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SOCIO-PHARMACOECONOMIC AND ANTHROPOLOGIC IMPACTS OF THE COVID-19 PANDEMIC IN RESOURCE LIMITED COUNTRIES

Estella Achick Tembe-Fokunang¹, Pascal Kum Awah², Andrew Nyuyki Banin³, Dobgima John Fonmboh⁴, Christian Nubia Kaba⁵, Joseph Fokam^{6,7}, Lovet Benyella Fokunang⁸, Ben Enoluomen Ehigiator⁹, Zelinjo N. Igweze⁹, Ralf Duerr³, Marie-Therese Abena Ondoua¹⁰, Sarah Tiskoff¹¹ and Charles Ntungwen Fokunang^{1*}

¹Department of Pharmacotoxicology and Pharmacokinetics, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Cameroon.

²Department of Anthropology, Faculty of Arts and Social Sciences, University of Yaoundé 1, Cameroon.
³Department of Pathology, New York University School of Medicine, New York, NY 10016, USA.
⁴Department of Nutrition, Food Science and Bioresource Technology in the College of Technology, University of Bamenda, Cameroon.

⁵Department of Clinical Research, Revance Therapeutic Incorporated, Newark California, USA. ⁶Department of Medical Laboratory Sciences, Faculty of Health Sciences, University of Buea, Cameroon. ⁷Virology Laboratory, Chantal Biya International Reference Center (CIRCB), Yaoundé, Cameroon. ⁸Lead Scientist GE Life Sciences CYTIVA, Logan, Utah, USA.

⁹Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Madonna University, Elele,

Nigeria.

¹⁰Department of Pediatrics, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Cameroon. ¹¹Department of Genetics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA.

*Corresponding Author: Charles Ntungwen Fokunang

Department of Pharmacotoxicology and Pharmacokinetics, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Cameroon.

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ABSTRACT

During the early month of the Coronavirus disease 2019 (COVID-19) pandemic, ignited in Wuhan China, the most reported cases and deaths have been reported in high-income countries (HIC) by the middle of 2021. On the other hand, the challenges of lack of and limited access to testing facilities contributed to an underestimation of infections in many low middle-income countries (LMIC), most especially in sub-Saharan Africa. With the increase of global testing and confirmed infection cases, the impact of the pandemic on individuals and communities in LMIC became very evident. This negative impact of COVID-19 in its forms has motivated research in diversified domains to address potential response for the management of the pandemic within the framework of LMIC strategic health plan. with particular references to the transmission patterns of SARS-CoV-2, the clinical characteristics of the disease, and the impact of pandemic prevention and response measures. Sub-Saharan Africa is faced with many setbacks from the pandemic due to the unpreparedness for disasters epidemiology of global magnitude, as created by COVID-19. This paper has been motivated by the COVID-19 pandemic global effect that has permitted us make a review using a multidisciplinary approach. We have taken into consideration the socio, pharmacoeconomic and anthropological impact potential burden of COVID-19 in LMIC countries, faced with limited human resources, funding, or medical supplies from response activities.

KEYWORDS: COVID-19 pandemic, socio-pharmacoeconomic impact, anthropology, global health, epidemiology, vaccine, therapeutics.

INTRODUCTION

From the late 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causal agent for COVID-19, has spread throughout the world. Although the pandemic began in China, paradoxically, most reported cases and deaths occurred in Western high-income countries (HICs) in the early months of the pandemic, while the low- and medium-income countries exhibited low number of infections.^[1,2] While it was still uncertain how LMICs were to perform, confirmed cases

in these countries continue to increase and could soon overtake confirmed cases in HICs. The quest to address the COVID-19 pandemic has motivated scientist in sub-Saharan Africa countries in particular to join others globally to address some broad research questions that can go a long way to inform public health and policy makers responses to COVID-19 in LMICs: (1) how do the patterns of SARS-CoV-2 transmission differ in resource-poor settings? (2) how does disease severity in LMICs, particularly among vulnerable populations, differ from observations elsewhere? (3) what will be the impact of pandemic prevention and response measures on the health and wellbeing of the diverse individuals and communities found in LMICs?^[3,4]

Focus on the scope of Epidemiology of COVID-19.

The transmissibility of infectious diseases, including COVID-19, is driven by characteristics of the causative agents, the host (i.e., biological and behavioural factors), and the environment called the epidemiologic triangle or host-pathogen-environment interactions.^[5-8] SARS-CoV-2 transmission occurs predominantly within households as compared to diffuse social interactions.^[4,9] Is SARS-CoV-2 transmission different in dense living conditions and larger household sizes common in many LMICs? Demographic profiles are younger in most of Africa, Asia and Latin American countries, but crowded multigenerational households are common and therefore could also affect the course of the pandemic.^[6,10-12] As in many LMIC which permits the use, sharing, adaptation, distribution and reproduction in any medium or format, we have exploited data mining tools while giving the right credit to the original author(s) and the sources.

Studies have identified SARS-CoV-2 in the faeces of infected individuals suggesting possible faecal-oral transmission.^[7,13,14] Research is still needed to understand how long the virus is viable in environments typically found in LMIC settings and if lack of access to clean water and sanitation facilities exacerbates faecal-oral transmission, as has been observed for at least one other respiratory virus (ie, avian influenza).^[8,15,16] In a broader sense, does a lack of clean water and soap or hand sanitizer modify transmission through established routes? Emerging evidence also suggests that temperature and absolute humidity and transmissibility of SARS-CoV-2; although, this reduction is insufficient to fully disrupt transmission.^[3,17,18] A more thorough understanding of the relationship between climate, seasonality, and virus transmissibility could provide more information into the potential course of the pandemic in LMICs that tend to be warmer and more humid, supporting preparedness and response efforts in these settings.^[10,19]

Disease incidence and severity

It is important to understand disease incidence and severity in LMICs, particularly case fatality ratios among vulnerable groups, such as young children the elderly and immunocompromised subjects/volunteers, is very relevant.^[11,20] COVID-19 has been reported to cause less severe disease in children who are asymptomatic compared to adults in HICs with ready access to quality treatment.^[3-4,21] However, the experience with pneumonia, the leading cause of death among children in LMICs and the most common clinical feature of severe COVID-19 cases is of concern that COVID-19 might be more severe among children in settings where pediatric respiratory disease risk factors, including multiple severe comorbidities, are more prevalent and advanced.^[12,22] The treatment for pneumonia is often absent or delayed

in LMICs and more so, the prevalence of respiratory disease risk factors is much higher in LMICs for all age groups, including under nutrition, indoor and ambient air pollution, being immunocompromised (eg, those infected with human immunodeficiency virus), first and second-hand smoke, and multiple coinfections.^[12-14,23]

The impact of prevention and control interventions, understanding the effect and unintended consequences of current COVID-19 prevention and control will help governments and communities to improve and adjust these efforts in real-time within the population settings in sub-Saharan Africa. Implementation research can efforts support such and non-pharmaceutical interventions (NPIs) have been adopted by many LMICs to prevent transmission and reduce morbidity and mortality associated with COVID-19.^[2,14,24] However. the effectiveness of NPIs in such contexts is not fully understood nor have they been adapted to local contexts.^[15]

Healthcare in LMICs

The COVID-19 pandemic has caused an unprecedented challenge for healthcare systems worldwide, in particular, the risk to healthcare workers is one of the greatest vulnerabilities of healthcare systems worldwide.^[16,25] Considering most healthcare workers are unable to work remotely, strategies including the early deployment of viral testing for asymptomatic and/or frontline healthcare staff is imperative.^[3,17,26] High healthcare costs, shortages of protective equipment including N95 face masks, and low numbers of intensive care units (ICU) beds and ventilators have ultimately exposed weaknesses in the delivery of patient care. In the US, there is concern regarding uninsured individuals, who may work in jobs predisposing them to viral infection which may lead to significant financial consequences in the event of illness.^[17,27]

Pharmaceutical industry

Profound changes to the dynamics of healthcare have undergo dynamic transformation, leading to massive investment into disease prevention infrastructure, and the accelerated digital transformation of healthcare delivery.^[28] Studies have highlighted the change in healthcare policy and clinical management as new evidence emerges.^[18] In the USA for example, active pharmaceutical ingredients are imported largely from India (18%) and the EU (26%), $^{[12,29]}$ China is also the biggest exporter of medical devices to the US, accounting for 39.3%. Currently, production slow-downs and limitations in supply would inadvertently lead to revenue loss.^[7,19,30] In the UK, AstraZeneca have indicated that COVID19 was likely going to affect its 2020 revenue growth. Conversely, opportunities for companies engaged in vaccine and drug development have simultaneously emerged, with US-based companies including Johnson & Johnson, Vir Biotechnology, and NanoViricides having announced Novavax collaborative plans to develop a viral vaccine.^[9,31-33] A

Phase 1 clinical trial evaluating an investigational COVID-19 vaccine was put in place, and enrolled 45 healthy adult volunteers ages 18–55 years over approximately 6 weeks.^[20] These vaccines have been fast racked for development and approved by the FDA for use worldwide.^[11,21,34]

Pharmacoeconomic impact of COVID-19

Consequences secondary to the coronavirus disease 2019 (COVID-19) pandemic has been observed in the healthcare service for many years. The coronavirus disease 2019 pandemic have affected many ongoing clinical trials and left large deficits in the budgets of many jurisdictions.^[22,35,36] The potential difficulties with data from these trials includes excess deaths; issues with extrapolation and evidence synthesis; and lack of generalizability of cost, utility, and discontinuation data.^[37]

In LMIC funding for other treatments, in particular new treatments, have become more constrained than expected. Therefore, a robust health previously technology assessment (HTA) system is vital but unfortunately HTA is not a common occurrence in most sub-Saharan countries.^[11,37] Many clinical trials carried out in the population of LMIC during the pandemic have been temporarily halted, while others have had to change their protocols.^[15,38] Even trials that continue as normal have experience external changes as other aspects of the healthcare service are not available to the patients in the trial, or the patients themselves have contracted COVID-19.^[14,23,39] Consequently, many limitations are likely to arise in the provision of potential HTAs, in LMIC which could have profound consequences on the availability of new treatments. Therefore, funds for other treatments, in particular new treatments, have become more constrained than previously expected. Hence, a robust health technology assessment (HTA) system is important to be in put in place with the public health structures.^[40] Drawing the experience of the National Centre for Pharmacoeconomics (NCPE) in Ireland which is a national HTA agency, responsible for assessing the costeffectiveness and budget impact of new medicines submitted by applicant pharmaceutical companies (herein the applicant) for potential reimbursement by the state health payer (Health Service Executive) are known to be effective in alleviating patients out of pocket payment burden of medications and health related products.^[17,41] Such NCPE are still at its infancy or nonexistent in LMIC to support patient health spending at this era of the coronavirus 19 pandemic.^[9,24]

It is important to understand how the pandemic has affected the estimation of the treatment effect, costs, lifeyears, utilities, discontinuation rates, and methods of evidence synthesis and extrapolation. It has been reported that trials conducted during the pandemic are subjected to a higher degree of uncertainty than before.^[25,42] It is also very important that applicants clearly identify any parameters that may be affected by the pandemic such that these parameters could require considerably more scenario and sensitivity analyses to account for this increase in uncertainty. Due to the pandemic, many limitations have arisen in the provision of robust services where HTAs are in operation, increasing the time taken to develop and assess costeffectiveness and budget impact models.^[43] This has also increased the uncertainty in the outputs from these models and has led to a delayed and less certain recommendations being communicated to the decision maker, which could have profound consequences on the availability of new treatments.^[3,26,44] Both manufacturers and decision makers in the health and insurance sectors face more complex and uncertain HTA assessments, compounded by budget deficits, which have affected the willingness-to-pay thresholds. For example, historically the cost-effectiveness threshold in Ireland varies between €20 000 and €45 000 per quality-adjusted life-year.^[27,45] At the moment, treatments below the upper threshold are considered cost-effective; however, it is unknown if that may change as the healthcare budget becomes more constrained. Therefore, it is imperative that the issues of cost-effective threshold are discussed and introduced now and planned for accordingly with ample time for these HTAs to be prepared and assessed or put in place where the resources are available in LMICs.^[29,46]

As another example, among others, the European Medicines Agency (EMEA) and the U.S. Food and Drug Administration (FDA), also discuss statistical issues and missing data arising from trials conducted during the COVID-19 pandemic.^[5,30,47] There are some additional issues that could affect HTA, over and above those considered by regulators. Clinical trial investigators and regulators use statistical models to infer treatment effects and the HTA models use this inference and build on it to predict patient outcomes, costs, and quality of life^[31,48], identified more issues concerning the impact of a pandemic on HTA. It is important to discuss and understand what is considered to be the most pertinent concerns, identify additional issues relating to the HTA process, and make some recommendations for applicants.^[14,32]

Quality-of-Life Data

The pandemic is imposed a significant level of stress, anxiety for individuals, families and he communities for many and challenges of economic concerns, predicted or real has impacted on health outcomes, and restrictions on movement and social contact has negatively affected physical health and mental well-being.^[33,49] These considerations may have affected health-related quality-of-life measures collected during the pandemic. This may limit the generalizability of utility values derived from these measures. Some community subgroups of the population (including the elderly and people with particular underlying health conditions) are at higher risk of mortality and complications arising from COVID-19^[34-36,50] and therefore, the survival level may be affected in certain trials where they are volunteers.

Difficulties with access to testing, issues with testing accuracy, and the presence of comorbidities implies that it may be difficult to know which of these deaths can be attributed to COVID-19.^[2,37] Therefore, the situation may affect both costs and life-years which may be underestimated. In a hypothetical randomized controlled trial in which COVID-19 presents an increase in baseline hazard of death, the treatment effect of an intervention (measured as a hazard ratio) would be unchanged; however, the life-years gained would be reduced.^[38,51] It has been observed that general population mortality tables collected during the pandemic have been affected by excess deaths or incidence of mortality.

Healthcare Resource Utilization Data

There is evidence that fewer patients are attending emergency departments or primary care providers, and non-urgent hospital appointments have been delayed or cancelled^[52, 53] For example, there was a 23% reduction in emergency department attendance in March 2020 versus March 2019 in England.^[39] On the other hand, there may be an increase in costs and resource use if some patients in a clinical trial develop COVID-19. Therefore, the generalizability of data on healthcare resource utilization collected during trials at this time may not be reflective of future patients' activities.^[9,40] In LMIC data generation on COVID patients are complicated to manage, as majority of cases of underlying comorbidities are grouped as COVID-19 cases.

Information technology, media, research & development

With the WHO raising COVD-19's status to a pandemic, 35 companies and academic institutions started racing to develop an effective vaccine. Four potential vaccines have been tested on humans.^[41,54] The Coalition for Epidemic Preparedness Innovations (CEPI), is leading various efforts to finance and coordinate COVID-19 vaccine development.^[21] They announced a \$4.4m partnership fund with Novavax and University of Oxford to develop a viable solution.^[22,55] The Gates Foundation, Wellcome and MasterCard also committed \$125m to find new treatments for COVID-19.^[42]

Social distancing precautions are paramount to the containment effort. Additionally, COVID-19 has left several hospitals in turmoil, having reached maximal capacity. As a result, various countries are turning towards technological solutions, to care for patients and at the same time, minimizing the risk of person to person transmission.^[44,56] In various cities across China, teleresponse powered by fifth-generation wireless networks are being utilized to the extent that allow health care staff to communicate with patients, monitor their health and deliver medical supplies.^[9,24,57] Drones that deliver medication and work-from-home apps are also being adopted in an increasing pattern. Automation of services has been a major goal for China. COVID-19 has helped

to accelerate uptake and has taken them one step closer to this goal. $\ensuremath{^{[46,58]}}$

The demand for respiratory ventilators has increased exponentially due to the outbreak of COVID-19. However, it is evident that the current supply across the United States and Europe does not meet demand. It is estimated that the USA alone has more than 260,000 ventilators.^[25] This is 580,000 short of what would be required in a severe pandemic.^[5] Governments around the world are attempting to buy ventilators to cope with the emergency hospitalized cases. In developed countries like in the United Kingdom, the prime minister asked some major companies to divert their manufacturing power to medical supplies.^[26,59] However, industry leaders have stated that this is easier said than done as many of these companies do not produce medical equipment such as ventilators. $^{\left[59\right] }$ In LMIC where there are little or no manufacturing of medical equipment except in China, but face with overpopulation the production of ventilators requires strict regulation and testing to ensure their safety which can be a lengthy process.^[27] On the other hand, LMIC are far from getting enough access and supply of ventilators and they need funding mobilization for acquisition of ventilators.^[48,60]

Effect on the Food sector

The food sector, including food distribution and retailing, has been put under strain as a result of people panicbuying and stockpiling of food.^[27,49] This has led to increased concerns about shortages of food products such as long-life milk, pasta, rice and tinned vegetables. Panic buying has resulted in an increase of billion worth of food in many countries with economic challenges.^[61] This high demand on food products has also affected online food delivery and companies are struggling with excessive bookings, with deliveries arriving late or not at all.^[28,51] In land lock countries, and poor communication network internet shopping and deliveries is a big challenge. Moreover, food banks have also been affected by panic-buying and food stockpiling as donations have reduced. Concerns about food running out also means that vulnerable populations who can not afford to stockpile, may not find food.^[2,11,52] Countries in LMIC under political crises, economic decline state are hard hit, with internally displaced population, refugees under extreme food shortage and starvation.^[62]

In response to these concerns, the most income limited government has made efforts to provide certain populations with food parcels and free meals to collect and take home. These populations include high-risk vulnerable individuals such as the elderly who have no support network, and school children of low-income families.^[52]

Some governments in LMIC has also reduced restrictions on delivery hours for retailers in order to allow stores to restock with basic food products. Furthermore, some retail consortium, community engagement action groups have been created in some countries to reassure the public that despite low inventory of certain food products in local stores, there are no such shortages of food. Similar statements have been made by the US Food and Drug Administration (FDA).^[14,63]

In addition, despite reassurance by the government, stores have made drastic changes by restricting the amount of each product that an individual can buy, providing more than 30,000 new jobs to meet the high pressure of restocking shelves, and setting special shopping hours for the elderly, vulnerable populations. Further changes being implemented include a decrease in the range of products being made by manufacturers, with the aim of focusing on products that are in greater need.^[53,64]

Independent supermarkets in well-developed countries have also been affected by the high demand on food products. Some measures implemented by these local stores include free delivery of food products to customers to avoid panicbuying, putting restrictions on the number of customers allowed in at any given time to avoid overcrowding, and expanding on the number of suppliers whom they buy their products from to avoid food shortage.^[34] On the other hand, LMIC suffer from food supplies that importation is not possible or supplies significantly reduced. Food supplies to the villages significantly reduced and creating hunger and misery.^[65] Although supermarkets have seen a huge demand on food products, restaurants and cafes have been forced to close down and as a result, many of these stores are at risk of permanent closure and many of their employees have lost their jobs.^[13, 66] The impact of COVID-19 on the food industry has forced some Agri industries to change their line of business, turning into shops that sell refrigerated ready -meal-type plastic pouches.^[35]

Economic impact

The COVID-19 pandemic has created unprecedented development challenges in low- and middle-income countries. Governments, international aid agencies, civil society organizations, and the private sector need evidence to mitigate the potentially devastating socio-economic impacts of the pandemic in developing regions, while also building the conditions for a more resilient future.^[36,67] Many countries have mobilized a rapid response to support sound, policy-relevant research in three areas:

- Monetary, fiscal, and regulatory policies to mitigate the economic impacts related to the pandemic and to rebuild in better ways of revamping the economy;
- Measures in the public and private sectors to support vulnerable groups, while addressing disparities and promoting gender equality;
- Accountable responses to the pandemic that safeguard democratic freedoms, enhance security, and harness opportunities for the empowerment of women and youth.^[3,68]

Up to 25 scholars networks, and consortia in developing countries are shortlisted to receive funding as part of the initiative to combat the negative economic impact of COVID-19.^[69] Efforts to address the COVID-19 pandemic in developing countries must contend with under-financed healthcare systems, the limited number of healthcare workers, lack of infrastructure including clean water and sanitation, crowded living conditions that prohibit physical distancing, and limited social safety nets to support people who have lost their sources of income.^[9,70] The world's response must ensure that lowand middle-income countries can emerge from the pandemic without reinforcing or exacerbating the existing gender, social, and economic fault lines that put women and girls and other vulnerable populations disproportionately at risk.^[71] The pandemic also represents an opportunity to build stronger and more resilient societies in the face of climate change and future disease outbreaks. Capacity infectious building initiatives to support local capacities for knowledge and innovation is more relevant than ever to drive effective domestic policies and actions that are based on sound evidence and data.^[3,38,71]

Implication for Finance industry

COVID-19 has affected rural communities in particular in LMIC, businesses and organizations globally, and therefore affecting the financial markets and the global economy.^[72] The economic meltdown worsens by the non-coordinated action by the state responses and lockdowns have led to a disruption in the supply chain. In Cameroon and the Central Africa subregions for example, lockdown restrictions significantly reduced the production of goods from factories, while quarantine and self-isolation policies decreased consumption, demand and utilization of products and services within and imported.^[32,73] As COVID-19 has progressed to affect the rest of the world, Africa has joined the others in the economic recovery process in the countries, strengthening its trade negotiating power against the developed countries. In addition to the disruption in the supply chain, the capital market sector has also been affected.

In the US, the S&P 500, a stock market index that measures the stock performance of 500 large companies on the US stock exchange, the Dow Jones Industrial Average and the Nasdaq fell dramatically until the US government secured the Coronavirus Aid, Relief, and Economic Security (CARES) Act, with the indexes $7.3\%^{[33,74]}$, $7.73\%^{[34]}$ and $7.33\%^{[35]}$ raising by respectively. On the contrary in the sub-Saharan countries the economy is not shares and stock driven due to low productivity of products for export or large manufacturing firms in place. Europe's bond yields mostly declined, reaching market stress hit levels faced in the eurozone crisis of 2011–2012.^[40] Germany's DAX, the UK's FTSE 100 and the Euro Stoxx 50 were all down on March 23rd, but rose significantly after the EU's rescue package was agreed. Gold dropped against the

dollar by 0.65%.^[41] The decline in global stock markets has festered a volatile environment with critical liquidity levels.^[42] To combat these effects, Central banks globally have intervened to ensure liquidity is maintained and mitigate the economic shock, with several leaders embarking on a 'Whatever it takes' approach.^[43,74]

Focus on the World's Most Vulnerable Countries due to Lack of the Capacity to Respond to a Global Pandemic Credit

The COVID-19 pandemic is impacting people across the world. Cases of the COVID-19 coronavirus have now been detected with the exception of a handful of countries in the majority of the world's Least Developed Countries (LDCs), Landlocked Developing Countries (LLDCs) and Small Island Developing States (SIDS); three vulnerable country groups with a combined population of over 1 billion.^[39] From the Middle East countries like Afghanistan, to the Caribbean, Trinidad and Tobago and many others, West and East Africa down to South Africa international borders have shut down, national emergencies have been declared and restrictions in the movement of people and goods have been enforced. By their very nature, these LMICs are particularly vulnerable to external shocks given their limited means to respond.^[17,40]

The pandemic threatens to impact the LDCs, LLDCs and SIDS disproportionately with potentially devastating impacts on human health, including through social and economic effects of the virus and containment policies through the months and years to come. The lack of domestic financial resources, high debt levels and fragile health systems presents an urgent challenge. What has emerged as a health crisis in the short term may well have far reaching impacts on education, human rights, food security and economic development in the long term.^[41,74] The pandemic is also having a dramatic restriction effect on global migration and tourism. Remittances to these regions comprise important revenue for most LDCs, LLDCs, and SIDS, which overall provides more funds than Official Development Assistance.^[42] As the trade impacts of the fast pandemic are emerging, an estimated \$50 billion drop in global exports has been recorded as far back as in February 2020 alone. This has the potential to impact severely the ability of vulnerable countries to access what are increasingly delicate international markets. LDCs for instance, account for less than 2 % of world GDP and about 1% of the global trade in goods. LLDCs are highly dependent on international trade and in particular, on commodities. A fall in commodity prices and reduction in demand for exports poses a balance of payment challenges and further marginalization of LLDCs in global trade.

Due to the nature of the landlocked geographical location, restrictions on trade and cross-border transport have interrupted needed aid, medical equipment and basic goods flowing into the LLDCs.^[43] As advanced

economies announce large-scale economic assistance and healthcare interventions, it is important that the international community do not neglect the fundamental responsibility to support those vulnerable members of the global family who have the least capacity to respond.^[1,44] Supporting these vulnerable country groups will need a three-cardinal approach to: (1) provide resources to stop the spread of COVID-19, (2) rapidly strengthen capacity to reduce the outbreak and (3) provide resources to avoid economic collapse. Both financial and technical support are relevant to limit the impact on the most vulnerable countries.^[45]

A statement by the High Representative for the Least Developed Countries, Landlocked Developing Countries and Small Island Developing States, Fekitamoeloa Katoa 'Utoikamanu, emphasized that to avoid a truly devastating global tragedy, the pandemic it will be critical that the international community urgently support vulnerable countries to strengthen their health systems and their capacity to manage the disease transmission. In the powerful world of information technology, we are only as strong as our weakest health system.^[46]

Health and Socio-Economic Impact on the Landlocked Developing Countries and Small Island Least Developed Countries

Least Developed Countries (LDCs) are facing both a health crisis and significant economic slow-down brought about by a collapse in commodity prices. These multi-faceted shocks interact in a complex manner and limit fiscal space to respond to the pandemic and to recover in a manner that does not leave the LDCs further behind.^[47,71] The high prevalence of malaria, HIV/AIDS, tuberculosis and malnutrition adds additional burdens for LDCs, especially as the pandemic is likely to coincide with peak malaria season in 2020.^[48] The pandemic is also impacting countries which are only just recovering from epidemics. After more than a year of battling an ebola virus outbreak that killed more than 2,200 people, the UN is cautiously optimistic that the epidemic in the northeast Democratic Republic of the Congo (DRC) will soon be history as the country gears up to face the threat of COVID-19. As in other developing countries, COVID-19 has diverted the available national health capacity and resources, and left millions of children affected by measles, malaria, polio and many other fatal diseases.^[48] That notwithstanding, the health impacts of COVID-19, with commodity markets in turmoil, the pandemic presents a major economic crisis for LDCs. Oil, minerals, food and other commodities account for more than 70 per cent of the merchandise exports from LDCs.[49]

In addition to the problems is the global demand and supply-side shocks arising from the impact of COVID-19, which is seriously affecting LDCs that are dependent on exporting manufactured goods, particularly textile food crop. Six LDCs – Bangladesh, Cambodia, Haiti, the Gambia, Nepal and Lesotho – receive more than 50% of their export revenue from exporting manufactured goods, therefore the fall in exports will likely lead to current account deficits.^[21,50]

Remittances

The pandemic is likely to severely shrink remittance inflows as migrant workers face large scale job losses and are forced to return to their home countries. Remittances to LDCs are projected to fall by more than 20 per cent, representing a loss of a crucial financing lifeline for many vulnerable households.^[52]

Furthermore, many migrant workers have already lost their jobs without any compensation or unemployment benefits. COVID-19-related travel restrictions across the world are creating an unprecedented impact on labor mobility, new migration and remittances. A recent World Bank report says remittances to low and middle-income countries (LMICs) are projected to fall by 19.7 percent to \$445 billion, representing a loss of a crucial financing lifeline for many vulnerable households.^[53]

Food Security

The pandemic is impacting food systems globally and pushing the world's poorest and most vulnerable people toward greater food insecurity. Hunger remains a major challenge and has further deteriorated as a result of COVID 19.^[4,54] Any decline in external demand will disproportionately hurt poor households employed in labor intensive manufacturing and agriculture sectors, which will further undermine their efforts to eradicate extreme poverty and achieve SDG 1.^[55] LDCs are seeing a growing number of cases and include: Bangladesh, Afghanistan, Guinea, Djibouti and Burkina Faso.

Conformed Social Behaviors required to reduce SARS-CoV-2 transmission

COVID-19 is the disease caused by the SARS-CoV-2 virus, which is a novel form of coronavirus.^[8,44] The virus is transmitted in communities either directly by travelling through the air from an infected person's airways, mouth or nose to a recipient's eyes, nose or mouth (the T-zone), or by the virus contaminating an object or surface (fomite) that is touched by a recipient who then goes on to touch their T-zone.^[19] The T-zone is the primary route for the virus to cause infection because the virus enters cells of mucous membranes and lung epithelial tissue.^[38] It does not enter through the skin. The evidence suggests that, in community settings, the virus is carried primarily on respiratory droplets (relatively large particles that typically travel a short distance before falling to a surface) rather than aerosol (small particles than can stay airborne for an extended period)^[12,18], but this view has been contested.^[12] Figure 1 shows the putative transmission paths and the behaviours that can block them in community (as opposed to healthcares) settings.

Governments have mainly used isolation (keeping vulnerable and infected or potentially infected people

physically away from others) and what has been termed social distancing' (staying at home except for essential journeys) to block transmission. Isolation and social distancing measures appear to be effective in controlling the pandemic However, they come with an enormous cost to people's livelihoods, education and mental health, as well as to the global economy.^[43] Adherence to isolation and social distancing behaviours faces strong practical, motivational and social barriers and also imposes considerable costs on people and society. These costs are borne disproportionately by people who are already disadvantaged.^[35,59] Even with the availability of vaccine the social distancing measures still applies but not very respected in the population of developing economies. Due to resurgence of infection it is not likely that these measures shall be relaxed sooner. Widespread and rigorous adherence to 'personal protective behaviours' (individual behaviours aimed at protecting oneself and others) have been put in place. These behaviours are also needed to protect people who have to put themselves at risk of catching the disease in the course of vital functions they perform in society. Figure 1 gives an illustration on the social distance strategic scheme in a define community to control the SARS-COV-2 transmission pathways of infections.



Fig. 1: Pathways to SARS-CoV-2 transmission and behaviours to block this. Large circles, stages in the pathway; red arrows, routes of transmission; crosses in small circles, blocks to transmission; filled rectangles, personal protective behaviours to block transmission routes. Dotted arrows point to the blocking points. The blue vertical bar shows the points at which isolation and social distancing measures work.^[16]

The biomechanics of transmission mean that it could be reduced at source by the infected person making sure that they cough or sneeze into a tissue that is immediately disposed of in a way that does not cause further contamination as shown in (Box 1 in Fig. 1). Face masks (Box 2 in Fig. 1) can act as a physical barrier to the spread of droplets, but their effectiveness in reducing virus transmission may be offset by people failing to use them appropriately, and what limited evidence is available as of the end of April 2020 has not clearly shown a benefit in community settings.^[16]

Physical distancing (Box 3 in Fig. 1) aims to minimize the risk of direct transmission of the virus via inhaled droplets. The distance at which people are thought to be at risk from direct inhalation of contaminated droplets in normal circumstances is currently estimated at up to 2 m.^[7] However, it has been suggested that under certain conditions droplets or aerosol may travel further than this.^[18]

Given importance potential role of fomites in transmission of the virus^[19], washing hands with soap or hand sanitiser (Box 4 in Fig. 1) and disinfecting objects and surfaces (fomites) (Box 5 in Fig. 1) may reduce

transmission. Transmission by fomites occurs because people touch their T-zone after touching them. The fomite route to transmission of the virus although has been reported that the virus can survive on some surfaces for several days, it is hardly functional.^[23] Therefore, not touching the T-zone (Box 6 in Fig.1) may be an important behaviour to target. Although the above personal protective behaviours are included in government advice in a number of countries^[8,13]</sup>. little guidance, training or support is given to promote adherence, even though failure to do so is critical to the transmission of the virus. There has been reports of outbreaks of COVID-19 in some closed settings like restaurants, nightclubs, places of worship and work places. This indicates that aerosol transmission, especially indoor places where there are crowded and poorly ventilated. When infected persons spend long periods in these spaces, there is possibility of COVID-19 transmission. WHO has called for more studies to investigate areosols transmission in poorly ventilated crowded place.

Focus on understanding behaviour and how to change it.

Ideally, we would be able to draw on high-quality intervention evaluations to identify ways to increase protective enactment of personal behaviours. Unfortunately, there is a dearth of studies on this. There are some suggestions on how best to promote adherence to social distancing, for example.^[3,7] While a considerable amount of research has been undertaken on hand-hygiene in certain settings.^[11,24,29], generalisability to community settings is limited. We could find no published evaluations of interventions to reduce T-zone touching. There is some research on psychological interventions to reduce itch scratching in people suffering from atopic dermatitis, but no firm conclusions have been reached.^[13,22]

In the absence of strong direct evidence to guide interventions, we can draw on behaviour-change principles to generate ideas as to what strategies to adopt. A staged process has been proposed for doing this, known as the 'behaviour change wheel'.^[8, 23] This was derived from a synthesis of 19 major behaviour-change frameworks. This starts with an analysis of the capability, opportunity and motivation required to enact each behaviour. This is followed by mapping these requirements to relevant types of intervention (education, incentivization, coercion, persuasion, training, restriction, environmental restructuring, modelling and enablement).

Some interventions to promote behaviors to limit virus transmission

The behaviour change wheel sets out nine broad categories of intervention that can be included in any behaviour change strategy: education, persuasion, training, incentivization, coercion, enablement, restriction, environmental restructuring and modeling.¹ ^{24]} It also specifies criteria for evaluating intervention options. Thus, an intervention may likely be effective but have unacceptable spill-over effects, or it may be impracticable or unacceptable to key stakeholders. An example of applying this approach to reducing COVID-19 transmission can be seen in a behavioural science paper presented to UK's Scientific Advisory Group in Emergencies outlining intervention options for increasing adherence to social distancing measures and consideration of them using the APEASE criteria.^[42] It is emphasized that this is a preliminary analysis, and for formal recommendations, a much fuller and more systematic analysis would condition: (i) unconflicted inertia when the risks of inaction are not judged to be serious, (ii) unconflicted change when risks of action are seen as minimal, (iii) defensive avoidance when there seems little hope of avoiding negative outcomes, and (iv) hypervigilance when there is strong time pressure and some hope of finding a solution. Following the decision, suboptimal modes of decision-making lead to defective strategies for coping with negative outcomes, whether or not these were avoidable.^[25]

Some examples of insights relevant to behaviours to limit transmission of SARS-CoV-2

Messaging to the public is aimed at creating a strongly felt 'need' to engage in protective behaviours rather than just a belief that one 'should' do them. People should be supported to develop plans that are specific and strongly linked to identity through development of personal rules (for example, always washing hands when entering one's home).^[52] Interventions should recognize the balance of impulses and inhibitions at key moments, and promote development of habits that come into play when needed. Educational materials should include modelling of desired behaviours. Interventions need to ensure that perceived benefits of protective actions outweigh the costs, and support should be provided to mitigate the costs.^[12] Benefits should be framed in terms of certainties and avoidance of negative outcomes, and they should be made readily imaginable. Messaging and support should create 'concern' that motivates action rather than anxiety that could lead to defensive avoidance. This involves providing a clear indication of practical and realistic steps that can be taken to address the risk with a strong sense that these will work.

Messaging to the public should aim to heighten dissonance linked to nonadherence, and to prevent people engaging in 'exceptionalism', where they add beliefs about their situation being a special case that means they do not have to adhere.^[9] Communications promoting protective behaviours should aim at bringing the benefits into people's immediate time horizon, and any use of incentives and or punishments should focus on creating immediate contingencies. Interventions, including communications, should maximize the visibility and approval of desired behaviours and should minimize the visibility of undesired ones by groups with which the target groups identify.^[20,46]

Social rewards, for example, through praise, should be liberally used to maintain desired behaviours, and people should be encouraged to support each other in this way. Where sanctions are used, it is important for these to be consistently applied.^[11,35] Resources supporting protective behaviours should help people to identify and train the required habits, including habits that conflict with behaviours one is attempting to prevent.

Impact of COVID-19 on psychosocial problems

What is the effect of COVID-19 on risk of anxiety, depression, and other outcomes, such as self-harm and suicide? Although a rise in symptoms of anxiety and coping responses to stress are expected during these extraordinary circumstances, there is a risk that prevalence of clinically relevant numbers of people with anxiety, depression, and engaging in harmful behaviours (such as suicide and self-harm) will increase in LMIC where unemployment is a common phenomenon.^[41] Although there is high community culture of life in LMIC, there could however be a possible rise in suicide, especially when life becomes unbearable for the

vulnerable neglected groups like the elderly. The potential fallout of an economic downturn on mental health is likely to be profound on those directly affected and their caregivers. The severe acute respiratory syndrome epidemic in 2003 was associated with a 30% increase in suicide in those aged 65 years and older; around 50% of recovered patients remained anxious; and 29% of health-care workers experienced probable emotional distress.^[18-20]

Patients who survived severe and life-threatening illness were at risk of post-traumatic stress disorder and depression. Many of the anticipated consequences of quarantine, and associated social and physical distancing measures are themselves key risk factors for mental health issues.^[15,16] These include suicide and self-harm, alcohol and substance misuse, gambling, domestic and child abuse, and psychosocial risks (such as social disconnection, lack of meaning or anomie, entrapment, cyberbullying, feeling a burden, financial stress, bereavement, loss, unemployment, homelessness, and breakdown).^[45-49] A major adverse relationship consequence of the COVID-19 pandemic is likely to be increased social isolation and loneliness which are strongly associated with anxiety, depression, self-harm, and suicide attempts across the lifespan.^[22-25] Tracking loneliness and intervening early are important priorities and crucially, reducing sustained feelings of loneliness and promoting belongingness are candidate mechanisms to protect against suicide, self-harm, and emotional problems within our community^[7,20-22] Social isolation and loneliness are distinct and might represent different risk pathways.

To inform management of COVID-19, it is important to understand the socioeconomic effect of the policies put in place by the government to manage the pandemic, which will inevitably have serious effects on mental health by increasing unemployment, financial insecurity, and poverty.^[25,29] The implication of population with lived experience and rapid qualitative research with diverse people and rural communities will help to identify ways in which this negative effect might be managed. Attaining the right balance between infection control and mitigation of these negative socioeconomic effects needs to be taken into consideration^[23,34] The immediate research priorities of African scientists are to monitor and report rates of anxiety, depression, selfharm, suicide, and other mental health issues both to understand mechanisms and crucially to inform on potential interventions which in most cases are neglected. This should be adopted across the general population and vulnerable groups, including front-line workers. COVID 19 monitoring and surveillance platform must go beyond ministry of public health record linkage to capture the real incidence in the community, because self-harm might become more hidden. There is the need to harness existing datasets and ongoing longitudinal studies, and establish new cohorts with new

ways of recording including detailed psychological factors. $^{\left[52-55\right] }$

The future for vaccines and therapeutics for Low middle income countries

WHO and partners learnt their lesson from the mis-steps in the response to the 2009 H1N1 influenza pandemic and then established the Access to COVID-19 Tools (ACT)^[75] which is an accelerator to promote equitable access vaccines, therapeutics, to and diagnostics. Unfortunately, many high-income countries already have bilateral agreements with manufacturers of COVID-19 vaccines. The COVAX Facility of the ACT Accelerator has agreements to access 2 billion doses of WHO pre-qualified vaccines during 2021, but this represents only 20% of the vaccine needs of participating countries.^[76,77] Most low-income and middle-income countries (LMICs) are face with the challenges of accessing and delivering vaccines and therapeutics for COVID-19 to their populations which in most cases are enclaved communities.^[78] COVAX require serious decisive to be taken by Gavi, the Vaccine Alliance, WHO, and the Coalition for Epidemic Preparedness Innovations (CEPI), back up by the countries they serve and with financing for vaccine purchasing, in order to ensure that people and communities worldwide have equitable access to COVID-19 vaccines.^[78-80] For 80% of the populations in LMICs that may not benefit from COVAX-provided COVID-19 vaccines, may desperately need funding for the purchasing or donations will be needed. Government measures in response to COVID-19 and the broader global financial situation have led to increasing fiscal imbalances of heavily indebted countries.^[4,81]

Multinational agencies, financial institutions, and developed countries need to consider strategic measures that could provide relief package to indebted LMICs. The World Bank, the International Monetary Fund, and others need to lead an international initiative to mobilize support for LMICs in need.^[82]

Many LMICs face the challenge of not having an established health emergency platform for vaccinating their adult populations. Although it is possible to deliver COVID-19 vaccines to health-care and other front-line essential workers, in some LMICs, it is still difficult to effectively reach and vaccinate with two doses all elderly populations vulnerable with underlined and comorbidities, considering the insufficient mechanisms to identify such target groups.^[57,83] Governments and policy makers, stake holders, international NGOs still need to use transparent, accountable, and unbiased processes when they make and explain evidence-based vaccine prioritization decisions, in the course of building confidence in COVID-19 vaccines and effective engagement with all the stakeholders.^[84]

The ultracold chain supplies requirements of mRNA COVID-19 vaccines is a big hurdle to overcome in

LMICs, outside of major cities. COVID-19 vaccine delivery needs a considerable investment of human and technical resources, health-care personnel, and a careful management planning to avoid opportunity costs, including a disruption of routine health services and a decline in essential childhood vaccination coverage, which could result in outbreaks of measles and other vaccine-preventable diseases.^[9,83,85] There were more deaths from measles than Ebola virus disease in 2019 with the aftermath of the Ebola outbreak in the Democratic Republic of the Congo, due to failure to maintain adequate childhood vaccinations.

The technical platform, infrastructure for vaccination in most LMICs is significantly inadequate, as reported by the 19.7 million under-vaccinated infants globally, most of whom are in sub-Saharan African countries.^[78] Thus, preparation for all aspects of COVID-19 vaccine delivery in LMICs have to start with the support of international partners. Capacity building of LMICs to do clinical trials and promoting LMIC participation in research are also crucial.^[33,82] There is the need to promote more research interest and funding of experts in LMICs to participate and be major actors in in future vaccine trials and in testing the clinical effectiveness of different therapeutic agents to ensure that interventions and implementation are suitable for local application and well defined programme for participation in vaccine therapeutic monitory in contexts.

CONCLUSIONS

The current upsurge of COVID-19 in LMICs has increased the fears of a new recession and financial collapse, and times like these call for resilient and strong leadership in healthcare, business, government and wider society. Enforced and timely relief measures are needed to be implemented and adjusted for those that are serious victims of the pandemic. Medium- and long-term planning is needed to re-balance and re-energize the economy following this crisis. Broad socioeconomic strategic sectorial development plans are highly encouraged with the creation of an ecosystem that encourages entrepreneurship so that those with consolidated and sustainable business models can blossom. It is promising for governments and financial institutions to constantly re-assess and re-evaluate the state of the economy, health interventions, and social economy of the population in order to ensure that the 'whatever it takes' promise is well executed.

In addition to isolation and social distancing measures, enactment of key personal protective behaviours is vital in order to reduce the transmission of SARS-CoV-2 and other respiratory viruses. Interventions to target individual behaviours such as these could potentially lead to substantial population-level effects, and behavioural science models and methods can be used to develop and evaluate such interventions. There is currently a dearth of evidence on interventions to achieve these behaviour changes and an urgent need to rectify this. Given the urgency of the current situation, there may be merit in establishing an online hub for helping with the design of pragmatic evaluations, piloting of interventions, and rapid reporting of experiences and outcomes using a standardized approach.

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