domain; thus, neither ethical approval nor individual consent was applicable. All data used in this work were publicly available from press releases from the Centre for Health Protection (CHP) of Hong Kong⁴ and the COVID-19 outbreak situation reports of the Shenzhen Municipal Health Commission,⁵ and the key R code is provided as a supplementary file online.

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7113032/>

DOI: 10.1017/ice.2020.64

67. Zhao S, Gao D, Zhuang Z, et al. Estimating the serial interval of the novel coronavirus disease (COVID-19): A statistical analysis using the public data in Hong Kong from January 16 to February 15, 2020. *medRxiv*. 2020:2020.02.21.20026559. DOI: 10.1101/2020.02.21.20026559

ABSTRACT: Backgrounds: The emerging virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused a large outbreak of novel coronavirus disease (COVID-19) in Wuhan, China since December 2019. Based on the publicly available surveillance data, we identified 21 transmission chains in Hong Kong and estimated the serial interval (SI) of COVID-19. Methods: Index cases were identified

and reported after symptoms onset, and contact tracing was conducted to collect the data of the associated secondary cases. An interval censored likelihood framework is adopted to fit a Gamma distribution function to govern the SI of COVID-19. Findings: Assuming a Gamma distributed model, we estimated the mean of SI at 4.4 days (95%CI: 2.9~6.7) and SD of SI at 3.0 days (95%CI: 1.8~5.8) by using the information of all 21 transmission chains in Hong Kong. Conclusion: The SI of COVID-19 may be shorter than the preliminary estimates in previous works. Given the likelihood that SI could be shorter than the incubation period, pre-symptomatic transmission may occur, and extra efforts on timely contact tracing and quarantine are recommended in combating the COVID-19 outbreak.
URL: <http://medrxiv.org/content/early/2020/02/25/2020.02.21.20026559.abstract>
DOI: 10.1101/2020.02.21.20026559

68. Zheng KI, Wang XB, Jin XH, et al. A Case Series of Recurrent Viral RNA Positivity in Recovered COVID-19 Chinese Patients. J Gen Intern Med. 2020. DOI: 10.1007/s11606-020-05822-1

Introduction: The outbreak of coronavirus disease 2019 (COVID-19) has been recently declared a pandemic by the World Health Organization.¹ Cases of positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) results in patients recovered from coronavirus disease 2019 (COVID-19) have been recently reported.² However, little is currently known about the prevalence of recurrent positive RT-PCR test results in these patients.

Methods: We examined twenty patients successfully treated for COVID-19 who had a 2-week post-discharge follow-up period who were admitted to the First Affiliated Hospital of Wenzhou Medical University and Wenzhou Central Hospital in Wenzhou, China, between January 25, 2020, and February 26, 2020. Of note, Wenzhou City was the second epicenter of the SARS-CoV-2 outbreak and had the second largest number of cases reported.³

Discharge criteria were as follows: (1) > 3 days of normal body temperature, (2) resolved respiratory symptoms, (3) substantially improved acute exudative lesions on chest computed tomography (CT), and (4) negative RT-PCR test results for both two consecutive salivary tests (with at least 1 day between tests) and one fecal nucleic acid (RNA) test.⁴ In all these patients, treatment included nebulized α -interferon, as recommended by the Chinese COVID-19 Management Guidance,⁵ until the aforementioned criteria for hospital discharge were met. Discharged patients were asked to follow strict protocols for self-isolation at designated hotels and away from family or relatives for 2 weeks. This study was approved by our local IRB, waiving informed consent for de-identified data.

Results: At baseline, all SARS-CoV-2 infection–confirmed patients (14 men, 6 women) with age ranging from 23 to 57 years had fever, while 9 also had cough. Their white blood cell (WBC) and lymphocyte counts, expressed as mean \pm SD, were $5.02 \pm 1.47 \times 10^9/L$ and $1.31 \pm 0.49 \times 10^9/L$, respectively. Their chest CT scans showed ground-glass opacities and consolidation that affected varying numbers of lobes with or without bilateral pulmonary involvement.

Seven days after hospital discharge, 3 patients who initially tested negative at discharge developed positive RT-PCR test results. One tested positive by fecal RNA, while two tested positive by both salivary and fecal RNA tests at 1 week of follow-up. Interestingly, all 20 patients returning for the week 2 follow-up tested negative for SARS-CoV-2, irrespective of sampling route. All three cases had improved with no increase in their temperature, and improvement in WBC and lymphocyte counts, as well as their CT scans. Compared with 17 patients with negative RT-PCR results at week 1 follow-up, there were no significant differences in WBC (6.0 vs. 4.9, $p = 0.38$) or lymphocyte counts (1.9 vs. 1.6, $p = 0.25$).

URL: <https://www.ncbi.nlm.nih.gov/pubmed/32314129>

DOI: 10.1007/s11606-020-05822-1

69. Zheng S, Fan J, Yu F, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. BMJ. 2020;369:m1443-m. DOI: 10.1136/bmj.m1443

ABSTRACT: Objective To evaluate viral loads at different stages of disease progression in patients infected with the 2019 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during the first four months of the epidemic in Zhejiang province, China. Design Retrospective cohort study. Setting A designated hospital for patients with covid-19 in Zhejiang province, China. Participants 96 consecutively admitted patients with laboratory confirmed SARS-CoV-2 infection: 22 with mild disease and 74 with severe disease. Data were collected from 19 January 2020 to 20 March 2020. Main outcome measures Ribonucleic acid (RNA) viral load measured in respiratory, stool, serum, and urine samples. Cycle threshold values, a measure of nucleic acid concentration, were plotted onto the standard curve constructed on the basis of the standard product. Epidemiological, clinical, and laboratory characteristics and treatment and outcomes data were obtained through data collection forms from electronic medical records, and the relation between clinical data and disease severity was analysed. Results 3497 respiratory, stool, serum, and urine samples were collected from patients after admission and evaluated for SARS-CoV-2 RNA viral load. Infection was confirmed in all patients by testing sputum and saliva samples. RNA was detected in the stool of 55 (59%) patients and in the serum of 39 (41%) patients. The urine sample from one patient was positive for SARS-CoV-2. The median duration of virus in stool (22 days, interquartile range 17-31 days) was significantly longer than in respiratory (18 days, 13-29 days; P=0.02) and serum samples (16 days, 11-21 days; P<0.001). The median duration of virus in the respiratory samples of patients with severe disease (21 days, 14-30 days) was significantly longer than in patients with mild disease (14 days, 10-21 days; P=0.04). In the mild group, the viral loads peaked in respiratory samples in the second week from disease onset, whereas viral load continued to be high during the third week in the severe group. Virus duration was longer in patients older than 60 years and in male patients. Conclusion The duration of SARS-CoV-2 is significantly longer in stool samples than in respiratory and serum samples, highlighting the need to strengthen the management of stool samples in the prevention and control of the epidemic, and the virus persists longer with higher load and peaks later in the respiratory tissue of patients with severe disease.

URL: <http://www.bmj.com/lookup/doi/10.1136/bmj.m1443>

DOI: 10.1136/bmj.m1443

70. Zhou B, She J, Wang Y, et al. The duration of viral shedding of discharged patients with severe COVID-19. *Clinical Infectious Diseases*. 2020. DOI: 10.1093/cid/ciaa451

ABSTRACT: The 2019 coronavirus disease (COVID-19) has drawn global intensive attention¹⁻³. Most of studies paid attention to epidemiological, clinical, and radiological features of inpatients with COVID-19¹⁻³. However, little studies have focused on clinical characteristics of discharged patients with severe COVID-19, especially the duration of viral shedding.

URL: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa451/5821307>

DOI: 10.1093/cid/ciaa451

71. Zhou F, Yu T, du r, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*. 2020. DOI: [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)

ABSTRACT: Background Since December, 2019, Wuhan, China, has experienced an outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Epidemiological and clinical characteristics of patients with COVID-19 have been reported but risk factors for mortality and a detailed clinical course of illness, including viral shedding, have not been well described. Methods In this retrospective, multicentre cohort study, we included all adult inpatients (≥18 years old) with laboratory-confirmed COVID-19 from Jinyintan Hospital and Wuhan Pulmonary Hospital (Wuhan, China) who had been discharged or had died by Jan 31, 2020.

Demographic, clinical, treatment, and laboratory data, including serial samples for viral RNA detection, were extracted from electronic medical records and compared between survivors and non-survivors. We

used univariable and multivariable logistic regression methods to explore the risk factors associated with in-hospital death. Findings 191 patients (135 from Jinyintan Hospital and 56 from Wuhan Pulmonary Hospital) were included in this study, of whom 137 were discharged and 54 died in hospital. 91 (48%) patients had a comorbidity, with hypertension being the most common (58 [30%] patients), followed by diabetes (36 [19%] patients) and coronary heart disease (15 [8%] patients). Multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1.10, 95% CI 1.03–1.17, per year increase; $p=0.0043$), higher Sequential Organ Failure Assessment (SOFA) score (5.65, 2.61–12.23; $p<0.0001$), and d-dimer greater than 1 $\mu\text{g/L}$ (18.42, 2.64–128.55; $p=0.0033$) on admission. Median duration of viral shedding was 20.0 days (IQR 17.0–24.0) in survivors, but SARS-CoV-2 was detectable until death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days. Interpretation The potential risk factors of older age, high SOFA score, and d-dimer greater than 1 $\mu\text{g/L}$ could help clinicians to identify patients with poor prognosis at an early stage. Prolonged viral shedding provides the rationale for a strategy of isolation of infected patients and optimal antiviral interventions in the future.

URL: <https://www.thelancet.com/pb-assets/Lancet/pdfs/S014067362305663.pdf>

DOI: [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)

72. Zhu L, Gong N, Liu B, et al. Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China. European Urology. 2020.

DOI: <https://doi.org/10.1016/j.eururo.2020.03.039>

ABSTRACT: Background Previous studies on coronavirus disease 2019 (COVID-19) have focused on populations with normal immunity, but lack data on immunocompromised populations. Objective To evaluate the clinical features and outcomes of COVID-19 pneumonia in kidney transplant recipients. Design, setting, and participants A total of 10 renal transplant recipients with laboratory-confirmed COVID-19 pneumonia were enrolled in this retrospective study. In addition, 10 of their family members diagnosed with COVID-19 pneumonia were included in the control group. Intervention Immunosuppressant reduction and low-dose methylprednisolone therapy. Outcome measurements and statistical analysis The clinical outcomes (the severity of pneumonia, recovery rate, time of virus shedding, and length of illness) were compared with the control group by statistical analysis. Results and limitations The clinical symptomatic, laboratory, and radiological characteristics of COVID-19 pneumonia in the renal transplant recipients were similar to those of severe COVID-19 pneumonia in the general population. The severity of COVID-19 pneumonia was greater in the transplant recipients than in the control group (five severe/three critical cases vs one severe case). Five patients developed transient renal allograft damage. After a longer time of virus shedding (28.4 ± 9.3 vs 12.2 ± 4.6 d in the control group) and a longer course of illness (35.3 ± 8.3 vs 18.8 ± 10.5 d in the control group), nine of the 10 transplant patients recovered successfully after treatment. One patient developed acute renal graft failure and died of progressive respiratory failure. Conclusions Kidney transplant recipients had more severe COVID-19 pneumonia than the general population, but most of them recovered after a prolonged clinical course and virus shedding. Findings from this small group of cases may have important implications for the treatment of COVID-19 pneumonia in immunosuppressed populations. Patient summary Immunosuppressed transplant recipients with coronavirus disease 2019 infection had more severe pneumonia, but most of them still achieved a good prognosis after appropriate treatment.

URL: <http://www.sciencedirect.com/science/article/pii/S0302283820302141>

DOI: <https://doi.org/10.1016/j.eururo.2020.03.039>

73. Zhu Y, Chen YQ. On a Statistical Transmission Model in Analysis of the Early Phase of COVID-19 Outbreak. Statistics in Biosciences. 2020:1-17. DOI: 10.1007/s12561-020-09277-0

ABSTRACT: Since December 2019, a disease caused by a novel strain of coronavirus (COVID-19) had infected many people and the cumulative confirmed cases have reached almost 180,000 as of 17, March

2020. The COVID-19 outbreak was believed to have emerged from a seafood market in Wuhan, a metropolis city of more than 11 million population in Hubei province, China. We introduced a statistical disease transmission model using case symptom onset data to estimate the transmissibility of the early-phase outbreak in China, and provided sensitivity analyses with various assumptions of disease natural history of the COVID-19. We fitted the transmission model to several publicly available sources of the outbreak data until 11, February 2020, and estimated lock down intervention efficacy of Wuhan city. The estimated R_0 was between 2.7 and 4.2 from plausible distribution assumptions of the incubation period and relative infectivity over the infectious period. 95% confidence interval of R_0 were also reported. Potential issues such as data quality concerns and comparison of different modelling approaches were discussed.

URL: <http://link.springer.com/10.1007/s12561-020-09277-0>

DOI: 10.1007/s12561-020-09277-0

74. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. The New England journal of medicine. 2020;10.1056/NEJMc2001737. DOI: 10.1056/NEJMc2001737

To the Editor: The 2019 novel coronavirus (SARS-CoV-2) epidemic, which was first reported in December 2019 in Wuhan, China, and has been declared a public health emergency of international concern by the World Health Organization, may progress to a pandemic associated with substantial morbidity and mortality. SARS-CoV-2 is genetically related to SARS-CoV, which caused a global epidemic with 8096 confirmed cases in more than 25 countries in 2002–2003.¹ The epidemic of SARS-CoV was successfully contained through public health interventions, including case detection and isolation. Transmission of SARS-CoV occurred mainly after days of illness² and was associated with modest viral loads in the respiratory tract early in the illness, with viral loads peaking approximately 10 days after symptom onset.³ We monitored SARS-CoV-2 viral loads in upper respiratory specimens obtained from 18 patients (9 men and 9 women; median age, 59 years; range, 26 to 76) in Zhuhai, Guangdong, China, including 4 patients with secondary infections (1 of whom never had symptoms) within two family clusters (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). The patient who never had symptoms was a close contact of a patient with a known case and was therefore monitored. A total of 72 nasal swabs (sampled from the mid-turbinate and nasopharynx) (Figure 1A) and 72 throat swabs (Figure 1B) were analyzed, with 1 to 9 sequential samples obtained from each patient. Polyester flock swabs were used for all the patients.

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7121626/>

DOI: 10.1056/NEJMc2001737

SEARCH STRATEGIES

CINAHL

Date Run: April 25, 2020 11:05

S14	S7 AND S11	Limiters - English Language	69
S13	S7 AND S11		72
S12	S7 AND S11		72
S11	S8 OR S9 OR S10		56,764
S10	TI ((transmi* or infecti* or communicab* or contagious* or shedding) N2 (period or duration or time or length or days)) OR AB ((transmi* or infecti* or communicab* or contagious* or shedding) N2 (period or duration or time or length or days))		5,500

- S9 TI (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral RNA" or "RNA shedding" or "discharge criteria") OR AB (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral RNA" or "RNA shedding" or "discharge criteria")
7,687
- S8 (MM "Disease Transmission+") OR (MM "Viral Load") OR (MM "Polymerase Chain Reaction+") OR (MH "Patient Discharge+") 45,458
- S7 S1 OR S2 OR S3 OR S4 OR S5 Limiters - Published Date: 20191201-20201231 1,416
- S6 S1 OR S2 OR S3 OR S4 OR S5 4,591
- S5 (TI (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) OR (AB (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) 537
- S4 ((TI "2019-nCov" OR "COVID-19" OR covid 19 OR "SARS-CoV-2" OR covid19) OR (AB "2019-nCov" OR "COVID-19" OR covid 19 OR "SARS-CoV-2" OR covid19)) OR ((TI (coronavirus* OR corona-virus*) AND (wuhan OR shanghai OR Beijing OR Italy OR south-korea OR china OR chinese)) OR (AB (coronavirus* OR corona-virus*) AND (wuhan OR shanghai OR Beijing OR Italy OR south-korea OR china OR chinese)))
1,386
- S3 ((TI "COVID-19" OR "2019-nCov" OR "SARS-CoV*" OR 2019-nCov OR 2019 coronavirus* OR 2019 corona virus* OR covid19) OR (AB "COVID-19" OR "2019-nCov" OR "SARS-CoV*" OR 2019-nCov OR 2019 coronavirus* OR 2019 corona virus* OR covid19)) OR MH "Coronavirus+" OR MH "Coronavirus Infections+" OR (TI ((novel or new or nouveau or "2019") N2 (coronavirus* or corona virus* or pandemi*)) OR AB ((novel or new or nouveau or "2019") N2 (coronavirus* or corona virus* or pandemi*))) 4,305
- S2 (TI coronavirus* OR corona-virus OR covid19 OR "covid 19" or SARS-Cov*) OR (((TI (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) OR (AB (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) AND ((MH "China+" OR (TI china OR Chinese) OR (AB china OR chinese) OR MH "Italy" OR (TI Italy OR AB Italy) OR MH "Korea" OR MH "South Korea" OR (TI korea OR AB korea)) OR ((MH "Pneumonia+" OR (TI pneumonia OR AB pneumonia)) AND (TI Wuhan OR AB Wuhan))) 1,120
- S1 ((MH "Coronavirus+" OR MH "Coronavirus Infections+") OR (TI coronavirus* OR corona-virus) OR (AB coronavirus* OR corona-virus)) AND ((TI wuhan or beijing or shanghai or Italy or South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*) OR (AB wuhan or beijing or shanghai or Italy or South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*)) 1,273

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Date Run: April 25, 2020 11:15

- 1 (exp coronavirinae/ or coronavirus*.mp. or corona-virus.mp.) and (wuhan or beijing or shanghai or Italy or South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*).mp. (7845)
- 2 (coronavirus* or Corona-virus or covid19 or "covid 19" or SARS-Cov*).ti. or (((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus*)).mp. and (exp china/ or china.mp. or Chinese.mp. or exp Italy/ or Italy.mp. or exp south korea/ or south korea.mp.)) or ((pneumonia.mp. or exp pneumonia/) and Wuhan.mp.) (13540)
- 3 ("COVID-19" or "2019-nCoV" or "SARS-CoV*" or 2019-nCov or 2019 coronavirus* or 2019 corona virus* or covid19).mp. or exp coronavirus Infection/ or ((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus* or Pandemi*2)).mp. (19682)
- 4 ("2019-nCov" or "COVID-19" or covid 19 or "SARS-CoV-2" or covid19).mp. or ((coronavirus* or corona-virus*) and (wuhan or shanghai or Beijing or Italy or south-korea or china or chinese)).ti,ot,ab. (6840)
- 5 ((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus*)).mp. (3634)
- 6 1 or 2 or 3 or 4 or 5 (24022)

7 6 and 20191201:20201231.(dc). (7042)
 8 exp *disease transmission/ or *virus shedding/ or *viral load/ or exp *polymerase chain reaction/ or
 hospital discharge/ (232222)
 9 (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral
 RNA" or "RNA shedding" or "discharge criteria").ti,ab. (94219)
 10 ((transmi* or infecti* or communicab* or contagious* or shedding) adj2 (period or duration or time or
 length or days)).ti,ab. (30808)
 11 8 or 9 or 10 (344436)
 12 7 and 11 (442)
 13 limit 12 to english language (421)
 14 limit 13 to exclude medline journals (50)

Ovid MEDLINE(R) ALL <1946 to April 24, 2020>

Date Run: April 25, 2020 10:30

1 (exp coronavirus/ or coronavirus*.mp. or corona-virus.mp.) and (wuhan or beijing or shanghai or Italy or
 South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*).mp. (7252)
 2 (coronavirus* or Corona-virus or covid19 or "covid 19" or SARS-Cov*).ti. or (((novel or new or nouveau or
 "2019") adj2 (coronavirus* or corona virus*)).mp. and (exp china/ or china.mp. or Chinese.mp. or exp Italy/ or
 Italy.mp. or exp Republic of korea/ or south korea.mp.)) or ((pneumonia.mp. or exp pneumonia/) and
 Wuhan.mp.) (13993)
 3 ("COVID-19" or "2019-nCoV" or "SARS-CoV*" or 2019-nCov or 2019 coronavirus* or 2019 corona virus* or
 covid19).mp. or exp Coronavirus Infections/ or ((novel or new or nouveau or "2019") adj2 (coronavirus* or
 corona virus* or Pandemi*2)).mp. (18912)
 4 ("2019-nCov" or "COVID-19" or covid 19 or "SARS-CoV-2" or covid19).mp. or ((coronavirus* or corona-
 virus*) and (wuhan or shanghai or Beijing or Italy or south-korea or china or chinese)).ti,ot,ab. (7780)
 5 ((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus*)).mp. (3164)
 6 1 or 2 or 3 or 4 or 5 (22075)
 7 6 and 20191201:20201231.(dt). (7773)
 8 exp *Disease Transmission, Infectious/ or *Virus Shedding/ or *Viral Load/ or exp *Polymerase Chain
 Reaction/ or Patient Discharge/ (127703)
 9 (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral
 RNA" or "RNA shedding" or "discharge criteria").ti,ab. (73862)
 10 ((transmi* or infecti* or communicab* or contagious* or shedding) adj2 (period or duration or time or
 length or days)).ti,ab. (24453)
 11 8 or 9 or 10 (216355)
 12 7 and 11 (321)
 13 limit 12 to english language (298)

PubMed

Date Run: April 25, 2020

((((((((coronavirus[MeSH Terms]) OR ((coronavirus* OR corona-virus* or corona virus*))) OR (((coronavirus* OR
 corona-virus*) and (wuhan OR beijing OR shanghai OR italy OR italian OR south-korea* OR south korea* OR
 china OR chinese OR 2019-nCoV OR nCoV OR COVID-19 OR Covid19 OR SARS-CoV*)))))) OR
 (((coronavirus*[Title] OR corona-virus*[Title] OR covid19[Title] OR covid-19[Title] OR "covid19"[Title] OR "covid-
 19"[Title] OR SARS-Cov*[Title]))) OR (((((novel OR new OR nouveau OR "2019") and (coronavirus* OR corona-
 virus*))) AND (((((china[MeSH Terms]) OR (china OR chinese)) OR italy[MeSH Terms]) OR (italy OR italian)) OR
 korea, republic of[MeSH Terms]) OR south korea*)) OR (((pneumonias[MeSH Terms]) OR penumonia*)) AND
 wuhan)))))) OR (((("COVID-19" OR "2019-nCoV" OR "SARS-CoV*" OR 2019-nCov OR 2019 coronavirus* OR 2019
 corona virus* OR covid19)) OR coronavirus infections[MeSH Terms]) OR ((novel OR new OR nouveau OR 2019

AND (coronavirus* OR "corona virus*" OR Pandemi*)) OR (((("2019-nCov" OR "COVID-19" OR covid 19 OR "SARS-CoV-2" OR covid19))) OR (((coronavirus*[Title/Abstract] OR corona-virus*[Title/Abstract])) AND (wuhan[Title/Abstract] OR shanghai[Title/Abstract] OR Beijing[Title/Abstract] OR Italy[Title/Abstract] OR south-korea[Title/Abstract] OR china[Title/Abstract] OR chinese[Title/Abstract]))) OR (((novel OR new OR nouveau OR "2019") and (coronavirus* OR corona virus*)))) AND (((((disease transmission, communicable[MeSH Terms]) OR disease transmission, infectious[MeSH Terms]) OR (((transmissibility[tiab] OR infectiousness[tiab] OR infectivity[tiab] OR communicability[tiab] OR "viral shedding"[tiab] OR "viral load"[tiab] OR "viral RNA"[tiab] OR "RNA shedding"[tiab] OR "discharge criteria"[tiab])))))) Filters: Publication date from 2020/01/01 (Results 325)

Search terms for other resources used in various combinations:

- Viral RNA, RT-PCR, viral shedding, viral load, infectivity, communicability, transmissibility