COMMENTARY

COVID-19 in Nigeria: Implications for Management of Related Co-morbidities, Prevalent Public Health Challenges, and Future Epidemic Preparedness

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Abstract

The Coronavirus Disease-2019 (COVID-19) pandemic is now well-established in Africa with cases reported from all countries on the continent. Despite the significant progress that has been made in the response to the pandemic in Nigeria, relative to the period of Ebola epidemic, the currently reported number of COVID-19 cases are likely under-estimates of the true number of cases. This is attributable to restricted testing capacity due to limited technical, infrastructural, financial, and logistical capacity to rapidly scale-up testing. In this article, we explore the impact of the COVID-19 pandemic on management of related co-morbidities and the major prevalent public health challenges, including mental health, in Nigeria, Africa's most populous country. We also discuss the most current knowledge about candidate vaccines for the control of the novel coronavirus (SARS-CoV-2) strain. The interactions between COVID-19 and the endemic public health challenges in Nigeria further highlight the linkage between infectious diseases and poverty, and emphasise the need for a sustained increase in investments in the general public health system that is geared toward achieving Universal Health Coverage in Nigeria.

Keywords: *COVID-19; Nigeria; Comorbidity; Mental Health; Epidemic preparedness*

INTRODUCTION

The Coronavirus Disease-2019 (COVID-19), caused by the novel *severe acute respiratory syndrome coronavirus-2* (SARS-CoV-2), was declared a pandemic by the World Health Organization (WHO) on 11th March 2020 (World Health Organization, 2020a). While the COVID-19 pandemic is now well-established in Africa with cases reported from all countries on the continent, the epidemic is still unfolding in the region. As at the time of compiling this report on 25thAugust 2020, a total of 1,195,702 confirmed cases of COVID-19 and 28,007 deaths have been reported on the African continent, with South Africa (611,450), Egypt (97,478), Morocco (53,252), Nigeria (52,548) and Ethiopia (42,143) having the largest numbers of confirmed COVID-19 cases (African Centre for Disease Control and Prevention, 2020).

While the initial cases on the continent were "imported" from travellers who came from Europe and Asia in most cases, the recent increase in the number of COVID-19 cases and the associated transmission pattern suggest the establishment of community transmission of the novel SARS-CoV-2 virus, particularly in African countries with cases in thousands. However, it has been suggested that the currently reported numbers of COVID-19 cases in Africa are very likely under-estimating the true number of cases, given the reality of restricted testing capacity in most countries due to the limited technical, infrastructural, financial and logistical capacity to scale-up testing (Kavanagh et al., 2020). In spite of this, significant progress has been made in the mounting of coordinated and rapid epidemic responses on the continent, relative to the period of Ebola epidemic, due to the leadership provided by the Africa Centre for Disease Control and Prevention (Africa CDC), World Health Organization (WHO) Regional Office for Africa (WHO-AFRO), and the strong leadership and commitment by governments of African countries themselves (Kavanagh et al., 2020).

Over the past five months, there has been considerable increase in morbidity and mortality due to the COVID-19 pandemic in Nigeria. There are currently more than 50,000 cases reported from all six geo-political zones in Nigeria, comprising of 11,730 active cases, 1,010 deaths and 40,281 recovered patients as at 27th August 2020 (Nigeria Centre for Disease Control, 2020). A comprehensive response to the rising COVID-19 challenge in Nigeria has been coordinated by a multidisciplinary Presidential Task Force (PTF) established by the President of Nigeria, which shows clear political commitment toward reversing the epidemic. The major objectives of the PTF and the Federal Ministry of Health (FMoH) of Nigeria are primary and secondary prevention of man-to-man transmission, provision of isolation and quarantine facilities, provision of diagnostic and laboratory facilities, research to produce specific treatment and vaccine, and minimization of the socio-economic impact on the general populace (World Health Organization, 2020a).

SCOPE

In this paper, we explore the impact of the COVID-19 pandemic on related co-morbidities and the major prevalent public health challenges, including mental health, in Nigeria, Africa's most populous country, as well as the most current knowledge about candidate vaccines for the control of SARS-CoV-2. We also discuss the need to build clinical research capacity to design and conduct clinical trials in Nigeria. These are with a view to identifying immediate priorities and potential long-term strategies that will further strengthen Nigeria's epidemic preparedness.

COVID-19 and Co-Morbidities

The clinical presentation of COVID-19 can be classified based on severity into mild, moderate, severe, and critical cases (Cascella et al., 2020; Wang et al., 2020). Some of the most frequent presenting symptoms of COVID-19 are fever, cough, dyspnea, sore throat, headache, rhinorrhea, fatigue, myalgia, and conjunctivitis (Di Gennaro et al., 2020). These symptoms are like those of many other common infectious diseases in Africa, including malaria, viral and bacterial respiratory diseases among others, thus posing significant challenge for accurate diagnosis in health care settings. Early studies have shown that majority of subjects with real-time reverse transcription-polymerase chain reaction-(RT-PCR)-positive throat swabs for SARS-CoV-2 are asymptomatic, majority of COVID-19 cases are mild or moderate cases, and that the disease is characterised by a virus-induced severe acute respiratory distress syndrome in its most severe form (Hassan et al., 2020; Pascarella et al., 2020). The pathophysiological mechanism of COVID-19 is still not fully understood and is a subject of ongoing research. However, several clinical studies have reported that severe COVID-19 cases or the need for intensive care unit (ICU) admission and mortality are more likely to occur in the elderly, in men, and/or in patients with underlying co-morbidities including diabetes mellitus (DM), cardio-cerebrovascular diseases, hypertension, renal diseases, cancers, and chronic pulmonary diseases such as asthma (Guan et al., 2020; Hussain et al., 2020; Wu and McGoogan, 2020; Zhou et al., 2020).

There are currently no reliable population-based estimates of the burden of the non-communicable disease (NCD) conditions that might predispose COVID-19 cases to develop more severe disease in Nigeria, and in most of Africa. While the burden of diseases in Nigeria continues to be dominated largely by infectious diseases, a recent Global Burden of Disease study suggests that the age-standardized rates of many NCDs such as diabetes mellitus, cancers and cardiovascular diseases are on the increase in many African countries, Nigeria inclusive (Gouda et al., 2019). A recent survey conducted by the WHO in 155 countries found that prevention and treatment services for NCDs have been severely affected since the COVID-19 pandemic began, with low- and middle-income countries (LMICs) most affected (World Health Organization, 2020b). There is no published empirical data of the numbers of available ICU beds and/or ventilators in public health facilities in Nigeria. However, report from the WHO shows that there are only about five ICU beds per million population in 43 African countries, while there are fewer than 2000 functional ventilators available in public health facilities in 41 countries, with 10 countries having none at all (World Health Organization, 2020a). The routine public health service in Nigeria that is used by most of the population is already over-stretched, and characterized by insufficient financial and human resources, accompanied by incessant strike actions by the medical, nursing and allied health staff. Taken together, these suggest that an unmitigated COVID-19 epidemic in Nigeria will pose a significant challenge for medical management of patients who might develop severe or critical forms of COVID-19, particularly those with underlying co-morbidities as highlighted.

Contrary to the prediction of millions of COVID-19 cases and deaths in Africa due to large population densities and weak national health systems on the continent, the reported morbidity and mortality from COVID-19 in African countries are relatively lower compared to countries in Europe and the Americas, more than four months after the first case was reported in Africa (Mbow et al., 2020). A recent study reported relatively lower case fatality rates of COVID-19 in Kenya and Nigeria when compared to Italy and United States of America (USA), using data from publicly available repositories collected since the first case of COVID-19 was reported in Africa (Njenga et al., 2020). The authors opined that Africa's more youthful population, with a

median age of <20 years compared with Europe and USA (median age >38 years), may have contributed to the low numbers of severe COVID-19 cases and mortality, while the "favourable" warm weather conditions on the continent might decrease the transmissibility of SARS-CoV-2 in Africa. However, it is important to state such opinion needs to be interpreted within the context that the reported numbers of COVID-19 cases and deaths in Africa is a function of the strength and coverage of the testing and surveillance system in each country. COVID-19 testing capacity in Africa is known to still be mostly insufficient, when compared to testing rates in high-income countries in Europe and the Americas (Our World in Data, 2020). Also, there is still no scientific evidence that warm weather conditions will reduce the effectiveness of SARS-CoV-2 transmission to an extent that few additional interventions are needed to curb its spread (O'Reilly et al., 2020). Taken together, it therefore remains unclear if Africa is spared from substantial COVID-19 cases and/or deaths or whether the observed COVID-19 experience reflect differences between Africa and the most affected countries in testing capacity, reliable reporting and death registration, lockdown stringency, demography, environmental exposures, and genetics among others (Mbow et al., 2020).

Available definitive treatment options for COVID-19 are limited. Remdesivir, an anti-viral drug previously developed for treatment of Ebola virus, is the only medication that was recently granted accelerated approval for treatment of COVID-19 by the United States Federal Drug Agency (FDA) (U.S Food and Drug Administratin (FDA). This followed evidence in the preliminary report from a randomised controlled trial that it shortens time to recovery in hospitalised COVID-19 patients, when compared to placebo (Beigel et al., 2020). This drug is still mostly unavailable in Nigeria and in the rest of Africa. There are now several on-going multi-country clinical trials, including trials in Nigeria, evaluating the efficacy of other possible treatment options for COVID-19. These include, among others, Lopinavir/Ritonavir, hydroxychloroquine and chloroquine taken together with azithromycin, Tocilizumab, which is a recombinant humanized monoclonal antibody that binds to the interleukin-6 receptor, as well as the use of convalescent plasma for treatment (Di Gennaro et al., 2020; Jin et al., 2020).

Covid-19 and Mental Health

The COVID-19 pandemic has profoundly shaken the fabric of our global society including the sustaining background of physical and mental health (Djalante et al., 2020). While the physical effects have been explored further, discourses on the fulcrum of mental component upon which the beam of physical health stands often do not appear (Kar et al., 2020). A recent online survey in three of COVID-19 hotspots in Nigeria (i.e. Lagos and Ogun States, and the Federal Capital Territory in Abuja) found relative increases in mental health issues among the general population (Olibamoyo *et al.*, in print). The increasing mental health concerns likely will affect vulnerable populations such as the elderly, children, pregnant women, those with chronic illnesses, those with pre-existing mental health problems, those with substance use disorders, migrant workers, healthcare professionals and even patients with COVID-19 (Chen et al., 2020). To date, there are still no data-driven specific recommendations with respect to addressing the mental health issues during the COVID-19 pandemic in Nigeria.

A review of studies on past pandemics has highlighted that quarantine, isolation and social distancing are risk factors for mental health issues across lifespan, such as anxiety, depression, suicide, domestic violence, alcohol and substance abuse and cyber bullying (Wind et al., 2020). Also, stigma and fear can be important barriers against seeking healthcare, social inclusion and trust in orthodox health agencies, while public perceptions of risk can lead to mass panic among

the general population, as well as disproportionate allocation of healthcare resources (Barrett and Brown, 2008). Research studies that include people with lived experience are needed to understand the psychological and socio-economic outcomes of policies used to manage a pandemic, such as unemployment, financial insecurity and poverty, and these will help in finding ways to address these issues (Baldwin and Tomiura, 2020; Frasquilho et al., 2016; Holmes et al., 2020).

Some extant studies have highlighted difficulties for persons with pre-existing mental ill-health with the measures taken to contain spread of the virus. These include the perception of the use of facemasks as threatening and that it amplifies pre-existing inequalities both in the society and at health care facilities (Wind et al., 2020). Apart from these, there is a need for repeated community surveys to obtain snapshots of the current situation, and a grasp of the effects of COVID-19 on the risk of anxiety, depression and other outcomes such as rape, self-harm, domestic violence, and suicide. More than 90% of enrolled learners are currently out of school (Lee, 2020). For a large proportion of children and adolescents, this means lack of access to resources they engage with routinely in schools, including mental health or peer support (Eshraghi et al., 2020). Children with special educational needs are particularly at increased risk for mental ill-health when daily routines are disrupted; they miss out on therapeutic sessions to develop essential skills (Eshraghi et al., 2020). Social distancing measures can result in social isolation and domestic abuse and increased risk of child maltreatment in homes with pre-existing family dysfunctions (Lee, 2020). Accordingly, sensitive frameworks for detecting and managing these are important.

Taken together, it is essential to incorporate mental health-related interventions in the COVID-19 responses in Nigeria. These will allow short term responses that include monitoring of reported rates of mental ill-health and anxiety-related issues, organization of appropriate services, determination of the efficacy of digital and non-digital interventions, and evaluation of models of implementation (Greer et al., 2019). And for the long term, there is a need to determine the mechanisms that could explain rates of common mental health issues, to understand the role of psychosocial factors in buffering the impact of COVID-19 on mental health, and to ascertain the long-term consequences of COVID-19 on the well-being of the general population with particular attention to the vulnerable groups (Holmes et al., 2020). Pertinent questions would include what the optimal structures for mental healthy life and social distancing are, as well as what are the psycho-structural factors that protect or worsen mental health of different categories of populations? Consequently, findings will help to develop interventions that enhance identified protective factors and mitigate the identified risk factors in differential populations. These call for an interdependent framework that includes: (1) the inclusion of mental health perspective to the COVID-19 pandemic response to inform Nigerian population-level behaviour change; (2) rigorous scientific and ethical reviews of collaborative protocols to safeguard patients, participants, and uphold research standards; and (3) a framework for prioritisation and coordination of policy that is relevant for psychological, social and neuroscientific researches in Nigeria (Holmes et al., 2020).

Therefore, it is important to have a multidisciplinary network whereby professionals in fields such as psychiatry, psychology, clinical medicine, public health, health economics, behavioural/social sciences and neuroscience, collaborate with people with lived experience of mental health issues in COVID-19 pandemic to address these mentioned priorities. Such organised collaborative multidisciplinary networks will open doors to understanding the

psychosocial and neuroscientific effects of COVID-19 pandemic on mental health and allow us as a nation to respond to the immediate needs, while applying these lessons to the likely future demands.

COVID-19, Tuberculosis, and HIV

Long before the emergence of the COVID-19 pandemic, tuberculosis (TB) and HIV have remained perennial health priorities in sub-Saharan Africa. Currently, Nigeria ranks among the high-burden countries worldwide for both diseases, with approximately 40,000 new TB cases each month, and about two million people living with HIV (PLWH) (UNAIDS, 2018; World Health Organization, 2019a). In Africa, Nigeria inclusive, HIV drives TB epidemic while TB-HIV co-morbidity impacts on mortality; consequently, TB co-occurring with HIV has stretched the capacities of already vulnerable health systems, and therefore has been targeted as a main priority for control efforts (Adepoju, 2020). The common thread linking these diseases is that they have natural capacities to stretch the already vulnerable health systems in different ways. While it is still unclear how COVID-19 influences TB and HIV, it is rational to expect poorer outcomes especially in populations like Nigeria with a relatively higher prevalence of TB and HIV infection, as well as in patients with significant post-TB lung damage (Motta et al., 2020; Togun et al., 2020). However, the pandemic offers an opportunity to assess the shared aspects of COVID-19, TB and HIV, as well as the challenges and lessons learned from the control efforts of each of them that could be of mutual benefit (Alagna et al., 2020).

COVID-19 and TB

TB and COVID-19 are similar in the way they present, and this is challenging for the control measures of both diseases. For example, a patient with cough, fever or breathlessness could be COVID-19, TB, or any other respiratory disease (Amimo et al., 2020). Due to the social stigma which is currently associated with having a cough or being unwell, TB patients are more likely to be viewed with more scrutiny, given the fear of COVID-19. This could result in people being afraid to go to healthcare facilities when they have such symptoms that, in fact, could be caused by TB (Saunders and Evans, 2020; Togun et al., 2020). Overall, people are less enthusiastic about hospital visits due to the fear of infection during travel or at the hospitals (Pang et al., 2020).

At health facilities, the competing needs of COVID-19 have necessitated reassignment of TB-staff and diversion of TB-diagnostic materials such as GeneXpert machines to be used for COVID-19 services (Erunke, 2020; Saunders and Evans, 2020). This may further reduce the access to services for patients with TB symptoms seeking care with an inevitable delay in diagnosis and treatment (Pang et al., 2020; Togun et al., 2020).

Furthermore, with current TB patients spending prolonged time indoors and with reported difficulties with starting or continuing anti-TB treatment due to the lockdown, we expect an increase in household TB exposure and transmission especially among susceptible populations like children below five years and PLWH (Egere et al., 2017). Likewise, isoniazid preventive treatment (IPT) for household members is likely to be severely weakened due to the strained health systems that focus limited resources on diagnosis and treatment of COVID-19 (Saunders and Evans, 2020; Togun et al., 2020). Other expected challenges may include disruptions in the production and transportation of anti-TB medicines and supplies, including child-friendly formulations, interruption of treatment, and the indirect negative impact of lowered household

income, missed health visits and vaccination further increasing the risk of poor outcomes (Pang et al., 2020; Saunders and Evans, 2020). COVID-19 will likely worsen the quality and reach of TB control efforts in Nigeria, given the likely negative impact of the pandemic at both individual and health system levels (Togun et al., 2020). This will potentially increase the number of the "missing" TB cases, and further set Nigeria back in achieving the WHO's target of ending the TB epidemic by 2035 (World Health Organization, 2015a).

In view of the above, it is reasonable to assume that the gains made against TB are at risk of being reversed by the COVID-19 epidemic in Nigeria. Priorities need to be given to key populations that are vulnerable to TB service interruptions and more harm during and after COVID-19. Strategies may include HIV services linked to COVID-19 screening and care, sustained access to HIV services that integrate physical distancing measures, provide virtual consultations, as well as monitoring and evaluation service for continuity and improved outcomes. We suggest that the preservation of essential TB services for key populations, the promotion of safety and responsibilities of stakeholders for TB and the sustenance of the response strategies to COVID-19 in ways that are sensitive to the current realities of TB populations and stakeholders are right-based strategies that are viable.

COVID-19 and HIV

The effect of COVID-19 on the clinical course of HIV, or vice-versa, is not yet fully understood (Xu et al., 2020). HIV-infected individuals with comorbidities, lower CD4 cell counts, or unsuppressed viral load might be at an increased risk of severe COVID-19 (Vizcarra et al., 2020). Also, there is still no evidence that any specific antiretroviral drug (ARV) alters COVID-19 severity (Vizcarra et al., 2020). Therefore, caution is needed when interpreting the incidence and clinical course of COVID-19 among PLWH compared with the HIV-negative population (Jones et al., 2020).

The COVID-19 pandemic has disrupted the existing HIV care continuum, with an ensuing negative impact on the relationship between frontline staff and their clients (Pinto and Park, 2020). HIV testing has been stifled by the restrictive measures put in place to curb the COVID-19 pandemic, thus threatening the realisation of the UNAIDS goal to end AIDS by 2030 (Mhango et al., 2020). Furthermore, the restrictions come with other unintended consequences such as the global slowdown in drug production lines and the restriction of flights affecting logistic services, with consequent shortage of ARVs. Movement restrictions within the country may also lead to challenges for PLWH in accessing health facilities for their medicines. This could lead to losses-to-follow-up, poor adherence, higher risk of transmission and a rise in new infections (Oladele et al., 2020). All of these could be worsened by the redirection of dedicated HIV donor funds to COVID-19 related services (The Global Fund, 2020). Therefore, Nigeria's HIV control efforts must be maintained during this COVID-19 crisis or else there could be a resurgence of HIV (Oladele et al., 2020).

Significant progress in the control of HIV might be upturned if adequate care and caution are not proactively taken. The right-based and social justice approaches to continued HIV services adjusted to the realities of COVID-19 are essential. Rapid survey of key populations including the experiences of persons with HIV and AIDS are required to inform contextualized feasibility studies of digital and non-digital interventions for these key populations.

In summary, with COVID-19 at the front-and-centre globally, it is essential to remember that TB and HIV have not disappeared from Nigeria. If so, we can do more than watch as our existing health problems become increasingly neglected, and thus prevent predictable adverse outcomes. TB and HIV remain global and local health emergencies and need our attention more than ever, given that significant resources are now being diverted to COVID-19 management. Priorities and informed strategies need to be upheld for these populations where the preservation of essential services for them are not denied but instituted in ways that are reflective of current data-driven realities of COVID-19.

COVID-19 and Malaria

The incidence rate of malaria declined globally between 2010 and 2014, but the decline slowed down and has remained at similar levels from 2014 through to 2018 (World Health Organization, 2019d). This raises concerns that the targets set to reduce the global malaria morbidity from 2015 levels by 75% in 2025, and 90% in 2030, may not be achieved (World Health Organization, 2015b).

In 2018, Nigeria accounted for an estimated 25% of malaria cases worldwide (WHO, 2019), with 76% of the population living in high transmission areas across ecological zones that define the intensity, seasonality of transmission and mosquito vector species (President's Malaria Initiative, 2019). The impact of COVID-19 on malaria burden vis-à-vis control and intervention efforts in a high malaria burden country like Nigeria would be of great importance. The similarity in general presentation of both diseases, with common symptoms such as fever, headache, body pains and flu-like symptoms, poses questions for the entire malaria research community, such as:

i. Would health-seeking behaviour change to significantly impact the current burden and death due to malaria?
ii. What safety measures are adequate to ensure protection of health facility staff and other patients?
iii. How would COVID-19 impact on malaria diagnosis and case management?
iv. Could COVID-19 increase risk and outcome of malaria in infected patients?
v. How can the effect of increased drug pressure on malaria parasites be determined as several antimalarial formulations are being used or proposed for treatment and prevention of COVID-19?
vi. What strategies and control measures can be put in place to track an upsurge or outbreak of malaria during the COVID-19 pandemic?

There is no doubt that these are uncharted territories, which raise more questions than solutions. Therefore, substantive research is needed to generate evidence that could inform the design of policies and interventions. Public health strategies would need to be tailored to address social behaviours such as COVID-19 stigmatisation, self-medication for malaria and general health-seeking behaviour, as these could potentially reverse any gains achieved in malaria control within the past decade. Frontline healthcare practitioners that routinely carry out malaria diagnostic tests are at risk of being exposed to possible COVID-19 cases, and appropriate protective gears need to be available to them (World Health Organization, 2020e). Information on the minimum protective gears, or safety measures to implement in various health facilities, particularly primary health care facilities in peripheral areas, need to be determined.

Due to the non-specificity of malaria symptoms, individuals in a malaria endemic country like Nigeria who present to health facilities with fever or history of fever and no other obvious cause are routinely offered a rapid malaria test (World Health Organization, 2015c). However, routinely eliminating COVID-19 would present peculiar challenges as this requires specialised molecular tests, which are not readily available. Therefore, case management in high malaria burden areas and management of malaria-negative, febrile cases need to be addressed to minimise undue presumptive treatment for malaria.

The prognosis of COVID-19 and malaria co-infection is also a major cause for concern, particularly in vulnerable malaria populations such as in children and pregnant women with malaria-associated anaemia(M Afolabi and Olukosi, 2018; Oladeinde et al., 2012). Their already compromised immunity raises concerns regarding the effect of co-infection with COVID-19. Malaria surveillance needs to be ramped up to get a clearer picture of the malaria situation in Nigeria within the context of the COVID-19 pandemic, and to monitor potential malaria outbreaks or parasite selection for antimalarial resistance.

COVID-19 and Maternal, Newborn and Child Health

The year 2020 is a pivotal time in the history of global maternal, newborn and child health (MNCH). This year, the world begins the final decade in the countdown to the end of the Sustainable Development Goals (SDGs); goal number three of the SGDs include direct emphasis on reducing maternal, newborn and child mortality and stillbirths, and achieving universal health coverage, while also highlighting the importance of moving beyond survival (United Nations, 2015). The year also marks the end of the "Decade of Vaccines" - an ambitious world vision guided by the multisectoral WHO-led Global Vaccine Plan (GVAP) 2011 – 2020, in which all individuals and communities enjoy lives free from vaccine-preventable diseases through universal access to immunisation (World Health Organization, 2019b).

Despite significant progress towards improving maternal, newborn and child survival, as well as immunisation coverage over the last two decades, progress has been uneven across regions and countries, being particularly slow in most of sub-Saharan Africa. It goes without saying that a global health crisis such as the current COVID-19 pandemic risks undermining decades of improvements in health outcomes and care achieved for women and their children in the sub-region (Graham et al., 2020a).

While global mortality rates for COVID-19 appear to be low in children and in women of reproductive age, modelled estimates have shown that collateral damage from the indirect effects of the pandemic on maternal, newborn and child mortality in LMICs could be enormous, and potentially more severe than that of the outbreak (Roberton et al., 2020). Nigeria bears a large proportion of the global burden of maternal, newborn and child deaths, and is at risk of missing all health-related SDG targets (United Nations Inter-agency Group for Child Mortality Estimation (UN IGME), 2019; World Health Organization, 2019c). In 2017, Nigeria's estimated maternal mortality ratio was 917 maternal deaths per 100,000 live births, with approximately 67,000 maternal deaths during that year and accounting for 23% of global maternal deaths (World Health Organization, 2019c). Similarly, high rates are reported for neonatal mortality (36 deaths per 1,000 live births), under-five mortality (120 deaths per 1,000 live births) (United Nations Inter-agency Group for Child Mortality Estimation (UN IGME), 2019). Decades of nationwide disparities in coverage of essential health interventions such as antenatal care, skilled attendance at birth and routine immunisation services, as well as the absence of quality data-

capturing and reporting systems, have masked the true burden of maternal, newborn and child deaths including stillbirths.

Furthermore, endemic poverty and complex humanitarian emergencies resulting from pockets of conflict and civil unrest have compromised access to health care thereby posing an increased risk of death, and a challenge to achieving global targets. It is against this backdrop that the COVID-19 pandemic with the attendant disruption of health systems, decreased access to food, as well as the overall economic fallout (brought about by public health and social measures to flatten the rate of transmission, and intentional choices in responding to the pandemic), is expected to lead to reduced coverage of health interventions that have an impact to reduce maternal, newborn and child deaths, and thereby indirectly increase mortality in these vulnerable groups in the coming months (Roberton et al., 2020). It is expected that most of the additional maternal deaths would be due to post-partum haemorrhage, maternal sepsis and eclampsia, as a result of reduced coverage of childbirth interventions such a parenteral administration of uterotonics, antibiotics and anticonvulsants, as well as clean birth environment (**Table 1**). Additional deaths among newborns and children would result from reduced coverage of antibiotics for neonatal sepsis and pneumonia, and oral rehydration solution for diarrhoea. The immediate impact on nutrition-related mortality would be an increase in the prevalence of wasting to 12.2 – 16.4% (from 10.9%), wasting also being a risk factor for death from other infectious causes. Other nutritional changes such as an increase in the prevalence of stunting (low height-for-age), and its effect on mortality, would only be evident in the long term.

As Nigeria joins the rest of the world in easing the "lockdown" we need to keep in view the fact that the pandemic is far from over as community transmission is widespread in the face of low community testing. In the absence of robust reporting structures, the effect of the pandemic on health service provision or utilisation and on the magnitude of the potential 'excess mortality' remain unknown; both of these are dependent on the severity and duration of the pandemic, as well as government choices in response to the pandemic. Rather than become complacent, we need to optimise strengthening of our health system with view to maintaining routine and essential maternal, newborn and child health services whilst preventing further spread of the virus and caring for those infected (The Lancet, 2020). This will be achieved by providing adequate funding for health facilities to enable them rapidly adapt and/or modify service delivery in response to different COVID-19 transmission scenarios and stages of the pandemic – a so-called 'safety net' around maternal newborn and child health services (Graham et al., 2020b). Despite the set-back to our efforts to achieve national and global health-related SDG targets, with sustained political and financial commitment, it is possible to get back on track and even double the rate of acceleration of progress.

Moving forward, Nigeria needs to invest in research to provide the much-needed robust and reliable local data essential to improve the quality of care, prevent deaths, improve vital statistics, allocate resources, and inform policy and development.

Table 1: Indirect effect of COVID-19 on coverage of maternal, newborn and child health services in Nigeria

Health system component		Underlying Nigerian context (Adeloye et al., 2017; UNICEF, 2020)	Effect of COVID-19 on the health system (Graham et al., 2020b; Roberton et al., 2020)	Potential effects of COVID-19 on coverage of some reproductive, maternal, newborn and child health services (Graham et al., 2020b; Roberton et al., 2020)
Provision of health services (service readiness)	**Availability of healthcare workers**	- Chronic shortage of health workers. (0.4 physicians and 1.2 nurses/midwives per 1,000 population) - Recurrent local and nationwide industrial action by health workers - Low coverage of skilled attendance at birth (only 43% of births attended by skilled personnel)	Further decreased workforce due to: - Government imposed movement restrictions - diversion of healthcare workers to COVID-19 activities - sickness or poor emotional/mental well-being of healthcare workers - less skilled/unqualified health workers assigned to maternity care (locum staff, students, house officers, auxiliary staff)	Reduced availability of essential medical supplies: - hormonal contraceptives - antenatal micronutrient supplementations - antimalarials - childbirth commodities (e.g. uterotonics, anticonvulsants, antibiotics, corticosteroids) - routine child vaccines - treatments for common illnesses (e.g. antibiotics, antimalarials, oral rehydration solution)
	Availability of supplies & equipment	- Poor infrastructure and working environment. - Reliance on importation of medical supplies/equipment - Lack of investment in drug discovery and manufacturing -Low budgetary allocation for health	- Re-allocation of resources to the COVID-19 response - Disruption of domestic supply chains	Drop in coverage of the following interventions: - Parenteral administration of uterotonics to 17.8% – 30.2% (baseline coverage 35.2%) - Parenteral administration of anticonvulsants to 14.3% – 24.2% (baseline coverage 28.2%) - Parenteral administration of antibiotics to 14.9% – 25.3% (baseline coverage 29.5%) - Parenteral antibiotics for neonatal sepsis to 18.9% - 32.1% (baseline coverage 39.4%) - oral rehydration solution to 20.3 – 34.3% (baseline coverage 40%)
Utilization of health services	**Demand for health services**	- Low coverage of ANC (only 57% of women aged 15 – 49 years attended at least 4 visits) - Low coverage of facility births (only 39% of deliveries occurring in a health facility) - Low coverage of health insurance	Decreased use of services due to: - Government imposed movement restrictions - fear of infection and/or separation from family - economic pressure from reduced income	Reduced care-seeking for and delayed access to: - family planning (leading to unintended pregnancies) - antenatal care (leading to reduction in the ANC coverage) - childbirth care (leading to fewer facility births, cancellation/postponement of elective procedures e.g. caesarean section) - postnatal care (lack of post-partum family planning) - routine newborn/child vaccines (skipped or postponed) - curative and preventive services (fewer inpatient beds available; delay in seeking care for illness due to fear of admission)
	Access to health services		Decreased access due to: - lost/reduced income for out-of-pocket expenses/travel costs - lack of trust in the official health system.	

COVID-19 Candidate Vaccines

Globally, vaccination has been recognized as the most potent control strategy for infectious diseases. This approach underscores the unprecedented activities triggered to accelerate the clinical development of vaccines against COVID-19, following its declaration as a pandemic by WHO (World Health Organization, 2020c). As of 25 August 2020, 31 candidate vaccines are at various stages of clinical development while additional 142 candidate vaccines are undergoing pre-clinical testing (World Health Organization, 2020f). **Table 2** gives a summarized outline of the 31 candidate vaccines currently in clinical development.

Preliminary results from leading candidate vaccines evaluated in China (National Institutes of Health, 2020a; Zhu et al.), United Kingdom (Health Research Authority, 2020), and USA (National Institutes of Health, 2020b), showed promising safety and immunogenicity profiles, with concerted efforts geared towards rolling out efficacious COVID-19 vaccines by the end of 2020; a feat that would ordinarily take 10-20 years to achieve. The urgency to stem the tide of the pandemic to minimise the attendant social disruption, humanitarian crisis and negative impact on global economy may justify this radical approach. Nevertheless, the scientific community needs to balance the momentum to roll-out a COVID-19 vaccine within a year, with a few compelling ethical, safety and logistical concerns.

First, some vaccine platforms being adopted to tackle COVID-19 are akin to solving one problem and creating a bigger one in the nearest future. For example, shortening or circumventing pre-clinical studies in vaccine development could potentially miss important safety findings such as antibody enhanced disease (AED) in which people who receive a vaccine become infected with wild virus strain (Poland, 2020). Also, given that SARS-CoV-2 is an RNA virus, it has an unpredictable potential to mutate, leading to disease enhancement following exposure or to vaccines that have short-time effectiveness. More importantly, mutations in the S protein of SARS-CoV-2 raises concerns about the efficacy of an S protein-based vaccine (Jia et al., 2020). It is therefore essential to consider adding more than one relevant SARS-CoV-2 viral antigens to the existing S gene of the virus or identify potential human Angiotensin Converting Enzyme receptor 2 (ACE2) to reduce this risk; although this process would take more time to develop and evaluate, and may possibly frustrate the fast-tracked timelines for a COVID-19 vaccine roll-out.

Second, human challenge studies are being proposed as a method to rapidly evaluate the vaccines for efficacy and thereby accelerate pathways to licensure. However, there is yet to be an ethical framework to implement this approach in the current pandemic. Also, robust ethical and regulatory pathways are needed to implement COVID-19 vaccination schedule for different age groups and people with different co-morbidities. For example, it is uncertain if the same or different vaccines will be required by a healthy adolescent, elderly people with co-morbidities such as Diabetes Mellitus or cardiac diseases, pregnant women or immuno-compromised young people, when limited opportunity exists to carefully evaluate the vaccines in these populations (Poland, 2020).

Lastly, vaccine ‘nationalism’ has emerged as a new phenomenon in the race to defeat COVID-19, with countries leading the vaccine development efforts prioritizing their citizens in the event that the vaccine is proven efficacious. Huge amount of monies has been allocated for mass production of the vaccines in these countries, but similar plans for developing countries such as Nigeria are being championed by COVAX to ensure commitments to vaccine ‘diplomacy’ and equitable access to an effective vaccine across the world (World Health Organization, 2020g).

Nevertheless, given that protecting the entire global community from COVID-19 through vaccination will require significant manufacturing capacity, mutually beneficial cooperation from governments, academic institutions, industry, and global philanthropic partners are needed to fund the bio-manufacturing infrastructure. Also, logistical challenges in the eventual delivery of vaccines, including cost, distribution systems and cold chain requirements need to be thoroughly considered and meticulously planned in low and middle-income countries such as Nigeria.

Table 2: WHO DRAFT landscape of COVID-19 candidate vaccines –25 August 2020 (World Health Organization, 2020f).

COVID-19 Vaccine developer/manufacturer	Vaccine platform	Type of candidate vaccine	Number of doses	Timing of doses	Route of Administration
University of Oxford/AstraZeneca	Non-Replicating Viral Vector	ChAdOx1-S	1		IM
Sinovac	Inactivated	Inactivated	2	0, 14 days	IM
Wuhan Institute of Biological Products/Sinopharm	Inactivated	Inactivated	2	0, 14 or 0, 21 days	IM
Beijing Institute of Biological Products/Sinopharm	Inactivated	Inactivated	2	0,14 or 0,21 days	IM
Moderna/NIAID	RNA	LNP-encapsulated mRNA	2	0, 28 days	IM
BioNTech/Fosun Pharma/Pfizer	RNA	3 LNP-mRNAs	2	0, 28 days	IM
CanSino Biological Inc./Beijing Institute of Biotechnology	Non-Replicating Viral Vector	Adenovirus Type 5 Vector	1		IM
Anhui ZhifeiLongcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences	Protein Subunit	Adjuvanted recombinant protein (RBD-Dimer)	2 or 3	0, 28 or 0, 28, 56 days	IM
Curevac	RNA	mRNA	2	0, 28 days	IM
Institute of Medical Biology, Chinese Academy of Medical Sciences	Inactivated	Inactivated	2	0, 28 days	IM
Inovio Pharmaceuticals/ International Vaccine Institute	DNA	DNA plasmid vaccine with electroporation	2	0, 28 days	ID
Osaka University/ AnGes/ Takara Bio	DNA	DNA plasmid vaccine + Adjuvant	2	0, 14 days	IM
Cadila Healthcare Limited	DNA	DNA plasmid vaccine	3	0, 28, 56 days	ID

Genexine Consortium	DNA	DNA Vaccine (GX-19)	2	0, 28 days	IM
Bharat Biotech	Inactivated	Whole-Virion Inactivated	2	0, 14 days	IM
Janssen Pharmaceutical Companies	Non-Replicating Viral Vector	Ad26COVS1	2	0, 56 days	IM
Novavax	Protein Subunit	Full length recombinant SARS CoV- 2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M	2	0, 21 days	IM
Kentucky Bioprocessing, Inc	Protein Subunit	RBD-based	2	0, 21 days	IM
Arcturus/Duke-NUS	RNA	mRNA			IM
Gamaleya Research Institute	Non-Replicating Viral Vector	Adeno-based	1		IM
ReiThera/LEUKOCARE/ Univercells	Non-Replicating Viral Vector	Replication defective Simian Adenovirus (GRAd) encoding S	1		IM
Clover Biopharmaceuticals Inc./GSK/Dynavax	Protein Subunit	Native like Trimeric subunit Spike Protein vaccine	2	0, 21 days	IM
Vaxine Pty Ltd/Medytox	Protein Subunit	Recombinant spike protein with Advax™ adjuvant	1		IM
University of Queensland/CSL/Seqirus	Protein Subunit	Molecular clamp stabilized Spike protein with MF59 adjuvant	2	0, 28 days	IM
Medigen Vaccine Biologics Corporation/NIAID/Dynavax	Protein Subunit	S-2P protein + CpG 1018	2	0, 28 days	IM
Instituto Finlay de Vacunas, Cuba	Protein Subunit	RBD + Adjuvant	2	0, 28 days	IM
Institute Pasteur/Themis/Univ. of Pittsburg CVR/Merck Sharp & Dohme	Replicating Viral Vector	Measles-vector based	1 or 2	0, 28 days	IM
Imperial College London	RNA	LNP-nCoVsaRNA	2		IM
People's Liberation Army (PLA) Academy of Military Sciences/Walvax Biotech.	RNA	mRNA	2	0, 14 or 0, 28 days	IM
Medicago Inc.	VLP	Plant-derived VLP adjuvanted with GSK or Dynavax adjs.	2	0, 21 days	IM
FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo	Protein Subunit	Peptide	2	0, 21 days	IM

Routine immunisation during COVID-19 pandemic

During the ongoing COVID-19 pandemic, many countries, including Nigeria, adopted public health control measures, such as physical distancing, imposing travel bans and whole population lockdowns, which led to closure of schools and public places. These strict approaches have merits and demerits. While human-to-human transmission of the virus has been drastically curtailed in settings where adherence is enforced, the measures have hugely disrupted routine immunisation against vaccine preventable diseases for children and pregnant women. The Global Polio Eradication Initiative recommended suspending polio vaccination campaigns until the second half of 2020 (Roberts, 2020). Also, the Strategic Advisory Group of Experts on Immunisation (SAGE) of WHO recommended that all preventive mass vaccination campaigns should be paused because of social distancing issues, making more than 117 million children in 37 countries to be at risk of missing age-appropriate vaccinations (World Health Organization, 2020d).

In Nigeria and many other African countries, vaccine hesitancy and refusal have become an important problem in recent years (Hotez et al., 2020). This is further worsened by restrictive measures during the COVID-19 pandemic where parents demonstrated reluctance and fear to attend health care services for their child's immunisation. In other instances, health care centres offering immunisation services were shut down and even after the lockdown was relaxed or lifted, minimal efforts are made to track the unvaccinated children for 'catch-up' immunisation. Given that an empirical study has shown that 140 deaths can be prevented for every one excess COVID-19 death by sustaining routine childhood immunisation, ensuring the continuation of timely administration of routine childhood vaccines is crucial for Nigeria and similar countries. This becomes imperative as no one could objectively predict when COVID-19 curve would flatten in Nigeria. Effective deployment of control measures to protect vaccine providers, children who will be vaccinated, and parents/caregivers who accompany them to the clinics, will be required to reduce the risk of transmission.

Development of clinical/vaccine trial capacity in Nigeria

With a population of more than 200 million people and arguably the largest economy in Africa, Nigeria has a huge potential to become a leader in translational research on the continent. The key attractive elements include an extremely large and diversified population of more than 250 ethnic groups and significant number of health centres and skilled health care practitioners. Notwithstanding the prevalent systemic and infrastructural challenges, the unacceptably high burden of infectious and non-communicable diseases in Nigeria could serve as an impetus to foster the development of an organised clinical/vaccine trial capacity that could entrench the research culture/integrity and scientific rigor required for credible research endeavours.

Paucity of credible data on many vital statistics probably stems from the lackluster attention given to clinical research in Nigeria, resulting in public health policies and planning not being data-driven and evidence-based. Inadequate investments manifesting in poor health performance indices seem to have become a permanent defining factor of Nigeria clinical research system. These challenges could be overcome with political will, commitment of investments and efficient allocation of resources. More importantly, current approaches should foster meaningful collaborations with established research centres in the West African sub-region for opportunities of research attachment programs to obtain hands-on experience at these centres. This approach could guarantee acquisition of practical skills in conducting top-notch clinical research and in attracting competitive grants to conduct translational research in Nigeria.

CONCLUSION

There is still no approved vaccine for the control of SARS-CoV-2. Therefore, preventive options are currently limited to public health interventions that minimise the spread of the virus in the general population, and the optimisation of infection control during provision of clinical care for sick patients. Without gainsaying, the public health and socio-economic impacts of COVID-19 in Nigeria will be disproportionately worse on the poorest and most disadvantaged people in the population, who often bear the largest burden of both communicable and non-communicable diseases and also have the least access to health care. These interactions between COVID-19 and the endemic public health challenges in Nigeria further highlight the linkage between infectious diseases and poverty. The current mandate to conduct research as part of the ongoing comprehensive response to COVID-19 should include the conduct of a large-scale population-based sero-prevalence survey nationwide to accurately determine the prevalence of SARS-CoV-2 in Nigeria. Such a survey could also be an opportunity to establish a proper demographic and health surveillance system (DHSS) in Nigeria, which could be a platform for generating reliable data on the epidemiology of both communicable and non-communicable diseases of public health importance. There is an urgent need for increased and sustained investment in the general public health system in Nigeria, especially at the primary health care level, that is geared toward a time-bound target for the achievement of Universal Health Care (UHC) in Africa's most populous country.

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