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COVID-19: Current Response

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RESEARCH SUPPORT SERVICE

March, 2020

Intelligence Brief Question

What is the COVID-19 outbreak and how has it been tackled?

The COVID-19 pandemic is impacting the entire world in an unprecedented way. Collecting information on the COVID-19-causing virus, called the SARS-CoV-2 virus, how it changes, and how it acts will be crucial to understand how to developed strategies to manage the outbreak and ultimately tackle the virus.

In Part 1 of this Intelligence Brief, we present basic epidemiologic and biologic information on the SARS-CoV-2 virus: What are the current standards for treatment, diagnostics, and prevention?

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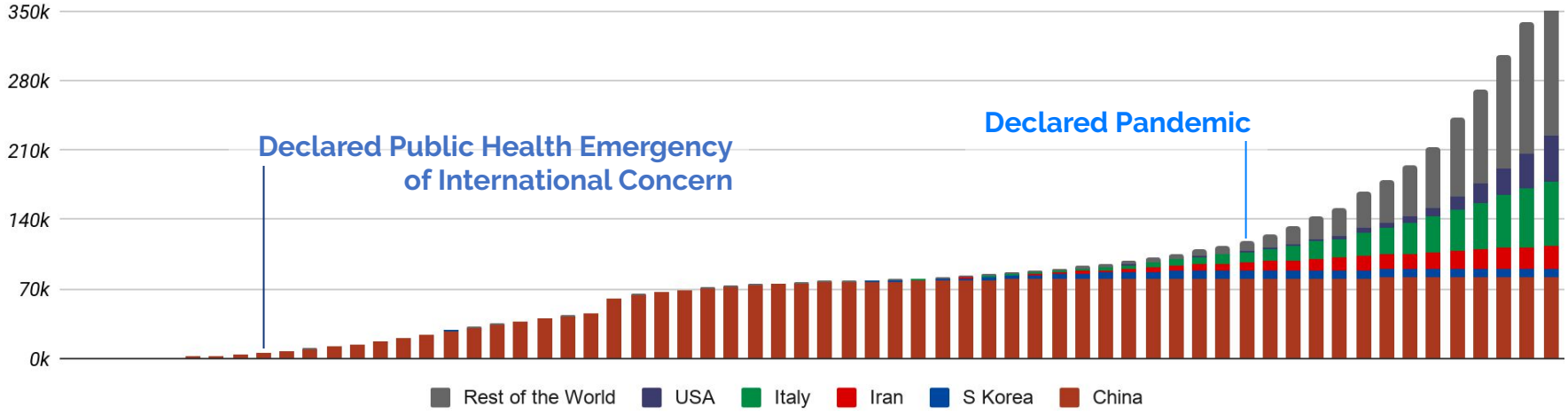
Executive Summary

The COVID-19 pandemic is already being described as the ***worst public health crisis in a generation***.

In the first 30 days of 2020, it went from ~50 confirmed cases to ~10,000 cases, mostly in China. It was then declared to be a public health emergency of international concern by the World Health Organization (WHO). Since then, it has jumped to more than **400,000 confirmed cases** across 193 countries and regions and **~18,000 fatalities**.

The current growth rate has the pandemic doubling in number of infected people every 7 days; the same applies for fatalities. What started as a Chinese problem quickly became a global crisis, with governments scrambling to contain the disease, gather key resources, and develop a cure.

COVID-19 confirmed cases evolution according to the European CDC



Executive Summary

What is the SARS-CoV-2 Virus?

SARS-CoV-2 is a positive-sense single-stranded RNA virus from the severe acute respiratory syndrome–related coronavirus species.

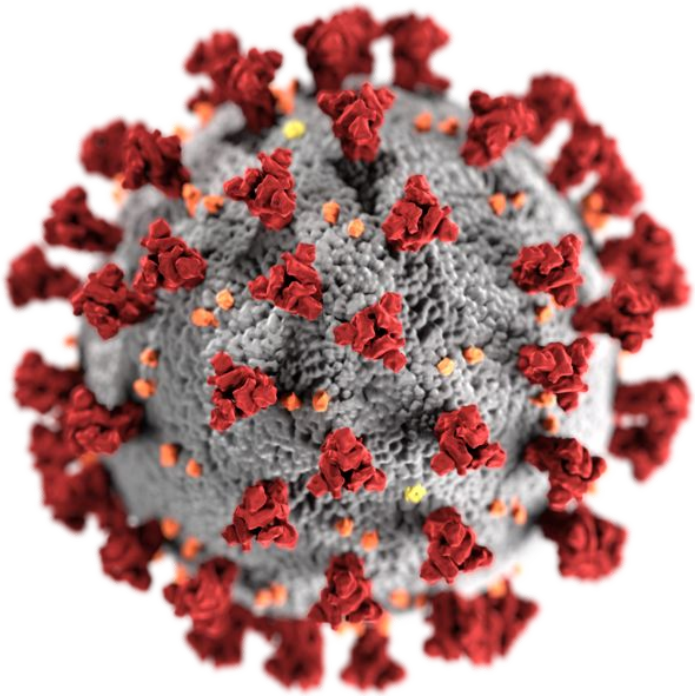
It emerged in China in December 2019, in a wet market of Wuhan.

Early studies demonstrated that SARS-CoV-2 binds a **membrane receptor** called human angiotensin converting enzyme 2 (hACE2).

hACE2 is expressed in different organs, such as the **lung, heart, kidney, and gastrointestinal tract.**

Once the virus binds and enters the host cell through the receptor, it **bypasses the host cell mechanisms and replicates**.

Cellular damage results either from the **virus that controls the host cell's mechanisms** or the **immune cells that kill the infected host cells, resulting in massive cell death**.



SARS-CoV-2 - Source: CDC

Executive Summary

Diagnosis:

Current guidelines from the WHO are for patients to be screened for the virus with a polymerase chain reaction (PCR)-based test (NAAT - nucleic acid amplification test).

Some initial studies reported that the approved assays had a sensitivity of 60-80%, often requiring a second test due to possible false negatives, particularly for suspect cases.

As such, computed tomography (CT) imaging is also often performed. As a chest CT scan with contrast takes about 40 minutes to perform, it has been utilized as a primary diagnostic tool to sort out suspected cases and predict severe complications such as acute respiratory diseases.

Manual NAAT-based tests are typically slow, requiring specialized equipment and personnel. They are not performed at the point of care (POC), potentially resulting in a turnaround time of several days for the results. Automated semi-POC or POC tests eliminate several of the pain points but are still typically slow and require expensive equipment.

The WHO's Global Research Forum that aims to identify research gaps and priorities for COVID-19 identified the development of a rapid point-of-care diagnostics for use at the community level as an immediate research need.

Executive Summary

There has been a strong response in regard to diagnosis development. **There are currently 96 manual and 30 automated NAAT assays commercialized, with at least 20 more in development.** The FDA just approved the first rapid near-POC NAAT assay from Cepheid on March 22, which can return results in just 40 minutes, but still requires specialized equipment that runs only one test at a time.

Only a fraction of automated NAAT assays are near point of care, with the majority still requiring lab processing. One notable exception is the **NINAAT from Self-Diagnostics**, initially developed for STDs, measuring less than 10 cm and returning results in just 30 minutes.

The greatest hope for rapid diagnostic test kits relies on immunoassays that detect the presence of anti-SARS-CoV-2 antibody levels (IgG and/or IgM). So far, there are over 70 such kits being commercialized, mostly from Chinese companies, with several others in development.

New assays need to be approved by each country's health authorities (a process that is a lot faster than drug approval under emergency status) and ramp up production to meet the current millions per day required around the world, which explains the shortage still felt by several countries.

A POC NAAT - NINAAT - *Self Diagnostics*

A rapid immunoassay - OnSite SARS-CoV-2 IgG/IgM Rapid Test, *CTK Biotech, Inc.*

A lab-based near-POC automated kit - QIAstat-Dx Respiratory Panel, *QIAGEN GmbH*

Executive Summary

Treatment:

There is no approved treatment for COVID-19. The current standard of treatment is to manage symptoms.

Several existing and new therapies are being investigated for treatment and prevention of COVID-19 - **we showcase 35 and highlight 2 in this report.**

Several of the world's major pharma and biotech companies have answered the call for a treatment with several antiviral drugs, vaccines, immunotherapies (mAB), and even cell therapies currently being developed.

One of the most promising drugs has been the antiviral drug **Remdesivir** from Gilead - initially developed for the Ebola virus. The drug has shown good antiviral activity against single stranded RNA viruses such as coronaviruses, inhibiting virus proliferation.

The number of COVID-19 studies registered so far:

468
Registered within the Chinese CT database

125
Registered within the FDA

REGENERON abbvie BAYER gsk GlaxoSmithKline SANOFI janssen PHARMACEUTICAL COMPANIES OF Johnson&Johnson GILEAD

Some of the companies currently working on a vaccine or therapy for COVID-19.

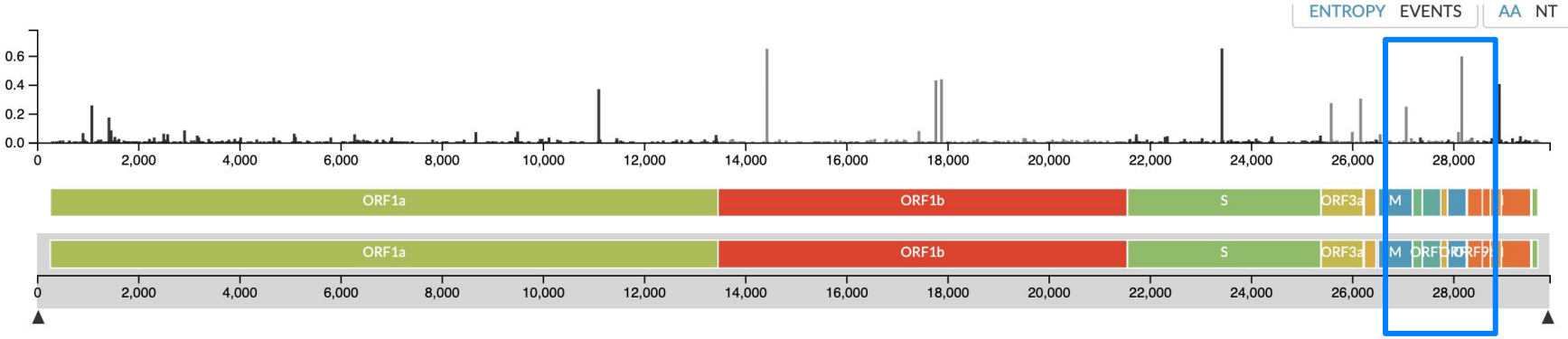
Executive Summary

Latest research in genomic information:

For the first time ever during a global outbreak, scientists are extensively using computational protein modeling and machine learning algorithms to identify viral protein targets and to predict which FDA-approved antiviral drug molecules can interact with SARS-CoV-2 proteins.

Major findings include:

1. A high sequence similarity (>99%) between all sequenced SARS-CoV-2 genomes available. This means that **a drug or vaccine would likely cover all of the strains thus far known.**
2. The spike protein (a major capsid) is highly similar to SARS-CoV, which means that **drugs and vaccines directed to SARS could be repurposed to target SARS-CoV-2.**
3. Despite the low heterogeneity of the SARS-CoV-2 genomes, at least two hyper-variable genomic hotspots were found (one is in the viral ORF8-encoded protein).



The genomic diversity plotted over the whole genome (numbers indicate nucleotide position) for all the 303 sequenced SARS-CoV-2 strains so far. One major variable region is ORF8. This region is thought to be involved in the suppression of the human immune system (blocking interferon gamma production). **Click here to access the interactive genomic database NextStrain.**

Executive Summary

The speed at which research moves against outbreaks has ramped up. Here's how the SARS-CoV-2 pandemic will have implications on future outbreaks:

1. Machine learning approaches identified possible antiviral drugs **within 2 weeks** of the publication of the first genome sequence. Several studies combined identified over **30 possible drug candidates**: The repurposing of FDA-approved drugs allows that some drugs can immediately be tested in patients and can immediately benefit treatment of the outbreak.

2. This is the first time that during an outbreak open access paper repositories are being used. All the newest, high-impact research is **immediately published** on sites such as bioRxiv before peer review. This increases the speed at which other scientists can build on findings dramatically.

3. Updates on genomic databases with tools to visualize and download genome and protein sequences are almost instantaneous, and the **newest sequencing tools** allow genome sequencing within a day. This greatly aids the mapping of mutations that might block the mode of action of certain drugs and can be analyzed *in silico*.

EPIDEMIOLOGY

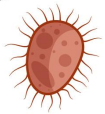
What is the coronavirus?

Coronaviruses (CoV) are a large family of viruses responsible for illnesses ranging from a normal cold to severe disease (Middle East Respiratory Syndrome or Severe Acute Respiratory Syndrome). CoV are **zoonotic**, meaning that they are transmitted between animals and people[5].

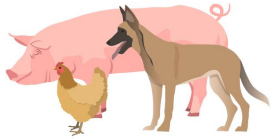
2019-novel Coronavirus (SARS-CoV-2) is a **new strain** that emerged in China in December 2019 in a wet market of Wuhan selling seafood and other animals (potential source of infection)[6]. New cases indicate a **human-to-human and asymptomatic transmission**[7].

On January 30, WHO declared a **Public Health Emergency of International Concern** (PHEIC) and on March 11, it classified the COVID-19 outbreak as a **pandemic**. As of March 23, **193 countries / territories / areas** have been affected.

1 Common host reservoirs/stock



Before infecting humans, viruses live in host animals.



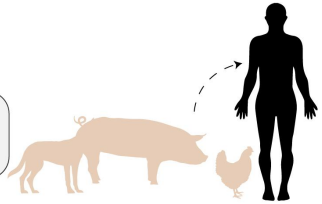
Studies on batCoV and hCoV genome suggested that in the case of Covid19, the host reservoir could be bats (1,2)

However, because the virus cannot directly infect humans, an intermediate host has been suggested: pangolins. Genome sequencing of the coronavirus from this species showed a high level of sequence identity (3)

99% similarity

2 Cross-species transmission

This occurs after direct contact with an infected animal or ingestion of contaminated food.



3 Human-to-human transmission

The virus in the population adapts and mutates to overcome barriers to infection leading to an outbreak. Movement (i.e. travelling) is an important fact in the spread of the virus (4)

Pathogenesis & how SARS-CoV-2 causes pneumonia

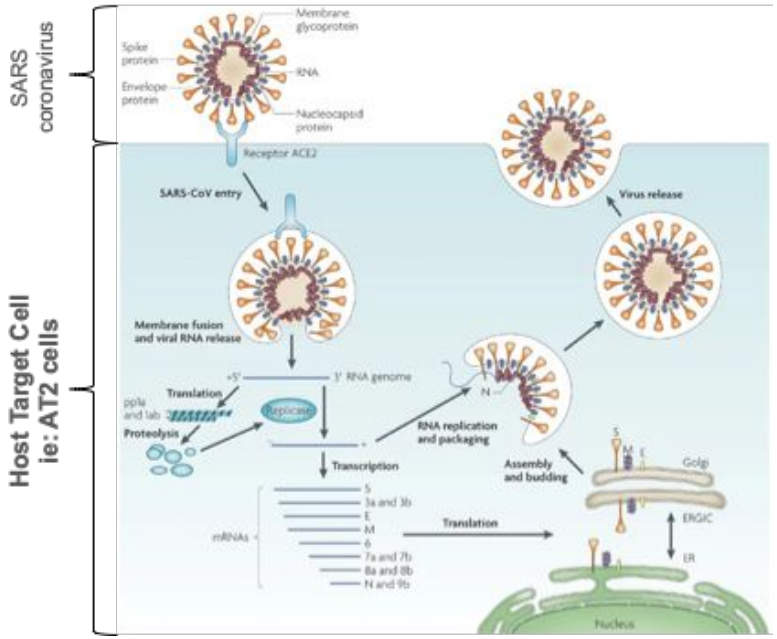
Scientists and health authorities are still retrospecting SARS-CoV-2 pathogenesis, although it is likely that this virus causes **direct viral damage** leading to disease up to death.

Early studies demonstrated that SARS-CoV-2 binds a **membrane receptor** called human angiotensin converting enzyme 2 (hACE2). hACE2 is expressed in different organs, such as the **lung, heart, kidney, and gastrointestinal tract** (why SARS-CoV-2 does not affect the heart is still unclear). This receptor is the same one that the SARS coronavirus uses to infect organs[8,9].

Once the virus binds and enters the host cell through the receptor, it **bypasses the host cell mechanisms and replicates**. Cellular damage results either from the **virus that controls the host cell's mechanisms** or the **immune cells that kill the infected host cells, resulting in massive cell death**[10].

A recent study showed that hACE2 is expressed in a **small population of cells in the lung (type II alveolar cells, AT2)**. SARS-CoV-2 could cause pneumonia in two ways[11,12]:

- by taking over the AT2 cells, leading to their death and consequently to a lung failure (pneumonia)
- by being associated with a secondary bacterial pulmonary infection (i.e., bacterial co-infection, as it has been shown for influenza, although there is no evidence so far for this explanation regarding SARS-CoV-2)



Symptoms, incubation period & mortality

The main symptoms are fever, cough, and shortness of breath. But people can also suffer from muscle ache, confusion, headache, bilateral pneumonia, and acute respiratory distress syndrome. These symptoms can worsen in a short period of time, leading to multiple organ failure and eventually death[13].

The incubation period can take anywhere from 2 to 14 days. A study dated March 10 showed the average incubation period to be 5.1 days (95% CI, 4.5 to 5.8 days), and 97.5% of those who develop symptoms will do so within 11.5 days (CI, 8.2 to 15.6 days) of infection, being in line with the current recommendation of 14 days as the isolation period.

Incubation period*: from 2 to 14 days (average 5.1 days)[30, 31]

Transmission Rate*: R0=2-3 (variable depending on the study or WHO report situation)

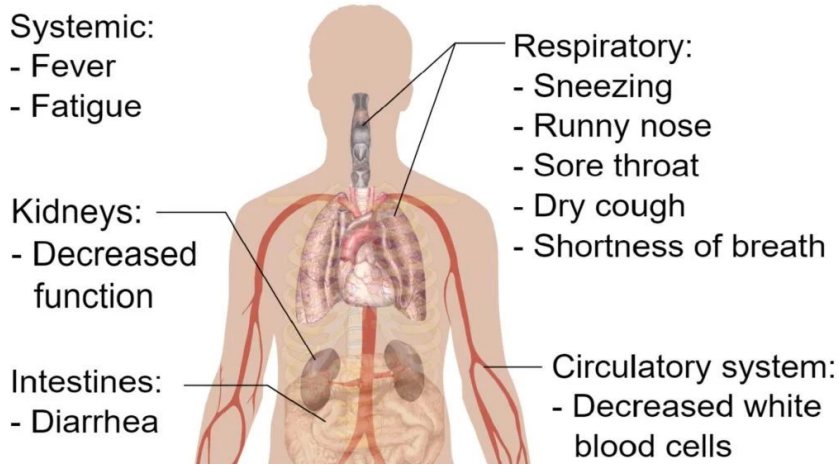
Case Fatality Rate:** CFR=15.3% (worldwide), 4.3% China.

Mortality Rate*:** 4.5% (worldwide), 4.0% China

**: estimation[14-16]*

Case Fatality Rate (CFR) = total death / (total death + total cured) - **high overestimation

****Mortality Rate = total deaths / total cases (open + closed) - likely overestimation due to low testing / asymptomatic patients.*

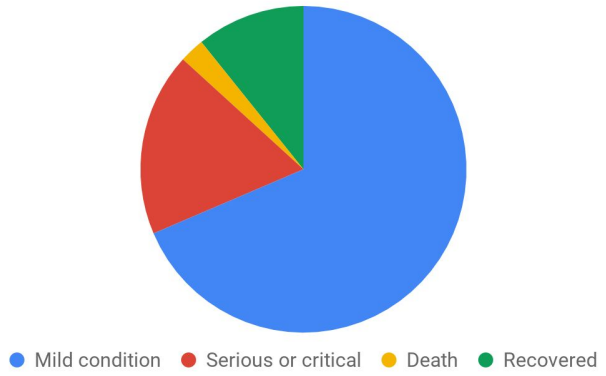


The potential symptoms for COVID-19. Photo: Mikael Häggström, M.D./WikiCommons

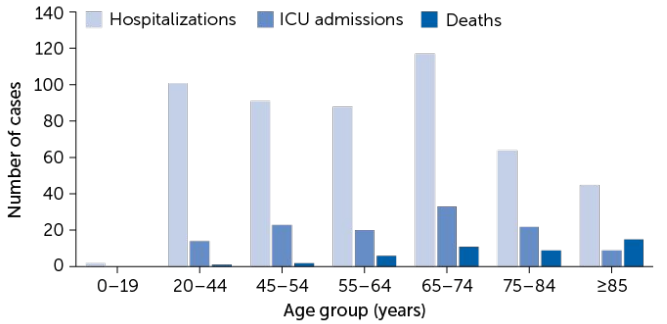
Symptoms, incubation period & mortality

The study of the first 17 deaths in China (to January 22) revealed that the **median days from first symptoms to death were 14**. These numbers can be shorter among people **older than 70**. In addition, these **older patients** and people with **pre-existing medical conditions** are more affected by the virus[17-19]. The majority of COVID-19 cases will be mild or even asymptomatic. Severe outcomes are more likely for people aged 65 and older; still, hospitalizations, ICU, and even deaths can happen in every age group.

Infected patient population breakdown



Severe outcomes of U.S. COVID-19 cases by age



Source: CDC

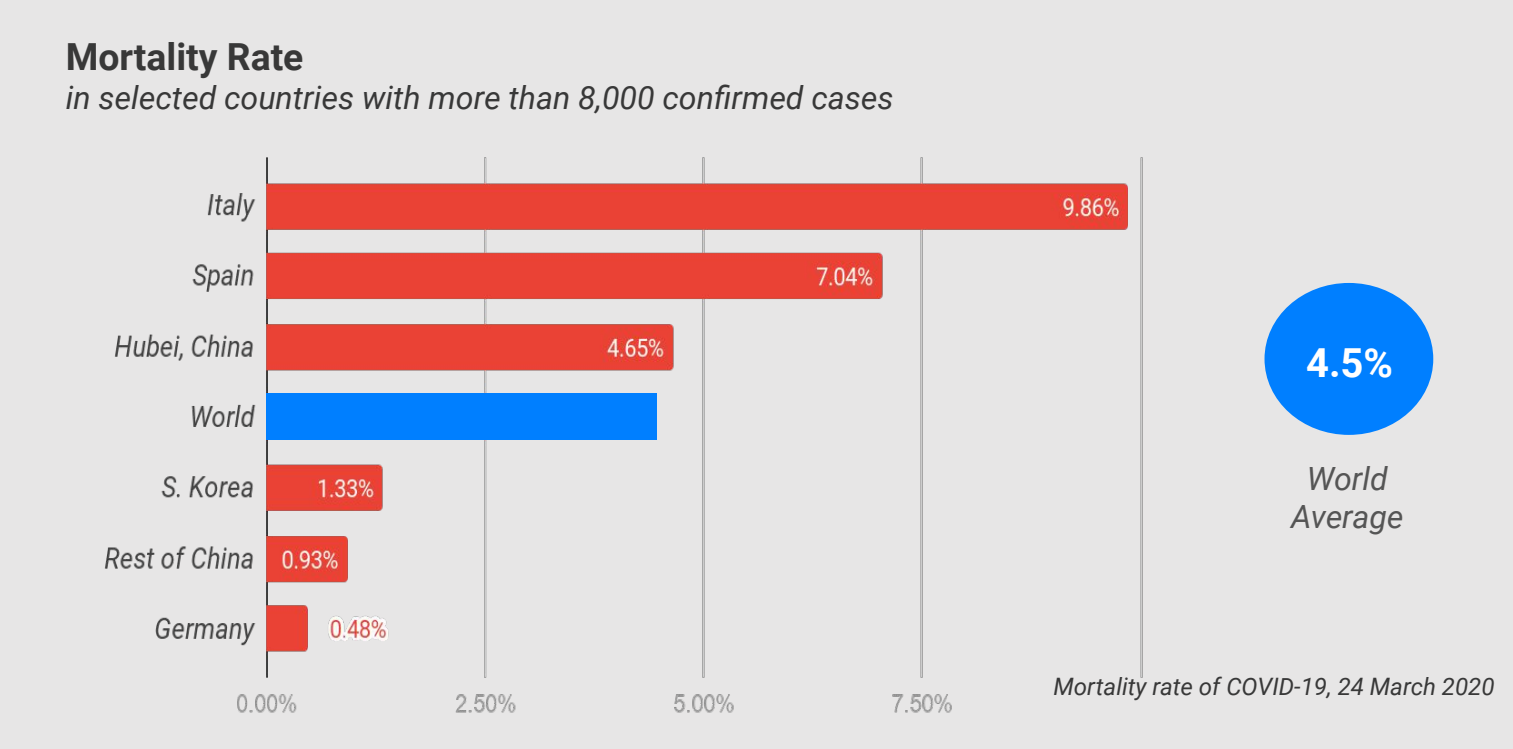
Among all patients, mild conditions are the majority. Public sectors and specialized organizations should focus on different patient populations.

Mild: *patient with fever, cough, and shortness of breath.*

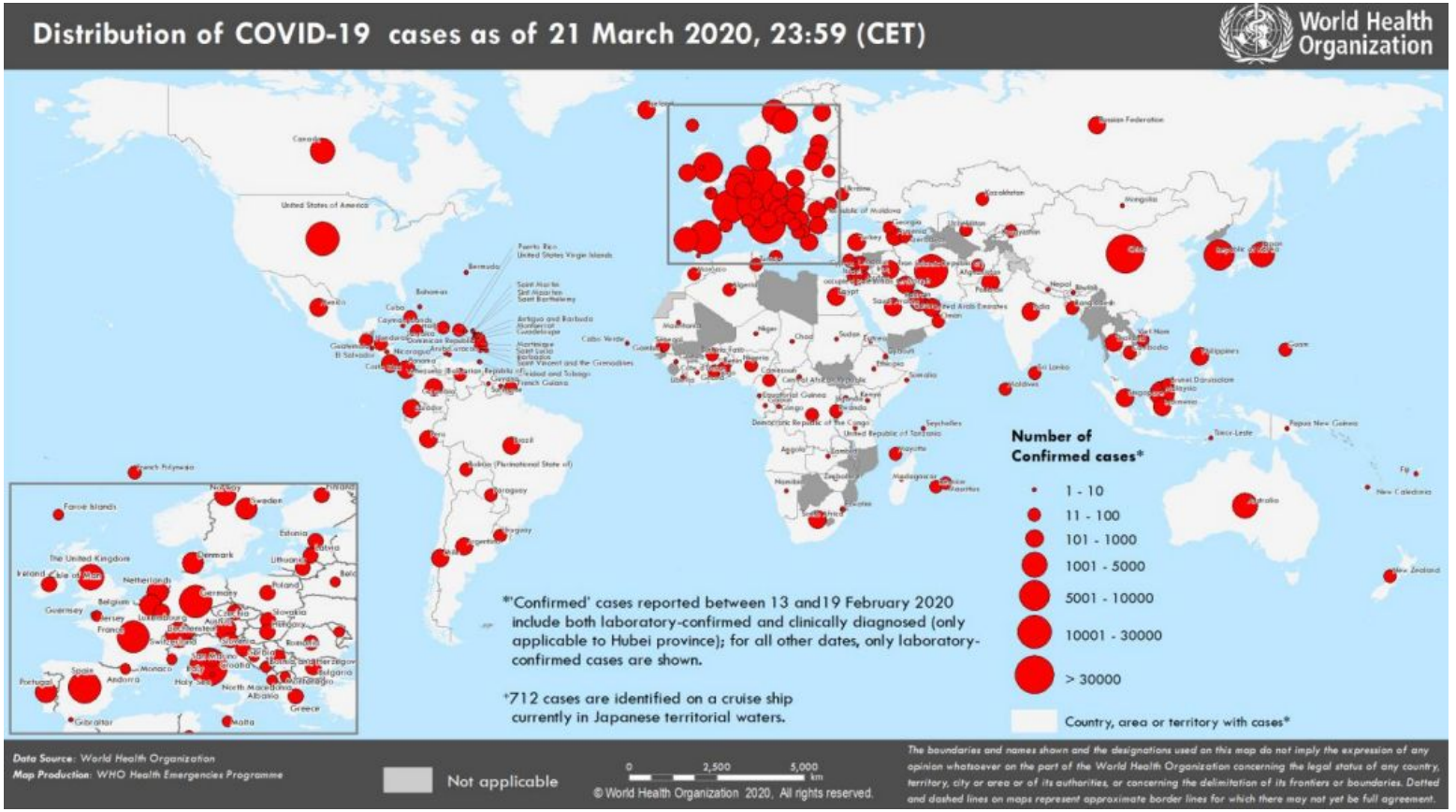
Severe: *patient with severe acute respiratory infection: severe pneumonia, acute distress respiratory syndrome, multiple organ failure, sepsis, and septic shock*

Symptoms, incubation period & mortality

The current 4.5% mortality rate reported worldwide is likely not representative of the true value. Not all countries have been testing extensively, and thus there is a bias toward testing and detecting the most serious cases. With that in mind, there has been a large disparity across different regions. Several countries show mortality rates below 1%. When the healthcare system is overburdened, not enough resources (e.g., intensive care, ventilators) will be available and the mortality can quickly rise, as was the case in Hubei, and later in Italy and Iran. **The lower mortality rates seen in some regions has been associated with the existence of enough hospital resources and containment strategies, showing the outbreak can be manageable.**



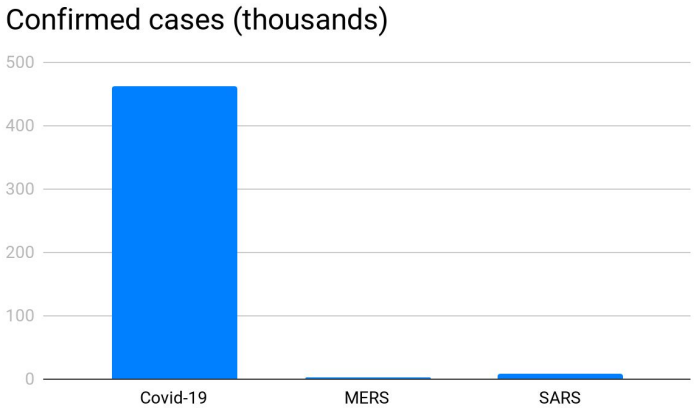
Patient population (geography)

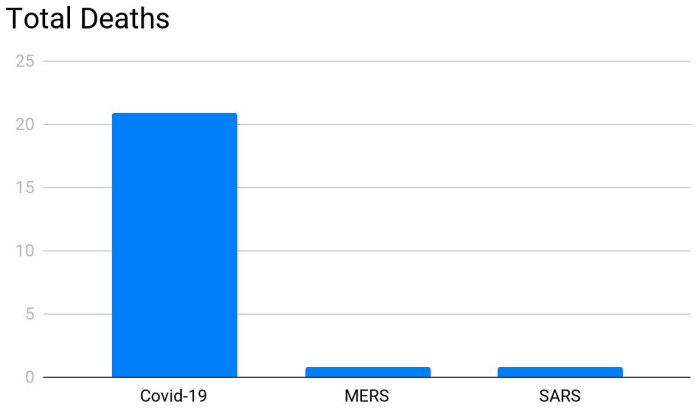


Countries, territories, and areas with reported confirmed cases of COVID-19, 22 March 2020

The WHO provides an updated daily visualization of SARS-CoV-2 distribution (above), but several other entities have been providing interactive maps and infographics as well. John Hopkins University put this visualization together that we recommend for up-to-date information.

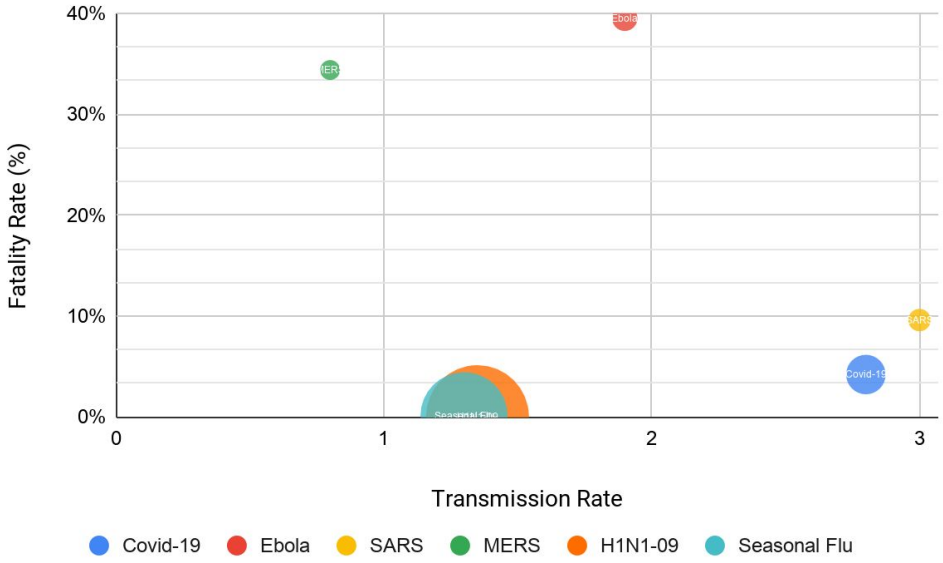
Virulence comparison with past virus outbreaks





Numbers updated on 18 March 2020

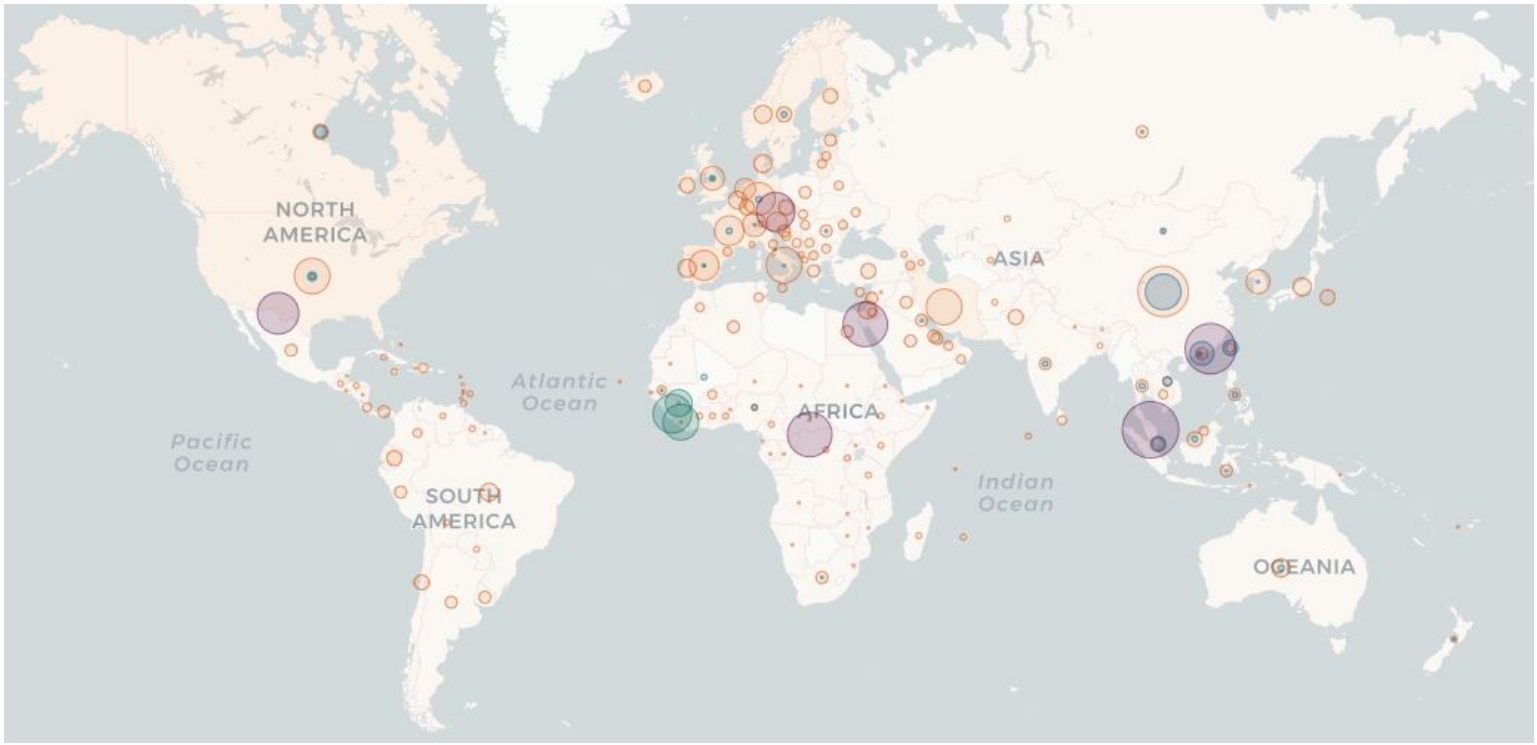
Although with a lower transmission rate, **SARS-CoV-2 has infected many more people in a shorter timeframe than coronavirus outbreaks such as SARS.** The fact that asymptomatic carriers can still be contagious has made containment very challenging across the world[16,20].



A comparison of the number of infected people, fatality rate, and transmission rate of Ebola, SARS, and SARS-CoV-2

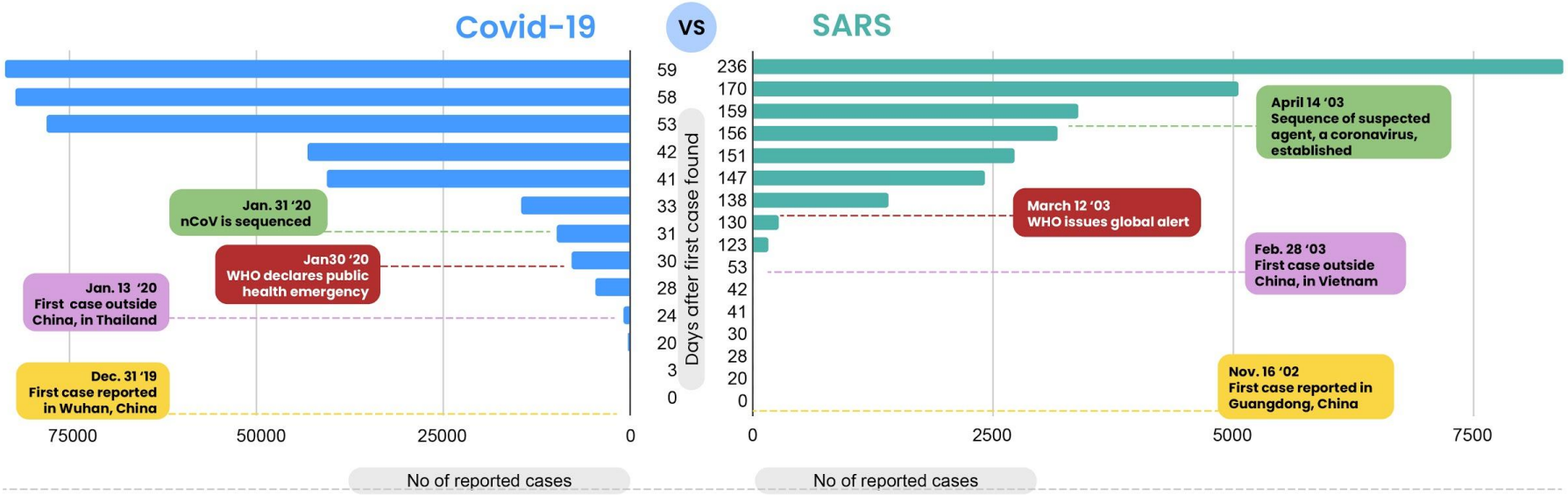
Comparison with past virus outbreaks

The last decade has seen several virus outbreaks that raised concern around the world. Ebola was one of the deadliest to date but was successfully geographically contained. On the other hand, SARS, with the virus closest to COVID-19, had a wider spread but was limited to a few localized outbreaks. This was thought to be the benchmark for COVID-19 in the first months after detection of the disease. The reality would be very different, with COVID-19 having now spread to virtually the entire world.



Source: https://vac-lshtm.shinyapps.io/ncov_tracker/

Timeline comparison of Initial Outbreak for COVID-19 & SARS



Covid-19 TIMELINE

Number of reported cases			
	First case reported in Wuhan, China	Dec. 31 '19	
44	Seafood market closed	Jan. 1 '20	
282	China identifies nCoV as outbreak cause	Jan 7 '20	
	First fatality	Jan. 9 '20	
	First case outside China, in Thailand	Jan. 13 '20	
	WHO reports human to human spread	Jan. 21 '20	
846	Reported in US, Japan and EU	Jan. 24 '20	
7818	WHO declares public health emergency	Jan. 30 '20	
9826	nCoV is sequenced	Jan. 31 '20	
14557	First death outside China, in Philippines	Feb. 2 '20	
43103	WHO assigns official name - COVID-19	Feb. 11 '20	
49053	First report in Africa (Egypt)	Feb. 14 '20	
83652	80k confirmed global infections with a death toll of 2.8k	Feb 28 '20	

SARS TIMELINE

			Number of reported cases
Nov. 16 '02	First case reported in Guangdong, China		
Feb 28 '03	First case outside China, in Vietnam	167	
March 11 '03	Hong Kong and Vietnam report outbreaks in hospital workers		
March 12 '03	WHO issues global alert	264	
March 19 '03	Reported in US and EU	1408	
March 27 '03	WHO issues travel advisories	2416	
April 5 '03	China admits coverup, SARS top priority	2722	
April 9 '03	Reported in Africa	3169	
April 14 '03	SARS sequenced	3389	
April 17 '03	Reported in India	5050	
April 28 '03	Virus contained in Vietnam	8439	
July 3 '03	Last case reported in China		

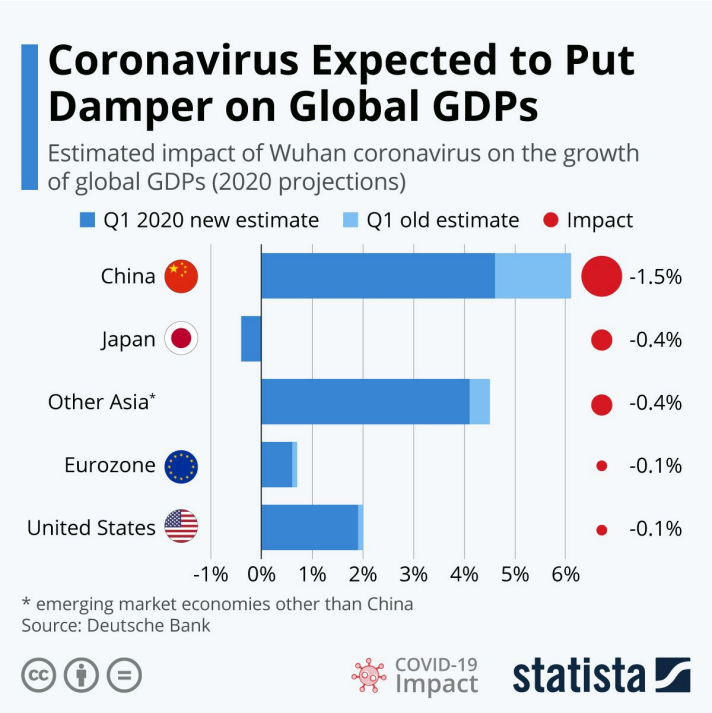
Economic impacts of the COVID-19 outbreak

The economic impact of the outbreak will depend on its duration and its severity. The consequences likely be unprecedented and widely surpass what was observed in other main outbreaks (SARS, MERS, H1N1).

While the initial concerns were focused on decrease travel demand and potential disruptions on the supply chain from China, as the outbreak spread and isolation measures became commonplace, hardly any industry will be left unscathed.

The stock market has already been seriously affected with major indexes (Dow, S&P 500, Nasdaq, FTSE 100) all losing more than 25% in value in the month since February 18th.

The Director of the Division on Globalization and Development Strategies at the United Nations Conference on Trade and Development announced that the outbreak could cost the global economy up to **$2 trillion** this year in March 9th. The OCDE also announced that global GDP growth could plummet to almost half of the initially 2.9% forecasted, the lowest since 2008-09 financial crisis and lower than the dot-com crash in 2000-2001.



Source: Statista[29]

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CURRENT STANDARD OF CARE

DIAGNOSIS

Methods used to diagnose patients

Nucleic acid amplification tests (NAAT)[1,2]

According to the latest guidance for laboratory testing of SARS-CoV-2 in suspected human cases issued by WHO, patients who meet the case definition for suspected COVID-19 should be screened for the virus with polymerase chain reaction (PCR). Confirmation of cases of the novel virus infection will be based on specific detection of unique sequences of viral nucleic acid by **reverse transcriptase polymerase chain reaction (RT-PCR)**, which is generally called a **nucleic acid amplification test (NAAT).**

Different companies currently provide the primers required to conduct the NAAT assay at **$5-$10 per test,** and the technique can deliver results within **4 hours**. Still, commercial solutions available to patients can cost thousands of dollars and take several days, as samples need to be collected, stored, and transported to an approved diagnostic center.

Example of commercial primers being sold to detect SARS-CoV-2 Source: Genesig.

Those with one of the following pathogenic evidence is a confirmed case:
(1) Positive to a validated specific SARS-CoV-2 nucleic acid test or,
(2) has the virus identified by electron microscopy or viral culture.

Methods used to diagnose patients

Nucleic acid amplification tests (NAAT)[1,2]

Limitations:

1. **Non-optimal specimens**. Analysts should be trained and familiar with testing procedures and interpretation of results prior to performing the assay. There is still only limited information about the best point in time for specimen collection.
2. **Error during collection, transport, or handling.** A false negative result may occur if inadequate numbers of organisms are present in the specimen due to improper collection, transport, or handling. Specimens should be kept at 2-4°C (≤4 days) or frozen at -70°C or below.
3. **Genetic variability of RNA viruses.** Although efforts were made to design RT-PCR assays to conserved regions of the viral genomes, variability resulting in mis-matches between the primers and probes and the target sequences can result in diminished assay performance and possible false negative results.

Nucleic acid amplification tests cannot be relied on alone.

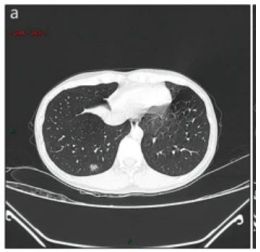
While results are still scarce, initial studies place RT-PCR sensitivity at 66-80%. For emergency cases in Hubei, lack of testing kits, testing staff, kit performance, and NAAT limitations all lead to difficulty of diagnosis. The epidemiological history of patients, common signs of infection including respiratory symptoms, fever, cough, and breathing difficulties, as well as clinical manifestation through chest imaging and blood tests need to be considered comprehensively for early diagnosis and effective control of nCoV infection.

Methods used to diagnose patients

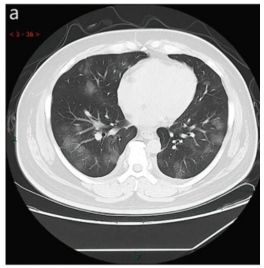
Computed tomography (CT) imaging[3,4]

Computed tomography (CT) imaging, a routine imaging tool for pneumonia diagnosis, is fast and relatively easy to perform. A chest CT scan with contrast takes about 40 minutes. It has been utilized as a **primary diagnostic tool to sort out suspected cases and predict severe complications** such as acute respiratory diseases. According to clinical data from Zhongnan Hospital of Wuhan University, CT imaging demonstrates 5 stages according to the time of onset and the response of body to the virus: ultra-early stage, early stage, rapid progression stage, consolidate stage, and dissipation stage, with characteristics of viral pneumonia showing ground-glass opacity and bilateral patchy shadowing.

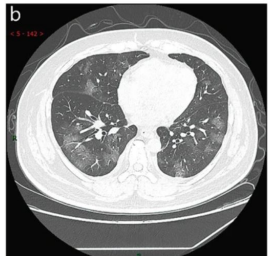
In general, costs of a CT ranges from **$270 to nearly $5,000**, depending on the facility, location, and factors such as method of payment (direct, subsidized, insurance, etc.).



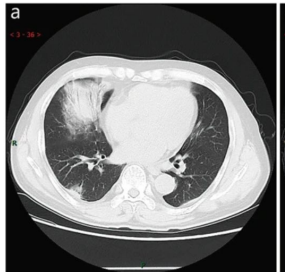
a. Ultra-Early Stage



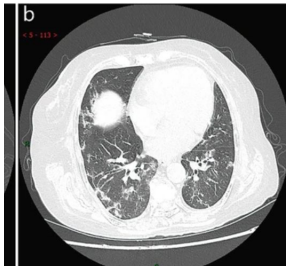
b. Early Stage



c. Rapid Progression Stage



d. Consolidate Stage

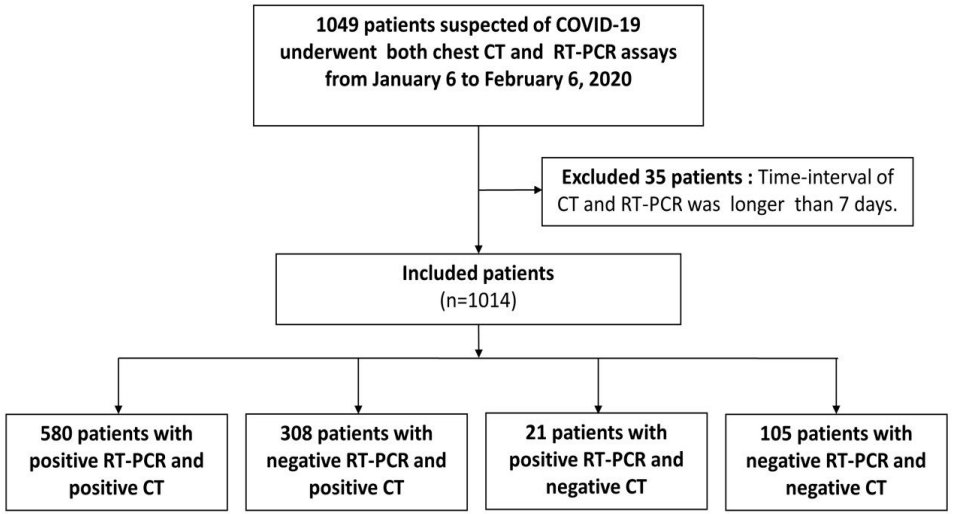


e. Dissipation Stage

Methods used to diagnose patients

Diagnostic value and consistency of CT compared with NAAT (RT-PCR) testing[5,6]

1. The positive rates of RT-PCR assay and chest CT imaging in this study were 59% (601/1014), and 88% (888/1014) for the diagnosis of suspected patients with COVID-19, respectively.
2. With RT-PCR as a reference, the sensitivity of chest CT imaging for COVID-19 was 97% (580/601). In patients with negative RT-PCR results but positive chest CT scans (n=308 patients), 48% (147/308) of patients were re-considered as highly likely cases, with 33% (103/308) as probable cases by a comprehensive evaluation.
3. With analysis of serial RT-PCR assays and CT scans, 60% to 93% of patients had an initial positive chest CT consistent with COVID-19 before the initial positive RT-PCR results. 42% of patients showed improvement of follow-up chest CT scans before the RT-PCR results turning negative.



A study of chest CT in comparison to the initial and serial RT-PCR results in 1014 patients with suspected COVID-19. Source: Radiology

Chest CT has a higher sensitivity for diagnosis of COVID-19. A single negative RT-PCR should not exclude COVID-19 if clinical suspicion and positive chest CT. Availability of chest CT for diagnosis should be expanded.

Methods used to diagnose patients

Summary table of available protocols suggested by WHO[7]

Country	Institute	Gene targets
China	China CDC	ORF1ab and N
Germany	Charité	RdRP, E, N
Hong Kong	HKU	ORF1b-nsp14, N
Japan	National Institute of Infectious Diseases, Department of Virology III	Pancorona and multiple targets, Spike protein
Thailand	National Institute of Health	N
U.S.	US CDC	Three targets in N gene

World Health Organization

Overview of all SARS-CoV-2 tests in development for the diagnosis of COVID-19: WHO convened a forum to identify research gaps and priorities for COVID-19, co-hosted by GloPID-R, due to the urgent need for access to accurate and standardized diagnostics for SARS-CoV-2. An overview of all SARS-CoV-2 tests in development for the diagnosis of COVID-19 can be found here with their current status addressed.

Methods used to diagnose patients

WHO appointed COVID-19 referral laboratories for NAAT testing[8]

Country	Referral laboratories for COVID-19
China	China CDC (TBD), School of Public Health, University of Hong Kong
EU	https://www.ecdc.europa.eu/en/novel-coronavirus/laboratory-support
UK	Public Health England
Japan	Institute of Tropical Medicine, Nagasaki University (WHOCC for Reference and Research on Tropical and Emerging Viral Diseases)
Thailand	National Institute of Health, Department of Medical Sciences, Ministry of Public Health
US	Respiratory Viruses Diagnostic Laboratory, US-CDC

Methods used to diagnose patients

WHO appointed COVID-19 referral laboratories for NAAT testing[8]

Country	National specialized laboratory for COVID-19
Singapore 	National Public Health Laboratory
Australia 	Victorial Infectious Diseases Reference Laboratory
India 	ICMR - National Institute of Virology
South Africa 	Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases
Senegal 	Institut Pasteur Dakar
Russia 	The State Research Center of Virology and Biotechnology VECTOR

TREATMENT

Strategies to cure/treat/manage patients' symptoms

Additional information

Ideally, infected patients should be treated with a customized treatment plan. However, currently, no specific antiviral therapies are available for COVID-19. **Citing information from WHO, the data suggests that 80% of infections are mild or asymptomatic, 15% are severe and require oxygen, and 5% are critical, requiring ventilation[9,10].**

For mild infections: Supportive treatment to help relieve symptoms through plenty of rest, drinking fluids, and over-the-counter (OTC) medicines for pain, fever, and cough. Although it is recommended to treat patients in an isolated hospital setting, in emerging conditions treatment at home is allowed.

For severe cases (severe acute respiratory infection/SARI): Optimized supportive care for supporting vital organ functions, and infection prevention and control (IPC) are needed. Treatment must be performed in the hospital setting.

Strategies to cure/treat/manage patients' symptoms

Guidelines suggested by WHO[9] in its latest report on clinical management of severe acute respiratory infection when 2019-nCoV infection is suspected:

1. Triage: recognize and sort patients with **SARI**
2. Immediate implementation of appropriate infection prevention and control (IPC) measures
3. Early supportive therapy and monitoring (supplemental oxygen therapy, conservative fluid management, empiric antimicrobials, etc.)
4. Collection of specimens for laboratory diagnosis (blood cultures, specimens from both the upper respiratory tract and lower respiratory tract)
5. Management of hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS)
6. Management of septic shock
7. Prevention of complications
8. Specific anti-nCoV treatments
9. Special considerations for pregnant patients

PREVENTION

Strategies used to prevent people from infection

Suggested by World Health Organization

It has been suggested by WHO[11] to globally adopt the following strategies for infection prevention and control in the latest infection prevention guidance report:

1. Ensuring triage, early recognition, and source control (isolating patients with suspected SARS-CoV-2 infection)
2. Applying standard precautions for all patients
3. Implementing additional empirical precautions (droplet, contact, and, whenever applicable, airborne precautions) for suspected cases of SARS-CoV-2 infection
4. Implementing administrative controls
5. Using environmental and engineering controls

The UN health agency's major concern is that the virus could reach countries without the capacity to detect infections. Urgent support is needed to bolster weak health systems to detect, diagnose, and care for people with the virus to prevent further human-to-human transmission and protect health workers.

WHO has been very vocal in asking affected regions to take the outbreak seriously and apply serious containment measures to prevent further spreading of the disease. Several countries are now following WHO guidelines.

Strategies used to contain outbreak

Summary - China & Other Countries[11]

Country	Confirmed cases (as of Mar 24)	Death cases (as of Mar 24)	Recovered cases (as of Mar 24)
China	81,171	3,277	73,159
Rest of the World	327,703	14,983	33,913

China has taken very strong measures in order to block the spread of the epidemic:

1. **Effective quarantine.** Wuhan, a city of over 10 million, was placed under quarantine starting January 23 by restricting air, rail, and road access, followed by other cities in Hubei province, encompassing a total of over 40 million people.
2. **Delay of work and school.** Enterprises in Hubei province were closed until Feb 13. Enterprises outside Hubei province were closed until Feb 9. Online courses were introduced to primary and high schools.
3. **Port-of-exit screening.**
4. **Strengthen medical supplies.** Two notable examples of speed and efficiency include the construction of the 1000-bed Huoshenshan Hospital and the 1600-bed Leishenshan Hospital in Wuhan, both built in under 10 days.

Strategies used to contain outbreak

Summary - Western Pacific & South East Asia[13,14]

Country	Measures
Japan 	Government has announced measures to contain the spread.
South Korea 	The president put the country on “red alert”. No lockdown so far. Active cases being tracked
Vietnam 	Restaurants closed
Malaysia 	2 week partial lockdown
Singapore 	Shutdown borders to tourists and short-term visitors
Thailand 	State of emergency declared - stronger measures to be announced

Strategies used to contain outbreak

Summary - Western Pacific & South East Asia Region[13,14]

Country	Measures
Indonesia 	Asked people to self isolate and work from home when possible. Police to disperse public gatherings.
India 	Nationwide lockdown.
Philippines 	Placed half the country on *Enhanced community quarantine* - lockdown.
Australia 	Non-essential stores and activities shutdown. Citizens told to self-isolate.
New Zealand 	State of emergency declared.

Strategies used to contain outbreak

Summary - European Region[15-17]

Country	Measures
Spain	Nationwide lockdown.
Germany	School closures, strict social distancing measures in place.
France	Nationwide lockdown.
Switzerland	State of emergency declared
Italy	Nationwide lockdown.
Russia	Shutdown borders, limited air travel, closing schools, economic stimulus.
Denmark	Events with more than 100 people are banned. Entered phase of “domestic lockdown.”
Sweden	Travel ban plus economic measures.
UK	Nationwide lockdown.
Netherlands	Partial lockdown announced until June.
Austria	Outdoor events with more than 500 people are banned. People advised to work from home. Banned arrivals from main infection focus.

Strategies used to contain outbreak

Summary - Region of the Americas[18,19]

Country	Measures
US 	Population advised to work from home when possible. Several businesses / schools / cities shut down. Travel restrictions.
Canada 	Only 4 airports remain open. Travel restrictions for foreigners. Closed border with the US.
Brazil 	The country's authorities are ramping up measures to attempt to control the spread.
Chile 	The country's authorities are ramping up measures to attempt to control the spread.
Diamond Princess Cruise ship 	Failed quarantine. CDC urged additional travel restrictions and quarantine measures for passengers after assessing the situation.

Strategies used to contain outbreak

Summary - Eastern Mediterranean Region[18,20]

Country	Measures
Iran	School closures and travel bans. Quarantine measures failing.
Qatar	School closures and travel bans.
Bahrain	School closures and travel bans.
Kuwait	School closures and travel bans.
Saudi Arabia	School closures and travel bans within country imposed.
Egypt	School closures and travel bans. Night curfew imposed.
Lebanon	Nationwide lockdown. Stay at home order in place.
United Arab Emirates	School closures and travel bans. Emirates Airlines suspends passenger flights.
Syria	School closures, night curfew imposed.

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KEY PROTECTIVE EQUIPMENT

Calling for key protective equipment suppliers worldwide

Summary

To help contain and properly deal with the crisis, the following key protective equipment has been put to use, mostly by health professionals across the world, but also by the infected and the general public. This created a high demand and resulted in shortages for a lot of these. Below are some of the key types of equipment. In this section, a summary of the types of equipment and the standards are provided[1].

Respirators	N95 Respirator (disposable) or surgical mask for medical staff as daily work protection KN95 Respirator (disposable) for medical staff or general public
Protection Suits	Medical protective clothing - Surgical isolative gown Surgical drapes, gowns, and clear air suits
Protective masks/Goggles	Eye and face protection for medical protection Medical goggles for protecting medical staff in treatment
Protective Accessories	Single-use medical protective hood (thicked cap) Single-use latex gloves for medical use
Thermometers	Infrared forehead thermometer
Disinfectants	Ethyl alcohol (70%), Chloroxylenol (0.12%), Alcohol-based hand sanitizer, etc.

Key protective equipment & main suppliers

N95 Respirator (disposable) or surgical mask[2,3]
Type: Surgical mask
Standard: CNS 14774 - general medical mask, China GB 19083, EN 14683 Type I, EN 14683 Type II, EN 14683 Type IIR, Europe EN 149 FFP3, GOSTR 58396 type HR, GOSTR 58396 type I, GOSTR 58396 type II, Premarket notification 510K submission, Taiwan CNS 14774 Surgical Mask Level 2, USA ASTM F2100 level 2, USA ASTM F2100 level 3, USA NIOSH N95, YY 0469, YY/T 0969
Uses: This type of mask is used by medical staff as daily work protection. It can also be used by the general public during the special (new coronavirus) period. It can filter ≥95% of non-oily particles and effectively block particles, droplets, blood, body fluids, secretions, etc. Recommended for medical staff as daily work protection.
Main Suppliers: Winner Medical Group, Ogilvy Medical, 3M, Halyard Health, Honeywell

Key protective equipment & main suppliers

KN95 Respirator (disposable)[2,3]
Type: Civilian mask
Standard: Aus AS/NZS 1716 P2, China GB 2626 KN 100, China GB 2626 KN 95, China GBT/T 32610 Protection level A / filtration efficiency level I, Europe EN 149 FFP2, GOST R 12.4.294 FFP2, Japan JIS T 8151-2005 DS2(PFE antibacterial), Korea MFDS standard KF 94, USA NIOSH standard N95, USA NIOSH standard N99
Uses: This respiratory protective mask gives protection for special occupations and the general public. It can filter ≥94% of non-oily particles, effectively block particles, droplets, body fluids, etc. Recommended for the general public presenting COVID-19 symptoms
Main Suppliers: 3M, Honeywell, UVEX, Schimer, SG Health, Dettol

Key protective equipment & main suppliers

Eye and Face Protection for medical protection[2,3]
Type: Medical protective mask
Standard: China GB 14866, Europe EN 166, ISO 4849, Japan JIS T8147, USA ANSI Z87.1
Uses: This type of equipment works well to protect medical staff in the following situations: 1. Blood, body fluids, secretions of patients may be splashed when medical staff is in treatment and nursing operations; 2. When medical staff is in close contact with patients with infectious diseases transmitted by droplet; 3. Blood, body fluids, secretions of patients may be splashed when medical staff performs tracheotomy and tracheal intubation for patients with respiratory infections
Main Suppliers: Shanghai Xiangxu Industrial Development Co. Ltd

Key protective equipment & main suppliers

Medical Goggles for protect medical staff in treatment[2,3]
Type: Medical goggles
Standard: China GB 14866, Europe EN 166, ISO 4849, Japan JIS T8147, USA ANSI Z87.1
Uses: This type of equipment works well to protect medical staff in the following situations: 1. Blood, body fluids, secretions of patients may be splashed when medical staff is in treatment and nursing operations; 2. When medical staff is in close contact with patients with infectious diseases transmitted by droplet.
Main Suppliers: 3M, Honeywell

Key protective equipment & main suppliers

Single-use medical protective hood (thicked cap)[2,3]
Type: Protective cap
Standard: China YY/T 1642
Uses: Used for medical staff, disease control, and epidemic prevention workers in contact with potentially infectious pollutants.
Main Suppliers: ULINE

Key protective equipment & main suppliers

Medical protective clothing - Surgical isolative gown[2,3]
Type: Medical protective clothing
Standard: ANSI/AAMI PB70-2012, China GB 19082, China WSB 58-2003, EN 14126, JIS T 8060 8061 8062, USA NFPA 1999
Uses: Disposable protective clothing provides barrier and protection for medical personnel in contact with blood, bodily fluids, secretions of potentially infectious patients.
Main Suppliers: Dupont, 3M, Winner Medical Group, Xiangsen Medical, Lakeland Industries

Key protective equipment & main suppliers

Surgical drapes, gowns, and clear air suits[2,3]
Type: Surgical gowns / sheets
Standard: China YY/T 0506.1 & 0506.2, Europe EN 13795, USA ANSI/AAMI PB70-2012
Uses: These prevent the spread of infectious agents between patients and healthcare workers during surgery and other invasive examinations. They can also be used as single-use medical surgical sheets and surgical gowns for patients, medical staff, and instruments.
Main Suppliers: Dupont

WORLD DEMAND

Protective equipment demand

Introduction

There have been two main shortages of equipment associated with the COVID-19 outbreak. The first has been in hospital critical care equipment, mainly ventilation units. The second has been in protective equipment. China reported a respirator shortage early on, even though the country is one of the main producers.

As the pandemic expanded into the Western world, the message from WHO and governments was clear: Respirators should only be used by the infected and medical professionals. The main reason behind the advice is the fact that there are not enough respirators to support healthcare professionals. There have been reports of doctors and nurses having to reuse protective equipment or simply running out. Governments have put in requests and different players have responded to try to bring production up to par with demand.

China - protective equipment demand

Protective equipment demand estimation[1,2]

There are an estimated 500,000 medical staff across the Hubei province alone. Medical advice in China is to change face masks regularly, as often as four times a day. Hence, medical teams in Hubei would require about 2 million masks each day. Given the infected population in Hubei and other parts of China, it is estimated there is at least another 0.5 million masks needed for medical usage per day (proportional to the number of infected population).

For non-medical use, if 1% of the Chinese population needs a mask each day, it would add another 14 million demand. In total, the demand of masks is no less than 16 million per day. **It is reported that 50-60 million masks are needed each day in China.**

It is also predicted that the number of infected people in Wuhan alone would to be greater than 190 thousand (prediction interval, 132,751 to 273,649), while the Ministry of Industry and Information Technology in Beijing estimated that Hubei province alone was in need of 100,000 pieces of protective clothing and equipment every day. Using the same estimation method, other parts in China need 20 thousand pieces of protective clothing and equipment each day. That is 360 thousand per month.

It is estimated that **50- 60 million** masks are needed per day in China. Among them, at least **2.5 million N95 respirators** are needed for medical use per day.

China - protective equipment supply

Protective equipment supply situation[3-7]

There are approximately 40 manufacturers in China capable of producing 20 million masks daily, and currently running at a ~60% capacity, according to authorities. However, only ~600,000 high-quality N95 masks can be produced per day. N95 masks are capable of preventing the inhalation of 95% of particles and are widely recommended for medical workers. Despite these numbers, there is still a huge demand in China for masks, wIth the suppliers from overseas importing an average of 56 million masks to China per week (8 million per day). The daily supply is still under 30 million masks per day.

Compared with the daily demand (50-60 million surgical masks and 2.5 million N95 masks per day), there is still a gap of 20 million masks and 2 million N95 masks to fill.

It is estimated that the demand for at least **20 million masks and 2 million N95 masks** are not met by Chinese domestic supply per day.

Major personal protective equipment (PPE) suppliers:

- Ak-Yel Medikal Company from Turkey
- Kukje Pharma from South Korea
- Many US private sector companies and foundations, such as Pfizer, Eli Lilly, Grandstream Networks, 3M, and Amazon

Rest of the World - demand & supply

Demand estimation[8-15]

With the spreading of SARS-CoV-2 all across the world, the main need and shortages have been around N95 respirators. The US Health and Human Services Secretary said that there were 30 million N95 respirators in the National Stockpile, but the nation **would need 300 million** to adequately supply its health care workers (1).

An estimate from WHO from the beginning of March places the estimated need for medical masks at **89 million per month (3 million per day)**, **examination gloves at 76 million per month, and goggles at 1.6 million per month for healthcare workers.** WHO estimates a need to increase manufacturing by 40% to meet the world demand just for the healthcare workers that need it.

3 million N95 masks are needed per day, requiring a **40% increase in manufacturing** to to meet the demand from just healthcare workers.

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Yaying Feng, PhD | PreScouter

Professional Summary:

Yaying earned his PhD in Materials Science and his MS in Electrical and Computer Engineering from Duke University. Before that, he earned a BS in Materials Physics from the University of Science and Technology, Beijing, in China. During Yaying's PhD tenure, he built expertise in nanomaterial synthesis, energy devices, advanced manufacturing, and telecommunications. At PreScouter, Yaying leads projects in the energy industry.

Subject Matter Expert

Christy Hui, PhD in Chemical Biology (McMaster University, Canada)

Professional Summary:

Christy received her PhD in Chemical Biology from McMaster University. Her primary research interest is in the area of developing bioanalytical instruments using proteins and DNA- or RNA-based receptors (DNA/RNA aptamers). Her expertise lies in constructing functional devices for detecting a wide range of molecules that can be indicative of environmental pollutions, early diagnosis for infections and diseases, etc.

Subject Matter Expert

Maikel Boot, PhD in Microbiology (VU University, Amsterdam, NL)

Professional Summary:

Maikel Boot is a Postdoctoral Fellow at the Rego Lab in the department of Microbial Pathogenesis at the Yale University School of Medicine. His research focuses on mapping the consequences of bacterial cell-to-cell variation of the causative agent of tuberculosis, *Mycobacterium tuberculosis*, on macrophage infection. He uses live-cell super-resolution microscopy (3D-SIM) to study long-term mycobacterial-macrophage infections. Maikel has been a part-time consultant at PreScouter for roughly two years and has worked on several projects as a research scholar or team leader. He enjoys puzzles, challenges and working together with other people to solve those. Besides his work at Yale, Maikel is a Fellow at Yale's Jonathan Edward College and current Chair of the Yale Postdoctoral Organization, leading a team of volunteers that organize 180+ events for 1250 Postdocs at Yale University. In his free time he enjoys listening to music and going to concerts.

Subject Matter Expert

Luyao Zhang, PH.D in Economics (Ohio State University, USA)

Professional Summary:

Luyao (Sunshine) Zhang is a tenure-tracked Assistant Professor in Business Management at East China Normal University in Shanghai, China. She has an abiding passion for interdisciplinary collaborations, especially related to Artificial Intelligence (Machine Learning), Fintech (Cryptocurrency and Blockchain), and Big Data (from all industries). She is also keenly interested in seeking creative solutions to challenging problems and transferring in-depth insights into practical impacts. She is a part-time consultant at PreScouter and works with industry pioneers on big-data paradigm shifts and digital transformations. She has dedicated herself to services with empathy, which she believes is one critical cornerstone of any civil society. She has served many local and international communities. She is the Ambassador for Startup Genome in Shanghai and was the Founding President for Dance Illumination, an NPO aiming at promoting diverse dance histories.

Subject Matter Expert

Yiran Cao, MSc in Chemistry and Science-Based Business (Leiden University, NL)

Professional Summary:

Yiran Cao has a combined education background in chemistry and business. Her research is focused on physical chemistry and surface science. She utilizes cyclic voltammetry with the use of rotating disk electrode and OLEMS to enhance insight of the kinetic impact of bromide on the chloride oxidation reaction. Her prior experiences include different management functions in MNCs and high-growth startups/unicorns, as well as international relations between China and Europe. She's passionate about technology and interdisciplinary collaboration, especially in the sectors of artificial intelligence, healthcare, and sustainability, with extensive knowledge and understanding in innovative trends and digital ecosystem in China and abroad.

Subject Matter Expert

Sophie Ramas, PhD in Developmental Biology (Goethe University, Frankfurt am Main, DE)

Professional Summary:

Sophie Ramas is a postdoctoral researcher in the Pharmacology department of Pr. Dr. Offermanns at the Max Planck Institute for Heart and Lung Research (Bad Nauheim, Germany). Her work focuses on the biological function of receptors in pancreatic beta cell functions, by combining in vitro and in vivo models. Her former work on zebrafish cardiovascular development during her PhD enabled her to strengthen a strong knowledge in molecular and cellular biology and genetic engineering.

In addition to her lab work, she has recently joined the PreScouter program as a scholar researcher. Combining lab work and consulting projects fulfills her scientific career. She is passionate about Life Science, always trying to improve her work efficiency. Interdisciplinary collaborating work is, for her, critical to a successful project.

Sophie is the mother of two children and successfully manages to balance her work, her family life, and swimming thanks to her organizational skills and her ability to adapt to different work environments.

Next Steps

SOME POSSIBILITIES THAT PRESCOUTER CAN OFFER FOR CONTINUATION OF OUR RELATIONSHIP

- ☑ COMPETITIVE INTELLIGENCE
- ☑ TECHNOLOGY ROADMAPPING
- ☑ TECHNOLOGY & PATENT LANDSCAPING
- ☑ MARKET RESEARCH & ANALYSIS
- ☑ TRENDS MAPPING
- ☑ REVIEW BEST PRACTICES
- ☑ PATENT COMMERCIALIZATION STRATEGY
- ☑ DATA ANALYSIS & RECOMMENDATIONS
- ☑ ACQUIRE NON-PUBLIC INFORMATION
- ☑ SUPPLIER OUTREACH & ANALYSIS
- ☑ CONSULT WITH INDUSTRY SUBJECT MATTER EXPERTS
- ☑ INTERVIEWING COMPANIES & EXPERTS

WE CAN ALSO DO THE FOLLOWING

- ✔ **CONFERENCE SUPPORT:** Attend conferences of interest on your behalf.
- ✔ **WRITING ARTICLES:** Write technical or more public facing articles on your behalf.
- ✔ **WORKING WITH A CONTRACT RESEARCH ORGANIZATION:** Engage with a CRO to build a prototype, test equipment or any other related research service.

For any requests, we welcome your additional questions and custom building a solution for you.

About PreScouter

PRESCOUTER PROVIDES CUSTOMIZED RESEARCH AND ANALYSIS

PreScouter helps clients gain competitive advantage by providing customized global research. We act as an extension to your in-house research and business data teams in order to provide you with a holistic view of trends, technologies, and markets.

Our model leverages a network of 3,000+ advanced degree researchers at tier 1 institutions across the globe to tap into information from small businesses, national labs, markets, universities, patents, startups, and entrepreneurs.

CLIENTS RELY ON US FOR:

Innovation Discovery: PreScouter provides clients with a constant flow of high-value opportunities and ideas by keeping you up to date on new and emerging technologies and businesses.

Privileged Information: PreScouter interviews innovators to uncover emerging trends and non-public information.

Customized Insights: PreScouter finds and makes sense of technology and market information in order to help you make informed decisions.

500+ CLIENTS WORLDWIDE

4,000+ RESEARCH REPORTS CREATED

150,000+ HOURS OF RESEARCH COMPLETED FOR CLIENTS