ABU DHABI PUBLIC HEALTH CENTRE | مركز أبوظبي للصحة العامة

Scientific Research Monitoring on COVID-19

17 April 2020

Summary on COVID19

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SARS-COV2 virus

- The virus have been sequenced and found to be similar to MERS-CoV and SARS-CoV. Research revealed that the virus originated in a bat reservoir.
- New designation for the disease and the virus: COVID-19 and SARS-COV2.
- SARS-COV2 stay viable in aerosol for hours and in surface up to 3 days.
- Two strain have been identified for SARS-COV2 (L type (more aggressive) and S type .

Transmission

- Transmission from human to human has been confirmed. Incubation period ranges from 5 days and can reach up to 14 days.
- Suggested human-to-human transmission occurs through droplets, contact and fomites, similar to Severe Acute Respiratory Syndrome (SARS).
- Isolation is the best measure to control transmission.

Clinical features and outcome

- Non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death.
- Highest risk for severe disease and death include people aged over 60 years and those with underlying conditions
- Pregnant women infected with SARS-COV2 may experience symptoms similar to those of non-pregnant adults. No evidence suggests transmission from mother to newborn if infected late in pregnancy. No evidence of transmission through breast milk.

Therapies and vaccination

- Efforts currently in developing therapies for this virus focus on previously known medications and vaccination for MERS-CoV and SARS-CoV. In addition to other type of medication.
- WHO forum held 11-12 Feb 2020 to mobilize research on COVID19 vaccinations and therapies.

Summary on COVID19 (Cont.)

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COVID19 in figure

- 80% of laboratory confirmed patients have had mild to moderate disease
- 13.8% have severe disease.
- 6.1% are critical
- Children account for 2.4% of all reported cases.(less than 19 years)

Todays' Highlights

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All articles presented in this report represents the authors' views and not necessarily represents Abu Dhabi Public Health Center views or directions.

Scientific Research

- **Treatment:** article showed that COVID-19 disease is different from classical ARDS and causes two types of phenotypes: the L type specific to COVID-19 and the H type typical of ARDS.CT scan is needed to differentiate the two type as the management is different.
- **Treatment:** Multiple article reviews about Stem cell therapy in COVID19 around the world , most promising stem cell in management of COVID19 could be Umbilical cord derived.

Due to abundant COVID19 information resources and given the urgent need to keep up with the updates .Below is a cluster of other academic articles for interested reviewer.
Listed articles may represent information that has been previously shared in the report and/or may target specific technical audience.

Others

Potential Neurologic and Oncologic Implications of the Novel Coronavirus
COVID-19 in patients with HIV: clinical case series
Immune Thrombocytopenic Purpura in a Patient with Covid-19

WHO daily report

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WHO daily report 16 April 2020

- No new country/territory/area reported cases of COVID-19 in the past 24 hours.
- Drinking alcohol does not protect you against COVID-19: existing rules and regulations to protect health and reduce harm caused by alcohol such as restricting access, should be upheld and even reinforced during the outbreak.
- In India, WHO is deploying its national polio surveillance network and other field staff to help with the COVID-19 response.
- Oxygen therapy plays an extremely important role in case management:
  - While the majority of patients with COVID-19 have mild or moderated illness, it is estimated that 20% of affected patients will need oxygen. The ability to boost capacity to deliver oxygen therapy is critical to being able to treat those patients and it has implications for the functioning of the entire system. WHO has recently published “Oxygen sources and distribution for COVID-19 treatment centers” that describes in detail how to surge oxygen systems and distribution.
  - In many resource-limited settings, oxygen supply and delivery systems are limited, and thus rapid gap analysis should be done to inform surge activities. To do so, the COVID-19 Essential Supply Forecast Tool (ESFT), can be used to forecast the total needs of oxygen and associated consumables and accessories (i.e. essential oxygen delivery devices and pulse oximeters). The forecast can then be compared to the existing oxygen supply availability. This method provides a way to identify a contextually appropriate oxygen surge strategy based on structures, capabilities, practices and technologies. Decision-makers can then use this strategy to frame and implement a surge plan.

Epidemiology

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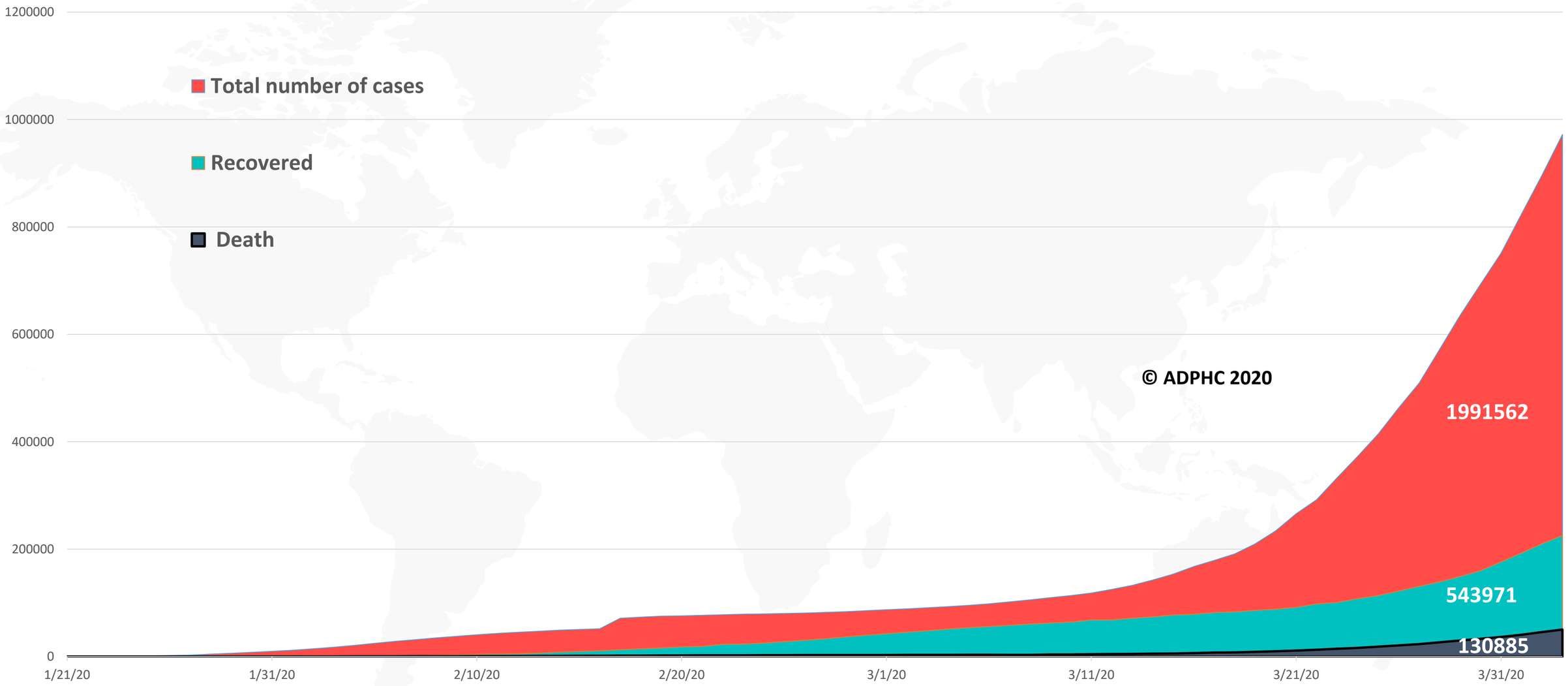
Figure 1: Total number of infected, recovered , and death cases (January 21st to April 16th , 2020)



Line graph published by Abu Dhabi Public Health Center 2020.

Data resources: WHO, : John Hopkins University

Epidemiology

Figure 2: Daily new infected COVID-19 cases reported between (January 21 to April 16h, 2020).

Line graph published by Abu Dhabi Public Health Center 2020.
Data resources: WHO

Epidemiology

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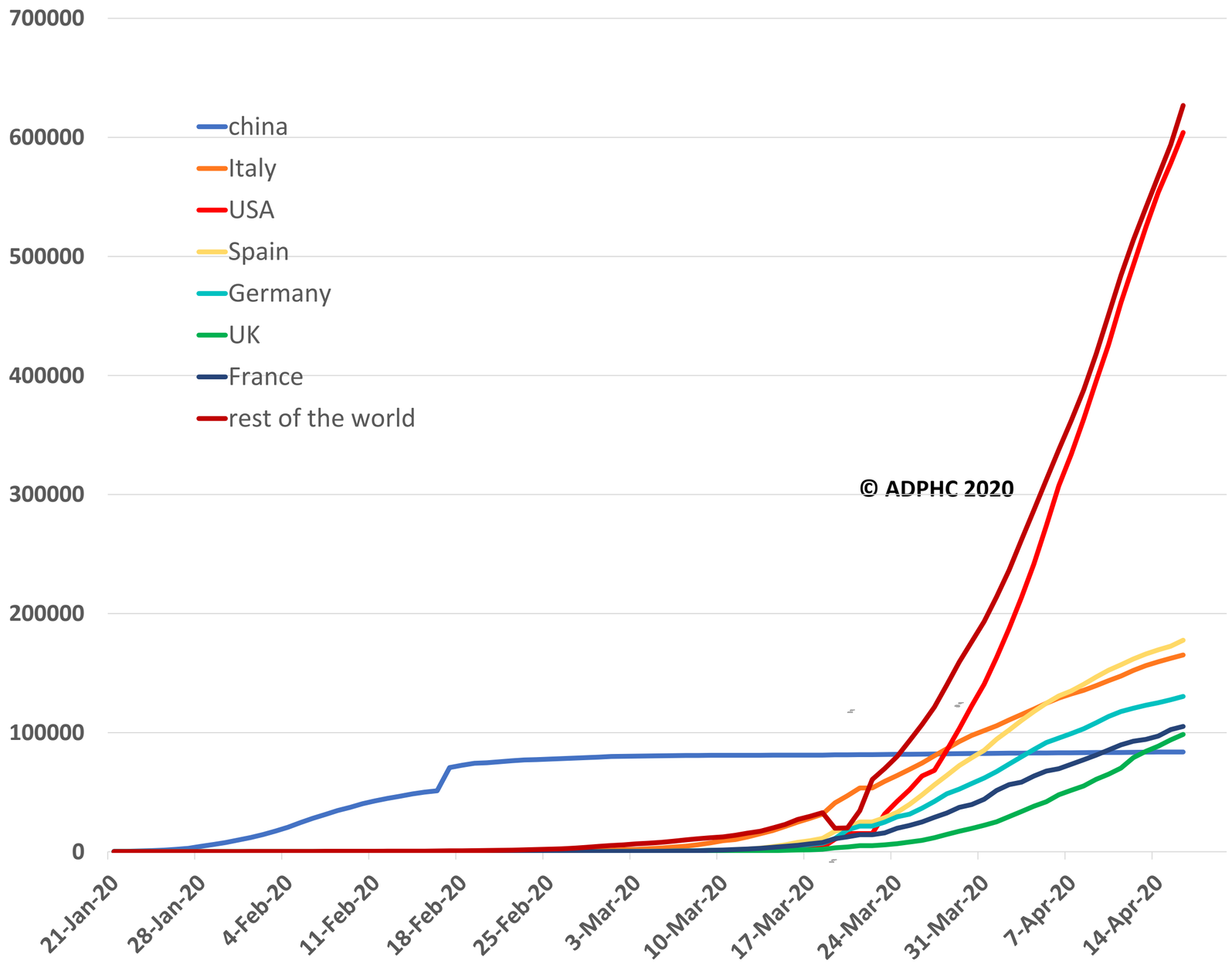
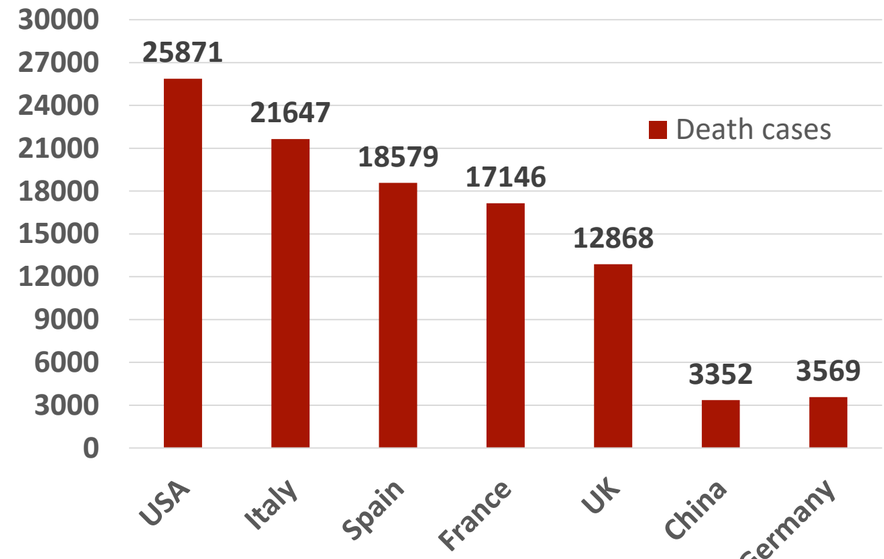
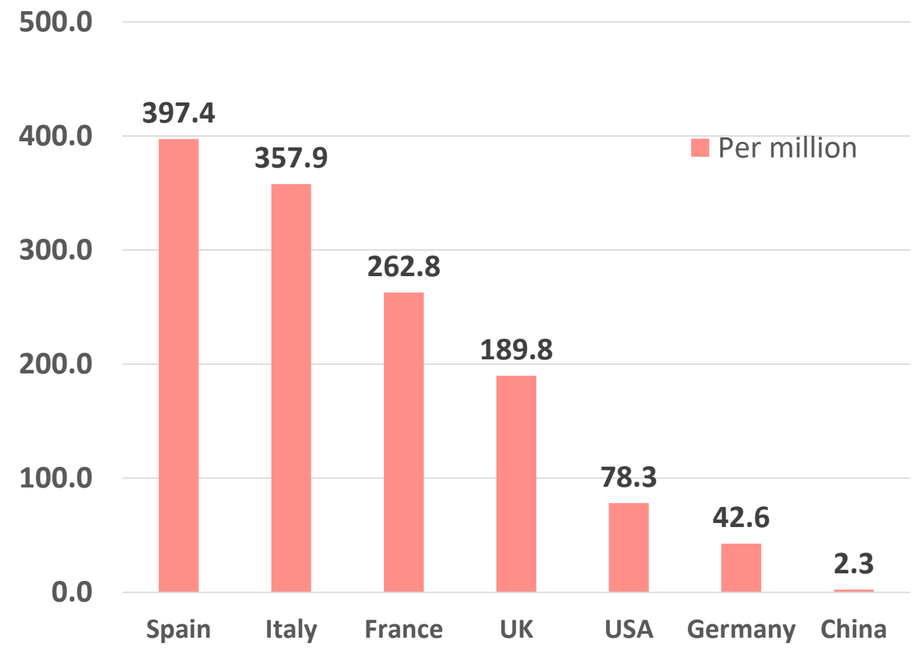
Figure 3 : Top 7 countries in the total number of cases due to COVID-19 (January 21 to April 16th, 2020).



TOTAL DEATHS



DEATHS PER MILLION

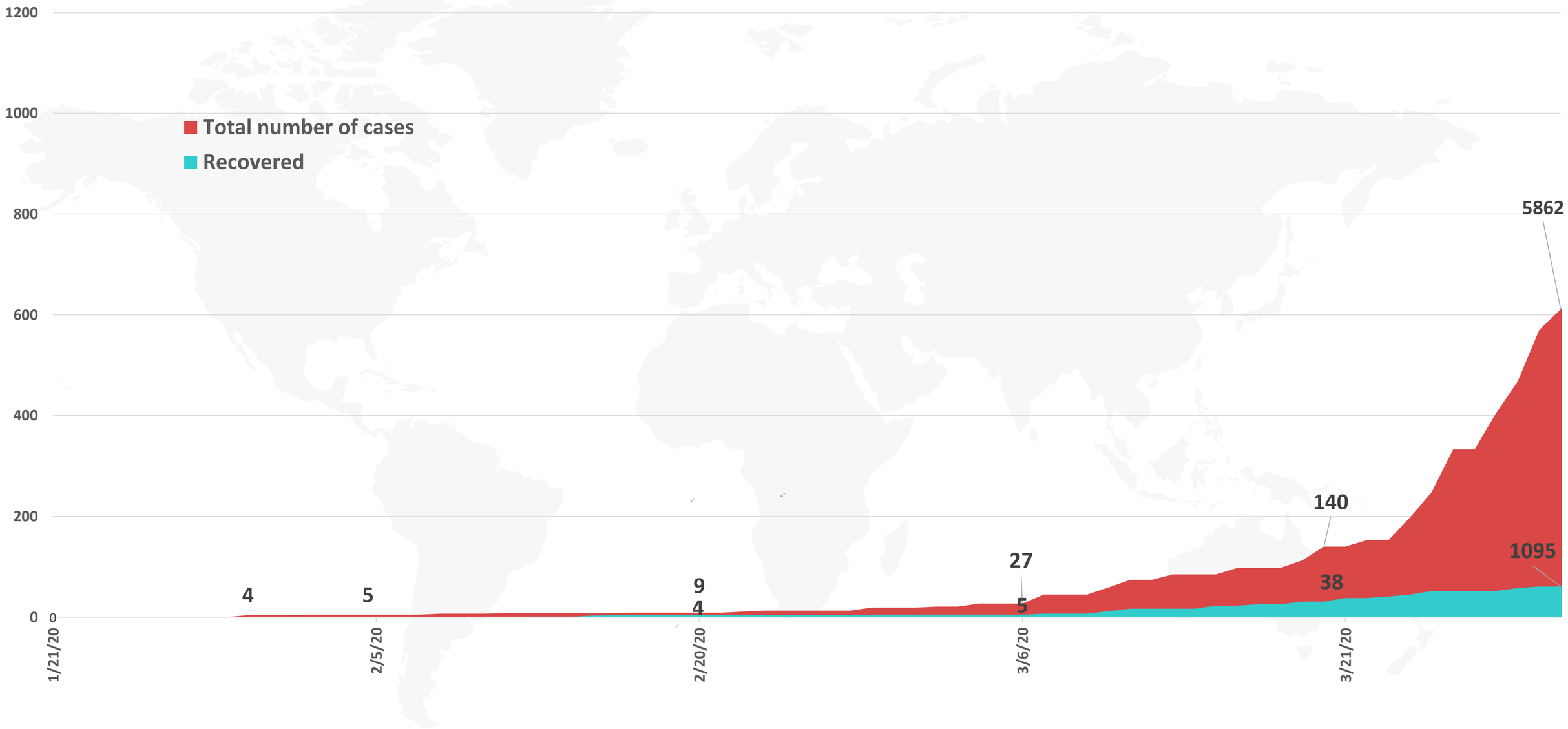


Line graph published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

Epidemiology

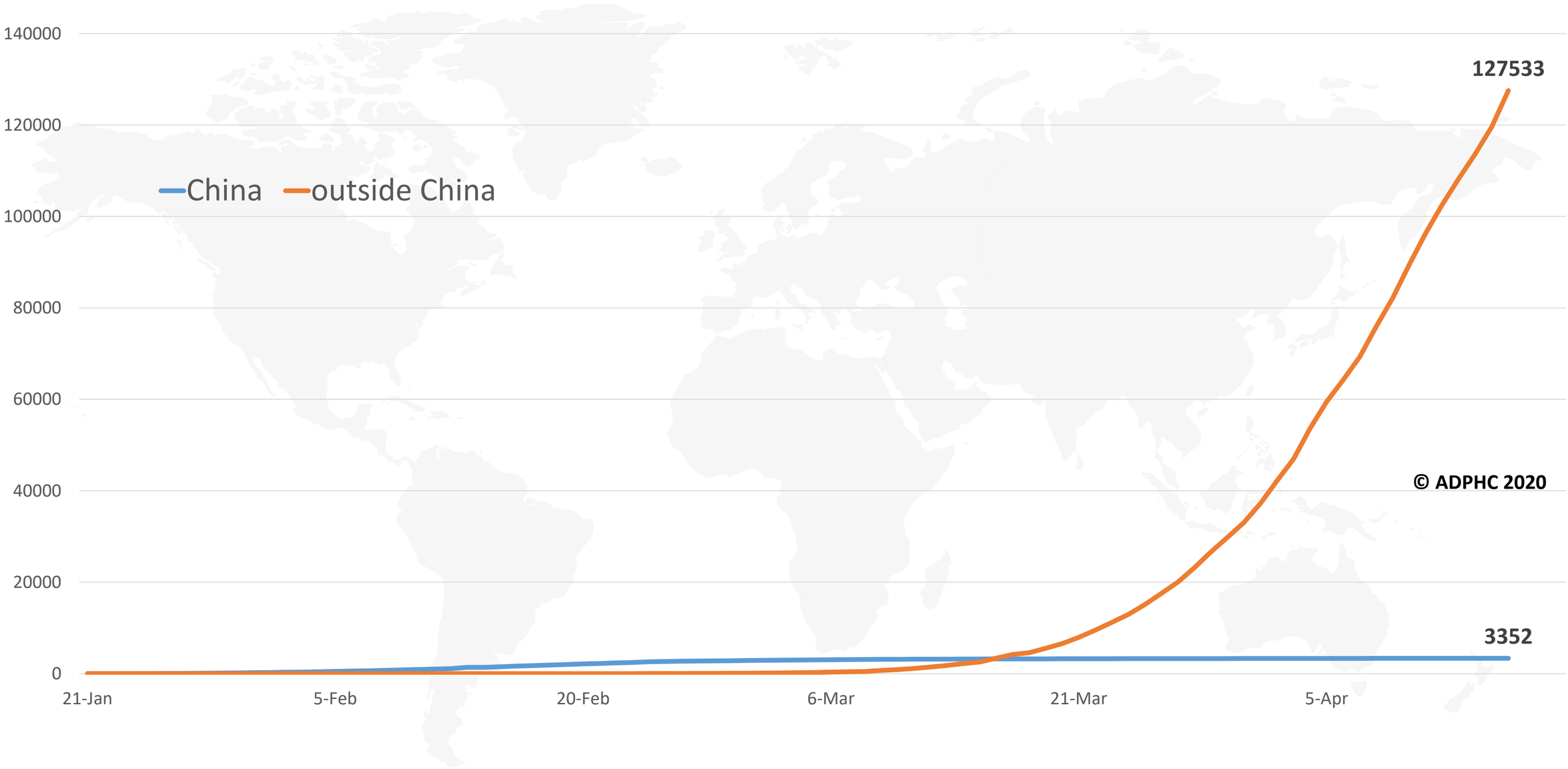
Figure 4: Total number of COVID-19 infected and recovered cases in UAE over time



Line graph published by Abu Dhabi Public Health Center 2020.
Data resources: WHO, : John Hopkins University

Epidemiology

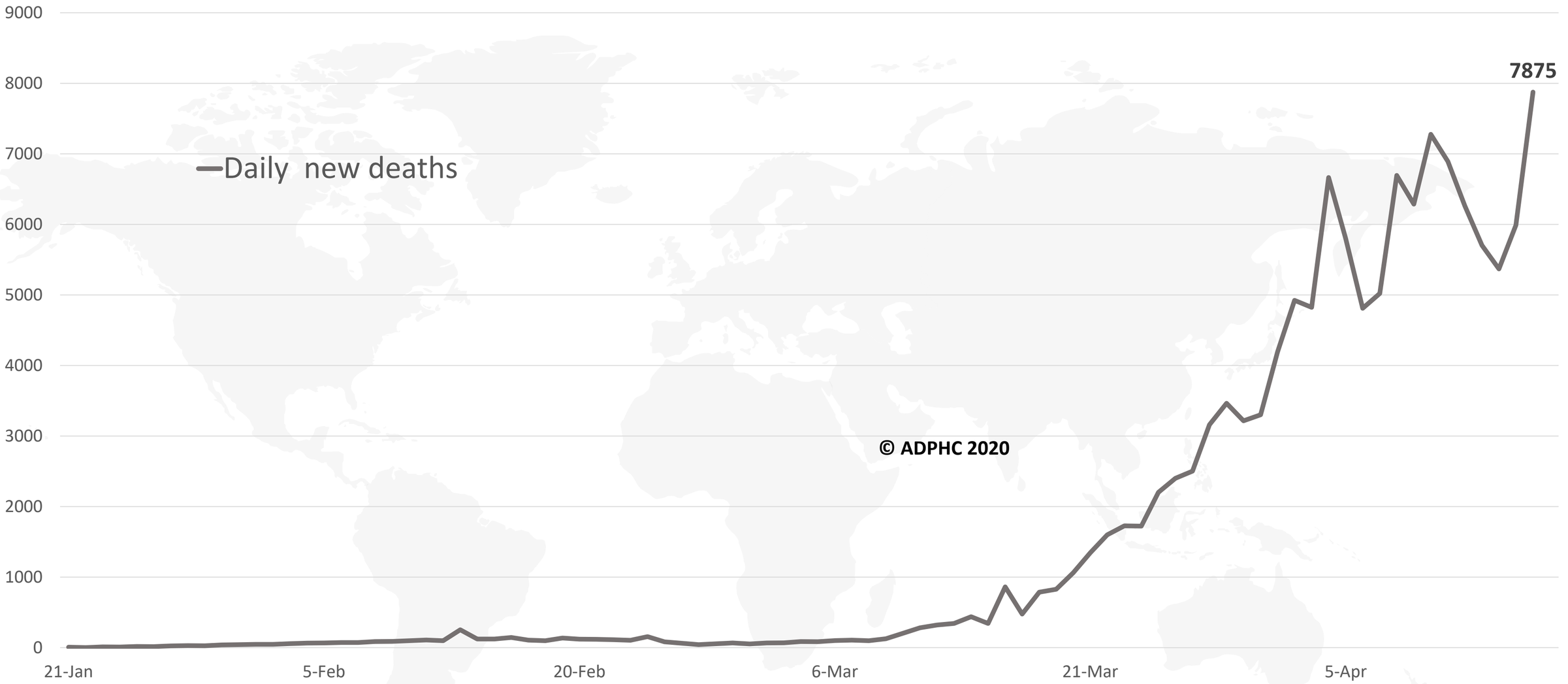
Figure 5: Total number of death due to COVID-19 reported by China and the rest of the world (January 21 to April 16th, 2020).



Line graph published by Abu Dhabi Public Health Center 2020.
Data resources: WHO

Epidemiology

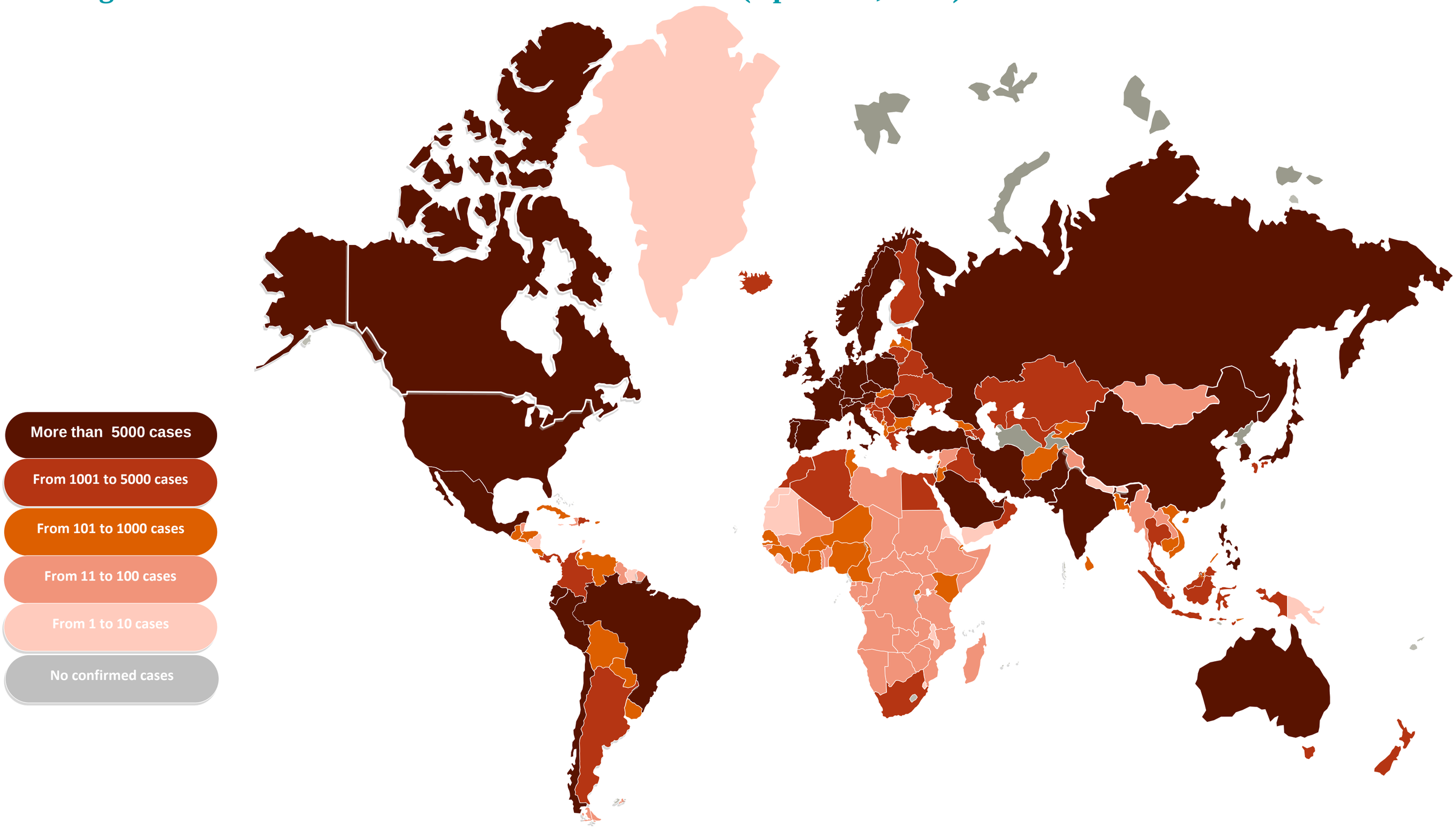
Figure 6: Global daily new deaths due to COVID-19 (January 21 to April 16th, 2020).



Line graph published by Abu Dhabi Public Health Center 2020.
Data resources: WHO

Epidemiology

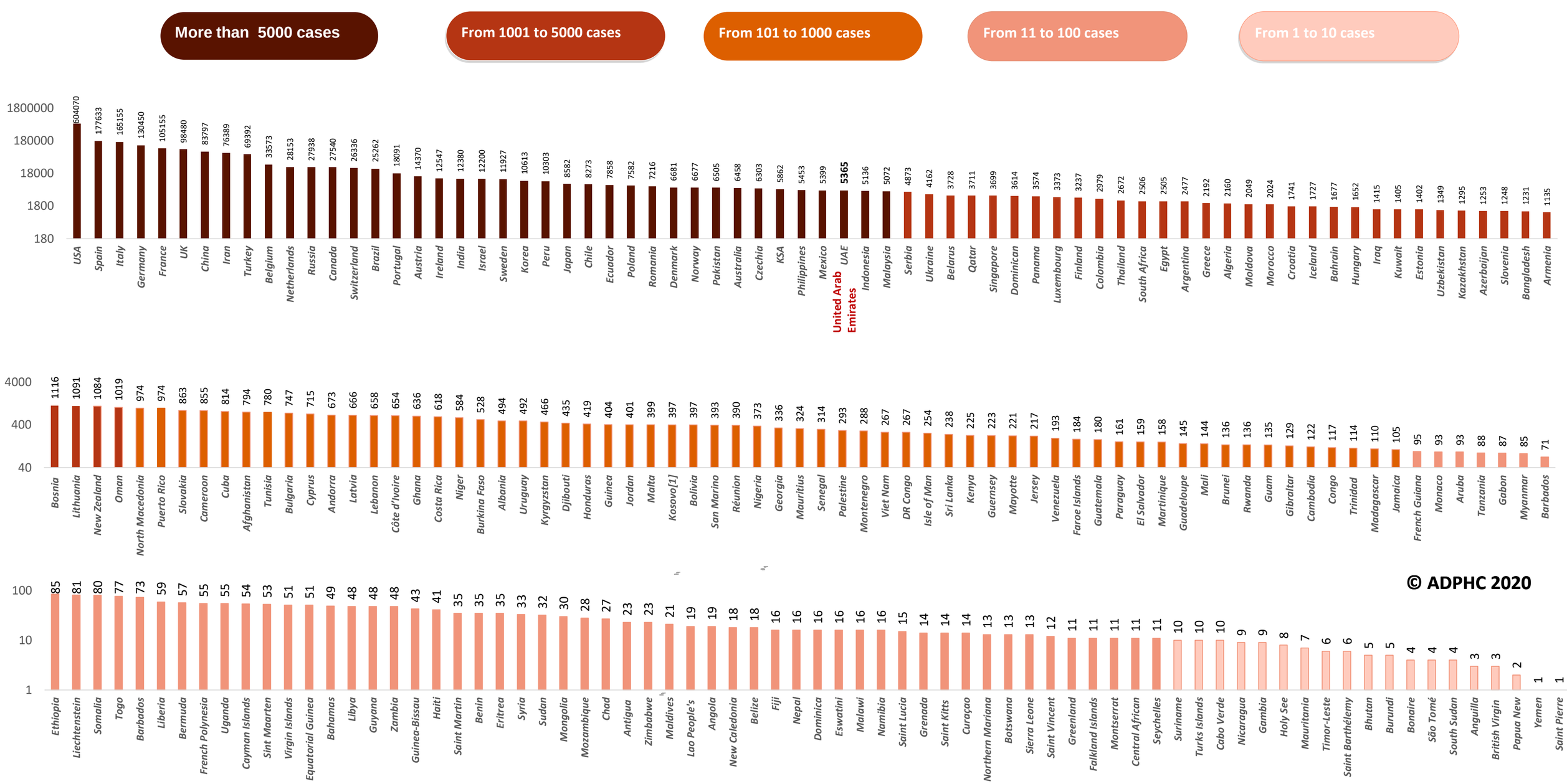
Figure 7a : Global distribution of COVID-19 cases (April 16th, 2020).



Map chart published by Abu Dhabi Public Health Center 2020.

Epidemiology

Figure 7B: Bar chart illustrate the global distribution of COVID19 cases April 16th, 2020)



Map chart published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

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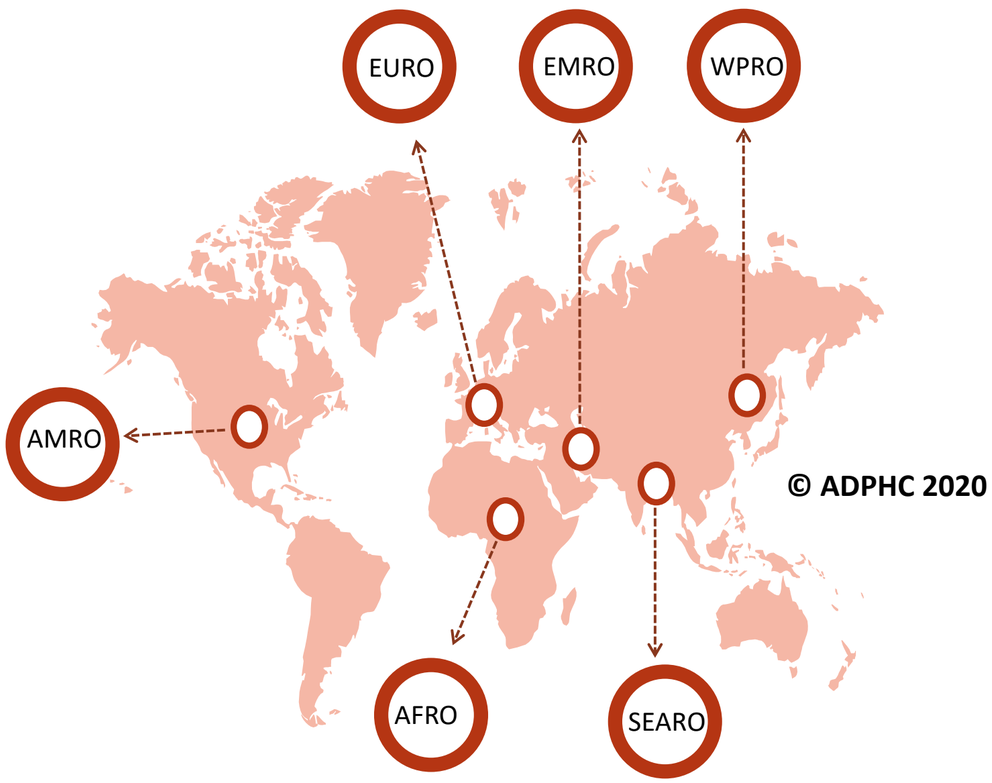
Figure 8: illustrate the Global distribution of COVID19 cases per region (April 16th, 2020)



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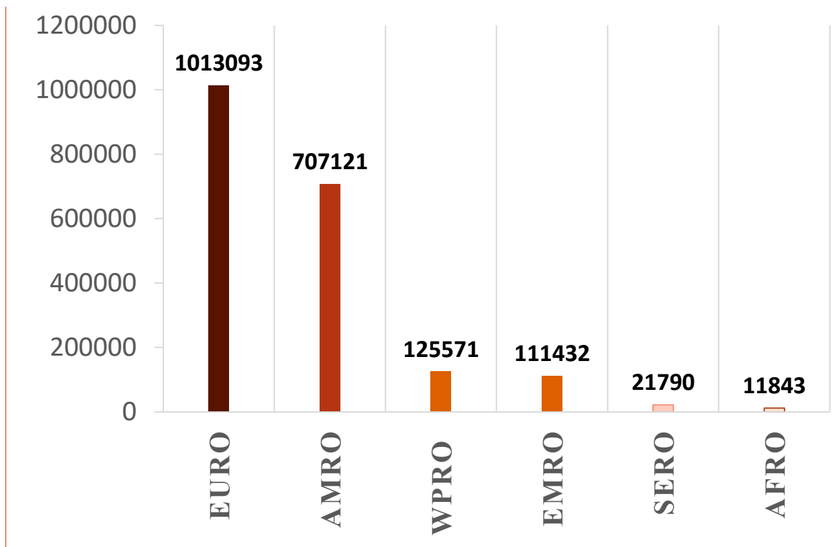
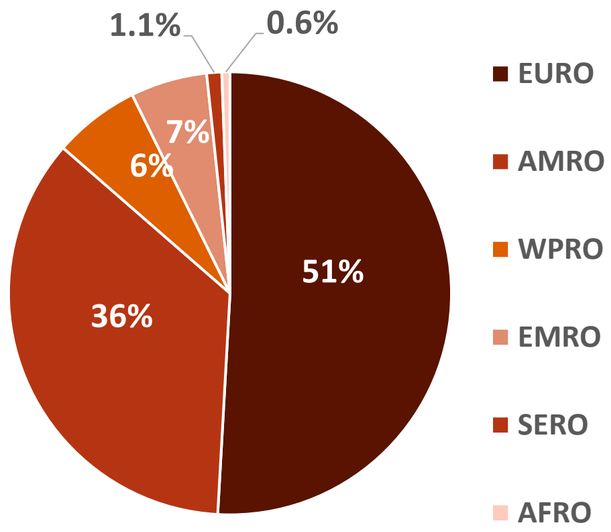
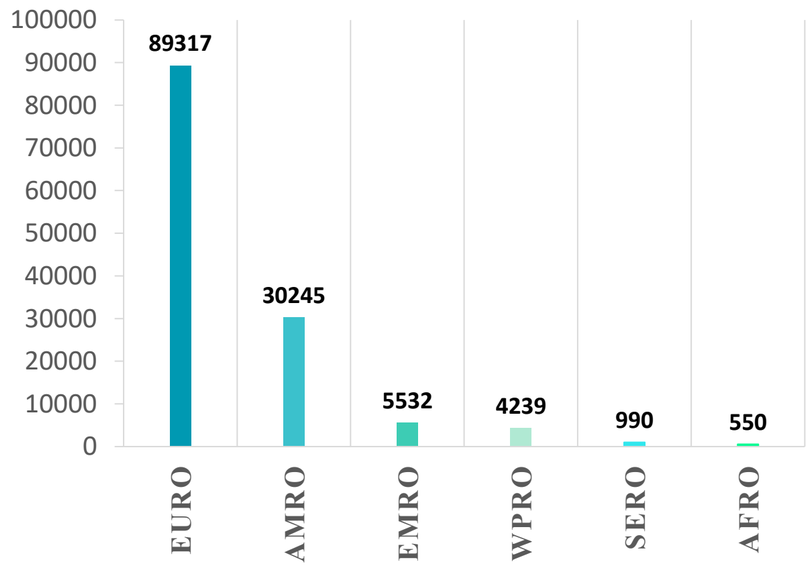
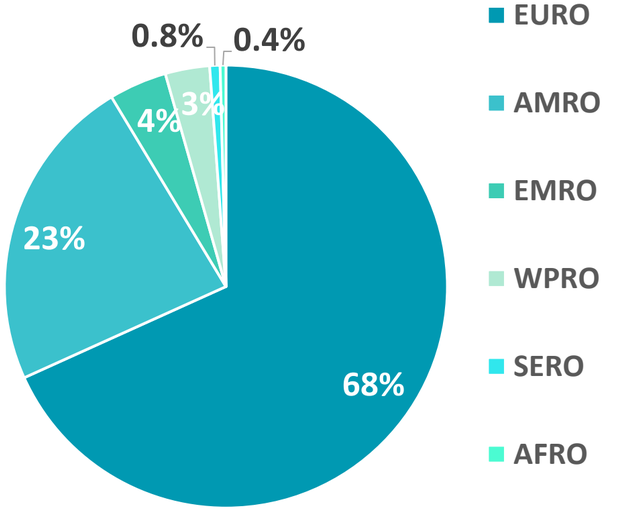
INFECTED





DEATH





Map chart published by Abu Dhabi Public Health Center 2020.
Data resources: WHO

Epidemiology

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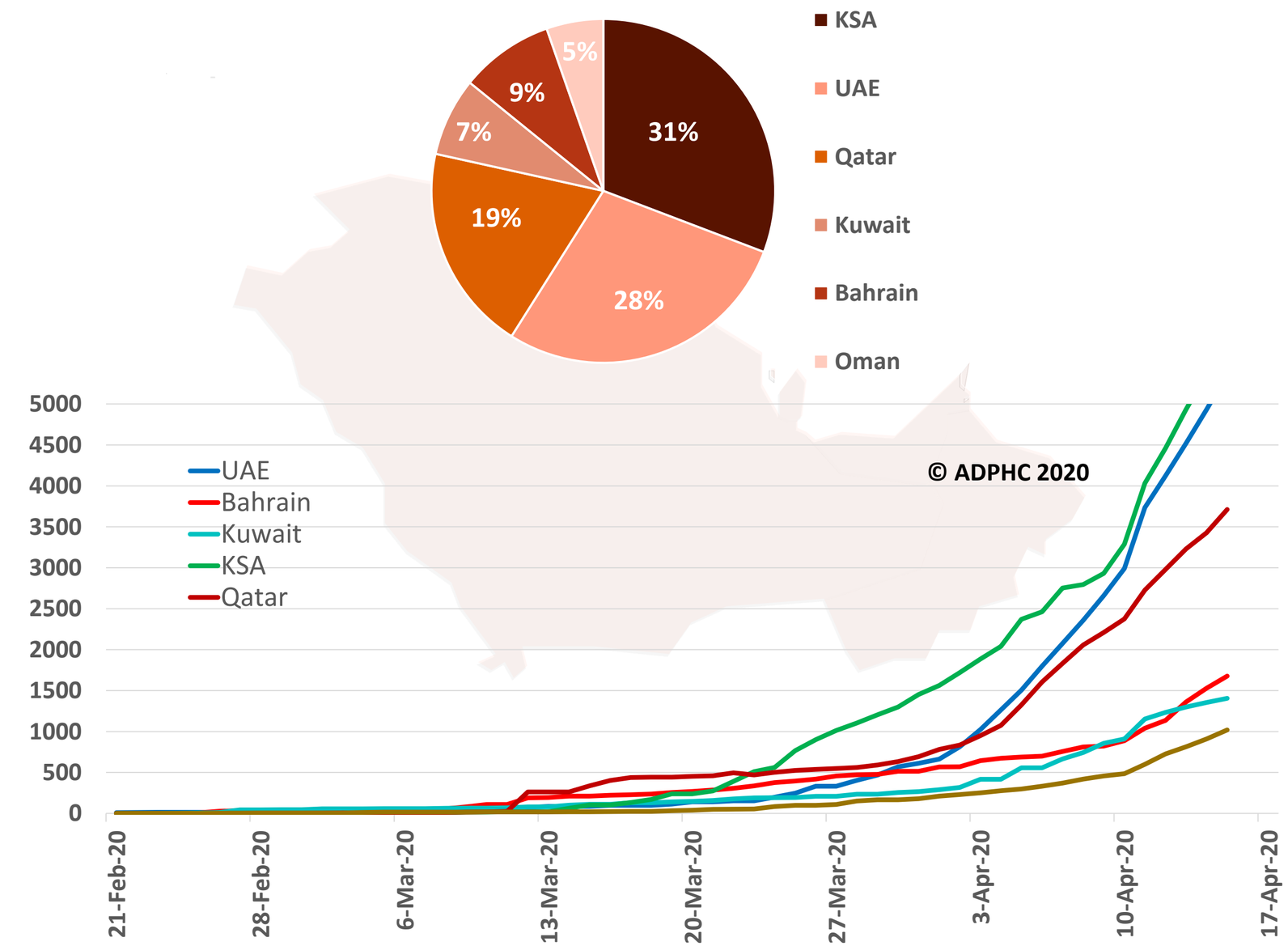
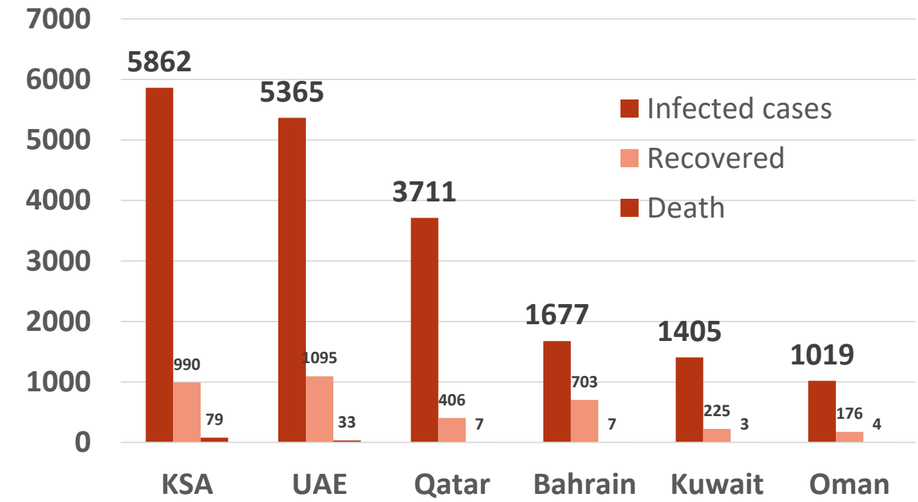
Figure 9: Comparative analysis of the distribution of COVID19 cases in GCC countries (April 16th, 2020)

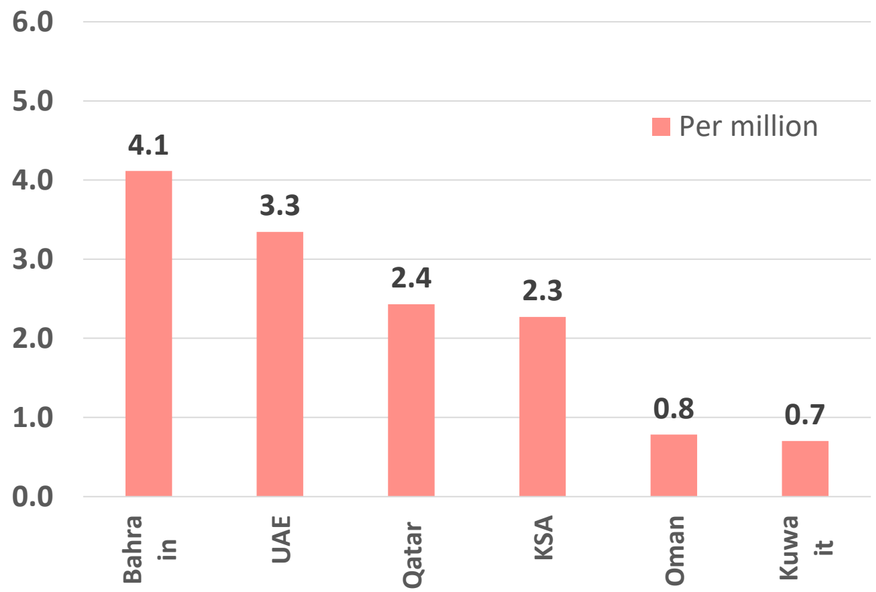
TOTAL NUMBER OF INFECTED CASES



Total number of infected, recovered and Deaths



Death per million



charts published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

Treatment

Article: COVID-19 pneumonia: different respiratory treatments for different phenotypes?
Published: April 14, 2020 *Intensive Care Medicine* (2020)

Summary:

This is an important study written by a group of intensive care physicians from Italy and UK who have been at the forefront of fighting COVID-19 in their respective countries. Based on their experiences, they highlight a critical observation that may be leading to the high death rates of severe COVID-19 patients. They suggest that even though the pneumonia caused by COVID-19 has been categorized under the Berlin definition of acute respiratory distress syndrome (ARDS), it is a distinct disease, manifesting a temporal (time-dependent) progression in severity, and requiring different management strategies. Based on current literature and their personal experiences, they suggest that COVID-19 pneumonia could be classified as either "L (low)" or "H (high)", a combination that is rarely seen in ARDS. They further hypothesize that patients experiencing COVID-19 pneumonia initially present with the L type characterized by "low elastance (normal gas in the lung), low ventilation-to-perfusion ratio(pulmonary artery pressure should be near normal.), low lung weight (ground-glass densities are present on CT scan, and lung volume moderately increase) and low recruitability (The amount of tissue with fluid is very low); . The patients may only present with L type followed by recovery, or the condition may worsen, further progressing to the "H" type which is characterized by "high elastance (The decrease in gas volume due to increased edema), high right-to-left shunt of heart to perfuse the edematous lung tissue , high lung weight and high recruitability (increased amount of non-aerated tissue) ", the typical manifestations of ARDS ("hypoxemia, bilateral infiltrates, decreased respiratory system compliance, increased lung weight, and potential for recruitment"). Most importantly, they suggest that while the progression to the H type may be due to disease severity, it could also be due to the result of damage from "high stress" ventilation which affects "depth of the negative intrathoracic pressure associated with the increased tidal volume in spontaneous breathing".

Treatment

Thus, based on this model, they suggest that treatment modalities of the COVID-19 pneumonia patients must also be different. They suggest that hypoxemia should be reversed in the L type patients by increasing FiO2, while L type patients with dyspnea can be treated with high flow nasal canula (HFNC), continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV). However, when the degree of inspiratory pleural pressure increases from 5-10 cmH2O to above 15 cmH2O, it leads to an increased risk of lung injury and intubations must be performed at the earliest to prevent transition to H type. The type H patients, on the other hand, should be treated as a severe cases of ARDS, "with hemodynamics, prone positioning and extracorporeal support".

Conclusions:

COVID-19 disease is different from classical ARDS and causes two types of phenotypes: the L type specific to COVID-19 and the H type typical of ARDS, both with their own specific signs and symptoms. The CT scan should be used to differentiate between the two conditions. If CT scan is not available, respiratory system elastance and recruitability should be used to differentiate between the two pathophysiological states of the disease that have been described. This is critical in deciding upon the appropriate treatment for the patient.

Implications:

COVID-19 patients with pneumonia should be treated differently depending upon whether they have the L or H type of pneumonia.

Treatment

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TRIAL LOCATIONS ON STEM CELL THERAPY FOR Treatment COVID19

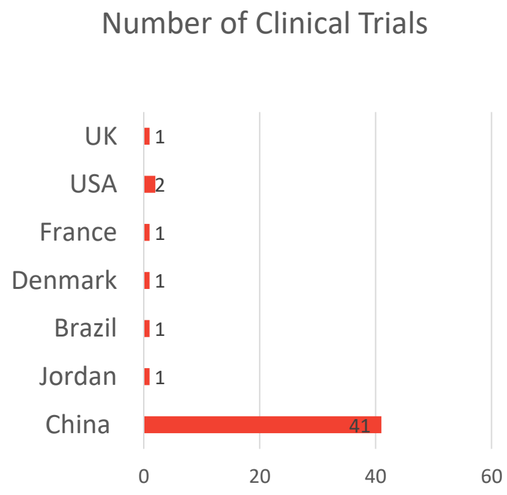
CLINICAL TRIALS AND PUBLICATIONS ON STEM CELL THERAPY FOR TREATMENT OF COVID19

INTRAVENOUS INFUSION **Best Route of Administration**

UMBILICAL CORD **Best Stem Cells To Treat Coronavirus**

48 Registered Clinical trials

More than 3 Publications



***Most of the current trial are using Umbilical cord stem cell**

Results of published research

PUBLISHED RESEARCH

	Publication1	Publication 2
Country	China	China
Patient Severity	Critical	Critical/Severe/Non-Severe
Enrolment Number	1	7
Study Type	Interventional	Compassionate
Antiviral Treatment	YES	YES
Clinical Improvement	• Umbilical cord MSC (hUCMSC) using three intravenous infusions of 5×107 hUCMSC, three days apart. • Within four days of second cell infusion, patient was off the ventilator and able to walk. • All measured parameters, including circulating T-cell counts, returned towards normal levels within 21 days.	• Single intravenous dose of clinical grade MSCs, 1 × 106 cells per kilogram of weight. • No adverse effects, and within 2 days. • All patients had significantly improved pulmonary function 2-4 days, including the one severe and two non-severe COVID-19 pneumonia cases discharge after 10 days.

Links to published research:
Publication 1 : March , 2020
Publication 2 :February 28 ,2020 (previously summarized in ADPHC 1.4.2020 report
Review summery on stem cell and COVID19 available here

This work is done in collaboration with the UAEU Research office

Treatment

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Article 3 : Expanded Umbilical Cord Mesenchymal Stem Cells (UC-MSCs) as a Therapeutic Strategy In Managing Critically Ill COVID-19 Patients: The Case for Compassionate Use

Published: April 2020, Pain Physician Journal

Summary:

The article give some review of umbilical stem cell therapy in COVID19 .

Role of Stem Cells

MSCs would appear to have some natural immunity to the coronavirus owing to their powerful immunomodulatory ability. They may also have beneficial effects for preventing or attenuating the cytokine storm by secreting powerful anti-inflammatory factor.

Safety:

Safety and effectiveness have been clearly documented in many clinical trials, especially in the immune-mediated inflammatory diseases.

Umbilical cord stem cells seem to be the most desirable for the following reasons:

What is the Best Route of Administration?

Intravenous infusion seems to be the most desirable route of administration. Fortunately, most of the stem cells injected IV, get trapped in the lung.

What Are The Best Stem Cells To Treat Coronavirus?

Umbilical cord stem cells seem to be the most desirable for the following reasons:

High concentration of stem cells. It is one of the richest sources of MSC	They are scalable which will be important given the large number of expected coronavirus patients
Extensive source of stem cells.	UC-MSCs can be extracted noninvasively No procedure
Fast doubling times, they can be efficiently expanded in the lab	An afterbirth tissue and is considered medical waste
UC-MSCs show a gene expression profile more similar to that of (ESCs)which means they have faster doubling times, more plasticity and possibly more potency	They seem to be immunoevasive as they express low levels of major histocompatibility complex (MHC) class I molecules, but not MHC class II on their cell surface, allowing their transplantation across MHC barriers

How to Assure Safety of this Treatment?

The source of stem cells should be from legitimate labs which are compliant with the FDA standards. There should be zero tolerance for negligence in these labs.

Donors should be strictly screened. There should be no room for contamination right from the procurement of the cord tissue to the production of the final product. This product must be analyzed for cell viability, quality of the stem cells and sterility and must meet the highest standards.	The appropriate cell dose, cell concentration, cell infusion rate should be determined to maximize efficacy and safety. Cell passage numbers should be limited to increase potency and decrease cell size.