Review Article

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A Comprehensive Review of Coronavirus Disease 2019: Epidemiology, Transmission, Risk Factors, and International Responses

Han Li[1], Seung Won Burm[2], Sung Hwi Hong[2,3], Ramy Abou Ghayda[3,4], Andreas Kronbichler[5], Lee Smith[6], Ai Koyanagi[7,8], Louis Jacob[7,9], Keum Hwa Lee[10], and Jae Il Shin[10]

[1]University of Florida College of Medicine, Gainesville, FL, USA;
[2]Yonsei University College of Medicine, Seoul, Korea;
[3]Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, MA, USA;
[4]Urology Institute, University Hospitals System, Case Western Reserve University School of Medicine, Cleveland, OH, USA;
[5]Department of Internal Medicine IV (Nephrology and Hypertension), Medical University Innsbruck, Innsbruck, Austria;
[6]The Cambridge Centre for Sport and Exercise Science, Anglia Ruskin University, Cambridge, UK;
[7]Research and Development Unit, Parc Sanitari Sant Joan de Déu, CIBERSAM, Barcelona, Spain;
[8]ICREA, Pg. Lluis Companys 23, Barcelona, Spain;
[9]Faculty of Medicine, University of Versailles Saint-Quentin-en-Yvelines, Versailles, France;
[10]Department of Pediatrics, Yonsei University College of Medicine, Seoul, Korea.

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused a worldwide pandemic. The first reports of patients with COVID-19 were provided to World Health Organization on December 21, 2019 and were presumably associated with seafood markets in Wuhan, China. As of October 25, 2020, more than 42 million cases have been confirmed worldwide, with more than 1.1 million deaths. Asymptomatic transmission contributes significantly to transmission, and clinical features are non-specific to the disease. Thus, the diagnosis of COVID-19 requires specific viral RNA testing. The disease demonstrates extensive human-to-human transmissibility and has infected healthcare workers at high rates. Clinical awareness of the epidemiology and the risk factors for nosocomial transmission of COVID-19 is essential to preventing infection. Moreover, effective control measures should be further identified by comprehensive evaluation of hospital and community responses. In this review, we provide a comprehensive update on the epidemiology, presentation, transmission, risk factors, and public health measures associated with COVID-19. We also review past insights from previous coronavirus epidemics [i.e., severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)] to suggest measures to reduce transmission.

Key Words: Infectious disease transmission, SARS virus, Middle East respiratory syndrome coronavirus, Severe acute respiratory syndrome coronavirus 2, Coronavirus infections

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Corresponding author: Jae Il Shin, MD, PhD, Department of Pediatrics, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Tel: 82-2-2228-2050, Fax: 82-2-393-9118, E-mail: shinji@yuhs.ac

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INTRODUCTION

At the beginning of 2020, a new coronavirus detected in Wuhan, China gave rise to a massive global health concern.[1] The first report of a cluster of patients with pneumonia from an unknown cause was provided to the World Health Organization (WHO) China Country Office on December 31, 2019.[2] Subsequently, multiple cases of this pneumonia grew rapidly throughout Wuhan and were primarily linked with exposures in seafood wholesale markets.[1,3] The causative agent was isolated on

January 7, and its whole genome sequence was analyzed.[4] On February 11, 2020, the WHO named the novel coronavirus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its accompanying disease as coronavirus disease 2019 (COVID-19).[5] Despite efforts to contain the virus, infectious outbreaks spread globally from China.[5] WHO designated the outbreak, which had at the time reached multiple continents outside Asia, as a pandemic on March 11 in an effort to help coordinate international efforts to mitigate spread of the contagion.[6]

As of October 25, 2020, there have been more than 42 million confirmed cases and more than 1.1 million deaths.[7] Although the novel coronavirus is being investigated worldwide, many questions lay unanswered. Here, we review the epidemiology, risk factors, and transmission of SARS-CoV-2. We seek to outlines measures for individuals, organizations, and nations to minimize the risk of household, nosocomial, and local community transmission. We also investigated preventive methods through which to inhibit further transmission via comparison with the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012 and the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002.[8]

EPIDEMIOLOGY

Reproduction number (R0)

Calculating the mean doubling time of a disease using reproduction numbers (R0) allows researchers to understand the speed and extent of a disease's transmission. Current R0 estimates for COVID-19 are not at consensus: the exact numbers of infected people cannot be appropriately surveyed due to asymptomatic spread, increased likelihood of detection of severe cases, and low availability of PCR test kits.[9] One research team at Boston Children's Hospital estimated R0 to be between 2.0 and 3.3 by applying an Incidence Decay and Exponential Adjustment (IDEA) model.[10] By fitting a deterministic Susceptible-Exposed-Infected-Recovered (SEIR) epidemiological model, a team at Lancaster University suggested R0 to be approximately 3.1.[11] They assumed Poisson-distributed daily increments using daily reported data in Chinese cities and in other countries. Another group of researchers at York University also used a deterministic SEIR compartmental model, but proposed an R0 value of 6.47.[12] A simplified version of the Bats-Hosts-Reservoir-People transmission network model, the Reservoir-People transmission network model, was created by a team at Xiamen University and calculated R0 values for each stage of transmission.[13] Under this model, R0 values for reservoir-to-person and person-to-person were assessed as 2.3 and 3.58, respectively. Epidemiologists in London estimated that 1.5–3.5 people were infected by each case in the early stage of the outbreak.[14] Overall, low numbers of reported cases and a lack of detection methods at the early stage of this crisis gave high uncertainty to modeling.[9] Further studies with larger sample sizes are needed to approximate the true value.

Incubation period

The incubation period of COVID-19 is widely believed to be 1 to 2 weeks.[15] A study published on March 26 reported a 5.2-day [95% confidence interval (CI), 4.1–7.0] incubation period.[16] Another study reached a similar estimate of 5.1 days (95% CI, 4.5–5.8) and reported that 97.5% of symptomatic cases developed symptoms within 11.5 days (95% CI, 8.2–15.6).[17] The WHO reported that patients who contract COVID-19 mostly develop signs and symptoms after 5–6 days from infection.[18] Accordingly, the WHO recommends travelers returning from affected areas to self-monitor for symptoms for 14 days and to follow the national protocols of receiving countries.[19] However, some outliers exist. One Japanese woman tested positive on February 6 after previously testing negative, and case number 25 in Korea was confirmed positive again on February 28, six days after discharge.[20] However, it is currently unclear whether these cases suggest a dormancy period longer than 14 days, the possibility of reinfection, or sustained viral load following functional recovery. Further research on the incubation period or recurrence of the virus is needed to eliminate hidden transmission.

Non-specific clinical features

Since early clinical features are not disease-specific, early diagnosis of the disease requires clinical awareness about the SARS-CoV-2 infection.[21] According to two studies aggregating 100596 cases, 80–81% of symptomatic patients show mild symptoms, and 13.8% show severe disease.[18,22] Reported symptoms include dry cough, fever, malaise, nasal congestion, fatigue, shortness of breath, sputum production, headache, sore throat, myalgia or arthralgia, diarrhea, dyspnea, hemoptysis, anosmia, ageusia, headache, and nausea or vomiting.[23-25] Anosmia and ageusia specifically occur in 47–88% of mild to moderate COVID-19 cases and often co-occur.[26,27] Females are more likely to have anosmia and ageusia with COVID-19. The limited data available suggest that such dysfunction is self-resolving within 14 days after disease recovery, with over half recovering from anosmia in the first 8 days.[27] In early cases reported in Wuhan, severe acute respiratory infection symptoms were shown, and some patients rapidly developed acute respiratory distress syndrome (ARDS) and other serious complications.[25]

Comparison to SARS and MERS

SARS and COVID-19 share similar transmission routes, risk factors, and disease progression. The SARS epidemic reported 8098 cases with 774 deaths and was controlled within 8 months.[28] Twenty-six countries experienced infections, but most cases were concentrated in China, Taiwan, Hong Kong, Singapore, and Canada. SARS is only transmissible by symptomatic patients, with viral load peaking 6–11 days after onset of illness.[29]

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However, COVID-19 differs from SARS in three aspects: asymptomatic transmission, a well-connected initial outbreak site, and strain on public health resources. With SARS, the co-occurrence of symptoms with viral shedding allowed for a sensitive case definition and isolation of high-risk patients.[28] Household secondary attack rates for SARS were 6.2% in Singapore and 10% in Toronto, compared to a secondary attack rate of 30% for COVID-19 by some higher estimates.[30-32] SARS also has both a longer time to peak viral load from onset and a shorter incubation period than COVID-19, explaining the decreased likelihood of asymptomatic transmission in SARS.[33,34] The R0 of SARS general transmission ranges from 0.58−1.17, partially due to isolation control measures.[35] Three out of five super spreading events in Singapore were possible largely because of atypical case presentations. Two additional super spreading events were propagated by inadequate plumbing or ventilation, instead of the failure to detect infected cases.[35-38] In contrast, asymptomatic transmission of COVID-19 leads to increased community and household transmission. In February, Liu, et al.[39] documented eight COVID-19 super spreading events in China through restaurants. Difficulty tracing asymptomatic carriers, combined with high international traffic through Wuhan, allowed community transmission and made tracing patients more difficult. The resulting demand on hospital resources impaired quarantining efforts on hospital staff, and the existence of asymptomatic carriers lessened the effectiveness of patient isolation.

The 2012 MERS epidemic infected 2553 people as of March 2020 with 876 associated deaths.[40] MERS also shares a similar disease course, transmission routes, and risk factors with SARS and COVID-19.[40] Like COVID-19, MERS can be transmitted by asymptomatic carriers.[41] However, the virus requires prolonged exposure before transmission and is primarily spread sporadically by animal-to-human transmission, decreasing the likelihood of a large-scale outbreak.[42] For example, the peak viral load occurs 7 days after onset in cases without needing supplemental oxygen and 14−21 days in cases delivered oxygen, in contrast to the 3-day peak viral load in COVID-19.[34] However, the incubation of MERS, 4.5−7.8 days, is more similar to SARS than COVID-19. The estimated secondary attack rate for MERS ranges from 0.42−15.8%.[43] In one study by Drosten, et al.,[44] only 14 out of 280 secondary household contacts among 26 index patients tested positive by antibody tests or reverse transcription polymerase chain reaction (RT-PCR). Nosocomial transmission accounts for a significant portion of human-to-human transmission: 18.6% of MERS cases involved healthcare workers (HCW).[45] While the R0 for general transmission of MERS ranges from <1 to 3,[11] but the R0 specific for nosocomial transmission is estimated to be between 1.9 and 4.04.[46] Table 1 summarizes the comparisons of SARS, MERS, and COVID-19.

PERSON-TO-PERSON TRANSMISSION

Nosocomial transmission of SARS, MERS, and COVID-19

The previous 2003 SARS outbreak led to over 966 infections among health care staff.[47] A low minimum distance between beds, previously performing resuscitation in the ward, low availability of washing facilities for staff, staff working while sick, and using ventilation or oxygen therapy have been shown to be associated with SARS nosocomial transmission.[48] Effective strategies against nosocomial transmission were to isolate known carriers, ban hospital visitors, and close infected wards.[49] Patients with fever or respiratory distress in sites of the outbreak were isolated until SARS was ruled out.[28] If the index patient could be identified before the estimated second incubation period, HCWs in contact with the patient were quarantined. If the index patient could not be identified, entire hospitals were closed.[49] Some intensive care units (ICUs) were entirely converted to negative pressure airflow, with hot, warm, and cold zones that necessitated full airborne precautions, droplet precautions, and no personal protective equipment (PPE), respectively.[50] In Toronto, the transmission was primarily nosocomial.[51] Enactment of hospital control, including droplet PPE and negative airflow isolation, 20 days after the first SARS death reduced the number of cases to 0 for 20 consecutive days. However, subsequent relaxation of hospital control led to a resurgence of infections.[51]

With MERS, a sensitive case definition was critical to identify sources of and to eliminate transmission.[46] In Thailand, nosocomial transmission was avoided entirely from three index

Table 1. Characteristics of SARS, MERS, and COVID-19 Transmission

	SARS	MERS	COVID-19
Asymptomatic transmission	N[33,34]	Y[41]	Y[22,23]
Peak viral load after onset	6–11 days[29]	7 days (mild) 14–21 days[34]	3 days[34]
Secondary attack rate	6.2–10%[30-32]	0.42–15.8%[43]	Up to 30%[30-32]
Primary mode of transmission	Human-to-human	Animal-to-human[42]	Human-to-human
R0 (general transmission)	0.58–1.17[35]	<1–3[11,46]	1.5–6.47[12,14]
Incubation period	3.6–4.4 days[33,34]	4.5–7.8 days[43]	5.1–11.5 days[17]

COVID-19, coronavirus disease 2019; SARS, severe acute respiratory syndrome; MERS, Middle East respiratory syndrome; R0, reproduction number.
Prominent characteristics of SARS, MERS, and COVID-19 are aggregated. Numerical values for secondary attack rate, R0, etc. were retrieved as ranges of the lowest and highest estimations described in each respective reference.

cases by directing all patients with acute respiratory illness traveling from countries with MERS outbreaks to designated entrances and airborne isolation rooms until MERS could be ruled out.[52] HCWs were required to adopt droplet precautions when working with suspected patients, as per the Centers for Disease Control and Prevention guidelines. In the United States, HCWs exposed to suspected cases were required to undergo home quarantine for 14 days and to test negative before returning to work.[53] Compared to COVID-19, MERS is a more fatal condition that may also spread before confirmatory diagnosis,[41] and its nosocomial transmission was controlled by similar early identification, isolation, and PPE guidelines as with SARS.

By February 11, 2020, 1716 health staff members in China were confirmed SARS-CoV-2 positive.[54] In a cohort of 138 patients, Wang, et al.[55] estimated that 41% were infected by nosocomial transmission. WHO recommends droplet and contact precautions for patients suspected of COVID-19 and airborne precautions while performing aerosol-generating procedures (intubation, cardiac resuscitation, high-flow nasal cannula, bronchoscopy), though some recommend airborne precautions in all cases.[56] Insights from the SARS outbreak have been used to create a number of recommendations for controlling COVID-19, which are summarized in Table 2. In short, it is recommended to place symptomatic hospital staff under self-quarantine, equip patients with N95 masks, and inform receiving hospitals of suspected infectious arrivals beforehand.[54,57] Patients with cough, dyspnea, and fever should be isolated in daily-disinfected, single negative pressure rooms until testing negative for COVID-19. Airborne precautions, including N95 respirator masks, gown, double-layered gloves, coverall, and protective shoes, have also been recommended.[57] Patients with mild symptoms may be sent for home care, but with the stipulations that home isolation necessitates careful prior assessment and that patients who do not recover should immediately seek further treatment.[57]

Table 2. Effective Measures against Nosocomial Transmission of COVID-19 and SARS

COVID-19
• Rapid isolation of HCWs, patients, and wards suspected of contacting infection[56]
• Daily chlorine-containing disinfection[89]
• PPE consisting of N95 respirator, gown, double-layered gloves, coverall, shoe covers[46]
• Separation of patient and HCW entrances and exits[58]
• Limiting patients per room[58]
• Equipping patients with masks[46]
• Adopting oxygen administration techniques that minimize droplet spread[56]
• Adopting airborne precautions for aerosol-generating procedures[46,52]
SARS
• Rapid isolation of HCWs, patients, and wards suspected of contacting infection[26]
• Construction of SARS-specific hospitals[45]
• Banning hospital visitors[45]
• Spacing patient beds[44]
• Conversion of ICUs to negative-pressure environments, with hot zones, warm zones, and cold zones[46]

COVID-19, coronavirus disease 2019; HCW, healthcare worker; SARS, severe acute respiratory syndrome; PPE: personal protective equipment, ICU intensive care unit.
Measures against nosocomial transmission described to be effective are aggregated for SARS and COVID-19. Measures against MERS nosocomial transmission were similar to SARS in the articles evaluated and were not included to avoid redundancy.

An elevated risk of hospital transmission has been described subsequent to treating critically-ill patients.[50,58,59] For the critically ill, it is recommended to adopt airborne precautions. Additional critical care measures include equipping patients with masks during high flow nasal cannula treatments, using ventilators with filters and heat-moisture exchangers, and using masks during bronchoscopy.[59] When possible, rapid intubation techniques should be utilized, bag-mask ventilation should be avoided, and early planned intubations should be prioritized rather than emergency intubations.[50,60] For prolonged procedures, powered air-purifying respirators may be an alternative to N95 masks, but no trials have demonstrated improved or equivalent risk reduction, compared to the N95.[50] One group described an increased risk of transmission with pulmonary function tests and recommended, in addition to isolation and disinfection procedures, suspending tests for suspected COVID-19 cases and for patients without an immediate need.[61] Oxygen therapy can disperse particles in varying patterns depending on the devices used. Continuous positive airway pressure (CPAP) via an oronasal mask and non-invasive ventilation (NIV) via an air-cushioned helmet showed minimum room contamination among nasal cannula, oronasal mask, Venturi mask, non-rebreathing mask, CPAP via an oronasal mask, CPAP via nasal pillows, high flow nasal cannula, NIV via a full face mask, NIV via a helmet without tight air cushion, and NIV via a helmet with tight air cushion.[60]

Transmission by asymptomatic individuals

Asymptomatic and pre-symptomatic transmission of COVID-19 have been documented. Studies in January 2020 were among the first to show the possibility of asymptomatic transmission by demonstrating mild or asymptomatic cases in an estimated 80% of patients, as well as an asymptomatic infection of a child.[22,23] On March 6, Luo, et al.[62] traced three SARS-CoV-2 infections from patients who otherwise had no contact with Wuhan or animals to asymptomatic carrier sources. Asymptomatic transmission was also demonstrated by a Wuhan resident to five family members and by clusters of patients in Singapore.[63,64] Asymptomatic infection is consistent with the longer incubation period, shorter time to peak viral load, and shorter serial interval of COVID-19. Nishiura and colleagues estimated the serial interval by following 28 infector-infected pairs as 4.6 days (95% CI, 3.5–5.9), shorter than many incubation period estimates, suggesting transmission during subclinical infection.[65]

Pre-symptomatic and asymptomatic infections are expected to contribute significantly to COVID-19 transmission. On March 13, Nishiura and colleagues used data from 565 Japanese citizens to estimate the proportion of asymptomatic infections as 30.8%.[66] With greater access to antibody testing, a Stanford group in Santa Clara County recruited 3330 people used lateral flow immunoassays to estimate the population-weighted seroprevalence of antibodies to SARS-CoV-2 as 2.49% (95% CI, 1.80–3.17%) to 4.16% (95% CI, 2.58–5.70%).[67] Another group in a northern Iran province used a cohort of 528 people to estimate the population antibody seropositivity prevalence as 33% (95% CI, 28–39%). Of the sample, 65 subjects (18%) had no symptoms, but had antibodies to SARS-CoV-2.[68] Contact tracing of 100 patients revealed similar secondary attack rates between pre-symptomatic and symptomatic exposures.[69] Byambasuren, et al.[70] recently found in a meta-analysis of 663 positive cases that 17% were asymptomatic, with a 42% lower relative risk of asymptomatic transmission. It is estimated that up to 62% of transmissions occurs pre-symptomatically, with true asymptomatic transmission being uncommon.[71]

Severity of illness and transmission

Preliminary evidence from epidemiological and biological studies have suggested both increased and prolonged viral transmission associated with severe illness in COVID-19. Reports have identified an increased risk of contracting the disease for HCWs who care for or resuscitate critically ill people with COVID-19.[50,59] The median duration of viral shedding for severely ill patients was calculated as 31 days from illness onset by one study, higher than the estimations of median viral shedding duration (17 days) for the collective population.[72,73] In a cohort of 113 patients, severe illness, emergent treatments (corticosteroid therapy and mechanical ventilation), and delayed recovery were associated with longer viral shedding times.[72] A separate cohort of 32 ICU and non-ICU patients with COVID-19 demonstrated a viral shedding time about 7 days longer in the ICU group.[74] However, He, et al.[75] found no differences in either viral load or shedding time between 94 mild and severe patients. Given ambiguous findings relating severity to increased transmission, it is currently unclear whether the apparent increased infection rates from patients who are critically ill intrinsically result from elevated viral load or are generated from aerosol-generating emergent techniques.

RISK FACTORS

Demographics and comorbid conditions

The most well-documented demographic risk factor for infection and morbidity is old age. Jing, et al.[76] reported that older individuals (aged ≥60 years) are the most susceptible to household transmission of SARS-CoV-2. Out of 799 patients, Chen, et al.[77] described that patients who died were older on average than those who survived. Male sex, obesity, and smoking have also been shown to be associated with mortality, though it is difficult to quantify the relative risks thereof due to possible confounding and limited sample size.[78]

Novel comorbidities associated with poor COVID-19 outcomes are continuously being described. Among those discovered early, hypertension occurs most frequently with infection and has been validated across multiple studies as a risk factor for mortality.[79,80] Respiratory disease, cardiovascular disease, diabetes, kidney disease, and cancer have also been linked to increased risks of death.[79,80] In some studies, coagulopathies and inflammation appear to be linked to severe outcomes or death. In a cohort study of 201 patients, neutrophilia, higher lactate dehydrogenase, and D-dimer were associated with the development of ARDS and death.[81] The inflammatory biomarkers procalcitonin, interleukin-6, tumor necrosis factor alpha, and neutrophil to lymphocyte ratio are also thought to be risk factors for fatal outcomes.[82] In a meta-analysis of nine studies, Lippi, et al.[83] linked thrombocytopenia with COVID-19 severity and mortality. Kidney disease and markers of abnormal kidney function have also been shown to be associated with death in COVID-19.[84] Although further work is necessary to confirm current prognostic markers for vulnerability to COVID-19, it seems likely that poor cardiovascular and respiratory function predispose people to adverse outcomes.

Environmental factors

SARS-CoV-2 environmental risk factors comprise surface contamination, fecal-oral transmission, and airborne transmission.[85,86] In an experimental study aerosolizing SARS-CoV-2-WA1-2020 viral particles, SARS-CoV-2 remained viable on plastic and stainless steel for up to 72 hours.[87] In some hospital wards in China, the virus was detected on floors, computer mice, trash cans, and on handrails.[88] SARS-CoV-2 has been detected in feces during and after symptomatic infection.[86] Routine disinfection has been shown to reduce contamination: none of the surfaces or sewage disinfection pools in wards with SARS-CoV-2 patients were positive for SARS-CoV-2 RNA when daily chlorine-containing disinfection was followed.[89]

WHO guidelines encouraging social distancing of at least 2 meters are based on early evidence suggesting that COVID-19 is primarily spread by large droplets (above 5 μm), which generally fall to surfaces before traveling 2 meters.[85,88] However, there is some evidence that SARS-CoV-2 distributes widely by aerosol and beyond 2 meters by droplets. SARS-CoV-2 has been detected in the air 3 hours following manual aerosolization and in the air up to 4 meters from COVID-19 patient rooms.[87,88] Aerosolized viral RNA has been detected in protective apparel removal rooms, suggesting resuspension of viral particles, and in crowded public spaces.[90] In a systematic review of 10 studies by Bahl, et al.[56] eight studies suggested that droplets travel above a 2-meter distance when coughing or sneezing. However, Liu, et al.[90] found negligible viral air contamination in hospitals with negative ventilation and chlorine-containing disinfection, suggesting the effectiveness of proper sanitation.

CONTROLLING MEASURES

Diagnostic testing

It is known from previous MERS and SARS outbreaks that early detection of infection is critical for blocking further transmission.[52,91] Genome sequencing of SARS-CoV-2 enabled the rapid development of screening methods. Clinical testing for COVID-19 comprises either RT-PCR, which is more widely used, or antibody-based tests. Currently, the majority of cases worldwide are confirmed through nucleic acid laboratory tests.

Early eligibility criteria typically required an epidemiological link, the onset of symptoms, and negative ruling for other respiratory diseases in many countries. HCWs or those vulnerable to severe infection were eligible for testing after initial signs of fever or respiratory illness. By February 20, only China, Taiwan, Vietnam, the Philippines, Oman, Turkey, Colombia, Gabon, and Rwanda offered testing to anyone with symptoms, and only South Korea provided asymptomatic testing,[92] A large majority had no testing policy. By March 2, the majority of nations around the world had developed testing policies, though many nations necessitated patients to demonstrate an epidemiological or vulnerability status. Some regions, including Singapore, northern Italy, and South Korea, effectively employed liberal testing eligibility criteria, in which any citizen with a phy-

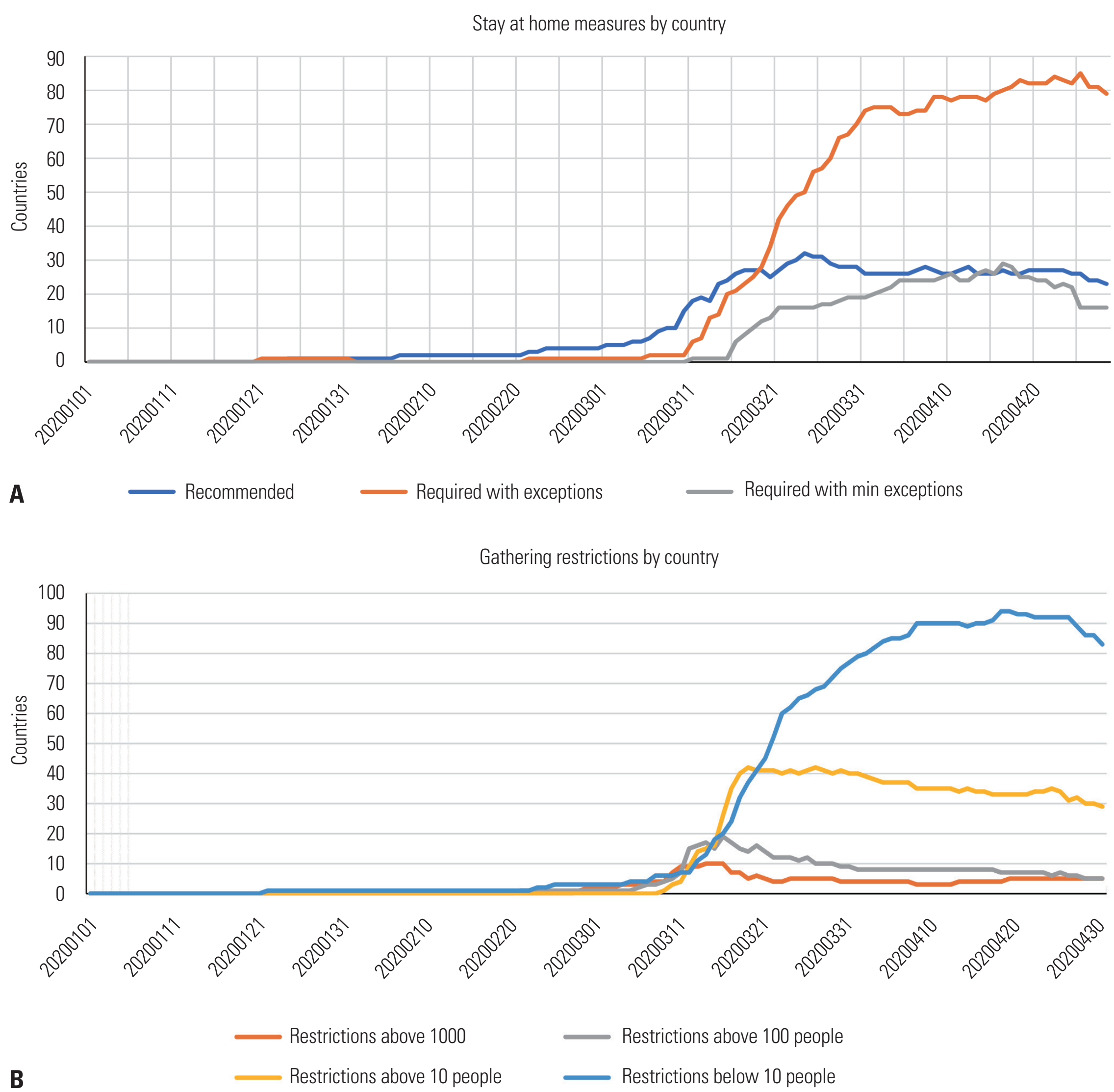

Fig. 1. (A) Number of countries with stay at home measures over time, stratified by level of enforcement. Restrictions with exceptions allow excursions for grocery shopping, exercise, and "essential trips." Restrictions with minimal exceptions allow only one member per household to leave and only for certain periods. (B) Number of countries with restrictions on gatherings over time, stratified by gathering size. Data were obtained from the Oxford COVID-19 Government Response Tracker (https://data.humdata.org/dataset/oxford-covid-19-government-response-tracker).

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sician's recommendation (Singapore) or with personal concern (South Korea, Northern Italy) could receive testing. On April 29, 20 nations offered testing to all people; 43 offered testing to all those who showed symptoms; and 48 offered testing only to vulnerable populations or those with epidemiological links after showing symptoms.[92]

Testing capacity has increased over time, with more accurate laboratory equipment and test kit supply production. By April 21, hotspots like Italy, New Zealand, Denmark, Canada, the US, and South Korea cumulatively conducted 23.98, 19.66, 17.36, 14.99, 12.65, 12.08, and 11.14 tests per 1000 people respectively. Thirty-five nations offered 0–5 tests per 1000 people; 13 nations offered 5–10 tests per 1000 people;[93] and 27 nations offered above 10 tests per 1000 people. The mean number of tests per 1000 conducted by all nations was 11.45. If the virus continues to spread on a global level, it will be increasingly important to scale the production of accurate tests to match diagnostic demand.

Lockdown and movement restriction

The number of countries enforcing stay-at-home measures or gathering restrictions are summarized in Fig. 1, and effective lockdown measures are shown in Table 3. From February 10 to March 1, fewer than 15 countries combined imposed either stay-at-home measures or gathering restrictions.[94] By March 10, 21 countries restricted gatherings, and 18 countries enforced stay-at-home measures. Thirty-five recommended or required the closing of public schools. By April 1, 131 countries restricted gatherings, of which 79 countries restricted gatherings below 10 people. On the same date, 196 countries enforced stay-at-home measures, with 70 enforcing home quarantine except for grocery shopping, exercise, and "daily trips." By April 30, 83 countries restricted all gatherings, and 79 countries allowed home excursions only for essential trips (Fig. 1). Sixteen countries limited home excursions, including essential trips, to once every few days for each household (minimal exceptions). Large-scale screening and training programs in COVID-19 recognition and isolation were also established by both hospitals and WHO.[95,96]

Precautions against SARS nosocomial transmission encompassed lockdown measures similar to those of the COVID-19 pandemic. In Beijing, local police, community health workers, and volunteers coordinated quarantining efforts.[91] Beijing closed all public entertainment sites on April 24, 2003, within 2 months of the initial importation of the virus. All schools, except universities, were closed. Restaurants and businesses were not closed, but screened for fever at entry. Travel advisories and screenings were implemented in multiple locations instead of travel bans.[28,97] Singapore utilized widespread temperature testing and encouraged its citizens to check for fever several times per day.[28]

By April 30, 122 countries had closed educational institutions, including universities. The efficacy of school closures in reducing transmission is based on previous influenza outbreaks and is expected to be highest if the reproductive number is <2, if closures are implemented early, and if attack rates are higher in children.[98] The attack rate in children for influenza is 15.2% (95% CI, 11.4–18.9%). However, the attack rate of COVID-19 in children has been estimated at only 7.2% (95% CI, 3.0–14.3%) and 3.8% (95% CI, 0.8–10.6%) in males and females, respectively.[99,100] A systematic review by Viner and colleagues found little evidence that school closures during the SARS and COVID-19 epidemics contributed significantly to curbing transmission, as transmission rates in schools were already low.[98] One mod-

Table 3. Effective Lockdown and Quarantine Measures for COVID-19 and SARS

Screening	Gathering restriction	Mobility restriction
COVID-19		
• Monitoring confirmed cases[19] • Using widely available testing[92] • Development of clinical referral systems for suspected cases[96] • Global education resources for screening and control[96]	• Restricting gathering sizes[94] • Closing public schools[96] • Limiting the maximum number of people per room[95]	• Administering early travel bans from infection hotspots[95] • Limiting trips outside the household[94] • Screening for infection at airport entry
SARS		
• Using thermometers for temperature screening[97] • Monitoring confirmed cases[28] • Using community volunteers to coordinate quarantine[91] • Development of clinical referral systems for suspected cases	• Closing public schools[97] • Restricting gathering sizes[97]	• Administering travel advisories on infection hotspots[28] • Screening for infection at airport entry[97]

COVID-19, coronavirus disease 2019; SARS, severe acute respiratory syndrome; MERS, Middle East respiratory syndrome.
Measures for lockdown and quarantine described as effective against COVID-19 and SARS are aggregated. Community lockdown measures against MERS were unable to be found and thus not included.

eling study using the UK population estimated that school closures in the COVID-19 epidemic have only reduced transmission by 2–4%.

CONCLUSION

As of May 26, 2020, more than 5 million cases and 300000 deaths associated with COVID-19 have been recorded worldwide. Likely to have resulted from bat-to-human transmission, SARS-CoV-2 exhibits high human-to-human transmission across households, hospitals, and communities. A major proportion of cases are asymptomatic, and it is likely that asymptomatic transmission contributes significantly to transmission. Efforts curbing transmission primarily comprise 1) early identification, either through targeted or indiscriminate testing and 2) lockdown and patient isolation. Previous lessons from SARS and MERS to reduce nosocomial and community transmission, such as isolating patients with respiratory illness, placing infected HCWs under quarantine, creating designated spatial pathways for suspected patients, and enabling the rapid development of testing, have been and should continue to be implemented. Novel studies describing methods to minimize aerosol generation during common hospital procedures can also be employed to curb transmission. Disinfection, precautionary social distancing beyond the recommended 2 meters, and hand hygiene are valuable measures through which to prevent environmental spread of the virus.

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AUTHOR CONTRIBUTIONS

Conceptualization: all authors. Data curation: Han Li and Seung Won Burm. Formal analysis: Han Li and Seung Won Burm. Investigation: Han Li and Seung Won Burm. Methodology: Han Li and Seung Won Burm. Project administration: Jae Il Shin. Resources: Han Li and Seung Won Burm. Software: Han Li and Seung Won Burm. Supervision: Jae Il Shin. Validation: Han Li and Seung Won Burm. Visualization: Han Li and Seung Won Burm. Writing—original draft: all authors. Writing—review & editing: all authors. Approval of final manuscript: all authors.

ORCID iDs

Han Li	https://orcid.org/0000-0002-9800-9948
Seung Won Burm	https://orcid.org/0000-0002-1808-8587
Sung Hwi Hong	https://orcid.org/0000-0002-9781-4822
Ramy Abou Ghayda	https://orcid.org/0000-0002-5170-3983
Andreas Kronbichler	https://orcid.org/0000-0002-2945-2946
Lee Smith	https://orcid.org/0000-0002-5340-9833
Ai Koyanagi	https://orcid.org/0000-0002-9565-5004
Louis Jacob	https://orcid.org/0000-0003-1071-1239
Keum Hwa Lee	https://orcid.org/0000-0002-1511-9587
Jae Il Shin	https://orcid.org/0000-0003-2326-1820

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