SCIENTIFIC RESEARCH MONITORING ON COVID-19

27 DECEMBER 2020

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SCIENTIFIC RESEARCH MONITORING ON COVID-19 (ISSUE 327)

Abu Dhabi Public Health Center (ADPHC) is gathering the latest scientific research updates and trends on coronavirus disease (COVID-19) in a daily report. The report provides summaries on breakthrough or updated research on COVID-19 to allow health care professionals and public health professionals get easy and fast access to information.

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Research

Updated

Statistics

Articles

Summary

Note : All articles presented in this report represent the authors' views and not necessarily represents Abu Dhabi Public Health Center views or directions. Due the nature of daily posting , some minor language errors are expected.
For further inquiries you may communicate with us as PHP@adphc.gov.ae

RESEARCH UPDATES

The views and opinions expressed in this report are those of the authors and do not reflect the official policy or position of the Abu Dhabi Public Health Center (ADPHC).

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Treatment

Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19

Treatment

Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia

Treatment

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19

Clinical Feature

Infectivity of asymptomatic versus symptomatic COVID-19
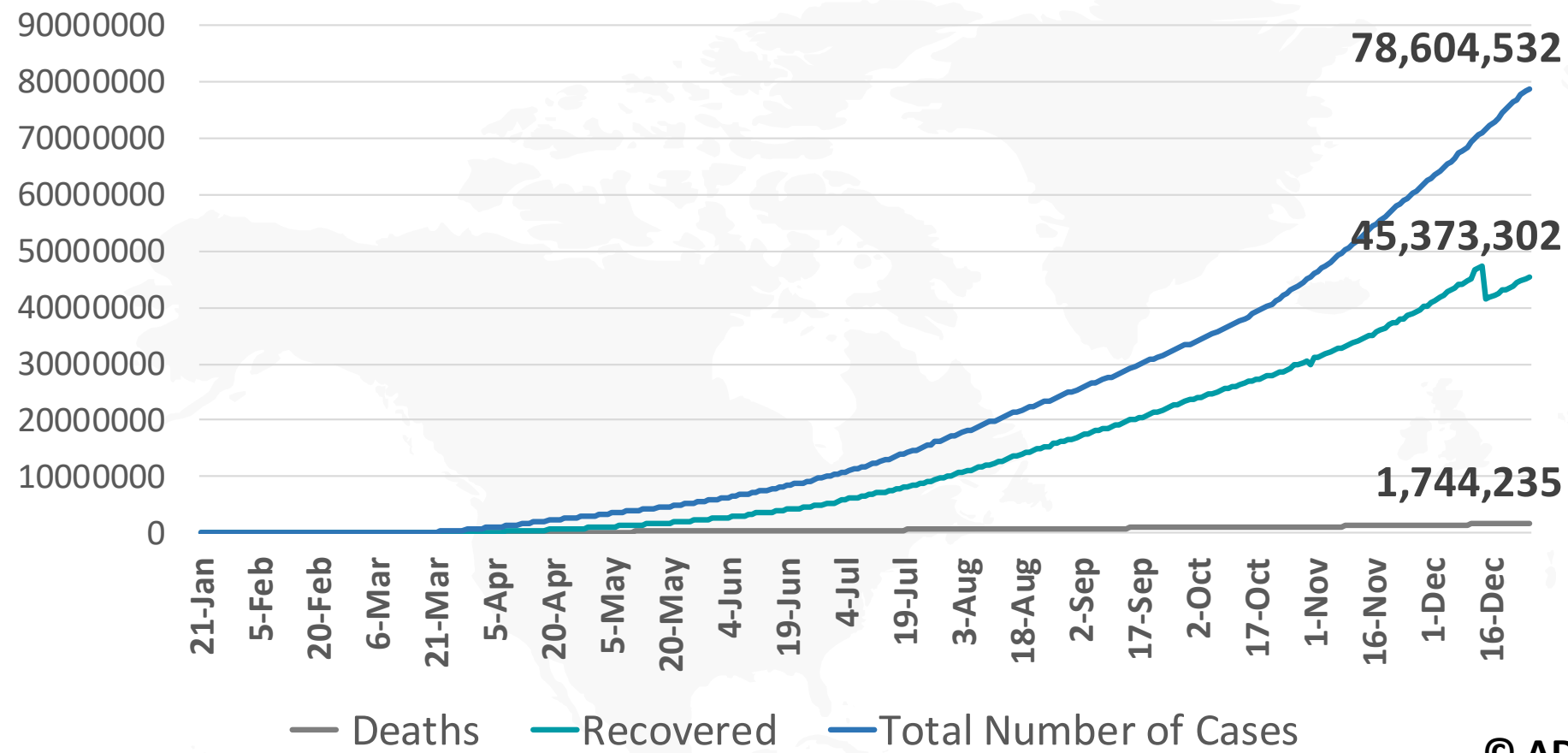
Public health response

Long COVID guidelines need to reflect lived experience

Diagnosis
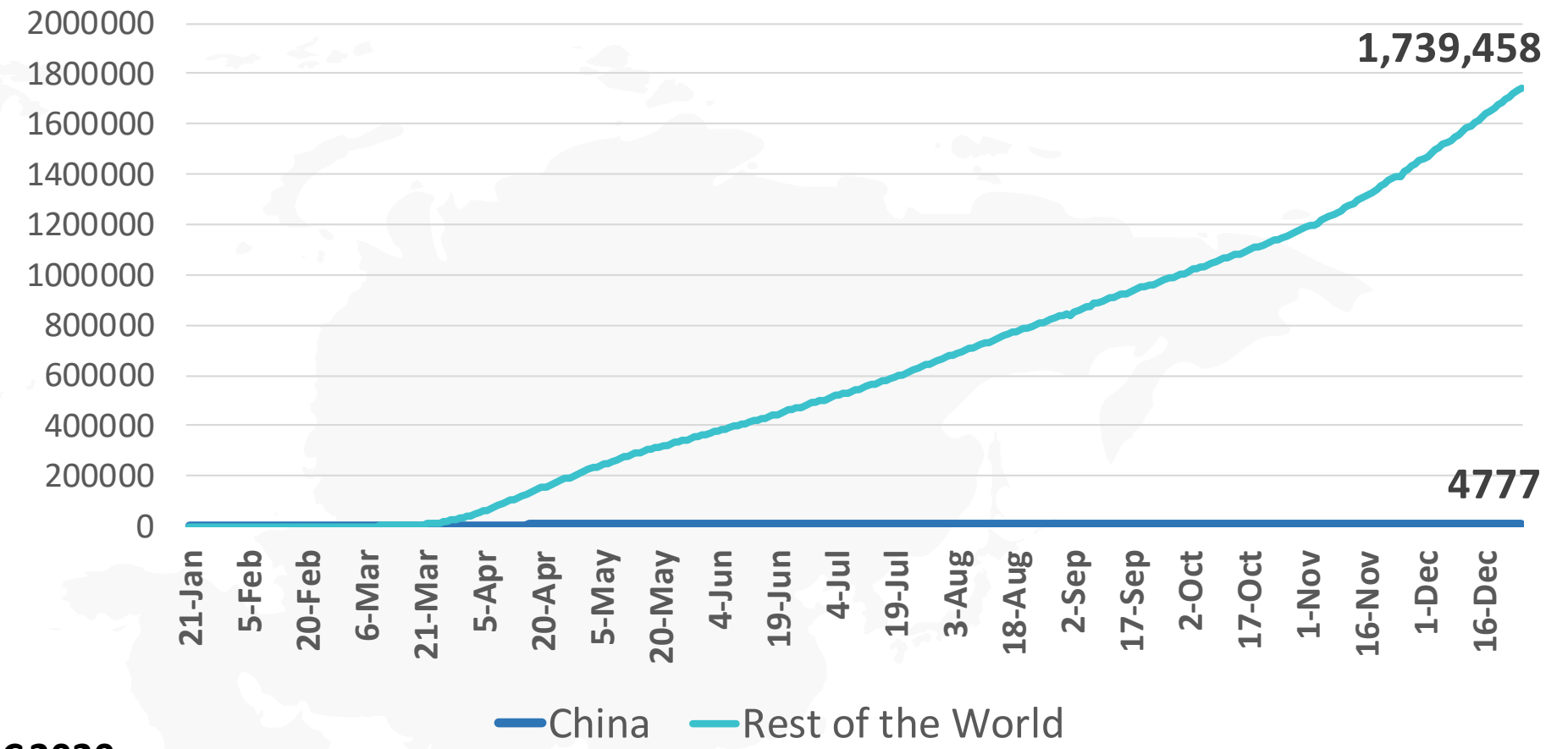
Persistence of IgG response to SARS-CoV-2

EPIDEMIOLOGY

FROM 21 JAN TO 26 DEC 2020

Figure 1: Total Number of Infected, Recovered, and Death Cases

78,604,532
45,373,302
1,744,235

Legend: — Deaths — Recovered — Total Number of Cases

Note: the number of recovered cases in 31th October recorrected from 30 million to 29 million, and in 15th December recorrected from 47 million to 41 million in Johns Hopkins website
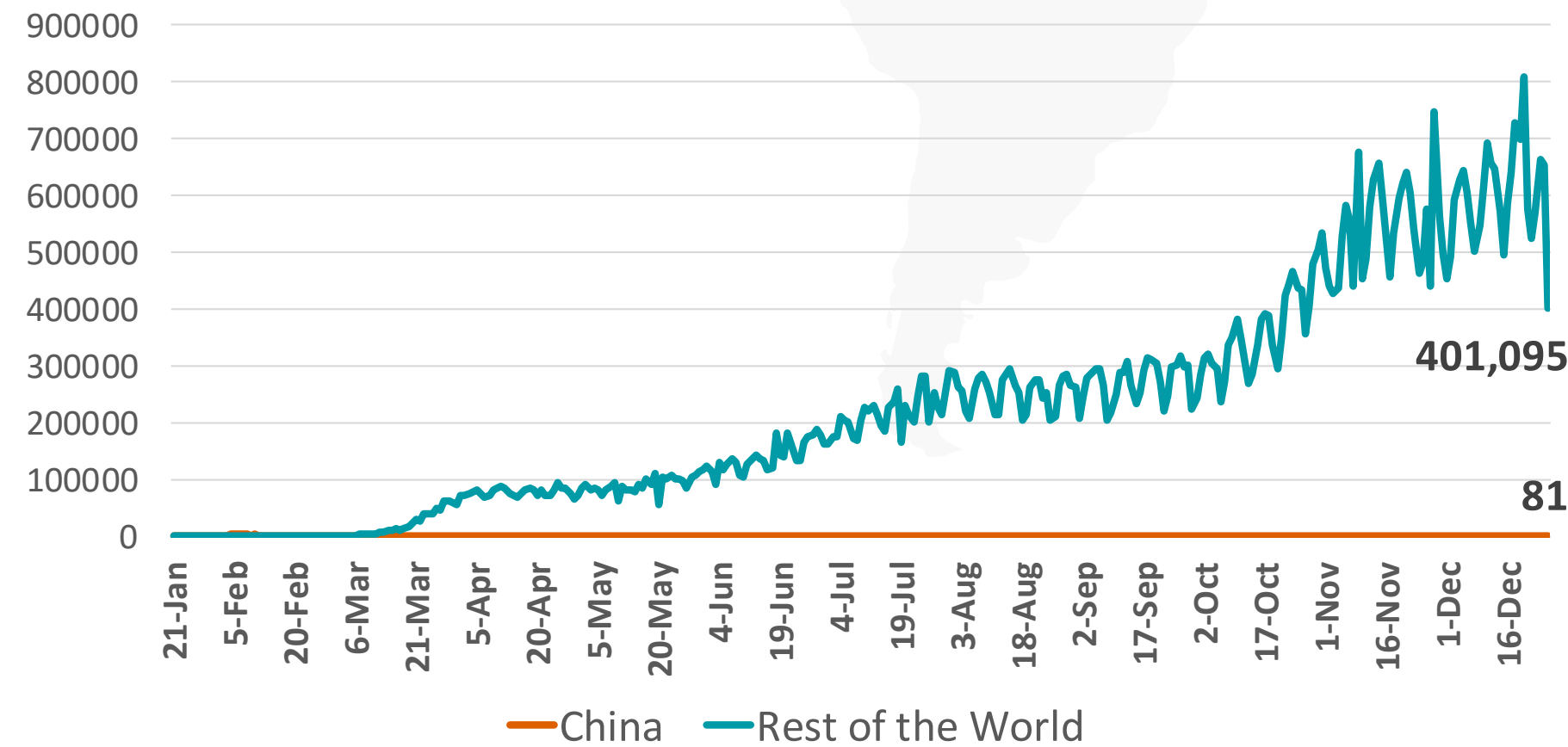
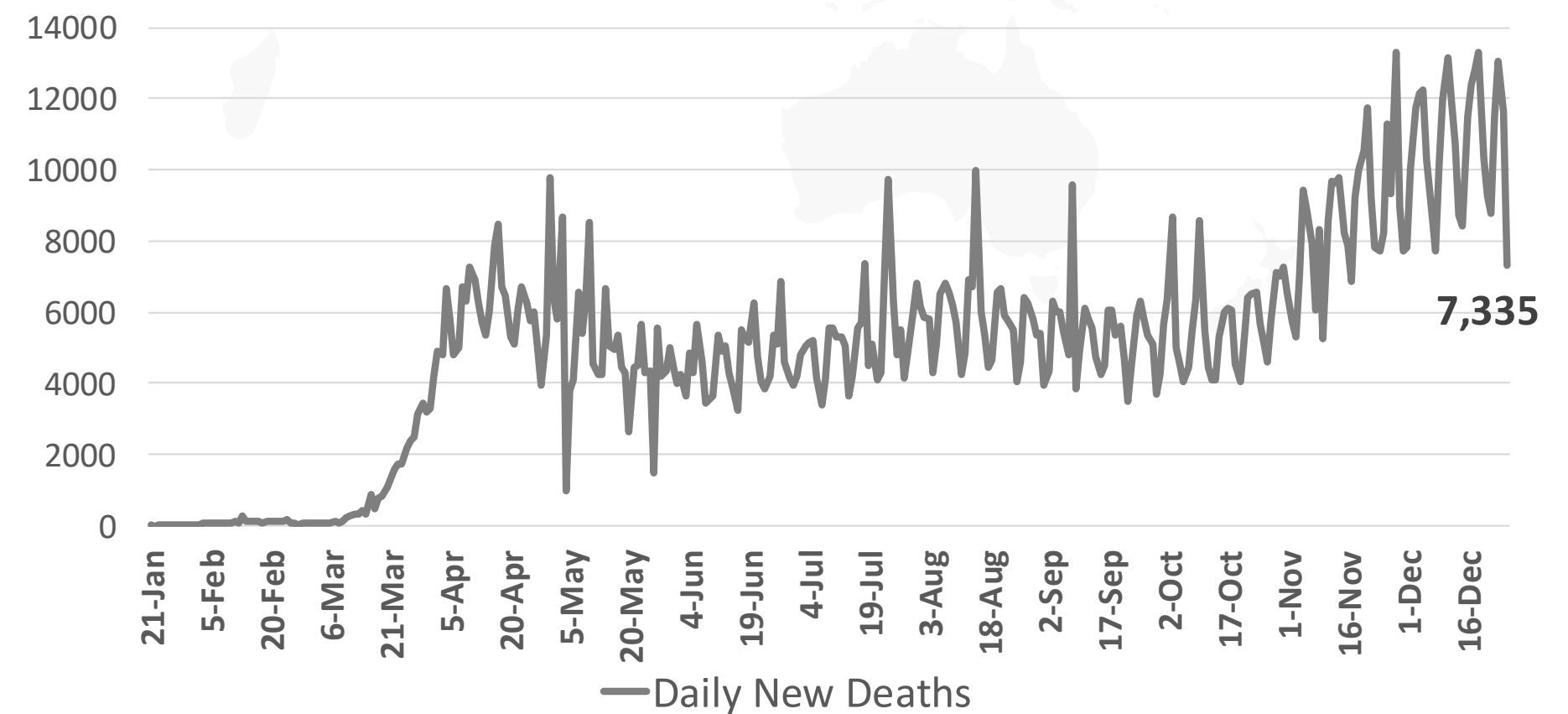**Figure 3: Total Number of Death Due to COVID-19** (china and result of the world)

1,739,458
4777

Legend: — China — Rest of the World

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Figure 2: Daily New Infected COVID-19 Cases (China and rest of the world)

401,095
81

Legend: — China — Rest of the World

Figure 4: Global Daily New Deaths Due to COVID-19

7,335

Legend: — Daily New Deaths

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Figure 5: Top 10 Countries in the Total Number of Cases Due to COVID-19

TOTAL DEATHS

Country	Total Deaths
USA	323,527
Brazil	190,006
India	147,343
Italy	71,359
UK	70,195
France	62,051
Russia	54,226
Spain	49,824
Argentina	42,392
Germany	29,422

DEATHS PER MILLION

Country	Deaths per Million
Italy	1180.23
Spain	1065.65
UK	1034.01
USA	977.42
France	950.63
Argentina	937.96
Brazil	893.9
Russia	371.58
Germany	351.17
India	106.77

TOTAL INFECTED CASES

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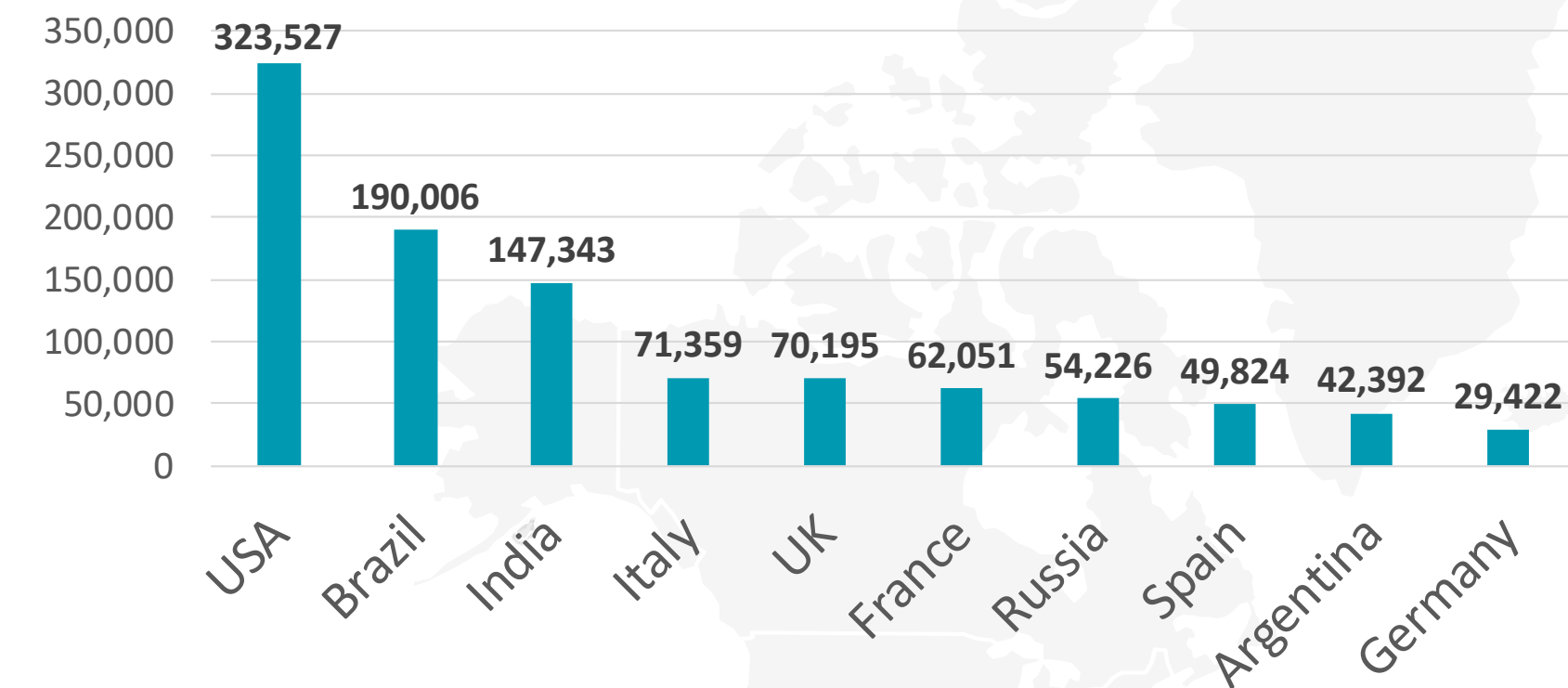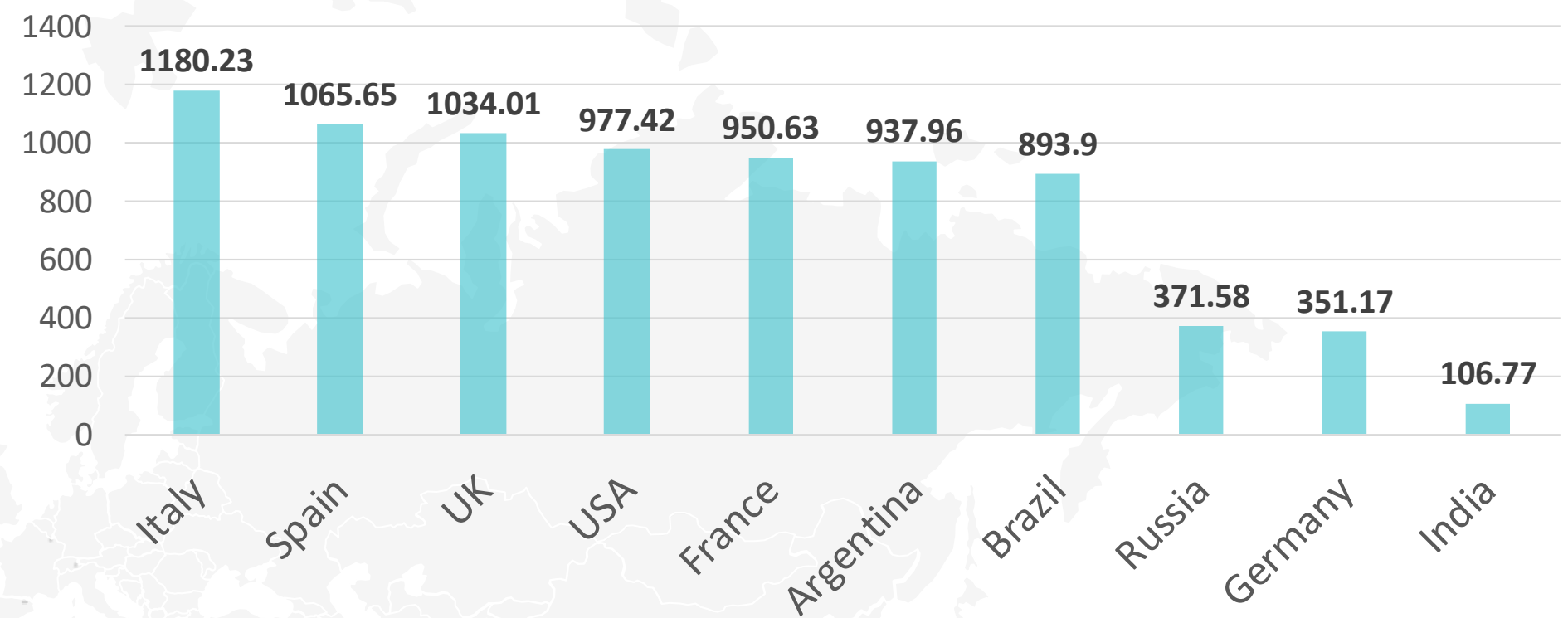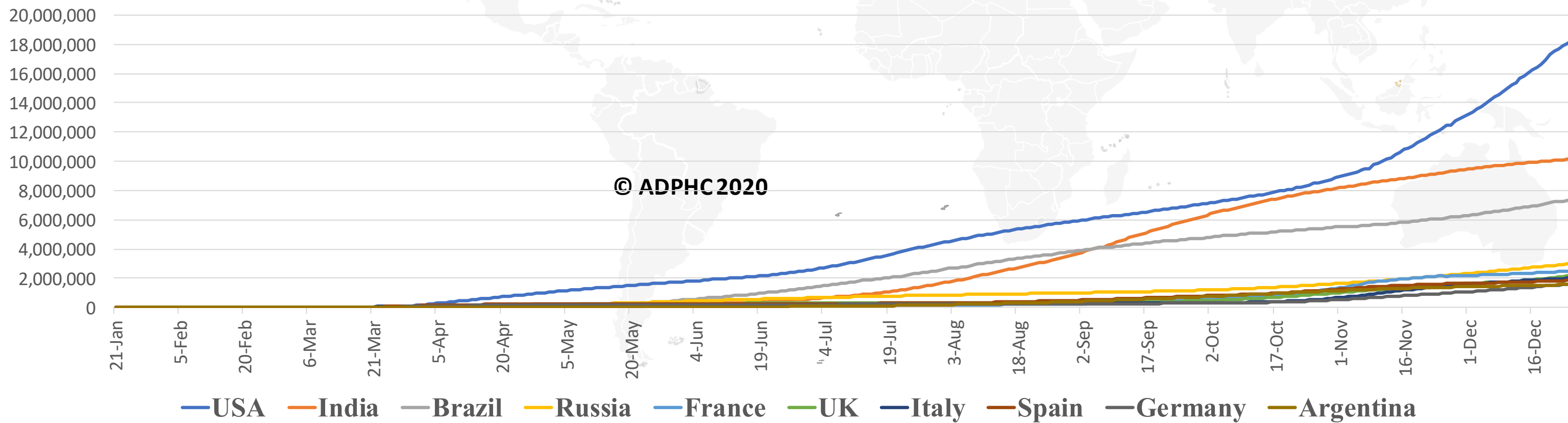
Country	Total Infected Cases
USA	18,311,405
India	10,169,118
Brazil	7,425,593
Russia	3,021,964
France	2,505,074
UK	2,221,316
Italy	2,028,354
Spain	1,854,951
Germany	1627103
Argentina	1,571,680

Legend: USA — India — Brazil — Russia — France — UK — Italy — Spain — Germany — Argentina

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Figure 6: COVID-19 Status in the UAE (Federal Competitiveness and Statistics Authority Dashboard)

Daily Tests
135,617.6 Average Tests
1,371.2 per 100k population
0.9% Positive Rate

Daily Cases
1,212.6 Average Cases
12.3 per 100k population

Daily Recovered
1,325.4 Average Recovered
13.4 per 100k population

Daily Deaths
3.0 Average Deaths
0.0 per 100k population
0.2% Case Fatality Rate
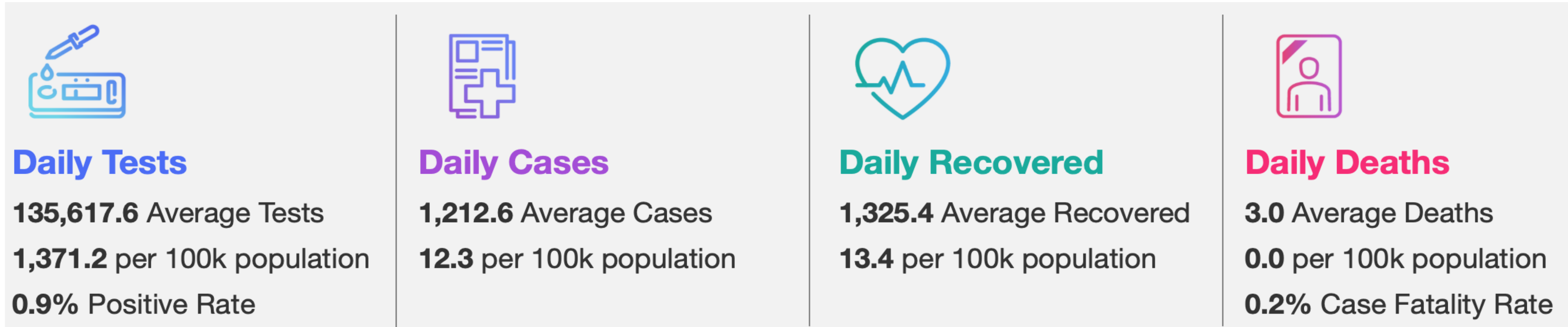
TOTAL NUMBER OF INFECTED AND RECOVERED CASES DUE TO COVID-19 REPORTED BY THE UAE

199,665

177,407

— Total number of cases   — Recovered cases

EPIDEMIOLOGY

Date: 26 DEC 2020

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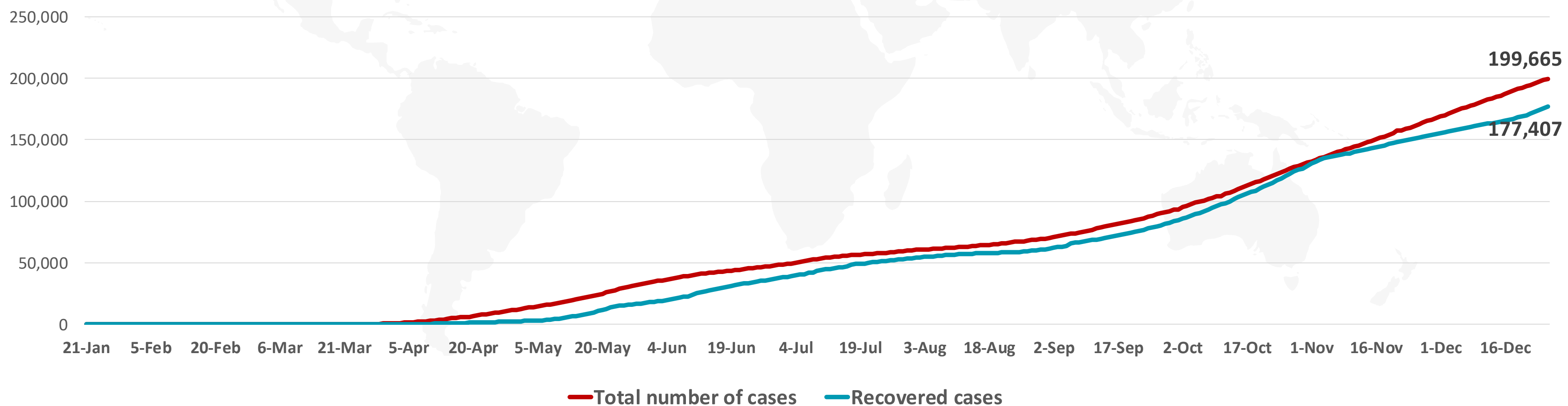
Figure 7A : **Global Distribution of COVID-19 Cases**
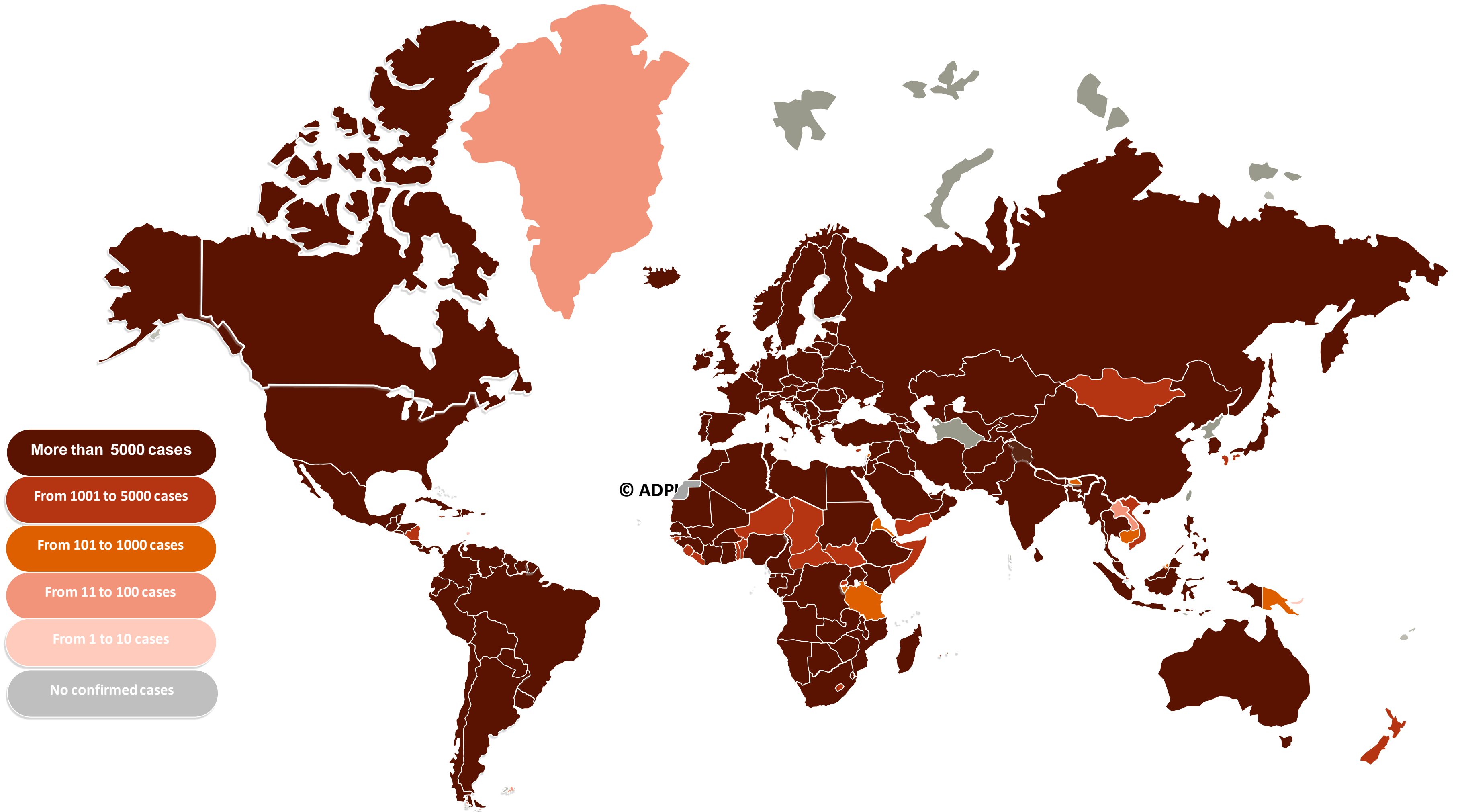
More than 5000 cases

From 1001 to 5000 cases

From 101 to 1000 cases

From 11 to 100 cases

From 1 to 10 cases

No confirmed cases

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EPIDEMIOLOGY

Date: 26 DEC 2020

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Figure 7B: Bar Chart Illustrates the Global Distribution of COVID19 Cases

| More than 5000 cases | From 1001 to 5000 cases | From 101 to 1000 cases | From 11 to 100 cases | From 1 to 10 cases |
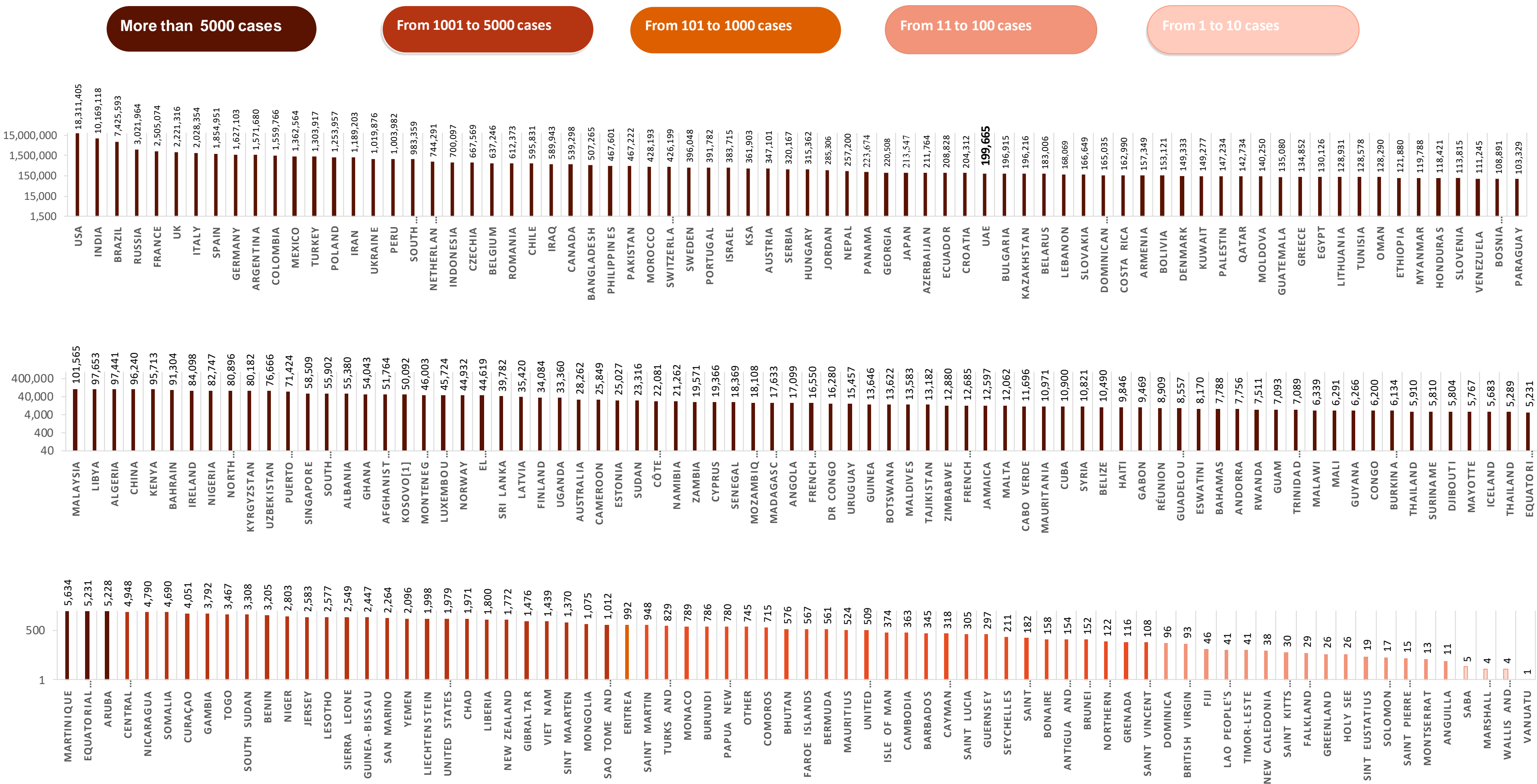
Other*: includes cases and deaths reported under the international conveyance (Diamond Princess)

EPIDEMIOLOGY

Date: 26 DEC 2020

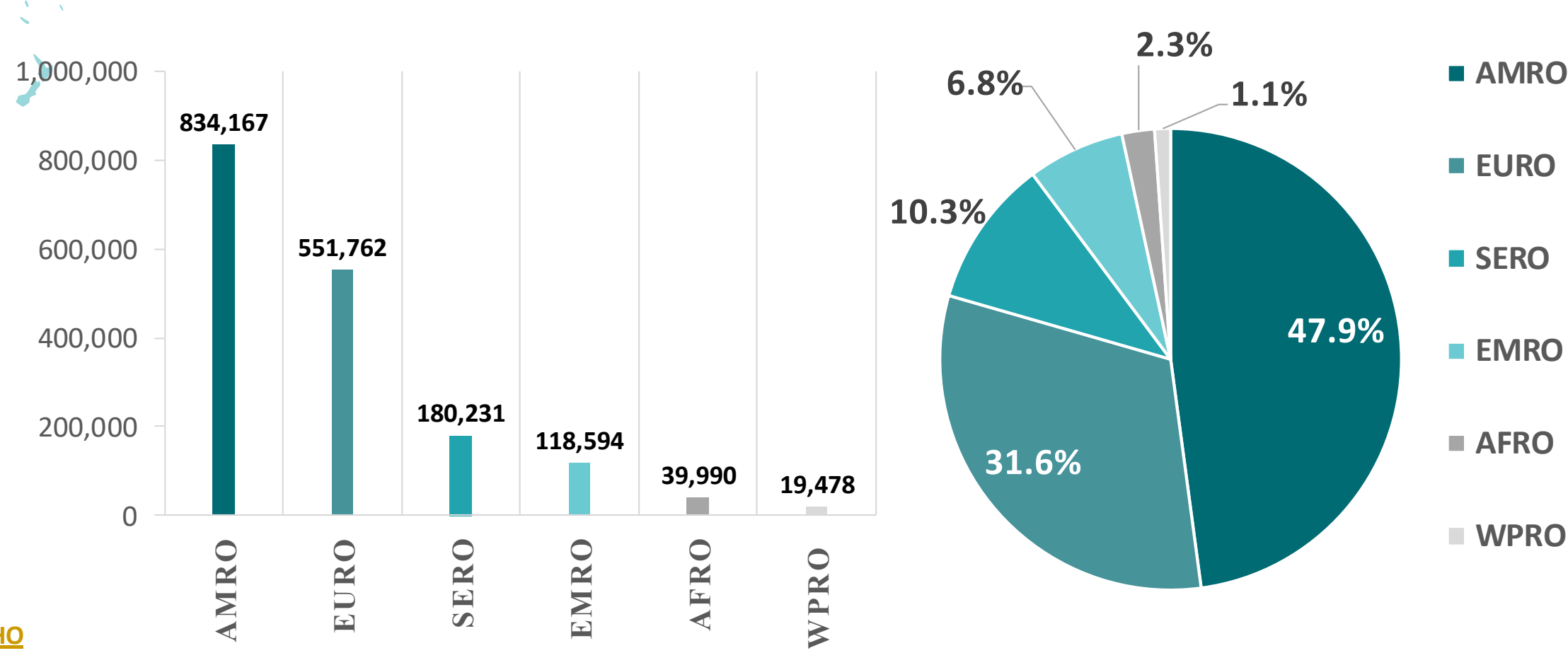مركز أبوظبي
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Figure 8: Global Distribution of COVID-19 Cases per Region

INFECTED

Region	Infected
AMRO	34,002,757
EURO	25,118,109
SERO	11,813,360
EMRO	4,803,191
AFRO	1,815,247
WPRO	1,051,123

Pie chart (INFECTED):
- AMRO 43.26%
- EURO 31.96%
- SERO 15.03%
- EMRO 6.11%
- AFRO 2.31%
- WPRO 1.34%

DEATHS

Region	Deaths
AMRO	834,167
EURO	551,762
SERO	180,231
EMRO	118,594
AFRO	39,990
WPRO	19,478

Pie chart (DEATHS):
- AMRO 47.9%
- EURO 31.6%
- SERO 10.3%
- EMRO 6.8%
- AFRO 2.3%
- WPRO 1.1%

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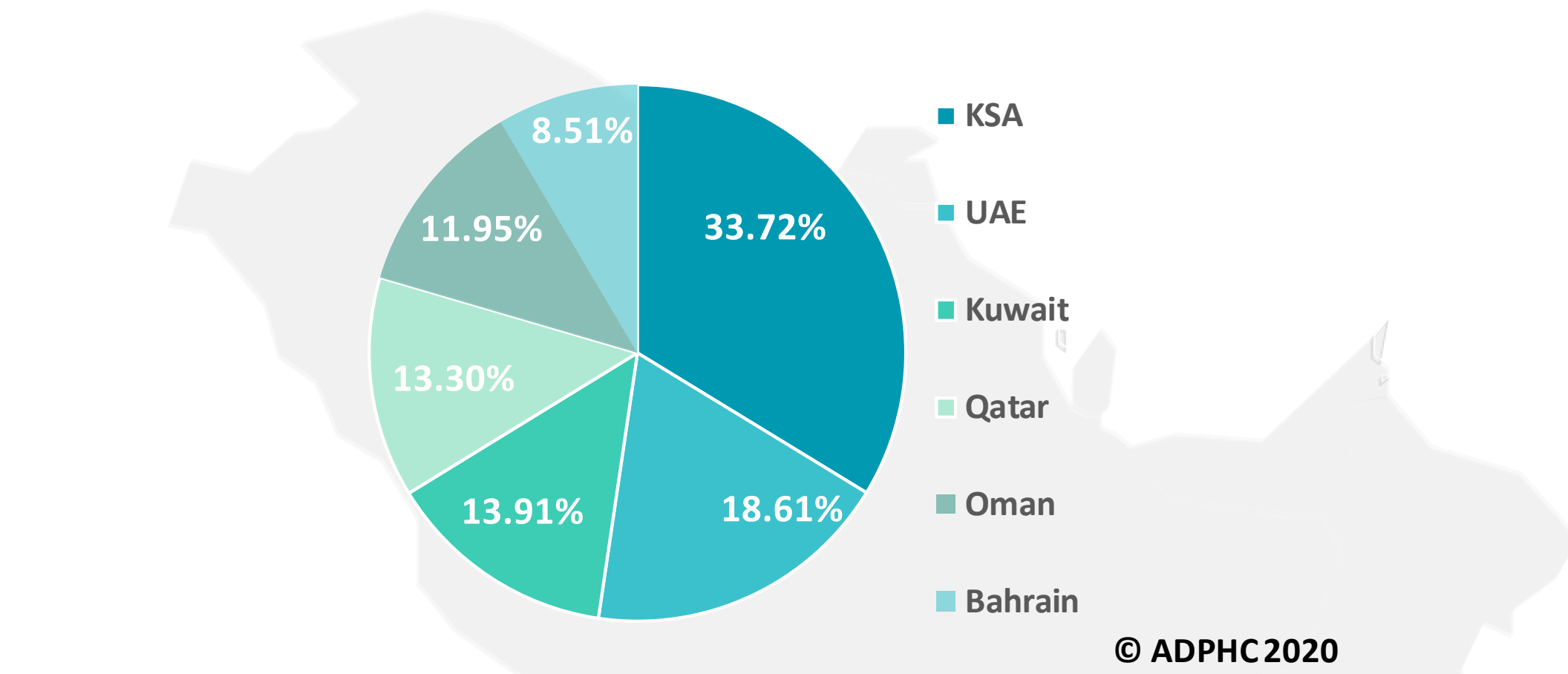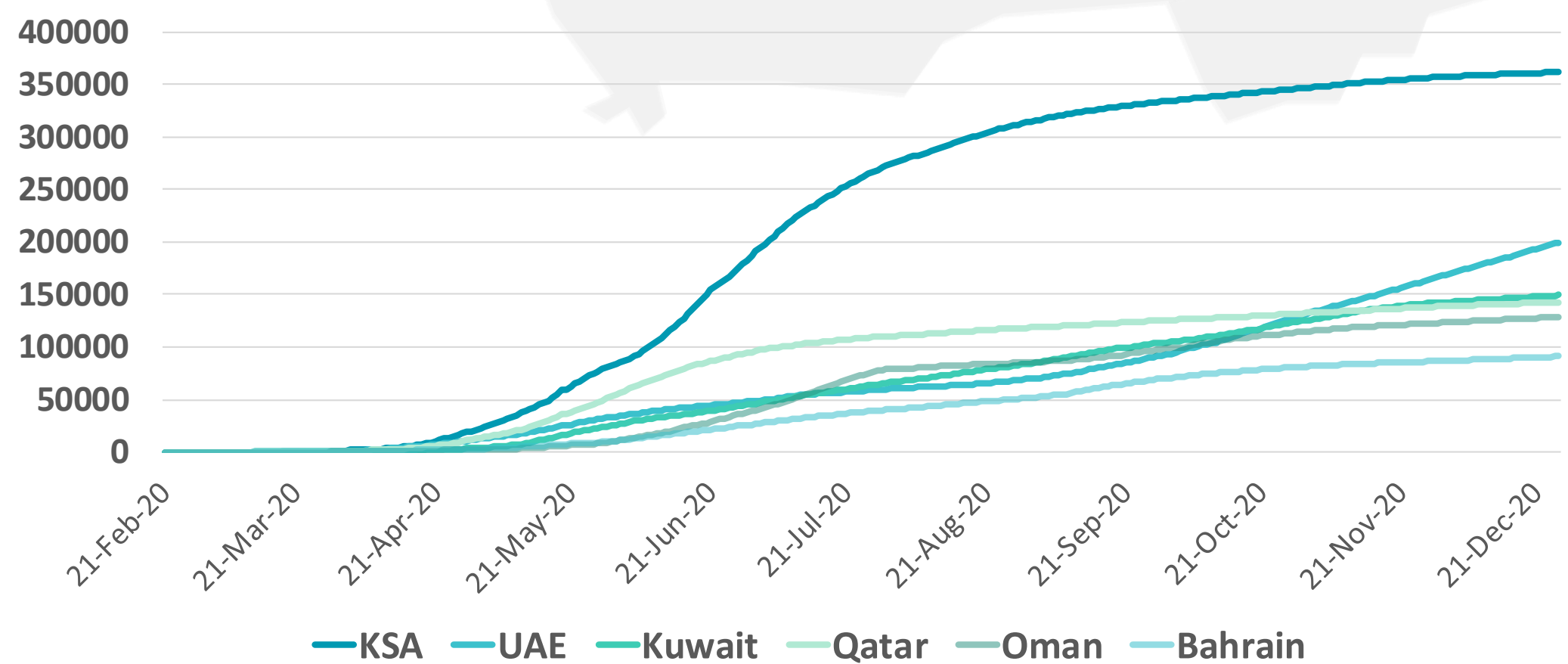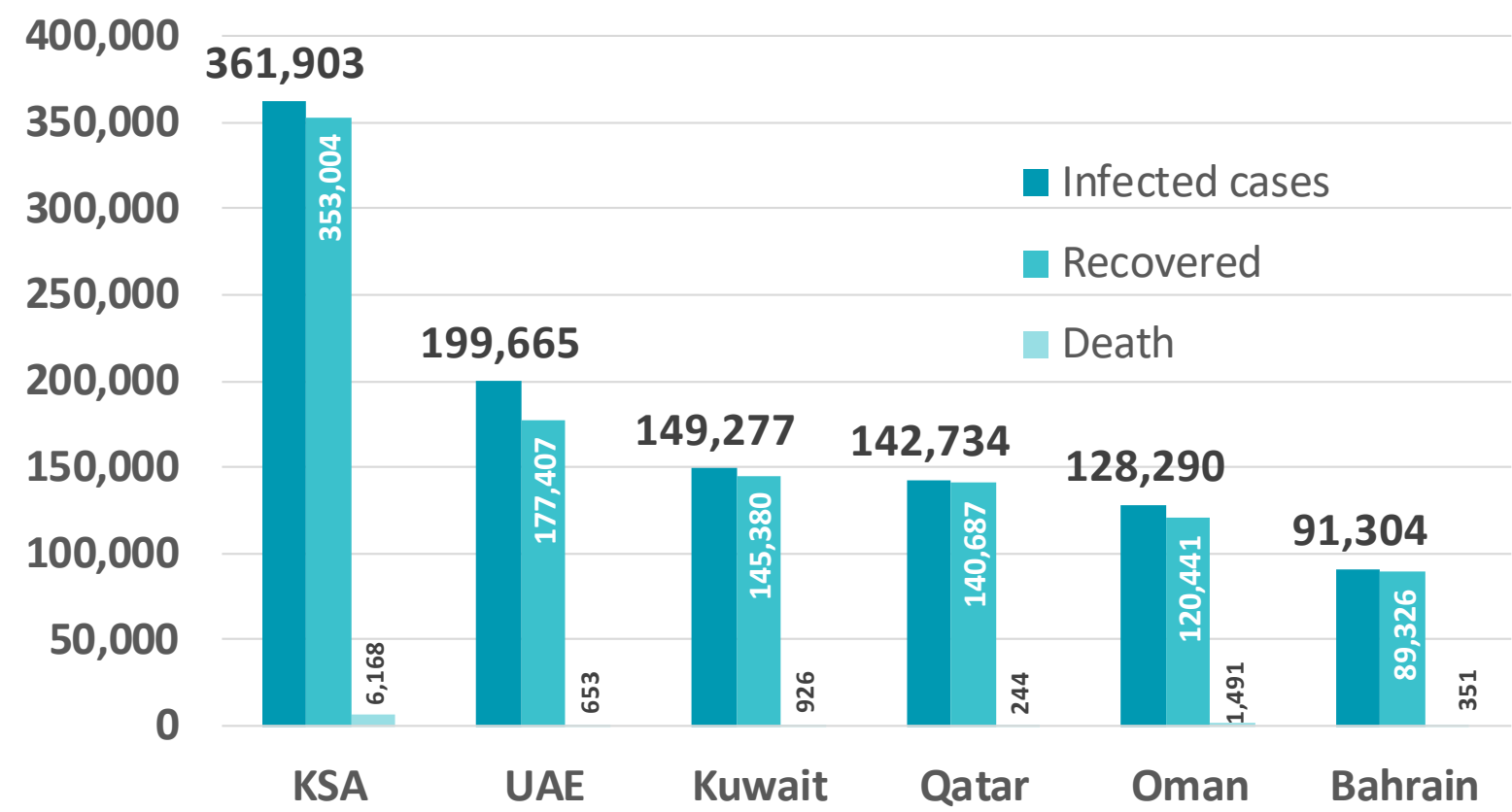**Graphs published by Abu Dhabi Public Health Center 2020 | Data resources: WHO**

Figure 9: Comparative Analysis of the Distribution of COVID-19 Cases in GCC Countries

TOTAL NUMBER OF INFECTED CASES

Pie chart:
- KSA: 33.72%
- UAE: 18.61%
- Kuwait: 13.91%
- Qatar: 13.30%
- Oman: 11.95%
- Bahrain: 8.51%

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TOTAL NUMBER OF INFECTED, RECOVERED AND DEATHS

Bar chart (Infected cases, Recovered, Death):
- KSA: 361,903 / 353,004 / 6,168
- UAE: 199,665 / 177,407 / 653
- Kuwait: 149,277 / 145,380 / 926
- Qatar: 142,734 / 140,687 / 244
- Oman: 128,290 / 120,441 / 1,491
- Bahrain: 91,304 / 89,326 / 351

DEATHS PER MILLION

Bar chart (Per million):
- Oman: 291.97
- Kuwait: 216.83
- Bahrain: 206.28
- KSA: 177.17
- Qatar: 84.69
- UAE: 66.02

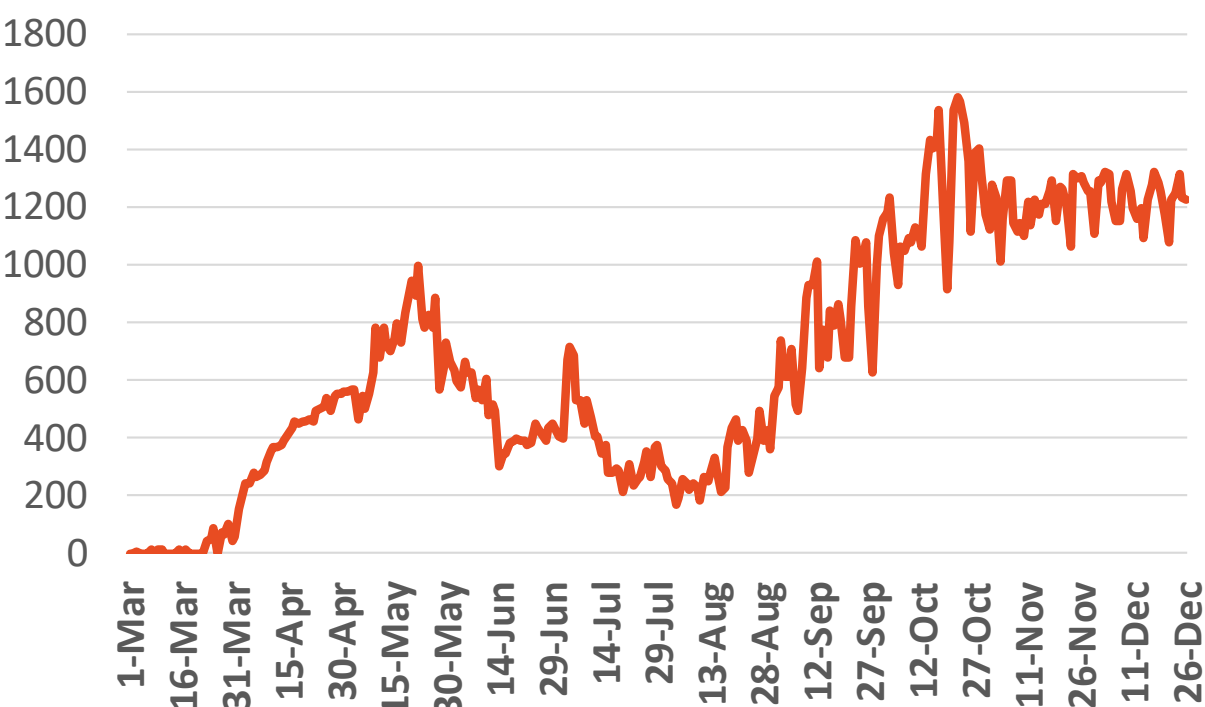Line chart from 21-Feb-20 to 21-Dec-20 for KSA, UAE, Kuwait, Qatar, Oman, Bahrain.
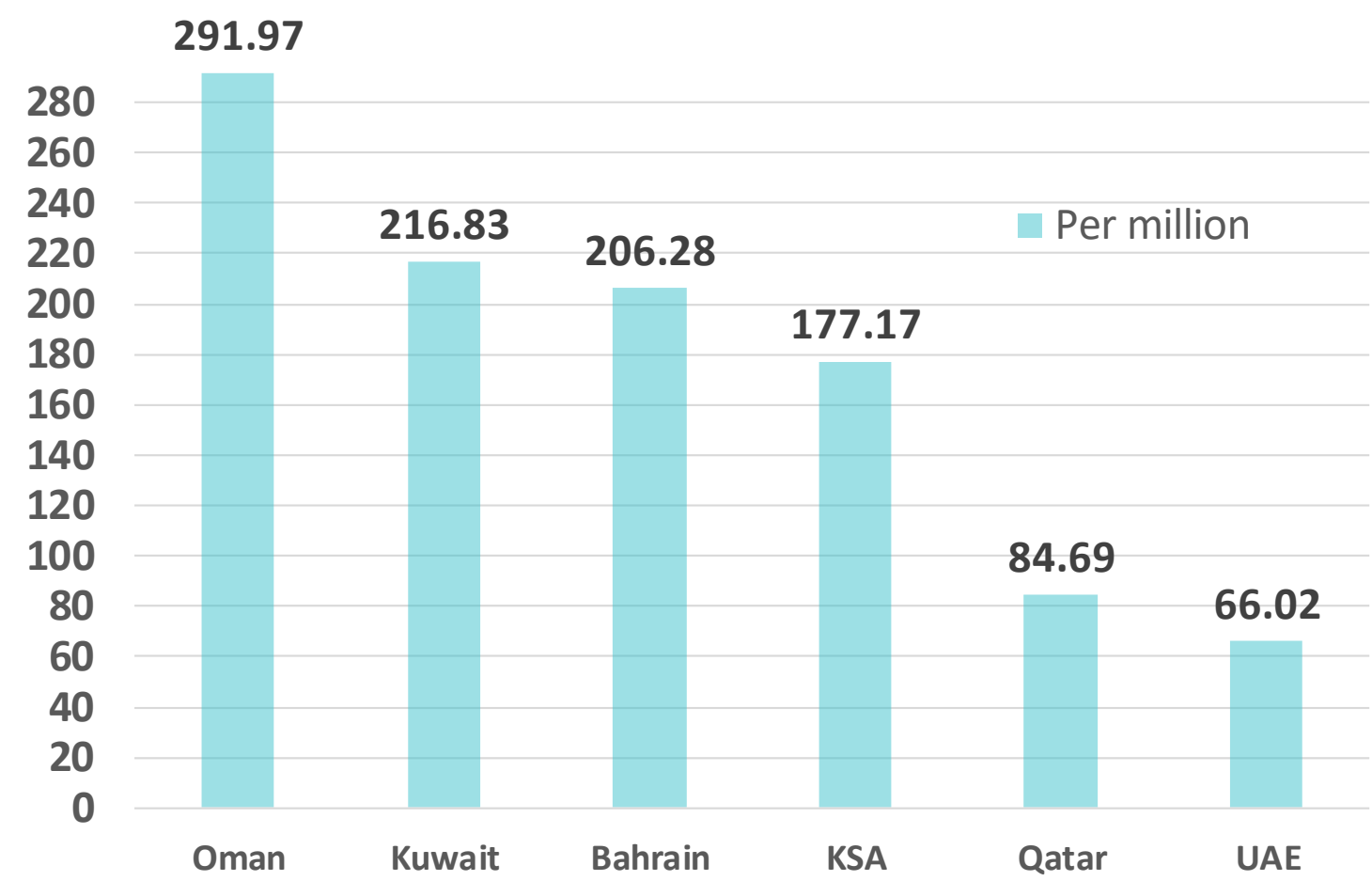
Graphs published by Abu Dhabi Public Health Center 2020 | **Data resources:** John Hopkins, WHO
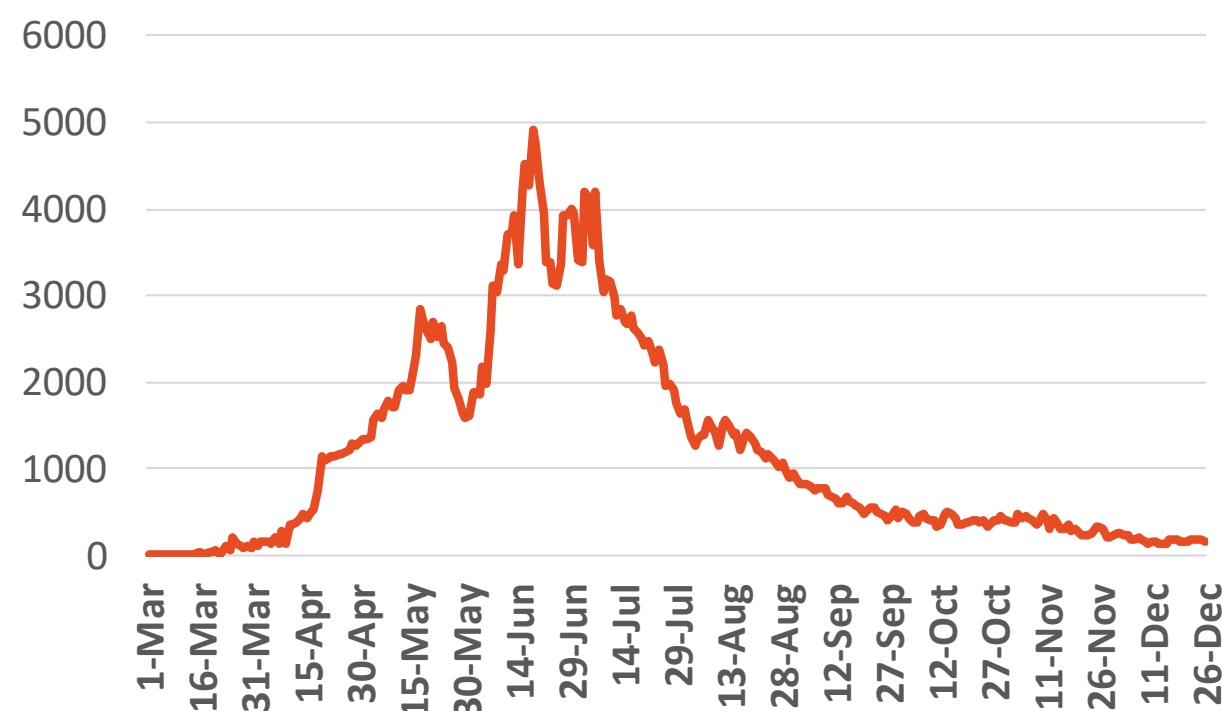
Figure 10: Comparative Analysis of the Distribution of COVID-19 New Cases in GCC Countries

UAE
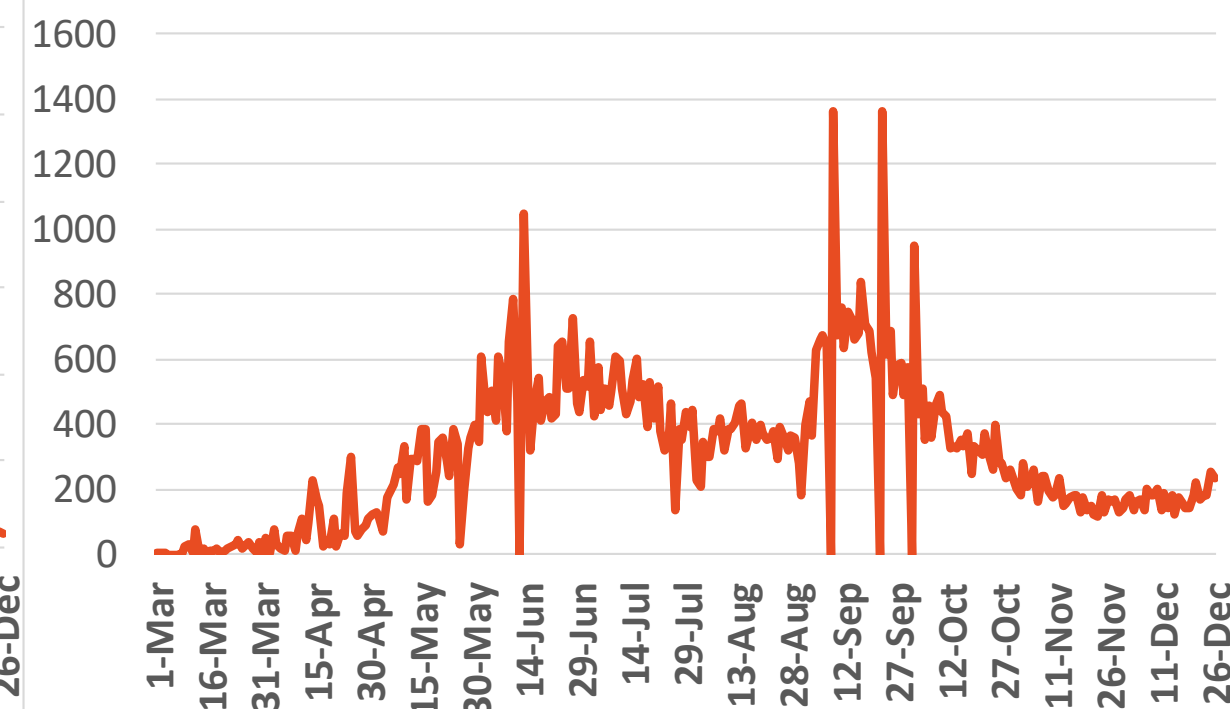Source : National Emergency Crisis and Disaster Management Authority
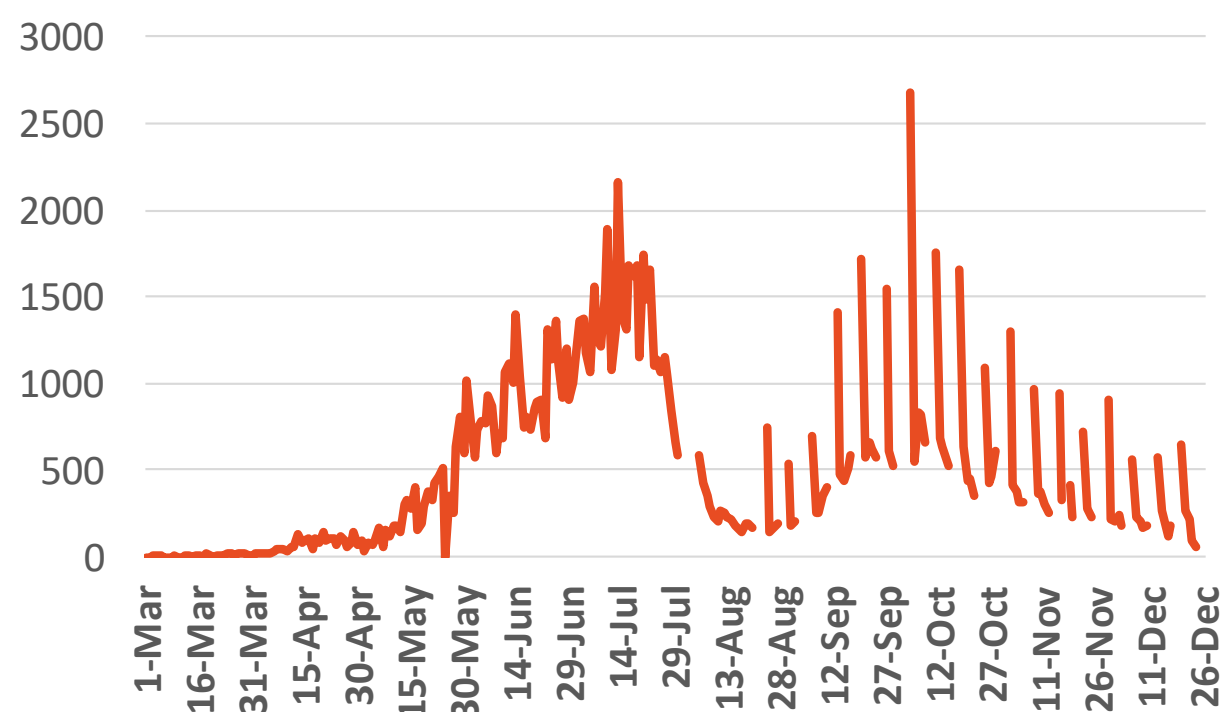
KSA
Source : KSA ministry of health

Bahrain
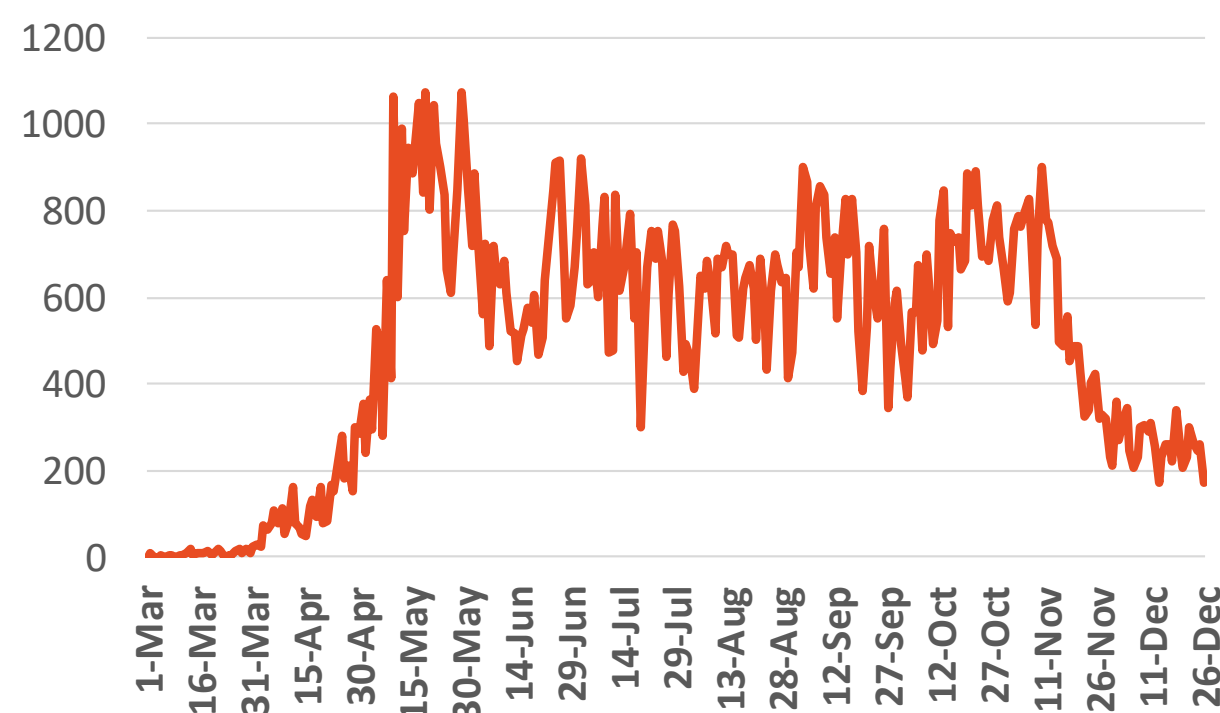Source :WHO

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Oman
Source :Oman ministry of health
*No announced statistic data from 31 JUL to 4 AUG, 21,23,28,30 AUG 2,4 5,11,12,18,19,25 ,26,30 SEP,1,2,9,10,16,17,23,24,30,21 OCT, 6,7,13,14,17,20,21, ,27,28 NOV,4,5,11,12,18,19,25,26 DEC
*No announced statistic data on weekends and official holidays.

Kuwait
Source : Kuwait ministry of health

Qatar
Source : Qatar ministry of health

Figure 11: Comparative Analysis of the Distribution of COVID-19 Newly Recovered Cases in GCC Countries

UAE

Source : National Emergency Crisis and Disaster Management Authority

KSA

Source : KSA ministry of health

Bahrain

Source : Bahrain ministry of health

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Oman

Source :Oman ministry of health

*No announced statistic data from 31 JUL to 4 AUG, 21,23,28,30 AUG 2,4 5,11,12,18,19,25 ,26,30 SEP, 1,2,9,10,16,17,23,24,30,21 OCT, 6,7,13,14,17,20,21, ,27,28 NOV,4,5,11,12,18,19,25,26 DEC

*No announced statistic data on weekends and official holdays.
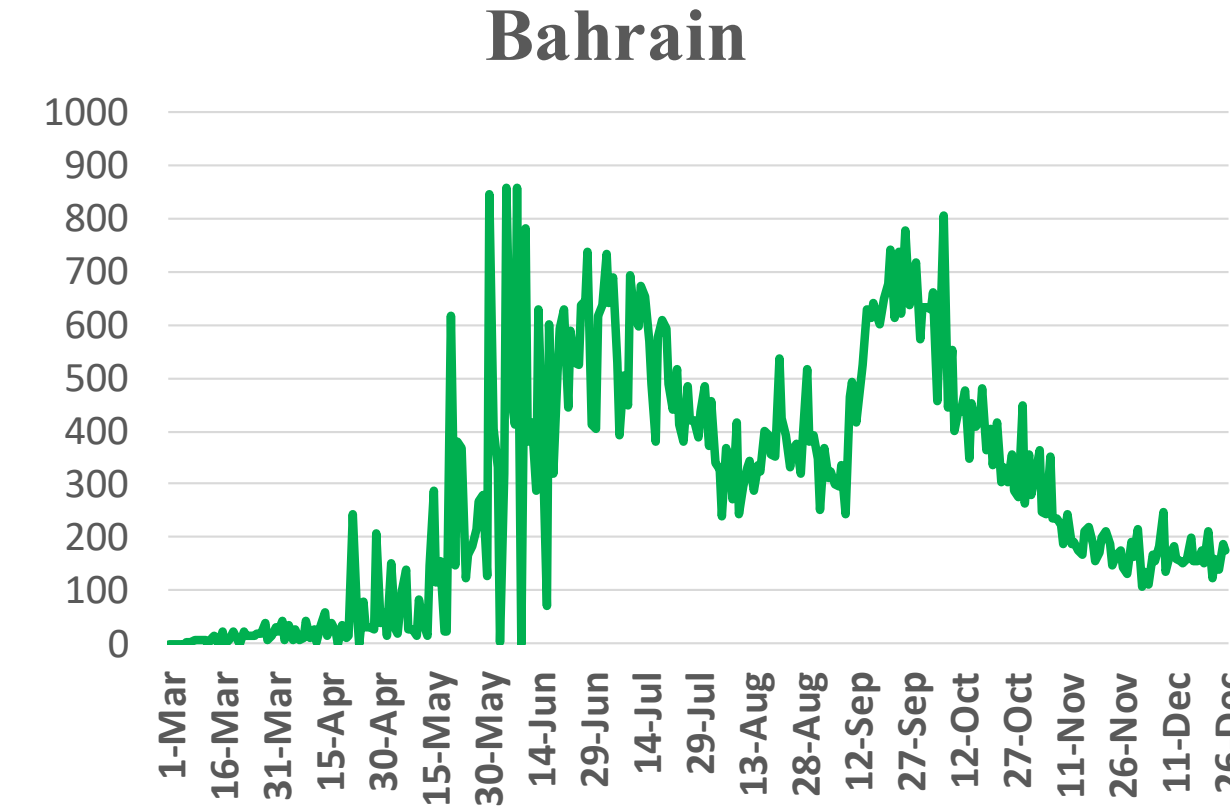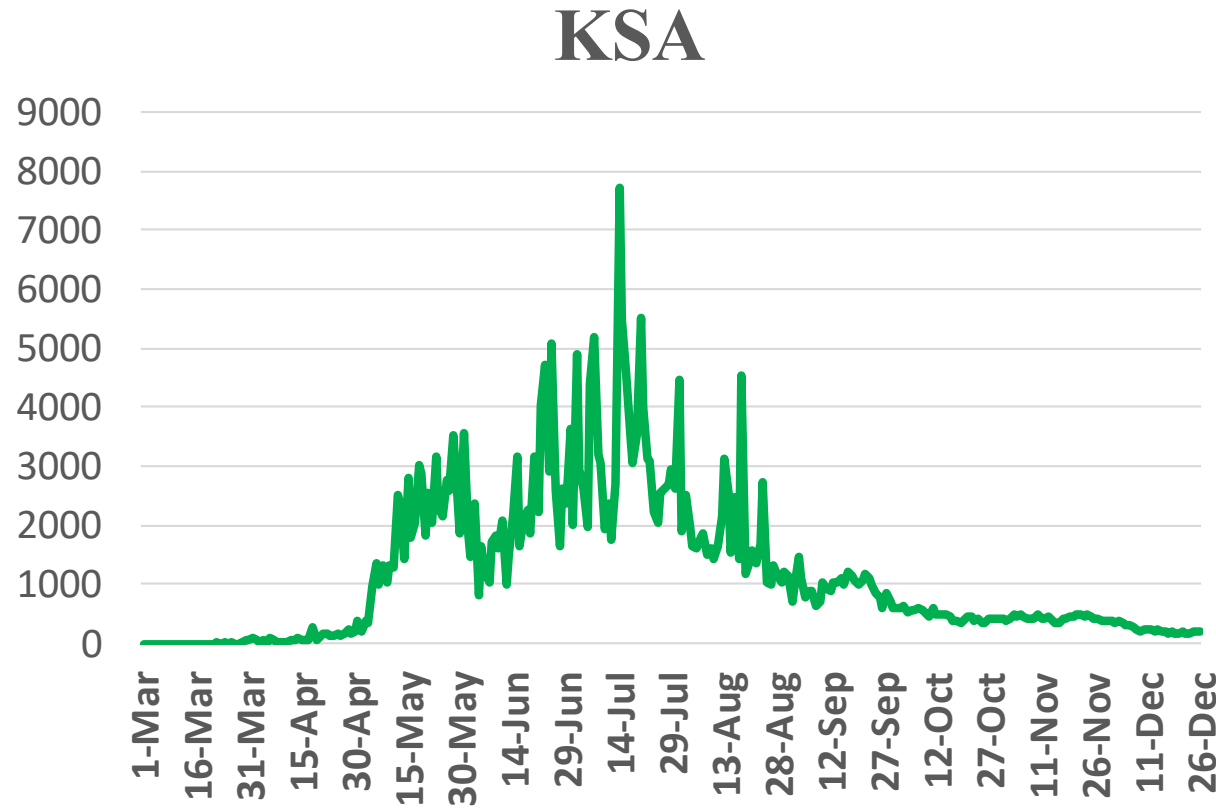
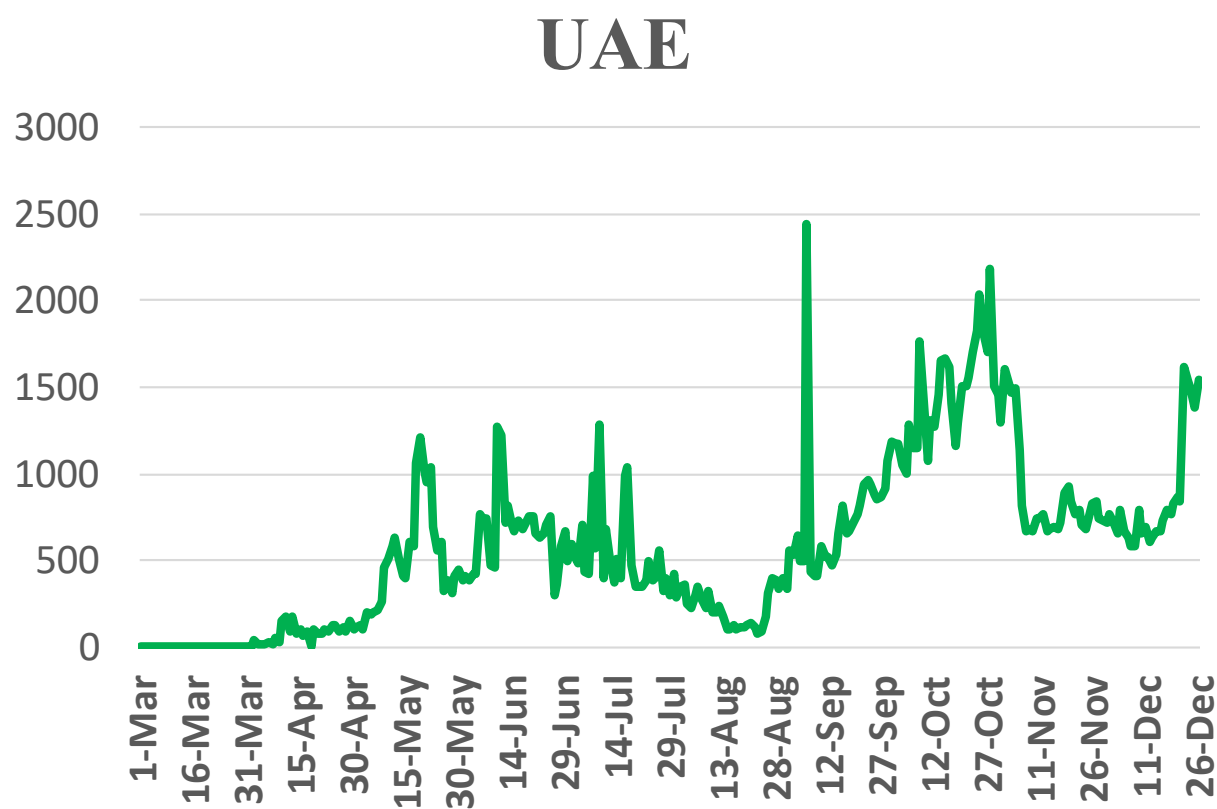### Kuwait

Source : Kuwait ministry of health
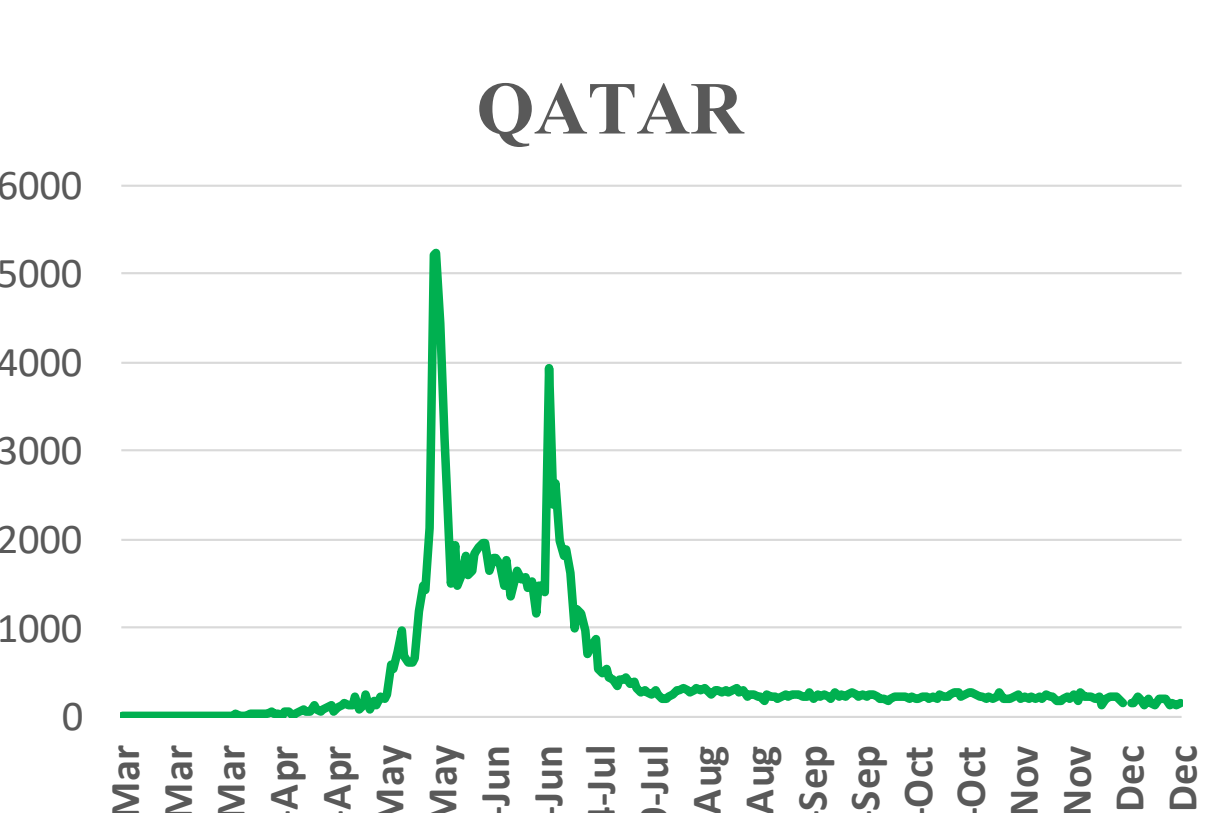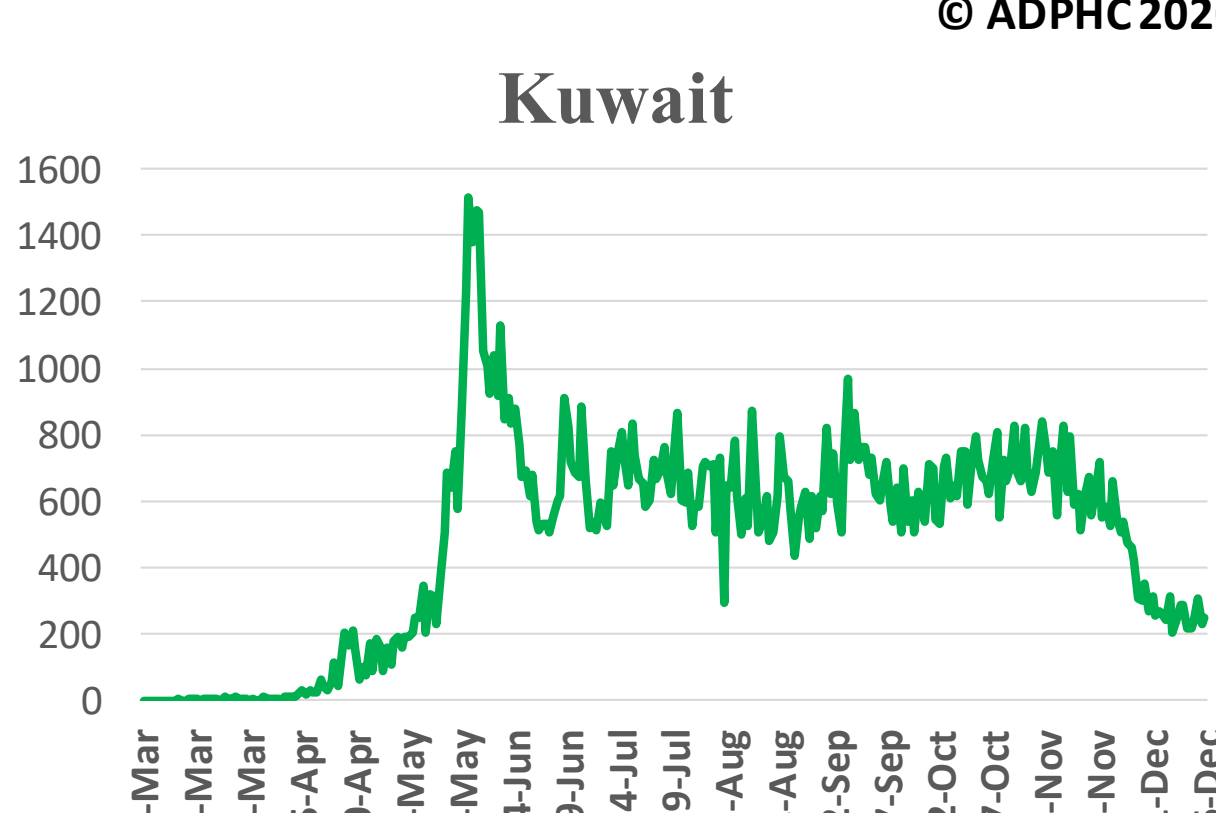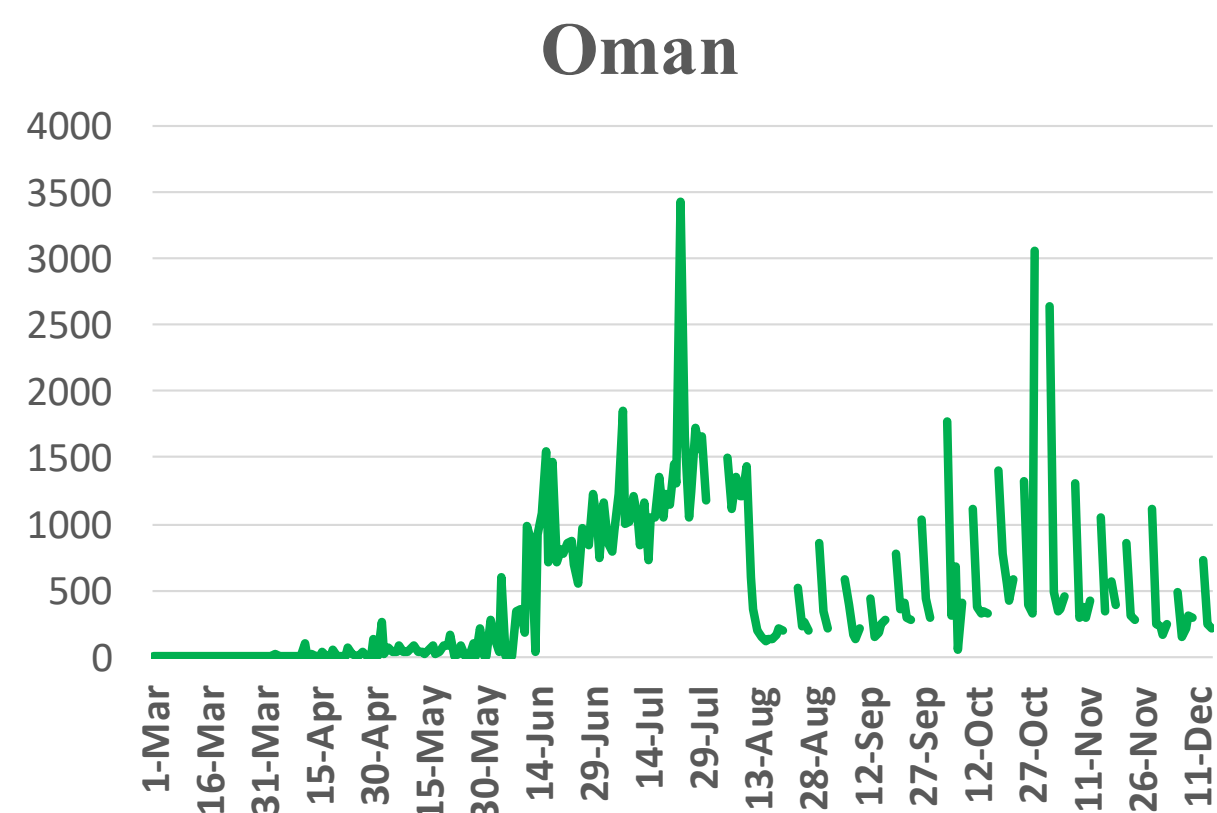
QATAR

Source : Qatar ministry of health

Figure 12: Comparative Analysis of the Distribution of COVID-19 New Death Cases in GCC Countries

UAE

Source : National Emergency Crisis and Disaster Management Authority

KSA

Source : KSA ministry of health

Bahrain

Source :WHO

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Oman

Source :Oman ministry of health

*No announced statistic data from 31 JUL to 4 AUG, 21,23,28,30 AUG 2,4 5,11,12,18,19,25 ,26,30 SEP, 1,2,9,10,16,17,23,24,30,21 OCT, 6,7,13,14,17,20,21, ,27,28 NOV,4,5,11,12,18,19,25,26 DEC
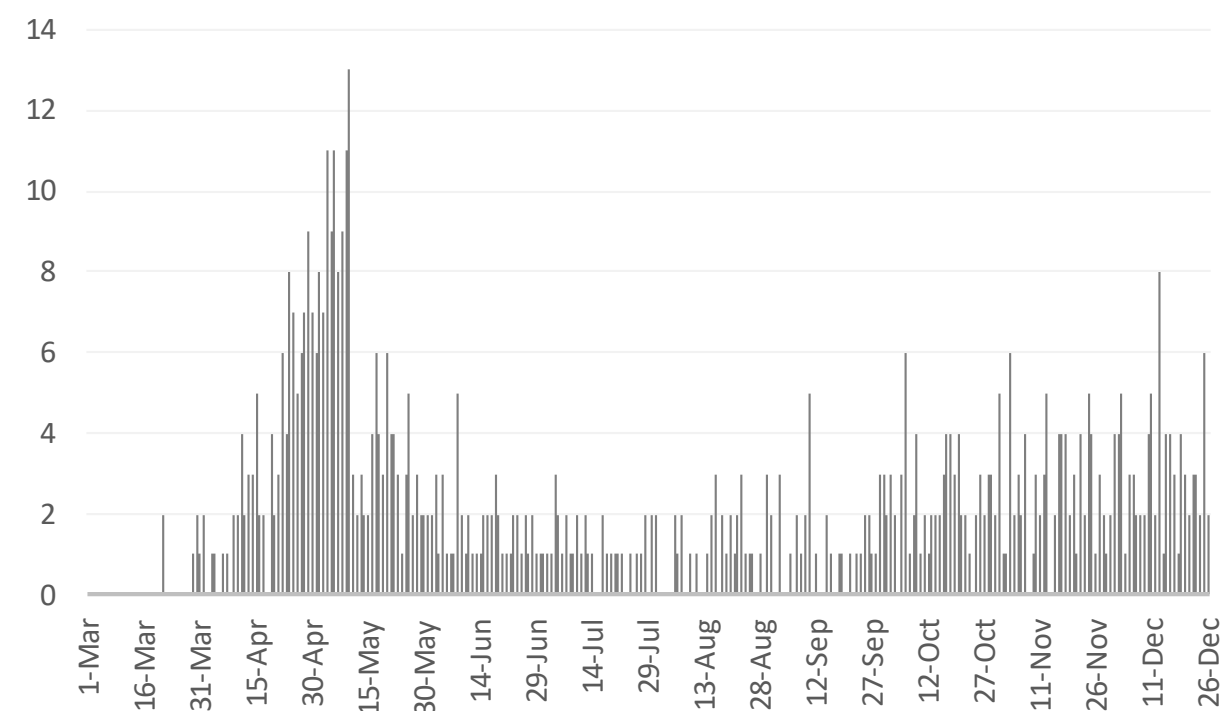*No announced statistic data on weekends and official holidays.

Kuwait

Source : Kuwait ministry of health

Qatar

Source : Qatar ministry of health

Article 1

Published

A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19

Objective

- To study the effect of LY-CoV555 (a neutralizing monoclonal antibody) in patients who are hospitalized with Covid-19.

Methodology

- Hospitalized patients who had Covid-19 without end-organ failure were randomly assigned in a 1:1 ratio to receive either LY-CoV555 or matching placebo.

- LY-CoV555 (at a dose of 7000 mg) or placebo was administered as a single intravenous infusion over a 1-hour period.

- The primary outcome was a sustained recovery during a 90-day period, as assessed in a time-to-event analysis.

- An interim futility assessment was performed on the basis of a seven-category ordinal scale for pulmonary function on day 5.

Conclusion

- Monoclonal antibody LY-CoV555, when co-administered with Remdesivir, did not demonstrate efficacy among hospitalized patients who had Covid-19 without end-organ failure.

Continued

A Pulmonary Ordinal Outcome on Day 5

Category		LY-CoV555	Placebo
		no. of patients (%)	
Better ↑	1	31 (19.3)	33 (22.0)
	2	50 (31.1)	48 (32.0)
	3	29 (18.0)	31 (20.7)
	4	17 (10.6)	11 (7.3)
	5	25 (15.5)	22 (14.7)
Worse ↓	6	8 (5.0)	5 (3.3)
	7	1 (0.6)	0 (0.0)

Category
- Can independently undertake usual activities with minimal or no symptoms
- No supplemental oxygen; symptomatic and unable to independently undertake usual activities
- Supplemental oxygen <4 liters/min
- Supplemental oxygen ≥4 liters/min or end-organ manifestations
- Noninvasive ventilation, high-flow oxygen, or severe stroke (NIHSS score, >14)
- Invasive ventilation, ECMO, mechanical circulatory support, renal-replacement therapy, or vasopressor
- Death

Summary Odds Ratio
0.85 (95% CI, 0.56–1.29)
P=0.45

B Time to Sustained Recovery

Recovery Rate Ratio
1.06 (95% CI, 0.77–1.47)

No. at Risk

LY-CoV555	87	86	41	9	3
Placebo	81	81	41	10	4

C Time to Hospital Discharge

Discharge Rate Ratio
0.97 (95% CI, 0.78–1.20)

No. at Risk

LY-CoV555	163	38	17	6	3
Placebo	151	36	13	6	4

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Article 2

Published

Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia

Objective
- To study the safety and efficacy of the anti–interleukin-6 receptor antibody Tocilizumab in patients from among underserved and racial and ethnic minority populations who are hospitalized with Covid-19 pneumonia.

Methodology
- Patients hospitalized with Covid-19 pneumonia who were not receiving mechanical ventilation were randomly assigned (in a 2:1 ratio) to receive standard care plus one or two doses of either Tocilizumab (8 mg per kilogram of body weight intravenously) or placebo.
- Site selection was focused on the inclusion of sites enrolling high-risk and minority populations.
- The primary outcome was mechanical ventilation or death by day 28.

Conclusions
- In hospitalized patients with Covid-19 pneumonia who were not receiving mechanical ventilation, Tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival. No new safety signals were identified.

TREATMENT

Continued

Table 2. Primary and Key Secondary Efficacy Outcomes by Day 28 in the Modified Intention-to-Treat Population.*

Outcome	Tocilizumab (N = 249)	Placebo (N = 128)	Hazard Ratio (95% CI)	Weighted Difference (95% CI)	P Value†
Primary outcome: mechanical ventilation or death — % (95% CI)‡	12.0 (8.5 to 16.9)	19.3 (13.3 to 27.4)	0.56 (0.33 to 0.97)	NA	0.04
Secondary outcomes					
Median time to hospital discharge or readiness for discharge (95% CI) — days§	6.0 (6.0 to 7.0)	7.5 (7.0 to 9.0)	1.16 (0.91 to 1.48)	NA	
Median time to improvement in clinical status (95% CI) — days§¶	6.0 (6.0 to 7.0)	7.0 (6.0 to 9.0)	1.15 (0.90 to 1.48)	NA	
Median time to clinical failure (95% CI) — days§	NE	NE	0.55 (0.33 to 0.93)	NA	
Death — no. (% [95% CI])‖	26 (10.4 [7.2 to 14.9])	11 (8.6 [4.9 to 14.7])	NA	2.0 (−5.2 to 7.8)**	

* NA denotes not applicable, and NE could not be estimated.

† The P value was calculated with the log-rank test. Significance testing was performed hierarchically to control the trial-wide type I error rate at a 5% significance level.

‡ The cumulative percentages of patients were estimated with the Kaplan–Meier method and compared with the use of the stratified log-rank test with age group (≤60 or >60 years) as a stratification factor. The stratified Cox proportional-hazards model with age group (≤60 or >60 years) as a stratification factor was used to estimate the hazard ratio and 95% confidence interval.

§ The median time to a secondary outcome event was estimated with the Kaplan–Meier approach.

¶ Improvement in clinical status was determined with the use of the seven-category ordinal scale.

‖ The Wilson method was used to estimate the 95% confidence interval for the observed proportion. The Cochran–Mantel–Haenszel weighting approach with age group (≤60 years or >60 years) as the stratification factor was used to calculate the weighted difference in percentages. The Newcombe method was used to estimate the 95% confidence interval for the weighted difference. Deaths by day 28 included all deaths reported from ordinal-scale scoring, adverse events reporting, and public death records during the hospital stay and after hospital discharge.

** The weighted difference is expressed as percentage points.

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Article 3

Published

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19

Objective

- To study the safety and efficacy of the anti–interleukin-6 receptor antibody tocilizumab in patients from among underserved and racial and ethnic minority populations who are hospitalized with Covid-19 pneumonia.

Methodology

- Patients hospitalized with Covid-19 pneumonia who were not receiving mechanical ventilation were randomly assigned (in a 2:1 ratio) to receive standard care plus one or two doses of either tocilizumab (8 mg per kilogram of body weight intravenously) or placebo.
- Site selection was focused on the inclusion of sites enrolling high-risk and minority populations.
- The primary outcome was mechanical ventilation or death by day 28.

Conclusions

- In hospitalized patients with Covid-19 pneumonia who were not receiving mechanical ventilation, Tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival. No new safety signals were identified.

Continued

Table 2. Change from Baseline in Viral Load.			
Variable	**LY-CoV555** **(N = 309)**	**Placebo** **(N = 143)**	**Difference** **(95% CI)**
Primary outcome			
Mean change from baseline in viral load at day 11		−3.47	
	700 mg, −3.67		−0.20 (−0.66 to 0.25)
	2800 mg, −4.00		−0.53 (−0.98 to −0.08)
	7000 mg, −3.38		0.09 (−0.37 to 0.55)
	Pooled doses, −3.70		−0.22 (−0.60 to 0.15)
Secondary outcomes*			
Mean change from baseline in viral load at day 3		−0.85	
	700 mg, −1.27		−0.42 (−0.89 to 0.06)
	2800 mg, −1.50		−0.64 (−1.11 to −0.17)
	7000 mg, −1.27		−0.42 (−0.90 to 0.06)
	Pooled doses, −1.35		−0.49 (−0.87 to −0.11)
Mean change from baseline in viral load at day 7		−2.56	
	700 mg, −2.82		−0.25 (−0.73 to 0.23)
	2800 mg, −3.01		−0.45 (−0.92 to 0.03)
	7000 mg, −2.85		−0.28 (−0.77 to 0.20)
	Pooled doses, −2.90		−0.33 (−0.72 to 0.06)

* Data regarding hospitalization, another key secondary outcome, are provided in Table 3.

Article 4

Published

Infectivity of asymptomatic versus symptomatic COVID-19

- In Singapore, this study was carried out with individuals who completed their quarantine (n=3,790) from August 1 to October 11, 2020, as a result of being close community contacts of people who were infected (n=628) and who had also undergone serology tests as part of their COVID-19 status assessment.

- 89 out of 3,790 (2%) close community contacts developed COVID-19 during the quarantine. Of those, 56% [50/89] contacts were quarantined because of an asymptomatic index case and 44% [39/89] contacts were quarantined because of a symptomatic case. Nearly half (48%) [43/89] of the contacts were quarantined because of a seronegative index case and little over half (52%) [46/89] were quarantined because of a seropositive index case. The incidence of COVID-19 among close contacts of a symptomatic index case was 3.85 times higher than for close contacts of an asymptomatic index case (95% CI: 2.06-7.19; p<0.0001).

- These findings indicated that individuals with asymptomatic COVID-19 are infectious; however, it might be less infectious than symptomatic cases. Furthermore, it was identified that the proportion of close contacts who became infected did not depend on the serology status of the index case. Future studies should investigate the relationship between viral loads, viable shedding, and transmission.

Continued

Variables of Index Case (628)		IRR	95% CI	p-value
Symptom Status*	Asymptomatic	1	-	-
	Symptomatic	4.22	2.32-7.66	<0.0001
Serology Status**	Seronegative	1	-	-
	Seropositive	1.08	0.62-1.88	0.80
Further adjusting for gender and age group of index case				
Variables of Index Case		IRR	95% CI	p-value
Symptom Status*	Asymptomatic	1	-	-
	Symptomatic	3.85	2.06-7.19	<0.0001
Serology Status**	Seronegative	1	-	-
	Seropositive	0.93	0.52-1.65	0.79

Table 2: Negative binomial regression of people who are quarantined contacts who became infected, based on symptomatic and serology status of index cases. *Symptom status analysis was adjusted for serology of people who were index cases. **Serology status analysis was adjusted for symptom status of people who were index cases.

Serology and Symptom Status of Index	No. of index cases (% of index cases)	No. of quarantined community contacts	No. and proportion of quarantined community contacts identified as COVID-19 cases (%)
(1) Seronegative	**232 (36.9)**	**1387**	**43 (3.10)**
Asymptomatic	196 (31.2)	836	14 (1.67)
Symptomatic	36 (5.7)	551	29 (5.26)
(2) Seropositive	**396 (63.1)**	**2403**	**46 (1.91)**
Asymptomatic	380 (60.5)	2199	36 (1.64)
Symptomatic	16 (2.6)	204	10 (4.90)
Total	628	3790	89 (2.35)

Table 1: Breakdown of index cases of people infected with COVID-19 and quarantined people in

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Article 5

Published

Long COVID guidelines need to reflect lived experience

- In England, according to the Office for National Statistics (ONS), 1 out of 5 individuals have symptoms >5 weeks and 1 out of 10 have symptoms for ≥12 weeks after acute COVID-19 infection. The National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the Royal College of General Practitioners (RCGP) have published a guideline on persistent effects of COVID-19 (long COVID) on patients. However, the guideline did not sufficiently address the following issues.

- The guideline needs to provide a more comprehensive description of the clinical features and physical nature of long COVID. It did not adequately mention what is known about the underlying pathology and the natural history of long COVID. There was no description of the three theories of persistent virus in immune privileged sites, aberrant immune response, or autoimmunity. Furthermore, a more thorough participative and open process is needed to consider and determine appropriate terminology by involving a broad range of experts including people with lived experience.

- Guidelines need to represent the complexity of long COVID including the areas where evidence is still emerging. Quick attempts to rename the condition or compare it to other conditions is a harmful to thousands of people, and could result in missed pathology to the detriment of the patient. Comprehensive guidelines are crucial to prevent an epidemic of long term, chronic disease as a result of early mismanagement of pathology, and the potential implications of such an epidemic for health systems and economies.

Article 6

Published

Persistence of IgG response to SARS-CoV-2

December 17, 2020, THE LANCET

- In Belgium, health care workers (n=850) are tested on a monthly basis since April 22, 2020 for the presence of SARS-CoV-2 with quantitative RT-PCR and for antibodies targeting S1 (spike subunit 1) protein with a commercial semi-quantitative ELISA (enzyme linked immunosorbent assay). Seven rounds of testing had been conducted by end of September, 2020. The duration of the presence of detectable IgG in the serum who were seropositive for SARS-CoV-2 were recorded in order to assess the longevity of the humoral immune response.

- 81 IgG positive health care workers had been identified by end of September, 2020. Antibodies became undetectable after intervals ranging from 107 to 159 days from presumed onset of infection in 9% [7/81] health care workers. Median duration of antibody persistence (time between the day IgGs were last detected and the day of presumed onset of infection) is 168.5 days in 91% [74/81] who remained seropositive. Of those, 96% [71/74] have already had antibodies for ≥90 days and 91% [67/74] have had them for ≥120 days. 82% [61/74] seropositive individuals had neutralizing antibodies in their most recent IgG positive serum sample. Of those 13 individuals with no detectable neutralizing antibodies, 8 had weak neutralizing antibody titers and 5 had no measurable neutralizing antibody titers from the start.

- A rapid decline of SARS-CoV-2 IgG sero-positivity or neutralizing capacity has not been found based on available data. These findings coincide with earlier observations of antibody persistence after infection with SARS-CoV (severe acute respiratory syndrome coronavirus) or MERS-CoV (Middle East respiratory syndrome coronavirus). The importance of neutralizing antibodies in long term immunity against SARS-CoV-2 remains to be determined.
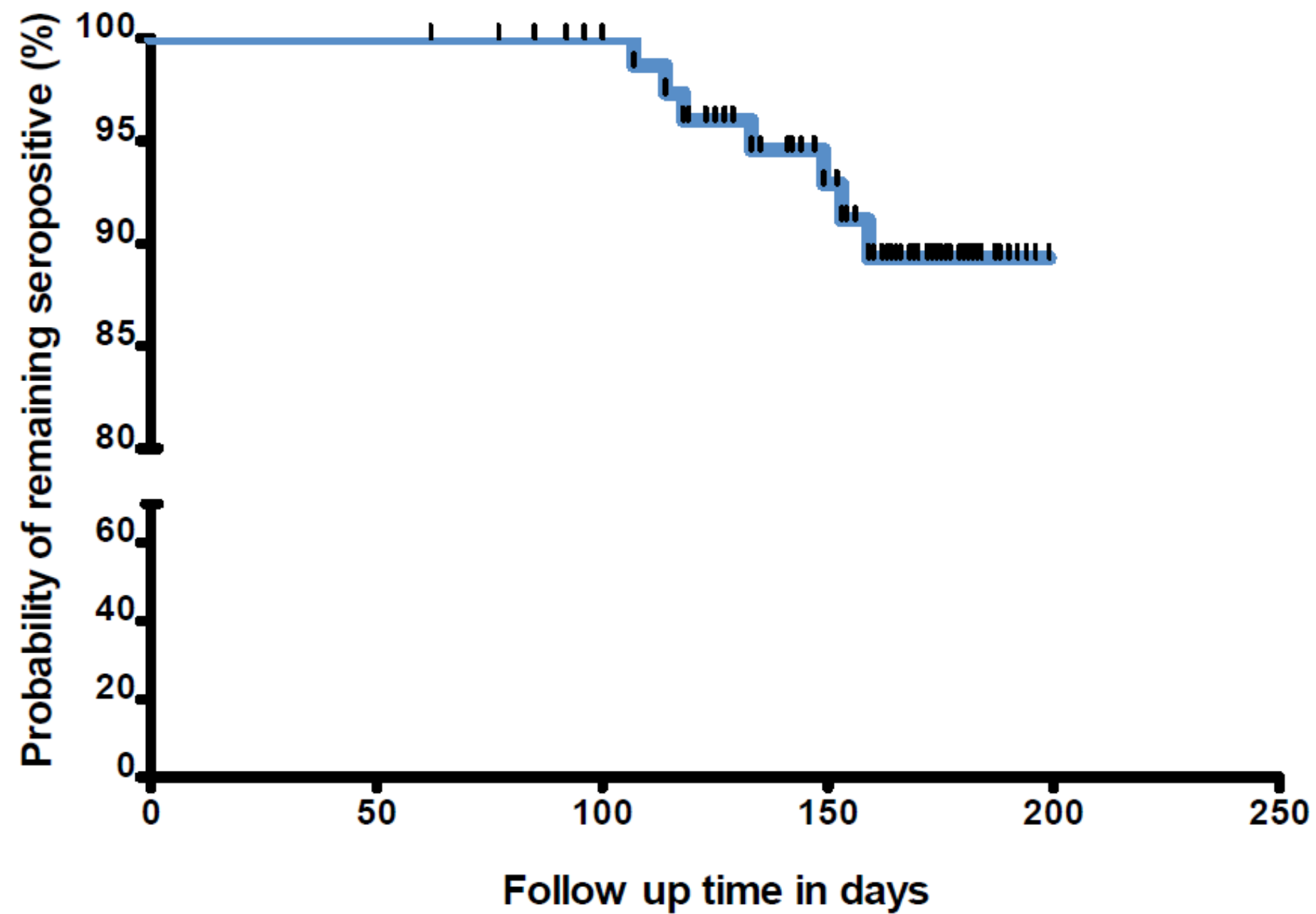
Continued

Figure: Kaplan-Meier curve showing the probability of remaining SARS-CoV-2 seropositive over time, follow-up of Belgian hospital healthcare workers between April and September 2020

THANK YOU

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