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Scientific Research Monitoring on COVID-19

27 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

- **Transmission:** study showed no positive viral cultures with a Ct greater than 24 or time of Symptoms To Test greater than 8 days. This data will assist in determining the clinical criteria for discontinuing isolation in positive cases of COVID19.
- **Clinical Feature and Transmission:** Korean CDC released an analysis of the cases which retested positive after isolation. Based on active monitoring, epidemiological investigation, and laboratory testing of re-positive cases and their contacts, no evidence was found that indicated infectivity of re-positive cases. viral cultures were negative , immune positive.
- **Treatment:** a retrospective study in patients with COVID-19 found that the **use of a regimen containing hydroxychloroquine or chloroquine (with or without a macrolide**) was associated with **no evidence of benefit**, but instead was associated with an increase in **the risk of ventricular arrhythmias and a greater hazard for in-hospital death with COVID-19**.
- **Treatment:** Avigan updates
- **Diagnosis:** More information about Antigen testing and its relation to other COVID19 testing (PCR , antibody)
- **Public Health Response:** Article discuss the impact of COVD19 on higher education institution

WHO daily report

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WHO daily report

25 May 2020,

WHO has partnered with Vital Strategies and other global partners to launch a new technical package: Revealing the Toll of COVID-19: A Technical Package for Rapid Mortality Surveillance and Epidemic Response. This is a technical package for rapid mortality surveillance and epidemic response to support national governments with surveillance and response planning surrounding COVID-19.

26 May 2020,

WHO Director-General Dr Tedros, in his regular media briefing, mentioned that "over 400 hospitals in 35 countries are actively recruiting patients and nearly 3500 patients have been enrolled from 17 countries" as part of the Solidarity Trial which was established to evaluate the safety and efficacy of four drugs and drug combinations against COVID-19.

- The DG general discussed about the pose in the HCQ arm of the SOLIDARITY TRIALs after the lancet observational study and ensure safety will be investigated*.
- The WHO Regional Office for Europe along with the European Centre for Disease Prevention and Control (ECDC), said that they will continue **to repurpose their influenza surveillance systems to also detect the COVID-19 virus.**
- Facing an unprecedented global demand for essential COVID-19 medical supplies, WHO is working with partners to help secure supplies to assist the most vulnerable countries
- WHO encourages Member States to submit requests for supplies through the COVID-19 Supply Portal, a tool to enable national authorities and all implementing partners supporting COVID-19 national plans to request critical supplies.
- An updated version of the Supply Portal was launched last week, with new features that: **▪ enable supplying agencies to list supplies. ▪ add a comments feature ▪ provide a 'Country viewer' of all requests submitted within one country; designed for country teams and government. ▪ and, provide a 'Global viewer' of all requests submitted globally; designed for regional offices and HQ.**

*More details on the study and the impact in this report

337,687

Epidemiology

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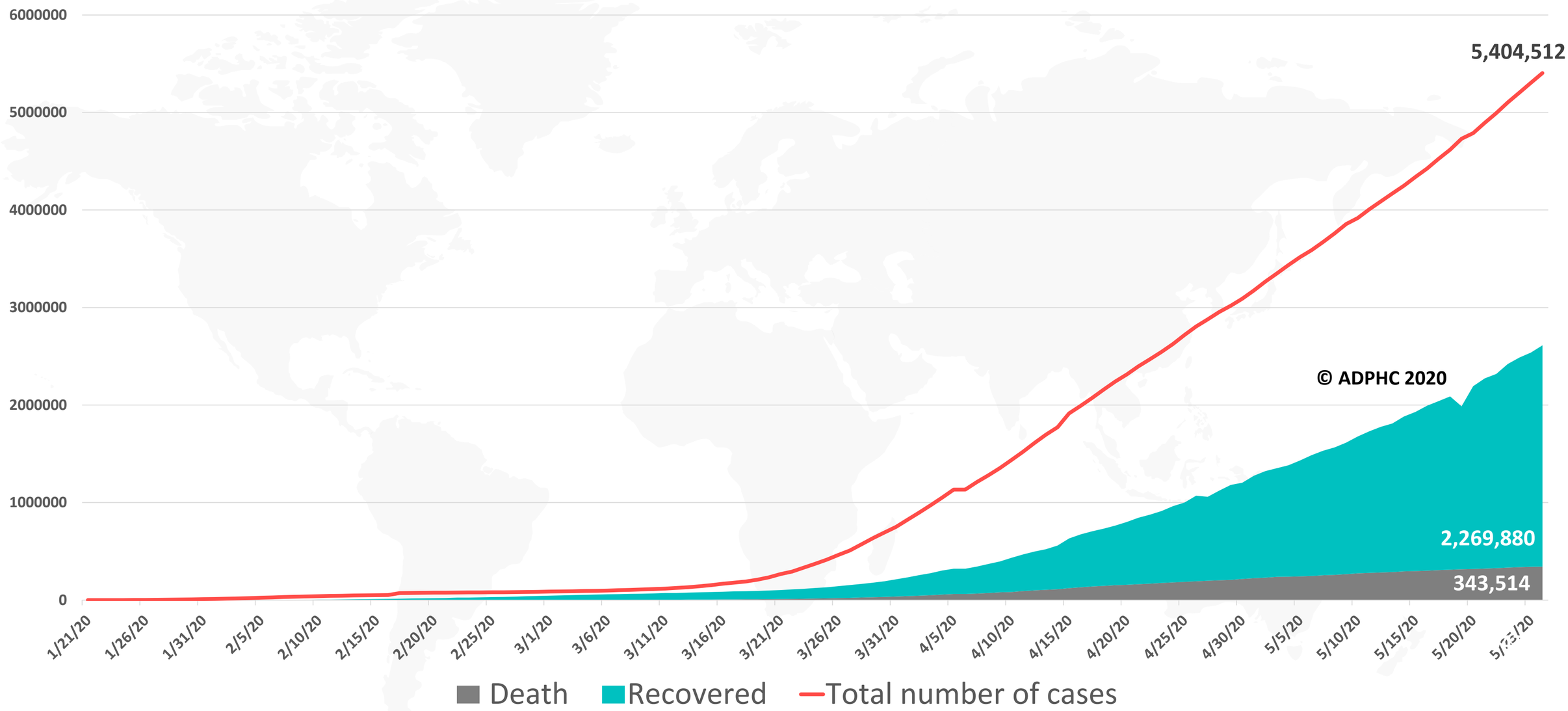
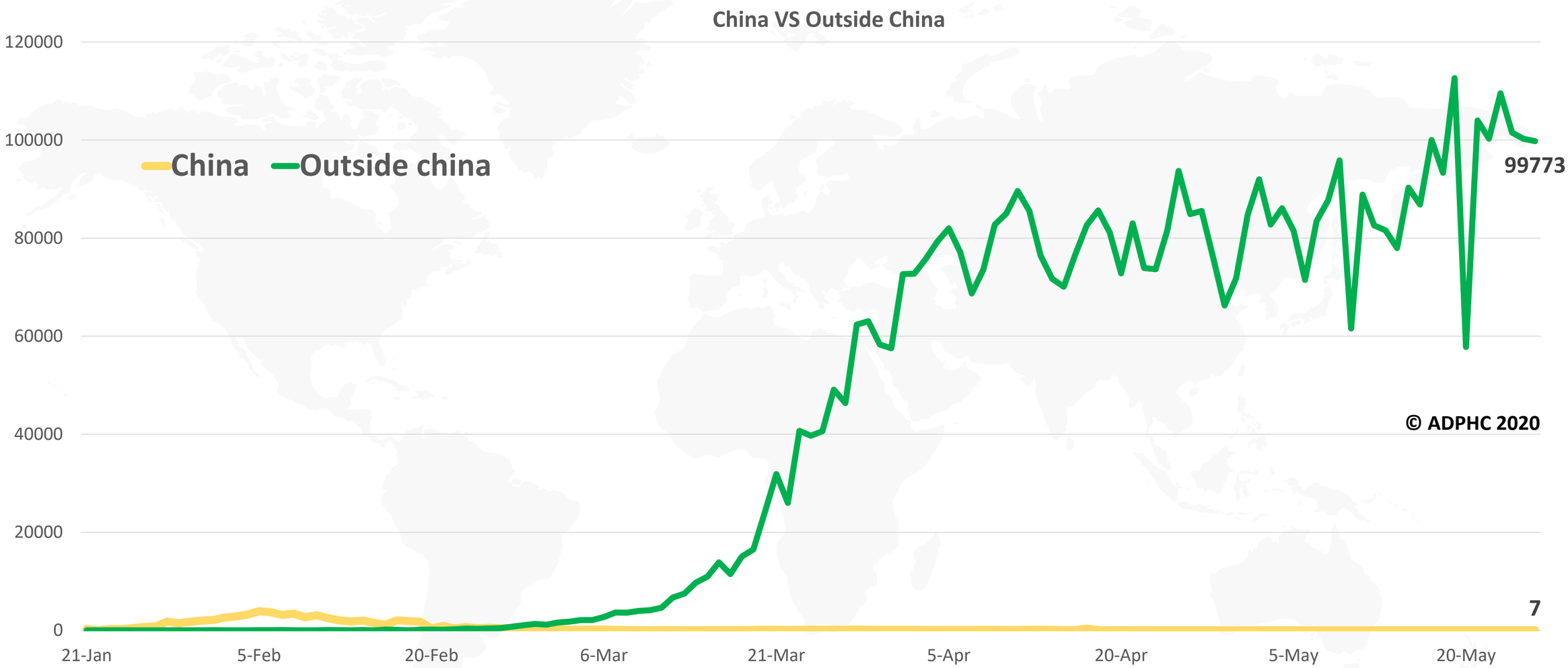
Figure 1: Total number of infected, recovered , and death cases (January 21st to May 26, 2020)



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 May 26, 2020).



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

Epidemiology

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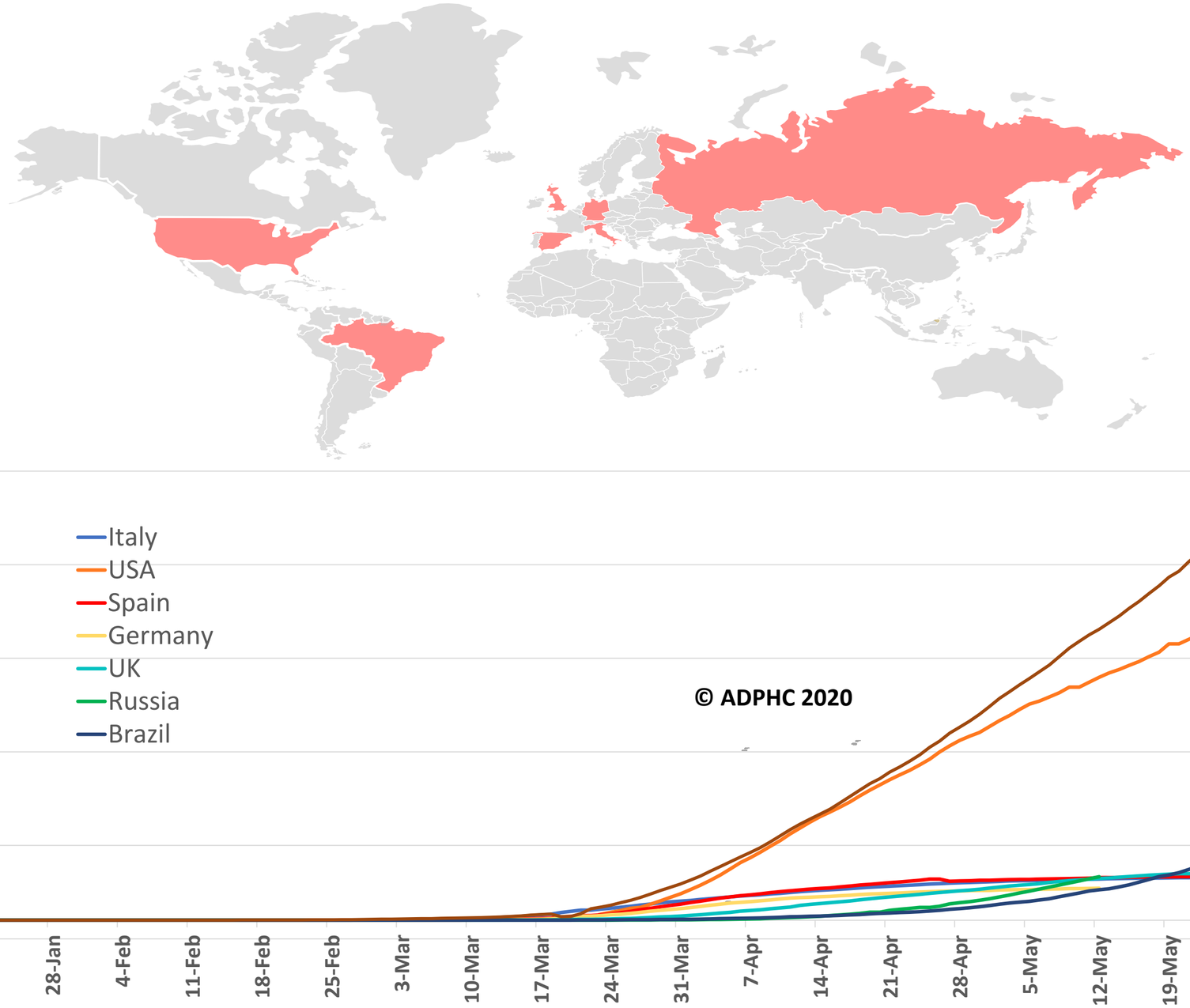
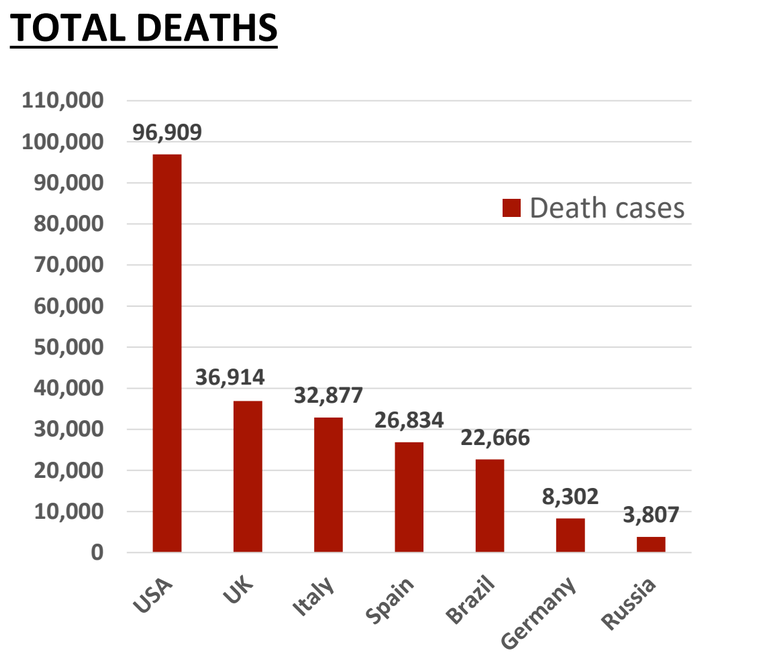
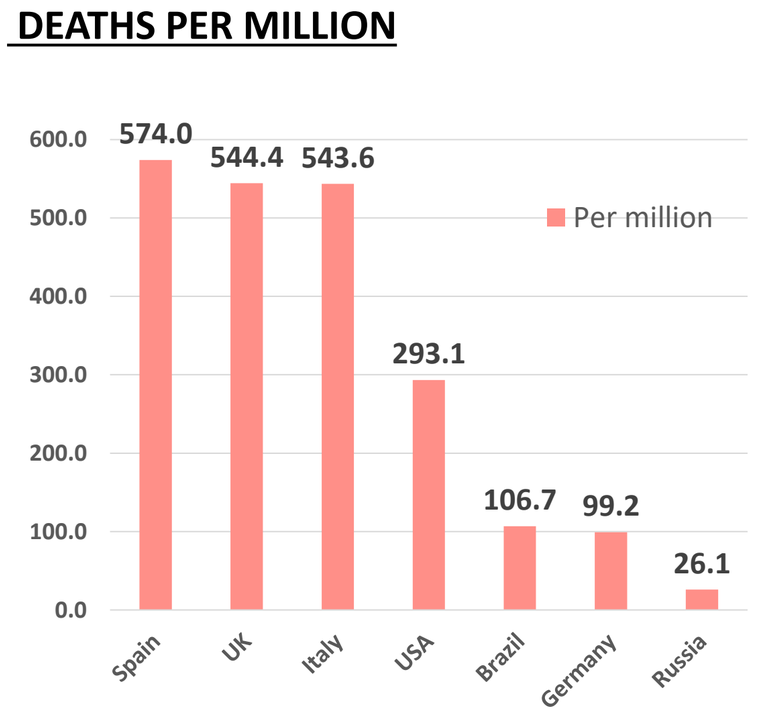
Figure 3 : Top 7 countries in the total number of cases due to COVID-19 (January 21 to May 26, 2020).





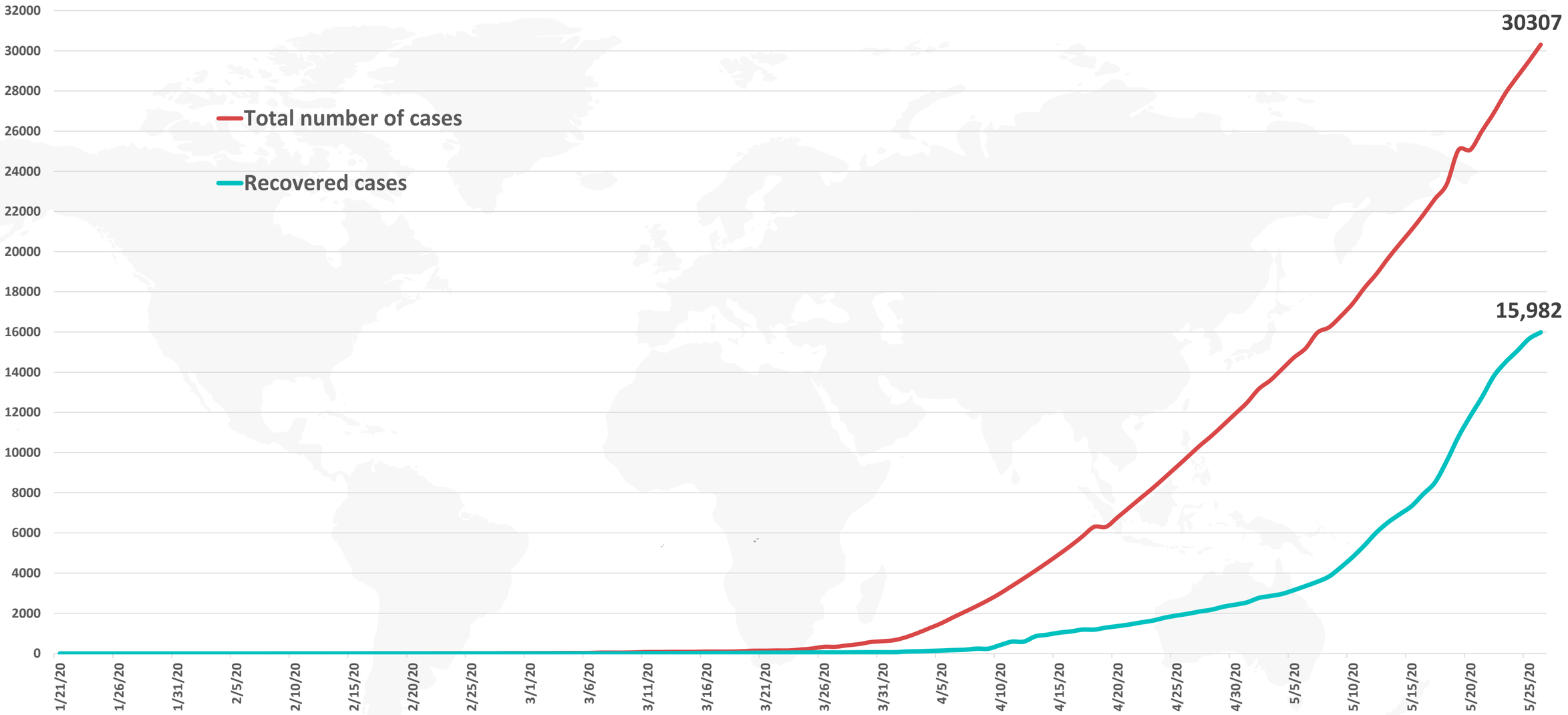


Line graph published by Abu Dhabi Public Health Center 2020.

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

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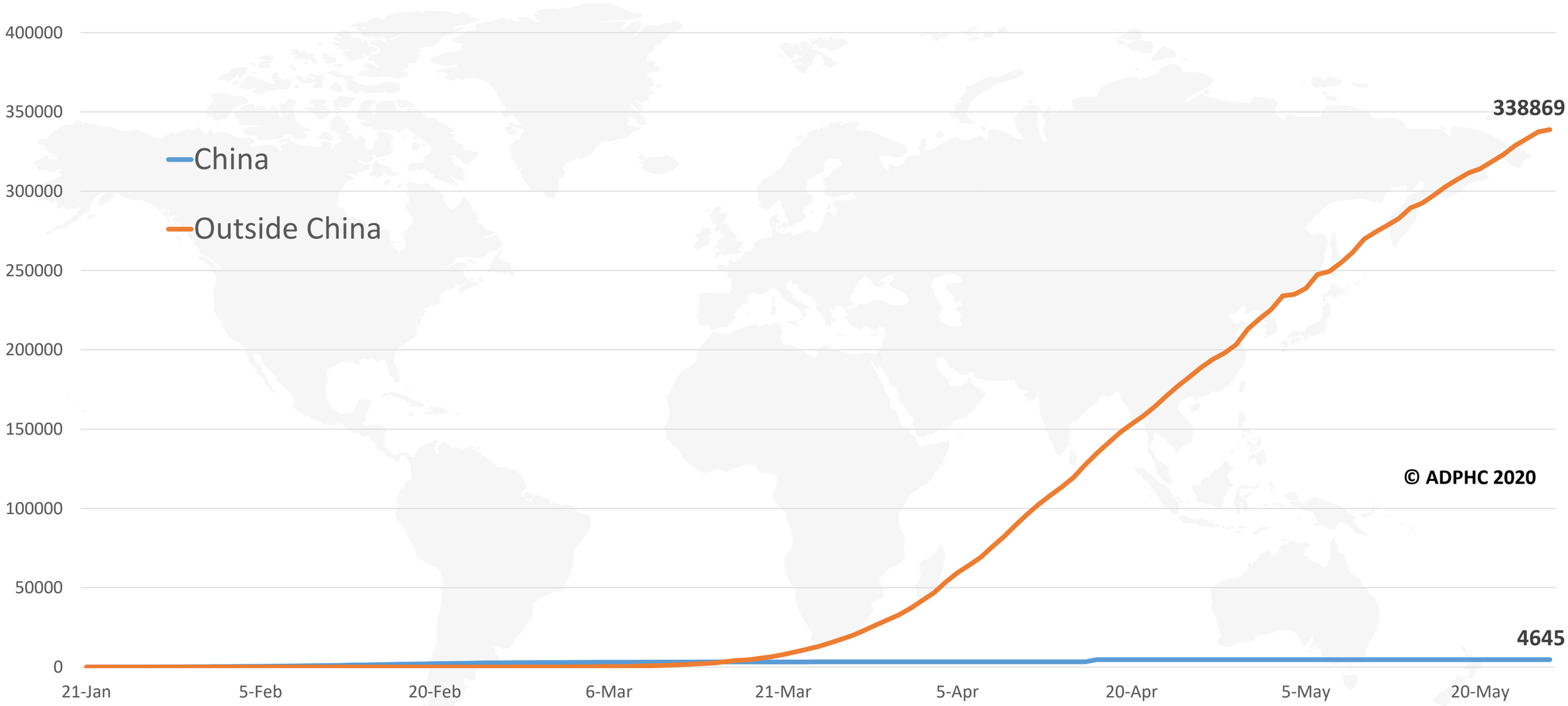
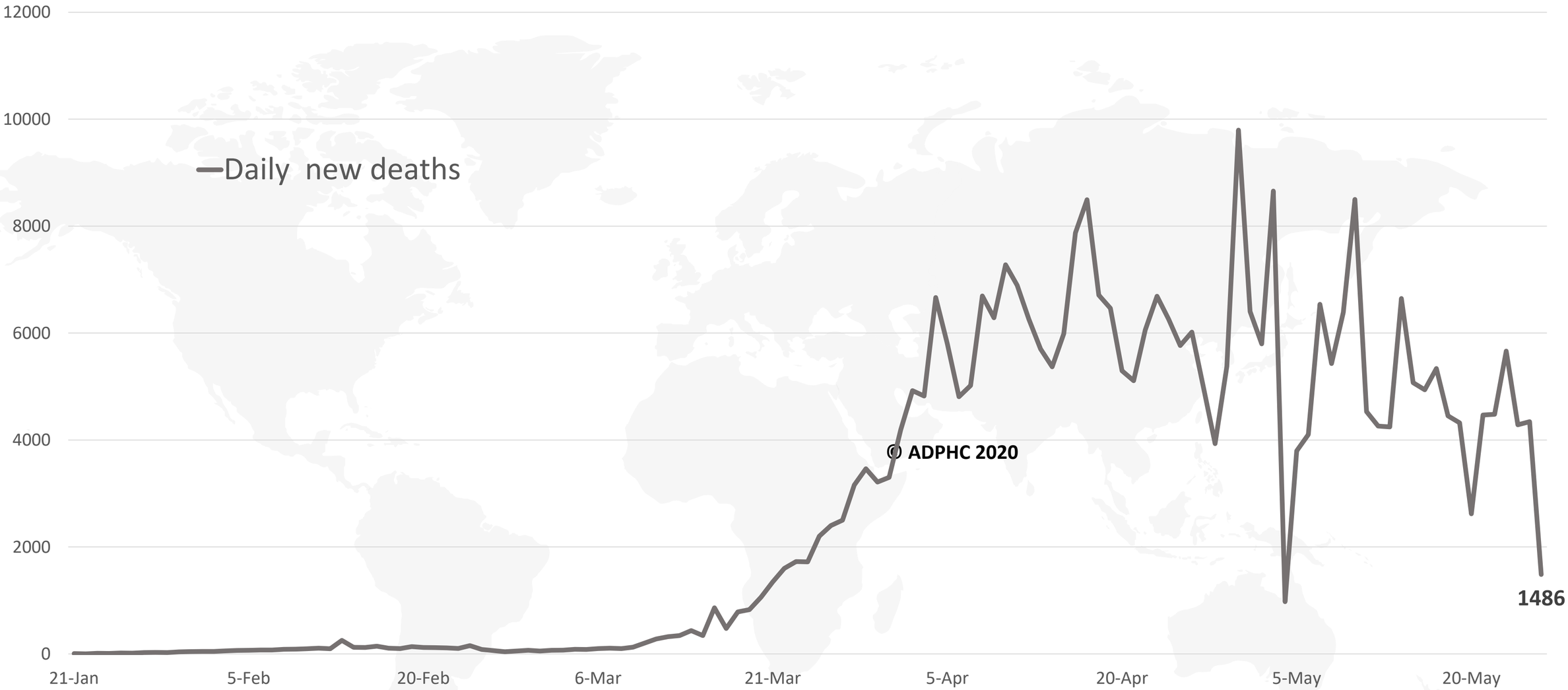
Figure 5: Total number of death due to COVID-19 reported by China and the rest of the world (January 22 to May 26, 2020).



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 May 26, 2020).



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

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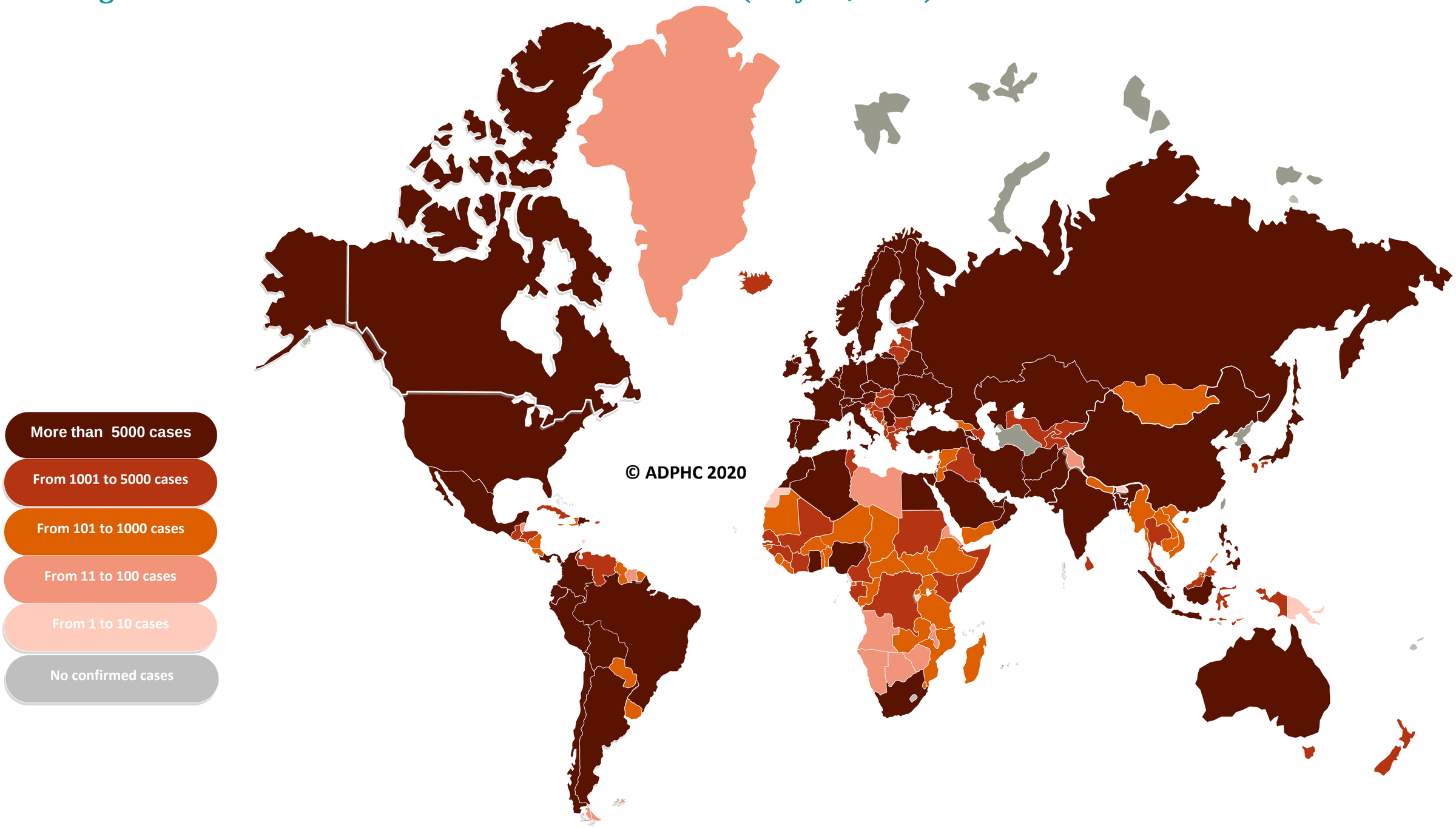
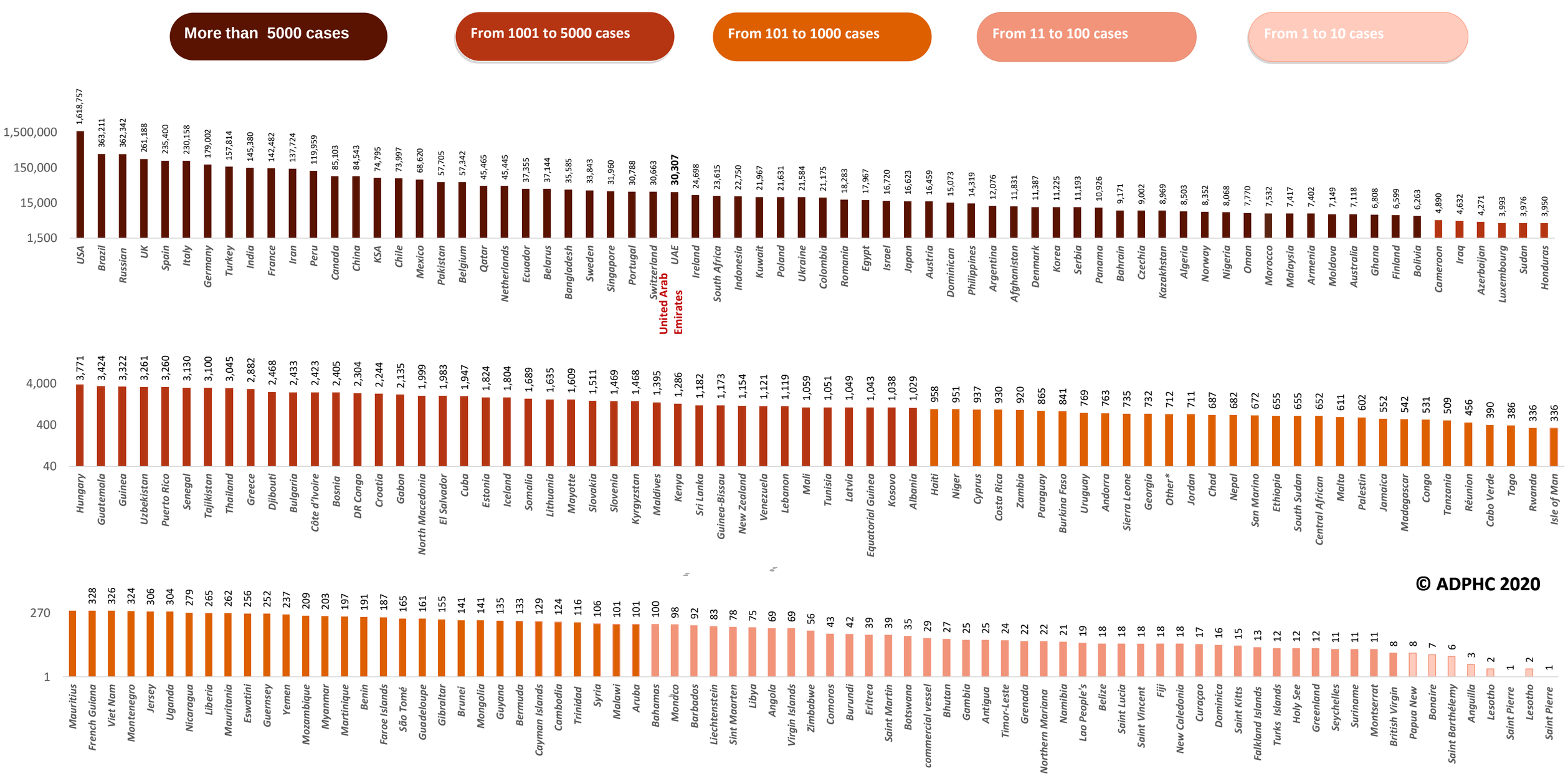
Figure 7a : Global distribution of COVID-19 cases (May 26, 2020).



Map chart published by Abu Dhabi Public Health Center 2020.

Epidemiology

Figure 7B: Bar chart illustrate the global distribution of COVID19 cases May 26, 2020)



Other*:includes cases and deaths reported under the international conveyance(Diamond Princess)

Map chart published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

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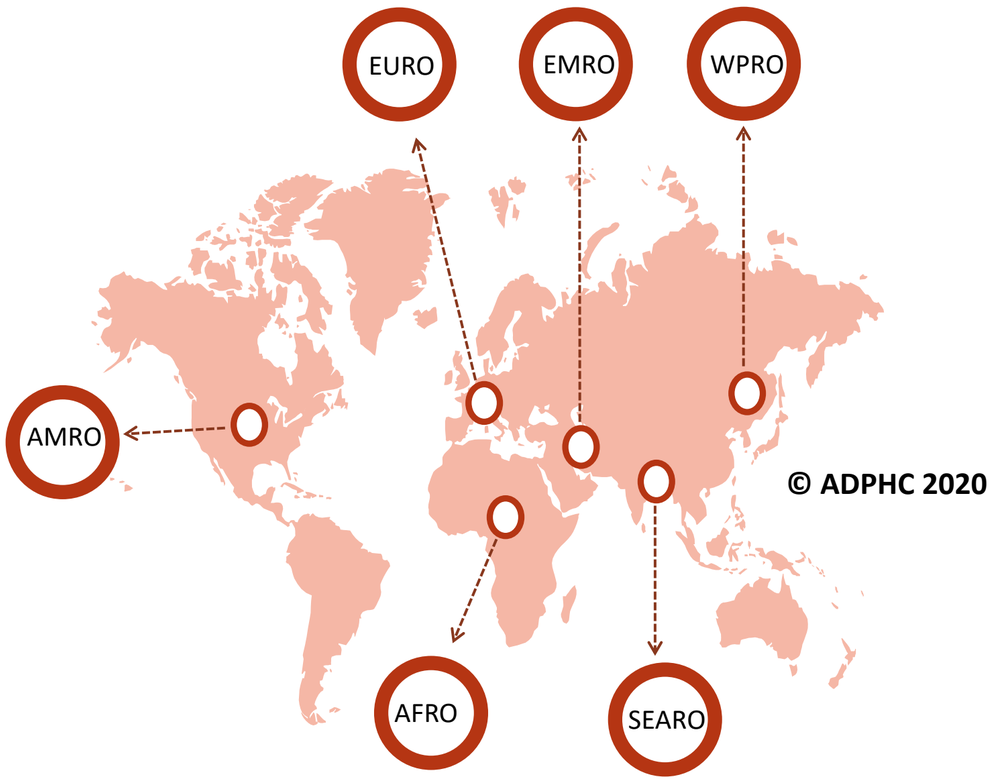
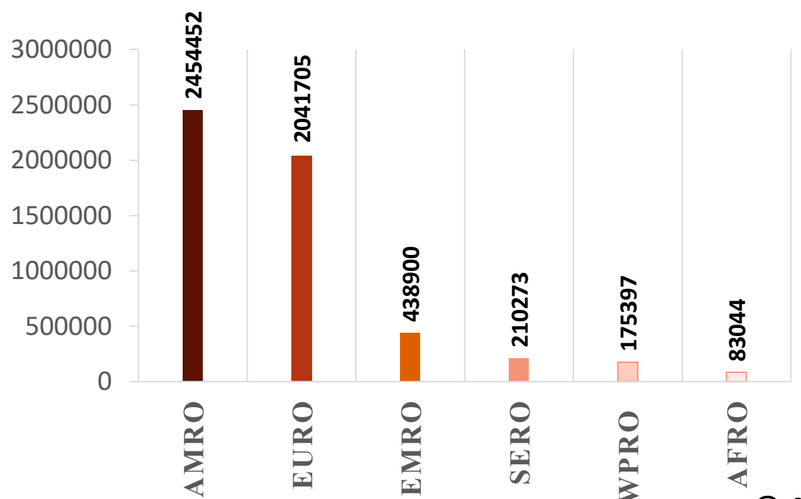
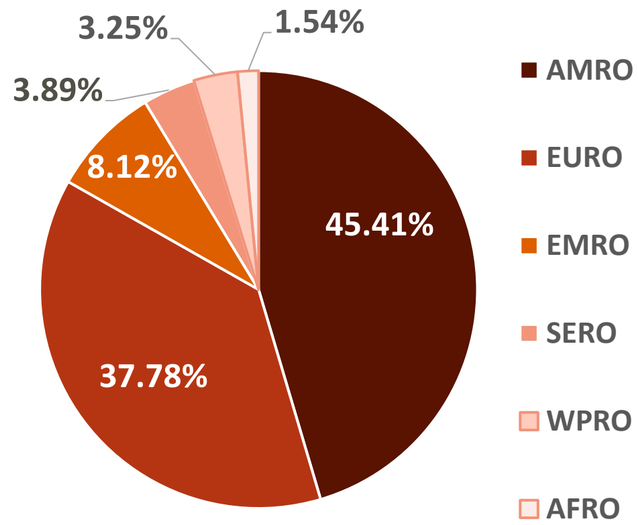
Figure 8: illustrate the Global distribution of COVID19 cases per region (May 26, 2020)

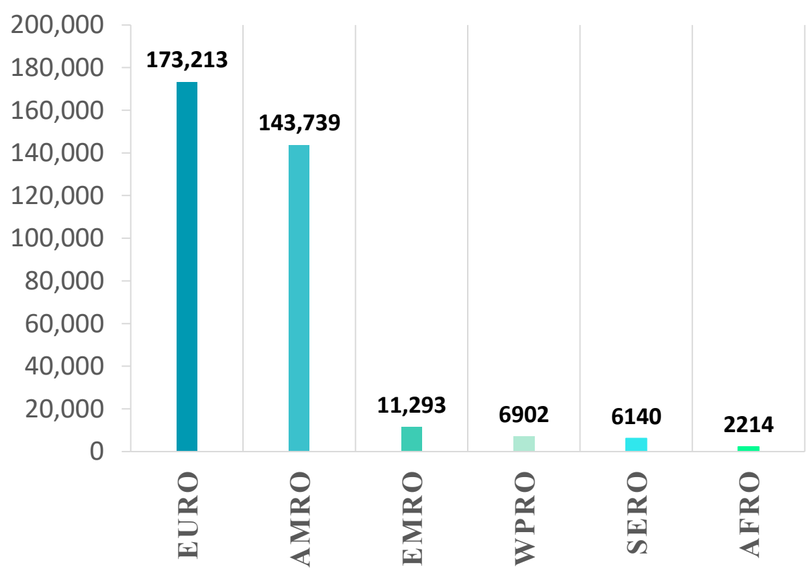


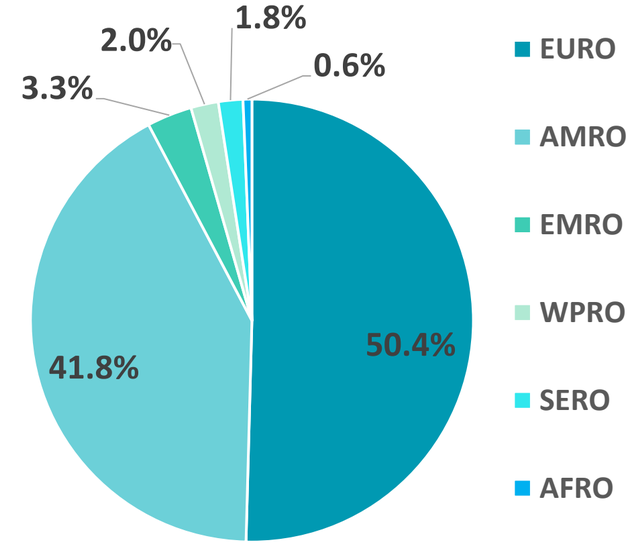
INFECTED





DEATH





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

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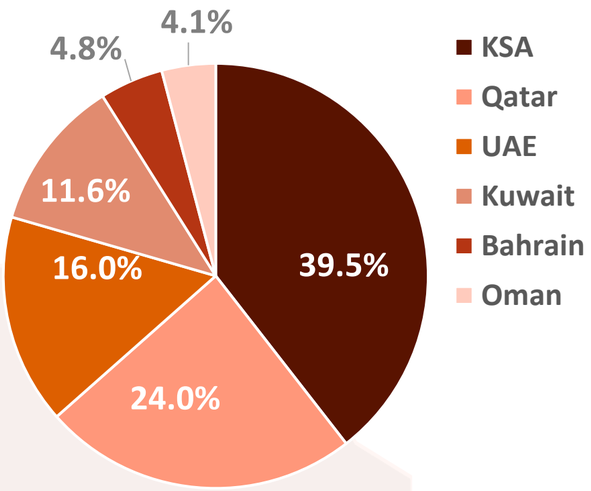
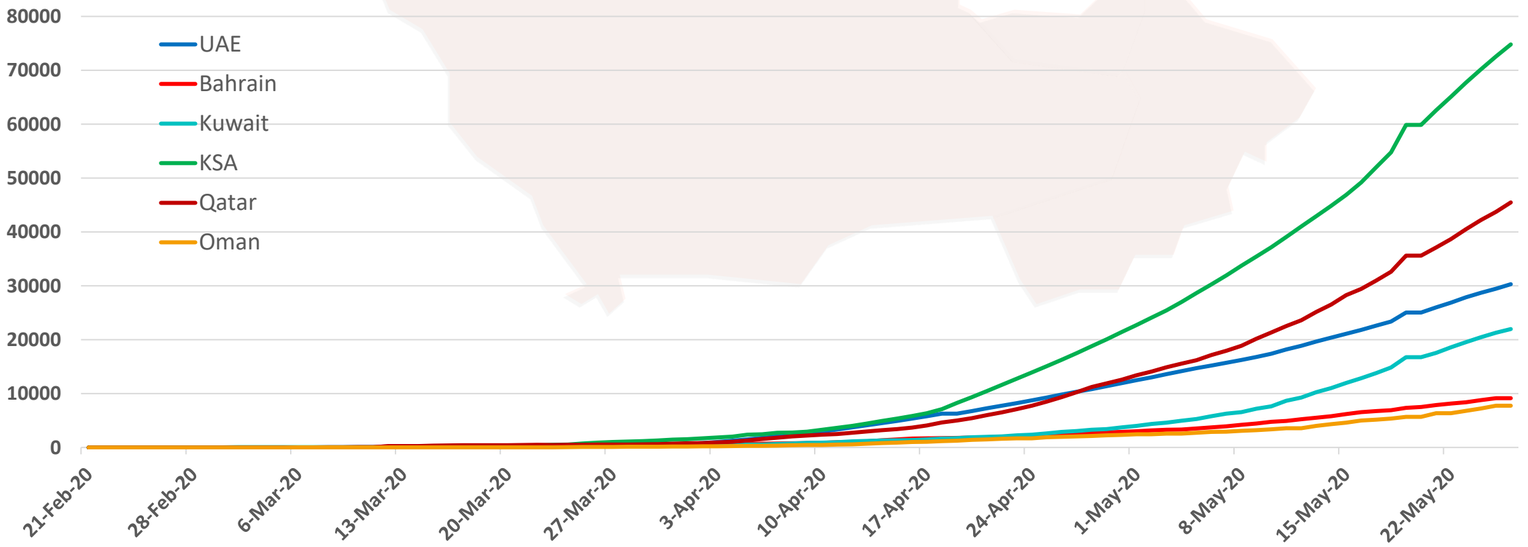
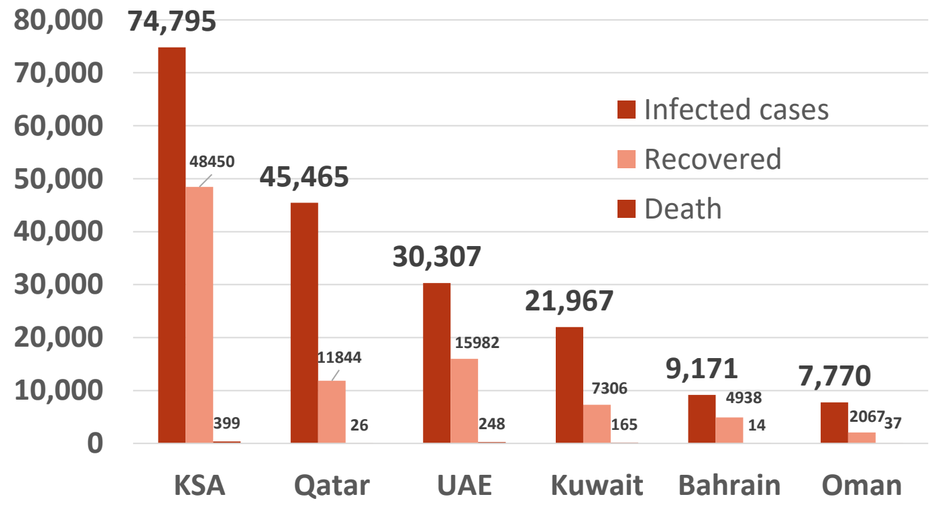
Figure 9: Comparative analysis of the distribution of COVID19 cases in GCC countries (May 26, 2020)

TOTAL NUMBER OF INFECTED CASES

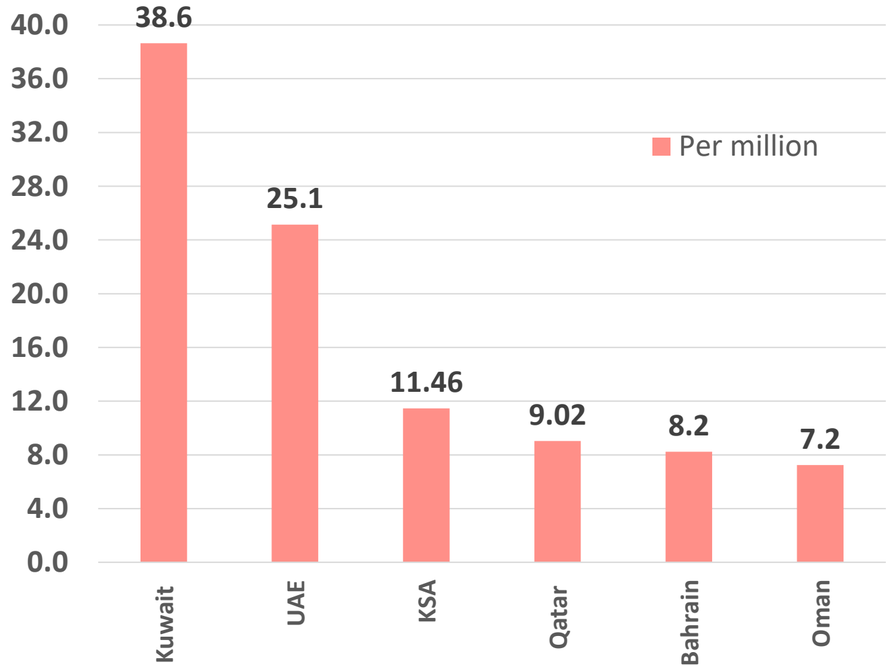




Total number of infected, recovered and Deaths



Death per million



charts published by Abu Dhabi Public Health Center 2020.

Data resources: WHO

Clinical Feature and transmission

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Article 1 : Predicting infectious SARS-CoV-2 from diagnostic samples

Published: : May22. 2020 in the OXFORD academic

Summary

- In this retrospective cross-sectional study aimed to address criteria of isolating Covid19 patients. A 90 RT-PCR samples were obtained from SARS-COV2 infected patients to determine the infectivity (as defined by growth in cell culture).
- **Two measures were used:**
  - The Ct value (a measure of viral load; the higher value means the sample have a less viral load)
  - The time symptoms to test (STT)). (defined as RT-PCR from day of symptom onset (Day 0) up to 21 days post symptom onset.)

Findings

- Out of the 90 samples 26 (28%) had a positive culture. Positive culture samples had a significantly lower Ct when compared to culture negative samples (**17** [16-18] vs **27** [22-33], p<0.001.
- Symptom to test time was also significantly lower in culture positive vs. culture negative samples (3 [2-4] vs. 7 [4-11], p<0.001.

Conclusion :

- As major drawback to PCR and other diagnostic approaches (including other NA, serology, antigen detection) is that they all fail to determine virus infectivity; The high specificity of Ct and STT suggests that **Ct values greater than 24,** along **with duration of symptoms greater than 8 days** may be used in combination to **determine duration of infectivity in patients**
- As some countries are using different Clinical criteria to discontinue isolation of hospitalized patient **includes:**
  1- a 14 days from symptom onset or 72 hours symptom free (whichever is longer).
  2- other jurisdictions are **using two negative NP RT-PCR results 48 hours apart after 14 days** of symptoms.
- This study supports the first approach since **RT-PC positivity persists significantly beyond infectivity;** the second approach may lead to unnecessary isolation, and use of PPE and testing resources.
- These data can be used efficiently to target case finding efforts by better defining the period of maximal transmission risk. This will be of particular importance in the maintenance phase of the response, where case finding efforts to rapidly interrupt chains of transmission will be essential

Clinical Feature and transmission

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Article 2 : Findings from investigation and analysis of re-positive cases **(South Korea)**
Published:19 May 2020 in the Korean CDC website.

Summary

- In response to reports of multiple cases testing positive for SARS-CoV-2 after being discharged from isolation, on 14 April, KCDC began managing such cases with measures similar to those for confirmed cases, **while further investigation, research and analysis continued.**
- On 18 May, KCDC announced the findings and the conclusions of the advisory committee

Findings:

- Based on active monitoring, epidemiological investigation, and laboratory testing of re-positive cases **and their contacts**, **no evidence was found that indicated infectivity of re-positive cases.**
  - **Of the 447 re-positive cases as of 15 May, epidemiological** investigation was conducted **on 285 cases and laboratory analysis on 108 cases**. (***473 as of 18 May**)
  - From monitoring **of 790 contacts** of the 285 re-positive cases, **no case was found that was newly infected solely from contact with re-positive cases during re-positive period**.
  - **Virus isolation in cell culture** of respiratory samples of 108 re-positive cases, **all result was negative (i.e. virus not isolated).**
  - Of the **23 re-positive cases** from which the **first and the second serum samples** were obtained, **96% were positive for neutralizing antibodies.**

Conclusion:

- **experts' recommendations, the terminology for referring to such cases will be changed from "re-positive" to "PCR re-detected after discharge from isolation".**
- **Based on this finding the KCDC have developed new protocols, that stated no additional tests are required for cases that have been discharged from isolation.**

Clinical Feature and transmission

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Article 2 : Cont.,
Summary

SYMPTOMS AND TESTING OF RE-POSITIVE CASES

		Re-positive cases	
Total		285	
Reason for testing	Symptoms present	107	(37.5)
	Investigation	170	(59.6)
	Requested (by self or guardian)	8	(2.8)
Symptoms *284 cases for which symptoms were checked	Symptoms present	126	(44.7)
	Symptoms absent	158	(56.6)

FINDINGS FROM MONITORING OF CONTACTS OF RE-POSITIVE CASES

		Re-positive cases	Contacts	Confirmed cases among contacts
Total		285	790	27*(3.4)
Presence of symptoms in re-positive cases * 284 cases for which symptoms were checked	Yes	126(44.2)	431(54.6)	18(4.2)
	No	158(55.4)	359(45.4)	9(2.5)
Type of contact	Family	-	351(44.4)	26(7.4)
	Other	-	439(55.6)	1(0.2)

*24 of the 27 are previously confirmed and re-positive cases (included in the re-positive cases)

Treatment (1/3)

Article 3: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis.

Published: May 22, 2020 in the lancet

Summary:

the study reports the largest observational study published to date **on the effects of chloroquine or hydroxychloroquine, with or without a macrolide, in 96 032 hospitalised pa**tients (mean age 53·8 years, 46·3% women) who tested positive for SARS-COV2.

Verified data from an international registry **comprising 671 hospitals** in **six continents** were used to compare patients with COVID-19 who received **chloroquine** (n=1868), **hydroxychloroquine** (n=3016), **chloroquine with a macrolide** (n=3783), or **hydroxychloroquine with a macrolide** (n=6221) within 48 h of COVID-19 diagnosis, with **81 144 controls** who did not receive these drugs.

The primary outcome was in-hospital mortality and the cardiac complications.

many confounding variables were adjusted in this study , including age, sex, ethnicity, comorbidities, other medications, and **COVID-19 severity**.

	Control group (n=81144)	Chloroquine (n=1868)	Chloroquine with macrolide* (n=3783)	Hydroxychloroquine (n=3016)	Hydroxychloroquine with macrolide* (n=6221)
Age, years	53·6 (17·6)	55·1 (18·0)	54·9 (17·7)	55·1 (17·9)	55·2 (17·7)
BMI, kg/m²	27·4 (5·4)	27·8 (6·1)	28·2 (5·8)	28·4 (5·9)	28·5 (5·9)
Sex					
Female	37716 (46·5%)	845 (45·2%)	1718 (45·4%)	1388 (46·0%)	2759 (44·3%)
Male	43428 (53·5%)	1023 (54·8%)	2065 (54·6%)	1628 (54·0%)	3462 (55·7%)
Baseline disease severity					
qSOFA <1	67316 (83·0%)	1530 (81·9%)	3051 (80·7%)	2477 (82·1%)	4994 (80·3%)
SPO_2 <94%	7721 (9·5%)	209 (11·2%)	413 (10·9%)	323 (10·7%)	651 (10·5%)
Outcomes					
De-novo ventricular arrhythmia	226 (0·3%)	81 (4·3%)	246 (6·5%)	184 (6·1%)	502 (8·1%)
Non-ICU length of stay, days	9·1 (6·4)	8·8 (6·2)	9·0 (6·6)	8·9 (6·2)	9·1 (6·7)
ICU length of stay, days	2·6 (5·0)	4·3 (6·8)	4·9 (8·1)	4·3 (6·8)	4·7 (7·8)
Total length of stay, days	11·7 (8·4)	13·2 (9·1)	13·8 (11·0)	13·2 (9·3)	13·8 (10·7)
Mechanical ventilation	6278 (7·7%)	403 (21·6%)	814 (21·5%)	616 (20·4%)	1243 (20·0%)
Mortality	7530 (9·3%)	307 (16·4%)	839 (22·2%)	543 (18·0%)	1479 (23·8%)
Ventilator or mortality	10703 (13·2%)	531 (28·4%)	1288 (34·0%)	877 (29·1%)	2120 (34·1%)

Data are mean (SD) or n (%). BMI=body-mass index. COPD=chronic obstructive pulmonary disease. qSOFA=quick sepsis-related organ failure assessment. SPO_2=oxygen saturation. ICU=intensive care unit. *Macrolides include only clarithromycin and azithromycin.

Table 2: **Patient demographics and characteristics by treatment group**

organ failure assessment Score called (qSOFA) was calculated for the start of therapy (including a scored calculation of the mental status, respiratory rate, and systolic blood pressure) and oxygen saturation (SPO2) on room air was recorded, were used **as measures of disease severity**. See the figure1.

Treatment (2/3)

Article 3 : Cont.,

Results:

The results showed a significant increase in the risk of in-hospital mortality with the four treatment regimens compared with the control group

The incidence of repetitive ventricular arrhythmias ranged from **4·3% to 8·1% in patients treated with a 4-aminoquinoline,** compared **with 0·3% in the control group (p<0·0001). See figure 1.**

conclusion:

- This real world study of patients with COVID-19 requiring hospitalization found that the use of a regimen containing hydroxychloroquine or chloroquine (with or without a macrolide) was associated with no evidence of benefit, but instead was associated with an increase in the risk of ventricular arrhythmias and a greater hazard for in-hospital death with COVID-19.
- These findings suggest that these drug regimens should not be used outside of clinical trials and urgent confirmation from randomized clinical trials is needed.

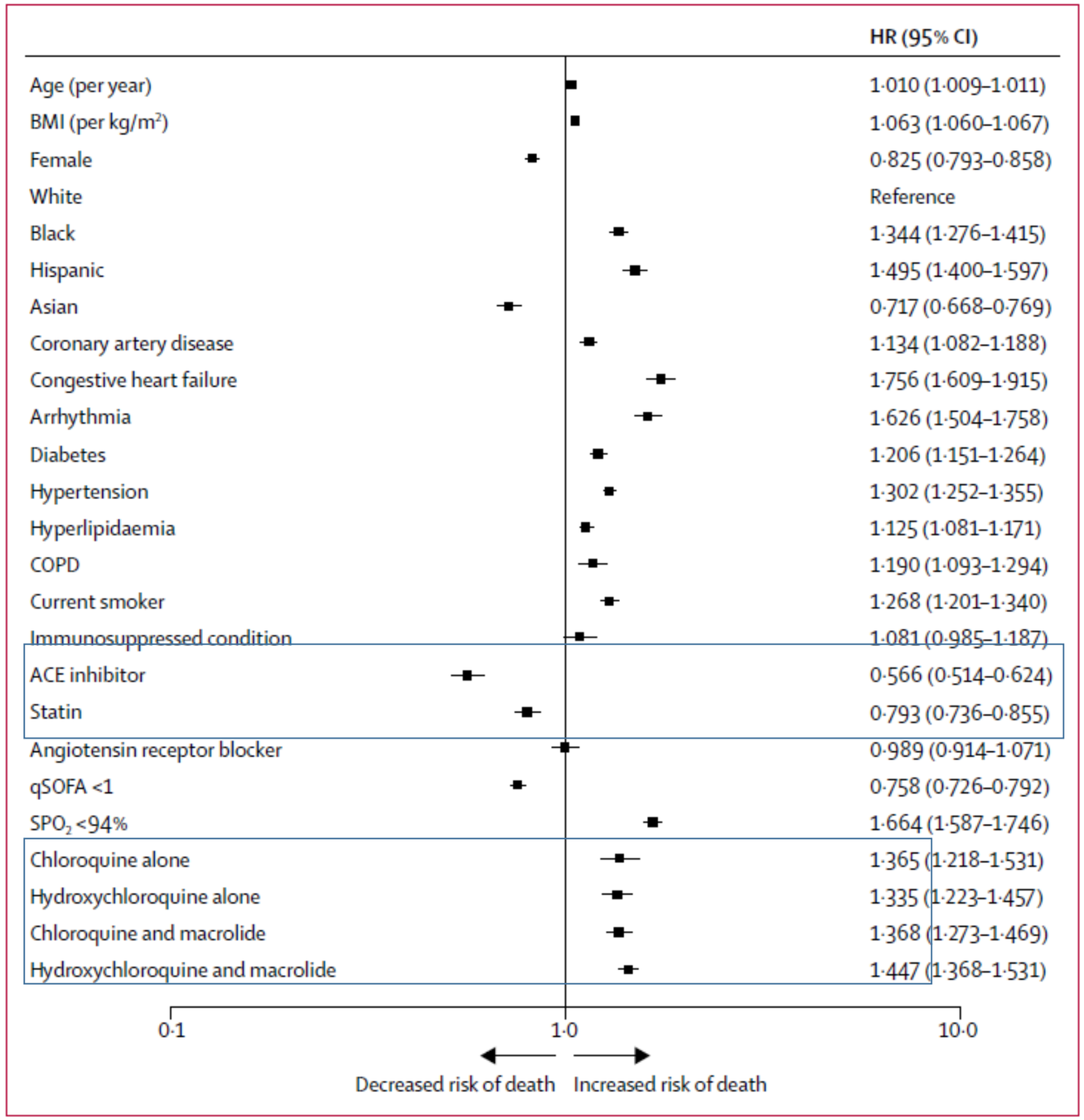

Figure 2: **Independent predictors of in-hospital mortality**

Treatment (3/3)

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Article 3 : Cont.,

Reflection on this study:

- WHO implement a temporary suspension **on 24 May 2020** of random allocation to the hydroxychloroquine arm within the Solidarity Trial while this review of the evidence occurs. See figure 1 from WHO solidarity team.
- Kingdom of Saudi Arabia have updated their guidelines on **23 May 2020** AND **removed HCQ/HC for the treatment of sever cases only**.

For further information:

- Read APDHC Sc. Report **on May 10, 2020,** summary of study found no benefit of HCQ group. Based on this results a hospital in the US **remove the drug from hospital guidelines for patients with moderate to sever cases**.
- Read ADPHC Sc. Report **on May 4 , 2020** , a summary of study explore the cardiac complication of HCQ with/out AZT. (90% of cases had prolonged QT syndrome)
- Read ADPHC Sc. Report on May 8,2020. review on 6 studies address the Antimalarial drug efficacy in treating COVID19 patient
- Read article titled : *Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State*" published on May 11,2020 observational study of >1000 cases showed treatment with hydroxychloroquine, azithromycin, or both, compared with neither treatment, was not significantly associated with differences in in-hospital mortality

WHO COVID-19 SOLIDARITY Trial
Executive Group of the steering committee
R&DBlueprint Powering research to prevent epidemics

Sunday 24 May 2020

To: National Principal Investigators of the Solidarity Trial
From: Executive Group Solidarity Trial

Subject: Emerging non-randomized evidence regarding use of hydroxychloroquine for the treatment of COVID-19 among hospitalised patients.

Dear Solidarity Trial Principal Investigator,

Recent publications of non-randomised observational evidence on the safety and efficacy of hydroxychloroquine (HCQ) for the treatment of hospitalized patients with COVID-19 have generated debate in the scientific community.

WHO COVID-19 SOLIDARITY Trial
Executive Group of the steering committee
R&DBlueprint Powering research to prevent epidemics

suspension of random allocation to the hydroxychloroquine arm within the Solidarity Trial while this review of the evidence occurs.

وزارة الصحة
Ministry of Health

Saudi MoH Protocol for Patients Suspected of/Confirmed with COVID-19

Supportive care and antiviral treatment of suspected or confirmed COVID-19 infection

(version 1.5) May 23rd, 2020

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
PCR Confirmed Cases	**Severe:** Symptoms ≥ 1 of the following: – Respiratory rate ≥30/min (adults); ≥40/min (children < 5 years) – Blood oxygen saturation ≤93% – PaO2/FiO2 ratio <300 – Lung infiltrates >50% of the lung field within 24-48 hours	– Treat symptoms – Follow instructions and recommendations published by Saudi CDC https://covid19.cdc.gov.sa/professionals-health-workers/ – ICU admission, decision by ICU treating team – Antibiotics and antifungals according to local antibiogram and institutional pneumonia management guidelines/ pathways.	**Do not start hydroxychloroquine or chloroquine.** – Triple combination therapy (for adults): Lopinavir /Ritonavir, Ribavirin and interferon beta-1b for 14-days. Start before 7 days from symptoms appearance. • Lopinavir /Ritonavir ○ Adult Dosing: 400/100 mg (2 tablets of 200/50 mg) every 12 hrs. • Ribavirin ○ Adult Dosing: 400mg every 12hrs • Interferon beta-1b ○ Adult Dosing: 8 MIU on alternative days for 3 doses	**Hydroxychloroquine & Chloroquine** *(see precautions above)* **Lopinavir/ritonavir** *(see precautions above)* **Ribavirin** *(see precautions above)* **Interferon beta-1b** *(see precautions above)*

Article 4

Updates on Favipiravir (Avigan)

Published: Thomson Reuters in May 26.2020

Summary:

Favipiravir, The Drug have not yet been approved in Japan for the treatment of CVID19. It was expected to get the approval by the end of May. However , according to the news agency, there was a report of an interim on the drug efficiency shared by the manufacturing company to the Japanese government. According to the news the interim study showed no clear evidence of the drug's efficacy in COVID-19 cases. *(no published information about the results of this report available online)*

Therefore the Japanese government will delay the approval of this drug until a good evidence of efficacy is available.

For Further Information On The This Drug:

Read the ADPHC Sc. Report on 23.3.2020 ; which presented a summary of an open label control trial comparing Favirpavir with LPV/RTV. Results showed positive results in the Favirpavir arm.

Diagnosis

Article 5 : COVID-19 Rapid Diagnostic Tests , use in low resource settings
Published: 30/04/2020 in the institute of tropical medicine antwerp

Summary

- **Rapid diagnostic tests (RDTs)** are small stand-alone tests that are simple to use. They can be used at the **point of care** –by minimally trained staff. **They provide test results within 15 minutes.** they are attractive for **decentralized testing particularly in low resource settings.**
- COVID-19 antigen and antibody detection RDTs are **"immunoassays"** or **"serology tests".**
- **COVID-19 antigen detection Rapid Diagnostic Tests (RDT) and COVID-19 antibody detection RDTs are different:**
  - COVID-19 antigen detection diagnose the presence **of a protein of the virus in body fluids** – mostly in secretions of the upper respiratory tract.
  - COVID-19 antibody detection diagnose antibodies produced by white blood cells of the infected person during the infection. They are mostly **detected in the blood**. But it takes **a few and up to 10 days after the onset of illness before the concentration of antibodies in the blood is high enough** to be captured by the RDT. (*Unlike other (laboratory-based) immunoassays, they do not provide quantitative information (information about the number of antibodies, expressed as dilution "titer")).*

What are the current recommendations for laboratory testing of COVID-19?

At time of writing, WHO recommends laboratory testing for COVID-19 as follow:

1. Identification of COVID-19 infections:

Nuclear acid amplification (NAAT) methods (molecular methods such as RT-PCR) are recommended. This comprises the following applications:

- clinical diagnosis for patient care (“test and treat”),
- identification at triage and investigation of clusters (“test and isolate”)
- confirmation of virus clearance after recovery

Respiratory tract specimens are recommended:

- upper respiratory specimens (nasopharyngeal and oropharyngeal swab or wash)
- lower respiratory specimens (sputum and/or endotracheal aspirate or bronchoalveolar lavage).

2. Serology tests are currently not recommended for case detection. But they will play a role in **research** and **surveillance.**

3. Rapid Diagnostic Tests for antigen detection for COVID-19 **need to be evaluated and is not currently recommended for clinical diagnosis nor for triage** and investigation of clusters pending more evidence on test performance and operational utility.

Public Health Response:

Article 6 :COVID-19: consequences for higher education
Published: May 21, 2020 in the lancet
Summary:

During COVID-19 pandemic, universities have been forced to increase online teaching that has involved unexpected expenditure. Universities have had to find money to continue paying their staff as well as other facilities. The shift to online learning looks set to continue until arrival of a successful vaccine. This situation raises questions about if institutions can justify a fee structure predicated on a model of face to face contact. In addition, online learning is not substitute for laboratory work.

The economic drop down will force thousands of students to delay entering university. Governments who wish to support commercial education, universities have come to depend on this money that represents about a third of the total income from tuition fees. A collapse in the international student market that seems unavoidable, would have serious consequences.

Economic recessions diminish the prospects for graduate employment that indicates downgrading of the student experience as well as the value of the degree. In this situation, it will be difficult for universities to sustain the same level of fees that they have been before. Furthermore, it will weaken domestic and international demand coupled with pressure to decrease fees. As a result, universities will be forced to make budget cuts, jobs will be lost, and vital research will be stopped.

Many universities worldwide are unlikely to survive during this pandemic in the absence of substantial financial support. Others will have to close large projects or sell properties.

Public Health Response:

Article 7 : Is It Safe for Me to Go to Work?" Risk Stratification for Workers during the Covid-19 Pandemic

Published: May 26,2020 in the NEJM

Summary:

This article propose a framework to help clinicians counsel patients about continuing to work in the midst of the pandemic that is based on their occupational risk of contracting SARS-CoV-2 and their risk of death if they are infected. See figure 1

The author recommends :

Government should develop strategy to protect at-risk workers needs at least three components:

- a framework for counseling patients about the risks posed by continuing to work,
- urgent policy changes to **ensure financial protections for people who are kept out of work**,
- and a data-driven plan for safe reentry into the workforce.

Figure 1