ABU DHABI PUBLIC HEALTH CENTRE | مركز أبوظبي للصحة العامة

# Scientific Research Monitoring on COVID-19

**25 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:** antihypertensive RAAS inhibitors shall not be stopped in COVID19 patient especially on those who have high risk.
- **Clinical Feature and transmission:** the first systematic review in children and adolescent in COVID19 patient confirm the mild disease in children, with hospital duration 1-2 weeks.
- **Diagnosis:** a study to assess the viral shedding in sever COVID19 patient found that patient might shed the virus more than 48 days.
- **virology** : A study on 11 patient sample observed the virus have 33 mutations

***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

- **From Mitigation to Containment of the COVID-19 Pandemic** Putting the SARS-CoV-2 Genie Back in the Bottle
- **Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study**
- **COVID-19 Comes to the United States**

# WHO daily report

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## WHO daily report 24 April 2020

- WHO has published an interim guidance ‘COVID-19 and Food Safety: Guidance for competent authorities responsible for national food safety control systems. The guidance document **provides advice and recommendations for national food safety authorities** to **optimize food control functions and prioritize critical services** that preserve the integrity of food safety systems.
- WHO has published an interim guidance ‘**Water, sanitation, hygiene, and waste management for the COVID-19 virus’.**
- WHO’s Health Security Learning Platform offers a number of online courses to help enhance knowledge on specific issues related to the implementation of the International Health Regulations (2005). A new course, “**Operational considerations for managing COVID-19 cases/outbreak in aviation.**
  - **Target audience are the aviation sector aim to provide** case definitions, management of suspected cases at airports and on-board aircraft, cleaning and disinfection, and other key topics

# Epidemiology

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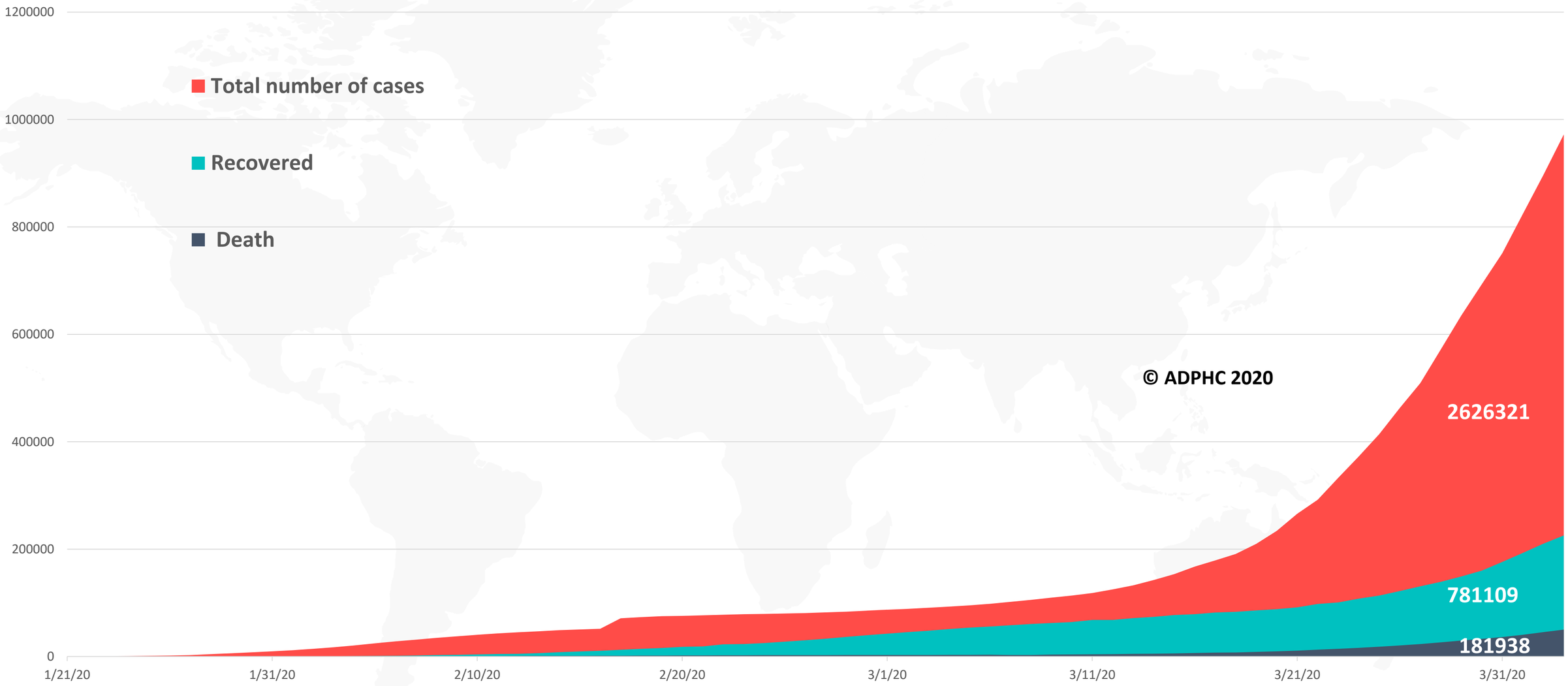
## Figure 1: Total number of infected, recovered , and death cases (January 21st to April 24 , 2020)

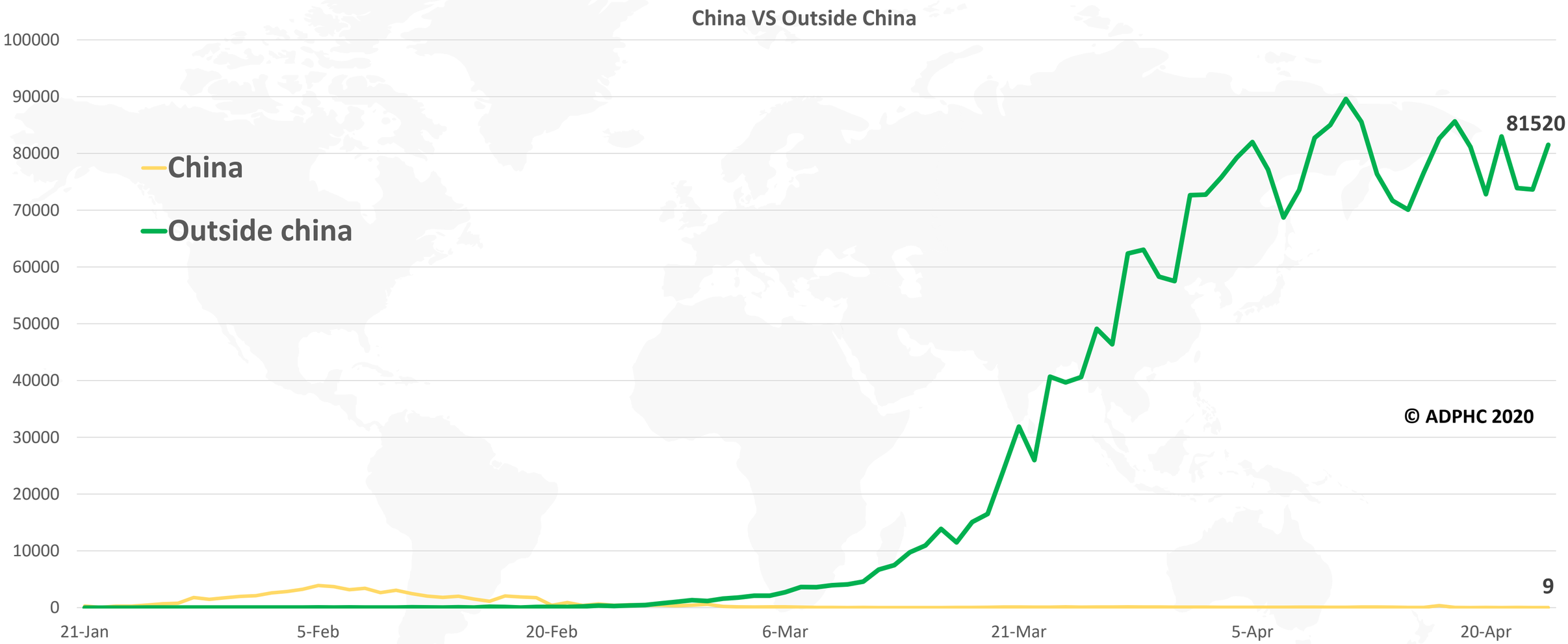



**Line graph published by Abu Dhabi Public Health Center 2020.**

**Data resources: WHO, : John Hopkins University**

# Epidemiology

## Figure 2: Daily new infected COVID-19 cases reported between (January 21 to April 24, 2020).




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

# Epidemiology

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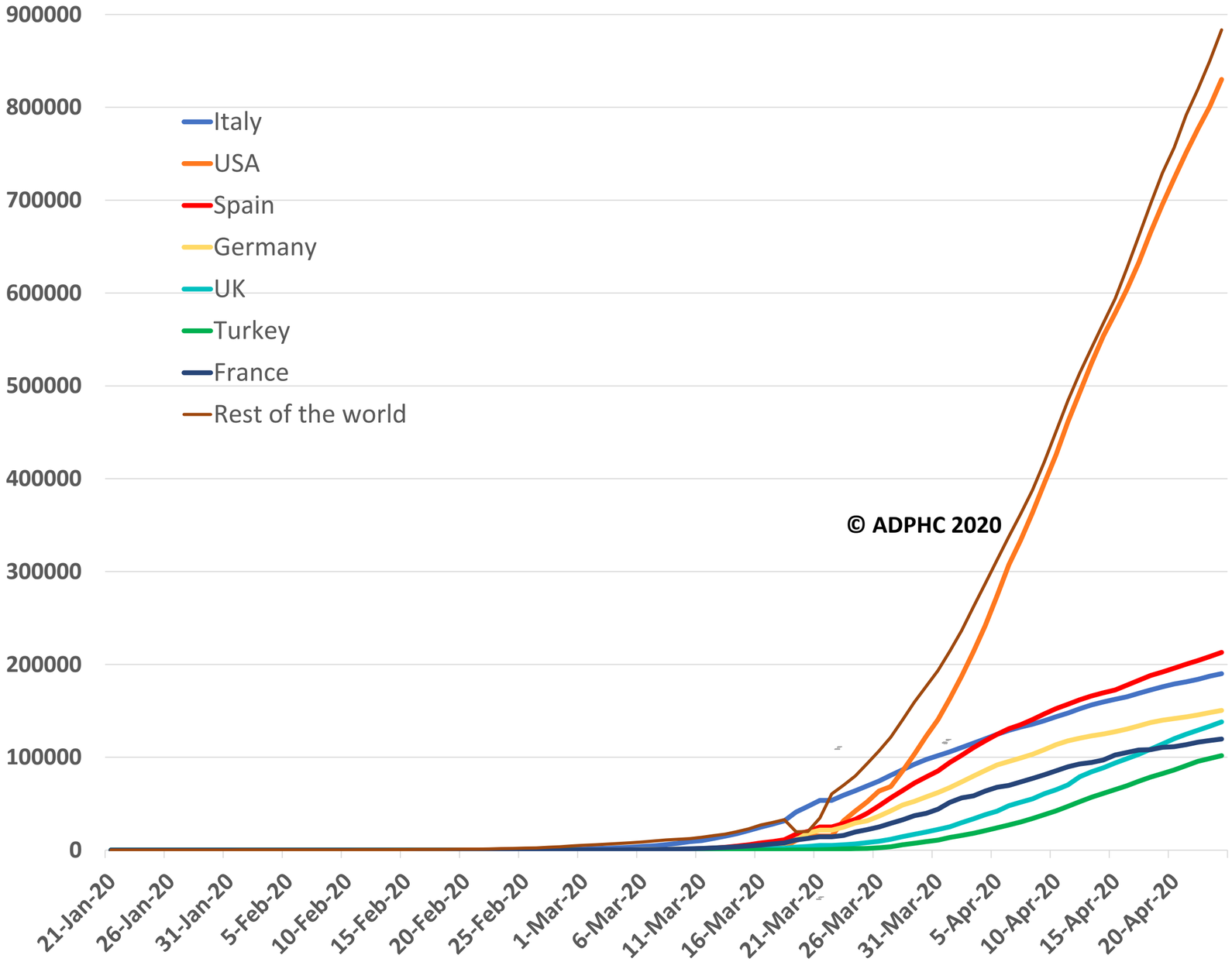
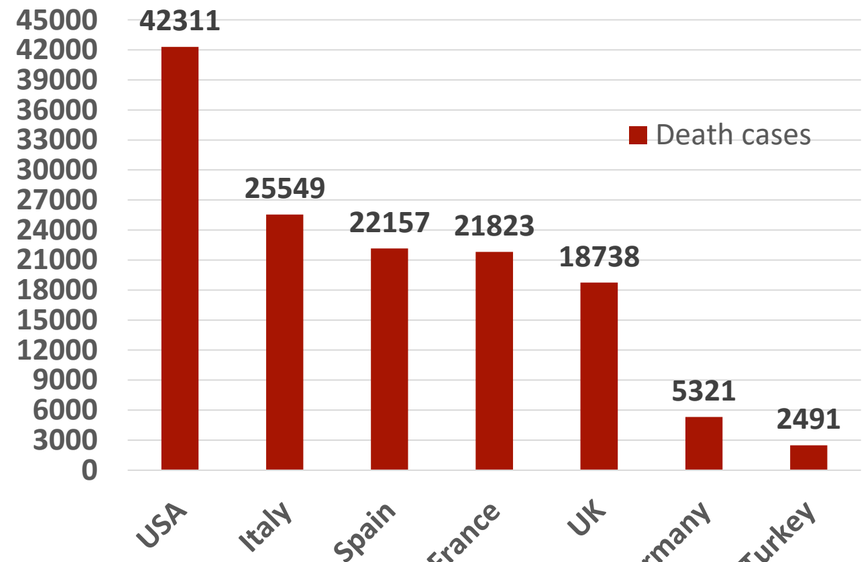
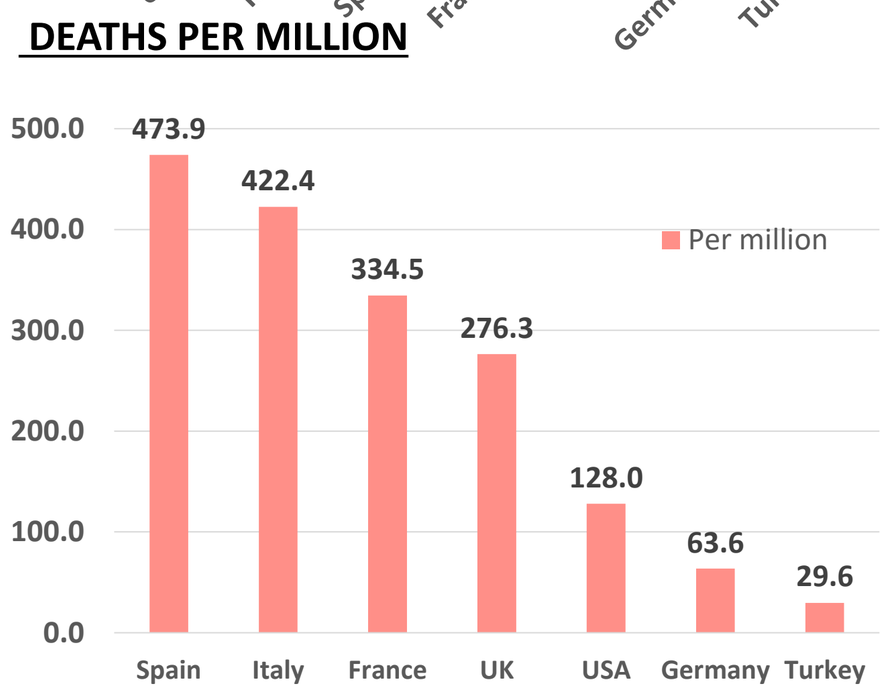
## Figure 3 : Top 7 countries in the total number of cases due to COVID-19 (January 21 to April 24 , 2020).




**Line graph published by Abu Dhabi Public Health Center 2020.**

**Data resources: WHO**

# Epidemiology

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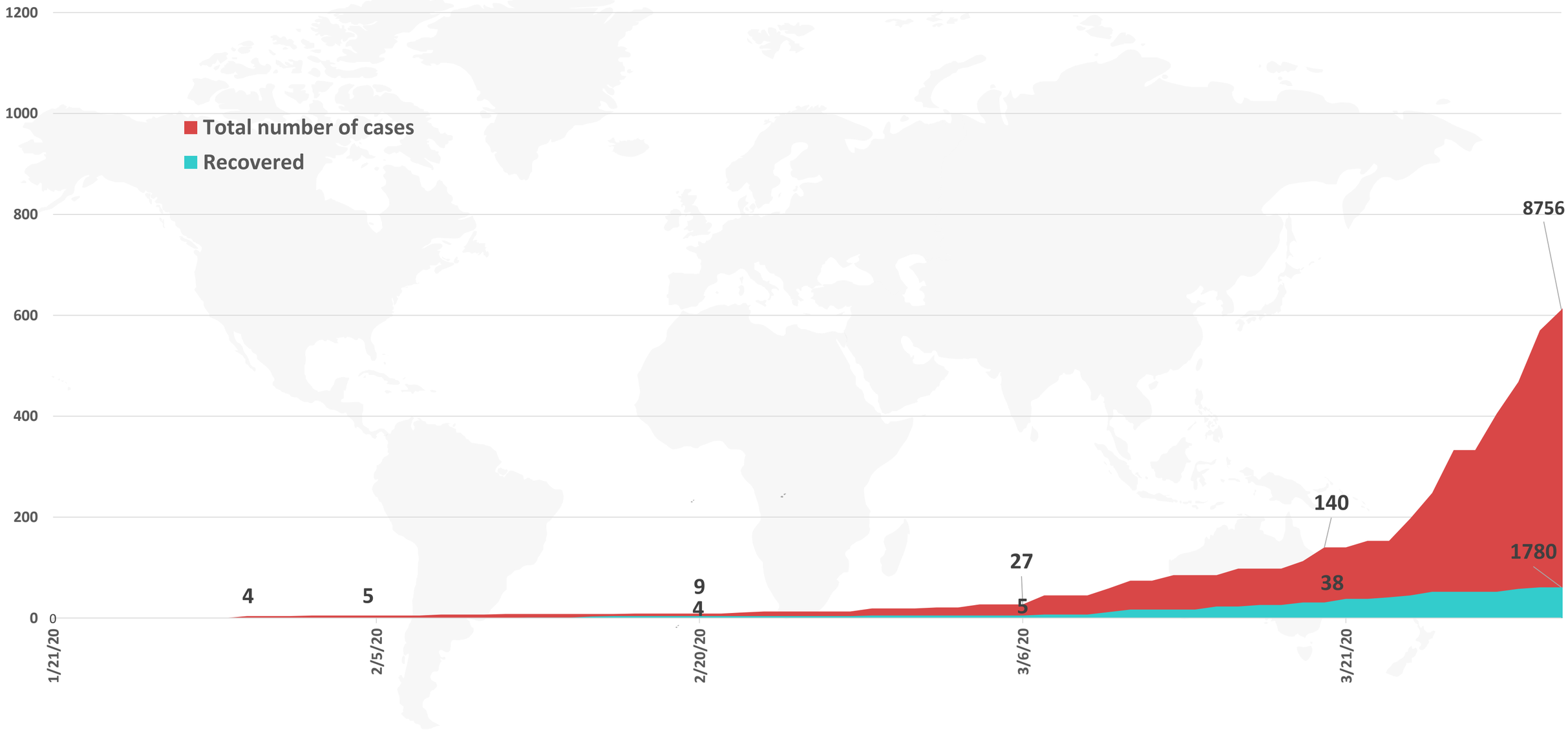
## Figure 4: Total number of COVID-19 infected and recovered cases in UAE over time

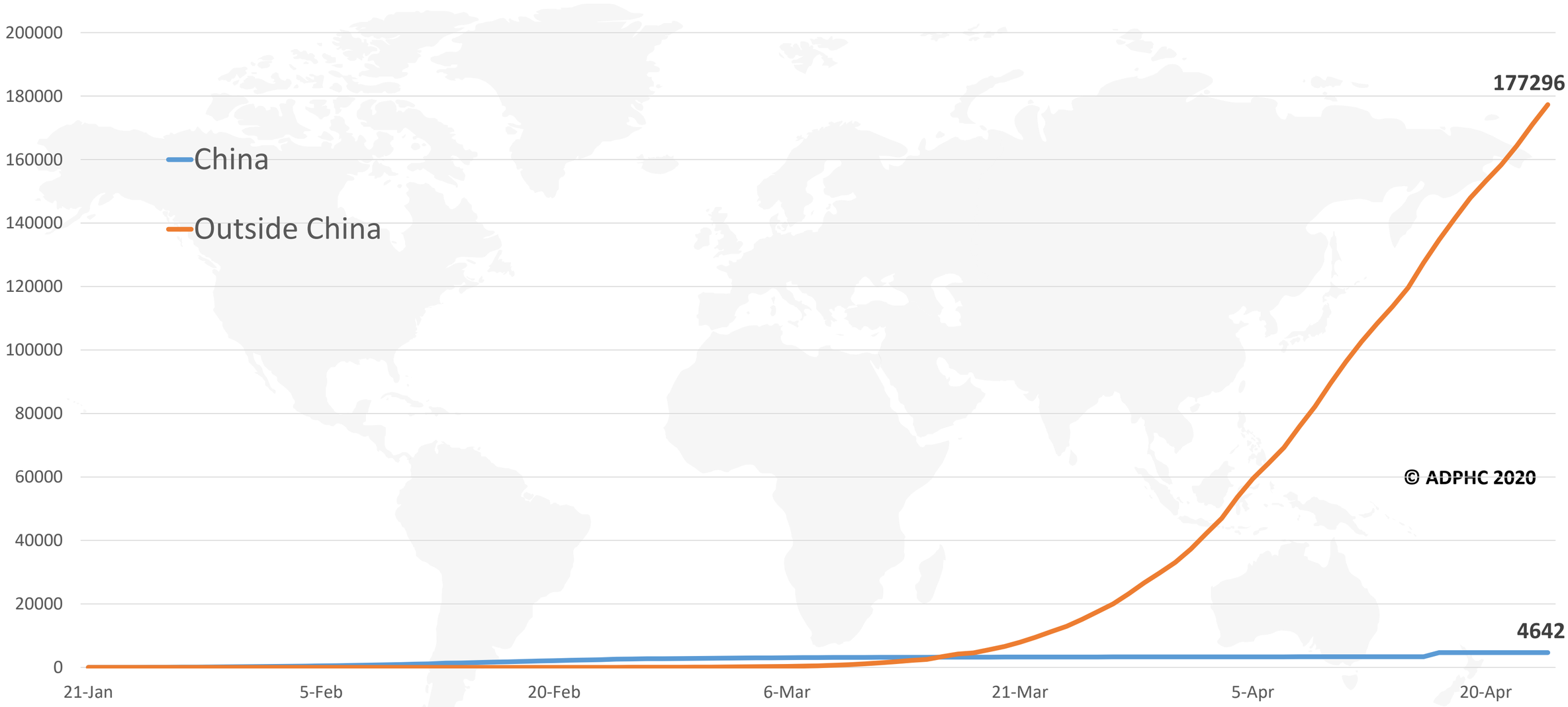



**Line graph published by Abu Dhabi Public Health Center 2020.**

**Data resources: WHO, : John Hopkins University**

# Epidemiology

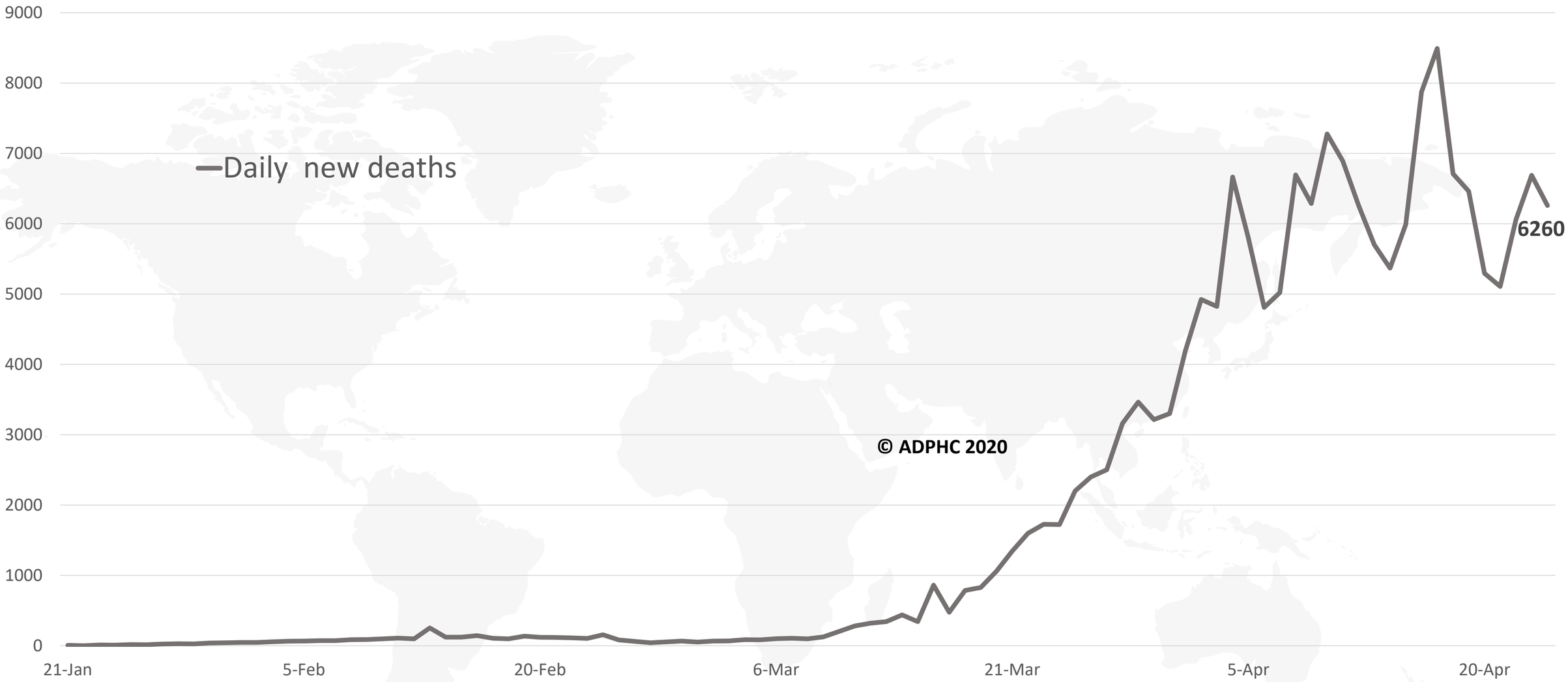
**Figure 5: Total number of death due to COVID-19 reported by China and the rest of the world (January 22 to April 24, 2020).**




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

# Epidemiology

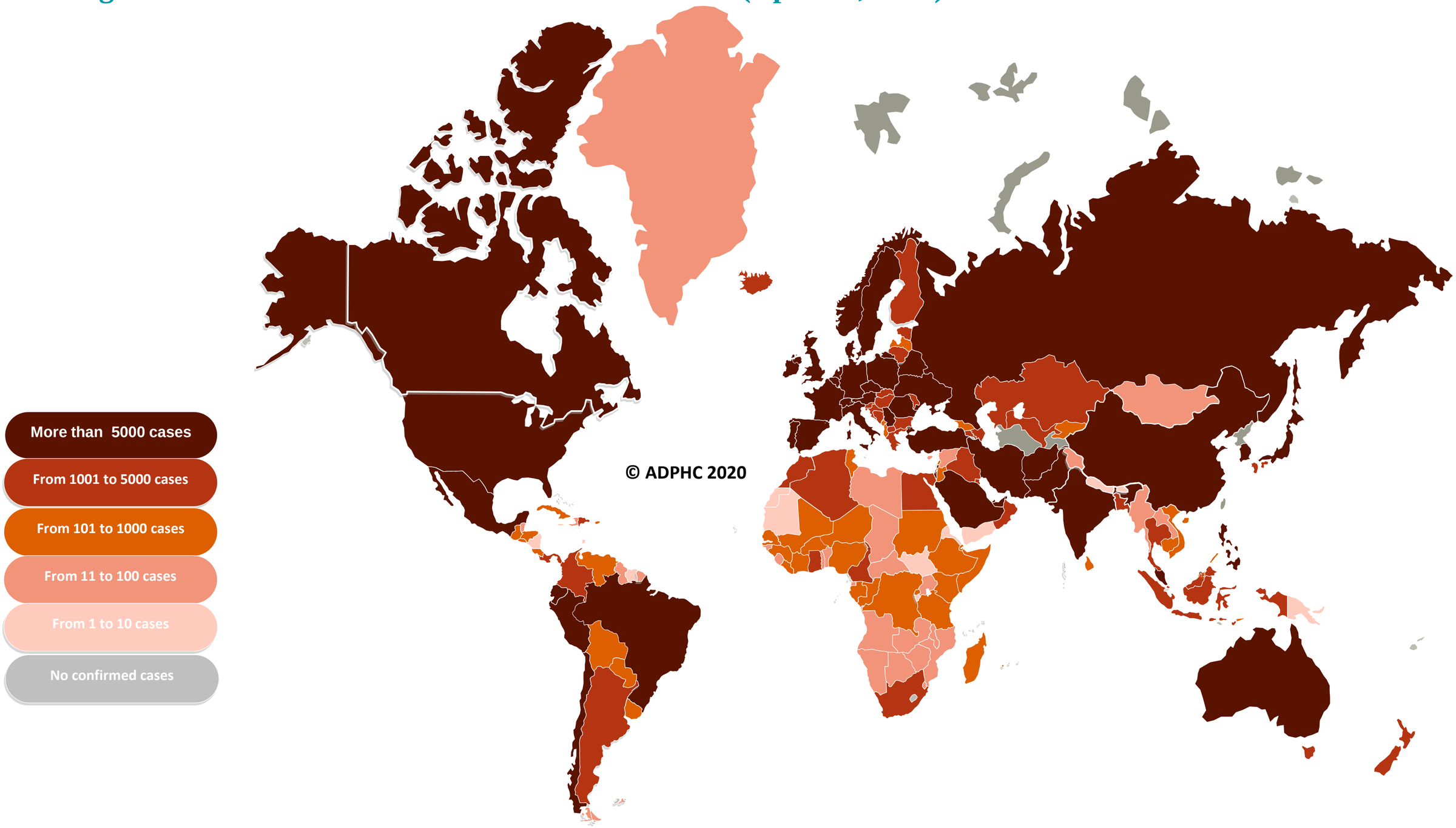
## Figure 6: Global daily new deaths due to COVID-19 (January 22 to April 24, 2020).




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

# Epidemiology

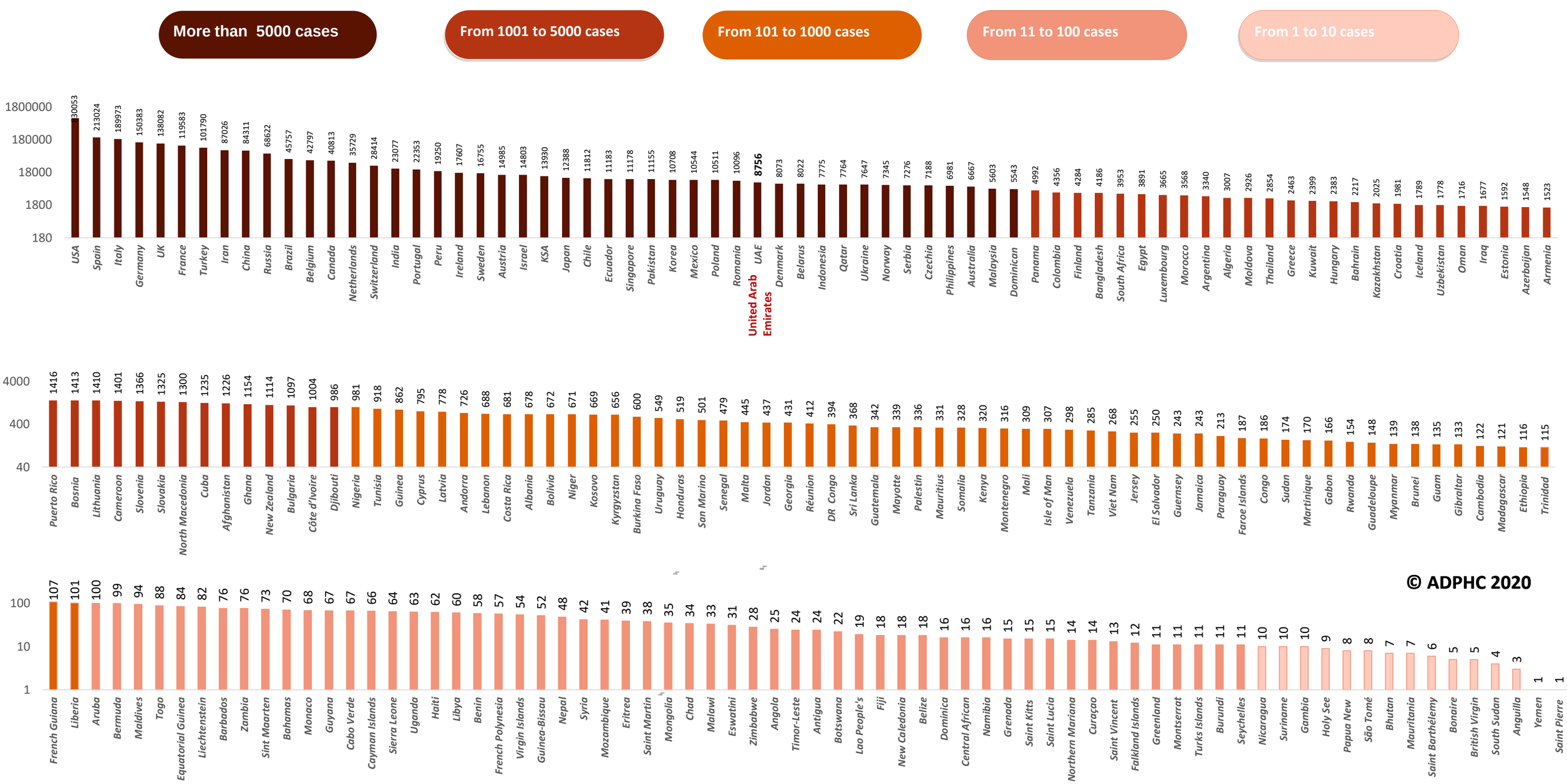
**Figure 7a : Global distribution of COVID-19 cases (April 24, 2020).**




**Map chart published by Abu Dhabi Public Health Center 2020.**

# Epidemiology

## Figure 7B: Bar chart illustrate the global distribution of COVID19 cases April 24 , 2020)

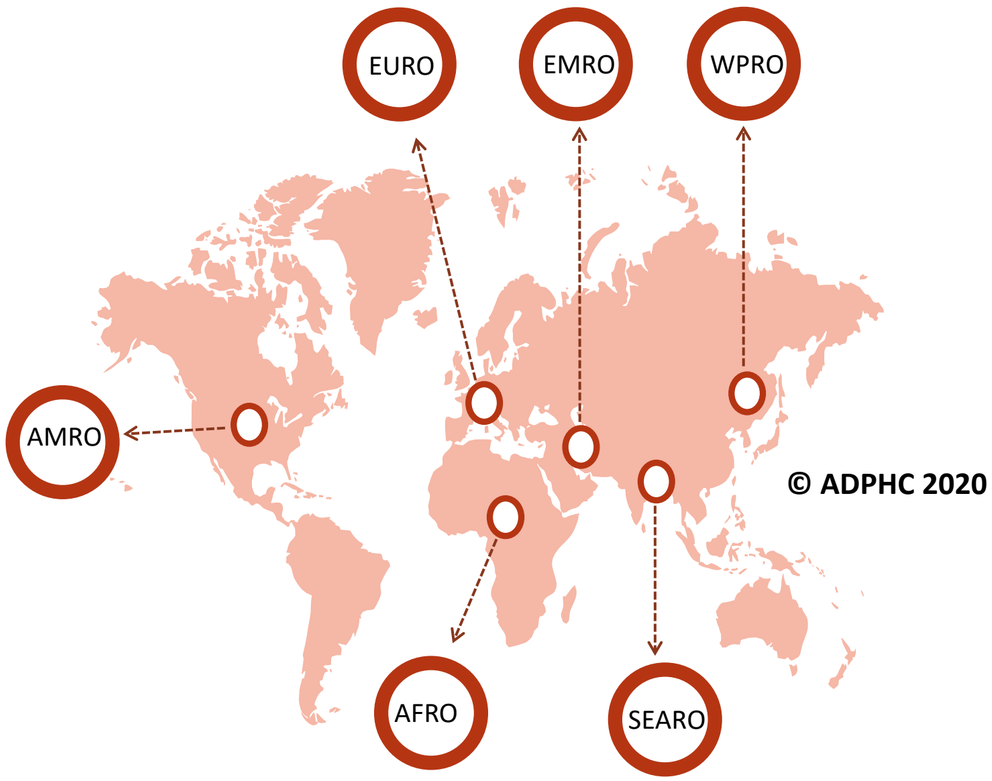



**Map chart published by Abu Dhabi Public Health Center 2020.**

**Data resources: WHO**

# Epidemiology

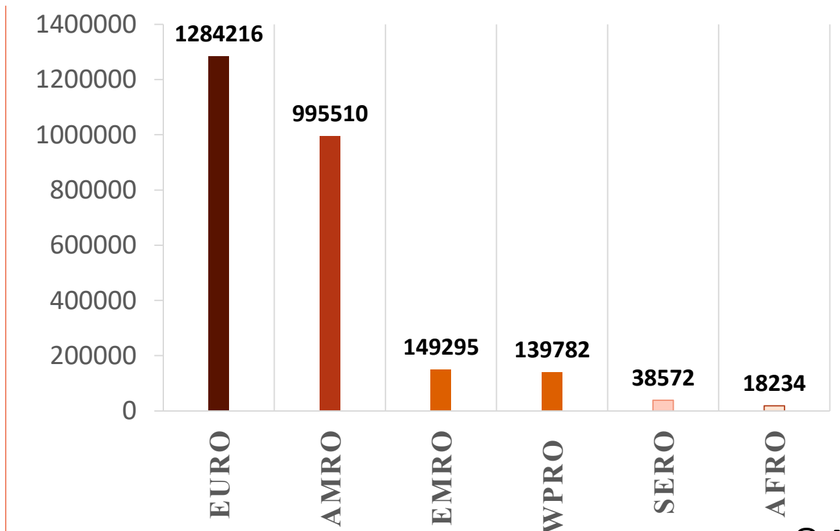
## Figure 8: illustrate the Global distribution of COVID19 cases per region (April 24, 2020)

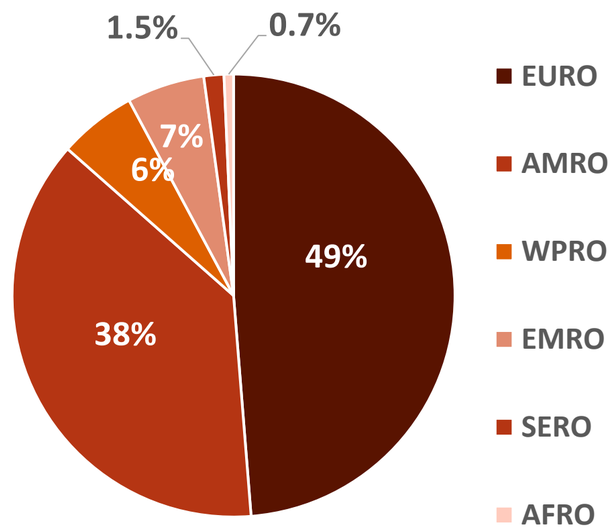





**Map chart published by Abu Dhabi Public Health Center 2020.**
**Data resources: WHO**

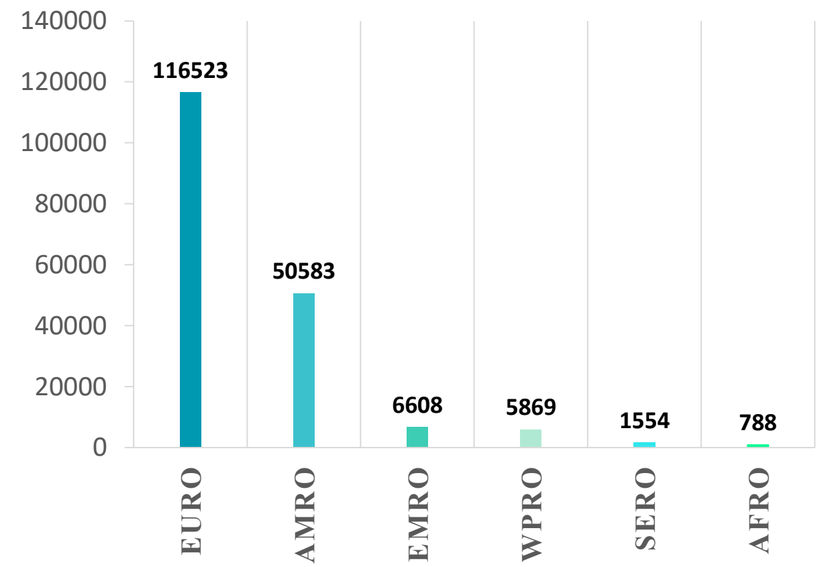
**INFECTED**

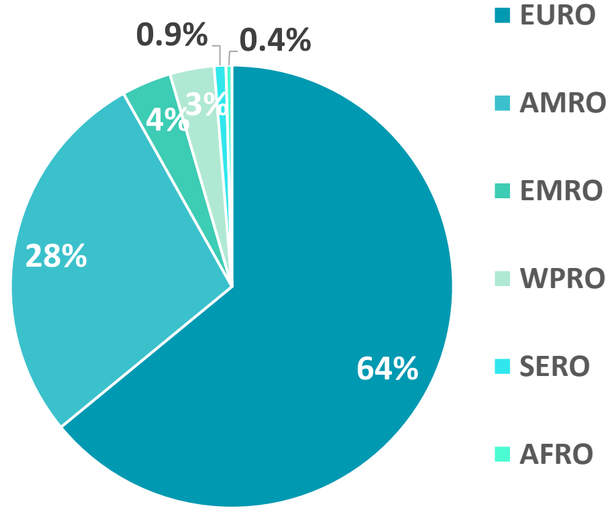





**DEATH**

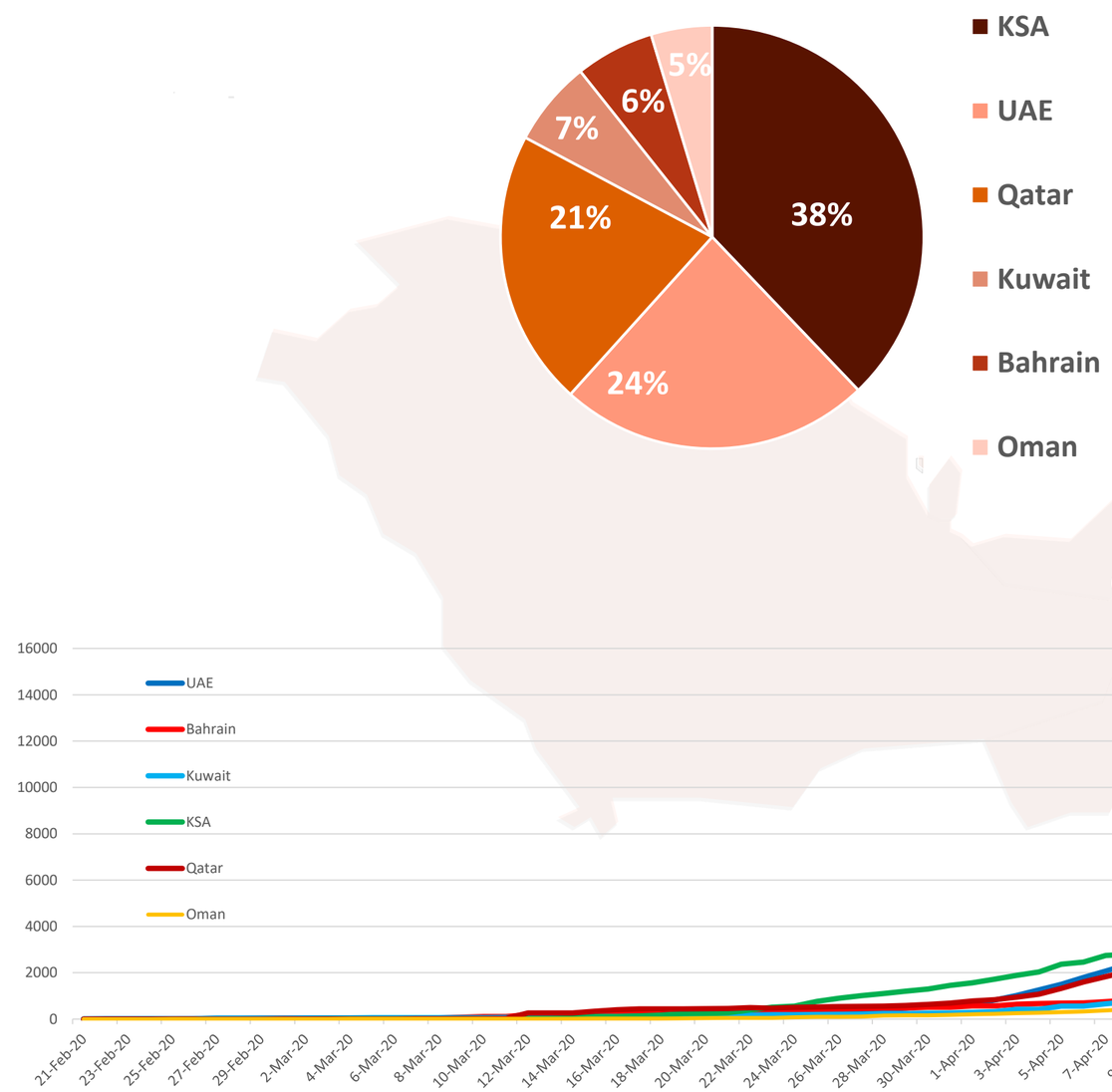


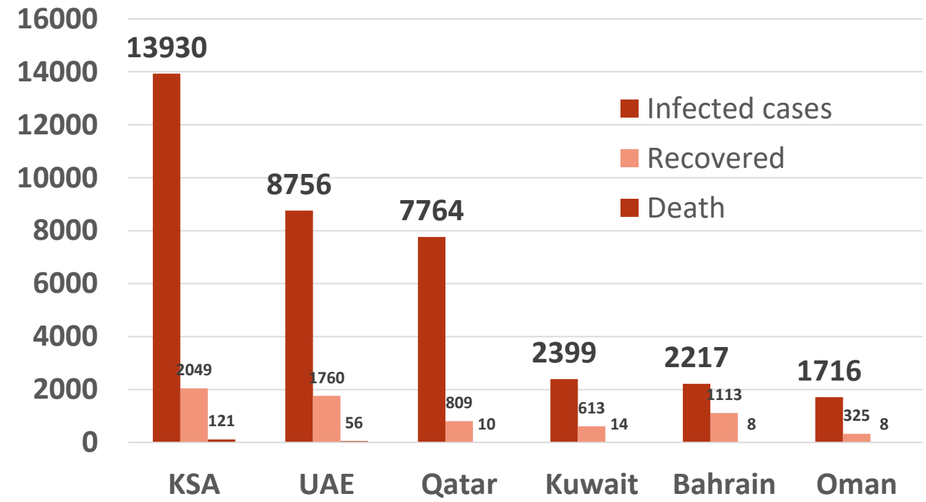
# Epidemiology

## Figure 9: Comparative analysis of the distribution of COVID19 cases in GCC countries (April 24, 2020)

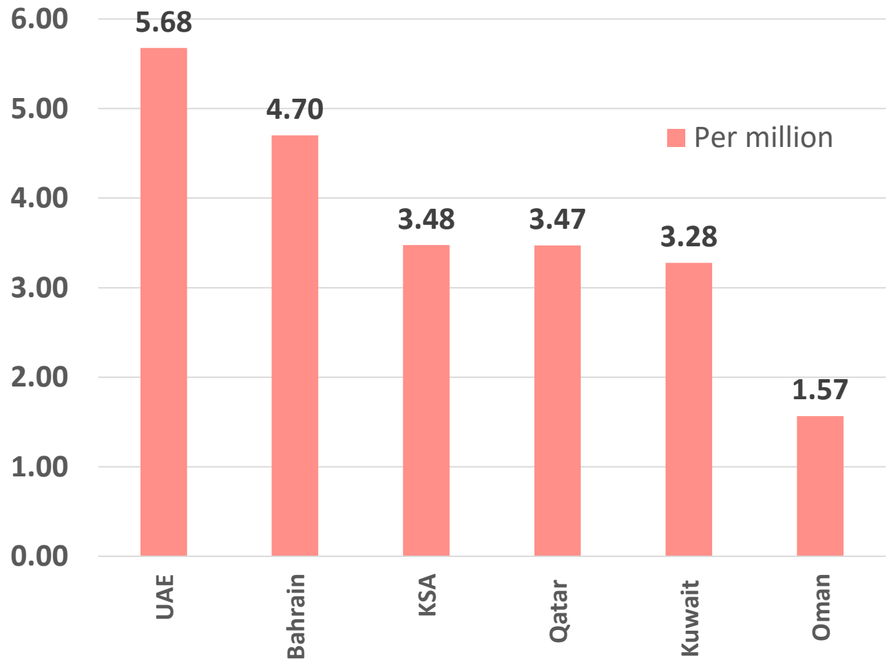
### TOTAL NUMBER OF INFECTED CASES




### Total number of infected, recovered and Deaths




### Death per million




**charts published by Abu Dhabi Public Health Center 2020.**

**Data resources: WHO**

# Treatment

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## Article 1: Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19

**Published: April 23, 2020 in NEMJ**


**Summary:**

This article provide a review on the evidence behind the use of antihypertensive drugs (Renin–Angiotensin–Aldosterone System inhibitors) which block one of the main receptors ( ACE2) involved in COVID19 pathogenesis (as many controversy have been made since the beginning of the pandemic that these medications might have adverse effects on COVID19 patient and some call for stopping these medication on Hypertensive patients. Below are the main points of this review:

- ACE2, an enzyme that physiologically inhibits RAAS activation, is the functional receptor to SARS CoV- 2, the virus responsible for the Covid-19 pandemic
- Select preclinical studies have suggested that RAAS inhibitors may increase ACE2 expression, raising concerns regarding their safety in patients with Covid-19
- **Insufficient data** are available to determine whether these **observations readily translate to humans**, and no studies have evaluated the effects of RAAS inhibitors in Covid-19
- Clinical trials are under way to test the safety and efficacy of RAAS modulators, including recombinant human ACE2 and the ARB losartan in Covid-19
- **Abrupt withdrawal of RAAS inhibitors in high-risk patients**, including those who have heart failure or have had myocardial infarction, **may result in clinical instability and adverse health outcomes**
- Until further data are available, **we think that RAAS inhibitors should be continued in patients in otherwise stable condition who are at risk for, being evaluated for, or with Covid-19**

# Treatment

**Article 2 : Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents**

**Published: April 22, 2020 in JAMA**

**Summary:**

This is the first systematic review addressing the clinical features of COVD-19 infection among children and adolescent population. A total of 815 articles were identified. Eighteen studies with 1065 participants (444 patients were younger than 10 years, and 553 were aged 10 to 19 years) with confirmed SARS-CoV-2 infection were included in the final analysis.

**Findings:**

Children mainly acquire SARS-CoV-2 infection from their family members but seem to experience less severe COVID-19 than adults, presenting mild symptoms, if any, good prognosis, and recovering within 1 to 2 weeks after disease onset.

**Chen et al reports:**

- The main radiologic features in symptomatic and asymptomatic pediatric are **bronchial thickening, ground-glass opacity, or inflammatory lung lesions, suggestive of pneumonia.**
- Most got infection from parents, **couple of infant acquired covid-19 during vaginal delivery** or through postpartum breastfeeding, on the other hand 9 cases of pregnant women with COVID-19 who underwent cesarean delivery, without transmitting COVID-19 to their infants. **Be noted that respiratory viruses, including MERS and SARS, did not show infection through vertical (intrauterine) and peripartum transmission or through breastfeeding.**
- The **Chinese Working Group** for the Prevention and Control of Neonatal SARS-CoV-2 Infection **recommends milk formula for child of infected mother** while **UNICEF recommends continuing breastfeeding with applying necessary precautions**

**Xu et al** reported that 8 pediatric patients tested positive on **rectal swabs**, even after nasopharyngeal testing was negative, suggesting viral shedding and the possibility of fecal-oral viral transmission to others.

- This shows the importance of extensive preventive strategies including quarantining and limitation of playing and school activities.

# Treatment

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## Article 2 :

## Summary:

Table. Results of Systematic Review

| Source | Publication date | Study type | Country | No. Patients | Age <10 y | Age 10-19 y | Age | Sex | Symptoms (yes/no); type of symptoms | Radiologic Tests | Radiologic Findings | Therapy (yes/no); type of therapy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cai et al[11] | February 4, 2020 | Case report | China | 1 | 1 | 0 | 7 y | M | Yes; the child presented with fever, cough, runny nose, dyspnea, nausea, and loss of appetite. | Chest radiograph and CT | Bronchial thickening | Yes; supportive care |
| Shen and Yang[12] | February 5, 2020 | Case series | China | 28 | NA | NA | 1 mo-17 y | NA | Yes; several patients gradually presented with fever, fatigue, and dry cough, accompanied by other upper respiratory symptoms including nasal congestion, runny nose, and seldom gastrointestinal symptoms such as nausea, vomiting, and diarrhea. Most pediatric patients had mild symptoms, without fever or pneumonia. They had good prognosis and recovered within 1 to 2 wk after disease onset. Only a few patients had lower respiratory tract infections. | Yes | Lung imaging examination revealed mild increase of lung markings or ground-glass opacity or pneumonia. | NA |
| Song et al[13] | February 6, 2020 | Retrospective study | China | 1 | 0 | 1 | 16 y | NA | NA | Chest CT | NA | NA |
| Chang et al[14] | February 7, 2020 | Case series | China | 2 | 1 | 1 | 2-15 y | NA | Yes; the youngest patient (age 2 y) had intermittent fever for 1 wk and persistent cough for 13 d before COVID-19 diagnosis. No symptoms were reported for the other child. | Yes | NA | NA |
| Schwartz and Graham[15] | February 10, 2020 | Case report with review of literature | China | 1 | 1 | 0 | 30 h | NA | Yes; the infant developed shortness of breath and showed abnormalities of liver function. | Chest radiograph | Abnormal chest radiographs | NA |
| Zhang et al[16] | February 11, 2020 | Case report | China | 1 | 1 | 0 | 3 mo | F | Yes; the patient developed fever. | Chest radiograph and CT | Bronchial thickening | Yes; the patient required antiviral therapy, antibiotics (azithromycin and ceftazidime), aerosol therapy, and supportive care. |
| Chen et al[17] | February 11, 2020 | Case report | China | 1 | 1 | 0 | 13 mo | M | Yes; the patient developed vomiting and diarrhea 6 d before he showed fever, dyspnea, cyanosis, and hepatomegaly. The patient developed shock with metabolic acidosis that required intensive care and the administration of vasoactive drugs (dopamine), IV rehydration, and assisted ventilation. The patient also showed acute kidney failure that required the dialysis. | Chest radiograph and CT | Imaging showed different area of lung thickening, suggesting pneumonia. | Yes; shock required dopamine, IV rehydration, blood transfusion, and assisted ventilation. Also, the patient was treated with antibiotic therapy (meropenem and linezolid), oseltamivir, IVIG and steroids, nebulized interferon, and dialysis. |
| Wei et al[18] | February 14, 2020 | Retrospective study | China | 9 | 9 | 0 | 1-11 mo | 2 M/7 F | Yes, but not all patients; 4 patients reported fever, 2 had mild upper respiratory tract symptoms, and 1 had no symptoms. For 2 patients, there were no available data on symptoms. None of the 9 infants required intensive care or mechanical ventilation or had any severe complications. | NA | NA | NA |

# Treatment

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## Article 2: Cont.,

Table. Results of Systematic Review (continued)

| Source | Publication date | Study type | Country | No. | | | Age | Sex | Symptoms (yes/no); type of symptoms | Radiologic | | Therapy (yes/no); type of therapy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Patients | Age <10 y | Age 10-19 y | | | | Tests | Findings | |
| Chan et al[19] | February 15, 2020 | Retrospective study | China | 2 | 2 | 0 | 7 and 10 y | 10-y-old M | No; patients were asymptomatic. | Chest CT | The 10-y-old patient showed ground-glass lung opacities. | NA |
| Zhang et al[20] | February 15, 2020 | Retrospective study | China | 1 | 0 | 1 | 15 y | M | Yes; the patient developed fever and fatigue. | Chest radiograph | NA | NA |
| Feng et al[21] | February 16, 2020 | Retrospective study | China | 15 | NA | NA | 4-14 y | 5 M/10 F | Yes, not all patients; 5 children were febrile, and 10 were asymptomatic. | Chest CT | At chest CT images, 6 patients had no lesions, while 9 patients had pulmonary inflammation lesions. Seven cases of small nodular ground glass opacities and 2 cases of speckled ground glass opacities were found. | NA |
| Zeng et al[22] | February 17, 2020 | Case report | China | 1 | 1 | 0 | 17 d | M | Yes; the newborn had a history of rhinitis and vomiting. | Chest radiograph and CT | Imaging showed different area of lung thickening and enlargement of lung hila, suggesting pneumonia. | Yes; the newborn required IV rehydration and supportive care. |
| Pediatric Branch of Hubei Medical Association et al[23] | February 22, 2020 | Case series | China | 14 | NA | NA | 6 mo-14 y | 6 M/8 F | Yes; fever, cough, fatigue, nausea, and vomiting were main symptoms. | NA | NA | NA |
| Wu and McGoogan[24] | February 24, 2020 | Retrospective study | China | 965 | 416 | 549 | 0-19 y | NA | NA | NA | NA | NA |
| Tian et al[25] | February 26, 2020 | Retrospective study | China | 11 | NA | NA | 0-12 y | NA | Yes; the most common symptoms of illness onset were fever, cough, fatigue, dyspnea, and headache. One severe case included dyspnea (patient age, <1 y). | NA | NA | NA |
| Kam et al[27] | February 28, 2020 | Case report | Singapore | 1 | 1 | 0 | 6 mo | M | Yes; the patient developed a transient temperature of 38.5 °C (1 episode). | NA | NA | No; no therapy |
| Cai et al[26] | February 28, 2020 | Case series | China | 10 | 10 | 0 | 3-131 mo | 4 M/6 F | Yes; 8 patients (80%) had fever, 6 (60%) had cough, 4 (40%) had sore throat, 3 (30%) had stuffy nose, and 2 (20%) had sneezing and rhinorrhea. None of the patients had diarrhea or dyspnea during the course of illness. Fever resolved 24 h after fever onset with the peak of fever ranging from 37.7 °C to 39.2 °C. | Chest radiograph | Chest radiograph revealed unilateral patchy infiltrate in 4 of 10 patients (40%). | Yes; all patients received symptomatic treatment with no need of oxygen therapy, and a few patients with pneumonia received empirical antibiotic therapy. |
| Tong et al[10] | March 3, 2020 | Case reports | China | 1 | 0 | 1 | 12 y | M | No; the patient was asymptomatic. | NA | NA | No; NA |

Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography; F, female; IV, intravenous; IVIG, intravenous immunoglobulin; M, male; NA, not available.

# Diagnosis :

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## Article 3: Duration of viral shedding of discharged patients with severe COVID-19

Summarized by subject matter experts

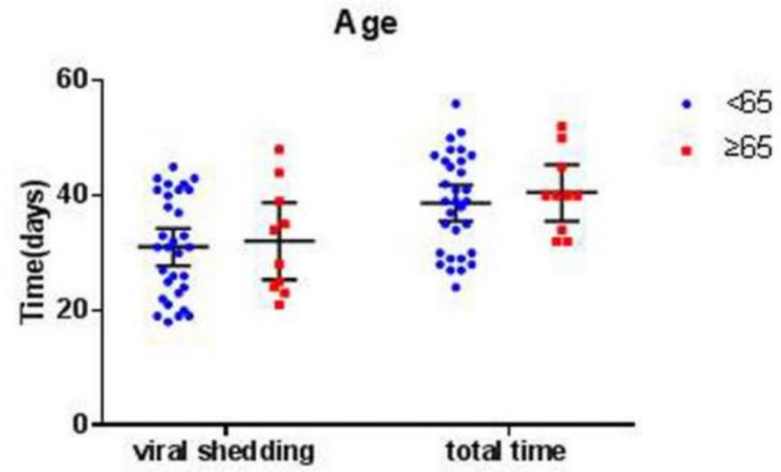
**Published: April 17 2020 by** Clin Infect Dis

**Summary:**

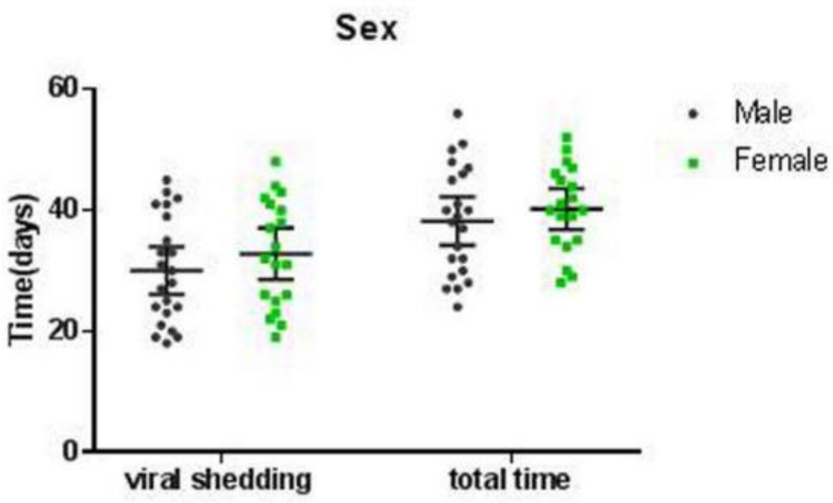
- **The study discussed the duration of shedding of COVID-19 in 41 sever patients.**
  Sever infection was defined if having either of:
  - Respiratory distress with respiratory rate was more than 30 times/min
  - Oxygen saturation ≤93% in resting state
  - PaO2/FiO2 ≤300mmHg (1mmHg=0.133kPa)
- **Hospital discharge should meet the following criteria**
  - Normal temperature lasting longer than 3 days
  - Resolved respiratory symptoms
  - Substantially improved acute exudative lesions on chest computed tomography (CT) images
  - Two consecutively negative RT-PCR test results separated by at least 1 day.

## Findings

- The median duration of viral shedding was **31.0** (IQR: 24.0-40.0) days from illness onset (**Range 18-48 days**)
- No significant difference with the viral shedding time between according to gender (Figure 1), and between patients <65 years old and patients ≥65 years old (Figure 2)




**(Fig. 1)** viral shedding time between male and female




**(Fig. 2)** viral shedding time between male and female

## Conclusion

This duration of viral shedding has clinical implications for :

- Taking isolation decision of discharged patients
- Guiding the duration of hospitalization for patients with severe COVID-19.

However, the study is limited with the small number of patients as well as with not including mild or moderate COVID-19 infection.

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## Article 4: Patient-derived mutations impact pathogenicity 1 of SARS-CoV-2

**Published:** April 19, 2020 in medRxiv

Summarized by subject matter expert

**Summary:**

SARS-CoV-2 is an (+) sense RNA virus that undergoes regular mutations in its genome as it replicates. Whether these randomly-generated mutations in infected individuals can be linked to differences in viral virulence (pathogenicity) was explored in this study. Eleven virus samples from mildly-, moderately-, or severely-ill patients were isolated from either sputum, stool, or nasopharyngeal swabs. Ultra-deep sequencing of the viral RNA was used to identify sequence differences in these viruses followed by their phylogenetic analysis. A total of 33 mutations were observed in these 11 patient isolates with 1-5 mutations per patient in the coding sequences of the virus of which 6 were in the spike glycoprotein (S protein), the protein critical for interaction with the host cell receptor, the ACE2 protein. The authors analyzed the effect of these mutations on the 11 patient isolates on viral loads and cytopathiticy (CPE) by conducting *in vitro* infectivity assays in monkey kidney Vero epithelial cells which is a standard cell line to study coronavirus infection. Using fluorescence assay, they showed that virus could attach to these cells and cause infection, as assessed by qRT-PCR, for three different genes of the virus. This was followed by a qualitative analysis of cytopathic effects of the virus on infected cells. An *in vitro* rather than *in vivo* assay was chosen for the replication and virulence analysis since viral pathogenicity in animals is highly affected by age, host genetics, comorbidities, immune status, etc. that can confound results.

**Conclusions:**

Test of these patient-derived viruses revealed that they could infect Vero cells and cause some cytopathic effects. However, great variation in viral load and CPE was observed between the eleven isolates with up to 270-fold differences in the virus load, assessed over 48 hours of infection. The authors conclude that the mutations acquired by SARS-CoV-2 over time are capable of changing viral pathogenicity and replication dynamics significantly.

**Implications and Study Limitations:**

This study suggests that mutations acquired by SARS-CoV-2 over time worldwide can affect viral virulence, an aspect which is crucial for understanding viral infection mechanisms and strategies for drug and vaccine development to deal with this pandemic. However, the study has several limitations. The authors used mixed viral populations (quasispecies) for their study rather than cloned mutations and did not present quantitative analysis of cell death, which challenges their conclusions on effects of the mutations on viral virulence.