

Assessing Changes in the Reproduction Number of COVID-19 in Cameroon

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Authors' contributions

This work was carried out in collaboration among all authors. Author SWY designed the analysis plan and ran it, carried out data verification with author DCA, under the supervision of author CK. All authors read and approved the final version.

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ABSTRACT

Aim: The purpose of this work is to assess changes that occur on COVID-19 infection in Cameroon since the start of the epidemic.

Study Design: We use a data-based analysis on longitudinal data of reported COVID-19 cases in Cameroon.

Place and Duration: The data for the study were obtained from the reports of confirmed COVID-19 cases from an official website between March 7, 2020 to September 29, 2021.

Methodology: A modified Susceptible-Infected-Recovered-Deceased (SIRD) model for the contagion was used to describe the cumulated cases of COVID-19 during different phases of the epidemic that correlated with highest spikes. The approach features several aspects: one is that model parameters can be time-varying, allowing us to capture possible changes of the epidemic behaviour, due for example to containment measures enforced by authorities or modifications of the epidemic characteristics, country events, and COVID-19 vaccine introduction; the second aspect is that the model accounts for a social distancing parameter. The time-varying parameters

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was handled using a phase-to-phase modelling in which initial parameters were the number of susceptible individuals at the end of each phase. In addition, daily incidence data were used to estimate daily reproduction number. Secondly, we used an Autoregressive Integrated Moving Average (ARIMA) approach to analyse the dynamic of the effective reproduction number R and forecast the new number of infected contacts.

Results: There was less than 54% compliance of social distancing during all phases. The reproduction number was above 1 during each phase of the analysis. As of September 2021, it was 2.43 suggesting a constant increase of infection. Time-series of the reproduction number was unseasonal and stationary. Forecasting of R gave a value of more than 2, suggesting a continued rise in the number of infected cases in the Country in the next coming months.

Conclusion: It is uncertain when the pandemic will last in the country. While social distancing is in decrease, prevention through vaccination is an option to reach more people and stop the propagation of the disease.

Keywords: COVID-19; reproduction number; social distancing; ARIMA modelling; vaccination.

1. INTRODUCTION

Over a couple of year ago, the world remains in the grip of the pandemic caused by the Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2), called COVID-19 by the World Health Organization (WHO). Barrier measures and prevention techniques were quickly implemented, up to a total lockdown observed in several countries. Epidemic curves sufficiently demonstrated the dangerous nature of the disease. Thus, the basic reproduction rates ranged from two to three, and up to six in the initial phases of the epidemic, leading to an effective reproduction number above 1 [1,2]. The disease consequences have been reported: the reduction of the human population, the decline in the economy [3,4]. As of August 23, 2021 and at the time of writing this paper, over 212 million cases and over 4 million of deaths have been reported worldwide ([http:// www.worldometers.info/coronavirus/](http://www.worldometers.info/coronavirus/)).

On the African continent, the epidemic has also wreaked havoc. In Cameroon, the first case of COVID-19 in the region was reported on March 7, 2020, and the first COVID-19 associated death was documented on March 24, 2020. Despite preventive measures provided by the government following different communiqué of the Minister of Public Health, the epidemic has continuing showing an increase. Since then, the local epidemic has spread rapidly with 7205 confirmed cases (up to August 03, 2020) and 1732 deaths (registered by August 01, 2020), and progressively increased as of July, 14 2021 from a total of 80858 to a total of 92303 of confirmed and probable cases, 1324 to 1459 deaths and 78224 to 80433 recovered as of September 29, 2021.

On May 31, 2020, the Cameroonian government declares the end of lockdown period, and schools re-opened. It has been shown that lockdown easing increases the daily contact rate and it is critically important to understand the extent to which such increase in the contact rate among people will affect control of COVID-19 transmission or lead to a secondary wave. Since June 1, 2020, the country experienced several events that may have contributed to an increase of contact: the continuity of inter-urban transport with buses with more than 70 seats, Christmas event, and new year celebration, football competition.

Since the onset of the epidemic, mathematical modelling has been widely used to understand the spread of COVID-19 across different settings, and to design optimal strategies to reduce the future burden and prevent a second wave. Different mathematical models have been utilised: deterministic models on whole populations and rooted in using equations tracking Susceptible-Exposed-Infectious-Removed (SEIR) populations, sometimes age-stratified [5-7], and stochastic i.e., individual-based models, and time series analysis approach for transmission between individuals in a population [8-10], and Markov chain modelling to estimate transition probabilities within COVID-19 states [11,12]. SIRD model appears as an old and simple model to describe interactions between COVID-19 cases independently of external agents [13-16]. Indeed, it describes the total cases, as well recovering and death and cases scenarios that can be observed within the population. Contact rate, as the daily number of contacts per person per day, is one of the key parameters within each group of models and physical/social distancing measures can be

modelled by varying the contact rate [17]. Contact rate is estimated from individual survey where daily contact from outside home is assessed for everyone [17]. However, in an absence of such data, contact rate estimation becomes tricky. However, an estimate of contagiousness which reflects the average number of people who may catch an infection from one contagious person is resumed in the reproductive number R_0 . In Cameroon, R_0 decreased from 6.80 to 2.25 over the period of March 7, 2020 to May 31, 2020 [18].

Determining the level of social distancing had been quantified as the reduction in daily number of social contacts per person, i.e., the daily contact rate, needed to maintain control of the COVID-19 epidemic and not exceed acute bed capacity in case of future epidemic waves, is important for future planning of relaxing of strict social distancing measures. These later parameters have been widely investigated in compartmental models to estimate COVID-19's R_0 value [14,15]. It was demonstrated that when the level of social distancing is less than 70%, it suggests a constant increase of the total cumulative cases [17].

One year since the beginning of the pandemic, the number of cases is still in increase. Indeed, total cases on May 31, 2020 was 6151, and total deaths of 191, and on August 23, 2021, it was 82 454, and 1338, respectively. The government and institutions have recommended massive test for citizen, and it has become a condition to access workplaces. Therefore, mass screening test had become regular to detect infected persons. In addition, vaccination had been deployed in the population to reduce the burden of the disease. Given these observations, there is still a need to assess structural changes of the epidemic characteristics and forecast the disease progression. In addition, at a time when COVID-19 is resurfacing in Europe and Asia, and at a time when summer travel is intensifying on the continent, it is more than urgent to provide indications on the evolution of COVID-19 in Cameroon.

In this paper, we describe COVID-19 pandemic and forecast daily new number of contacts. We first used a SIRD model with social distancing as a function of contact rate, to compare the epidemic in different phases. Variation of the reproduction number was assessed over time on a phase-to-phase basis using cumulative data and daily incidence cases. Secondly, we

proposed the use a time series analysis of estimated reproduction numbers to assess the future change in the epidemic behaviour.

2. MATERIALS AND METHODS

2.1 Data Sources

Publicly accessible data, including newly increased cases, cumulative numbers of confirmed cases, cured cases, and death cases were sourced from <https://worldometerinfo.com/coronavirus/cameroon>, the WHO report (WHO. Coronavirus disease (COVID-2019) situation reports. 2020), and the WHO dashboard (<https://covid19.who.int>). Cumulative number of the confirmed, recovered, death and active cases, as well as daily incidence data, were recorded through the range of the studied dates. As of August 23, 2021, and at the time of writing this paper, over 82,454 cases and over 1,324 deaths have been reported in the country, more elevated than the number of total cases of 19142, and 411 of deaths as of August 31, 2020 [19].

2.2 Analysis of the Aggregated Data for Cameroon

To enable a better understanding of the covid-19 pandemic in the country, several key events and dates need to be considered:

- March 7, 2020: formal date of the first reported covid-19 cases in Cameroon;
- March 18, 2020: first decree of the Prime Minister on prevention strengthening against the spread of this virus in our country, including restriction on gathering event, postponing of school and university competitions; Cameroon closed its land, air and sea borders.
- March 18 to May 31, 2020: lockdown period; schools closed; outdoors restriction, social distancing; this period was marked by several peaks of the epidemic
- On 30 March, the Minister of Health announced the imminent launch of a coronavirus test campaign in the city of Douala. Dedicated teams went door-to-door in the economic capital from April 2 to 6, says the minister;
- On 7 April, the Cameroonian government has suspended calls for public generosity

in the fight against COVID-19, a move that attracted criticism over political motives.

- On 10 April, the government took 7 additional measures to stop the spread of COVID-19 in Cameroon. These measures took effect from Monday, 13 April 2020
 - Measure 1: Wearing a mask in all areas opened to the public;
 - Measure 2: Local production of drugs, screening tests, protective masks and hydro-alcoholic gels;
 - Measure 3: Establishment of specialized COVID-19 treatment centers in all regional capitals;
 - Measure 4: Intensification of the screening campaign with the collaboration of the Center Pasteur of Cameroon;
 - Measure 5: Intensification of the awareness campaign in urban and rural areas in both official languages;
 - Measure 6: Continuation of activities essential to the economy in strict compliance with the directives of March 17, 2020;
 - Measure 7: Sanctions were put in place
- June 1 to September 2020: primary schools and Universities re-opened their doors; people's daily activities continued, and public transportation re-opened;
- In late June, the government announced that the 2021 Africa Cup of Nations would be postponed until 2022;
- December 2020: Cameroon hosted the African football competition;
- April 12, 2021: COVID-19 vaccine introduction in the country, and some people got vaccinated, while reluctance was present to others;
- May to July 2021: cases increased as well as deaths, and relaxation in communication around the pandemic;
- August to September 4, 2021: holidays period with lack of reporting.

Models: SIRD Model with Social Distancing

We follow standard notation in the literature [14]. There is a constant population of N people, each of whom may be in one of four states: $S_t + I_t + R_t + D_t = N$

- $S(t)$: the number of individuals susceptible of contracting the infection at time t ;
- $I(t)$: the number of individuals that are alive and infected at time t ;

- $R(t)$: the cumulative number of individuals that recovered from the disease up to time t ;
- $D(t)$: the cumulative number of individuals that deceased due to the disease, up to time t .

A susceptible person contracts the disease by coming into "adequate" contact an infectious person, assumed to occur at rate $\beta_t I_t / N$, where β_t is a time-varying contact rate parameter. The starting value of β_t , β_0 , reflects how the infection would progress if individuals were behaving as they did before any news of the disease had arrived. We think of β_0 as capturing characteristics of the disease, fixed attributes of the region such as density, and basic customs in the region. Over time, β_t varies depending on how strong is the social distancing and hygienic practices that different locations adopt, either because of policy or simply because of voluntary changes in individual behaviour. β_t was recovered from the data using a phase-to-phase modelling approach. In addition, the total number of new infections at a point in time is $\beta_t I_t / N \cdot S_t$. $S(t) + I(t) + C(t) = N$, $\forall t$, where $N = S(0) + I(0) + C(0)$ represents the fraction of the total population which is affected by the contagion

where β is the transmission rate of the disease, γ is the recovery rate, and ν is the death rate. Underlying hypotheses in this model is that the recovered subjects are no longer susceptible of infection,

$R_{ot} = \beta_t \times 1/\gamma$ under the current social distancing and hygienic practices i.e., the number of infections from sick person is expressed as β_t , the number of lengthy contact per day multiply by $1/\nu$, the number of days contacts are infectious. The effective reproduction number known as the average number of new infections caused by a single infected individual at time t , $R_{et} = R_{ot} \cdot S_t / N$,

2.3 Time Series Analysis of the Reproduction Number

Daily incidence data was pre-processed from March 2020 to July 2021. Analysis was done using the log-linear modelling. Weekly estimates of the reproduction number were extracted and plotted as a time series, and the trend estimated by Locally Weighted Scatterplot Smoothing (LOWESS) methods. Then a classical seasonal decomposition was performed to distinguish between seasonal, trend and irregular

components using moving averages. This allowed graphical visualization of seasonal variation. The Weibel-Ollech overall seasonality test (WO-test) was also performed to verify seasonality (seasonality if p-values are under 0.01 or 0.002). After testing for stationarity using Augmented Dickey-Fuller Test; when seasonality was present, a seasonal Autoregressive and Moving Average (ARMA) Model (Box-Jenkins models) was used for modelling, if not, an ARIMA was used. Models were identified using the sample autocorrelation function (ACF) and partial autocorrelation function (PACF) and then the parameters were estimated. The model adequacy was assessed with the diagnostic plots of standardized residuals, the ACF of the residuals, a boxplot of the standardized residuals, and the p-values associated with the Q-statistic. When the model passed the diagnostic, it was used for forecasting and determining a 3-month ahead 95% prediction interval for future effective reproduction number from July 2021 to December 2021.

We will identify periods where epidemic spikes are in the descending order, or increasing order, and carried out the SIRD model on this period. We will also use daily incidence data to study the fluctuation of the reproduction number over the period of March 7, 2020 to July, 14 2021. The fluctuation was studied using a time series approach with the objective of estimating the mean reproduction number by July 2021 and predict the evolution of contact rate. Data collected from July 15, 2021 to September 29, 2021 were used to validate the forecasting. All analysis was done using the R software version 4.0.3.

3. RESULTS

3.1 Data Visualization

The evolution of covid-19 pandemic revealed several fluctuations over the period of March 2020 to July 2021. This is potentially related to the various events that occurred in the country, as well as several dates with absence of reporting (Supplementary Fig. 1). Over the period of June 1, 2020 to September 29, 2021, the top first three peaks of the epidemic occurred between March and April 2021. Indeed, the highest peak of the epidemic revealed more than 9668 cases on April 1, 2021, following by 7045 cases on March 25, 2021, 6889 on September 29, and 6252 cases on April 29, 2021 (Supplementary Fig. 2).

3.2 SIRD to Describe Several Phases of the Total Cumulated Cases

During each phase of the epidemic, the reproduction number was estimated. Table 1 shows a variation of R0 from March 7, 2020 to September 29, 2021. All estimated values were found above 1.

June 1, 2020 to June 24, 2020: lockdown period release: From June 25, 2020 to July 6, 2020, no data was reported in the country. As a result, we presented the results from June 1 to June 24, 2020. During this period, the peak occurred on June 15, 2020 with 1183 new cases, allowing us to separate the period into two and estimate R0 from June 1 to June 15, then, from June 18 to June 24, 2020 because of absence of data during June 16 and June 17. Before the peak, R0 was 2.20, and 2.21 after the spike, suggesting that an infected individual could infect more than 2 others.

July 7 to November 30, 2020: This period was characterized by a several peaks of the epidemic with an overall trend in the descending order (Supplementary Fig. 3). For instance, 2324 occurred on July 7; 984 on July 16; 463 on August 04, and 328 on November 30.

December 1, 2020 to December 31, 2020: The epidemic peak was reached on December 24, 2020 with 428 new cases.

Overall, the social distancing parameter was less than 0.5 during all phases of the epidemic. As of July 14, the estimate was 0.464 i.e., 54% compliance of social distancing, and 56% as of September 29, 2021.

Modelling daily incidence data using log-linear modelling from March 7, 2020 to July 14, 2021: Daily incidence data reported during this period was very sparse with a distribution very similar to a normal distribution (Supplementary Fig. 4). Indeed, they were 153 dates with zero incidence data among 195 dates available over the same period, suggesting a very low rate of reporting. The highest peak was reached on April 1, 2021 with 9668 cases. The month of April 2021 was the period with the highest incidence value compared to previous months and year 2020, as well as zero-incidence data related to non-reporting (Supplementary Fig. 3). The estimated reproduction number varied greatly over time. The fluctuation reached more than 7 suggesting that an infected person

could transmit the disease to more than 7 others (Fig. 1). It is expected that R remains below 0.5 to say that the epidemic is under control. This seems to be the case as of July 14 according to Fig. 1. Values ranged from 0.00022 to 9.63. But it is not very certain that another outbreak will not be possible after July 2021. When zero-incidence data were removed, R_0 was always above 0.5 since March 7, 2020 (Supplementary Fig. 5).

Reproduction number estimates were obtained using a serial interval of mean 7.5, and standard deviation of 3.4.

Assess the temporal series of the reproduction number from March 7, 2020 to July 14, 2021: The temporal series of the reproduction number is displayed on Fig. 1. Despite values of R found below 1 as of July 14, there exists infected people in the population leading to an uncertainty of the end of the pandemic in Cameroon.

Based on the graph, we would not see any trend pattern. Despite it looks periodic, the highest value of R at each time is not in the same week of the month and is correlated to the epidemic peak. This graph does not have an increasing or decreasing trend on it. The WO seasonality test gave a p-value of 0.21, thus suggesting an unseasonal series. The Augmented Dickey-Fuller Test revealed a p-value of 0.01, thus rejecting the

null hypothesis of non-stationarity. Hence the series was unseasonal and stationary. Hence ARIMA(1,0,3) with non-zero mean was chosen as the best candidate for the unseasonal time series. Supplementary Fig. 6 shows model diagnosis results. The graph displays a plot of the standardized residuals, the ACF of the residuals, a histogram of the standardized residuals, and the p-values associated with the Q-statistics at lag 30. Inspection of the time plot of the standardized residuals shows no obvious patterns. The ACF of the standardized residuals shows no apparent departure from the model assumptions, and the Q-statistic is never significant at the first six lags. The normal Q-Q plot of the residuals shows that the assumption of normality is reasonable. Forecasting of the reproduction number within two months of forecasting period, and 95% confidence intervals, shows an increase of 1.4, for which values could reach up to 5, attesting that the epidemic will continue to grow in the next coming months Fig. 2. This observation well corroborates with the fluctuation observed during the months of August and September, all suggesting an increasing epidemic with value of the reproduction number up to 5 (Fig. 3).

The WO seasonality test gave a p-value of 0.18, thus suggesting an unseasonal series. The Augmented Dickey-Fuller Test revealed a p-value of 0.01, thus rejecting the null hypothesis of non-stationarity.

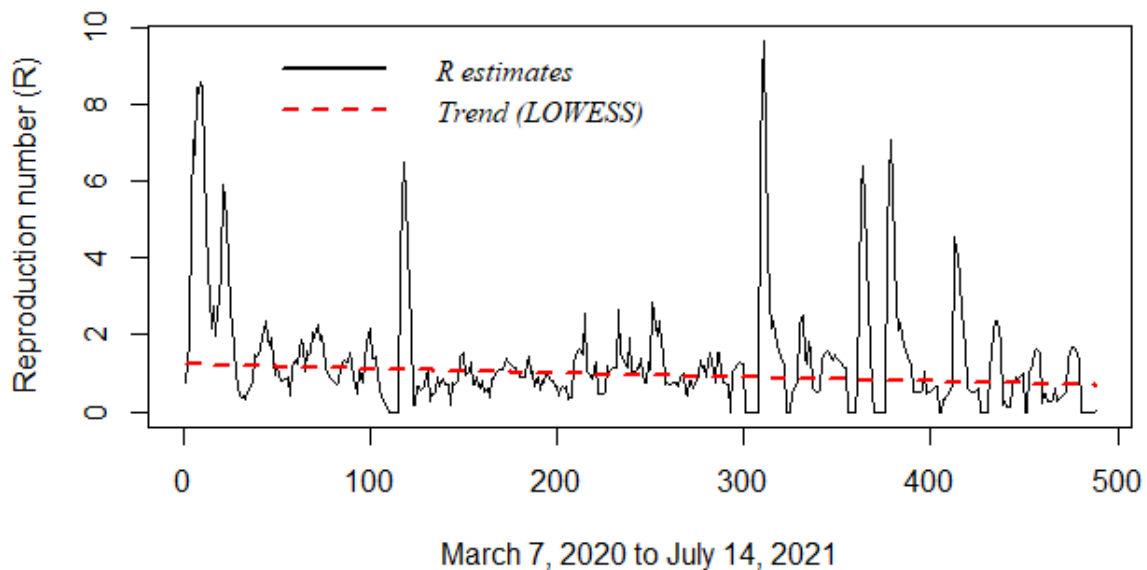


Fig. 1. Estimate of the weekly reproduction number and estimated trend (using the locally weighted scatterplot smoothing) of COVID-19 Cameroon, March 7, 2020 to July 14, 2021

Table 1. Phase-to-phase variation in the basic reproduction number of COVID-19 Cameroon, March 7, 2020 to July 14, 2021

	June 1 to June 24 2020	July 7 to November 30 2020	December 1 to 31, 2020	January 01 to March 25 2021	April 1 to July 14, 2021	July 15 to September 29, 2021
Parameters						
Epidemic peak Date	June_15_2021	June_7_2020	Dec_24_2020	March_25_2021	April-1_2021	September 29, 2021
# new cases	1183	2324	428	7047	9668	6889
$\hat{\beta}$ = infection rate	0.19356	0.245837	0.19329312	0.19477558	0.2015984	0.1534
$\hat{\gamma}$ =recovery rate	0.054263	0.06909	0.05413891	0.05409077	0.05406	0.0427
$\hat{\alpha}$ =social distancing	0.4591	0.49466	0.45891748	0.45991408	0.46448	0.4333
$\hat{\mu}$ = case fatality	0.0329	0.04911	0.03279064	0.03278166	0.03293	0.0204
R0	2.22	2.08	2.22	2.24	2.32	2.43

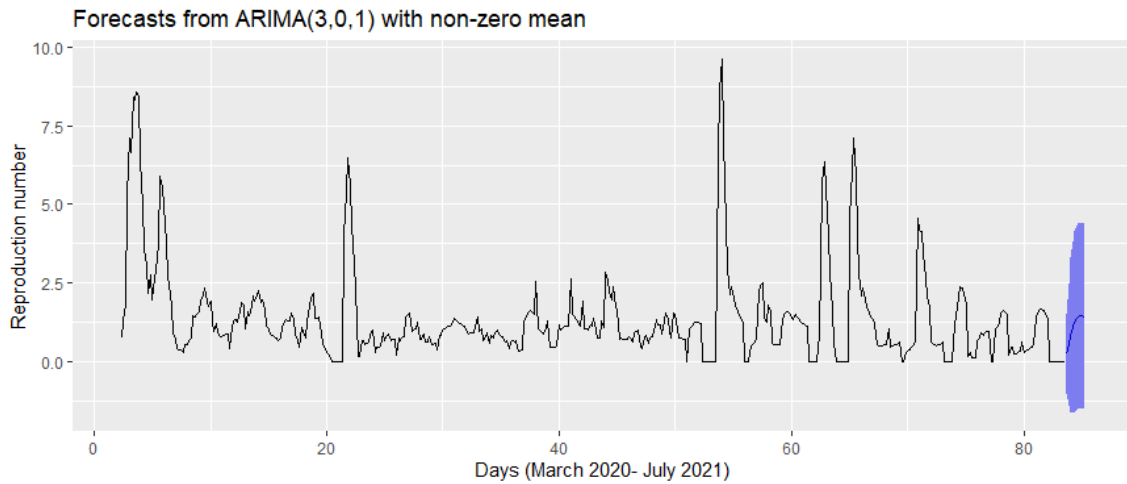


Fig. 2. Temporal series of the reproduction number and forecast of new infected of COVID-19 Cameroon, March 7, 2020 to July 14, 2021

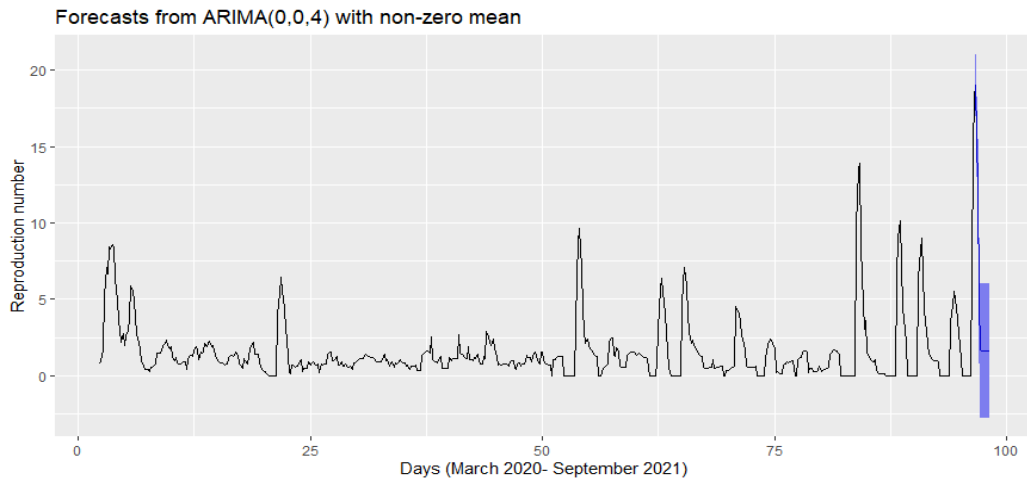


Fig 3. Temporal series of the reproduction number and forecast of new infected of COVID-19 Cameroon, March 7, 2020 to September 29, 2021

4. DISCUSSION

The purpose of this work was to update information on COVID-19 in Cameroon from its advent until the time of submission of this work. Phase -to-phase analysis of the total cumulative cases and the daily incidence data were used, as well as analysis of the variation in the reproduction number generated from the incidence cases. Results showed that the epidemic remains a reality, and because of its constant progression over time, it is very likely that this pandemic will rage for a long time in the country.

It was noted that the basic reproduction rate showed an increase between June 2020 and

March 2021. Indeed, as of September 29, 2021, it was almost 3, meaning that 3 individuals could be infected from an infected individual, and suggesting a daily contact of 4 to 5. Some authors argued that, keeping the daily contact rate lower than 5 or 6, can prevent an increase in the number of COVID-19 cases, and keep the effective reproduction number R_e below 1 to avoid new COVID-19 wave in Cameroun [20]. In addition, simulations showed that when the social distancing is less than 0.39 or more than 70% compliance in social distancing [17], one could expect constant cumulative cases i.e., zero daily cases. Our analysis showed only 54% compliance, which according to Nyabadza et al., is the case where the number of cumulative total cases will continue to grow [17].

These observations suggest that the epidemic is still in an increase, and the proportion of the population that needs to be effectively immunized to prevent sustained spread of the disease, known as the “herd immunity threshold”, has to be larger than $1 - (1/R_0)$ i.e., 66% of the population should be immunized to stop the spread of the infection [21]. With a population of approximately 27 million in Cameroon (<https://www.unfpa.org/publications/unfpa-strategy-2020-round-population-housing-censuses-2015-2024>. Accessed 12 Oct 2021), this translates into roughly 18 million of people that should be vaccinated to enable a collective immunity.

Coronavirus has become a challenge over the world. Pharmaceuticals firms brought new insights to slow down the disease especially to oldest persons through the development of vaccines. However, the gradual increase in the number of infected people will have fatal consequences for the most vulnerable strata, and in particular for the health system. It will be quite possible, if not certain, that the youngest are carriers of the virus and transmit it to others. In addition, with the spread of the delta variant of the virus, other mutant strains will be born, and the epidemic will grow. Indeed, as of July 2021, there were 13 cases of Delta variant detected in the main towns of Douala and Yaoundé (<https://reliefweb.int/report/cameroon/cameroon>). On another hand, out of 745 samples, they were 43 Alpha variants, 17 Beta, and 14 Delta variant detected as of August 2021 (<https://reliefweb.int/report/cameroon/cameroon>). Thus, the increase in infected people can generate serious forms, therefore lead to a rapid decrease in the population.

Indeed, the work carried out using these mathematical models predicts an uncertain future for the virus in Cameroon; the epidemic curves still reveal the hidden nature of the disease which could show a downward face, only under the assumption of a total restriction and fully immunized population. The coronavirus vaccine remains a promising way to reduce viral loads and counteract the advanced form of mutant strains of the virus. Cameroon set a goal to vaccinate 20% of its over 25 million population with a COVID-19 vaccine at the time the country experienced new surge of infections on April 2021. As of May 21, 2021, information from the Twitter handle of the Minister of Public Health, revealed that Cameroon has already administered 48,971 doses of the Covid-19 vaccine: 29,882 doses of the Sinopharm vaccine

and 19,089 doses of the AstraZeneca vaccine respectively. As of September 30, 2021, only 2.39% of the population fully or partially immunized leading to a huge drastic gap between observed and expected level of immunity. In Nigeria, as of July 2021, 2.58% got vaccinated, and in Ivory Coast, 6.05% were in favour to vaccination and got vaccinated [22].

Absence of constant mask protection, vaccination hesitancy, and absence of strong communication strategies are some of the factors that could be associated to such gap [23-25].

Data that we used could be inconsistent with the COVID-19 reality in Cameroon. However, we intended to learn from the reported observations to an extend of sounding the alarm about the constant progression of the epidemic in the country. Other modelling extension can be possible. Rather than using a deterministic model that enable homogeneity in the model compartment, it is also possible to use a stochastic process that accounts for the heterogeneity among individuals in the population (e.g., variations in individual health conditions and disease transmissibility) and patterns of contacts between them, as well as the COVID-19 delta-variant [26].

The end of the epidemic should not be celebrated immediately, but individual contributions are required in the fight against COVID-19. The world is experiencing another turning point in its history. At a time when COVID-19 is resurfacing with fourth waves following the appearance of the delta variant [27-28], as a result, some measures were observed in several countries: the imposition of the sanitary pass in restaurants, schools, universities, and public transport. It is more than urgent to adopt healthy behaviours especially during these holidays where travel is intensifying. The hesitation to vaccinate has become a challenge in the fight against COVID-19 [29], and the absence of the application of barrier measures via the absence of a protective mask, together with the absence of sensitive communication on the usefulness of the vaccine, are ways that could certainly cause other waves of epidemics to be more dangerous than previous ones. Therefore, a call for individual awareness is launched. Vaccination appears as a better mass protection measure against COVID-19 [30-31]. The infodemic should not prevent the achievement of the objectives set by the Cameroonian government, at the risk of

gathering more deaths than in previous phases of the epidemic.

5. CONCLUSION

It is uncertain when the pandemic will last in the country. While social distancing is in decrease, wearing of facial mask, use of hand sanitizer should continue to be applied by everyone. In addition, prevention through vaccination is an option to reach more people and stop the community expansion of the disease.

6. SUPPLEMENTARY MATERIALS

Supplementary materials available in:
<https://www.journalajrid.com/index.php/AJRID/libraryFiles/downloadPublic/4>

ETHIC APPROVAL

Not applicable

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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