ABU DHABI PUBLIC HEALTH CENTRE | مركز أبوظبي للصحة العامة

Scientific Research Monitoring on COVID-19

1 May 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:** a randomized double blinded control trial showed no difference between **Remdesivir** and placebo in clinical improvement.
- **Diagnosis :** Using artificial intelligence in CT diagnosis the pros and cons.
- **Treatment:** Article discuss the importance of physician push for clinical studies designed to meet the standards necessary to reach reasonable conclusions about the efficacy.
- **Public Health response**: a comparative analysis for four countries including UAE addressing metric measures to guide COVID19 exist plan .

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.

Others

A National Medical Response to Crisis — The Legacy of World War II
An Italian programme for COVID-19 infection in multiple sclerosis
Remdesivir for COVID-19: challenges of underpowered studies

WHO daily report

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WHO daily report 30 April 2020

- WHO reminds health authorities to take specific steps to protect health care workers and communities during essential immunization activities during the COVID-19 pandemic.

- WHO AMRO/PAHO Director, Dr Carissa F. Etienne, has urged for vaccination programs to continue during the COVID-19 pandemic: "**If we fall behind on routine immunizations, particularly for children, we risk outbreaks, thus overwhelming hospitals and clinics with preventable diseases in addition to COVID-19**."

- WHO/EURO Director, Dr Hans Henri P. Kluge, called for transparent knowledge-sharing, tailored support on the ground, and steadfast solidarity.

- WHO SEARO organized a meeting yesterday with vaccine manufacturers and national regulatory authorities to discuss future COVID-19 vaccine manufacturing in the Region.

Epidemiology

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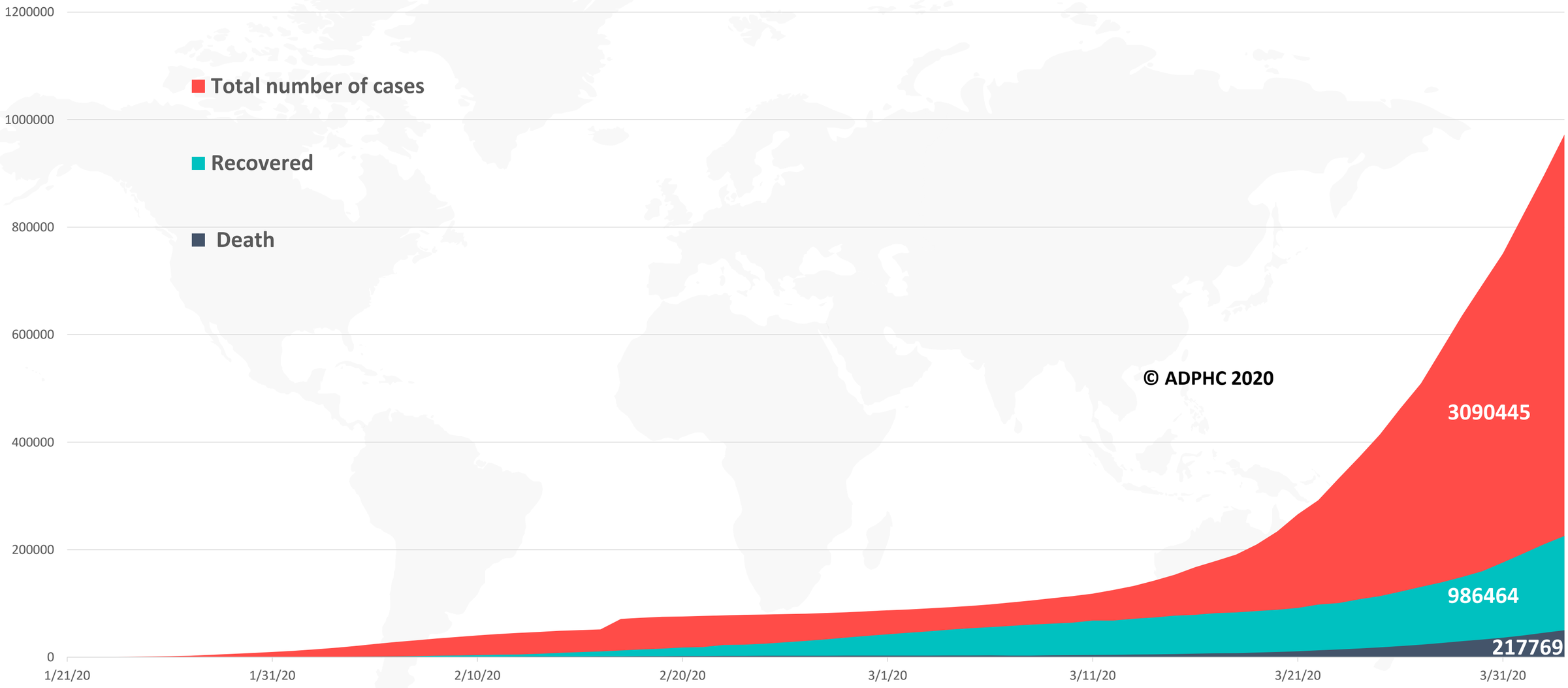
Figure 1: Total number of infected, recovered , and death cases (January 21st to April 30, 2020)

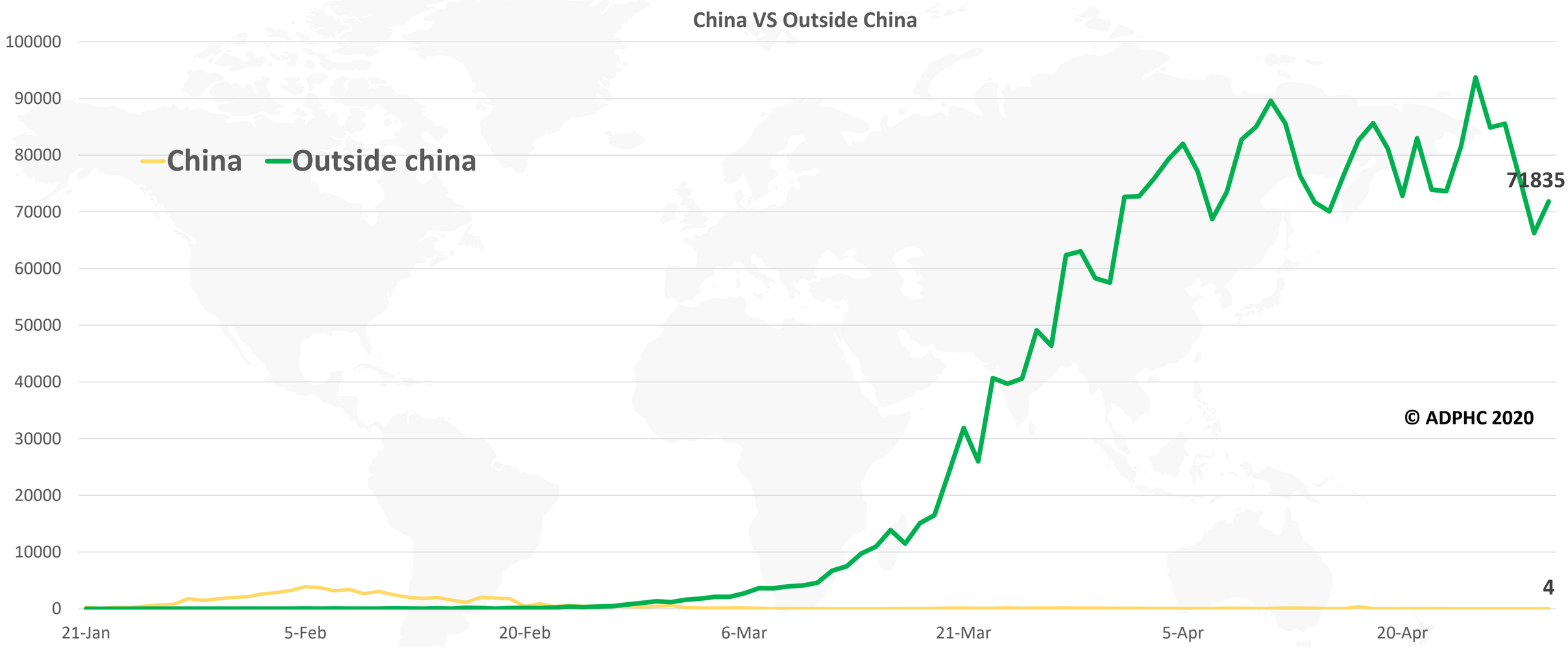


Line graph published by Abu Dhabi Public Health Center 2020.

Data resources: WHO, : John Hopkins University

Epidemiology

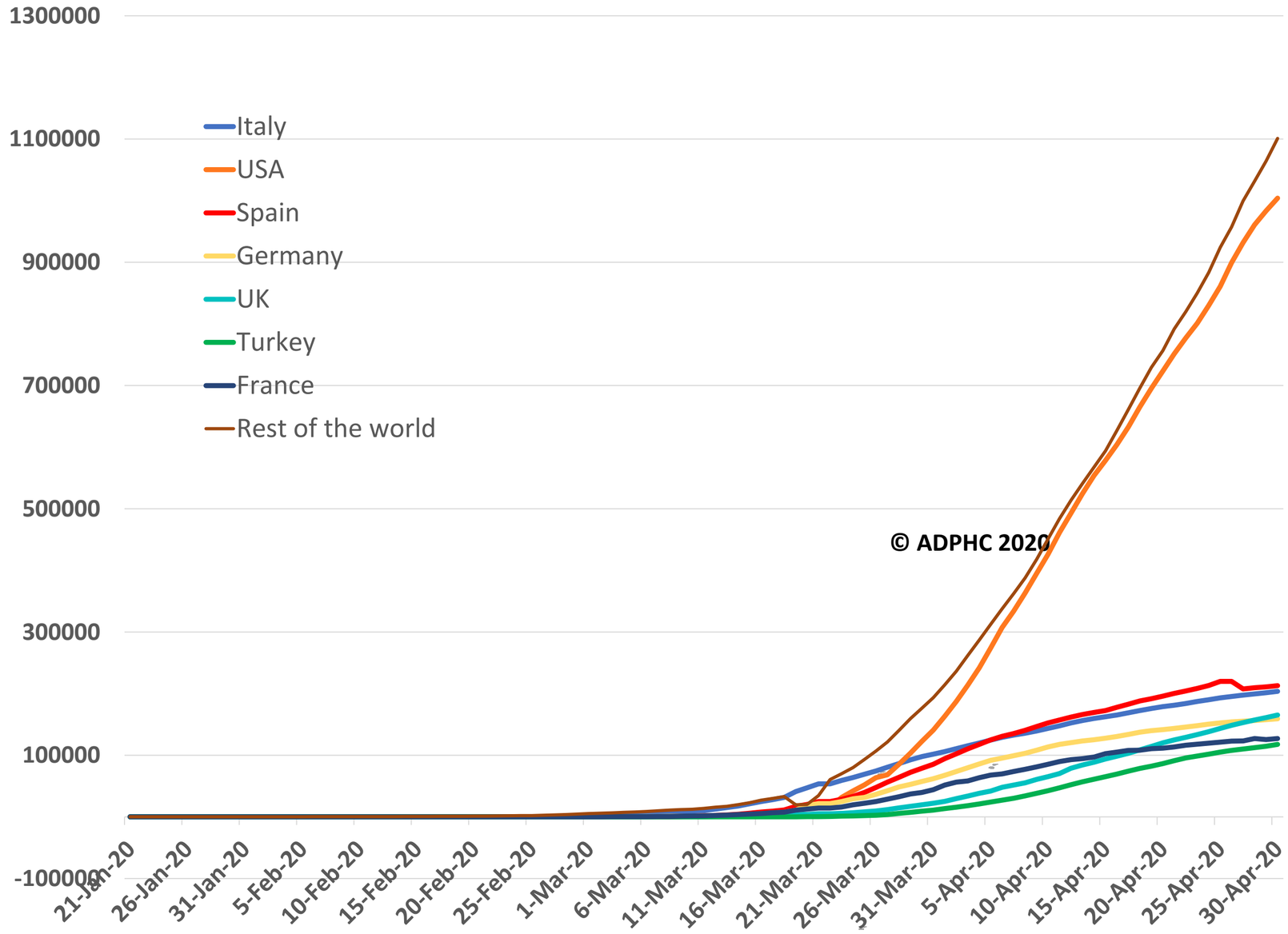
Figure 2: Daily new infected COVID-19 cases reported between (January 21 to April 30, 2020).

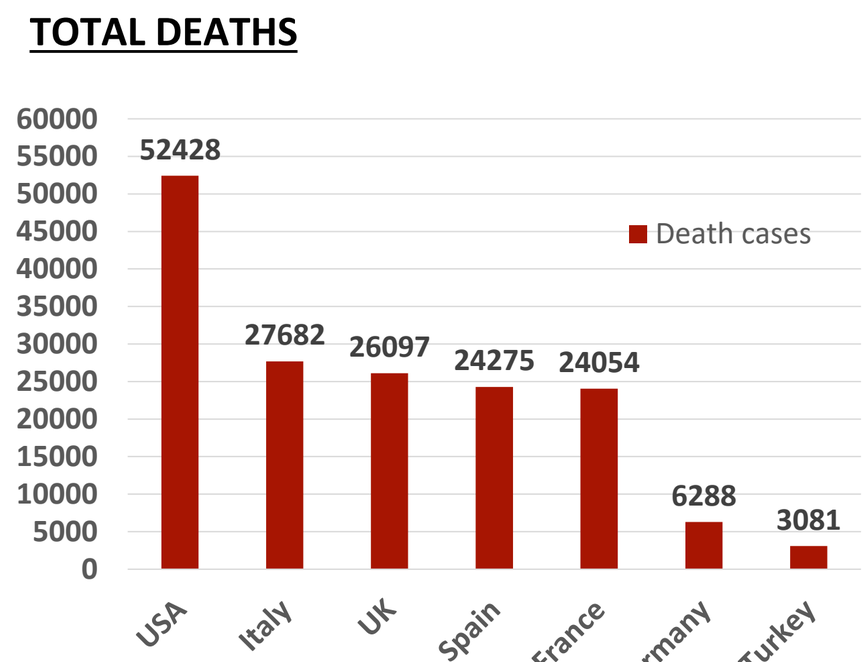


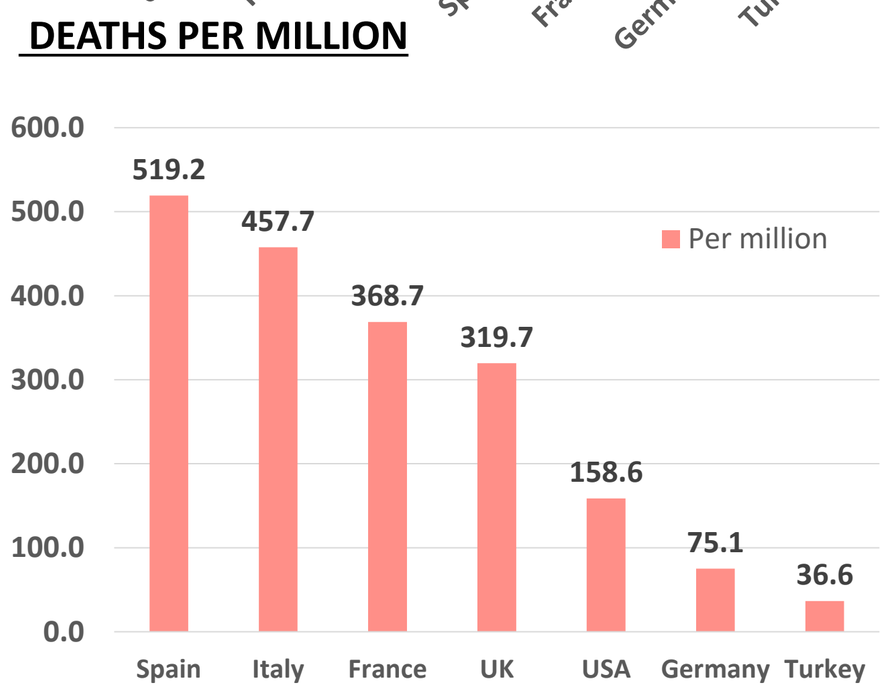
Line graph published by Abu Dhabi Public Health Center 2020.
Data resources: WHO

Epidemiology

Figure 3 : Top 7 countries in the total number of cases due to COVID-19 (January 21 to April 30, 2020).







Line graph published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

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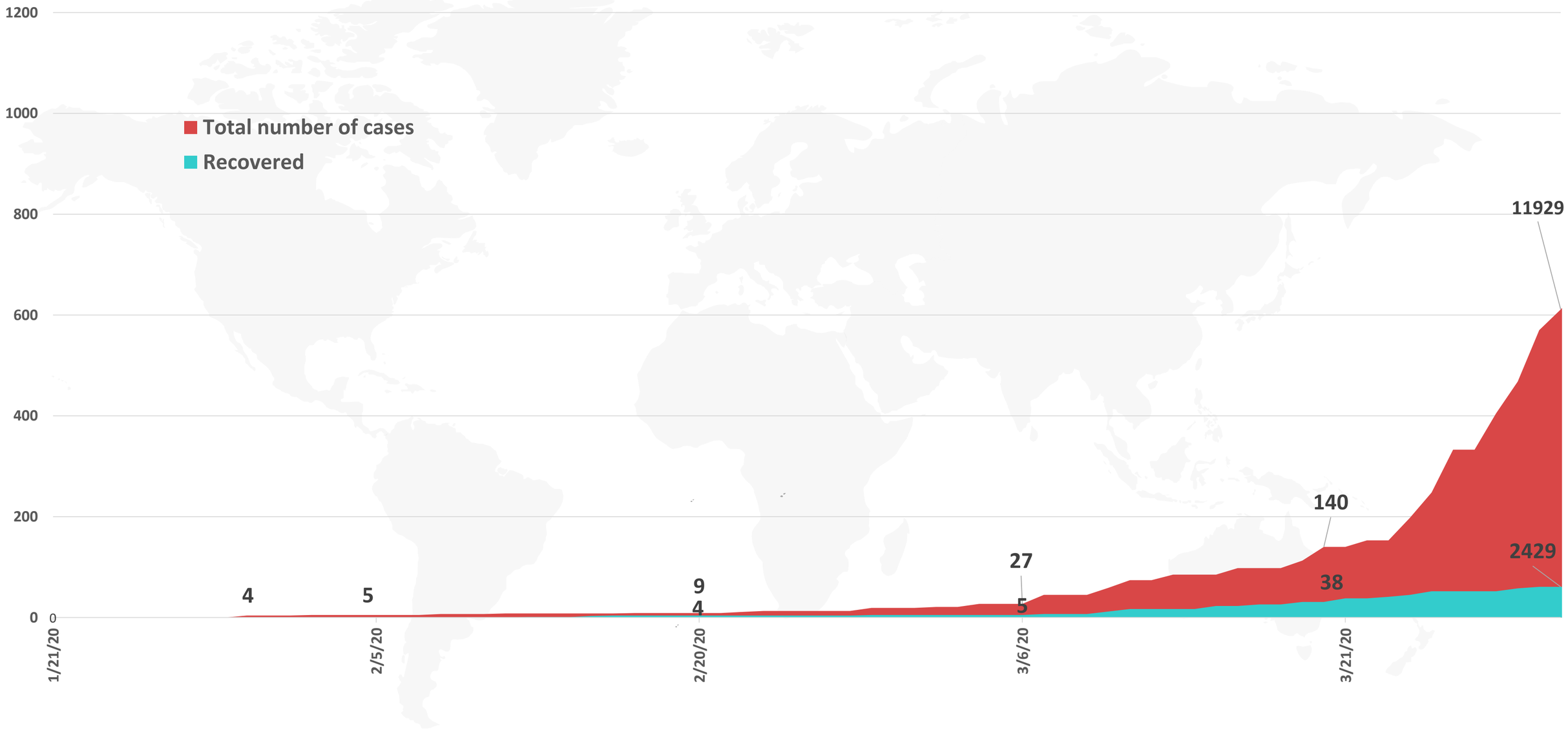
Figure 4: Total number of COVID-19 infected and recovered cases in UAE over time



Line graph published by Abu Dhabi Public Health Center 2020.

Data resources: WHO, : John Hopkins University

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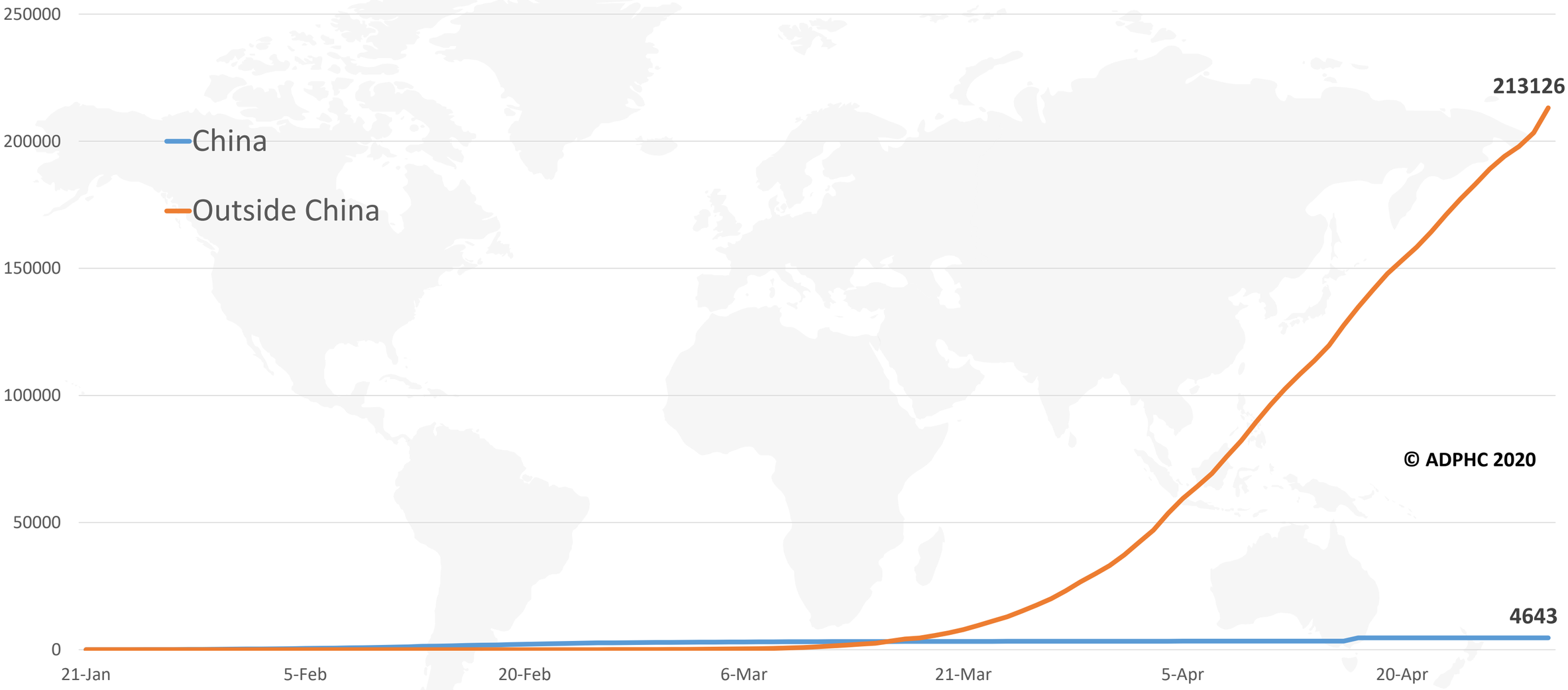
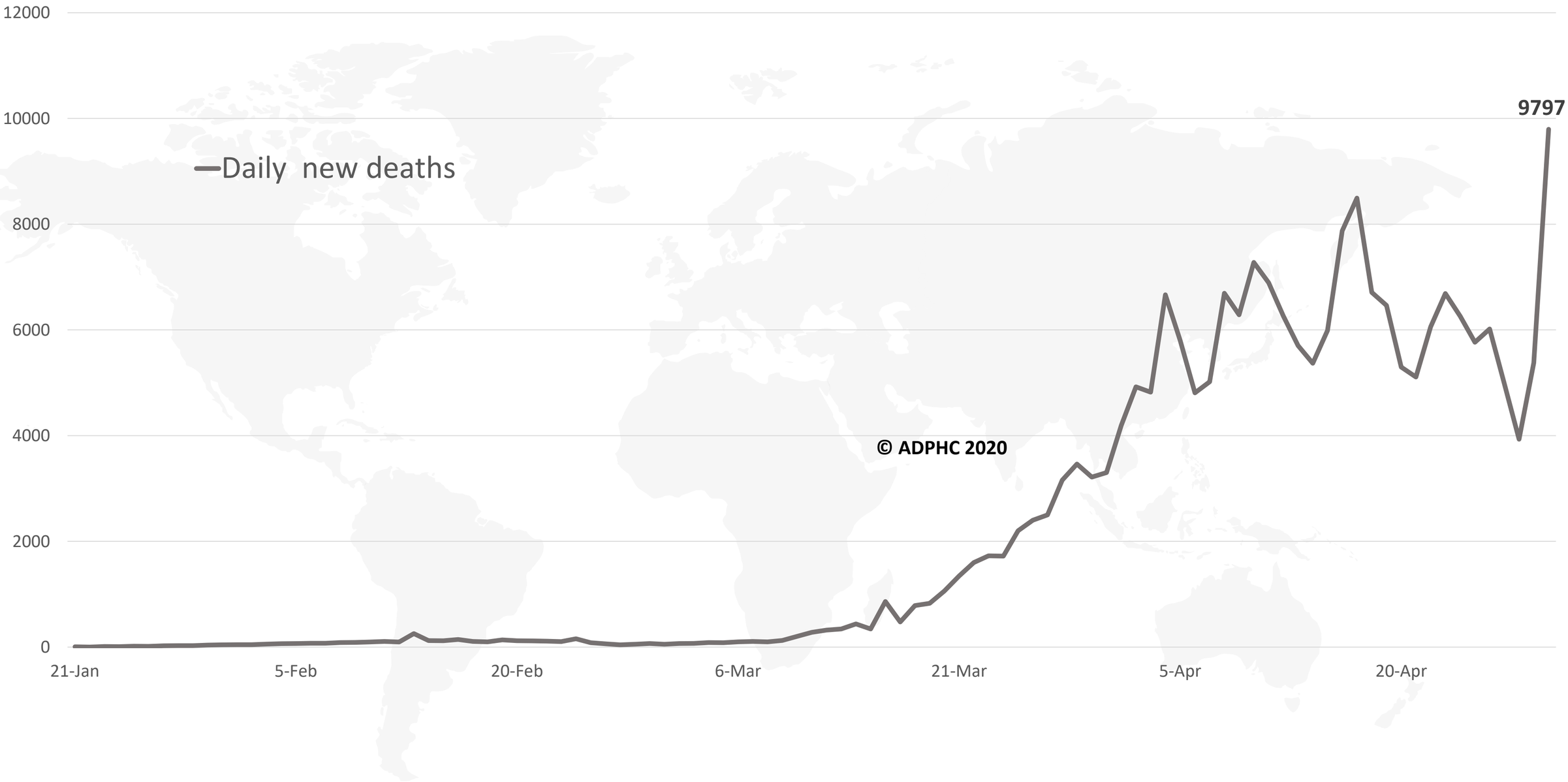
Figure 5: Total number of death due to COVID-19 reported by China and the rest of the world (January 22 to April 30, 2020).



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 30, 2020).



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

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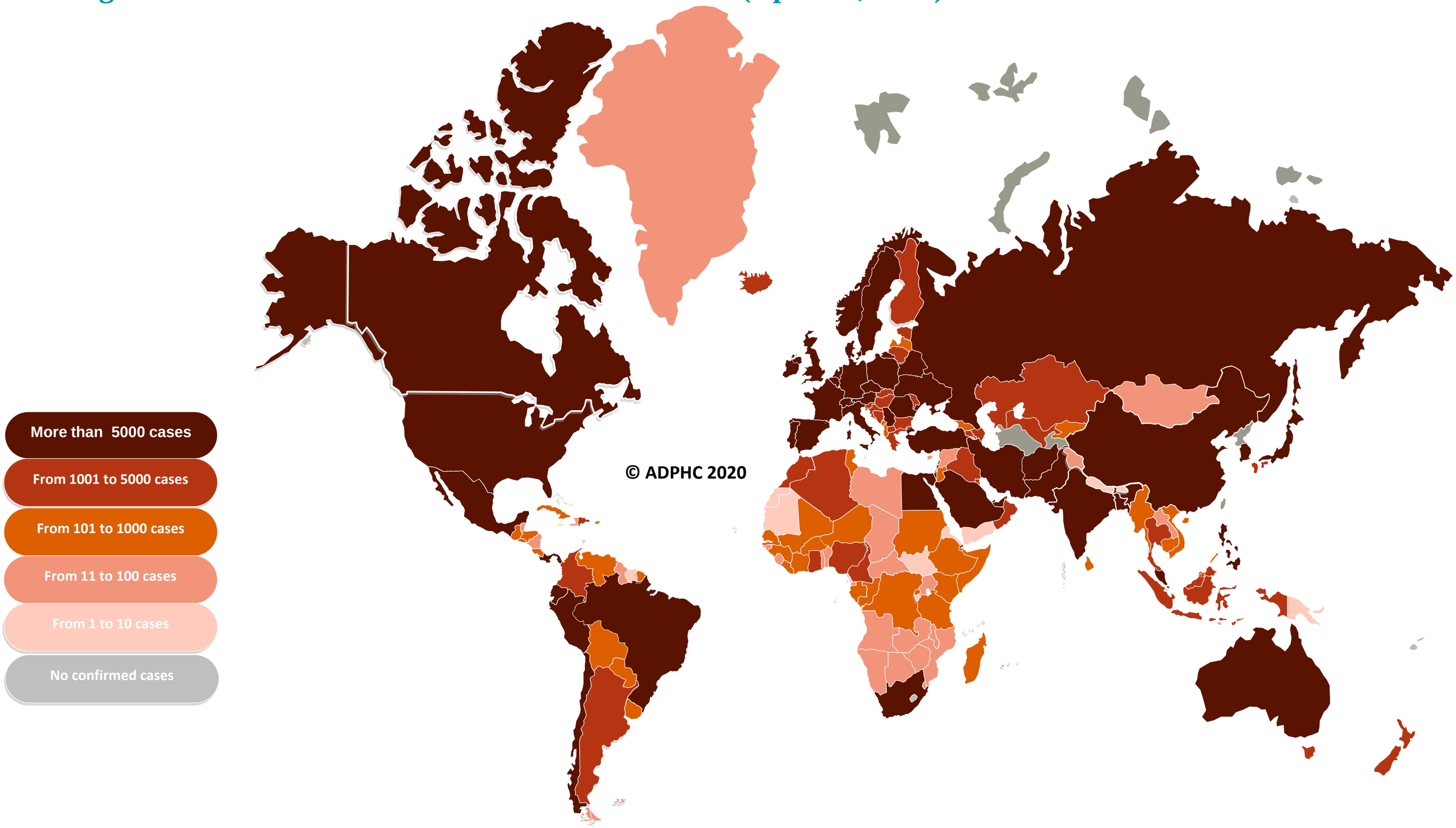
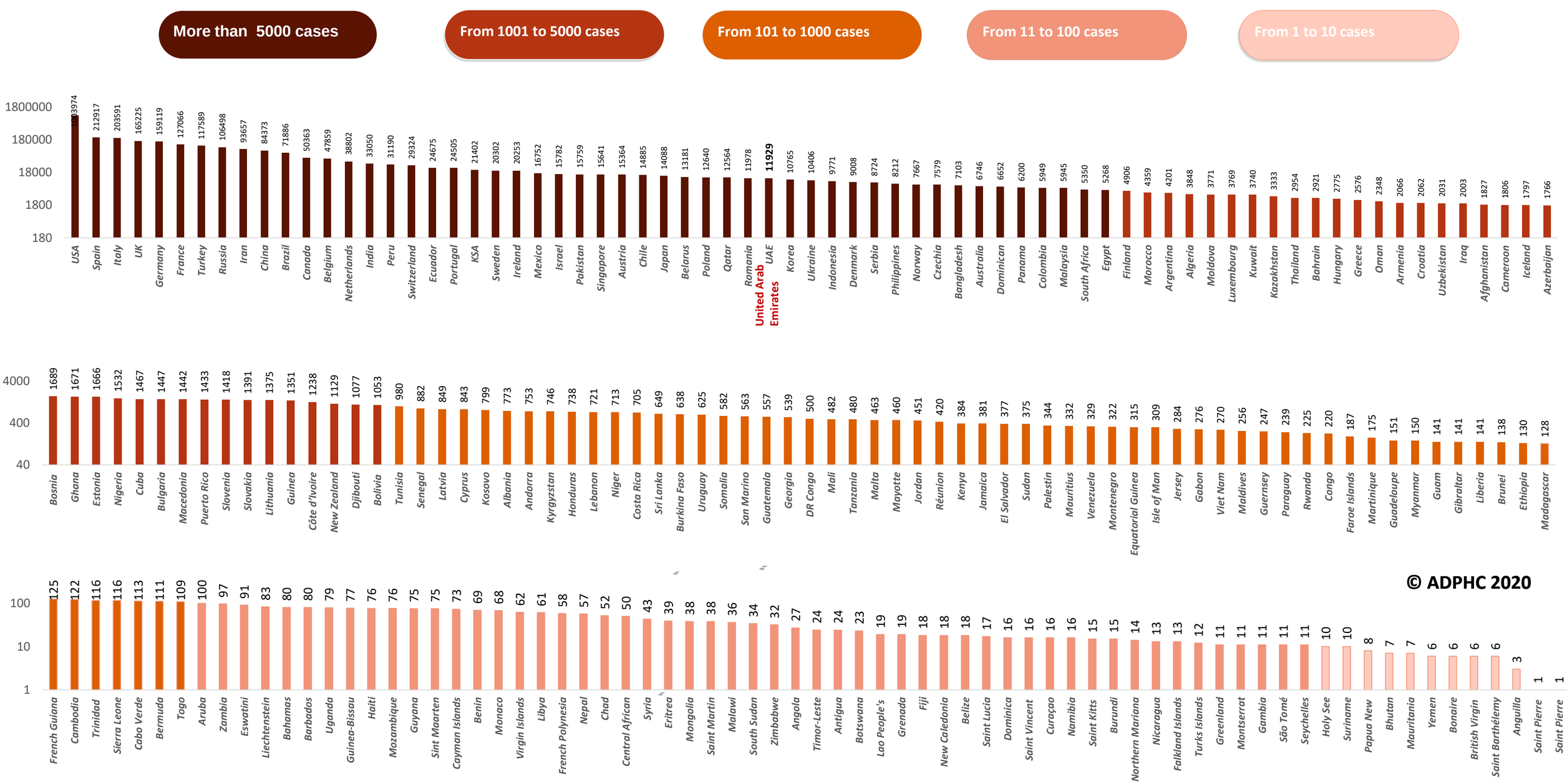
Figure 7a : Global distribution of COVID-19 cases (April 30, 2020).



Map chart published by Abu Dhabi Public Health Center 2020.

Epidemiology

Figure 7B: Bar chart illustrate the global distribution of COVID19 cases April 30, 2020)



Map chart published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

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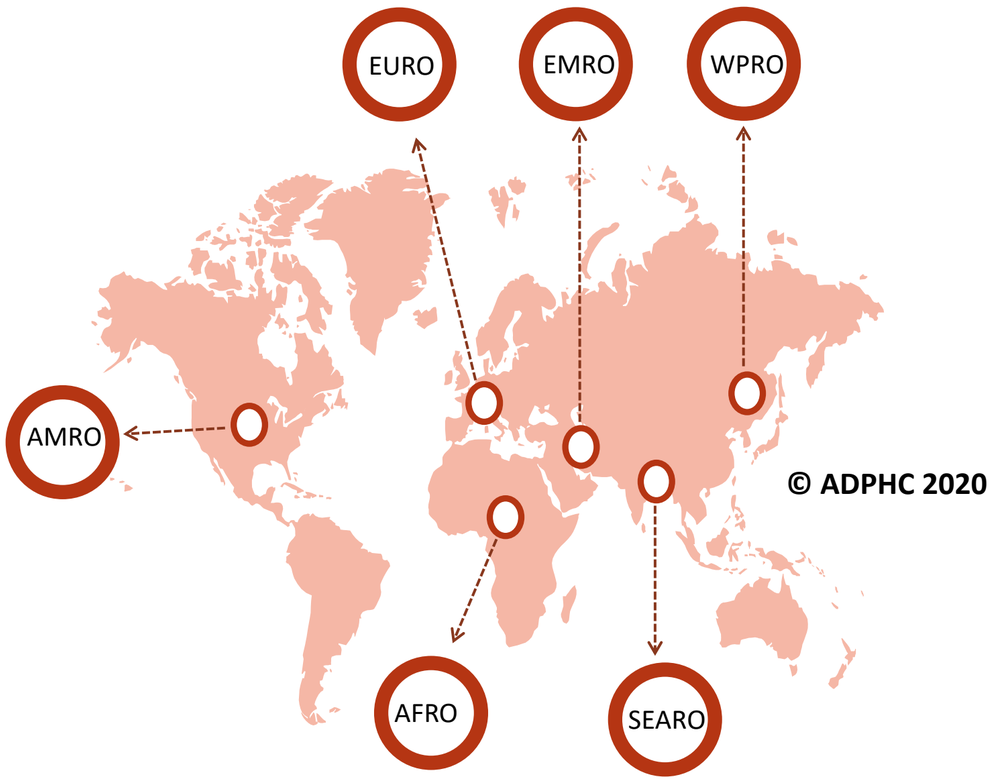
Figure 8: illustrate the Global distribution of COVID19 cases per region (April 30, 2020)



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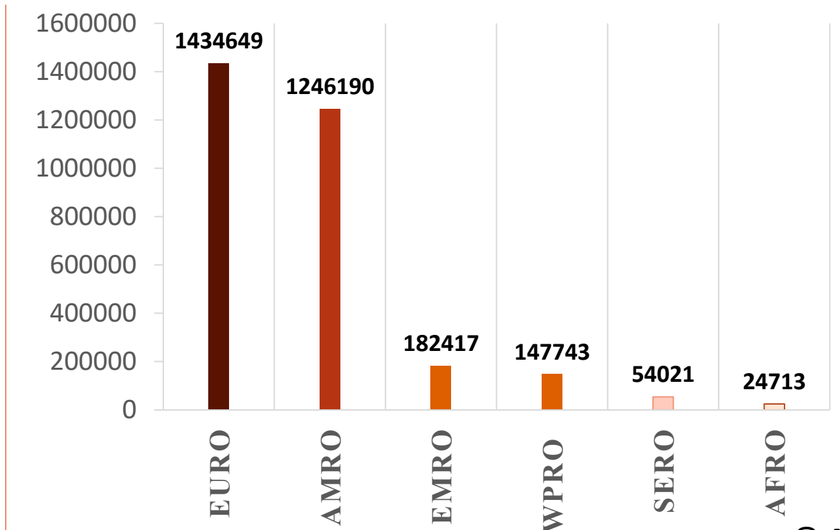
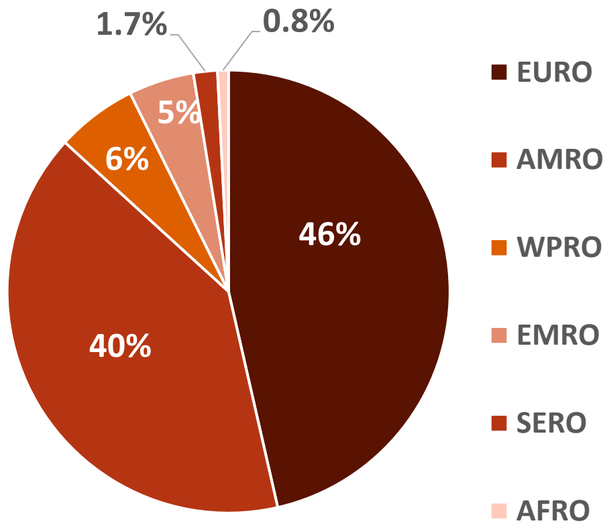
INFECTED





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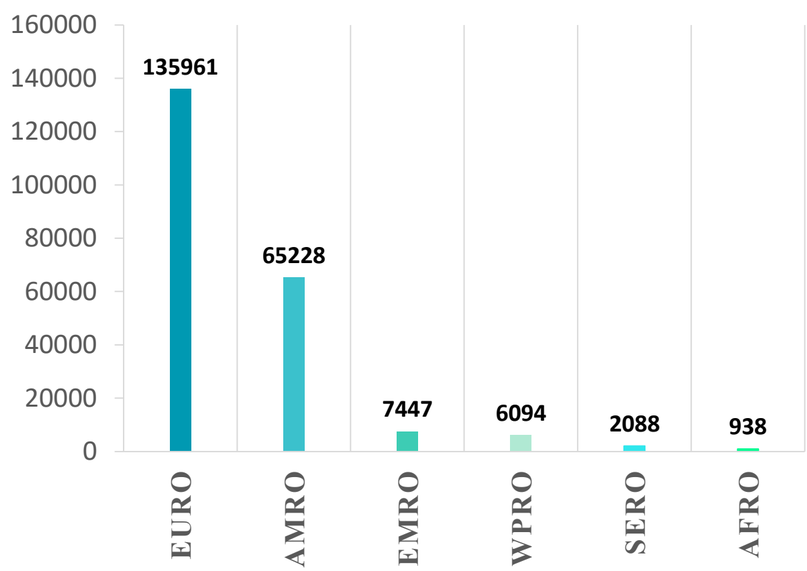
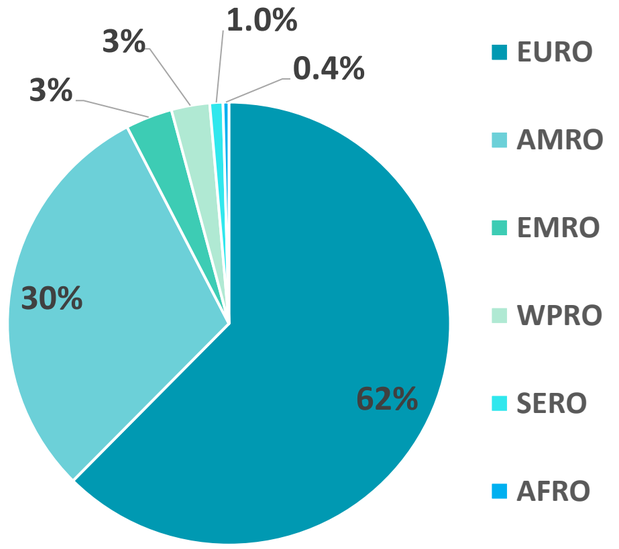
DEATH



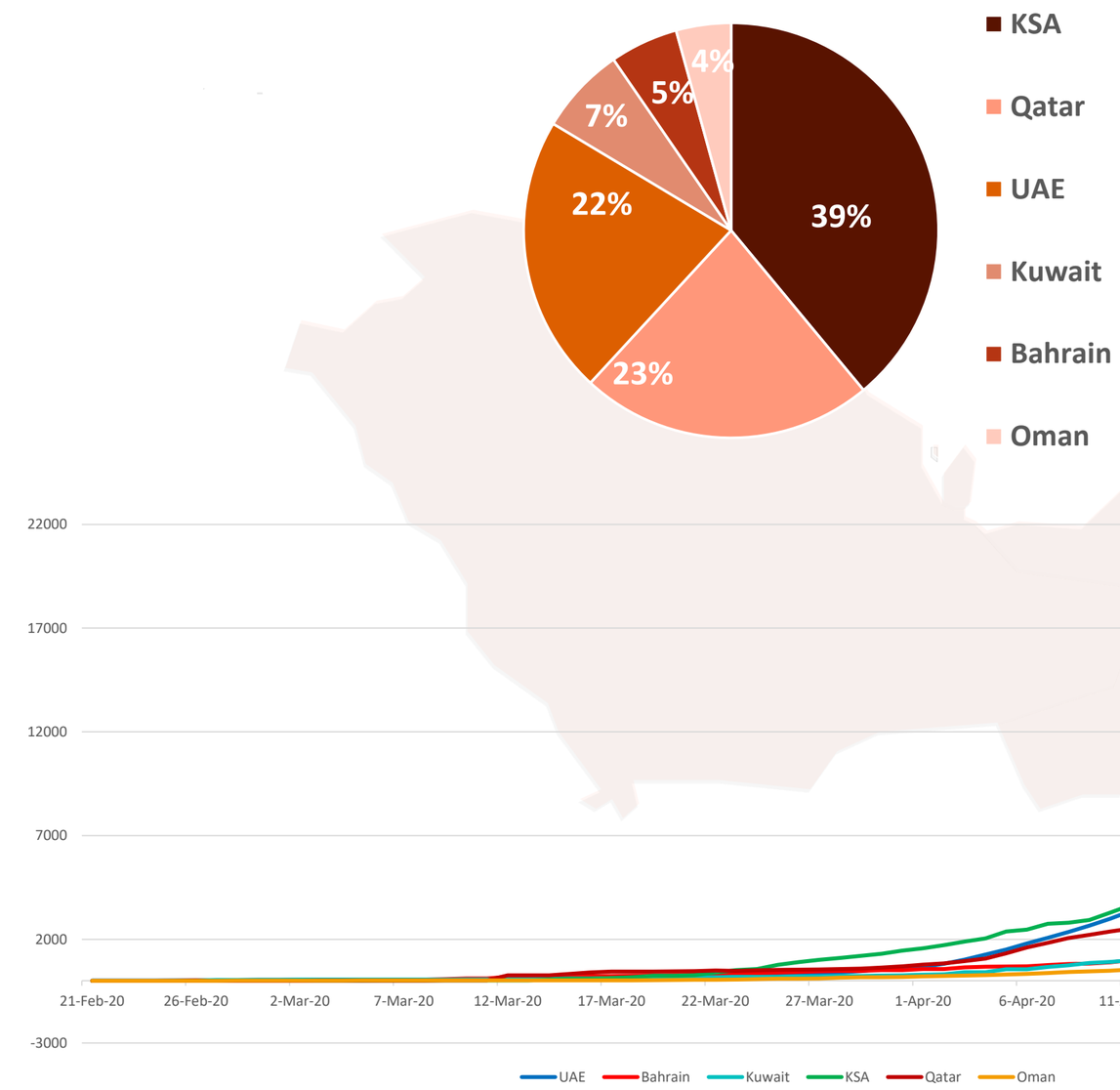


Map chart published by Abu Dhabi Public Health Center 2020.
Data resources: WHO

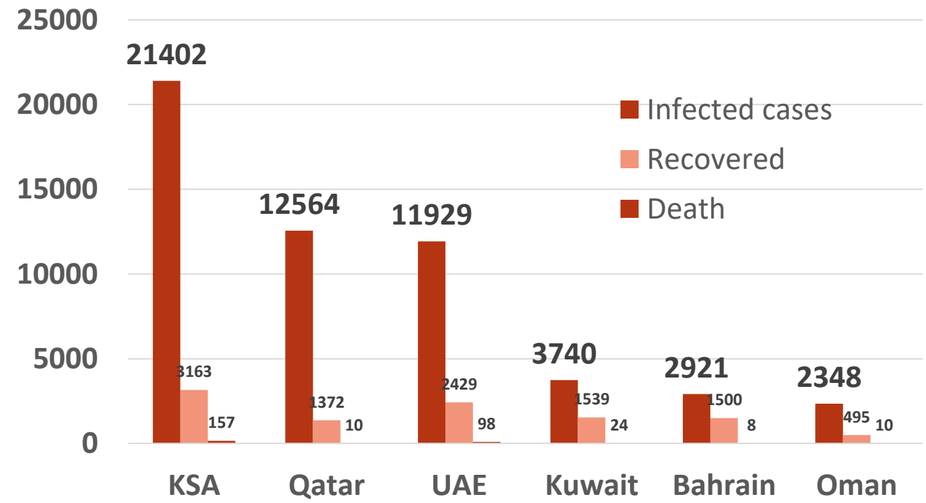
Epidemiology

Figure 9: Comparative analysis of the distribution of COVID19 cases in GCC countries (April 30, 2020)

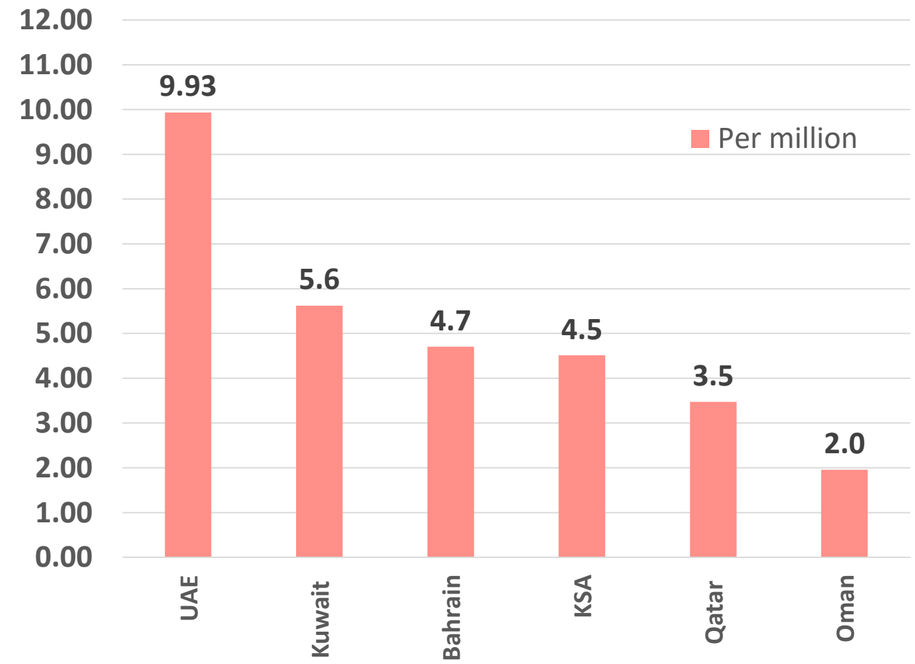
TOTAL NUMBER OF INFECTED CASES



Total number of infected, recovered and Deaths



Death per million



charts published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

Treatment

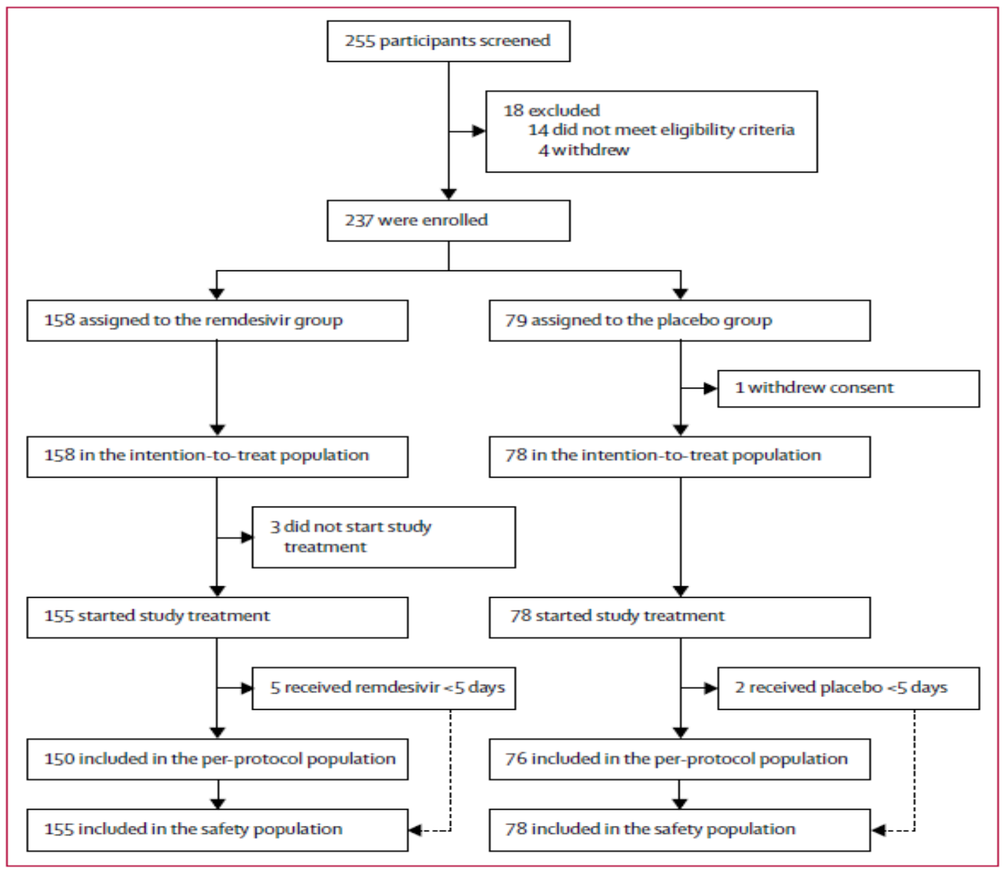
Article 1: Remdesivir in adults with severe COVID-19: a randomized, double-blind, placebo-controlled, multicenter trial.

Published: April 29, 2020 in the lancet

Summary:

Randomized, double-blind, placebo-controlled, multicenter trial at ten hospitals in Hubei, China. Patient were assigned (2:1). Firgure1

Patient demographic as in figure 2 . Patient were allowed treatment of LPN/TNV or steroids.



	Remdesivir group (n=158)	Placebo group (n=78)
Age, years	66·0 (57·0–73·0)	64·0 (53·0–70·0)
Sex		
Men	89 (56%)	51 (65%)
Women	69 (44%)	27 (35%)
Any comorbidities	112 (71%)	55 (71%)
Hypertension	72 (46%)	30 (38%)
Diabetes	40 (25%)	16 (21%)
Coronary heart disease	15 (9%)	2 (3%)
Body temperature, °C	36·8 (36·5–37·2)	36·8 (36·5–37·2)
Fever	56 (35%)	31 (40%)
Respiratory rate >24 breaths per min	36 (23%)	11 (14%)
Six-category scale at day 1		
2—hospital admission, not requiring supplemental oxygen	0	3 (4%)
3—hospital admission, requiring supplemental oxygen	129 (82%)	65 (83%)
4—hospital admission, requiring high-flow nasal cannula or non-invasive mechanical ventilation	28 (18%)	9 (12%)
5—hospital admission, requiring extracorporeal membrane oxygenation or invasive mechanical ventilation	0	1 (1%)

(Continued from previous page)

6—death	1 (1%)	0
Baseline viral load of nasopharyngeal and oropharyngeal swabs, log_{10} copies per mL	4·7 (0·3)	4·7 (0·4)
Receiving interferon alfa-2b at baseline	29 (18%)	15 (19%)
Receiving lopinavir–ritonavir at baseline	27 (17%)	15 (19%)
Antibiotic treatment at baseline	121 (77%)	63 (81%)
Corticosteroids therapy at baseline	60 (38%)	31 (40%)

	Remdesivir group (n=158)	Placebo group (n=78)
Time from symptom onset to starting study treatment, days*	11 (9–12)	10 (9–12)
Early (≤10 days from symptom onset)	71/155 (46%)	47 (60%)
Late (>10 days from symptom onset)	84/155 (54%)	31 (40%)

Treatment :

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Article 1: Cont.,

Findings:

- Remdesivir use **was not associated with a difference** in **time to clinical improvement**
- Although **not statistically significant**, patients receiving remdesivir had a numerically **faster time to clinical improvement** than those receiving placebo among patients with symptom duration of 10 days or less .
- **Adverse events** were reported in 102 (66%) of 155 remdesivir recipients versus 50 (64%) of 78 placebo recipients.
- Remdesivir was stopped early because of **adverse events** in **18 (12%)** patients versus four (5%) patients who stopped placebo early.
- **No differences in viral load** were observed when stratified by interval from symptom onset to start of study treatment

Figure3: Outocme

	Remdesivir group (n=158)	Placebo group (n=78)	Difference*
Time to clinical improvement	21·0 (13·0 to 28·0)	23·0 (15·0 to 28·0)	1·23 (0·87 to 1·75)†
Day 28 mortality	22 (14%)	10 (13%)	1·1% (−8·1 to 10·3)
Early (≤10 days of symptom onset)	8/71 (11%)	7/47 (15%)	−3·6% (−16·2 to 8·9)
Late (>10 days of symptom onset)	12/84 (14%)	3/31 (10%)	4·6% (−8·2 to 17·4)
Clinical improvement rates			
Day 7	4 (3%)	2 (3%)	0·0% (−4·3 to 4·2)
Day 14	42 (27%)	18 (23%)	3·5% (−8·1 to 15·1)
Day 28	103 (65%)	45 (58%)	7·5% (−5·7 to 20·7)
Duration of invasive mechanical ventilation, days	7·0 (4·0 to 16·0)	15·5 (6·0 to 21·0)	−4·0 (−14·0 to 2·0)
Duration of invasive mechanical ventilation in survivors, days‡	19·0 (5·0 to 42·0)	42·0 (17·0 to 46·0)	−12·0 (−41·0 to 25·0)
Duration of invasive mechanical ventilation in non-survivors, days‡	7·0 (2·0 to 11·0)	8·0 (5·0 to 16·0)	−2·5 (−11·0 to 3·0)
Duration of oxygen support, days	19·0 (11·0 to 30·0)	21·0 (14·0 to 30·5)	−2·0 (−6·0 to 1·0)
Duration of hospital stay, days	25·0 (16·0 to 38·0)	24·0 (18·0 to 36·0)	0·0 (−4·0 to 4·0)
Time from random group assignment to discharge, days	21·0 (12·0 to 31·0)	21·0 (13·5 to 28·5)	0·0 (−3·0 to 3·0)
Time from random group assignment to death, days	9·5 (6·0 to 18·5)	11·0 (7·0 to 18·0)	−1·0 (−7·0 to 5·0)

Conclusion:

In this study of adult patients admitted to **hospital for severe COVID-19**, remdesivir **was not associated with statistically significant clinical benefits**.

The study did not answer to whether **longer treatment** course and **higher dose of remdesivir** would be beneficial in patients with severe COVID-19. Recommend strategies to enhance the antiviral potency of remdesivir (eg, higher-dose regimens, combination with other antivirals, or SARS-CoV-2 neutralising antibodies)

Diagnosis

Article 2: Cautions about radiologic diagnosis of COVID-19 infection driven by artificial intelligence

Published: : early release May 2020 in The Lancet

Summary:

- experts shared their opinions about the possible role of artificial intelligence in tackling COVID-19 in particularly supporting radiologists with lung CT images' use & interpretation. Some have optimistic expectations about the value of lung CT images as outlined by McCall. Some said it has a **diagnostic value** that can confirm covid-19 infection and rule out other differential diagnosis. Others said it helps to faster the reading of the findings in 10 seconds rather than manual reading which takes 15 minutes by radiologists leading to **faster confirmation** of disease comparing to PCR-based diagnosis which takes too long (sometimes over a week) due to pressure on labs. In addition artificial intelligence applications can precisely measure the percentage of the pulmonary parenchyma involvement at time of diagnosis allowing monitoring the course of the disease and can be used as **prognostic value** to determine the choice of therapy. This precise quantification of lung involvement is an interesting application of artificial intelligence.

- Having said that this is not yet supported by scientific evidence and might generate unjustified expectations among doctors, policy makers, and citizens. As we know 50% of COVID-19 patients have a normal CT scan at early stage of symptoms. Therefore the American College of Radiology does **not** consider CT imaging as a **useful screening test** in asymptomatic individuals. Also it **can't be a pathognomonic** of COVID-19 as it overlaps with other entities (ie, H1N1 influenza, cytomegalovirus pneumonia, or atypical pneumonia). Moreover there are different lung findings over the course of disease. This all urge realistic expectations with use of artificial intelligence to be in line with the daily diagnostic reality and support the work of radiologists.

Treatment

Article 3: **Covid-19 - A Reminder to Reason**
Published: **April 28, 2020 in NEJM**
Summary:

- Physicians are treating COVID-19 patients with unsparing generosity using medications without approved uses and study protocols, with little scientific evidence supporting their administration beyond extrapolation from in vitro studies reporting their antiviral and anti-inflammatory properties. Intense desire to try new, unproven medicines may divert physicians from offering patients the best quality treatment. Prescribing medications based on case reports help little to advance science or ability to combat future recurrences of diseases.

- In spite of using untested medications, physicians should instead push for clinical studies designed to meet the standards necessary to reach reasonable conclusions about the efficacy although this is a difficult task during this outbreak. However, a blinded, randomized, controlled trial of remdesivir (antiviral), as well as a drug that inhibits the action of interleukin-6 is being conducted. Physicians should not rely on any therapeutic strategy until enough statistical evidence is gathered that would assure that one treatment is better than any other.

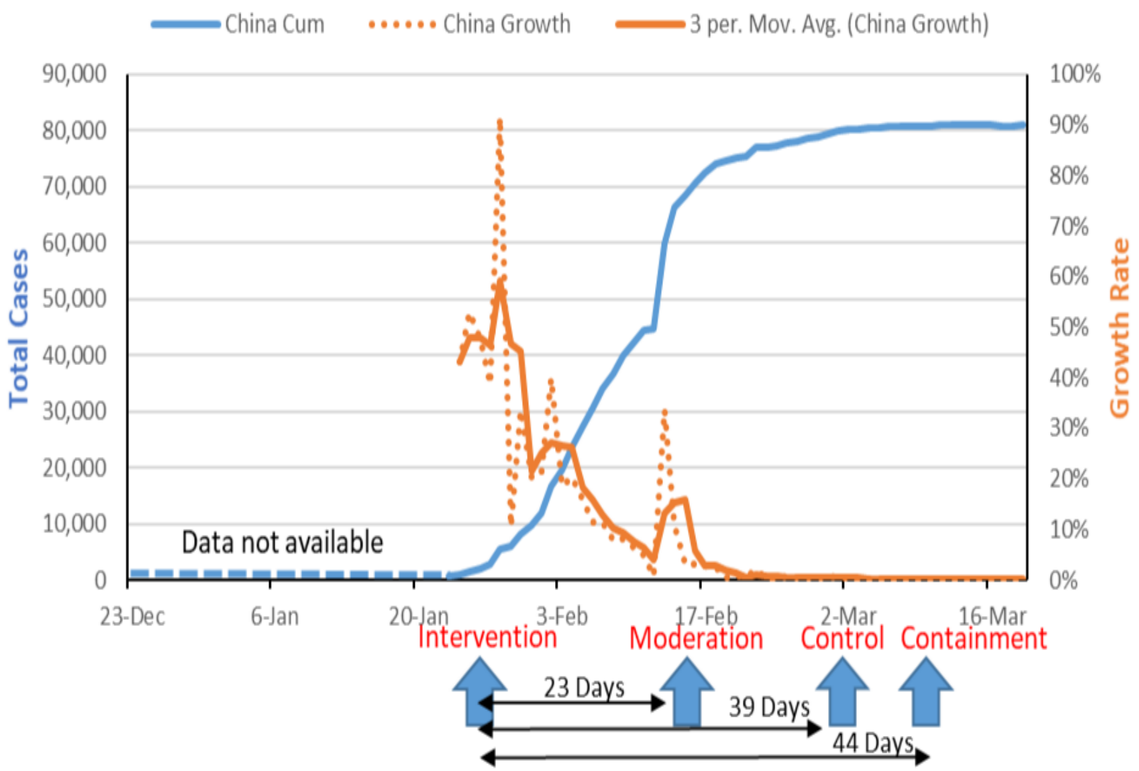
- It must be responded to the biases that may influence thinking processes, critically evaluate the evidence in deciding how to treat patients, and use anecdotal observations only to generate hypotheses for trials that can be conducted with clinical equipoise.

Public Health Response:

Planning for COVID19 exist ?

Based on previously summarized modelling study in ADPHC scientific report (April 15,2020) under the title "*How Long Should Social Distancing Last? Predicting Time to Moderation, Control, and Containment of COVID-19*"*. Here , we highlight a comparative analysis of four countries including the UAE; addressing important metrics of the spread of disease and defining three important measurable benchmarks that may guide in an exist strategy

Figure: Total Cases & Daily Growth in China



The **daily growth rate** and **doubling time** can allow measurable benchmarks for the epidemic response beyond the **acute intervention period**:

- **Moderation**: when growth rate stays below 10% and doubling time stays above 7 days
- **Control**: when growth rate stays below 1% and doubling time stays above 70 days
- **Containment**: when growth rate stays below 0.1% and doubling time stays above 700 days

This is a collaborative work between DOH, UAEU modelling team and ADPHC

* Note that this article have been published in preprint database SSRN

Public Health Response:

Cont., Planning for COVID19 exist ?

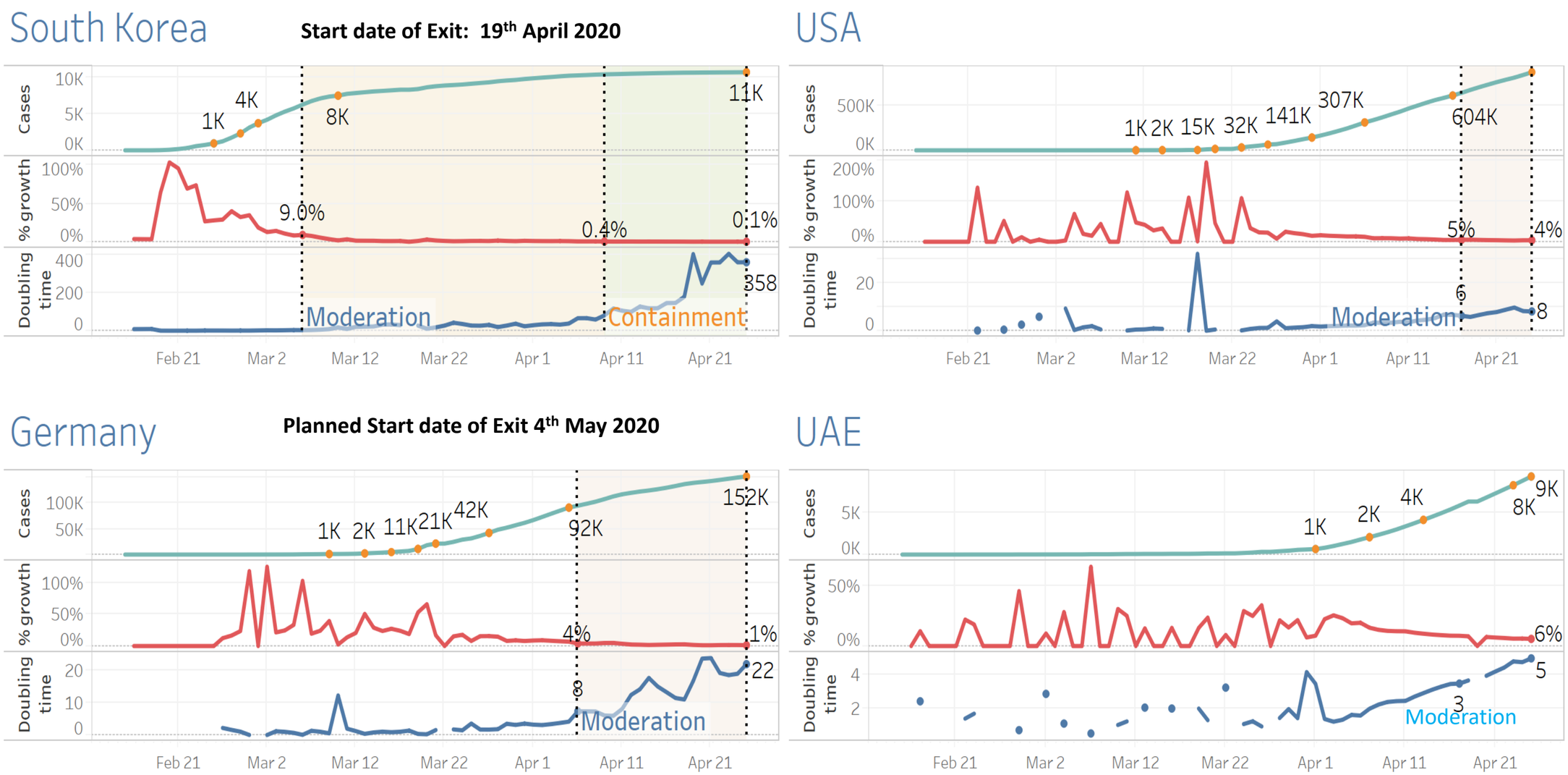


Figure 1: South Korea in containment phase with growth rate of 0.1% doubling time 358 days**, USA**: moderation phase: growth rate is 4% and doubling time is 8 days; **Germany** in moderation phase with 1% growth rate and doubling time of 22 days. **UAE** is in moderation phase with 6% growth rate and doubling time of 5 days.

Figure is published by the DOH/ UAEU modelling team based on ADPHC request
Data Source from WHO (data of the last 2 weeks before 25 of April 2020 was used in this analysis.