EHESP

Master of Public Health

Master de Santé Publique

Assessing the impact of the national anti-contagion interventions on the progression of COVID-19 epidemic within the first 63 days of its introduction in Nigeria: an interrupted time series (ITS).

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Table of Content

1 ACRONYMS

- COVID-19 - Novel Coronavirus Disease 2019 (COVID-19)
- SARS-CoV-2 - Severe Acute Respiratory Syndrome-related Coronavirus 2
- NCDC – Nigeria Centre for Disease Control
- PTF – Presidential Task Force on COVID-19 in Nigeria
- ACAPS – The Assessment Capacities
- OSI – Oxford Stringency Index
- PHSM – Public Health and Social Measures
- Rt – Time-varying reproduction number
- ITS – Interrupted Time Series

2 Abstract

Relevance Non-pharmacological interventions constitute the mainstay of Nigeria's response to the novel coronavirus disease 2019 (COVID-19) epidemic. The extent to which stringency level and compliance determine the success of these interventions deserves more attention.

Objective To assess the impact of national anti-contagion interventions on the progression of COVID-19 in Nigeria and the extent of dependence of impact on level of stringency and compliance to measures interventions.

Study Design and Population This study is a natural experiment using interrupted time series methods to examine the intervention effects and applying time series analyses of confirmed COVID-19 cases (and deaths) in Nigeria by date of reporting and symptom onset between 27th February 2020 and 10th June 2020 reported by the Nigeria Centre for Disease Control (NCDC).

Interventions National anti-contagion interventions with timelines collected from NCDC, PTF and ACAPS were divided into 4 time periods: period 1(< 30 Mar, pre-lockdown, suspension of international cross-border movements), period 2 (30 Mar-13 Apr, lockdown in 3 states, closure of schools, ban on mass gatherings and internal cross-border movements), period 3 (14 Apr -3 May, strict enforcement of restrictions, expansion of lockdown to other states) and period 4 (4 May onwards, phased easing of restrictions). Nonparametric multiple changepoint detection analysis was performed to identify periods during interventions in which change in the slope of daily case incidence occurred.

Key Outcome Measures Epidemic growth/decay rate, doubling/halving time, time-varying reproduction number (Rt), Oxford Stringency Index (OSI) and national mobility trend were assessed according to the four time periods. Growth/decay rate was estimated by fitting a log-linear model to each period, then doubling/halving time was calculated. Rt estimates were computed using a Bayesian procedure involving 4 steps: estimation of i.) daily new infection rates λ ii.) likelihoods of observing k new infections given λ iii.) posteriors of the probability distribution of Rt and iv.) probability distribution of Rt with 95% confidence intervals. Analyses of OSI and national mobility data from University of Oxford's Blavatnik School of Government and Google were performed. Outcome measures pre- and post-intervention periods were compared.

Results The growth/decay rates (with 2.5^{th} - 97.5^{th} percentiles) are 0.113 (0.086 to 0.140) in period 1, decreased by 115.9% to -0.018 (-0.110 to -0.073) in period 2, increased to 0.103 (0.0774 to 0.129) in period 3 but less than period 1 by 9% and, decreased by 83.5% to 0.017(0.008 to 0.025) in period 4. The epidemic doubled every 6.2 days (5.0 to 8.1) in period 1, halved every 37.7 days (6.3 to -9.5) in period 2, doubled every 6.7 days (5.4 to 9.0) in period 3 and 41.0 days (27.3 to 82.3) in period 4, representing a prolongation by 34.2 days from period 3. The Rt fell from above 3.5 to 1.65(95% CI 0.78 to 2.46) at end of period 1, 1.08 (95% CI 0.25 to 1.78) at the end of period 2 representing 39.4% decrease, 1.34 (95% CI 1.11 to 1.54) in period 3 (24.1% increase) and 1.21(95% CI 1.05 to 1.35) at the end of period (9.7% decrease). OSI rose from 11.2 initially and peaked at 82.9 at the end of 1st period, continued at 82.9 in 2nd period, climbed to 85.7 towards the end of 3rd period and 80.6 in the 4th period. The national movement trend began to fall at the end of period 1 but dropped sharply by at least 50% in period 2, remained at the same level with minor fluctuations in period 3 but climbed up steadily in period 4 following relaxation of restrictions. Non-parametric, multiple changepoint detection analysis identified 2020-04-13, 2020-04-27 and 2020-05-03 as changepoints, coinciding roughly with end first and second lockdowns in periods 2 and 3, and the eve of easing of lockdown (period 4).

Conclusions: A combination of national anti-contagion interventions appears to be linked with improvement in the control of COVID-19 epidemic in Nigeria, effectiveness appears to be higher with higher level of stringency of interventions and compliance to them. Although the expansion of the scope of interventions seemed to have worsened the control parameters of the epidemic in period 3 but overall, they represent an improvement from those in period 1.

3 Introduction

Emerging infectious diseases have continued to pose critical threats to global health in recent times [1]. The current pandemic of coronavirus disease 2019 (COVID-19) reportedly started in December of 2019 as a cluster of pneumonia cases of unknown etiology linked to a seafood market in the Wuhan City of China [2]. Subsequently, the etiological agent was identified and named Severe Acute Respiratory Syndrome-related Coronavirus 2 (SARS-CoV-2) due to its genetic similarity to the SARS-CoV and, compelling evidence in support of human-to-human transmission of the disease surfaced in January 2020 [3][4]. With 118,319 infections and 4,292 deaths worldwide, COVID-19 was declared a pandemic by the World Health Organization (WHO) on 11th of March 2020 [5]. Globally, a total of 7,145,539 confirmed COVID-19 infections and 408,025 deaths have been reported in about 214 countries/territories/areas as of 10th June 2020 [6].

3.1 Brief epidemiology overview

On 27th of February 2020, Nigeria's first confirmed case was reported in Lagos – a foreign worker of Italian nationality who had a recent travel history to Milan, Italy [7]. A co-worker of the index case became the country's second confirmed case and the first-known locally acquired COVID-19 infection on 13th March 2020. Sporadic cases were reported in the weeks following, mostly imported. Before long, the epidemic initially concentrated in Lagos and Federal Capital Territory (FCT) most probably due to their proximity to the 2 main international airports, gradually spread to other states, beginning from neighboring states. A notable driver of transmission was mass repatriation of Almajirai - children from poor homes sent to other states within northern Nigeria for Islamic education, among whom COVID-19 tests performed upon arrival in their respective states of origin showed high positivity rates [8], [9].

As of 10th June 2020, the epidemic has spread to all 36 states plus the FCT with a cumulative of 382 deaths and 13, 873 confirmed cases reported nationwide, 60 % of which are concentrated in the 3 worst hit states - Lagos (45%), FCT (8%) and Kano (7%) [7] . Overall, 72% (9934) of the cumulative cases have unknown epidemiological links, 26% (3650) had contacts with known cases and only 2% (289) were imported [7].

Like most governments around the world, the Nigerian government responded to the pandemic by implementing a range of non-pharmacological interventions such as cross-border movement restrictions, restrictions of mass gatherings, home confinements ('lockdowns'), closure of schools, testing, contact tracing and quarantine among other [10].

3.2 Current Evidence

Evidence from recent studies continue to shed more light on the association between anti-contagion policies and changes in some key epidemiological parameters of the novel respiratory disease - COVID-19. In a study by Islam *et al*, the authors found that implementation of national anti-contagion policies aimed at achieving physical (social) distancing in 149 countries reduced the overall incidence of COVID-19 by 13% and the reduction was bigger with early lockdown and vice versa [11]. In another study involving 28 European countries by Vokó *et al*, social distancing interventions were associated with decreasing epidemic growth rates and the decrease showed a dose-response relationship with increasing social distancing index [12]. According to findings from a study by Hsiang *et al*, a combination of non-pharmacological anti-contagion interventions including border restrictions, lockdowns and social distancing measures slowed down epidemic growths and averted 530 million COVID-19 infections across 1,717 localities in 6 countries – China, France, Iran, Italy, South Korea and United States [13]. In a study by Flaxman *et al,* a series of public health and social measures successfully drove down the time-varying reproduction number (Rt) to below 1 with 99.9% probability in 11 European countries [14]. In a separate study by Pan *et al* in which the authors examined the impact of anti-contagion interventions by 5 time periods according to timelines of key public health interventions, the Rt fell from above 3 to as low as 0.3 at the end of study period [15]. Benefits have also been widely reported in other studies with regards to control of epidemic using non-pharmacological anti-contagion measures [16], [17],[18], [19].

In Nigeria, Amzat et al in a narrative review of Nigeria's response to COVID-19 epidemic, noted that the country has recorded success in controlling the epidemic with non-pharmacological measures but risks reversing all the gains if the economy is re-opened too soon as case counts of COVID-19 infection have increased by 52% since businesses were re-opened [20]. Rutayisire et al identified lack of compliance as one of the barriers to winning the fight against COVID-29 in Nigeria and other African countries [21].
Therefore, this present study will explore the association between national anti-contagion interventions and the progression of COVID-19 epidemic in Nigeria and, the strength of the association (if any) on the level of stringency of interventions and compliance to them by the Nigerian population.

Hypothesis
The hypothesis of this study is that, stringency level of anti-contagion measures and buy-in or compliance to them by the Nigerian population are associated with improved control of COVID-19 epidemic in Nigeria in a dose-response manner.

Research question
What is the impact of national anti-contagion interventions on the progression of COVID-19 epidemic in the first 63 days since its introduction on 27th of February 2020 in Nigeria and to what extent is the impact dependent on level of stringency of the interventions and compliance to them?

3.3 Aims and objectives

The general aim of this study is to determine the impact of national anti-contagion policies on the progression of COVID-19 epidemic in Nigeria and the extent of its (impact) dependence on stringency of the policies and compliance to them.
The objectives of the study are outlined below

1. to estimate the epidemic growth/decay rate
2. to estimate the doubling/halving time
3. to estimate the time-varying reproduction number
4. to analyze the national mobility trends and stringency of anti-contagion interventions
5. to identify dates during the time periods of interventions when a shift in trend (or slope) of daily case incidence occurred

4 Materials and Methods

***Table 1** A summary study materials and methods*

Research Question

What is the impact of national anti-contagion interventions on the progression of COVID-19 epidemic in the first 63 days since its introduction on 27th of February 2020 in Nigeria and to what extent is the impact dependent on level of stringency of the interventions and compliance to them?

Design	Interrupted Time Series (ITS)
Participants	All confirmed COVID-19 cases (and deaths) on Nigeria's soil
Interventions (Exposures)	• cross-border movements restriction (local and international), • schools' closure • mass gatherings restriction • sit-at-home order • others including testing, contact tracing and quarantine
Outcome measures	• growth or decay rate • doubling or halving time • time-varying reproduction number (Rt) • Oxford Stringency Index (OSI) and national mobility pattern • Identified changepoints
Comparators	Outcome measures of each preceding period of key interventions (periods 2 vs 1, 3 vs 2 and 4 vs 3)
Data collected	• daily new cases and deaths by date of report and symptom onset (where reported) • anti-contagion measures with implementation timelines and stringency • national mobility data including movement patterns to transit stations, workplaces, pharmacy and grocery shops/markets, parks
Data sources	• NCDC, Presidential Task Force on COVID-19 (PTF) • Blavatnik School of Government (University of Oxford) • The Assessment Capacities (ACAPS) • Google COVID-19 Community Mobility Reports

4.1 Materials

Open-access data on daily newly detected COVID-19 cases (and deaths) by date of report and symptom onset (where reported) between 27th February and 10th June of 2020 were scraped from Nigeria Centre for Disease Control (NCDC)'s website [7]. Details of government's anti-contagion interventions including cross-border movements restriction (local and international), closure of schools, restriction of mass gatherings, sit-at-home order and others (testing, contact tracing and quarantine) were obtained from publicly available sources - NCDC, Presidential Task Force on COVID-19, The Assessment Capacities (ACAPS) [7], [10], [22]. Publicly available data on stringency of government public health countermeasures in response to COVID-19 were collected from the University of Oxford's Blavatnik School of Government [23], [24]. National mobility data for Nigeria including movements related to workplace, pharmacy and grocery, transit stations and parks were collected from Google COVID-19 Community Mobility Reports – open-access document published by Google in support of the fight against COVID-19 pandemic [26].

4.2 Methods

4.2.1 Study design and interventions

The study is a natural experiment which employed an interrupted time series (ITS) analysis – a quasi-experimental design used to evaluate the impact of population-wide interventions or 'interruptions' in which the outcome variable is a time series data [25]. In public health, ITS has been applied in recent studies to assess the effects of interventions or 'interruptions' on the transmission dynamics of COVID-19 and Ebola Virus Disease [26], [27].

The interventions have been divided into 4 key time periods: period 1 (< 30 Mar, pre-lockdown, international cross-border movement restrictions), period 2 (30 Mar-13 Apr, lockdown in 3 states, school closures, ban on mass gatherings, local cross-border movement restrictions), period 3 (14 Apr -3 May, strict enforcement of restrictions, expansion of lockdown to other states) and period 4 (4 May onwards, gradual easing of restrictions). Refer to ***Table 3*** (**Results)** and ***Table 5*** (***Appendix).***

4.2.2 Estimation of the epidemic growth or decay rate and doubling or halving time

First, as it is a standard practice to characterize epidemic growth profiles by date of symptom onset rather than date of reporting [28], missing dates of symptom onset were imputed using the global median reporting delay of 6 days. Then a simple log-linear model was fitted to each intervention period to estimate the epidemic growth or decay rate as expressed in the equation:

$\log(y) = \beta + r.t$[29]

where y represents incidence, r - epidemic growth rate (slope of regression line), t – time since the start of intervention, and β - intercept.

The doubling (or halving) time – time taken for the epidemic to double (or to halve) was estimated from the growth (or decay) rates using the formula:

$dt = \frac{\ln 2}{r}$[30]

where dt = doubling time, r = growth rate

Estimates of growth or decay rate and doubling or halving time following each time period of interventions were compared with those preceding the period of interventions (***Table 3, Figure 2)***

4.2.3 Estimation of time-varying reproduction number Rt with 95% credible intervals

Time-varying reproduction number Rt - defined as the average number of secondary cases of an infectious disease that would be generated by a primary case in a susceptible population at a given time *t* if conditions remain constant after *t* (for *t > 0)* [31], is an extremely important epidemiological metric for monitoring the effect of control efforts during an epidemic [32].To compute the most likely estimates of Rt with uncertainty bounds, a Bayesian procedure proposed by Bettencourt and Ribeiro was employed [33]. This method has been demonstrated to provide reliable real-time estimates of probability distribution of Rt with smaller computational overheat from sparse data, not only for Influenza outbreaks but also for COVID-19 pandemic [33], [34].The underlying principle of the approach is based on translation of time-series infection counts into probability distribution for the epidemiological parameter (Rt in this case) using Bayes' theorem:

$$\mathrm{P(Rt|kt)} = \frac{\mathrm{P(Rt)} \cdot \mathrm{P\ (kt|Rt)}}{\mathrm{P(kt)}}$$

where $\mathrm{P(Rt|kt)}$= *probability distribution of Rt given k number of new infections,*
$P\ (kt|Rt)$ *= likelihood of observing k new cases given Rt,*
P(Rt) = prior, initial beliefs of distribution of Rt,
$P(kt)$ *= probability of k number of infections*

Estimation of probability distribution of Rt given k number of new infections $\mathrm{P(Rt|kt\ )}$ involved 4 steps [33], [34]. First, daily new infection (arrival) rate λ was computed but in preparation for this, the number of new daily infections k were smoothed over a 7-day window using a Gaussian smoother to account for reporting lags which are usually quite pronounced during weekends. The relationship between λ, k and Rt is expressed below

$$\lambda = (\mathrm{kt} - 1)\ \mathrm{e}^{\gamma(\mathrm{Rt}-1)}$$

where γ *represents reciprocal of serial interval (serial interval ~ 4 days*[35]*), kt−1 = daily new (smoothed) infections at time interval t-1 in days, Rt−1 represents range of possible values of R over time t-1 (assumed range of Rt from 0 to 12)*

Second, $\mathrm{P\ (kt|\lambda\ )}$ - the likelihoods of observing k new infections given λ was computed using the relationship:

$$\mathrm{P\ (kt|\lambda\ )} = \frac{\lambda \mathrm{k\ e} - \lambda}{\mathrm{k!}}$$

Third, the posteriors of the probability distribution of Rt were computed. The formula showing the relationship between Rt, likelihood and posterior is expressed below

$$\mathrm{P(Rt|kt)} \propto \mathrm{P}(\mathrm{R}_{t-1}|\ \mathrm{k}_{t-1}) \cdot \mathrm{P(kt|Rt)}$$

where P(Rt-1| kt-1) = posterior distribution of Rt given k new cases at time interval t-1
P(Rt|kt) = posteriors of the probability distribution of Rt given k new cases at time interval t-1
P(kt|Rt) = likelihoods of k cases given Rt.

Finally, estimates of most likely values of Rt with 95% credible intervals were computed from the posteriors of the probability distribution of Rt (***Table 3, Figure 3, 4).***

4.2.4 Identifying changepoints: nonparametric multiple changepoint detection analysis

A non-parametric multiple changepoint detection analysis was applied to detect changepoints - dates during the epidemic in which a change in slope of the daily case incidence occurred [27]. The main assumption of this model is that of a distinct distribution of time series data pre- and post-changepoints. The model is non-parametric - does not impose assumption of parametric distribution, it is suitable for identifying multiple changepoints [27]. To identify the changepoints, the method applied by Jombart *et al* was used. First, a total of 250 changepoint analyses were run by adjusting the segment length between 1 and 5 weeks while simultaneously varying quants between 1 and 50. Then, changepoints with frequencies of at least 20 % of the 250 runs were selected and the process was repeated for frequencies at least 16%. Identified changepoints were compared against dates of implemented anti-contagion interventions (***Table 4, Figures 6, 7)***.

4.2.5 Oxford Stringency Index and national movement trend

Oxford Stringency Index (OSI) is composite metric for assessing the stringency level of government anti-contagion policies with values ranging from 0 to 100 (increasing order of stringency), calculated from 9 indicators including restrictions on mass gatherings, cross-border movement restrictions, sit-at-home order and closure of schools [23]. Both OSI and mobility data were visualized to assess the trend in stringency of interventions and the national mobility which used data on movements made to transit stations, workplaces, grocery and pharmacy stores and parks [23], [24]. See ***Table 3, Figures 3, 4, 5.***

4.2.6 Analytical tools

All analyses and data management were executed in version 3.2 of R Software. Data management was performed using various packages including *tidyverse, dyplyr* and *lubridate among others.* Estimation of the growth or decay rate and doubling or halving time was done using the package *Incidence*. In the estimation of probability distribution of Rt process, case counts were smoothed with *smoother,* likelihoods were computed using *dpois,* posteriors of Rt probability distribution were computed with *cumprod* and finally, Rt estimates were computed and corresponding 95% credible intervals were estimated with *hdi*.

Unsupervised multiple changepoint detection analysis was performed with the packages *changepoint and changepoint.np.* The national mobility trends, Oxford Stringency Index, results of change point analysis, growth rate and Rt were visualized with *ggplot2.*

Table 2 *A summary of analytical tools (R packages) used in data management/analysis*

Analysis/data management	**R package used**
Data management	*tidyverse, dyplyr, lubridate..*
Growth or decay rate, doubling or halving time	Incidence
Time varying reproduction number, Rt	smoother, dpois, cumprod and hdi
Change point analysis	changepoint and changepoint.np
National mobility trend, Oxford Stringency Index	ggplot2

4.2.7 Ethical Considerations

All data used in this study are open-access, secondary and fully anonymized. However, ethical permission was granted by the University of Sheffield Ethical Committee for the main data used for this research.

5 Results

This analysis has been divided into 4 main periods based on the timelines of implementation of key public health and social measures (PHSMs):

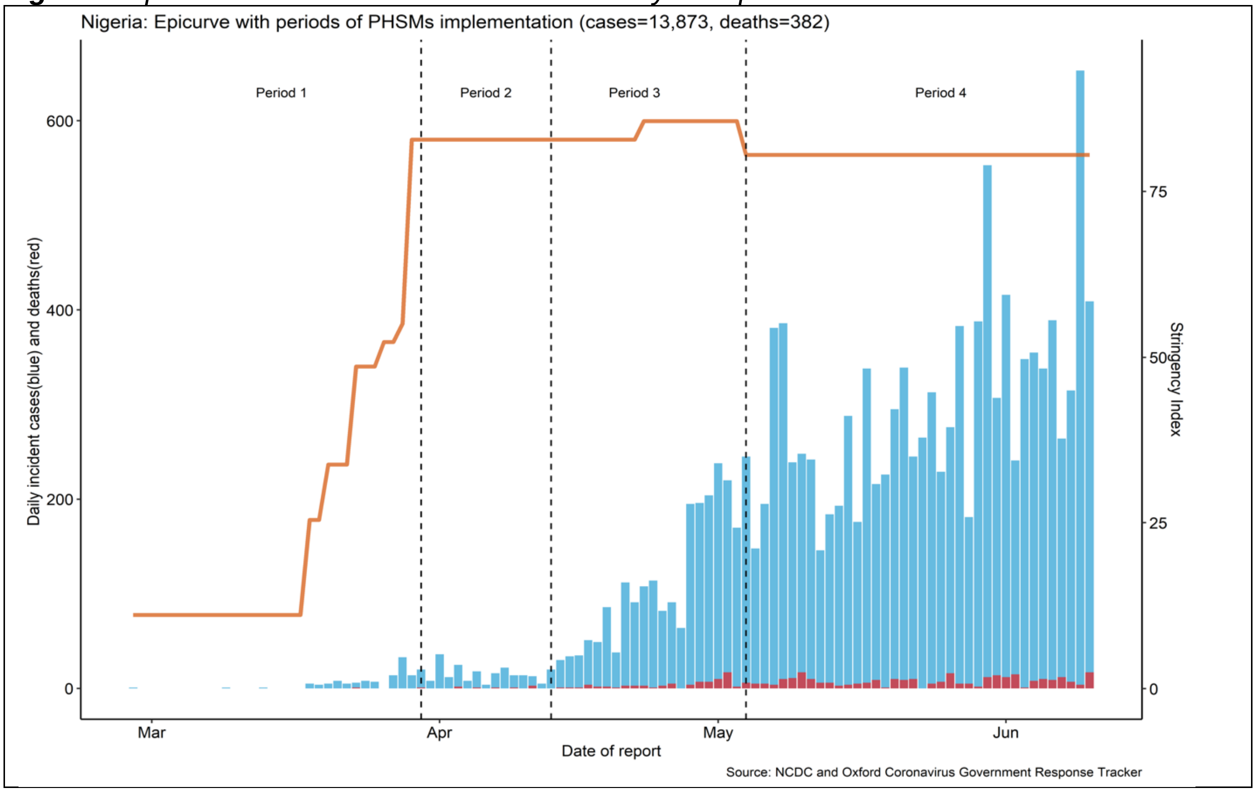
i.) period 1 (< 30 Mar, pre-lockdown, international cross-border movement restrictions)
ii.) period 2 (30 Mar-13 Apr, lockdown in 3 states, school closures, ban on mass gatherings, local cross-border movement restrictions)
iii.) period 3 (14 Apr -3 May, strict enforcement of restrictions, expansion of lockdown to other states) and iv.)
iv.) period 4 (4 May onwards, gradual easing of restrictions). See ***Tables 3*** & ***5***

Table 3: *A summary of key outcome measures by periods of analysis*

	Pre-lockdown	Lockdown		Post-lockdown
Period (Timeline) See ***Table 5 (Appendix)***	Period 1 (Early PHSMs) <30 March	Period 2 (Sit-at-home) 30 March-13 April	Period 3 (Further restrictions) 14 April -3 May	Period 4 (Return to work) 4 May – 10 June
Epidemiological situation (Figure 1)	Sporadic cases-mostly imported, established local transmission, 1 death ,	Decreasing case incidence trend, 6 new deaths	Increasing transmission, ~ 4 deaths/day	Stable transmission, ~8 deaths per day
Epidemic growth/decay rate	0.113 (0.086-0.140)	-0.018 (-0.110 to -0.073) [-115.9%]	0.103 (0.0774 -0.129)	0.017 (0.008-0.025) [-83.5%]
Doubling/Halving time (days)	6.2 (5.0-8.1)	37.7 (6.3 to -9.5)	6.7 (5.4 - 9.0)	41.0 (27.3-82.5) prolonged by 34.3 days
Time-varying Rt at end of period **[%change in Rt]**	1.65 (95% CI 0.78 - 2.46) from 3.77 (95%CI 0 - 7.42)	1.08 (95%CI 0.25 -1.78) [-39.4%]	1.34 (95% CI 1.11 - 1.54) [+24.1%]	1.21 (95% CI 1.05-1.35) [-9.7%]
Oxford Stringency Index: Median (i.q.r) **[Maximum]**	11.1 (i.q.r. 11.1 – 33.8) [82.9]	82.9 (i.q.r 82.9 – 82.9) [82.9]	85.7 (i.q.r 82.9 – 85.7) [85.7]	80.6 (i.q.r 80.6 – 80.6) [80.6]

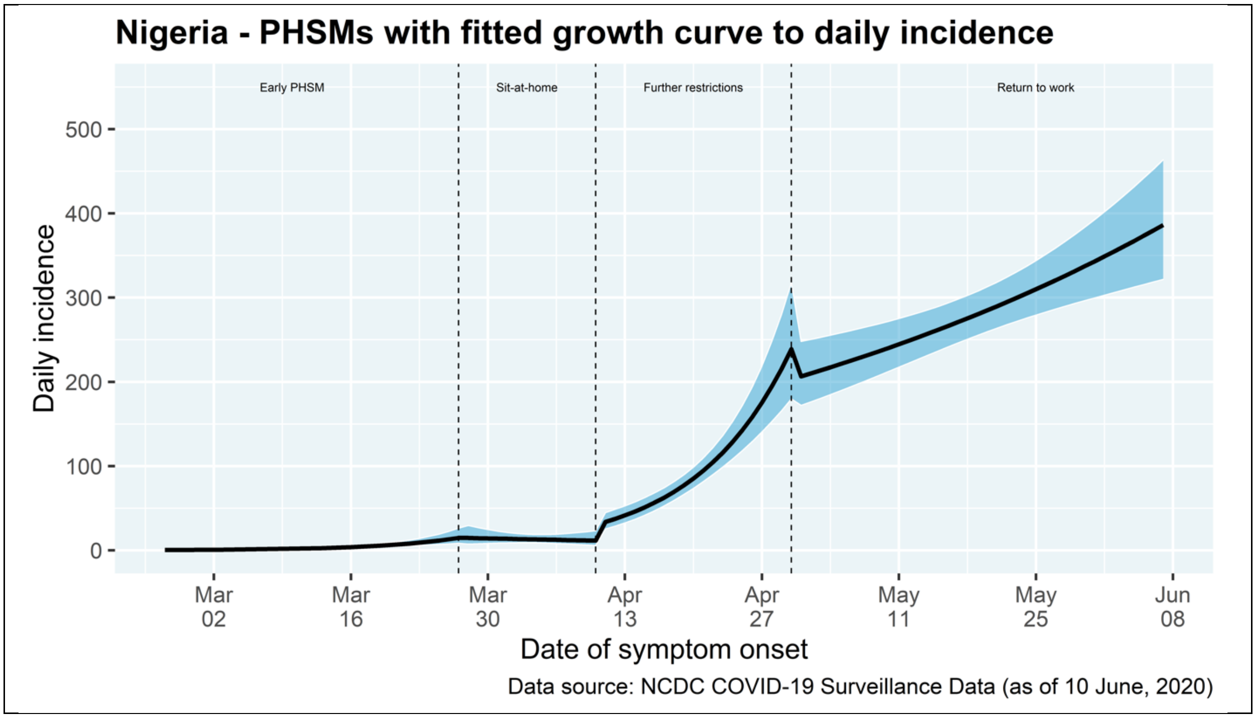
As shown in ***Figure 1***, the median OSI (pink line) rose from 11.2 in period 1 to 82.9 in period 2, climbed to 85.7 from around middle of period 3 and dropped to 80.6 in period 4. In other words, the national anti-contagion measures were least stringent in period 1 and most stringent from around middle of period 3 followed by period 2 and 4.

Figure 1 *Epicuve of cases and deaths with OSI by time periods of interventions*



As shown in ***Figure 2*** & ***Table 3,*** the epidemic grew at the rate of 0.113 (0.086-0.140) in period 1 but decreased by 115.9% to decay at the rate of -0.018(-0.110 to -0.073) with the implementation of sit-at-home order and other measures in period 2. Similarly, the epidemic which doubled every 6.2 days in period 1 began to halve every 37.7 days with the implementation of sit-at-home order and other measures in period 2. Following the expiration of the first sit-at-home order in period 2, growth was resumed at the rate of 0.103 (0.0774 -0.129) with a doubling time of 6.7 days (5.4 - 9.0) in period 3 but growth was slowed down by 83.5% (0.017) in period 4.

Figure 2 *Fitted growth rate by the 4 time periods of anti-contagion interventions*



As in F***igure 3, 4***, at the start of first period, the Rt was highly variable with large degree of uncertainties [3.77(0 - 7.42)] partly due to low incidence, declined to 1.65 (0.78 - 2.46) at the end of the period, further dropped by 39.4 % [1.08 (95%CI 0.25 -1.78)] at the end of period 2, then rose by 24.1 % [1.34 (95% CI 1.11 - 1.54] and with a 9.7%, Rt fluctuates around 1 in period 4.

Figure 3 *Time-varying reproduction number by 4 periods of analysis*

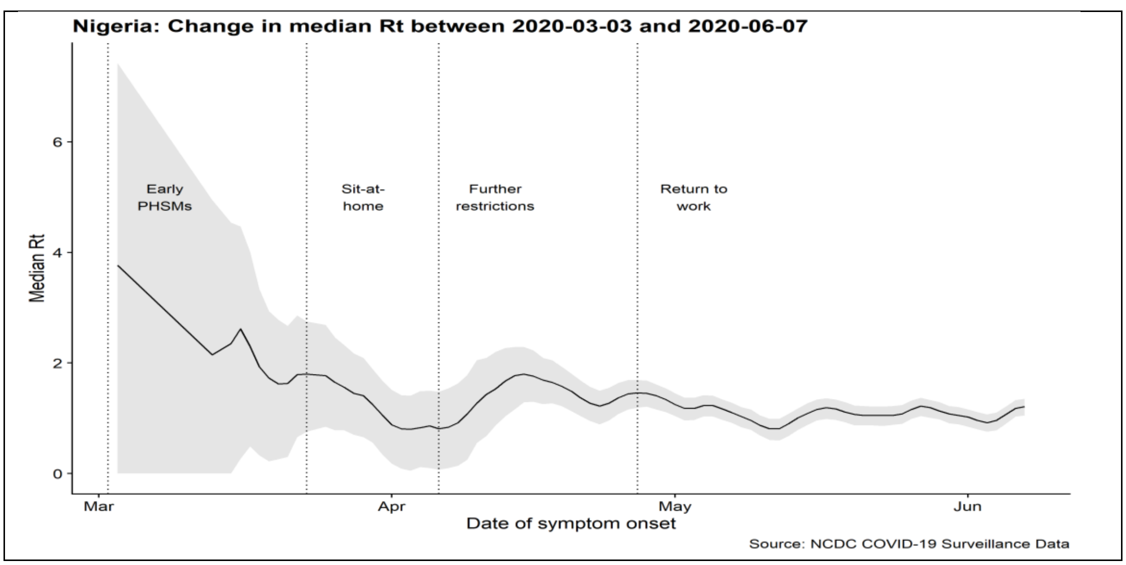
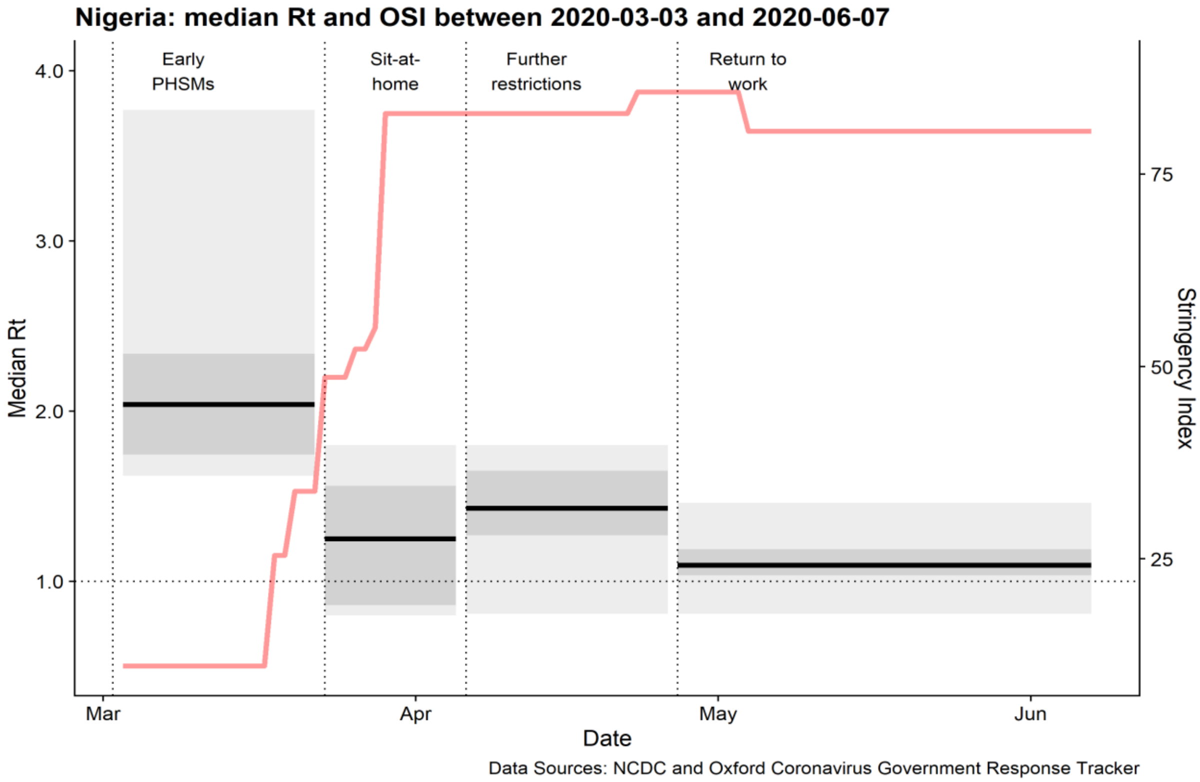


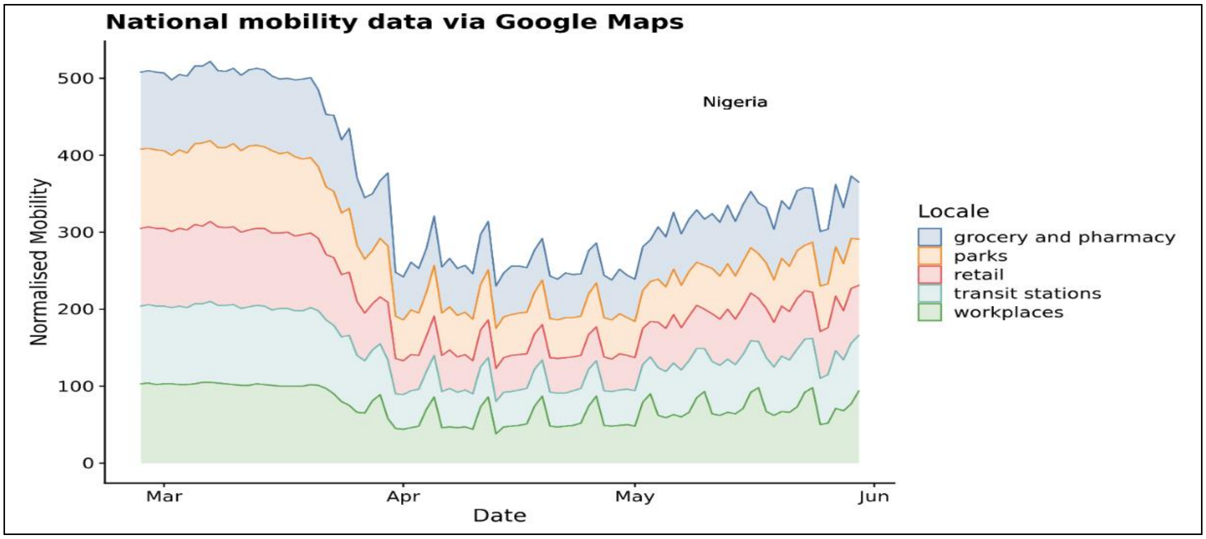
Figure 4 *Time-varying reproduction number and stringency index by period of analysis*



As observed from ***figure 4***, as OSI (represented by the pink line) increases, Rt dropped in period 2 with a further decrease in period 4 following most stringent implementation of anti-contagion measures towards period 3 ending and start of period 4.

As a proxy for compliance, the analyzed national mobility data (***figure 5***) shows a decreasing trend in national mobility in all categories from late March and plummeting just before mid-April, coinciding with period 2 when Rt was lowest following the implementation of sit-at-home order. The trend was maintained with a few spikes around mid-April and further decreased slightly around late April before increasing again with the relaxation of restrictions in early May. The decrease in Rt with increase in mobility in period 4 could be indicative of increased compliance to PHSMs as recommended by NCDC.

Figure 5 *Nigeria's mobility trend between 27th February 2020 and 10th June 2020*



As may be seen in ***figure 6*** *&* ***7,*** the non-parametric multiple changepoint detection analysis yielded 2 changepoints (using a frequency cut-off of at least 20%): 13th and 27th of April coinciding with the ends of first and second lockdowns in periods 2 and 3 respectively. The date 3rd May is among additional changepoints identified (using a frequency cut-off of at least 16%), coincide with eve of lockdown relaxation. Further details are presented in ***Table 4.***

Figure 6 *Identified changepoints (frequency cut-off of 20% or more of model runs)*

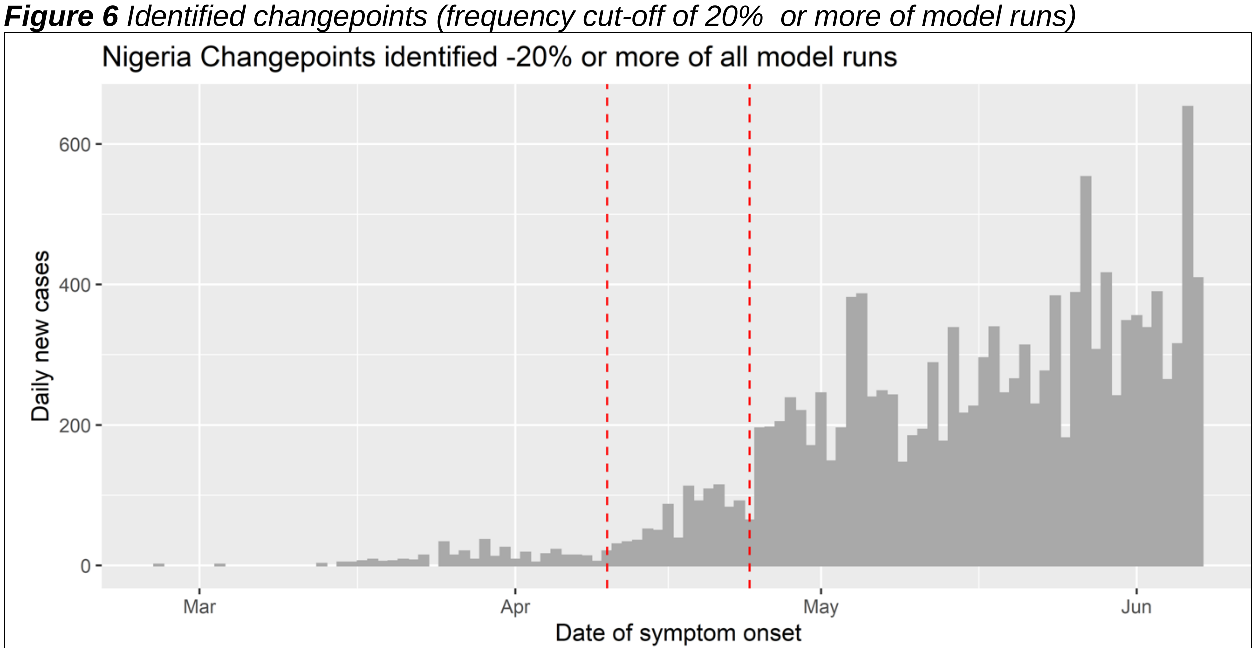


Figure 7 *Identified changepoints (frequency cut-off of 16 % or more of model runs)*

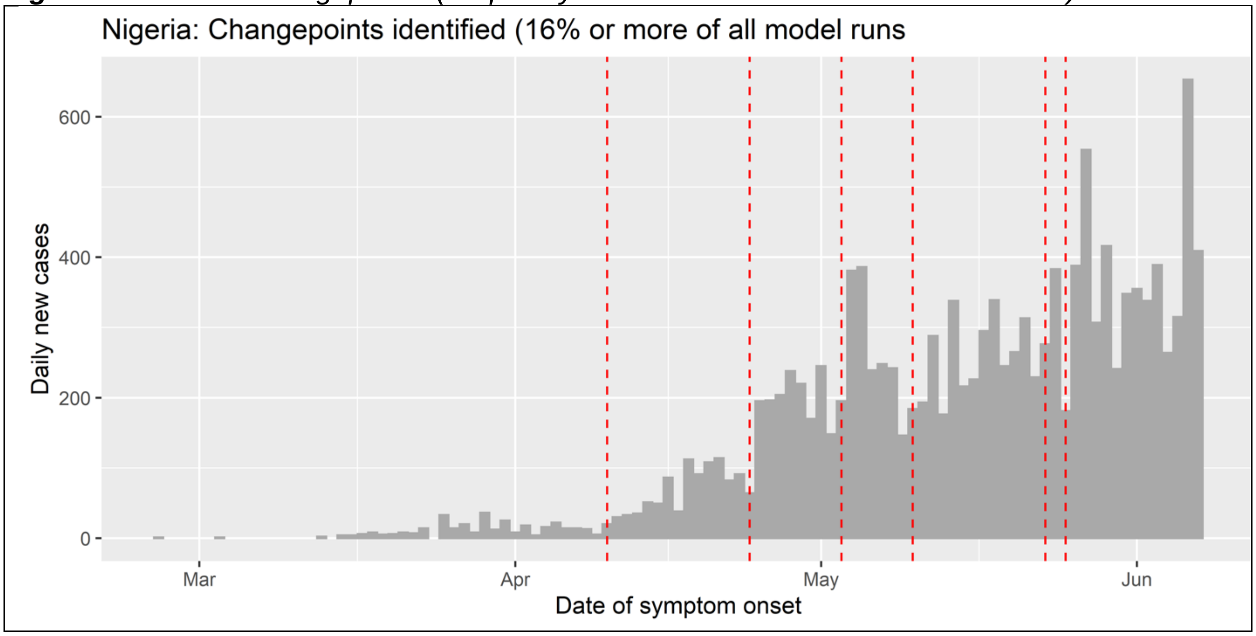


Table 4 *Identified changepoints*

Cut-off used	Change points identified	Significance
20 % or more	2020-04-13	End date of first sit-at-home order/lockdown
	2020-04-27	End date of extension of first sit-at-home order/lockdown
16 % or more	2020-04-13	As above
	2020-04-27	As above
	2020-05-03	Eve of relaxation of restrictions
	2020-05-10	It's a Sunday – perhaps due to reporting delay
	2020-05-23	-
	2020-05-25	-

6 Discussion and Recommendations

6.1 Discussion

This study examines the effect of national anti-contagion interventions on the trajectory of COVID-19 epidemic in Nigeria and the roles of stringency of the interventions and compliance in achieving improved control of the epidemic. There was a huge decline in growth rate (115.6% decrease) in second period of the analysis following the implementation of several drastic PHSMs including sit-at-home order in 3 Nigerian states-hotspots, a ban of outdoor gathering of all sizes and closure of schools. This observation aligns with findings from studies by Voko *et al* and Hsiang *et al* in which a combination of non-pharmacological interventions was found to be associated with decrease in epidemic growth rate [12],[13]. In period 3 when sit-at-order was extended to more Nigerian states (***Table 5*** *in* ***Appendix****)*, the epidemic grew again but the growth rate was still less than the pre-lockdown growth rate by about 9 %. Like the decay rate, the epidemic transitioned from doubling every 6.2 days in period 1 to halving every 37.7 days following implementation of comprehensive physical distancing measures in period 2. Doubling time was prolonged by 34.3 days with gradual easing of restrictions in period 4 (compared to period 3). This could be attributed to increase in stringency index from 82.9 to 85.7 after middle of period 3 towards the start of period 4 (***Figure 5****)*.

With the exception of period 3, the Rt fell in every successive period from above 3.5 in period 1 to a little above 1 in period 4. Again, these observations are consistent with findings from studies by Pan *et al* and Flaxman *et al* in which a range of PHSMs successfully drove down the Rt below 1[15], [14] . The slight increase in growth rate, doubling time and Rt observed in period 3 (***Table 3****)* when OSI was most stringent and mobility at the lowest level could be explained by expansion of the scope of interventions to more Nigerian states and increased sensitivity of surveillance system to detect more cases. Since the re-opening of businesses on 3rd May 2020, the Rt values have remained around 1 as of 10th June 2020, possibly suggestive of good observance of social distancing and other safety guidelines as recommended by public health authorities.

6.1.1 Strengths

This study used real-time data from the ongoing COVID-19 epidemic to directly quantify the transmissibility metric (Rt) of the epidemic reliably using a computationally less intensive but equally reliable methods with minimal number of unknown epidemiological parameters (only serial interval) , thereby reducing the possibility of biases resulting from assumptions of values for several epidemiological parameters with unknown values, as is the case for many studies on COVID-19 using sophisticated modeling techniques. In addition to quantifying the effect of the anti-contagion measures, this study assessed the roles of stringency level and compliance in the control of the epidemic. Also, different methods were used to affirm/validate the dates of implementation of some key interventions using multiple changepoint detection analysis and to some extent, national mobility patterns.

6.1.2 Limitations

This study has some obvious limitations. First, the testing strategy in Nigeria is targeted mostly at symptomatic individuals and consequently, asymptomatic and pre-symptomatic cases are either not picked up at all or not diagnosed promptly. This could lead to under-ascertainment of cases and by extension, under-estimation of the true epidemic growth rate and doubling time and inaccurate estimation of Rt. However, the observed national trend in the Rt appears similar to those observed in Nigeria's 3 highest COVID-19 burdened states – Lagos, FCT and Kano (a decrease in period 2, slight increase in period 3 and fluctuation around 1 in period 4) as shown in ***Figure 9***. Furthermore, regardless of the assumed ascertainment rates – either 20% or 40%, the national trend in Rt appear similar to the observed trend (see ***Figure 10*****)**. Perhaps, a possible way to minimize potential bias resulting from differential testing strategies over time is to predict the expected daily new infections from the death counts (more reliable) using mathematical modeling as done by Flaxman *et al* [14] but it may be difficult to make reliable predictions with a very low COVID-19 death incidence of ~1.8 deaths per million population (382 deaths by 206 million) in the case of Nigeria. Estimates of Rt computed based on death counts were unstable and fluctuated around 1 (see ***Figure 8***).

Second, the lag time between laboratory case detection and reporting was quite an issue especially during weekends. The reporting delay could lead to allocation of some proportion of the intervention effect size to a wrong intervention time period. To minimize this, confirmed case counts were smoothed over a 7-day window period using a smoother.

Third, international air borders were closed a week (less than the 14-day incubation period) prior to the end of the period 1 and individual level data were not provided for imported cases. This could have contributed to over-estimating the true Rt before 23rd March in period 1.

6.2 Recommendations

The following are some of the recommendations (among others) to eliminate or minimize COVID-19 infections and deaths

- The government should continue to strengthen the surveillance system to be able to pick quickly up localized outbreaks, trace all contacts and quarantine as quickly as possible to avoid a potential of second wave.
- Aggressive nationwide awareness campaigns on COVID-19 (need to observe enough physical distance, proper cough etiquette, facemask where physical distancing is impossible…)
- Strengthening of health systems starting with the primary healthcare system to support the national surveillance efforts

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7 Conclusion

Despite some limitations of the data, findings from this study suggest that a combination of non-pharmaceutical anti-contagion policies with high stringency level and compliance are associated with improved control of COVID-19 epidemic in Nigeria. Although the expansion of the scope of interventions seemed to have worsened the control parameters of the epidemic in period 3 but overall, they represent an improvement from those in period 1.

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10 Appendix

***Table 5** Summary of Key Public Health and Social Measures (PHSMs) with Timelines*

	Pre-lockdown	Lockdown		Post-lockdown
	Period 1 (Early PHSMs)	Period 2 (Sit-at-home)	Period 3 (Further restrictions)	Period 4 (Return to work)
Characteristics	< 30 Mar; entry restrictions (plus POE testing, quarantine, contact tracing)	30 Mar - 13 April; Home confinement,	14 April -3 May Enforcement and expansion of PHSMs,	4 May onwards Phased easing of restrictions
Epidemiological situations	Sporadic cases mostly imported (*figure 1*).	Decreasing incidence of reported cases	Increasing trend of reported cases, local transmission	Decreasing trend of reported cases
Key PHSMs	18 Mar: • Point of entry screening • Quarantine • Mass gathering restrictions 20 Mar: • Int'l flights limited to 2 airports 23 Mar: • Int'l flights suspended	30 Mar: • Sit-at-home order in 3 states • Inter-state travel ban • School closures • Ban on all mass gatherings 4 Apr: • 2 reference labs activated, increased testing	14 Apr: • Sit-at-home order extended 15 Apr – 3May: • Stricter enforcement of PHSMs • Lockdowns were extended to other Nigerian states • Screening scale-up	4 May: • Phased easing of restrictions • Reduced working hours by 1/2 • Face masks mandated • Physical distancing • Hand washing practices • Gatherings of < 20 people allowed

Figure 8 *Median Rt (based on death counts) with periods of key interventions*

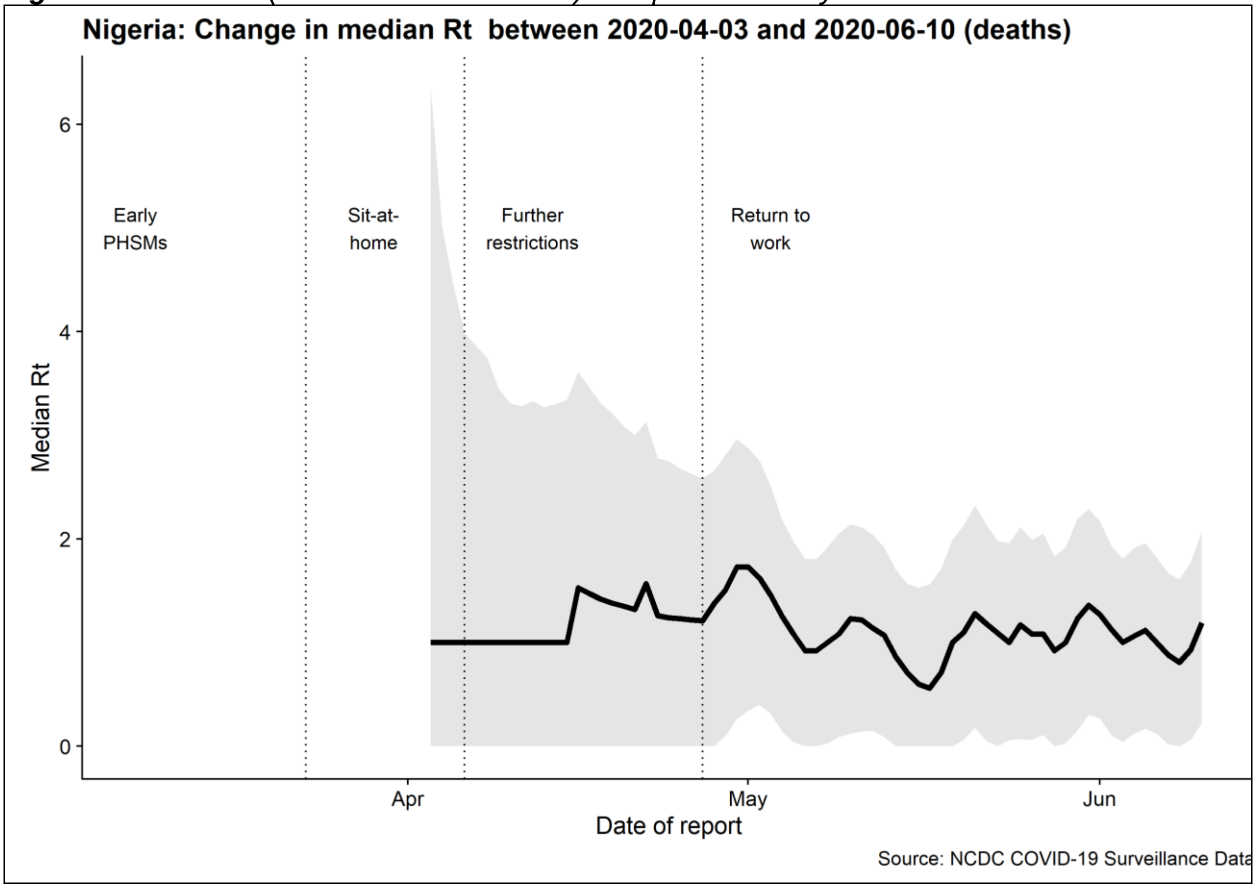


Figure 9 *Time-varying reproduction number in Nigeria's 3 most affected states-Lagos, FCT, Kano*

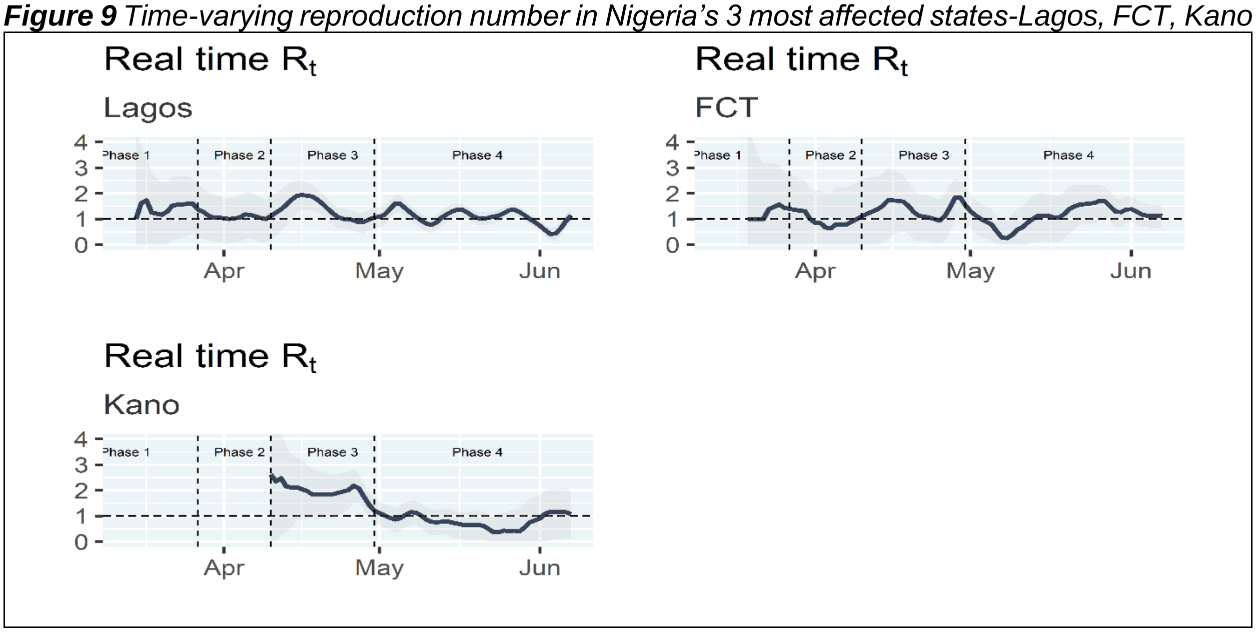
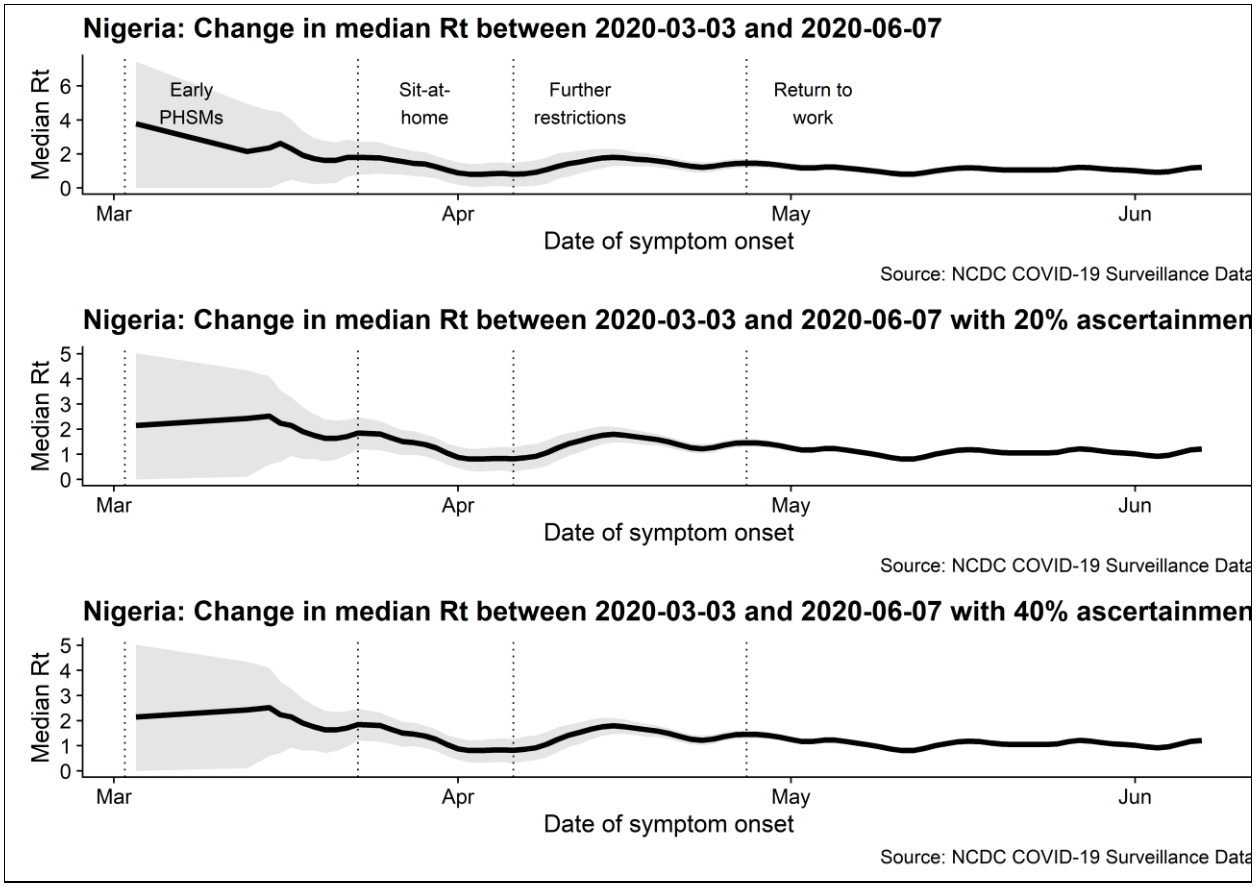


Figure 10 *Rt based on observed case count, 20 % and 40% case ascertainment rates*



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11 Abstract in French (Résumé en Français)

Pertinence Les interventions non pharmacologiques constituent le pilier de la réponse du Nigéria à l'épidémie de la maladie du nouveau coronavirus 2019 (COVID-19). La mesure dans laquelle le niveau de rigueur et la conformité déterminent le succès de ces interventions mérite plus d'attention.
Objectif Évaluer l'impact des interventions nationales anti-contagion sur la progression du COVID-19 au Nigéria et l'étendue de la dépendance de l'impact sur le niveau de rigueur et de conformité aux interventions.
Conception de l'étude et population Cette étude est une expérience naturelle utilisant des méthodes de séries chronologiques interrompues pour examiner les effets de l'intervention et appliquer des analyses de séries chronologiques de cas confirmés (et de décès) de COVID-19 au Nigeria par date de notification et apparition des symptômes entre le 28 février 2020 et 10 juin 2020 rapporté par le Nigeria Center for Disease Control (NCDC).
Interventions Les interventions nationales de lutte contre la contagion avec des échéanciers collectés auprès du NCDC, des PTF et de l'ACAPS ont été divisées: période 1 (<30 mars, pré-verrouillage, restrictions de mouvement transfrontalier international), période 2 (30 mars-13 avril, verrouillage dans 3 États , fermetures d'écoles, interdiction des rassemblements de masse, restrictions locales de mouvement transfrontalier), période 3 (14 avril -3 mai, application stricte des restrictions, extension du verrouillage à d'autres États) et période 4 (à partir du 4 mai, assouplissement progressif des restrictions). Une analyse non paramétrique de détection de points de changement multiples a été réalisée pour identifier les périodes d'interventions au cours desquelles un changement de la pente de l'incidence quotidienne des cas a été observé.
Principales mesures des résultats Le taux de croissance / décroissance épidémique, le temps de doublement / réduction de moitié, le nombre de reproduction variant dans le temps (Rt), l'indice de stringence d'Oxford (OSI) et la tendance de la mobilité nationale ont été évalués en fonction des quatre périodes. Le taux de croissance / décroissance a été estimé en ajustant un modèle log-linéaire par période, puis le temps de doublement / réduction de moitié a été calculé. Les estimations de Rt ont été calculées en utilisant une procédure bayésienne en 4 étapes: estimation de i.) Taux de nouvelles infections par jour λ ii.) Probabilités d'observer k nouvelles infections étant donné λ iii.) Postérieurs de la distribution de probabilité de Rt et iv.) Distribution de probabilité de Rt avec intervalles de confiance à 95%. Les données sur les OSI et les données nationales sur la mobilité recueillies auprès de la Blavatnik School of Government de l'Université d'Oxford et de Google ont également été analysées. Les mesures des résultats avant et après l'intervention ont été comparées.
Résultats Les taux de croissance / décroissance (2,5e - 97,5e centiles) sont de 0,113 (0,086-0,140) dans la période 1, ont diminué de 115,9% à -0,018 (-0,110 à -0,073) dans la période 2, augmenté à 0,103 (0,0774 -0,129)) dans la période 3 mais inférieure à la période 1 de 9% et, diminué de 83,5% à 0,017 (0,008-0,025) dans la période 4. L'épidémie a doublé tous les 6,2 jours (5,0 -8,1) dans la période 1, divisée par deux tous les 37,7 jours (6,3 à -9,5) dans la période 2, doublé tous les 6,7 jours (5,4 - 9,0) dans la période 3 et 41,0 jours (27,3 - 82,3) soit une prolongation de 34,2 jours. Le Rt est passé de plus de 3 à 1,65 (IC à 95% 0,78 - 2,46) à la fin de la période 1, 1,08 (IC à 95% 0,25 à 1,78) à la fin de la période 2, soit une diminution de 39,4%, 1,34 (IC à 95% 1,11 - 1,54) à la période 3 (augmentation de 24,1%) et 1,21 (IC à 95% 1,05-1,35) à la fin de la période (diminution de 9,7%). L'OSI est passé de 11,2 au départ et a culminé à 82,9 en fin de 1ère période, s'est poursuivi à 82,9 en 2e période, a grimpé à 85,7 vers la fin de 3e période et 80,6 en 4e période. La tendance des mouvements nationaux a commencé à baisser à

la fin de la période 1 mais a chuté brusquement d'au moins 50% pendant la période 2, est restée au même niveau avec des fluctuations mineures pendant la période 3 mais a augmenté régulièrement pendant la période 4 suite à l'assouplissement des restrictions. Une analyse non paramétrique de détection de points de changement multiples a identifié le 13/04/2020, le 27/04/2020 et le 03/05/2020 comme des points de changement, coïncidant approximativement avec la fin des premier et deuxième verrouillages des périodes 2 et 3, et la veille de l'assouplissement du verrouillage (période 4).

Conclusions: Une combinaison d'interventions nationales anti-contagion semble être liée à une amélioration du contrôle de l'épidémie de COVID-19 au Nigeria, l'efficacité semble être plus élevée avec un niveau plus élevé de rigueur des interventions et de respect de celles-ci. Bien que l'élargissement du champ des interventions semble avoir aggravé les paramètres de contrôle de l'épidémie au cours de la période 3, ils représentent globalement une amélioration par rapport à ceux de la période 1.