What could explain the late emergence of COVID-19 in Africa?

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Running title: **Emergence of COVID-19 in Africa**

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Abstract

At the end of November 2019, a novel coronavirus responsible for respiratory tract infections (COVID-19) emerged in China. Despite drastic containment measures, this virus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread in Asia and Europe. The pandemic is ongoing with particular hotspot in Southern Europe and America in Spring 2020. Many studies predicted a similar epidemic in Africa as that currently seen in Europe and the United States of America. However, reported data do not confirm these predictions. Several hypotheses that could explain the later emergence and spread of COVID-19 pandemic in African countries are being discussed, including the lack of health care infrastructure capable of clinically detecting and confirming COVID-19 cases, the implementation of social distancing and hygiene, international air traffic flows, the climate, the relatively young and rural population, the genetic polymorphism of the ACE2 receptor, cross-immunity and the use of antimalarial drugs.

Key words: COVID-19, SARS-CoV-2, malaria, antimalarial drugs, Africa.

1. Introduction

In December 2019, the Chinese health authorities reported the emergence of a novel coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) in Wuhan (China), after clinicians had published that this new Sarbecovirus is causing a disease subsequently named COVID-19 (coronavirus disease 2019) [1,2]. In fact, retrospective studies show that SARS-CoV-2 has already been circulating for several weeks, probably since October 2019, with a case of COVID-19 formally identified on November 17, 2019 [3]. Among 10,237 infected patients with SARS-CoV-2 included in a nationwide cohort in South Korea (January 24 to April 9, 2020), 6,350 patients (62%) were asymptomatic [4]. In another study on 1,096 patients in Kuwait (February 24 to April 20, 2020), 46.3% of the infected people were asymptomatic on sample day [5]. Thirty-five patients (6.9%) who were initially asymptomatic developed symptoms later [5]. Asymptomatic infection can occur at any age, but had a higher prevalence in patients under 45 year old compared with symptomatic people [6]. In a meta-analysis, the most frequent clinical signs and symptoms reported in symptomatic patients were fever (78.5%), cough (53.8%) and fatigue (25.0%) and 6.8% of the patients were admitted to the intensive care unit (ICU) and 7.7% died during hospitalization due to complications related to COVID-19 (pneumonia, secondary bacterial infection and respiratory failure) [7].

Because of its high transmission efficiency [8], SARS-CoV-2 spread worldwide, thus prompting the World Health Organization (WHO) to declare an international public health emergency on January 30, 2020 [9], and a pandemic on March 11, 2020 [10]. Following the early outbreak in China, COVID-19 spread to other Asian countries and western European countries and then to the United States of America in Spring 2020 (Figure 1). COVID-19 later spread to Central and South America, Africa, India and Southeastern Asia. Cities most affected by COVID-19 are

either the cities displaying intensive international economic exchanges, such as Hong Kong, Milan, London, Paris, Madrid, and more recently New York, or cities having recently hosted events bringing together many people. It is worth noting that in the ranking of countries that faced the most severe outbreaks, Italy was the first to be very strongly impacted in Europe.

Interestingly, it was reported that the Lombardia region, accounting for the highest number of COVID-19 in Italy, is the region with the highest percentage of Chinese residents (23% of its population being composed of Chinese residents) [11]. Although the pandemic has evolved rapidly at the global level (on March 23, 2020, 174 countries and territories had been affected by Covid-19, while on June 4, almost all countries were concerned (Figure 1)), the African continent has so far reported only a very small number of cases.

As of June 4, 2020, 54 countries are affected in Africa with 150,610 cumulative confirmed cases and 4,281 reported deaths [12]. The five most affected African countries are South Africa with 37,525 cases and 792 deaths, Nigeria with 11,166 cases and 315 deaths, Algeria with 9,733 cases and 673 deaths, Ghana with 8,548 cases and 38 deaths and Cameroon with 6,789 cases and 203 deaths, on June 4, 2020. The first African cases of confirmed detection of SARS-CoV-2 were reported on February 14, 2020 in Egypt for north Africa [13] and on February 27, 2020 in Nigeria for the Sub-Saharan Africa [14]. Gilbert *et al.* estimated the risk of importation of cases of COVID-19 to Africa according to air travel flows from infected provinces of China to Africa and taking into account the African country's capacity to detect COVID-19 [15]. The countries at highest importation risk from China were Egypt, Algeria, South Africa, Nigeria and Ethiopia. Three of these countries (South Africa, Algeria and Nigeria) are the 3 most affected countries and Egypt records 28,615 cases and 1,088 deaths. Another study predicted that a high risk of exposure in countries of small size like Mauritius (1,097,013 estimated cases for 1,265,303 inhabitants; 335 confirmed cases on June 4, 2020) or

Equatorial Guinea (819,289 estimated cases for 1,308,974 inhabitants; 1,306 confirmed cases on June 4, 2020) [16]. Using a branching process model, Pearson et al. estimated the number of cases of COVID-19 in each African country, and more especially the timing of reporting 10,000 cases for all African countries [17]. For instance, the timing of reporting 10,000 cases was between April 11 and 18 (3,836 cases on June 4, 2020) in Senegal, April 17 and 23 (6,585 cases on June 4, 2020) in Cameroon, May 7 to 21 (86 cases on June 4, 2020) in Angola and April 23 and May 3 (1,486 cases on June 4, 2020) in Ethiopia. The declared data to WHO indicated the spread of COVID-19 in Africa but with lower confirmed cases than expected. We discuss several hypotheses that could explain the later emergence and spread of COVID-19 pandemic in African countries.

2. Information gathering regarding COVID-19 cases and deaths

The gathering of available information regarding the number of infected people varies between countries depending on several factors. First, screening strategies vary considerably between countries according to the availability of virus-screening assay. For instance, in western countries, some countries (like France) have recommended to test only people with mild to severe symptoms, while other countries (like Germany) have adopted an opened strategy to detect asymptomatic persons and then isolate positive persons. At the beginning of February 2020, only two countries in Africa (Senegal and South Africa) had laboratories currently able to carry out RT-PCR tests, the gold standard in COVID-19 testing, in the absence of available and reliable rapid diagnostic test [18]. Between February 2, and March 1, 2020, the laboratory capacity for testing for SARS-CoV-2 had increased from two to 34 countries [19]. However, on April 1, 2020, South Africa had tested more than 47,000 people, while Zimbabwe had tested only 316 people and Namibia only 306 [20]. The lack of health care infrastructure capable of clinically detecting and

subsequently confirming COVID-19 cases is obviously the most important reason for the relatively low number of confirmed cases in Africa [21]. The country the most affected is South Africa with 37,525 cases and 792 deaths (June 4, 2020), one of the countries with the best diagnostic capacities with more than 3 million tests performed on August 13, 2020 [22]. However, between February 2 and April 15, 2020, laboratory testing capacity has increased from two (South Africa and Senegal) to forty-four countries in WHO African Region [23]. The situation is even more precarious in war zones and the many landlocked zones.

Another possible explanation of the weakness of epidemiological signals regarding COVID-19 in Africa is the hypothesis that epidemiological surveillance cannot be carried out appropriately and that syndromic surveillance is difficult due to confounding factors linked to other respiratory infections. For instance, COVID-19 cases have been reported in the same areas in Brazil where cases of dengue fever, with similar clinical and laboratory characteristics, have been identified [24].

3. Physical distancing and enhanced hygiene

WHO anticipates a rapid increase in the number of COVID-19 patients on the African continent and Africa has responded quickly. African health ministers have quickly implemented the Africa Taskforce for Coronavirus Preparedness and Response on February 3, 2020 [25]. Physical distancing and enhanced hygiene are two of the response measures. Lockdown measures, like closing schools, churches, mosques or markets to promote social distancing or shutting down airports, have been rapidly implemented in some African countries [26-28]. However, lockdown and working from home are unlikely implementable in many areas of Africa due to cash economy, daily work requiring physical presence, electricity or internet inaccessibility [29]. Sanitary measures including access to soap, water, hydroalcoholic gel, are also difficult to set up [30,31]. More

than 50% of the population in sub-Saharan Africa was without access to handwashing in 2019 [31]. In 3 African countries (Nigeria, Ethiopia and Democratic Republic of the Congo), more than 50 million people were estimated to be without handwashing access [31]. Additionally, physical distancing and enhanced hygiene are unlikely implementable in refugee camps, shantytowns or overcrowded settings [32-34]. However, several African countries have benefited from previous initiatives to address Ebola [35,36]. For instance, the surveillance structure and screening measures in airport developed for Ebola virus disease became pillars in the COVID-19 response in Uganda [35] and Ebola standard operating procedures were updated for COVID-19 in Democratic Republic of Congo [36].

4. Delay in the dynamic of the COVID-19 Epidemic

The hypothesis of a marked delay of the onset of the epidemic in Africa could be linked to less frequent exchanges between China and Africa (a mono-directional exchanges model where it is especially the Chinese who travel to Africa) than between China and Europe or China and the United States (a bi-directional exchange model). According to air travel flows from infected provinces in China to Africa and the African country's capacity to detect COVID-19, Gilbert *et al.* estimated that Egypt, Algeria, South Africa, Nigeria and Ethiopia presented the highest risk of importation of cases of COVID-19 from China [15]. Another study, based on the analysis of 388,327 passengers traveling to 1,297 airports, estimated that the risk of transmission to Africa was very low [37]. The only African countries identified at high risk were Ethiopia (28^{th}) and South Africa (40^{th}). Egypt, Algeria and Nigeria were estimated at low risk (59^{th}, 88^{th} and 100^{th}, respectively). However, this hypothesis is questionable: the African continent has attracted 121 million Chinese visitors in 2017 (a tremendous growth compared to 2005 (31 million)) [38], while according to the China Tourism Academy, about six million Chinese visitors were recorded to travel to Europe in 2018 and with a 8%

increase in the first six months of 2019 [39]. But the status of Chinese visitors is different between Europe and Africa. Most of Chinese visitors in Europe are either students, tourists or business trips. To the contrary, most Chinese visitors to Africa are construction workers, engineers, translators, company executives who stay in Africa for a long time [40] and the number of Chinese ranged between 1 to 2 million in 2020 [41]. In 2017, Chinese tourists accounted only for 11 million flights for a total of 121 million visitors [42]. The Chinese workers typically fly back to China once or twice a year, and especially for Chinese New Year. At the opposite. Many Chinese tourists leave China for Europe on vacation days before the Chinese New Year Day. The majority of the first COVID-19 cases in Europe have been linked to Chinese tourists or people returning from China [43.44]: on January 29, 2020, two Chinese tourists from Hubei province coming to Italy [45], on January 27, 2020, a Chinese people working for a a company in Munich who had been in contact with their parents from Wuhan before visiting Germany [46], on February 4, 2020, a Belgian people returning from Wuhan [47], on January 27, 2020, two Chinese tourists coming to England [48] or on January 24, 2020, a french patient returning from Wuhan and two Chinese tourists from Wuhan [49].

What is interesting is that the majority of the inital cases of COVID-19 in Africa have been linked to European travel rather than China. The first case of SARS-CoV-2 in Nigeria was identified in Italian citizen on February, 27, 2020 [14], in Italian people on March 1, 2020 in South Africa [50], in Italian citizen on February, 17, 2020 in Algeria [51], in French citizen on February 24, 2020 in Cameroon [52], in French resident in Dakar returning from France on February 26, 2020 in Senegal [53], in two citizen arrived in Ghana from Norway and Turkey in March 12, 2020 [54], in Kenyan citizen back to Kenya returning from the United States of America via London on March 5, 2020 [55] or in Japanese man

who traveled from Japan to Burkina Faso before coming to Ethiopia March 13, 2020 [56]. Among the countries the most affected by COVID-19, only the first case in Egypt came from Wuhan [57].

First cases of SARS-CoV-2 were identified preferably in January-February 2020 in Europe and United States of America, and in February-March in Africa and Brazil. The dynamic of the expansion of COVID-19-related deaths was relatively different between the countries (figure 2). Deaths emerged rapidly in African countries but stayed low after the first 150 days, Logarithmic analysis of the cumulative deaths (figure 2C and 2D) showed that the number of deaths evolved in a similar way in South Africa and Algeria during the first 30 days to what was observed in US, Brazil or Europe. The dynamic was slower in Nigeria, Cameroon, Senegal, Ghana,.Kenya or Ethiopia than in South Africa or Algeria (figure 2D).

5. Demographic hypothesis

One hypothesis rarely mentioned to date to explain the weakness of the epidemiological signal in Africa regarding the COVID-19 epidemic (and potentially a delay in its dynamic) is the fact that its population is extremely young. In 2015, 40% of its population was aged 0-14 and 19% aged 15-24, while those over 65 accounted for only 3.5 % The proportion of people over 65 years of age in 2019 was higher in Southeastern Asia (7%), in Central America (7%) and South America (9%) but remained much lower than in Europe (21%) [58]. The relatively young and rural population has certainly limited the spread and severity of COVID-19 in Africa [59]. Yet, there is a consensus, to consider that Covid-19 is far less severe in children than in adults, and that in this group, most of them are asymptomatic. For example, in China, in a study conducted on 7736 patients who had been hospitalized with COVID-19, only 0.9% were younger than 15 years old [60]. Disease severity in patients under 15 years

of age represented only 0.6% of the total number of cases. Patients over 65 years of age accounted for 15.1% of the patients and 27.0% of the total severity. In an investigation of 72 314 cases, Wu et al. reported that children under 9 and 10 to 19 years old represented 1% of the total number of cases, respectively [61]. In a clinical and epidemiological study conducted on 36 children, 28% were asymptomatic versus <5% in adults, 36% showed fever versus 89% in adults, 0% showed severe disease versus 23% in adults [62].

6. Role of climate

Environmental factors, especially temperature and relative humidity, may influence SARS-CoV-2 transmission [63]. High temperature and high humidity may reduce coronavirus transmission [64], which could explain the relatively low confirmed cases in Africa. Around 60% of the world cases occurred in areas where temperature ranged from 5 to 15°C [65]. The rate of confirmed cases significantly decreased with maximum temperature above 22.5°C [66]. Mean daily cases and deaths were significantly lower in hottest countries with highest temperatures reported between December 29, 2019 and May 12, 2020 (26.3 °C; 407.1 daily cases and 17.8 daily deaths) than in coldest countries with lowest temperatures (6.2°C; 1876.7 daily cases and 100.4 daily deaths) [67]. The viral transmissibility is estimated by the reproduction number (R_0), which represents the number of people that will be infected by an individual who has an infection. The SARS-CoV-2 R_0 was above 2 for temperatures below 0°C, decreased to R_0=1 for temperatures increasing from 0 to 11°C, increased to R_0=1.6 for temperatures increasing from 11 to 20°C, and gradually decreased to R_0=1 for temperatures above 20°C [68]. However, a study carried out in Australia suggested that even with high temperature, COVID-19 could persist [69]. Another study showed that in Brazil, high temperatures and relative humidity favored the COVID-19 transmission [70].

7. Genetic polymorphism

Genetic polymorphism of angiotensin converting enzyme 2 (ACE2), the cell entry receptor for SARS-CoV-2 could play a role in SARS-CoV-2 transmission [71,72]. Analyses of different geographical populations demonstrated the existence of at least 32 variants of ACE2 (single mutation, deletion, truncation) [73]. Expression of a specific variant allele in African subpopulations could alter the process of interaction between the viral S protein and the ACE2 receptor on the alveolar cells of the lung. In addition, expression quantitative trait loci (eQTL) variants were reported to regulate the expression of ACE2 gene. ACE2 gene expression was down regulated by variants rs11271234 and rs75979613 and upregulated by the others variants [74–76].

Moreover, ACE1 gene, an analog of ACE2, can have insertion (I) or deletion (D) of a 287 base pair Alu repeat sequence in intron 16 [77]. Three different genotypes exist, II, ID and DD. The number of patients infected with SARS-CoV-2 and the number of deaths from COVID-19 were negatively associated with the ACE1 II genotype frequency [78]. The European population has a lower ACE1 II genotype frequency and a higher prevalence of infected patients and mortality due to COVID-19 than the Asian population [78]. These data are consistent with epidemiological study that reported a significant positive correlation of D allele with SARS-CoV-2 infection prevalence and mortality rate in Asian population [79]. The DD genotype was also increased in acute respiratory distress syndrome (ARDS) [80]. Increase of ID genotype frequency was found to increase recovery rate after COVID-19 [81]. The frequencies of D allele were different between ethnic groups: it ranged from 72 to 77% in North African (Moroccans, Egyptians, Algerians, Tunisians), 59% in West African (Nigerians), 64 to 73% in East African (Sudanese, Somalis), only 14% in South African (Zambians), 29% in Chinese, 9% in Samoans, 46% in Caucasian [82]. For instance, the DD

frequency was 43% for Sudanese [83], 51% for Somalis [83], 36% for Burkinabe [84], 34% for South African [85] or 30% for Europeans [86]. Prospective studies are needed to investigate ACE genotype frequencies in different world areas and a potential role in delayed transmission. Moreover, other SARS-CoV-2 receptor could be involved in COVID-19 cases and mortality rate, like the transmembrane protease serine 2 (encoded by *TMPRSS2*) [87]. *TMPRSS2*-upregulating variants were at higher frequencies in European and American populations than in the Asian and African populations, which implies that these populations might be relatively susceptible to SARS-CoV-2 infection [87].

8. Cross-immunity to SARS-CoV-2

Protective immune responses to viral infection occur following the combined actions of B cells (humoral immunity) and T cells (cellular immunity). In COVID-19, B cells produce IgM, IgG and IgA antibodies that neutralize SARS-CoV-2 entry by competition with ACE2 for binding the receptor-binding domain of the viral spike protein [88,89].

T helper cells (CD4) are responsible for cellular immunity and for helping B cells to produce neutralizing antibodies. Importantly, all B and T cells have immunological memory after a first contact with pathogen. Memory CD4+ T cells mediated protective immunity against respiratory coronaviruses as well as neutralizing antibodies that bind the receptor binding domain in the spike of SARS-CoV were reported [90,91], suggesting that similar immune response could be observed with COVID-19 patients. The SARS-CoV-2 Spike glycoprotein is closely related to that of SARS-CoV S and some antibodies identified in SARS-CoV-infected patients could also neutralize SARS-CoV-2 [92]. But although cross-reactivity in antibodies binding to the Spike protein is relatively common, cross-neutralization responses between SARS-CoV and SARS-CoV-2 remained rare [93]. Convalescent sera from SARS-CoV and SARS-CoV-2 patients showed only limited cross-neutralization [94,95]. Pre-

existing immunity could explain the relatively low confirmed cases in Africa. Pre-existing SARS-CoV-2-crossreactive CD4+ and CD8+ T cells responses were observed in healthy people [96-98]. SARS-CoV-2 Spike glycoprotein-reactive CD4+ cells were found in 20-60% of healthy individuals [96-98]. Very recently, the analysis of immune responses to SARS-CoV-2 from patients who recovered from COVID-19 identified targets of T cell responses to SARS-CoV-2 and revealed cross-reaction with circulating "common cold" betacoronaviruses due to past infections [97-102]. Children appear to be protected and develop mild COVID-19 or no disease [103-105]. Common human coronavirus (HCoV-229E, HCoV-NL63, HCoV-OC43, HCoV-HKU1) were isolated from 7 to 11% in children hospitalized for acute respiratory tract infections [106-108]. Cross-reactivity between SARS-CoV-2 and human coronavirus is a plausible explanation for why children appear to be protected.

Another explanation is protection against SARS-CoV-2 induced by vaccines used against other pathogens. It seems that bacillus Calmette-Guérin (BCG) vaccination could protect from COVID-19. A strong association was observed between BCG vaccination deployment and COVID-19 mortality [109,110]. Countries where BCG vaccination is given at birth showed lower numbers of COVID-19 cases and deaths [111]. In fact, a SARS-CoV-2 envelope protein is closely related to a Mycobacterium bovis protein and BCG vaccine could induce a specific immunity against SARS-CoV-2 by targeting its essential viral envelope protein [112]. Moreover, the fatality rate due to COVID-19 was lower in Asian countries where Japanese encephalitis immunization is recommended compared with those who were not vaccinated [113].

9. Protection by repeated antimalarial treatments?

There seems to be an inverse relationship in the overall number of COVID-19 cases and malaria cases [110,114-116]. For instance, three of the most affected African countries with COVID-19 on June 4, 2020, are South Africa (37,525 cases and 792 deaths), Algeria (9,733 cases and

673 deaths) and Egypt (28,615 cases and 1,088 deaths) and belong to the less affected countries with malaria [117]. The use of antimalarial drugs to treat uncomplicated malaria in Africa could be another hypothesis explaining the relatively low number of confirmed cases in Africa [118]. Since 2002, the World Health Organization (WHO) has recommended the use of artemisinin-based combination therapy (ACT) in the treatment of uncomplicated falciparum malaria (artemether-lumefantrine, artesunate-amodiaquine, dihydroartemisinin-piperaquine or artesunate-mefloquine) (Figure 3). In 2018, these ACTs were widely used (Figure 4). These ACTs, evaluated at plasma concentrations expected after oral uptake at recommended doses used in uncomplicated malaria treatment, showed an in vitro inhibition of SARS-CoV-2 replication that ranged from 30 to 70% [119]. The combination mefloquine-artesunate was found to be the most effective *in vitro* against SARS-CoV-2. A patient treated by ACT for uncomplicated malaria could be protected from SARS-CoV-2 during treatment. Another study reported that some artemisinin derivatives used alone (dihydroartemisinin and artesunate) showed in vitro activity with median effective concentration (EC_{50}) around 10 µM [120]. Moreover, amodiaquine, a quinoleine antimalarial and one of the partner of artemisinin derivative, was found to be active in vitro at micromolar concentration against SARS-CoV-1 (2.5 µM) [121]. Another ACT partner, mefloquine, exerts in vitro cytopathic effects on Vero cells infected by SARS-CoV-2 at 10 µM [122]. A molecular docking study showed that pyronaridine, another ACT partner (artesunate-pyronaridine) can interact with the non-structural protein5 (Nsp5), an essential protein for transcription and replication of SARS-CoV-2 [123]. Pyronaridine showed effective antiviral activity with EC_{50} of 0.72 µM and pyronaridine is 165 more concentrated in lungs than in plasma (Pradines B, unpublished data). The use of antimalarial drugs and the dynamics of COVID-19 should now be compared on a country-by-country basis to confirm the potential effects of antimalarial drugs on COVID-19 transmission. It could be necessary now to evaluate clinically the ACT

efficacy to treat COVID-19, and more particularly that of mefloquine-artesunate, and the potential prevention of ACT against SARS-CoV-2 during malaria season which currently begins in some African countries, taking into account the antimalarial drug, its dose, the number of treated patients, the number of cases of COVID-19 and deaths.

10. Conclusion

The comparison of European and African models of SARS-CoV-2 prevalence could provide important clues to the spread of the virus. However, it is essential to increase the capacity to clinically detect the COVID-19 cases and then to confirm them by RT-PCR or reliable rapid diagnostic tests in African countries. Epidemiological, clinical and pharmacological data should be carefully recorded to follow the evolution of the spread of COVID-19 over the coming months in malaria endemic areas in Africa.

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Conflict of Interest statement

CD declares a link of interest with the Sanofi company which sells hydroxychloroquine. The other authors have no competing interests to declare.

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Figures legends

Figure 1: Confirmed cases of COVID-19 by country (June 4, 2020). The color gradient (dark to light) represents the graduated number of confirmed cases (highest to lowest). The figure was generated by compiling the data on COVID-19 cases on June 4, 2020, in each world country (from Worldometer [124]).

Figure 2: Comparison of the cumulative total COVID-19 deaths reported in the first 200 days of the pandemic in United States of America, Brazil, France, Italia and the most affected countries in Africa (South Africa, Algeria, Nigeria, Cameroon, Senegal, Ghana, Kenya and Ethiopia). Figure 2A represents the cumulative deaths for the 12 selected countries, Figure 2B only for the 8 African countries and Figure 2C the cumulative deaths for the 12 selected countries in log. The number of death was evaluated every 10 days from the first SARS-CoV-2 detected case to August 18, 2020, in each country. The graph was generated with daily WHO data [12].

Figure 3: Global distribution of the two most artemisinin-based combination therapy (ACTs) used for the treatment of uncomplicated falciparum malaria in 2018, especially artemether-lumefantine and artesunate-amodiaquine, the most deployed ACT in malaria endemic countries. The figure was generated by compiling the data obtained by WHO in 2018 [117].

Figure 4: Number of artemisinin-based combination therapy (ACTs) used in 2018, by malaria-affected country. The color gradient (dark to light) depends on the graduated number of ACTs used (highest to lowest). The figure was generated by compiling the data obtained by WHO in 2018 [117].

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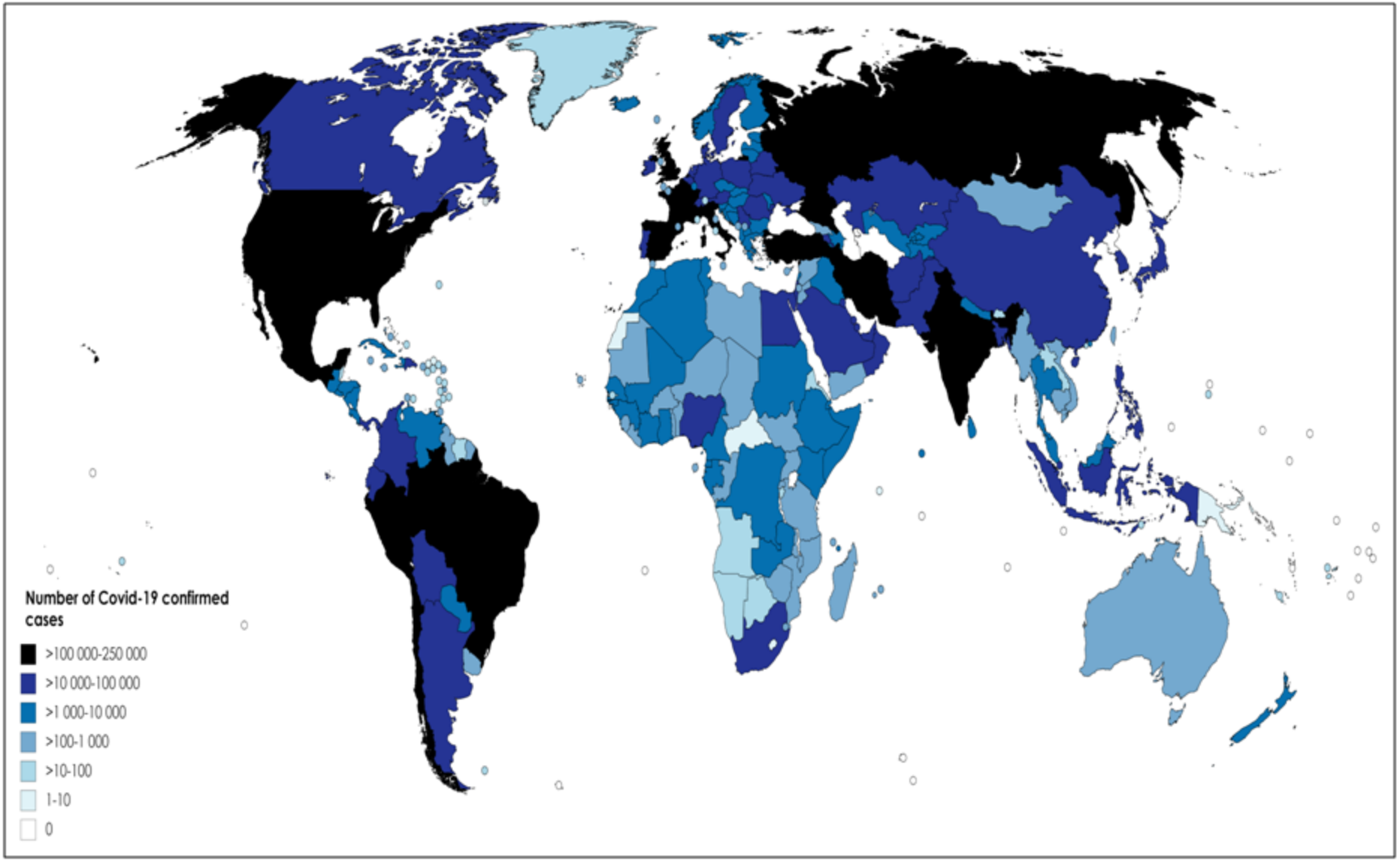
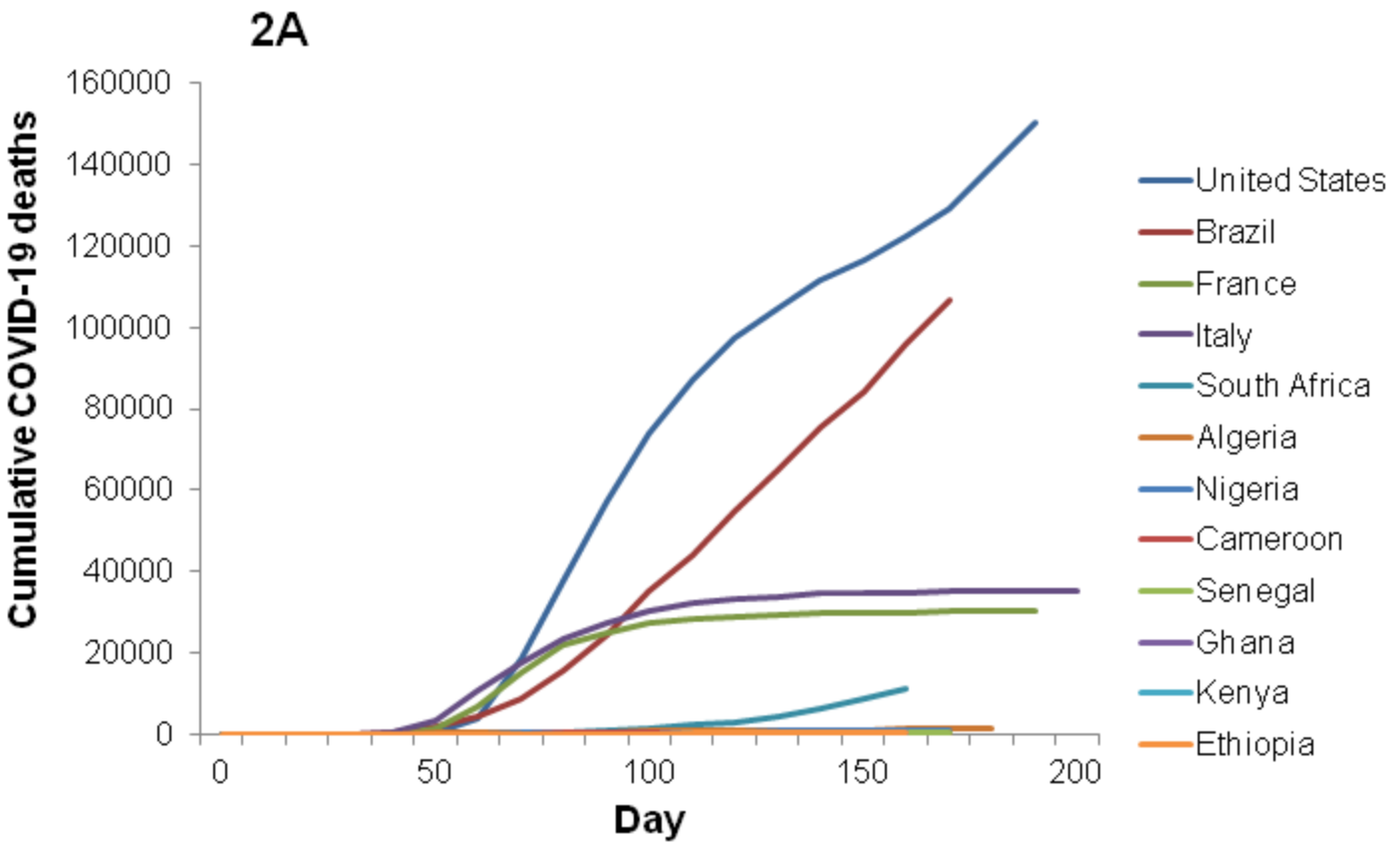
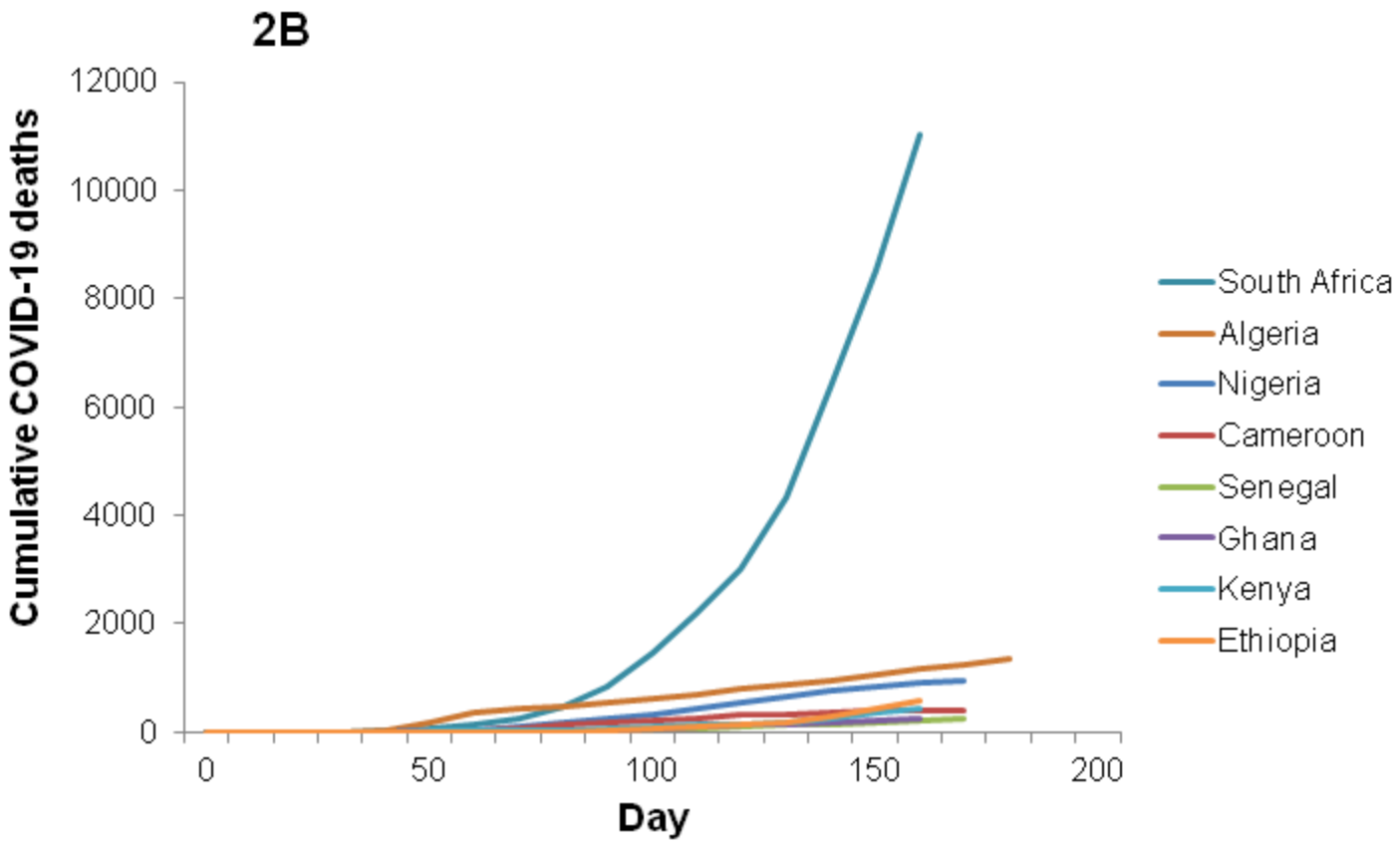
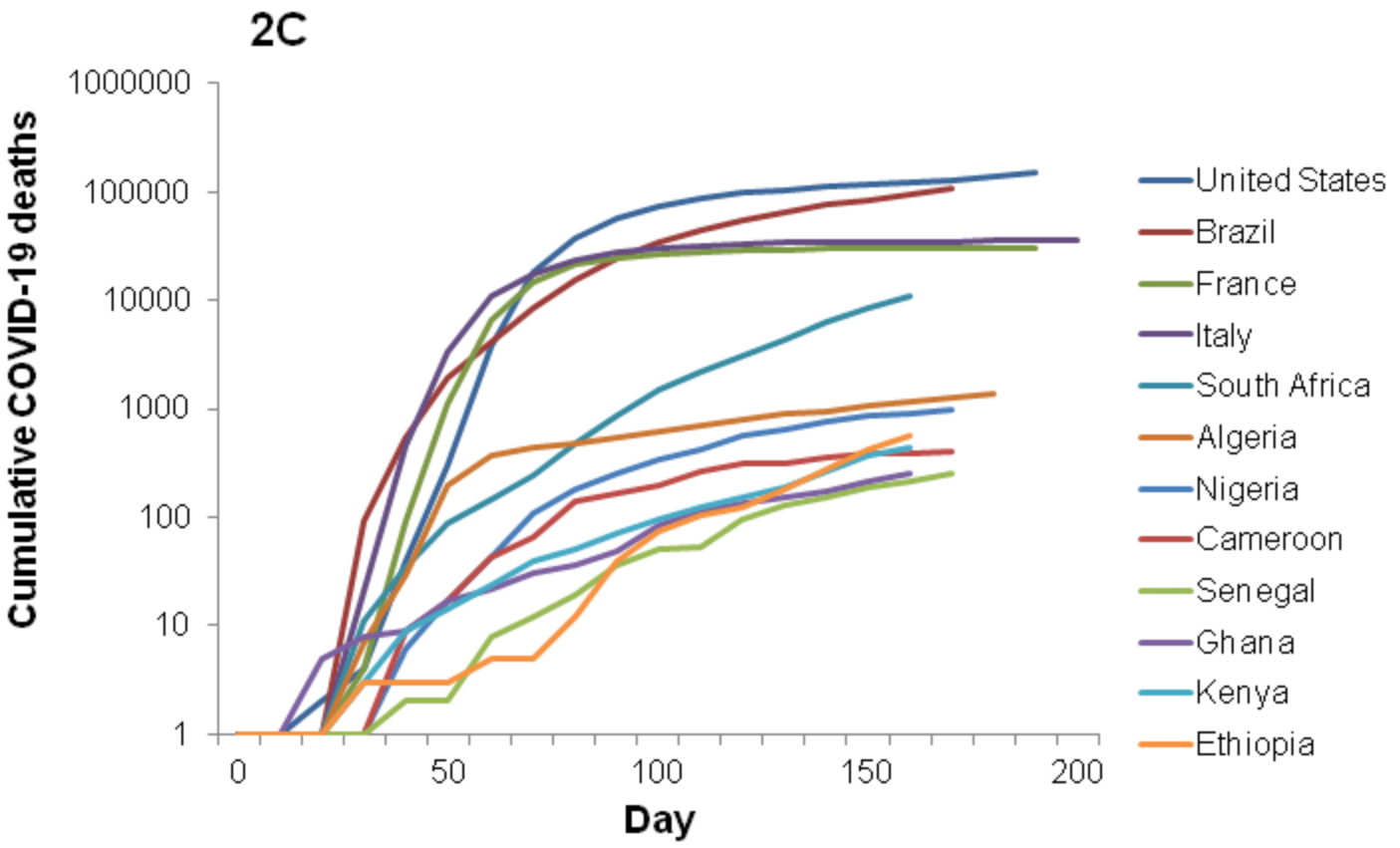
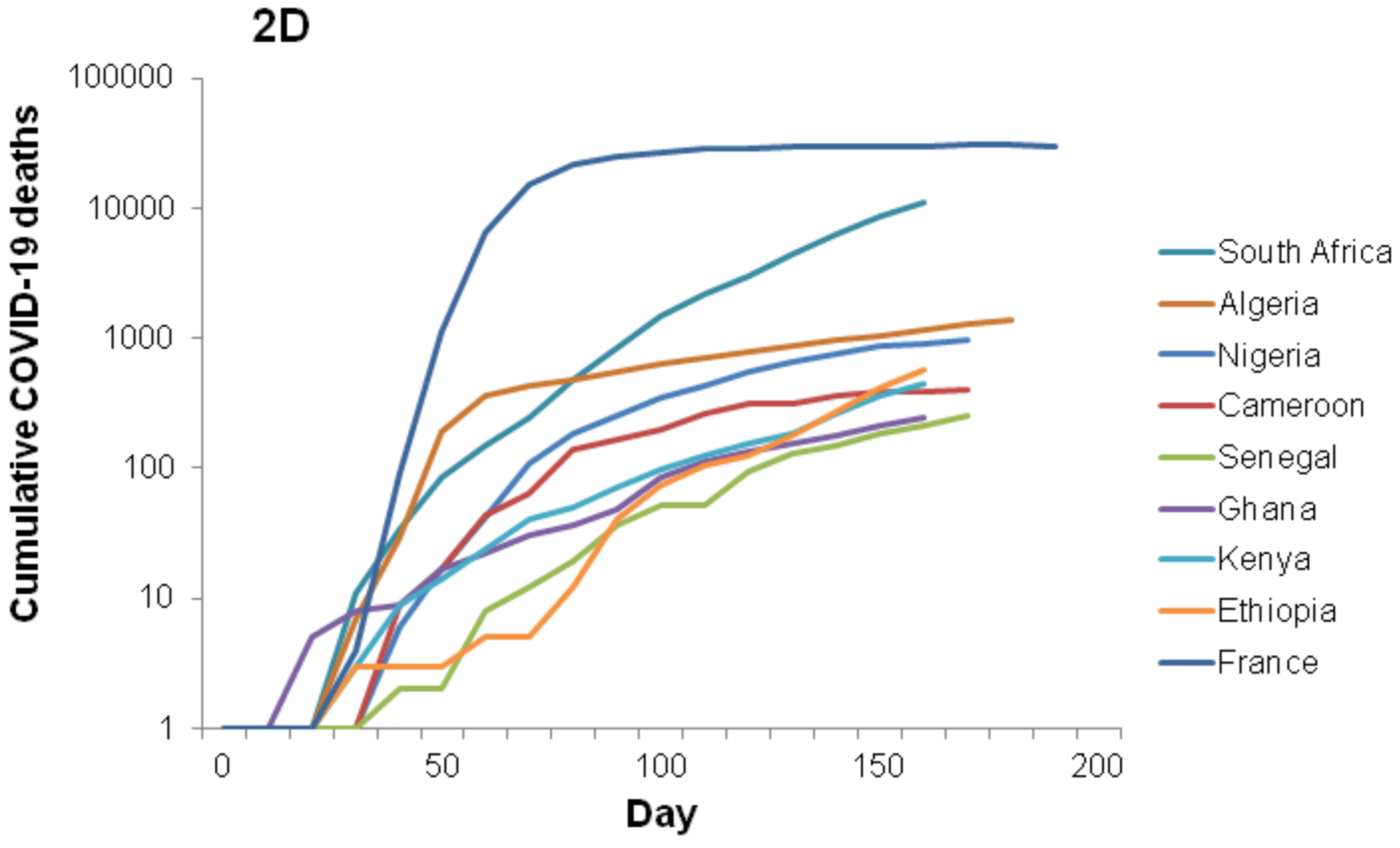
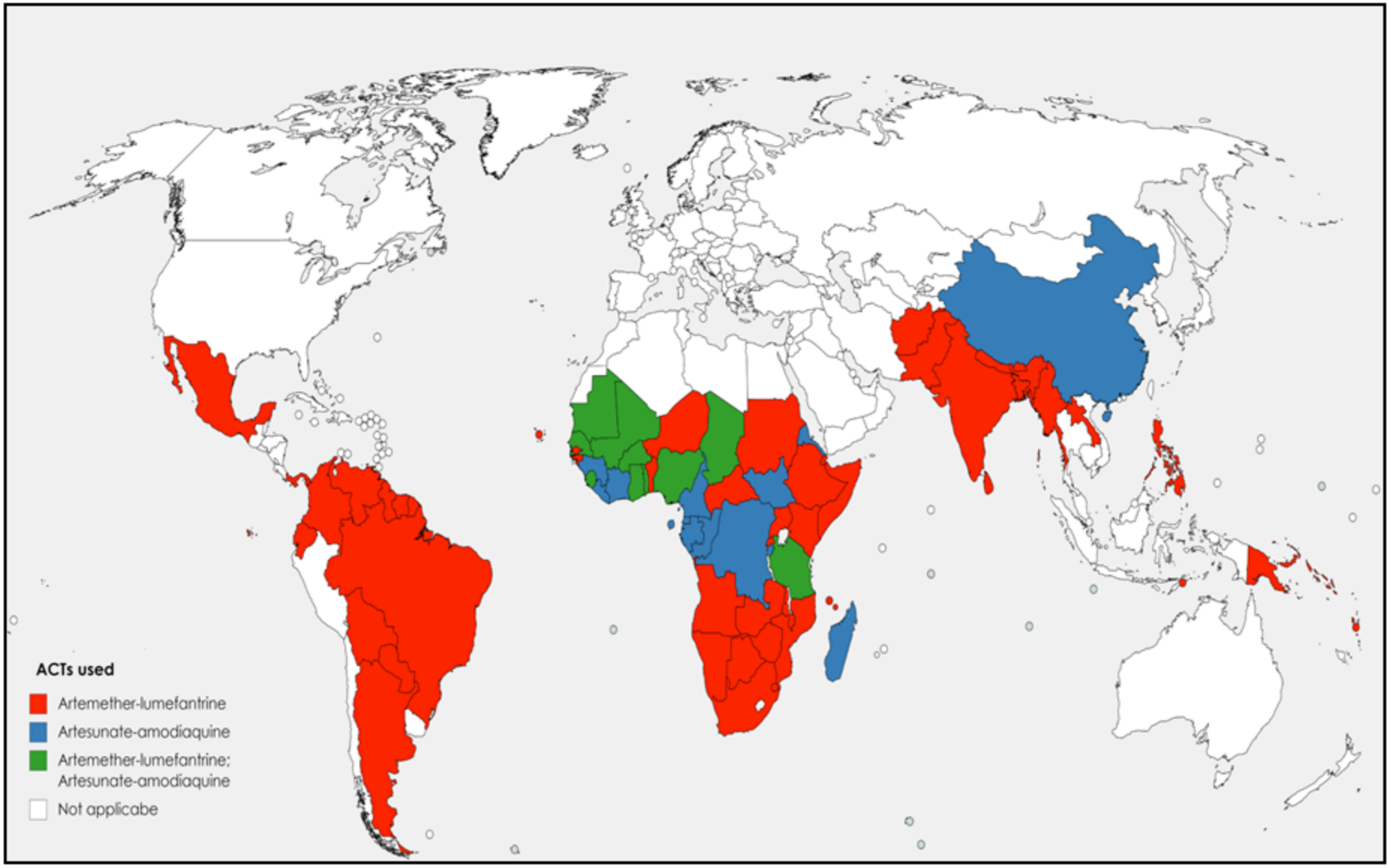

Number of Covid-19 confirmed cases
>100 000-250 000
>10 000-100 000
>1 000-10 000
>100-1 000
>10-100
1-10
0

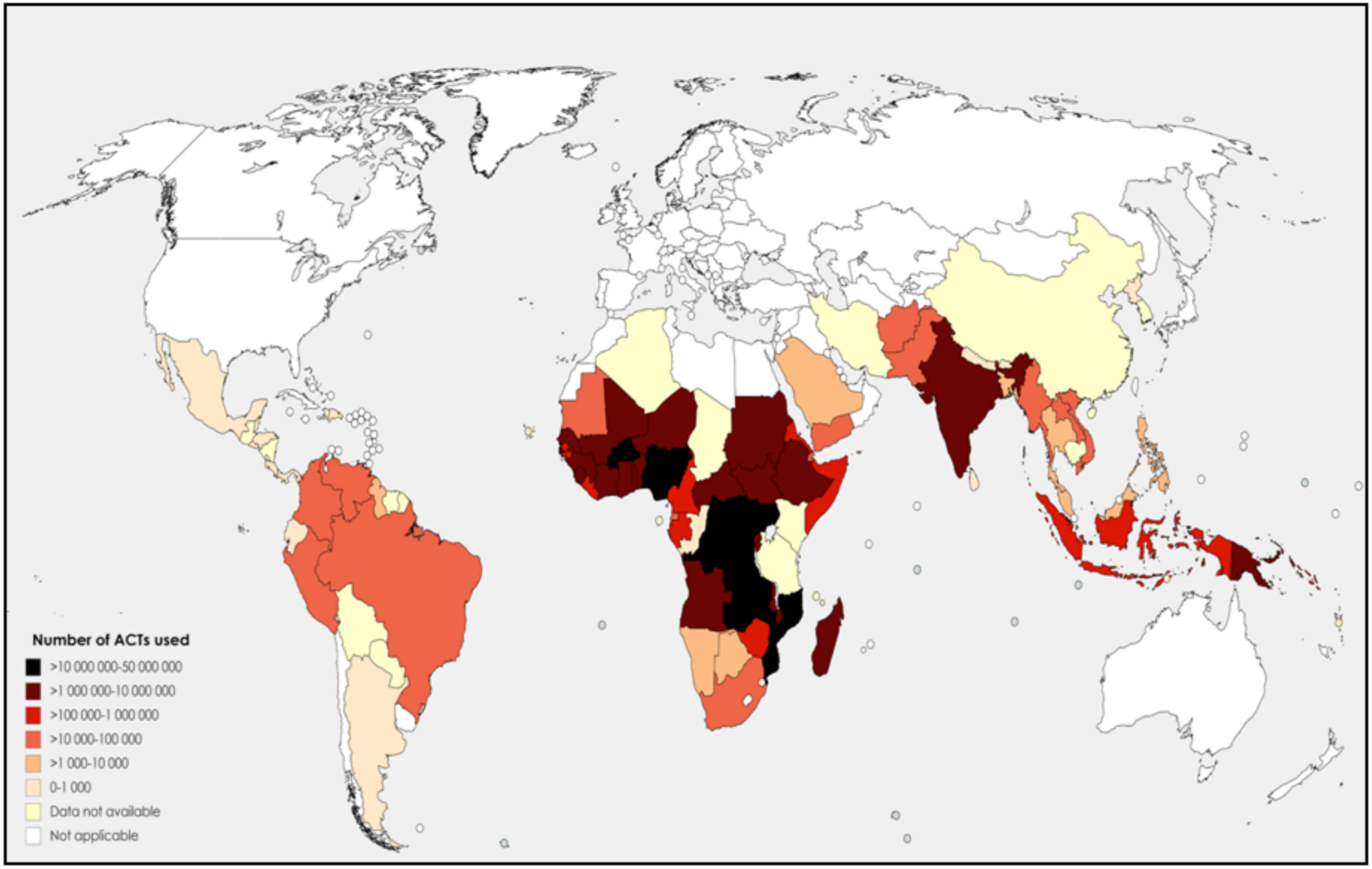

2A
Cumulative COVID-19 deaths
160000
140000
120000
100000
80000
60000
40000
20000
0
0
50
100
150
200
Day
United States
Brazil
France
Italy
South Africa
Algeria
Nigeria
Cameroon
Senegal
Ghana
Kenya
Ethiopia


2B
Cumulative COVID-19 deaths
12000
10000
8000
6000
4000
2000
0
0
50
100
150
200
Day
South Africa
Algeria
Nigeria
Cameroon
Senegal
Ghana
Kenya
Ethiopia


2C
Cumulative COVID-19 deaths
1000000
100000
10000
1000
100
10
1
0
50
100
150
200
Day
United States
Brazil
France
Italy
South Africa
Algeria
Nigeria
Cameroon
Senegal
Ghana
Kenya
Ethiopia


2D
Cumulative COVID-19 deaths
100000
10000
1000
100
10
1
0
50
100
150
200
Day
South Africa
Algeria
Nigeria
Cameroon
Senegal
Ghana
Kenya
Ethiopia
France


ACTs used
Artemether-lumefantrine
Artesunate-amodiaquine
Artemether-lumefantrine;
Artesunate-amodiaquine
Not applicabe


Number of ACTs used
>10 000 000-50 000 000
>1 000 000-10 000 000
>100 000-1 000 000
>10 000-100 000
>1 000-10 000
0-1 000
Data not available
Not applicable