FOREWORD

The Department of Homeland Security (DHS) is paying close attention to the evolving Coronavirus Infectious Disease (COVID-19) situation in order to protect our nation. DHS is working very closely with the Centers for Disease Control and Prevention (CDC), other federal agencies, and public health officials to implement public health control measures related to travelers and materials crossing our borders from the affected regions.

Based on the response to a similar product generated in 2014 in response to the Ebolavirus outbreak in West Africa, the DHS Science and Technology Directorate (DHS S&T) developed the following “master question list” that quickly summarizes what is known, what additional information is needed, and who may be working to address such fundamental questions as, “What is the infectious dose?” and “How long does the virus persist in the environment?” The Master Question List (MQL) is intended to quickly present the current state of available information to government decision makers in the operational response to COVID-19 and allow structured and scientifically guided discussions across the federal government without burdening them with the need to review scientific reports, and to prevent duplication of efforts by highlighting and coordinating research.

The information contained in the following table has been assembled and evaluated by experts from publicly available sources to include reports and articles found in scientific and technical journals, selected sources on the internet, and various media reports. It is intended to serve as a “quick reference” tool and should not be regarded as comprehensive source of information, nor as necessarily representing the official policies, either expressed or implied, of the DHS or the U.S. Government. DHS does not endorse any products or commercial services mentioned in this document. All sources of the information provided are cited so that individual users of this document may independently evaluate the source of that information and its suitability for any particular use. This document is a “living document” that will be updated as needed when new information becomes available.
Clinical
Protective
Incubation
Host Range
Infectious Dose
Table of Contents

REQUIRED INFORMATION FOR EFFECTIVE INFECTIOUS DISEASE OUTBREAK RESPONSE

SARS-CoV-2 (COVID-19)
Updated 4/14/2020

Table of Contents

Infectious Dose – How much agent will make a healthy individual ill? .......................................................... 3
The human infectious dose of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unknown by all exposure routes. SARS-CoV-2 is the cause of coronavirus disease 19 (COVID-19).
Identifying the infectious dose for humans by any exposure route is critical to diagnostics, decontamination, and model development. Animal studies are a plausible surrogate.

Transmissibility – How does it spread from one host to another? How easily is it spread? .......................... 4
SARS-CoV-2 is passed easily between humans, likely through close contact with relatively large droplets and possibly through smaller aerosolized particles.
Individuals can transmit SARS-CoV-2 to others before they have symptoms.
Undetected cases play a major role in transmission.
Identifying the contribution of asymptomatic or pre-symptomatic transmission is important for implementing control measures. Additionally, the relative contribution of different infection sources – fomites, droplets, aerosols, and potentially feces – are unknown.

Host Range – How many species does it infect? Can it transfer from species to species? .......................... 5
SARS-CoV-2 is closely related to other coronaviruses circulating in bats in Southeast Asia. Previous coronaviruses have passed through an intermediate mammal host before infecting humans. The identity of the SARS-CoV-2 intermediate host is unknown.
SARS-CoV-2 uses the same receptor for cell entry as the SARS-CoV-1 coronavirus that circulated in 2002/2003.
To date, ferrets, hamsters, cats, and primates have been shown to be susceptible to SARS-CoV-2 infection. Cats can transmit infection to other cats. It is unknown whether these animals can transmit infection to humans.
Several animal models have been developed to recreate human-like illness, though to date they have been infected with high dose exposures. Lower dose studies may better replicate human disease acquisition.

Incubation Period – How long after infection do symptoms appear? Are people infectious during this time? ........ 6
The majority of individuals develop symptoms within 14 days of exposure. For most people, it takes at least 2 days to develop symptoms, and on average symptoms develop 5 days after exposure. Some individuals never develop symptoms but can still transmit disease.
While the incubation period is well-characterized, less is known about how long individuals are infectious before, during, and after symptoms. Additionally, the possibility of reinfection warrants more research.

Clinical Presentation – What are the signs and symptoms of an infected person? ........................................ 7
Most COVID-19 cases are mild, but severe disease can be found in any age group. Older individuals and those with underlying medical conditions are at higher risk of serious illness and death.
Current modeling suggests the overall case fatality rate (CFR) of COVID-19 is approximately 2.4%,17 but varies substantially by patient age and underlying comorbidities.
Evidence suggests that African Americans are at elevated risk of severe symptoms. Additional data on vulnerable subpopulations is needed.
Children of all ages are susceptible to COVID-19,84 though generally show milder55,145 or no symptoms.
The true case fatality rate is unknown, as the exact number of cases is uncertain. Testing priorities and case definitions vary by location.

Protective Immunity – How long does the immune response provide protection from reinfection? .............. 8
Infected patients show productive immune responses, however, more data is needed.
Currently, there is no evidence that recovered patients can be reinfected with SARS-CoV-2.
Understanding the duration of protective immunity is limited by small sample sizes. Animal models are plausible surrogates.
Additional research to quantify the risk of reinfection after weeks, months, and years is needed.

Clinical Diagnosis – Are there tools to diagnose infected individuals? When during infection are they effective? ........ 9
Diagnosis relies on identifying the genetic signature of the virus in patient nose, throat, or sputum samples. These tests are relatively accurate. Confirmed cases are still underreported.
Validated serological (antibody) assays are being developed to help determine who has been exposed to SARS-CoV-2.

CLEARED FOR PUBLIC RELEASE
In general, PCR tests appear to be sensitive and specific, though robust estimates of false positive/negative rates are still lacking. The efficacy of serological testing should be confirmed.

**Pharmaceutical Interventions – Are there effective treatments? Vaccines?**

Treatment for COVID-19 is primarily supportive care including ventilation if necessary. Over 332 clinical trials are ongoing, but results are preliminary. Work is ongoing to develop a SARS-CoV-2 vaccine in human and animal trials. No preliminary results are available. In general, the efficacy of various therapeutic options for COVID-19 is unknown, though clinical trial results are beginning to be released.

**Non-pharmaceutical Interventions – Are public health control measures effective at reducing spread?**

Broad-scale control measures such as stay-at-home orders are effective at reducing movement, and modeling shows evidence that they reduce transmission. The effect of relaxing control measures is unknown, and research is needed to help plan for easing of restrictions. As US states have implemented differing control measures at various times, a comprehensive analysis of social distancing efficacy has not yet been conducted.

**Environmental Stability – How long does the agent live in the environment?**

SARS-CoV-2 can persist on surfaces for at least 3 days and on the surface of a surgical mask for up to 7 days depending on conditions. If aerosolized intentionally, SARS-CoV-2 is stable for at least several hours. The seasonality of COVID-19 transmission is unknown. Additional testing on SARS-CoV-2, as opposed to surrogate viruses, is needed to support initial estimates of stability.

**Decontamination – What are effective methods to kill the agent in the environment?**

Soap and water, as well as common alcohol and chlorine-based cleaners, hand sanitizers, and disinfectants are effective at inactivating SARS-CoV-2 on hands and surfaces. Methods for decontaminating N95 masks have been approved by the FDA under Emergency Use Authorization (EUA). Additional decontamination studies, particularly with regard to PPE and other items in short supply, are needed.

**PPE – What PPE is effective, and who should be using it?**

The effectiveness of PPE for SARS-CoV-2 is currently unknown, and data from other related coronaviruses are used for guidance. Healthcare workers are at high risk of acquiring COVID-19, even with recommended PPE. Most PPE recommendations have not been made on SARS-CoV-2 data, and comparative efficacy of different PPE for different tasks (e.g., intubation) is unknown. Identification of efficacious PPE for healthcare worker is critical due to their high rates of infection.

**Forensics – Natural vs intentional use? Tests to be used for attribution.**

All current evidence supports the natural emergence of SARS-CoV-2 via a bat and possible intermediate mammal species. Identifying the intermediate species between bats and humans would aid in reducing potential spillover from a natural source.

**Genomics – How does the disease agent compare to previous strains?**

Current evidence suggests that SARS-CoV-2 accumulates substitutions and mutations at a similar rate as other coronaviruses. Mutations and deletions in specific portions of the SARS-CoV-2 genome have not been linked to any changes in transmission or disease severity, though modeling work is attempting to identify possible changes. Research linking genetic changes to differences in phenotype (e.g., transmissibility, virulence, progression in patients) is needed.
### Infectious Dose – How much agent will make a healthy individual ill?

**What do we know?**

The human infectious dose of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unknown by all exposure routes. SARS-CoV-2 is the cause of coronavirus disease 19 (COVID-19).

**Work using SARS-CoV-2**

- A total dose of approximately 700,000 plaque-forming units (PFU) of the novel coronavirus SARS-CoV-2 infected cynomolgus macaques via combination intranasal and intratracheal exposure ($10^6$ TCID$_{50}$ total dose). Macaques did not exhibit clinical symptoms, but virus was shed from the nose and throat.\(^{185}\)
- Rhesus macaques are effectively infected with SARS-CoV-2 via the ocular conjunctival and intratracheal route at a dose of approximately 700,000 PFU ($10^6$ TCID$_{50}$).\(^{81,82}\)
- Rhesus macaques infected with 2,600,000 TCID$_{50}$ of SARS-CoV-2 by the intranasal, intratracheal, oral and ocular routes combined recapitulate moderate disease observed in the majority of human cases.\(^{157}\)
- Ferrets infected with 316,000 TCID$_{50}$ of SARS-CoV-2 by the intranasal route show similar symptoms to human disease. Uninfected ferrets in direct contact with infected ferrets test positive and show disease as early as 2 days post-contact. Direct contact is required to transfer infection between ferrets.\(^{118}\)
- Syrian Golden Hamsters infected with 100,000 PFU via the intranasal route closely resemble human respiratory infection. Uninfected hamsters in close contact with infected hamsters show symptoms within 4 days of exposure.\(^{51}\)
- Domestic cats exposed to 100,000 PFU of SARS-CoV-2 via the intranasal route developed severe pathological symptoms including lesions in the nose, throat, and lungs.\(^{197}\) Juvenile cats exhibited more severe symptoms than subadults.\(^{197}\)

**Related Coronaviruses**

- The infectious dose for severe acute respiratory syndrome coronavirus 1 (SARS) in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route).\(^{78,80}\)
- Genetically modified mice exposed intranasally to doses of Middle East respiratory syndrome coronavirus (MERS) virus between 100 and 500,000 PFU show signs of infection. Infection with higher doses result in severe syndromes.\(^{13,66,131,246}\)

**What do we need to know?**

Identifying the infectious dose for humans by any exposure route is critical to diagnostics, decontamination, and model development. Animal studies are a plausible surrogate.

- Human infectious dose by aerosol route
- Human infectious dose by surface contact (fomite)
- Human infectious dose by fecal-oral route
### What do we know?

**SARS-CoV-2 (COVID-19)**

**Transmissibility – How does it spread from one host to another? How easily is it spread?**

SARS-CoV-2 is passed easily between humans, likely through close contact with relatively large droplets and possibly through smaller aerosolized particles.

- Pandemic COVID-19 has caused 1,945,055 infections and 121,897 deaths in at least 185 countries and territories (as of 4/14/2020).[^4] 42, 192, 226
- In the US there are 584,073 confirmed SARS-CoV-2 cases across all 50 US states, with 23,709 deaths (as of 4/14/2020).[122] Sustained community transmission of COVID-19 is occurring in the US. 26
- High-quality estimates of human transmissibility (R₀) range from 2.2 to 3.1.[148] 169, 182, 233, 245
- SARS-CoV-2 is believed to spread through close contact and droplet transmission, with fomite transmission likely and close-contact aerosol transmission plausible but unconfirmed.[225]
- Aerosolized virus has been detected in COVID-19 patient rooms, with particle sizes within the human respirable range (0.25 – 2.5 μm).[^141]
- Extensive contamination of patient rooms indicates the potential for airborne transmission, though to date infectious virus has not been isolated from aerosol samples.[189]
- Limited evidence suggests that SARS-CoV-2 may be spread by conversation and exhalation in the absence of cough, however more work is needed.[7, 189, 11, 130]
- SARS-CoV-2 is present in infected patient saliva, lower respiratory sputum, and feces.[135]
- Up to 67% of patients with asymptomatic infection may still show CT evidence of pneumonia.[216]

**Individuals can transmit SARS-CoV-2 to others before they have symptoms.**

- SARS-CoV-2 replicates in the upper respiratory tract (e.g., throat), and infectious virus is detectable in throat and lung tissue for at least 8 days.[228]
- Pre-symptomatic[248] or asymptomatic[21] patients can transmit SARS-CoV-2; between 12%[85] and 23%[140] of infections may be caused by asymptomatic or pre-symptomatic transmission. Individuals may be infectious for 1-3 days prior to symptom onset.[219]
- Severe cases are more likely to transmit disease, and most new infections are within households of infected patients.[146]

**Undetected cases play a major role in transmission.**

- Models suggest up to 86% of early COVID-19 cases in China were undetected, and these infections were the source for 79% of reported cases.[133]
- Models estimate that the true number of cases may be approximately 11 times greater than the reported number of cases in the UK,[241] and between 5 and 10 times greater than the reported number of cases in the US.[114]

### What do we need to know?

**Identifying the contribution of asymptomatic or pre-symptomatic transmission is important for implementing control measures.** Additionally, the relative contribution of different infection sources – fomites, droplets, aerosols, and potentially feces – are unknown.

- Capability of SARS-CoV-2 to be transmitted by contact with fomites (phones, doorknobs, surfaces, clothing, etc.) – see also Experimental Stability
- Superspreading capacity needs to be refined.
- Updated person to person transmission rates (e.g., R₀) as control measures take effect.
- What is the underreporting rate?[110]
- Can individuals become re-infected with SARS-CoV-2?
- What is the difference in transmissibility among countries?
- Is the R₀ estimate higher in healthcare or long-term care facilities?
- How effective are social distancing measures?
- When will infections peak in various cities and countries?

[^4]: [1945055 infections and 121897 deaths](https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/country-specific.html)
<table>
<thead>
<tr>
<th>SARS-CoV-2 (COVID-19)</th>
<th>Host Range – How many species does it infect? Can it transfer from species to species?</th>
</tr>
</thead>
</table>
| **What do we know?**  | SARS-CoV-2 is closely related to other coronaviruses circulating in bats in Southeast Asia. Previous coronaviruses have passed through an intermediate mammal host before infecting humans. The identity of the SARS-CoV-2 intermediate host is unknown.  
• Early genomic analysis indicates similarity to SARS-CoV-1,\textsuperscript{5,6,7} with a suggested bat origin.\textsuperscript{5,6,7}  
• Positive samples from the South China Seafood Market strongly suggests a wildlife source,\textsuperscript{48} though it is possible that the virus was circulating in humans before the disease was associated with the seafood market.\textsuperscript{27,69,236,243}  
• Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.\textsuperscript{184} The identity of the intermediate host remains unknown.\textsuperscript{134-138}  
• Viruses similar to SARS-CoV-2 were present in pangolin samples collected several years ago.\textsuperscript{123}  
SARS-CoV-2 uses the same receptor for cell entry as the SARS-CoV-1 coronavirus that circulated in 2002/2003.  
• Experiments show that SARS-CoV-2 Spike (S) receptor-binding domain binds the human cell receptor (ACE2) stronger than SARS-CoV-1,\textsuperscript{231} potentially explaining its high transmissibility. The same work suggests that differences between SARS-CoV-2 and SARS-CoV-1 Spike proteins may limit the therapeutic ability of SARS antibody treatments.\textsuperscript{231}  
• Modeling of SARS-CoV-2 Spike and ACE2 proteins suggests that SARS-CoV-2 can bind and infect human, bat, civet, monkey and swine cells.\textsuperscript{213}  
• Receptor binding is not the only feature of coronaviruses that facilitate cell entry, however, changes in proteolytic cleavage of Spike protein can also affect animal host range.\textsuperscript{153}  
To date, ferrets, hamsters, cats, and primates have been shown to be susceptible to SARS-CoV-2 infection. Cats can transmit infection to other cats. It is unknown whether these animals can transmit infection to humans.  
• Animal model studies suggest that Golden Syrian hamsters, primates and ferrets may be susceptible to infection.\textsuperscript{51,118}  
• Domestic cats are susceptible to infection with SARS-CoV-2 (100,000 PFU via the intranasal route), and can transmit the virus to other cats via droplet or short-distance aerosol.\textsuperscript{197} Dogs exposed to SARS-CoV-2 showed limited evidence of infection, producing anti-SARS-CoV-2 antibodies but no clinical symptoms.\textsuperscript{397}  
• Wild cats (tigers)\textsuperscript{218} can be infected with SARS-CoV-2, although their ability to spread to humans is unknown.\textsuperscript{150,244}  
• Ducks, chickens, and pigs remained uninfected after experimental SARS-CoV-2 (30,000 CFU for ducks and chickens, 100,000 PFU for pigs, all via intranasal route).\textsuperscript{197} There is currently no evidence that SARS-CoV-2 infects livestock.\textsuperscript{109} |

| **What do we need to know?** | Several animal models have been developed to recreate human-like illness, though to date they have been infected with high dose exposures. Lower dose studies may better replicate human disease acquisition.  
• What is the intermediate host(s)?  
• What are the mutations in SARS-CoV-2 that allowed human infection and transmission?  
• What other animals can SARS-CoV-2 infect (e.g., pet dogs, potential wildlife reservoirs)?  
• Can infected animals transmit to humans (e.g., pet cats, pet dogs to humans)? |
# Incubation Period

The majority of individuals develop symptoms within 14 days of exposure. For most people, it takes at least 2 days to develop symptoms, and on average symptoms develop 5 days after exposure. Some individuals never develop symptoms but can still transmit disease.

- The best current estimate of the COVID-19 incubation period is 5.1 days, with 99% of individuals exhibiting symptoms within 14 days of exposure.\(^{126}\) Fewer than 2.5% of infected individuals show symptoms sooner than 2 days after exposure.\(^{126}\)
- Individuals can test positive for COVID-19 even if they lack clinical symptoms.\(^{21, 50, 100, 203, 248}\)
- Individuals can be infectious while asymptomatic,\(^{46, 186, 203, 248}\) and asymptomatic individuals can have similar amounts of virus in their nose and throat as symptomatic individuals.\(^{253}\)
- Infectious period is unknown, but possibly up to 10-14 days.\(^{10, 133, 192}\)
- On average, there are approximately 4\(^{41}\) to 7.5\(^{132}\) days between symptom onset in successive cases of a single transmission chain.
- Most hospitalized individuals are admitted within 8-14 days of symptom onset.\(^{250}\)

---

### What do we need to know?

While the incubation period is well-characterized, less is known about how long individuals are infectious before, during, and after symptoms. Additionally, the possibility of reinfection warrants more research.

- What is the average infectious period during which individuals can transmit the disease?
- Are individuals infectious after hospital discharge and clinical recovery, or are positive PCR tests only detecting non-infectious virus?
- Can individuals become re-infected after recovery? If so, how long after?
### Clinical presentation – What are the signs and symptoms of an infected person?

**What do we know?**

Most COVID-19 cases are mild, but severe disease can be found in any age group. Older individuals and those with underlying medical conditions are at higher risk of serious illness and death.

- The majority of COVID-19 cases are mild (81%, N = 44,000 cases).
- Initial COVID-19 symptoms include fever (87.9% overall, but only 44% - 52% present with fever initially), cough (67.7%), fatigue, shortness of breath, headache, and reduced lymphocyte count. Headache is uncommon. Diarrhea may be uncommon, though lack of appetite may be an early symptom.
- Complications include acute respiratory distress (ARDS), 17-29% of hospitalized patients leading to death in 4-15% of cases, pneumonia, cardiac injury (20%), secondary infection, kidney failure, arrhythmia, sepsis, and shock.
- Most deaths are caused by respiratory failure or respiratory failure combined with myocardial (heart) damage.
- Approximately 15% of hospitalized patients are classified as severe, and approximately 5% of patients are admitted to the ICU.
- Loss of taste and smell appears in 5-30% of patients who test positive, however ~18% of individuals who test negative also report this symptom. More work is needed.
- Ocular symptoms such as conjunctivitis have been seen in severe COVID-19 cases.

Current modeling suggests the overall case fatality rate (CFR) of COVID-19 is approximately 2.4%, but varies substantially by patient age and underlying comorbidities.

- The CFR depends on comorbidities. Cardiovascular disease, hypertension, diabetes, and respiratory conditions all increase the CFR.
- The CFR increases with age: individuals >60 are at higher risk of death, and >60% of confirmed fatalities have been male. In the US, 34% of hospitalizations have been individuals younger than 44 years old.
- Variation in the CFR between countries may be due to demographics, testing criteria, and how COVID-19 related deaths are defined.

Evidence suggests that African Americans are at elevated risk of severe symptoms. Additional data on vulnerable subpopulations is needed.

- A review of US COVID-19 patients revealed that African Americans are disproportionately represented in hospitalized populations (comprising 33% of hospitalized patients compared to only 18% of the base study population). Additional research highlighting potentially vulnerable subpopulations is needed.

Children of all ages are susceptible to COVID-19, though generally show milder or no symptoms.

- Up to 28% of children may be asymptomatic.
- Severe symptoms in children are possible, and infant deaths have been recorded.

**What do we need to know?**

The true case fatality rate is unknown, as the exact number of cases is uncertain. Testing priorities and case definitions vary by location.

- How long does it take for infected individuals to recover outside of a healthcare setting?
- Are reductions in CFR over time (e.g., China) an indication of better treatment, less overcrowding, or both?
- Are pregnant women at greater risk of complications during labor?
- How prevalent is loss of smell, loss of taste and gastrointestinal symptoms in COVID-19 patients?
<table>
<thead>
<tr>
<th>SARS-CoV-2 (COVID-19)</th>
<th>Protective Immunity – How long does the immune response provide protection from reinfection?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What do we know?</strong></td>
<td>Infected patients show productive immune responses, however more data is needed.</td>
</tr>
<tr>
<td></td>
<td>• In a limited study (n=9), hospitalized patients shed high levels of infectious virus for 7-days via the nasal-pharyngeal route, 50% of patients seroconverted within 7 days, and all patients by 14 days. Seroconversion did not correlate with lower viral load.(^{228})</td>
</tr>
<tr>
<td></td>
<td>• In a larger study (n=175), most patients developed neutralizing antibodies within 10-15 days after disease onset. Elderly patients had significantly higher neutralizing antibody titers than younger patients.(^{232})</td>
</tr>
<tr>
<td></td>
<td>• Based on one patient, a productive immune response is generated and sustained for at least 7 days.(^{204}) Previous studies on coronavirus immunity suggest that neutralizing antibody may wane after several years.(^{36,234}) More data are needed.</td>
</tr>
<tr>
<td></td>
<td>• A small subset of COVID-19 patients in China (8%) did not develop a serological response to infection, and the potential for reinfection in these patients is unknown.(^{232}) Interestingly, the majority of patients that failed to develop a quantifiable immune response were &lt; 40 years old.</td>
</tr>
<tr>
<td></td>
<td><strong>Currently, there is no evidence that recovered patients can be reinfected with SARS-CoV-2.</strong></td>
</tr>
<tr>
<td></td>
<td>• Experimentally infected macaques were not capable of being reinfected after their primary infection resolved.(^{23})</td>
</tr>
<tr>
<td></td>
<td>• According to the WHO, there is no evidence of re-infection with SARS-CoV-2 after recovery.(^{125})</td>
</tr>
<tr>
<td></td>
<td>• Patients can test positive via PCR for up to 37 days after symptoms appear,(^{210}) and after recovery and hospital discharge.(^{124}) The ability of these individuals to infect others is unknown.</td>
</tr>
<tr>
<td><strong>What do we need to know?</strong></td>
<td>Understanding the duration of protective immunity is limited by small sample sizes. Animal models are plausible surrogates. Additional research to quantify the risk of reinfection after weeks, months, and years is needed.</td>
</tr>
<tr>
<td></td>
<td>• How long does the immune response last?</td>
</tr>
<tr>
<td></td>
<td>• Is there evidence of waning immunity?</td>
</tr>
<tr>
<td></td>
<td>• Can humans become reinfected?</td>
</tr>
<tr>
<td></td>
<td>• Are patients who test positive weeks after discharge from hospital capable of transmitting infection?</td>
</tr>
<tr>
<td></td>
<td>• How does the patient immune response vary by age?</td>
</tr>
<tr>
<td>SARS-CoV-2 (COVID-19)</td>
<td>Clinical Diagnosis – Are there tools to diagnose infected individuals? When during infection are they effective?</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>What do we know?</strong></td>
<td>Diagnosis relies on identifying the genetic signature of the virus in patient nose, throat, or sputum samples. These tests are relatively accurate. Confirmed cases are still underreported.</td>
</tr>
<tr>
<td></td>
<td>• US CDC has expanded patient testing criteria to include symptomatic patients at clinician discretion.25</td>
</tr>
<tr>
<td></td>
<td>• PCR protocols and primers have been widely shared internationally.41, 71, 132, 196, 222, 227 PCR-based diagnostic assays are unable to differentiate between active and inactive virus.</td>
</tr>
<tr>
<td></td>
<td>• Broad testing in Iceland suggests that ~50% of those who test positive are symptom-free at the time of testing.19 155</td>
</tr>
<tr>
<td></td>
<td>• A combination of pharyngeal (throat) RT-PCR and chest tomography are the most effective diagnostic criteria (correctly diagnose 91.9% of infections).179 A single throat swab detects 78.2% of infections, and duplicate tests identify 86.2% of infections.179</td>
</tr>
<tr>
<td></td>
<td>• Nasal and pharyngeal swabs may be less effective as diagnostic specimens than sputum and bronchoalveolar lavage fluid,213 although recent evidence suggests this may not always be the case.228 More work is needed.</td>
</tr>
<tr>
<td></td>
<td>• RT-PCR tests can identify asymptomatic cases. The SARS-CoV-2 infection was identified in 2/114 individuals cleared by clinical assessment.106</td>
</tr>
<tr>
<td></td>
<td>• Combination RT-PCR and serology (antibody) testing may increase the ability to diagnose patients with mild symptoms, or identify patients at higher risk of severe disease.247</td>
</tr>
<tr>
<td></td>
<td>• The FDA released an Emergency Use Authorization enabling laboratories to develop and use tests in-house for patient diagnosis.23</td>
</tr>
<tr>
<td></td>
<td>• Updated tests from the US CDC are available to states.41, 46</td>
</tr>
<tr>
<td></td>
<td>• Multiple rapid or real-time test kits have been produced by universities and industry, including the Wuhan Institute of Virology,74 BGI,29 Cepheid212, Abbot,91 and Mesa Biotech.30</td>
</tr>
<tr>
<td></td>
<td>• The US CDC is developing serological tests to determine what proportion of the population has been exposed to SARS-CoV-2.116 A rapid antibody test by Cellex is now authorized by the FDA.105, 221</td>
</tr>
<tr>
<td></td>
<td>• Home tests are being developed; however none are FDA approved, nor are they useable as a diagnostic.158-159, 168</td>
</tr>
<tr>
<td></td>
<td>• Machine learning tools are being developed to predict severe and fatal COVID-19 cases based on CT scans.199</td>
</tr>
<tr>
<td></td>
<td>• Interleukin-6 levels of &gt;80 pg/mL were associated with respiratory failure in a small study (n=41).102 More work is needed.</td>
</tr>
<tr>
<td></td>
<td>Validated serological (antibody) assays are being developed to help determine who has been exposed to SARS-CoV-2.</td>
</tr>
<tr>
<td></td>
<td>• Researchers have tested a variety of enzyme-linked immunosorbent assays (ELISA) to determine their sensitivity and specificity to SARS-CoV-2 as well as other coronaviruses. Results show high specificity, though sample sizes for SARS-CoV-2 patients were small.161</td>
</tr>
<tr>
<td></td>
<td>• In one German town, serological testing has been used to identify the percent of the population already exposed to SARS-CoV-2 (14%), which can assist in public health response planning.177</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>What do we need to know?</strong></th>
<th>In general, PCR tests appear to be sensitive and specific, though robust estimates of false positive/negative rates are still lacking. The efficacy of serological testing should be confirmed.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• False positive/negative rates for tests</td>
</tr>
<tr>
<td></td>
<td>• Eclipse phase of infection (time between infection and detectable disease) in an individual</td>
</tr>
<tr>
<td></td>
<td>• With limited testing in many locations, how accurate are clinical diagnoses compared to genetic tests?</td>
</tr>
<tr>
<td></td>
<td>• How effective are different swab specimens as diagnostic samples?</td>
</tr>
<tr>
<td></td>
<td>• How many serological tests need to be done to obtain an accurate picture of underlying exposure?</td>
</tr>
<tr>
<td>What do we know?</td>
<td>Pharmaceutical Interventions – Are there effective treatments? Vaccines?</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Treatment for COVID-19 is primarily supportive care including ventilation if necessary. Over 332 clinical trials are ongoing, but results are preliminary. Convalescent sera is being tested at multiple sites across the US. WHO is tracking &gt;50 potential vaccines, and has begun two global clinical trials: Solidarity and Discovery that include remdesivir, hydroxychloroquine and chloroquine, ritonavir/lopinavir, and interferon-beta. Limited, preliminary evidence from clinical trials supports the efficacy of favipiravir, tocilizumab, intravenous immunoglobulin, and hydroxychloroquine with azithromycin. Additional work including sufficiently powered clinical trials are necessary to confirm therapeutic efficacy of any of these compounds. Limited, preliminary evidence shows mixed efficacy of chloroquine alone, and no efficacy from combination ritonavir and lopinavir. Favipiravir has been approved to treat COVID-19 in China. Antibody based therapeutics are planned to start clinical trials in 3-5 months. Teams across the USA are testing passive antibody therapy (convalescent serum) to patients (FDA Investigational New Drug approval). Corticosteroids are commonly given to COVID-19 patients at risk of ARDS, but their use is not recommended by the US CDC. Laboratory testing identified 17 repurposed drugs and remdesivir-like nucleoside inhibitors with significant antiviral activity, however more research is needed to confirm efficacy. A blood-cleaning device has been approved by the FDA under Emergency Use Authorization to filter cytokines from severely ill COVID-19 patients. Work is ongoing to develop a SARS-CoV-2 vaccine in human and animal trials. No preliminary results are available. Multiple entities are working to produce a SARS-CoV-2 vaccine, including HHS/NIH/NIAID, CEPI, Moderna Therapeutics, Pfizer, Gilead Sciences, Sanofi, and Johnson and Johnson. Moderna has begun phase 1 clinical vaccine trials.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>What do we need to know?</th>
<th>In general, the efficacy of various therapeutic options for COVID-19 is unknown, though clinical trial results are beginning to be released.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?</td>
<td></td>
</tr>
<tr>
<td>Is the GLS-5000 MERS vaccine cross-reactive against SARS-CoV-2?</td>
<td></td>
</tr>
<tr>
<td>Efficacy of antibody treatments developed for SARS and MERS</td>
<td></td>
</tr>
<tr>
<td>What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics?</td>
<td></td>
</tr>
<tr>
<td>Are viral replicase inhibitors such as beta-D-N4-hydroxycytidine effective against SARS-CoV-2?</td>
<td></td>
</tr>
</tbody>
</table>
## SARS-CoV-2 (COVID-19)

### What do we know?

**Non-pharmaceutical interventions – Are public health control measures effective at reducing spread?**

- Broad-scale control measures such as stay-at-home orders are effective at reducing movement, and modeling shows evidence that they reduce transmission.
  - Social distancing and other policies are estimated to have reduced COVID-19 spread by 44% in Hong Kong\(^{73}\) and reduced spread in China.\(^{119, 143}\)
  - Modeling demonstrates that multifaceted restrictions and quarantines in China reduced the \(R_0\) of SARS-CoV-2 from greater than 3 to less than 1 between January 23\(^{rd}\) and February 5\(^{th}\).\(^{165}\)
  - Models indicate that a combination of school closures, work restrictions, and other measures are required to effectively limit transmission.\(^{94}\)
  - Preliminary modeling results from Japan suggest that school closures alone were not sufficient to limit COVID-19 spread, though the school closures in question only applied to students between 6 and 18 years of age.\(^{111}\)
  - Globally, there is some evidence that implementing social distancing measures has reduced the amount individuals travel, though the data are based on planned rather than actual trips.\(^{149}\)
  - Restrictive lockdowns in China are estimated to have reduced disease transmission within only a few days.\(^{752}\)
  - Non-pharmaceutical interventions in China did not reduce transmission equally across all groups; transmission rates in younger individuals, particularly infants, as well as hospital workers continued to increase even while overall transmission rates declined.\(^{165}\)

**The effect of relaxing control measures is unknown, and research is needed to help plan for easing of restrictions.**

- Modeling suggests that premature lifting of social distancing measures will substantially increase the number of local COVID-19 cases in Wuhan, China.\(^{170}\)
  - Similarly, forecasts in the US estimate a resumption of exponential case growth if social distancing measures are relaxed.\(^{75}\)
  - In the UK, modelers are assessing the efficacy of rolling interventions, whereby social distancing measures are put into place every few weeks to keep healthcare demand below a critical point.\(^{241}\)
  - A modeling study using Chinese data estimated the impact of relaxing social distancing measures after an initial reduction in disease transmission. Results suggest that if \(R_0\) is allowed to rise above 1, tightening controls may not be enough to keep transmission low; rather, additional effort would be needed to drive \(R_0\) below 1 again, suggesting that carefully balancing control measures to maintain \(R_0\) below 1 would be more efficient than allowing \(R_0\) to increase again in the first place.\(^{127}\)
  - Robust contact tracing and case finding may be needed to control COVID-19 in the US, but would require additional staff and resources to conduct effectively.\(^{217}\)

### What do we need to know?

- As different US states have implemented differing control measures at various times, a comprehensive analysis of social distancing efficacy has not yet been conducted.
  - How many cases in the US have been averted due to social distancing restrictions?
  - How long does it take for various non-pharmaceutical interventions to show effects?
  - What are effective surrogate measures of social distancing efficacy (e.g., reduction in travel, contact, traffic, etc.)?
  - What are plausible options for relaxing social distancing and other intervention measures without resulting in a resurgence of COVID-19 cases?
### SARS-CoV-2 (COVID-19) Environmental Stability – How long does the agent live in the environment?

**What do we know?**

SARS-CoV-2 can persist on surfaces for at least 3 days and on the surface of a surgical mask for up to 7 days depending on conditions. If aerosolized intentionally, SARS-CoV-2 is stable for at least several hours. The seasonality of COVID-19 transmission is unknown.

**SARS-CoV-2 Data**

- SARS-CoV-2 can persist on plastic and metal surfaces for between 3 days (21-23°C, 40% RH) and 7 days (22°C, 65%RH). Infectious virus can be recovered from a surgical mask after 7 days (22°C, 65% RH).
- SARS-CoV-2 can persist for at least two weeks at refrigerated temperatures (4°C).
- SARS-CoV-2 genetic material (RNA) was detected in symptomatic and asymptomatic cruise ship passenger rooms up to 17 days after cabins were vacated. The infectiousness of this material is not known.

**Surrogate Coronavirus data:**

- Studies suggest that other coronaviruses can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV), and porous surfaces for up to 3-5 days (SARS-CoV) in air conditioned environments (20-25°C, 40-50% RH).
- Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH), though infectious virus can persist on surfaces for several days in typical office or hospital conditions.
- SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C) on surfaces.
- No strong evidence exists showing reduction in transmission with seasonal increase in temperature and humidity.
- One hour after aerosolization approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH).
- Porous hospital materials, including paper and cotton cloth, maintain infectious SARS-CoV for a shorter time than non-porous material.

### What do we need to know?

Additional testing on SARS-CoV-2, as opposed to surrogate viruses, is needed to support initial estimates of stability.

- Stability of SARS-CoV-2 in aerosol, droplets, and other matrices (mucus/sputum, feces)
- Particle size distribution (e.g., droplet, large droplet and true aerosol distribution)
- Duration of SARS-CoV-2 infectivity via fomites and surface (contact hazard)
- Stability of SARS-CoV-2 on PPE (e.g., Tyvek, nitrile, etc.)
### SARS-CoV-2 (COVID-19)

**What do we know?**

Soap and water, as well as common alcohol and chlorine-based cleaners, hand sanitizers, and disinfectants are effective at inactivating SARS-CoV-2 on hands and surfaces.

- **SARS-CoV-2**
  - Alcohol-based hand rubs are effective at inactivating SARS-CoV-2.\(^{120}\)
  - Chlorine bleach (1%, 2%), 70% ethanol and 0.05% chlorhexidine are effective against live virus in lab tests.\(^{60}\)
  - Twice-daily cleaning with sodium dichloroisocyanurate disinfected surfaces in COVID-19 patient hospital rooms.\(^{163}\)
  - EPA has released a list of SARS-CoV-2 disinfectants, but solutions were not tested on live virus.\(^{12}\)

**Other Coronaviruses**

- Chlorine-based\(^{224}\) and ethanol-based\(^{70}\) solutions are recommended.
- Heat treatment (56°C) is sufficient to kill coronaviruses,\(^{174, 249}\) though effectiveness depends partly on protein in the sample.\(^{174}\)
- 70% ethanol, 50% isopropanol, sodium hypochlorite (0.02% bleach), and UV radiation can inactivate several coronaviruses (MHV and CCV).\(^{188}\)
- Ethanol-based biocides effectively disinfect coronaviruses dried on surfaces, including ethanol containing gels similar to hand sanitizer.\(^{108, 229}\)
- Surface spray disinfectants such as Mikrobac, Dismozon, and Korsolex are effective at reducing infectivity of the closely related SARS-CoV after 30 minutes of contact.\(^{173}\)
- Coronaviruses may be resistant to thermal inactivation for up to 7 days when stabilized in stool.\(^{205, 206}\)
- Coronaviruses are more stable in matrices such as respiratory sputum.\(^{86}\)

**Methods for decontaminating N95 masks have been approved by the FDA under Emergency Use Authorization (EUA).**

- Hydrogen peroxide vapor can repeatedly decontaminate N95 respirators.\(^{181}\) Devices capable of decontaminating 80,000 masks per day have been granted Emergency Use Authorization from the FDA.\(^{90}\)
- The FDA has issued an Emergency Use Authorization for a system capable of decontaminating 10 N95 masks at a time using devices already present in many US hospitals.\(^{32}\)

### Table: Decontamination – What are effective methods to kill the agent in the environment?

<table>
<thead>
<tr>
<th>Decontamination</th>
<th>SARS-CoV-2 (COVID-19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soap and water, as well as common alcohol and chlorine-based cleaners, hand sanitizers, and disinfectants are effective at inactivating SARS-CoV-2 on hands and surfaces.</td>
<td></td>
</tr>
</tbody>
</table>
### SARS-CoV-2 (COVID-19)

#### What do we know?

The effectiveness of PPE for SARS-CoV-2 is currently unknown, and data from other related coronaviruses are used for guidance. Healthcare workers are at high risk of acquiring COVID-19, even with recommended PPE.

- Healthcare worker illnesses (over 1,000[203]) demonstrates human-to-human transmission despite isolation, PPE, and infection control.\(^{190}\)
- Risk of transmission to healthcare workers appears high, with up to 20% of healthcare workers in Lombardy, Italy becoming infected.\(^{178}\)
- “Healthcare personnel entering the room [of SARS-CoV-2 patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield).”\(^{44}\)
- WHO indicates healthcare workers should wear clean long-sleeve gowns as well as gloves.\(^{223}\)
- Respirators (NIOSH-certified N95, EUFFP2 or equivalent) are recommended for those dealing with possible aerosols.\(^{224}\) Additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation).\(^{34}\)
- Particular attention should be paid to the potential for transmission via exhaled air during supportive respiratory procedures.\(^{99}\)
- There is evidence both for\(^{141}\) and against\(^{163}\) the detection of SARS-CoV-2 RNA via air sampling in patient rooms and other hospital areas.
- Research at Johns Hopkins Center for Health Security has provided initial estimates of PPE needs in the US: 7.8 billion gloves, 668 million gowns, 360 million surgical masks, and 136 million N95 or similar respirators.\(^{208}\)

**Masks may be effective at slowing transmission.**

- Surgical face masks, respirators and homemade face masks may prevent transmission of coronaviruses from infectious individuals (with or without symptoms) to other individuals.\(^{128}, 209, 77\)
- More work is needed.
- On 4/3/2020, the US CDC recommended wearing cloth face masks in public where social distancing measures are difficult to maintain.\(^{45}\)
- The efficacy of homemade PPE, made with T-shirts, bandanas, or similar materials, is less than standard PPE, but may offer some protection if no other options are available.\(^{62, 76, 180}\)

### PPE – What PPE is effective, and who should be using it?

Most PPE recommendations have not been made on SARS-CoV-2 data, and comparative efficacy of different PPE for different tasks (e.g., intubation) is unknown. Identification of efficacious PPE for healthcare workers is critical due to their high rates of infection.

- What is the importance of aerosol transmission? What is the effective distance of spread via droplet or aerosol?
- How effective are barriers such as N95 respirators or surgical masks?
- What is the appropriate PPE for first responders? Airport screeners?
- What are proper procedures for reducing spread and transmission rates in medical facilities?
- How effective are homemade masks at reducing transmission?

---

**CLEARED FOR PUBLIC RELEASE**
<table>
<thead>
<tr>
<th>SARS-CoV-2 (COVID-19)</th>
<th>Forensics – Natural vs intentional use? Tests to be used for attribution.</th>
</tr>
</thead>
</table>
| **What do we know?**  | All current evidence supports the natural emergence of SARS-CoV-2 via a bat and possible intermediate mammal species.  
• Genomic analysis places SARS-CoV-2 into the beta-coronavirus clade, with close relationship to bat coronaviruses. The SARS-CoV-2 virus is distinct from SARS-CoV-1 and MERS viruses.  
• Genomic analysis suggests that SARS-CoV-2 is a natural variant and is unlikely to be human-derived or otherwise created by "recombination" with other circulating strains of coronavirus.  
• Genomic data support at least two plausible origins of SARS-CoV-2: "(i) natural selection in a non-human animal host prior to zoonotic transfer, and (ii) natural selection in humans following zoonotic transfer." Both scenarios are consistent with the observed genetic changes found in all known SARS-CoV-2 isolates.  
• Some SARS-CoV-2 genomic evidence indicates a close relationship with pangolin coronaviruses, and data suggests that pangolins may be a natural host for beta-coronaviruses. Additional research is needed.  
• Additionally, "[...] SARS-CoV-2 is not derived from any previously used virus backbone," reducing the likelihood of laboratory origination, and "[...] genomic evidence does not support the idea that SARS-CoV-2 is a laboratory construct, [though] it is currently impossible to prove or disprove the other theories of its origin."  
• Work with other coronaviruses have indicated that heparan sulfate dependence can be an indicator of prior cell passage, due to a mutation in the previous furin enzyme recognition motif. |
| **What do we need to know?** | Identifying the intermediate species between bats and humans would aid in reducing potential spillover from a natural source.  
• What tests for attribution exist for coronavirus emergence?  
• What is the identity of the intermediate species?  
• Are there closely related circulating coronaviruses in bats or other animals with the novel PRRA cleavage site found in SARS-CoV-2? |
<table>
<thead>
<tr>
<th>SARS-CoV-2 (COVID-19)</th>
<th>Genomics – How does the disease agent compare to previous strains?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What do we know?</strong></td>
<td>Current evidence suggests that SARS-CoV-2 accumulates substitutions and mutations at a similar rate as other coronaviruses. Mutations and deletions in specific portions of the SARS-CoV-2 genome have not been linked to any changes in transmission or disease severity, though modeling work is attempting to identify possible changes.</td>
</tr>
<tr>
<td></td>
<td>• There have been no documented cases of SARS-CoV-2 prior to December 2019.</td>
</tr>
<tr>
<td></td>
<td>• Preliminary genomic analyses, however, suggest that the first human cases of SARS-CoV-2 emerged between 10/19/2019 – 12/17/2019.</td>
</tr>
<tr>
<td></td>
<td>• The mutation rate of SARS-CoV-2 is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be $1.04 \times 10^{-3}$ substitutions per site per year ($N = 116$ genomes).</td>
</tr>
<tr>
<td></td>
<td>• Pangolin coronaviruses are closely related to both SARS-CoV-2 and closely related bat coronaviruses. Phylogenetic analysis suggests that SARS-CoV-2 is of bat origin, but is closely related to pangolin coronavirus.</td>
</tr>
<tr>
<td></td>
<td>• The SARS-CoV-2 Spike protein, which mediates entry into host cells and is the major determinant of host range, is very similar to the SARS-CoV-1 Spike protein. The rest of the genome is more closely related to two separate bat and pangolin coronaviruses.</td>
</tr>
<tr>
<td></td>
<td>• Analysis of SARS-CoV-2 sequences from Singapore has identified a large nucleotide (382 bp) deletion in ORF-8. The effect of this deletion on transmission or virulence is unknown.</td>
</tr>
<tr>
<td></td>
<td>• A recent report of virus mutations within patients needs more research. Additional analysis of data suggests that the results may be due to experimental methods.</td>
</tr>
<tr>
<td></td>
<td>• Structural modeling suggests that specific changes in the genetic sequence of the SARS-CoV-2 Spike Protein may enhance binding of the virus to human ACE2 receptors. More specifically, changes to two residues (Q493 and N501) are linked with improving the stability of the virus-receptor binding complex.</td>
</tr>
<tr>
<td><strong>What do we need to know?</strong></td>
<td>Research linking genetic changes to differences in phenotype (e.g., transmissibility, virulence, progression in patients) is needed.</td>
</tr>
<tr>
<td></td>
<td>• Are there similar genomic differences in the progression of coronavirus strains from bat to intermediate species to human?</td>
</tr>
<tr>
<td></td>
<td>• Are there different strains or clades of circulating virus? If so, do they differ in virulence?</td>
</tr>
</tbody>
</table>
Table 1. Definitions of commonly-used acronyms

<table>
<thead>
<tr>
<th>Acronym/Term</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE2</td>
<td>Angiotensin-converting enzyme 2</td>
<td>Acts as a receptor for SARS-CoV, allowing entry into human cells</td>
</tr>
<tr>
<td>Airborne transmission</td>
<td>Aerosolization of infectious particles</td>
<td>Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)</td>
</tr>
<tr>
<td>ARDS</td>
<td>Acute respiratory distress syndrome</td>
<td>Leakage of fluid into the lungs which inhibits respiration and leads to death</td>
</tr>
<tr>
<td>Attack rate</td>
<td>Proportion of “at-risk” individuals who develop infection</td>
<td>Defined in terms of “at-risk” population such as schools or households, defines the proportion of individuals in those populations who become infected after contact with an infectious individual</td>
</tr>
<tr>
<td>CCV</td>
<td>Canine coronavirus</td>
<td>Canine coronavirus</td>
</tr>
<tr>
<td>CFR</td>
<td>Case Fatality Rate</td>
<td>Number of deaths divided by confirmed patients</td>
</tr>
<tr>
<td>CoV</td>
<td>Coronavirus</td>
<td>Virus typified by crown-like structures when viewed under electron microscope</td>
</tr>
<tr>
<td>COVID-19</td>
<td>Coronavirus disease 19</td>
<td>Official name for the disease caused by the SARS-CoV-2 virus.</td>
</tr>
<tr>
<td>Droplet transmission</td>
<td>Sneezing, coughing</td>
<td>Transmission via droplets requires relatively close contact (e.g., within 6 feet)</td>
</tr>
<tr>
<td>Fomite</td>
<td>Inanimate vector of disease</td>
<td>Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.</td>
</tr>
<tr>
<td>HCW</td>
<td>Healthcare worker</td>
<td>Doctors, nurses, technicians dealing with patients or samples</td>
</tr>
<tr>
<td>Incubation period</td>
<td>Time between infection and symptom onset</td>
<td>Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible</td>
</tr>
<tr>
<td>Infectious period</td>
<td>Length of time an individual can transmit infection to others</td>
<td>Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods</td>
</tr>
<tr>
<td>Intransal</td>
<td>Agent deposited into external nares of subject</td>
<td>Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.</td>
</tr>
<tr>
<td>MERS</td>
<td>Middle-East Respiratory Syndrome</td>
<td>Coronavirus with over 2,000 cases in regional outbreak since 2012</td>
</tr>
<tr>
<td>MHV</td>
<td>Mouse hepatitis virus</td>
<td>Coronavirus surrogate</td>
</tr>
<tr>
<td>Nosocomial</td>
<td>Healthcare- or hospital-associated infections</td>
<td>Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
<td>PCR (or real-time [RT] or quantitative [Q] PCR) is a method of increasing the amount of genetic material in a sample, which is then used for diagnostic testing to confirm the presence of SARS-CoV-2</td>
</tr>
<tr>
<td>PFU</td>
<td>Plaque forming unit</td>
<td>Measurement of the number of infectious virus particles as determined by plaque forming assay. A measurement of sample infectivity.</td>
</tr>
<tr>
<td>PPE</td>
<td>Personal protective equipment</td>
<td>Gowns, masks, gloves, and any other measures used to prevent spread between individuals</td>
</tr>
<tr>
<td>R₀</td>
<td>Basic reproduction number</td>
<td>A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.</td>
</tr>
<tr>
<td>SARS</td>
<td>Severe Acute Respiratory Syndrome</td>
<td>Coronavirus with over 8,000 cases in global 2002-2003 outbreak</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>Severe acute respiratory syndrome coronavirus 2</td>
<td>Official name for the virus previously known as 2019-nCoV.</td>
</tr>
</tbody>
</table>
### Acronym/Term | Definition | Description
---|---|---
Serial interval | Length of time between symptom onset of successive cases in a transmission chain | The serial interval can be used to estimate $R_0$, and is useful for estimating the rate of outbreak spread.
Superspreading | One individual responsible for an abnormally large number of secondary infections | Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections.
TCID$_{50}$ | 50% Tissue Culture Infectious Dose | The number of infectious units which will infect 50% of tissue culture monolayers. A measurement of sample infectivity.
Transgenic | Genetically modified | In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection.
Literature Cited:


8. (U) Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. *MMWR 2020*. [https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm?s_cid=mm6912e2_w#suggestedcitation](https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm?s_cid=mm6912e2_w#suggestedcitation)


10. (U) [Wuhan Pneumonia] The hospital authority stated that 2 critically ill patients needed external life support treatment. [https://www.singtao.ca/4037242/202001082020](https://www.singtao.ca/4037242/202001082020)

11. (U) AAAS, You may be able to spread coronavirus just by breathing, new report finds. *Science* 2 April, 2020.


19. (U) Assunção, M., Iceland’s coronavirus testing suggests 50% of cases have no symptoms. NY Daily News 01 April, 2020.


54. (U) Changzheng, L. J. L., Experts in the medical treatment team: Wuhan’s unexplained viral pneumonia patients can be controlled more. [https://www.cn-healthcare.com/article/20200110/content-528579.html](https://www.cn-healthcare.com/article/20200110/content-528579.html)


63. (U) Ćirić, J., Is Iceland’s coronavirus testing showing that 50% of cases have no symptoms? *Iceland Review* 02 April, 2020.

64. (U) Clifford, T., Eli Lilly CEO aims to start testing coronavirus cure ‘this summer’. *CNBC* 13 March, 2020.


68. (U) Cohen, J., Vaccine designers take first shots at COVID-19. AAAS 2020, 368 (6486), 14-16. [https://science.sciencemag.org/content/368/6486/14](https://science.sciencemag.org/content/368/6486/14)


74. (U) Daily, H., Wuhan Institute of Virology, Chinese Academy of Sciences and others have found that 3 drugs have a good inhibitory effect on new coronavirus. Chen, L., Ed. 2020. [http://news.cnhubei.com/content/20200128/content_12656365.html](http://news.cnhubei.com/content/20200128/content_12656365.html)


117. (U) Karamitros, T.; Papadopoulou, G.; Bousali, M.; Mexias, A.; Tsiodras, S.; Mentis, A., SARS-CoV-2 exhibits intra-host genomic plasticity and low-frequency polymorphic quasispecies. *bioRxiv 2020*, 2020.03.27.009480. [http://biorxiv.org/content/early/2020/03/28/2020.03.27.009480.abstract](http://biorxiv.org/content/early/2020/03/28/2020.03.27.009480.abstract)


130. (U) Lewis, D., Is the coronavirus airborne? Experts can’t agree. Nature 2020. 10.1038/d41586-020-00974-w


CLEARED FOR PUBLIC RELEASE

27


142. (U) Lowe, D., Hydroxychloroquine Update For April 6. (accessed April 7).


159. (U) Nadi, A., An at-home finger prick blood test may help detect your exposure to coronavirus. NBC NEWS 04 April, 2020.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7081066/
https://doi.org/10.1016/S2468-2667(20)30073-6
https://link.springer.com/content/pdf/10.1007/s00430-004-0219-0.pdf
177. (U) Regalado, A., Blood tests show 14% of people are now immune to covid-19 in one town in Germany. Technology Review 2020.
https://doi.org/10.1016/S0140-6736(20)30627-9


CLEARED FOR PUBLIC RELEASE
http://stm.sciencemag.org/content/early/2020/04/03/scitransmed.eabb5883.abstract


https://science.sciencemag.org/content/sci/early/2020/04/07/science.abb7015.full.pdf


https://www.biorxiv.org/content/biorxiv/early/2020/03/12/2020.03.11.987222.full.pdf


epidemic diarrhea virus in swine feces on metal surfaces. *Journal of Swine Health and Production* 2015, 23 (2), 84.


https://jamanetwork.com/journals/jama/articlepdf/2761044/jama_wang_2020_oie_200019.pdf


https://www.biorxiv.org/content/biorxiv/early/2020/03/27/2020.03.25.008482.full.pdf


**CLEARED FOR PUBLIC RELEASE**