IMPACT OF LOCKDOWN ON COVID-19 TRANSMISSION DYNAMICS IN BOTSWANA: A MATHEMATICAL MODELING STUDY

BY

LEBANG JANET MATOKWANE

A thesis submitted to the University of Zambia in partial fulfillment of the requirements for the award of the Master of Science degree in One Health Analytical Epidemiology (OHAE)

The University of Zambia, Lusaka

School of Veterinary Medicine

COPYRIGHT DECLARATION

AURTHOR'S DECLARATION

I, **LEBANG JANET MATOKWANE**, student number **VET2100101**, do hereby declare that this dissertation is my original work, where assistance was sought it has been acknowledged accordingly, and has not been submitted for award of a degree at The University of Zambia or any other university.

………………………..   ………………………

Signature   Date

CERTIFICATE OF APPROVAL

This dissertation submitted by LEBANG JANET MATOKWANE is approved as fulfilling the partial requirements for the award of the Master of Science Degree in One Health Analytical Epidemiology by the University of Zambia.

Supervisor: Prof Martin C. Simuunza

……...................................	……………………
Signature	Date

…..……………………	………………………	………………………
Name	Examiner 1 Signature	Date
…………………………	…………..……….……	..……………………
Name	Examiner 2 Signature	Date
………………………… .	……………………..	……………………
Name	Examiner 3 Signature	Date
………………………..	………………………	……………………
Name	Chairperson Signature	Date

(Board of Examiners)

ABSTRACT

The COVID-19 pandemic is the biggest public health and economic challenge the world has faced for the past three years. Since there was no vaccine during the early phase of the pandemic, Botswana imposed lockdown as one of the non-pharmaceutical interventions to mitigate the COVID-19 burden. Various mathematical models have been used in the current and previous epidemics for analysis of disease spread, forecasting and identifying trajectories as well as assessing effect of imposed mitigation strategies to aid policy makers in making informed decisions. In this study, a deterministic mathematical model was formulated to assess transmission dynamics of COVID-19 and impact of control measures undertaken in Botswana to deal with the pandemic. This study aimed at informing future decisions about lockdown by retrospectively examining its impact of implementation using a mathematical modeling approach. The proposed model was fitted to actual COVID-19 data obtained from the Ministry of Health and Wellness. Publicly available COVID-19 data for the period of 23rd June till 22nd September 2020 was used to validate the model. Model simulations were conducted to estimate the number of cumulative cases without intervention, with lockdown alone as well as in combination with contact tracing. Furthermore, the model was used to estimate the impact of lockdown on reproduction number. According to the model projections, 4362 cumulative confirmed cases would have been recorded after a year in the worst-case scenario of no interventions. After inclusion of interventions in the proposed model, model simulation results showed that lockdown yielded a significant reduction in number of cumulative confirmed cases by a range of 37.28% to 77.94%. In addition, a combination of lockdowns and contact tracing was also found effective in reducing number of cumulative cases by 42.62% to 70.99% (lockdown and medium contact tracing) and by 47.33% to 65.55% (lockdown and high contact tracing). Furthermore, difference in reproduction numbers were noted with a significant reduction noticed after enforcing of lockdown when the reproduction number dropped from 3.9 before lockdown down to 0.4 after full lockdown was implemented. Among all scenarios, lockdown measure was evaluated as the most effective control strategy. These study findings suggest that in the absence of vaccination, lockdown (especially full lockdown) can be used as a possible control measure to culminate SARS-CoV-2 transmission and effectively reduce number of cumulative cases in Botswana. Additionally, combination of intervention strategies; lockdown and contact tracing, alongside other NPIs, is likely to be the most robust means of controlling COVID-19 transmission and spread.

DEDICATION

This work is dedicated firstly to the Almighty God, the source of strength. Secondly to my kids, Tyler Kgosi Matokwane and Hope Nandi Matokwane for their long endurance and sacrifice while I concentrated on my studies. Lastly to my grandmother Gabafetane Baumake, my friend Freeborn Magodoro and my entire family for moral and spiritual support. Remain Blessed always.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my supervisor Prof. Martin SIMUUNZA, Department of Disease Control, School of Veterinary Medicine, University of Zambia for the support and guidance throughout this research. My sincere gratitude also goes to Mr Joseph Sichone for the kind mentorship and valuable time dedicated to my work.

A special thanks to the Ministry of Health & wellness, Botswana for provision of data that I needed to complete my research. I am eternally grateful to the AFRICA CENTER OF EXCELLENCE FOR INFECTIOUS DISEASE OF HUMANS AND ANIMALS (ACEIDHA) for awarding me the scholarship to pursue this Master ‘s degree at The University of Zambia and providing the necessary support to ensure I carried out my study. I would further like to acknowledge the people whose support and contribution have made this work possible; Mr Wilfred Taika, Dr Marty Tsumbu, my course mates and friends.

TABLE OF CONTENTS

LIST OF TABLES

LISTS OF FIGURES

LIST OF ABBREVIATIONS AND ACRONYMS

CDC:	Centers for Disease Control and Prevention.
COVID-19:	Coronavirus Disease-2019
CoVs:	Coronaviruses
FAO:	Food Agriculture Organisation
GDP:	Gross Domestic Product
MERS-CoV:	Middle East Respiratory Syndrome Coronavirus
MoHW:	Ministry of Health & Wellness of the Republic of Botswana.
NPIs:	Non-Pharmaceutical Interventions.
PCR:	Polymerase Chain Reaction.
R_e:	Effective Reproduction Number.
R_0:	Basic Reproduction Number.
SARS:	Severe Acute Respiratory Syndrome.
SARS-CoV-2:	Severe Acute Respiratory Syndrome Coronavirus 2.
SIR:	Susceptible, Infectious, Removed.
SEIR:	Susceptible, Exposed, Infectious, Recovered.
WHO:	World Health Organization.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Coronavirus Disease-2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Sardar *et al.*, 2020). The disease was first identified in Wuhan, Hubei Province, China (Zhao and Chen, 2020). COVID-19 was declared a pandemic by the World Health Organization on March 11, 2020, following high death tolls witnessed in nations like China, Italy, and the United States of America(Kim *et al.*, 2020). Since its emergence in China, the highly transmissible virus has spread worldwide, and Botswana was not spared.

Botswana reported the first confirmed case of the disease on the 30th March 2020 (Siamisang, Kebadiretse and Masupe, 2021).The initial emergence of COVID-19 in Botswana was due to international travel to infected countries. The first three COVID-19 cases were reported to be returning from high risk countries; an index case was a male who had visited Thailand, while the other two cases were a couple returning from United Kingdom (Motlhatlhedi *et al.*, 2020). The local transmissions were driven by several factors including truck drivers who transported essential goods and services in and out of the country, travels across the country especially from Greater Gaborone Zone (the epicenter) to uninfected areas, crowding and non-compliance to public health prevention measures put in place (Motlhatlhedi *et al.*, 2020).

According to Africa CDC weekly report estimates, as of 23rd September 2020, Botswana had recorded 2567 coronavirus cases with 13 deaths. Likewise, on the same day, WHO and Africa CDC (2020) also reported COVID-19 cases for other states regionally and globally which were alarmingly high as compared to Botswana. For instance, Kenya 37076 cases and 650 deaths, Ethiopia 69 709 cases and 1108 deaths, South Africa 661 936 cases and15992 deaths, UK 429281 cases and 41971 deaths, Italy 308104 cases and 35818 deaths, India 5992532 cases and 7751deaths. On the other hand, on the same day, other countries reported lower cases than Botswana such as Tanzania 509 cases and 21 deaths, Seychelles 143 cases and 0 deaths, New Zealand 1477 cases and 25deaths. The skyrocketing COVID-19 cases witnessed in some countries were due to several factors including better surveillance, diagnostic and health care documentation system (i.e. South Africa, UK)) (Motlhatlhedi *et al.*, 2020), non-compliance to instigated public health control measures (i.e. Italy) (Bugalia *et al.*, 2020; Dwomoh *et al.*, 2021) , tourism hubs that receive high level of foreign travels (UK, South Africa, Italy) (Motlhatlhedi *et al.*, 2020) and high proportion of older population (UK, Italy) (Bugalia *et al.*, 2020). Other countries like Kenya, Ethiopia and India experienced high COVID-19 burden because of high population density coupled with suboptimal health facilities and weaker health care system (i.e. limited testing capacity), and poor Water, Sanitation and Hygiene(WASH) conditions (inadequate access to clean water and hand washing facilities) (Bwire *et.al*.,2022). The lower reported cases in some countries were because of limited testing and reporting (e.g. Tanzania) (Bwire *et.al*.,2022) , some had better surveillance, diagnostic capacity matched with early implementation of strict control measures(e.g. New Zealand)(Singh, 2021). Some states like Seychelles are isolated from the mainland and earlier restriction of international travels might have contributed to lower cases (Motlhatlhedi *et al.*, 2020).

In response to the pandemic, world governments including Botswana deployed a wide range of control measures like closure of boarders and airports, strengthening port health systems (i.e thermal checks, testing, capacity building of staff on infection and prevention control and case management),imposing lockdown, curfew, social distancing, contact tracing, community sensitization through public education, and isolation among others to contain the disease (Djaoue *et al.*, 2020; Motlhatlhedi *et al.*, 2020).These actions were employed to minimize virus dissemination and also to buy states some time to organize, mobilize and allocate the available resources to assist prepare for the surge (Gathungu *et al.*, 2020). The aim of these strategies was to prevent infection introduction, contain outbreaks and shrink peak epidemic size so that healthcare system was not overwhelmed (Haider *et al.*, 2020).

While stringent restrictions measure have been generally proven to be effective in controlling the infection spread, their potential benefits can be jeopardized by the detrimental socio-economic impacts associated with long term implementation (Siamisang *et al.*, 2022). Therefore, countries across the world instigated public health interventions with varying degree of stringency, timing and duration. According to Mander and Ruttenauer (2020), government subsidies to scale up testing and contact tracing affected national budgets, whereas physical distancing measures disrupted economic activities, thus exacerbating levels of poverty. Relatedly, Siedner *et.al* (2020) reported that Economic Commission for Africa projected that Sub Sahara African region would experience a 1.4% shrinkage in gross domestic product (GDP). Moreover, implementation of non-pharmaceutical interventions (NPIs) was reported to have also disrupted healthcare access and service delivery. There were some reports of closure of mobile clinic services (Haider *et al.*, 2020), decline in clinic attendance in Kwazulu-Natal, South Africa (Haider *et al.*, 2020) , closure of vaccination clinics in Zimbabwe (Siamisang, Kebadiretse and Masupe, 2021), augmented cases of malnutrition of under-5 children in Northern Ethiopia as well as a decline in HIV testing and enrollment into antiretroviral therapy (Bwire *et.al*.,2022). Furthermore, long term social restriction have been linked to the adverse mental health outcome in the population and decline in educational advancement (Sardar *et al.*, 2020).

An evaluation of public health measures implemented in Botswana or globally could help authorities in choosing the most cost-effective measure to control this and future pandemics. Since the global pandemic began, an increased number of techniques including mathematical models have been developed to forecast the effects of COVID-19 (Yang *et al.*, 2020). Mathematical models have been used for centuries to understand disease spread and analyze the effectiveness of control measures of different infectious diseases. According to Ambikapathy and Krishnamurthy (2020), the health system can use the predictions of such models as an intelligent tool to decide on the types of control measures to implement, as well as when and where they should be implemented. Therefore, the aim of this study was to use mathematical modeling to describe the SARS-CoV-2 transmission dynamics, COVID-19 trajectories, assess and quantify the impact of some implemented control measures (i.e lockdown) in Botswana.

1.2 Statement of the problem

The emergence and spread of human zoonotic coronaviruses in recent decades have provided a challenge to humanity, posing significant threat to global health, social and economic conditions of the global community. Since the announcement of COVID-19 as a pandemic, WHO has reported a total of 31174627 confirmed cases and 962613 deaths globally with 2567 confirmed cases and 13 deaths being recorded in Botswana as of 23rd September 2020 (WHO, 2020). Furthermore, the Botswana's already stretched healthcare system was put under pressure due to lower inpatient care facilities (i.e shortage of hospital beds and intensive care unit beds) (Tshitenge and Nthitu, 2022; Ncube, Mars and Scott, 2020; Kealeboga, Khutjwe and Seloilwe, 2022), shortage of skilled personnel (Tshitenge and Nthitu, 2022) and shortage of health commodities (essential medicine, testing kits and reagents, personal protective equipment etc) locally due to disruption in global supply chains of health products which in turn compromised the quality of care to patients(Goldschmidt and Stasko, 2022).

Aside from the substantial morbidities and fatalities brought about by COVID-19, this outbreak and the secondary effects of NPIs implemented also resulted in unanticipated far reaching economic and societal consequences that governments were not prepared to handle. According to the reports from World Bank in 2020, COVID-19 pandemic had a severe impact on the economy of Botswana; evidenced by the country's GDP growth shrinkage of 8.7 percent (World Bank,2020). Unemployment was reported to have increased to 26 percent by 2021 due to collapsing enterprises and subsequent job losses (Sambona *et al.*, 2020). SARS-COV-2 pandemic was also deemed as a food security threat, as it worsened the food insecurity situation in the country. Botswana being a net food importer was vulnerable to interruptions in global logistics and distributions (Kakaei *et al.*, 2020; Liu *et al.*, 2020)). Additionally, control measures which restricted movement heavily impacted the daily wage earners in informal sector (Kakaei *et al.*, 2020) which exacerbated the poverty levels. Some reports have highlighted that due to movement restriction and isolation there was a spike in Gender Based Violence and child abuse cases observed across the country with 37% of women reporting sexual, physical and emotional violence (Sambona *et al.*, 2020). Moreover, Bolaane *et al* (2020), conquered with Ntshwarang *et al* (2020), reporting that the education sector also suffered as a result of full lockdown highlighting increased dropout rates, decline in academic performance of pupils across the country due to prolonged school closures, limited ICT infrastructure, technology disparities among learners and most teachers lacking training or knowledge with remote teaching and learning among others.

Since there has been little or no evidence and research about the COVID-19 transmission dynamics nor impact of intervention strategies on SARS-CoV-2 containment, therefore it is still unclear how impactful lockdown and other NPIs were in reducing COVID-19 burden in the country. Henceforth, this warranted research considering the current situation of COVID-19 in Botswana as this will help to give a basis for the government and policy makers to find common ground on which preventive policies would be most effective in managing the current outbreak and future pandemics at the same time considering the economy of the country.

1.3 Study Justification

Since the announcement of the first COVID-19 case in March 2020, the government of Botswana had adopted different non-pharmacological intervention (i.e. lockdown) strategies to reduce the virus transmission. However, it is still not clear what the influence lockdown has had on the decline in reported incidence of COVID-19 cases because until now there have been no study to quantify the impact of such implemented control strategies used to control the rapid propagation of COVID-19 in the country. Therefore, due to that information gap coupled with the incomplete understanding of the epidemiology of the disease, authorities have faced challenges in terms of implementing disease control strategies, disease management and development of effective public health policies.

Therefore, this study will help in determining the effectiveness of implementing lockdown as a control strategy against Covid-19 in Botswana. To the best of the author's knowledge, no mathematical models has been developed using Botswana data to understand the impact of the control measures that were applied to mitigate the effects of COVID-19 during the early stages of the pandemic. Since, little has been done to explore effective policy scenarios that can achieve a balance between the control of the outbreak and economic growth, findings from this study can give highlights of the most efficacious options available to control the disease.

Also, this study findings can help support the establishment of mid- and long-term interventions to prepare containment strategies against further outbreaks. Moreover, the projections and comparison of COVID-19 cases using mathematical modeling under different lockdown scenarios (partial or full lockdown) in this study can help authorities on deciding where, when and how to uplift the lockdown. Therefore, this work will contribute to the body of knowledge of transmission dynamics of COVID-19 in Botswana.

1.4 Objectives

General objective

To generate knowledge to improve understanding of transmission dynamics of COVID-19 in the early stages of the pandemic in Botswana and use it to forecast number of cumulative cases under different intervention scenarios.

Specific objectives

- ✓ To develop and validate a mathematical model for COVID-19 transmission and predict number of cumulative cases without interventions.
- ✓ To study the impact of various lockdown scenarios (partial and complete) on the spread of the COVID-19 infectious disease.
- ✓ To estimate the effect of lockdowns in Botswana on the effective reproduction number (Re).
- ✓ To study the combined effect of lockdowns and other intervention strategies (contact tracing and quarantine) on the COVID-19 dynamics.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

This chapter presents a comprehensive discussion of literature review with respect to the research topic and research objectives. This section looks at the general overview of SARS-CoV-2 as an etiological agent of COVID-19 and reviewed the epidemiology of COVID-19 in global, regional and country specific literature in line with factors influencing transmission, risk of infection, clinical symptoms, diagnosis and control mechanisms. In addition, it also discussed the history of mathematical modeling in infectious disease control as well as mathematical modeling of COVID-19.

2.2 Etiology of Covid-19

Coronaviruses (CoVs) are a group of enveloped, non-segmented positive sense stranded RNA virus that belong to the family of *Coronaviridae*, the order *Nidovirales* and the subfamily *Coronavirinae* (Sardar *et al.*, 2020) which is divided into four genera being; alpha coronavirus, beta coronavirus, delta coronavirus and gamma coronavirus (Sardar *et al.*, 2020). Severe acute respiratory syndrome (SARS-CoV-2), which is the etiological agent of COVID-19 belongs to subfamily *Orthocoronavirinae a*nd genus *Betacoronavirus* (Sardar *et al.*, 2020). Other than SARS-CoV-2, there are six human infective coronaviruses that have been identified including; Human coronavirus-NL63, Human coronavirus-229E, Human coronavirus-OC43, Human coronavirus - HKU1, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV) (Sardar *et al.*, 2020).However, amongst other coronaviruses, studies have highlighted that SARS-CoV-2 is genetically related to SARS-CoV and MERS-CoV with 79.5% and 51% similarities, respectively (Sardar *et al.*, 2020). Coronaviruses are known to cause disease in mammals and have been found in humans since 1960 (Sardar *et al.*, 2020) .

Most human coronaviruses are endemic and responsible for causing mild respiratory diseases, but only the zoonotic coronaviruses (SARS-CoV, MERS-CoV and SARS-CoV-2) are considered of paramount health and socioeconomic importance because they are known to cause severe to deadly pneumonia in humans and also responsible for recent major outbreaks which occurred in 2003,2012 and 2019 (Garba, Lubuma and Tsanou, 2020). SARS-CoV-2, whose origin is linked to Huanan seafood market in Wuhan has been reported to be infectious not only to humans but to other mammalian animals such as lions, tigers, non-human primates, dogs, cats, mink, white tailed deer, giant anteater, hippopotamus and hamsters among others (CDC,2022; FAO, 2022). According to literature(Garba, Lubuma and Tsanou, 2020; Ouassou *et.al*.,2020), SARS- CoV-2 reservoir remains elusive, however bats and pangolins are thought to be its sources. Since COVID-19 pandemic began, there are several SARS-CoV-2 variants of concern that have been identified to influence transmission, disease severity and also contribute to unique trends observed globally namely; alpha variant (B.1.1.7), beta (B.1.351), delta (B.1.617.2,), gamma(GR/501Y.V3/P.1.1+P1.2) and Omicron (B.1.1529) (Africacdc.org, 2022;Sardar *et al.*, 2020).

2.3 Transmission

SARS-CoV-2 is mainly transmitted through the human population via direct and indirect contact and respiratory droplets transmission routes (WHO,2020; CDC,2020; (Zhao and Chen, 2020). Respiratory droplets transmission route which is considered a dominant route for spread of COVID-19 occurs when susceptible individuals inhales respiratory droplets and aerosols generated by infectious individuals when sneezing, talking or coughing (Rahman *et al.*, 2021). The SARS-CoV-2 virus can also be transmissible through direct physical contact with the infected person e.g. kissing, handshake (CDC,2020). According to WHO (2020) and Zhou *et al (*2020), formite transmission is also considered as a likely mode of SARS-CoV-2 transmission because respiratory droplets expelled by the infected individuals can contaminate the surrounding surfaces and objects. Thus, the transmission occurs due to self-inoculation in the mouth, nose and eyes after a susceptible individual touches a contaminated surfaces or objects. However, authors Zhou *et al (*2020) have concluded that this transmission mode is dependent on viral load on the inanimate surface, nature of the object and the environmental conditions. Some studies have also suggested that SARS-CoV-2 can be spread through fecal oral route since the virus can remain in the digestive tract of infected patients up to weeks; even after respiratory symptoms subsides, hence the excreta of such individuals are considered the primary source for cross contamination (Memon, Qureshi and Memon, 2021; Guo *et.al*.,2021). This assumption came about following reports of detecting SARS-COV-2 RNA in rectal swabs or feces samples from COVID-19 patients and viral RNA in sewage which raised possible fecal oral transmission route of SARS-CoV-2 in humans (Heller, Mota and Greco, 2020). However, some reports have highlighted that this mechanism of transmission does not significantly contribute to new infections (Sardar *et al.*, 2020).

2.4 Risk Factors associated with COVID-19 transmission.

There are several factors that have been reported to influence the spread of the COVID-19 pandemic within and across countries such as the agent, host, mitigating strategies deployed, socioecological factors (e.g. environmental conditions, socioeconomic status and healthcare system, and population density) and anthropological factors (socio-cultural and level of knowledge)

Agent: Viral factors such as genetic mutation has been proven in various studies to affect the pathogenicity, virulence and transmissibility of SARS-CoV-2 strains. Emerging SARS-CoV-2 variants of concern have been reported to be highly transmissible, more virulent and responsible for reinfections than the wild type of strain. For instance in a study done by Yang and Sharman (2021), omicron strain was 94% more transmissible than the ancestral strain and eroded more than 50% immunity acquired from prior infections and vaccination.

Host: The infection of humans by SARS-CoV-2 has been reported to depend on demographics (age, gender), comorbidities, immune status and genetics among others. Although SARS-CoV-2 can infect all ages, its severity and mortality is higher in elderly people(aged 65 and above) (Rothan and Byrareddy *et al.*, 2020; Ouasson *et.al.*, 2020; Gois *et al.*, 2020). Comorbidities have been linked to heightened risk of COVID-19 related deaths, with individuals experiencing one or more chronic underlying conditions suffering severe form of the disease(Gesesew *et al.*, 2020; Ouasson *et.al.*, 2020).Also studies have reported that individuals with low immunity are more susceptible to contracting the COVID-19 infection (Rothan and Byrareddy *et al.*, 2020; Ouasson *et.al.*, 2020).

Intervention measures: Public health control measures deployed by the authorities and timing of implementation is also a determining factor influencing the rate of disease spread. Many studies have suggested that to successfully suppress disease spread and reduce burden, early implementation of rigorous mitigation measures was of necessity. According to Singh (2021) those countries like New Zealand that implemented strict measures(lockdown) promptly, reported decreased rate of new infections and the death toll. On the other hand, Guzzetta *et al.*(2021) and Shattock *et al.*(2021) highlighted that other nations like Italy, USA and UK which delayed in implementing lockdown and/or ignored implemented public health measures until number of fatalities soared experienced uncontrolled morbidity and mortality.

Socioecological factors play a key role in the transmission of SARS-CoV-2. Environmental conditions such as temperature and humidity have been reported to have an effect on SARS-CoV-2 transmissibility e.g cold and dry conditions are associated with rapid viral spread while warm climatic conditions are linked to slower transmission rates (Su *et.al*.,2020;Fonchin *et.al*.,2022).However, conflicting results were reported in some studies whereby high SARS-CoV-2 transmission rates have been observed in areas (e.g Iran, Brazil) with warmer climatic conditions (Smith *et al.*, 2021), while some studies also reported no significant association between climatic conditions and COVID-19 transmission (Su *et.al*.,2020).Overcrowding in limited spaces has also been reported as a one of the catalyst to increased disease transmission. According to Iderus *et al* (2021) areas with high population densities are correlated with increased COVID-19 transmission rate due to higher interaction and close contact between individuals as compared to sparsely dense population.

Socio-economic status and healthcare system of a country has been strongly linked to the COVID-19 transmission rate and risk of severe COVID-19 outcome. Fernández-Martínez *et al* (2022) stated that, compared to countries of high socioeconomic status, economically undeveloped countries are characterized by poor sanitation, inadequate supply of freshwater, health inequalities and overstretched healthcare system which is likely to aggravate viral spread. In addition, Zsichla and Muller (2022) concluded that countries with effective healthcare system such as strong surveillance system, case detection and response programs had been reported to experience low disease transmission in terms of reported cases and reduced severity of COVID-19 outcome i.e had lower case fatality rates

Socio-cultural factors are also considered as one of the predictors of SARS-CoV-2 transmission rate. The communities' traditions and beliefs can precipitate the spread of COVID-19 infection; for example hand shaking, ceremonial gathering(wedding and burials) can accelerate the spread of the virus (Fonchin *et al.*, 2022). Furthermore, the level of knowledge, attitude and perception of the individual and/or community about infectious agent can also determine its transmission intensity; a knowledgeable and well informed community tend to be compliant to implemented public health measures thus lowering the risk of COVID-19 transmission (Lorettu *et.al*.,2020).

2.5 Clinical signs and symptoms

The symptoms of COVID-19 usually appear after an incubation period of 2-14 days, with an estimated average incubation of about 5.1days (Garba, Lubuma and Tsanou, 2020; Wangari *et al.*, 2021). Additionally, the viral shedding of COVID-19 among infected patient lasts about 10 days(Bugalia *et al.*, 2020). Common symptoms mostly include fatigue, cough, fever, headache, confusion, nausea, vomiting, shortness of breath, loss of appetite, taste and smell(Sewell and Miller, 2020; Kifle and Obsu, 2022). Complications from COVID-19 leading to death include pneumonia, acute respiratory distress syndrome, multiple organ failure, sepsis and septic shock(Bugalia *et al.*, 2020). There is a wide variety of symptom severity that has been reported in COVID-19 infected patients. WHO and most studies have pointed out that a larger proportion (60-80%) of infected individuals are usually asymptomatic or show mild symptoms of a disease and recover without needing hospital treatment. (Wangari *et al.*, 2021; Gu *et.al.*, 2022; WHO, 2022).In cases where individuals are infected and symptomatic, about 15% become severe cases requiring hospitalization and supplementary oxygen, while 5% become critically ill requiring treatment and mechanical ventilation in intensive care unit, whereas 1% of the cases die from the disease (Gois *et al.*, 2020; WHO, 2022) .

2.6 Diagnosis of COVID-19

Rapid and accurate detection of COVID-19 is crucial to control community outbreaks. Diagnosis of COVID-19 is considered in individuals with new onset of symptoms, travel history to hotspot areas/countries and close contact with confirmed COVID-19 case (CDC,2020; WHO,2020). There are several diagnostic assays that are relevant in COVID-19 patient management and pandemic control, and these tests are available as laboratory-based or point of care tests (CDC,2020; WHO,2020).

2.6.1 Molecular tests: Diagnosis of the infection is typically made by detection of SARS-CoV-2 RNA on upper respiratory specimen (nasopharyngeal swab) using nucleic acid amplification tests (NAATs) like real time polymerase chain reaction (RT-PCR) assay (Vandenberg *et al.*, 2021). These tests are considered more specific and sensitive because they are based on genome sequencing of SARS-CoV-2, hence are used as the reference standard diagnostic test (Vandenberg *et al.*, 2021). According to studies conducted by Hellou *et al.*(2021) and Kevadiya *et al.*(2021) , the pooled sensitivity and specificity of RT-PCR was reported to be around 90.4% (95% CI,83.7 to 94.5) and specificity of 98.1%(95% CI, 95.9 to 99.2) respectively. However, this method is expensive and requires specialized skills and equipment (Zhai *et al.*, 2020).

2.6.2 Rapid antigen test: These lateral flow assays detects viral proteins (e.g nucleocapside or spike proteins) in a nasopharyngeal swab specimen (CDC,2020). Rapid antigen tests are considered more convenient, accessible, cheaper and have shorter turnaround time (Zhai *et al.*, 2020) However, rapid antigen tests have low sensitivity, thus negative results of a symptomatic patients may need a further confirmatory test(NAATs) to avoid false negative results (Pascarella *et al.*, 2020) . Ebrahimzaden *et al.*(2021) reported sensitivity of antigen test to be 65.3% (95% CI, 56.8 to 73.1) and specificity was 99.9% (95% CI, 99.5% to 100%). Nonetheless some researches highlighted that the sensitivity of the test varied depending on the infectiousness state of a patient; showing high sensitivity in symptomatic individuals than asymptomatic counterpart (Jegerkhens *et al.*, 2020). This test is recommended by WHO and CDC in settings where there are unavailable molecular tests or delayed laboratory results as an alternative method for case detection and implementation of public health measures such as isolation and quarantine (Peeling *et al.*, 2020).

2.6.3 Serological tests: Serological assays like enzyme linked immunosorbent assay are used to detect host antibodies in response to SARS-CoV-2 infection in blood samples (serum or plasma)

(CDC, 2020). According to a CDC (2020) report, serologic tests are mostly used to identify past COVID-19 infection exposures, thus this testing approach is primarily employed for research and surveillance purposes to better understand the percentage of the population previously infected with SARS-CoV-2 as well as how the virus is spreading across the population over time. The use of serologic tests in acute settings is limited because detectable antibodies typically take days to weeks to develop in response to an infection (Caliendo and Hanson, 2022).

2.6.4. Radiological findings: Imaging techniques like chest X-ray, computed tomography (CT) and lung ultrasound can also be used to diagnose COVID-19. Imaging abnormalities in COVID-19 patients are characterized by diffuse, peripheral ground-glass opacities on peripheral and lower lobes (Pascarella *et al.*, 2020). At present the best radiological strategy remains unknown. According to some reports chest CT scan seems to have high sensitivity and specificity compared to other imaging techniques. A pooled sensitivity and specificity of 86.9%(95% CI, 83.6 to 89.6) and 78.3% (95% CI, 73.7 to 82.3), respectively was reported by Kevadiya *et al.*(2021). However since it is costly, it is only recommended for patients with undefined clinical picture (Long *et al.*, 2020; Pascarella *et al.*, 2020). Zhai *et al* (2020) reported that chest CT scan can be used to assess the severity of COVID-19, while ultrasound is commonly used for monitoring disease progression.

Achieving a correct diagnosis in a patient is crucial, however specificity and sensitivity of a test is dependent on various factors like the quality of specimen collected, proficiency at which the test is done, correct interpretation of results and timing of testing relative to stage of infection (i.e days after symptom onset) (Pascarella *et al.*, 2020). According to Caliendo and Hanson (2022), the highest sensitivity for molecular or antigen tests occurs when viral loads are high, which occurs in the first three days after onset of symptoms. Although most studies have suggested upper respiratory specimens as the ideal specimen for COVID-19 diagnostic testing, several other studies have reported positive SARS-CoV-2 in various specimens like stool, sputum and saliva (Vandenberg *et al.*, 2021).

2.7 Covid-19 Epidemiology: Global overview

The novel COVID-19 was first reported in Wuhan city, China in late December 2019 and rapidly spread throughout China and to all parts of the World (Kim *et al.*, 2020 ; Sardar *et al.*, 2020; WHO,2020). Since its discovery, the epidemic scale of COVID-19 disease has swiftly grown worldwide. Henceforth, following reports of increased spread, confirmed cases and deaths across the globe, WHO declared COVID-19 as a Public Health Emergency of International Concern and a global pandemic on the 30th January and 11th March 2020, respectively (Kim *et al.*, 2020 ; WHO,2020). As of 6th January 2022, nearly 289 million COVID-19 cases and over 5.4 million deaths had been reported globally by WHO: with Europe, America, Western Pacific, South-East Asia and Eastern Mediterranean reporting 103190 471 (36%), 104698449(36%),11391761(4%), 45034821(16%) and 17201367(6%) cumulative cases, respectively. The above-mentioned regions also recorded cumulative deaths as follows; 1674758(31%), 2411818(44%), 156515(3%),721940(13%), 316141(6%), respectively (WHO situation report, 2022). Although most countries globally registered significant death rates, it was also reported that most COVID-19 patients recover, with recovery rate estimated between 90%-99% (Worldometer, 2022). Studies have shown that although SARS-CoV-2 is highly transmissible, its case fatality rate is lower; 2.5 % as compared to SARS-CoV and MERS-CoV with 10% and 35%, respectively (Sardar *et al.*, 2020).

The first COVID-19 case in Africa was reported in Egypt on 14 February 2020 (Frost *et al.*, 2021), which later on spread to the rest of the continent. However, in Southern Africa, the first COVID-19 case was reported in South Africa on the 5th March 2020 (Nyabadza *et al.*, 2020). According to Africa CDC estimation, by 6th January 2022, Africa had reported over 9.8million COVID-19 cases which accounted for 3.3% of the COVID-19 total cases reported globally and over 229 000 deaths were reported which accounts for 4.2% of the deaths reported globally (Africacdc.org ,2022). In comparison to other continents, WHO reports indicated that Africa had lower number of COVID-19 cases and deaths (Kifle and Obsu, 2022). According to Diop *et al.* (2020) there are similar characteristics across African countries that are hypothesized to have had a hand in the noticeably lower COVID-19 cases recorded in Africa compared to other continent. For instance, Africa has young population with the median age of 18years with at least 3% of the African population being older than 65years (Frost *et al.*, 2021, Bwire *et.al.*,2022). This indicated that less percentage of African population was at high risk of developing severe COVID-19 illness. Secondly, there was limited testing capacity, contact tracing and insufficient data collection in Africa which might result in underreporting and underestimation of the true disease burden on the continent (Pearson *et al.*, 2020) . Thirdly, the similarity of COVID-19 symptoms to other diseases which are endemic in Africa (i.e. Malaria) can also result in underestimation of the actual COVID-19 cases (Bwire *et.al*.,2022). Moreover, the delayed arrival of pandemic in Africa, allowed countries to learn from the situation unfolding in other continents which helped in readiness and preparedness (i.e early imposition of lockdown and other interventions) by African countries thus contributing to the minimum COVID-19 spread (Sichone *et al.*, 2021).

2.7.1 Covid-19 in Botswana

On the 30th March 2020, one person with travel history was diagnosed of COVID-19 in Gaborone, and this marked the first confirmed COVID-19 case to be reported in Botswana (Siamisang, Kebadiretse and Masupe, 2021). According to Siamisang *et al* (2022), the majority of reported cases during the early phase of the pandemic were imported mostly by truck drivers. Additionally authors in Siamisang *et al* (2022) highlighted that, in Botswana, the emergence of COVID-19 was initially influenced by human behaviors such as overcrowding during celebration events (parties), noncompliance to intervention measures (i.e escaping from quarantine/isolation facilities, not wearing masks in public areas) and traveling from hotspot to uninfected areas among others. As of 6th January 2022, Botswana had recorded 229855 cases and 2497 deaths (Worldometer, 2022). Current reports have pointed out that more people recovered from COVID-19 disease and few succumbed to COVID-19 related diseases; with recovery rate of 99.2% and case fatality rate of 0.8% (MoHW,2022 ,Singini and Manda, 2022). In comparison to other African states, Botswana was least hit by the COVID-19 outbreak probably because of embarking on intensified disease surveillance and emergency preparedness as cases were escalating in neighboring countries, especially South Africa (Singini and Manda, 2022). For instance, early closure of boarders even before reporting the index case, implementation of lockdown immediately after reporting the first case and local travel restrictions helped to reduce the number of reported cases(Bolaane *et al.*, 2020; Sambona *et al.*, 2020; Motlhatlhedi *et al.*, 2020)). Moreover, Botswana has a younger population with a median age of 24 years and less than 5% of the population older than 65years old (World Bank,2022), hence the population was at low risks of COVID-19 severity. However it was not clear how the high prevalence of comorbidities(HIV,TB and non-communicable disease) in this young population would affect the COVID-19 severity in the country (Bwire *et.al*.,2022).

At the time of this write-up, Botswana was reported to be experiencing a 4^{th} COVID-19 epidemic wave and different circulating SARS-CoV-2 variants were identified and associated with each epidemic wave (Africacdc.org, 2022). According to Viana *et al.* (2020), the first variant that replaced the original strain was alpha variant (B.1.1.7), which caused a wave that peaked in June 2020 to September 2020.The second wave which peaked around November 2020 till February 2021 was driven by Beta (B.1.351). The delta (B.1.617.2,) variant followed soon causing the third wave which peaked in May 2021 and ended in September 2021. As of late November 2021, the fourth wave was dominated by the Omicron (B.1.1529) variant.

2.8 COVID-19 Control mechanism.

Currently, the World governments embarked on using pharmaceutical interventions to curtail the spread and severity of COVID-19 disease. Various vaccines including AstraZaneca-Covishield, Pfizer, Moderna, Sinovac and Johnson & Johnson were approved for administration by WHO and states authorities (CDC,2022). However, during the early phase of the outbreak, WHO issued several recommendations mostly NPIs, which were adopted by different countries to combat the pandemic. During this period, NPIs were the cornerstone, most accessible and vital interventions in the face of COVID-19 pandemic (Nyabadza *et al.*, 2020), particularly given the efficacy of such preventive measures in previous pandemics. According to Haider *et al.*, (2020) the goal of these interventions was to prevent infection introduction, contain outbreaks and reduce peak epidemic size so that healthcare system were not overburdened.

During the initial phase of the pandemic, countries resorted to using combination of NPIs such as closure of boarders and international airports, lockdowns, curfews, isolation, quarantine, social distancing, use of face masks, hand hygiene, public health awareness and contact tracing among others to contain the disease and also reduce its effects of spread on health care and economies (Djaoue *et al.*, 2020; Kucharski *et al.*, 2020). Although most countries agreed with WHO COVID 19 protocols, there were some countries which thought otherwise and were initially hesitant to embrace the proposed interventions such as Tanzania and Mauritius (Bwire *et.al.*,2022). Depending on the severity and number of cases, the social and economic effect of strategy, government willpower and capacity, acceptance and willingness of the public (Chen *et.al.*,2021) , different countries enforced different interventions of varying lengths and types to contain the outbreak.

2.8.1 COVID-19 control in Botswana.

After reporting the first confirmed case, the government of Botswana immediately implemented various preventive measures to reduce local transmission. The President declared a state of emergency for six months and announced a nationwide 49 days' lockdown starting midnight on 02nd April 2020 until 21st May 2020 (Motlhatlhedi *et al.*, 2020; Sambona *et al.*, 2020). This aggressive control measure was implemented mainly to curb transmission and to buy the state some time to prepare and mobilize the resource needed to contain the disease. Soon after, additional measures were concurrently instigated by the government to minimize community transmission. Schools were closed on the 23rd March 2020, Targeted testing and community contact tracing began on 21st April 2020 at Metsimotlhabe, Bobonong and Siviya, facemasks usage in public places was made mandatory on the 1st May 2020 and a national curfew was imposed on 24th December 2020 from 7pm to 04am (Bolaane *et al.*, 2020; Sambona *et al.*, 2020 ; MOHW,2020)). Other measures which were also implemented included hand hygiene, quarantine/isolation of suspected cases, awareness campaigns in both rural and urban areas, cancellation of events/public gatherings and closure of non-essential businesses, churches among others (MOHW, 2020). Because of socio-economic pressures in Botswana, the lockdown was relaxed and lifted in phases. The authorities provided few relaxations (i.e. conditional inter-state travel) during phase 2 (07 May 2020) and phase 3 (14 May 2020) of full lockdown respectively (MOHW, 2020). Furthermore, the government divided the country into nine COVID-19 zones (Greater Gaborone, Greater Francistown, Greater Palapye, Greater Phikwe, Kgalagadi, Ghanzi, Boteti, Chobe and Maun) for easy regulation and coordination; the largest being Greater Gaborone zone (Motlhatlhedi *et al.*, 2020).With all the aforementioned interventions that had been implemented with the aim of preventing the spread of COVID-19 and reducing the pandemic caseload in Botswana, still to date their efficacy and likely impact on the COVID-19 infection is unknown.

While there is ample amount of research (especially quantitative research) on relevance of NPIs such as lockdown in responding to COVID-19 crisis in developed countries, such kind of studies are missing in low- and middle-income countries like Botswana. Hence this study aimed to fill that gap. Botswana makes a good case study for this research because it is one of the Sub-Sahara African countries which instituted most of the NPIs including stringent nationwide full lockdown during the early phase of the pandemic.

2.9 Mathematical modeling history

Mathematical models are simple approximate description of reality using mathematical equations and assumptions that can be used to develop hypothesis by breaking down the behavior of the complex system (Bugalia *et al.*, 2020; Dwomoh *et al.*, 2021). According to Chintalapudi *et al.*, (2020) mathematical modeling is a tool of great veracity that study disease spread and trajectory, predict the future of an outbreak and evaluate intervention strategies. It is believed that the first use of mathematical modeling to study spread of epidemics dates back to 1760 when Daniel Bermoulli developed a smallpox model to study the efficacy of vaccination (Guan *et al.*, 2022). Subsequently, different scholars including Ross and Hamer did a lot of work which contributed to the advancement of mathematical modelling of emerging and re-emerging infectious diseases (Talihun, Demie and Eyob, 2020; Runge *et al.*,2020). In 1928, Kermack and McKendrick developed the first transmission dynamics model; Susceptible-Infected-Recovery(SIR) model to study plaque in London (Chen *et al.*, 2022). From there onwards, modified SIR models have been developed and used in many instances in different countries to inform health policy on control of various infections like dengue (Carvalho *et al.*, 2022), HIV (Chibaya, Kgosimore and Maasawe, 2013), Tuberculosis (Nyabadza and Kgosimore, 2012), H1N1 (Tan *et al.*, 2021) and Ebola (Denes and Gumel, 2019).

There are several advantages linked to using mathematical models, for instance modelling is quicker and less expensive and also allows for the exploration of the impact of multiple control measures and determination of the best intervention strategy (Marjan, Wahbi and Alridha, 2022). Additionally insight from modeling generally comes with lower risk and less ethical concerns than traditional experimental studies or field trials (Runge *et al.*, 2022).

2.9.1 Mathematical modeling of COVID-19.

In response to the COVID-19 pandemic, a variety of mathematical model types including deterministic models capable of providing worthy insight for healthcare policy making have been developed and analyzed extensively in different countries. For example; Yang *et al* (2020) used a Susceptible-Exposed-Infected-Recovered(SEIR) model and artificial intelligence approach to predict the epidemic peaks and sizes in China by assimilating COVID-19 epidemiological data and population migration. A modified SEIR model was proposed by Mugisha *et al* (2021) to study the dynamics of COVID-19 in Uganda and also to determine the implications of early easing of lockdown. Another study was done in South Africa by Garba, Lubuma and Tsanou (2020) using a compartmental model to scrutinize the transmission dynamics of the disease taking into consideration environmental contamination. In Frost *et al* (2021), the authors developed a compartmental model to study possible trajectory of SARS-CoV-2 under various intervention scenarios in 52 African countries. Sichone *et al* (2021), developed a deterministic model to determine the blanket testing rate of asymptomatic individuals required to combat the pandemic in Lusaka; Zambia. Al-Harbi and Al-Tuwairqi (2022) used a deterministic model to study the impact of lockdown and social distancing on the dynamics of COVID-19 in Saudi Arabia. The authors in Gosce *et al* (2021) developed modified SEIR model to predict the impact of lifting lockdown in London, UK and also assessed the combined effect of NPIs on future incidences of COVID-19. Therefore, it is with reference to the studies that the focus of this current research study is framed, to utilize a compartmental model to forecast the course of the COVID-19 in Botswana and investigate the impact of lockdown on COVID-19 cases.

Among the WHO recommended NPIs strategies, numerous modeling studies have upheld lockdown as the most efficient strategy for flattening the COVID-19 epidemic curve and to delay the epidemic peak in the absence of pharmaceutical intervention. For example Roques *et al* (2020) reported that in France, lockdowns were able to minimize the transmission of COVID-19 by 84%. Additionally Ivorra *et al.* (2020), pointed out that lockdown imposed in China had a significant effect on COVID-19 epidemic within two weeks corresponding to a decrease in effective reproduction number. Relatedly, Amouzouvi *et al* (2021) also reported gradual decline in basic reproduction number after the Kenyan government enforced travel restrictions. Moreover, Tiwari *et.al* (2020) endorsed nationwide public lockdown as an effective controlling policy for COVID-19 dissemination, not only in India but globally as well because it plays a critical role in epidemic peak suppression. Although a lot of mathematical models have been developed and used to analyze the impact of lockdown on COVID-19, very few studies have done that in the context of Botswana COVID-19 epidemic data and considering lockdown as a compartment.

Just like any other NPIs, the effectiveness of lockdown policy relies on several factors such as societal compliance, duration of implementation and socio-economic status of the country. Several studies indicated that containment measures must be implement early and for a sustainable period to suppress disease spread. According to Yang et al (2021) the earlier the strict implementation, the lower the peak and the earlier the flattening of the epidemic curve of cumulative cases. This was evident in Singh (2021), who report early adoption of strict lockdown measures in New Zealand even before a single death was reported, hence resulted in decreased rate of new infections and marginal death toll among developed countries. However, other nations like the USA and UK which delayed implementing lockdown and other measures until number of fatalities soared, experienced uncontrolled morbidity and mortality (Goscé *et al.*, 2020). Although most literature (Ambikapathy and Krishnamurthy, 2020, Talmoudi *et al.*, 2020, Daniel Deborah, 2020) supports the long implementation of lockdown for effective containment of the disease spread, some reports have indicated that it is possible that lockdown strategy could worsen COVID-19 transmission especially in high population density and overcrowded settlements with weak medical facilities. Nyabadza *et al.* (2020) stated that although lockdowns enforce social distancing, in some parts of South Africa, social distancing is nearly impossible due to the socialization of family units and the nature of settlement patterns thus contributing to increased disease spread. In addition some studies have highlighted that long-term implementation of lockdowns in low and middle income countries may not be feasible or sustainable due to challenges including sociocultural, political and economic factors (Haider *et al.*, 2020). Relatedly, Frost *et al* (2021) concluded that in Africa, approximately 40% of people are living under the poverty line and 85.8% of employment is informal, thus lockdowns that restrict movement may not be enforced. Dzobo, Chitungo and Dzinamarira (2020) also stated that it was a known fact that for some countries, the lockdown strategy could worsen the spread of the virus due to poor management and lack of facilities, palliatives and incentives.

Therefore, because of the above-mentioned shortcomings, it is of utmost importance to determine an effective lockdown policy that may reduce COVID-19 transmission in the community as well as saving the country's economy from drowning. As a resolution, most countries went into lockdown with different levels of restrictions. As much as countries were compelled to lift lockdown due to its negative impact on their economy, it would be of paramount importance for countries to devise ways to predict when or how to relax or uplift the lockdown measures because if done earlier in attempt to re-open the economy of a country, may trigger another pandemic wave (Ndaïrou *et al.*, 2020)). On evaluating how effectively lockdown restriction can be relaxed in UK, Rawson *et al (*2020) found out that the optimal strategy was a phased out release. Mugisha *et al.* (2021) also reported that avoiding the scenario of releasing too many people too soon was considered the optimal time of relaxing lockdown while mitigating the possibility of a second epidemic wave re-emerging. Another solution to cushioning the negative impact of lockdown to the economy would be through implementation of lockdown together with other mitigation strategies. This was supported by Bhadauria *et.al* (2021) stating that COVID-19 could only be controlled if complete lockdown was imposed otherwise disease would always persist in the population. Nonetheless it could be kept under control if lockdowns were imposed partially coupled with other preventive measure. Additionally, Mugisha *et al.* (2021) highlighted that although lockdowns may be inherently enough to suppress an outbreak other control measures must be scaled up as lockdowns were being relaxed. Moreover, Frost *et al.* (2021) reported that in all the 54 African countries they conducted their study on, hard lockdowns with continued post-lockdown interventions were the most effective in delaying and reducing peak infections. In contrast, some reports (Djaoue *et al.*, 2020; Sardar *et al.*, 2021) have indicated that any type of relaxation in lockdowns may lead to exponential transmission leading to resurgence in most countries. This was further supported by Ndaïrou et al, (2020) highlighting that even past epidemics have proven that mortality and incidence cases are lessened while interventions are strictly implemented, however, transmission bounced back once controls are relaxed.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Study Area

Botswana is a landlocked country in the center of Southern Africa bordered by Namibia to the West, Zambia to the North-East, Zimbabwe to the East, Angola to the North-West and South Africa to the South (Tapera *et al.*, 2018). Botswana had an estimated population of about 2.4 million in 2022, with 33% of it aged under 15years and 5% aged 65years and above (World Bank, 2022). Life expectancy at birth is 66 years for men and 72years for women, while birth and infant death rate currently stands at 23 per 1000 people and 26.7 per 1000 live births, respectively (World Bank, 2022). The country has a total land area of about 566 730 km^2 (World Bank, 2022), with a population density of 4 per km^2 and around 72.8% of the population living in urban areas (Worldometer,2022). Botswana is an upper middle-income country with its gross domestic product (GDP) per capita estimated to be $ 6805.2 by World Bank in 2021. The economic strength of the country rests on diamond mining, agriculture (cattle production) and tourism sectors (World Bank, 2022). The country is divided into 10 administrative districts, two cities, five towns and 11 sub-districts. Gaborone is the capital city with about 11.6% of the country's total population living there (Worldometer, 2022). There are six international airports in Botswana, the main one being Sir Seretse Khama international airport located in Gaborone, which has international direct flights from Zimbabwe, South Africa, Kenya, Namibia and Ethiopia (Mbenge *et al.*, 2020).

Just like most Sub-Saharan African countries, the healthcare system in Botswana is inefficient even in normal situations and faces several challenges. Botswana ranks amongst the world's highest burdened countries for both HIV and TB infections ranking number three and 30 respectively in the World, as well as rising rates of chronic health conditions that may increase the risk of COVID-19 complications (Mupfumi *et al.*, 2021). Relatedly, Tshitenge and Nthitu (2022) reported that the inadequacy of the country's healthcare system was highlighted in a WHO report which included Botswana as one of many Africa nations with gaps in preparedness for health emergencies including limited intensive care beds, ventilators, limited stockpiles of essential medicines, shortage of healthcare personnel especially those trained to manage major outbreaks. Healthcare service delivery in Botswana is pluralistic; however, the public health sector dominates the healthcare system in Botswana operating 98% of the health facilities(Tshitenge and Nthitu, 2022). For a population of around 2.4 million, Botswana has 356 health facilities including referral hospitals (3), general hospitals (18), primary hospitals (17), clinics (318), with service delivered by 7427 nurses and 830 doctors (Ncube, Mars and Scott, 2020; Kealeboga, Khutjwe and Seloilwe, 2022)). Besides having low doctor to patient ratio (3.8/10,000), Botswana has a hospital bed capacity of 1.8 hospital beds per 1,000 inhabitants which is much lower than the WHO recommended hospital bed capacity of 2.9 hospital beds per 1000 occupants (Ncube, Mars and Scott, 2020; Kealeboga, Khutjwe and Seloilwe, 2022)).

3.2 Model Formulation

The model proposed in this study was developed following steps of model constructions. COVID-19 epidemic data collected from MoHW was used to model the outbreak in the country. An appropriate model structure that can explain the natural history and evolution of COVID-19 epidemic was selected, created in Vensim software and represented as a stock-and flow diagram in Figure 3.1. Thirdly, a system of formulated ordinary differential equations was used to mathematically model the COVID-19 epidemic as a continuous dynamics process. Lastly the model was optimized to fit the actual reported data.

This study hypothesized that NPIS are a pre-requisite for the success of outbreak containment. Therefore, this modeling study aimed to examine this hypothesis by assessing the effect of lockdown alone and or combined with contact tracing on the R_0 of SARS-COV-2 and trajectory of COVID-19 epidemic in Botswana. For simplicity, this modeling study did not consider numerous economic concerns associated with the increased viral spread and the intervention policies put in place to combat the outbreak. Also, since the model focused on the early stages of the epidemic, the study assumed that only the primary strain was circulating and disregarded mutant strains. In addition, the study did not distinguish between self and mandatory quarantine, as it is only the efficacy and adherence to isolation regulations which affects probability of transmission.

In this section, the study presented model development, model assumptions, model flow diagrams and model equations. In the model development a general overview of the proposed deterministic compartmental model was discussed in detail.

3.2.1 Model Development

In this study a deterministic compartmental model developed by Mugisha *et al* (2021) was adopted and extended by introducing lockdown, contact tracing and isolation to study the transmission dynamics of COVID-19 outbreak in Botswana. The total population size of Botswana (N(t)) at any time t was divided into 10 compartments; S(susceptible), L(Lockdown), E (latently infected), I_a (asymptomatic infected) and I_s (symptomatic infected)], Quarantine asymptomatic (Qa), Quarantined symptomatic (Qs), H(hospitalized), R (Recovered) and D(Deaths). Thus, the total human population N(t) is given by the following equation:

$$N(t) = S(t) + L(t) + E(t) + Is\ (t) + Ia\ (t) + Qa(t) + Qs(t) + H(t) + R(t) + D(t)$$

Transition through compartments: The Susceptible individuals (S) are people in Botswana that have not been exposed to the virus but are at risk of contracting the infection once they come into effective contact with infectious individuals. Lockdown population (L) are individuals whose movement are restricted and have isolated themselves from the population. Hence full lockdown was alleged perfect and protective.

The population in lockdown was initially defined by the proportion ε of the total population N, while those who are susceptible (not in lockdown) were therefore defined by the proportion $(1- \varepsilon)$ of the total population N. Susceptible individuals get infected with SARS-CoV-2 from effective contact with infected individuals at rate ß and then moved to the exposed compartment (E). After the average incubation period of about five days, a fraction κ, of the exposed individuals became symptomatic infected (Is) while the remaining fraction $(1- \kappa)$ became asymptomatic infected (Ia) at the same rate σ (1/incubation period). Upon reaching this stage of the infection, symptomatic infected individuals were identified and isolated efficiently either based on normal surveillance based targeted testing and diagnosis of all suspected symptomatic persons as it was mandatory in Botswana during the COVID-19 pandemic at a rate d or through contact tracing at a rate c. The identified symptomatic infected individuals subsequently entered the group of isolated individuals' Qs and recovered at the rate γ_5 joining the recovered symptomatic Rec S class. On the other hand, asymptomatic infected individuals were assumed to be basically unnoticed in the community hence can only be identified and isolated through contact tracing at the rate *c* and entered the group of isolated asymptomatic individuals Qa and later recovered at the rate γ_4 and joined the recovered asymptomatic Rec A group. It was assumed that some infected individuals in the community can be missed during contact tracing or targeted testing, and these will be responsible for spreading the disease in the community. This group of undetected infected people, i.e. asymptomatic and symptomatic, recovered naturally at the rate of γ_1 and γ_2, respectively and joined the class of undetected community recoveries (undetected cRec). A fraction of those undetected symptomatic infected individuals in the community died from COVID-19 at the rate of θ_1 and entered the D class. Those individuals from symptomatic infected class (in community) who developed severe symptoms to an extent that they required hospitalization proceeded to the Hospitalized class (H) at the rate *h*. The population in this class either experienced COVID-19 related deaths and entered D class at the rate θ_2 or recovered from COVID-19 at the rate γ_3 and entered Rec S group. The total recovered population (R) consisted of individuals from asymptomatic, symptomatic, hospitalized and quarantined compartments who have recovered naturally or from supportive treatment. For the purpose of this model, the total recoveries were made up of Rec A, Rec S and undetected cRec. In regard to this study, Total cumulative confirmed cases at any given time (t) were made up of Qa, Qs, Rec A, Rec S, H and D. Additionally, this study defines confirmed cases as those individuals who were tested and identified either through contact tracing or targeted testing and reported to be SARS-CoV-2 positive at any given point in time.

In the model, the parameter ß (rate of effective contacts between susceptible and infectious individuals) is automatically estimated by model fitting to Botswana outbreak data. However, it is actually a complex parameter that comprises of various components including the average rate of contacts that occur between individuals in the population per unit time. Therefore, to accommodate the effect of lockdown on COVID-19 transmission in the population, the parameter ϱ defined as the contact rate dilution factor was introduced in the model. It is assumed in this study that the overall rate of contact between susceptible and infectious people will reduce as more susceptible people go into lockdown and thus ultimately also reducing the rate of effective contacts ß between susceptible and infectious people. Therefore, the parameter ϱ represents this fractional reduction (dilution) of the contact rate between susceptible and infectious people as a function of the proportion of susceptible people who go into lockdown in the population and this directly affects ß. Note that it is still assumed that people are mixing homogenously in this population except that the rate of effective contacts ß is reduced due to the lock down effect of some people in random parts of the population who are protected from having close physical contact with the infectious person.

3.2.2 Model assumptions

In addition to the above-mentioned assumptions, other assumptions were also considered in the model including.

- The spread and transmission of the COVID-19 virus was only via person-to-person.
- The population was constant (i.e effect of birth, natural mortality and migration were ignored) since the simulation period is very short.
- The members of the population mixed homogenously.
- With regards to transmission of infection, compared to symptomatic individuals, asymptomatic individuals had a lower transmission rate, will recover without requiring special treatment (i.e hospitalization) and were less likely to succumb to the disease.
- During the course of infection, some asymptomatic individuals will eventually start to experience symptoms as the illness progresses and may even need hospitalization, however such occurrences were considered negligible in this model.
- Isolated and hospitalized individuals do not mix with the general population in the community; thus, they do not contribute to the COVID-19 transmissions.
- The recovered population was immune from re-infection during the period of the study.
- The study defined *d* as d = 1/diagnosis delay (days) and an average value of 5.5 days was used to represent this slight delay in diagnosis of visibly symptomatic people (Is) due to various factors including shortages of testing kits, delays in receiving PCR results among other reasons (Sichone et al., 2021).

- The values of this contact tracing rate *c* are equivalent to 1/trace delay of 4 days to 1/trace delay of 20 days meaning it can take between 4 to 20 days to successfully find a contact of the infected individual depending on how efficient and fast the contact tracing is.

3.2.3 Model equations and model flow diagram

Based on the above assumptions and description, the corresponding compartmental model used to capture the COVID-19 transmission dynamics in Botswana without and with interventions was illustrated in Figures 3.1 and 3.2, and expressed mathematically using non-linear Ordinary Differential Equations as presented below:

Model without lockdown nor targeted testing nor contact tracing interventions (null model)

$$\frac{dS(t)}{dt} = -\frac{1}{N}\text{ßIs(t)S}(t) - \frac{1}{N}0.5\text{ßIa(t)S(t)}$$

$$\frac{dE(t)}{dt} = \frac{1}{N}\text{ß}Is\text{(t)S(t)} + \frac{1}{N}0.5\text{ßIa(t)S(t)} - \kappa\sigma E(t) - (1-\kappa)\sigma E(t)$$

$$\frac{dIa(t)}{dt} = (1-\kappa)\sigma E - \gamma 1\text{Ia(t)}$$

$$\frac{dIs(t)}{dt} = \kappa\sigma E(t) - \gamma 2\text{Is(t)} - h\text{Is(t)} - \theta 1\text{Is(t)}$$

$$\frac{dH}{dt} = h\text{Is(t)} - \gamma 3\text{H(t)} - \theta 2\text{H(t)}$$

$$\frac{dR}{dt} = \gamma 1\text{Ia(t)} + \gamma 2\text{Is(t)} + \gamma 3\text{H(t)}$$

$$\frac{dD}{dt} = \theta 1\text{Is(t)} + \theta 2\text{H(t)}$$

Model with lockdown, quarantine, targeted testing and contact tracing interventions

$$\frac{dL(t)}{dt}lock = \varepsilon N(t)$$

$$\frac{dS(t)}{dt} = -\frac{1}{N}\varrho ßIs(t)S(t) - \frac{1}{N}\varrho 0.5ßIa(t)S(t)$$ .... where here $S(t) = (1 - \varepsilon)N(t)$

$$\frac{dE(t)}{dt} = \frac{1}{N}\varrho ßIs(t)S(t) + \frac{1}{N}\varrho 0.5ßIa(t)S(t) - \kappa\sigma E(t) - (1-\kappa)\sigma E(t)$$

$$\frac{dIa(t)}{dt} = (1-\kappa)\sigma E - c\mathrm{Ia(t)} - \gamma 1\mathrm{Ia(t)}$$

$$\frac{dIs(t)}{dt} = \kappa\sigma E(t) - \gamma 2\mathrm{Is(t)} - \mathrm{dIs(t)} - \mathrm{cIs(t)} - h\mathrm{Is(t)} - \theta 1\mathrm{Is(t)}$$

$$\frac{dQa}{dt} = cIa - y4Qa$$

$$\frac{dQs}{dt} = cIs + dIs - y5Qs$$

$$\frac{dH}{dt} = h\mathrm{Is(t)} - \gamma 3\mathrm{H(t)} - \theta 2\mathrm{H(t)}$$

$$\frac{dR}{dt} = \frac{dRecA}{dt} + \frac{dRecS}{dt} + \frac{dUcRec}{dt}$$

$$\frac{dRecA}{dt} = y4Qa(t)$$

$$\frac{dRecS}{dt} = y3H(t) + y5Qs(t)$$

$$\frac{dUcRec}{dt} = y1Ia(t) + y2Is(t)$$

$$\frac{dD}{dt} = \theta 1\mathrm{Is(t)} + \theta 2\mathrm{H(t)}$$

The corresponding initial conditions used were; N= 2351627, L(0) ≥ 0, $S(0) \geq 0$, $E(0) \geq 0$, Ia(0) ≥ 0, $Is(0) \geq 0$, Qa(0) ≥ 0, Qs(0) ≥ 0, H(0) ≥ 0, R(0) ≥ 0 and D(0) ≥ 0, since the simulation began on the 23rd June 2020 when the epidemic had already started in Botswana.

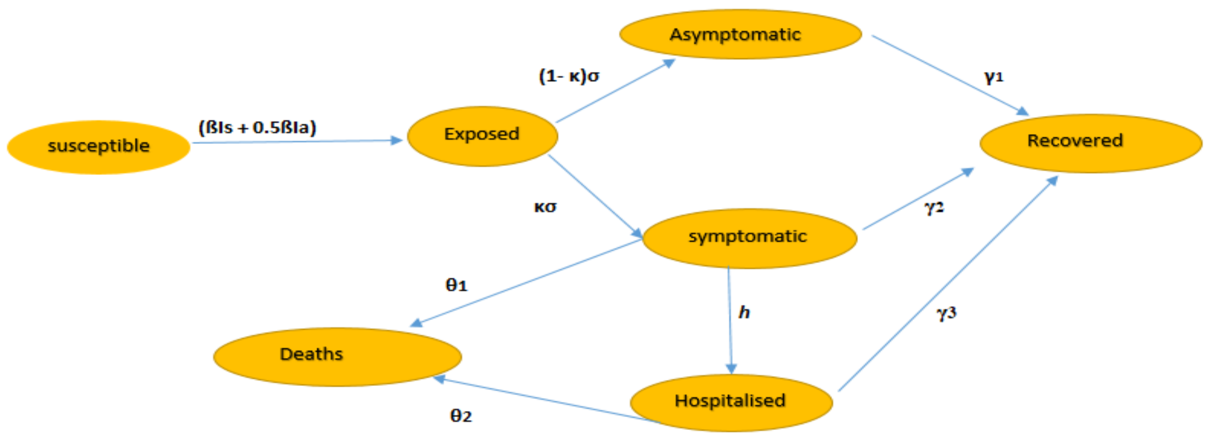


Figure 3.1: A compartmental model without lockdown nor targeted testing nor contact tracing interventions (null model)

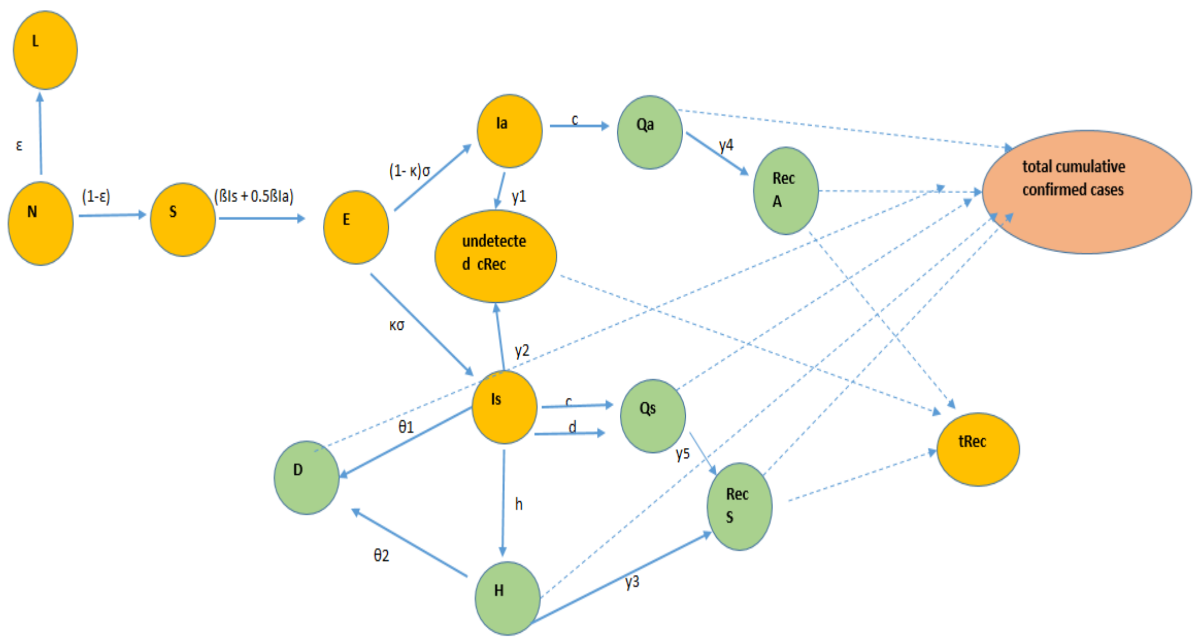


Figure3.2: A compartmental model with lockdown and other intervention (isolation through targeted testing (d) and contact tracing (c)).

Table 3.1: Description of the parameters used in the model for the spread of COVID-19 in Botswana

Parameter	Description	Value	Units	Reference
N	Total population	2,351,627	people	World Bank (2022)
ß	Effective contact rate	Data fitted	day^{-1}	-
σ	Rate from Exposed to COVID-19 infectious infected state	0.2	day^{1}	Mugisha *et al.* (2021)
κ	Fraction of exposed population that become symptomatically infected	0.4	dimensionless	Garba *et.al (2020)*
(1- κ)	Fraction of exposed population that become asymptomatically infected	0.6	dimensionless	Garba *et.al (2020)*
h	hospitalization rate of symptomatic infected individuals	0.01	day^{1}	Garba *et.al (2020)*
d	Quarantine rate of symptomatic infected individuals through targeted testing.	0.181(or same as 1/5.5 days)	day^{-1}	Bugalia *et.al (2020)*
c	Rate of contact tracing	0.05−0.25 (varying range)	day^{-1}	Wangari *et.al (2021)*
γ_1	recovery rate of undetected asymptomatic infected individuals	0.133 (same as 1/7.5 days)	day^{-1}	Sichone *et.al* (2021)
γ_2	recovery rate of undetected symptomatic infected individuals	0.08 (same as 1/12.5 days)	day^{-1}	Bugalia *et.al (2020)*
γ_3	recovery rate for hospitalized individuals	0.05 (or same as 1/20 days)	day^{-1}	Mugisha *et al.* (2021)
γ_4 , γ_5	recovery rate of self-quarantined/isolated individuals	0.08 (or same as 1/12.5 days)	day^{-1}	Bugalia *et.al (2020)*

θ_1	disease induced death rate of undetected symptomatic infected individuals	0.0008 (0.001-0.008)	day^{-1}	Wangari *et.al (2021)*
θ_2	disease induced death rate of hospitalized individuals	0.0016 (0.001-0.008)	day^{-1}	Wangari *et.al (2021)*
ε	Proportion of total population in total compliant lockdown	0.10-0.90 (varying range)	people	Assumed
ϱ	Dilution factor of the contact rate between susceptible and infectious individuals (approximate percentage reduction of the contact rate due to lockdown)	0.1 – 0.8 (varying range depending on percentage of people in lockdown)	day^{-1}	Approximated from ratio of susceptible people vs people in lockdown.

Table 3.2: Description of lockdown effect on contact rate

N = 2351627	People under locked down	susceptible people	Value of contact rate dilution factor (ϱ)
0% in lockdown	0	2351627	1
20% lockdown	470325.4	1881301.6	0.8
40% lockdown	940650.8	1410976.2	0.6
50% lockdown	1175813.5	1175813.5	0.5
60% lockdown	1410976.2	940650.8	0.4
80% lockdown	1881301.6	470325.4	0.2
90% lockdown	2116464.3	235162.7	0.1

N= total population of Botswana

3.3 Numerical analysis

In this section, the study optimized the null model depicted in Figure 3.1 was used for model fitting and estimation of some parameter values. The study also conducted model testing to ensure model verification and validation before it was regarded reliable to perform simulations. Afterwards, the study performed model simulations under different scenarios to determine the COVID-19 trajectory in the absence or presence of interventions (lockdown and contact tracing). Finally, the study investigated the impact of lockdowns on effective reproduction number. The systems dynamics modeling software Vensim- Personal learning edition (PLE) version 7.0 (Ventana Systems, Inc, USA) for windows was used for model optimization and simulation in this study.

3.3.1 Parameter estimation and Model calibration

The model was adapted to the Botswana context by optimizing it using the daily number of cases and information on the different types of NPIs carried out in Botswana. The formulated model was parameterized to assess the burden of COVID-19 in terms of Total cumulative confirmed cases in Botswana. Details of parameters for data fitting are summarized in Table 3.1. It is to be noted that the parameters used in this study were either estimated/assumed within the values where they make biological science or fitted while other parameters values were chosen from various well-established literature. COVID-19 daily reported data collected from the Ministry of Health and Wellness (MoHW) between the period of 30th March 2020 (when the index COVID-19 case was reported) until 30th December 2021 was used to configure the model and optimize parameters. Nonetheless, only data from 23rd June till 22nd September 2020 was used to calibrate the model. This cut off period was chosen because during this period, there was an observed exponential increase in recorded cases due to lockdown relaxation until an initial peak on the 22nd of September 2020. Additionally, in the course of this period, it was also assumed that disease transmission occurred naturally in the community with minimal or no interventions in place. Moreover, data capturing was more consistent, and the community transmission was already established around this time.

The initial conditions of the model were based on the available data at the start of simulation. Since the population of Botswana was assumed constant during the model period, the initial conditions were set as N=2351627, L(0)=0, S(0)= 2351627, E(0)=606, Ia(0)=400, Is=100, RecA(0)=21, ucRec(0)=52 and other variables were set at zero. The initial conditions for the exposed, asymptomatic, symptomatic infected and recovered individuals were estimated a bit higher to account for the possibility that the actual number of cases was likely much higher than that reported in Botswana as in other parts of the world due to limited testing (Flaxman *et al.*, 2020).The values of H and Q were taken as zero because of the paucity of information linked to the initial phase of outbreak for these compartments.

Model calibration was performed as shown Figure 3.1 with no control measures. The proposed model was calibrated using the initial conditions together with fixed parameter values presented in Table 3.1. This was done by subjecting the proposed model to several rounds of simulations and manually adjusting the value of infection rate (ß) in order to fine tune the model until a projection which was not significantly different from the outbreak data was achieved. This process was also used to estimate the unknown study parameter ß.

3.3.2 Model Testing

In order to develop the most accurate and reliable model, the study performed some tasks including model settings unit check, model check and goodness of fit.

For the simulation of the model, the following model settings were taken into account; INITIAL TIME= 0, FINAL TIME=91, simulation TIME STEP=1, with integration method of Euler. The unit of time was taken to be a day.

As part of model verification and validation, unit check was done to ensure consistency. Moreover, direct structure and behavior tests were conducted as part of model check, including white and black box tests. The white box test scrutinized the model structure and mathematical equations to ensure that the assumptions in the model were based on accepted theories and that all important variables or parameters were incorporated in the model. The black box test tested the behavior of the model ensuring that it behaved as per system dynamic theories at various test conditions.

A goodness of fit test (at a significance level of 0.05) and Pearson’s correlation coefficient (significance level of 0.010) were used to compare the model generated data with the outbreak data. All the statistical analysis were performed using SPSS Statistics version 21(IBM, USA) software.

Therefore, with the derived assumptions, the model was considered for generating reliable projections of COVID-19 trajectories in Botswana.

3.3.1 Simulation and analysis of mitigation strategies

In this section, numerical simulations were analyzed for two versions of the fitted model to evaluate impact of different intervention measure taken by the government. The primary model (null model) assumes no interventions against COVID-19 while the second model (intervention model) tested several scenarios investigating the potential impact of control measures.

The study ran simulations over 365- or 60-days using sets of parameter estimates for disease severity and NPIs conditions presented in Table 3.1. The outcomes of each intervention on the number of confirmed cumulative cases which acted as an indicator in this study were presented.

3.3.1.1 Prediction of cumulative number of positive cases with no (or relaxed) intervention

In this scenario, the study considered a situation where there were no interventions implemented. Also, in this scenario, it was assumed that there was no change in contact or transmission rate hence it was presumed that the population lived their normal lifestyle, all individuals in the population were susceptible to COVID-19 infection and that migration in and out of the country is approximately equal. It was important to start the simulation at this level (no control measures) so that significant and effective control measures could be easily identified. Thus, in this study the model depicted in Figure 3.1 was used to perform short term predictions to forecast the growth of cumulative cases by extending the modeling period to 365 days from 23 June 2020 until 23 June 2021.

3.3.1.2 Determining the impact of different interventions.

In this section, the study investigates two scenarios; the first scenario attempts to estimate the number of cases while considering enforcement of lockdown only while the second scenario attempts to estimate number of cases when lockdown and contact tracing are jointly implemented.

The effect of interventions on the dynamics of COVID-19 were explored by simulating effects of changes to values of the lockdown and contact tracing related parameters of the model over a time period of 60 days.

To show the effect of lockdowns, the proportion of the total population under lockdown were varied. The lockdown was presented by the function $0 \leq \mathcal{E} \leq 1$, where 1 represented complete lockdown and conversely 0 represents no lockdown. The study assumed that during full lockdown all services (mostly non-essential), except essential ones were suspended and interaction was removed whereas in partial lockdown most economy sectors were open hence more interaction between people. Since lockdown lessens contact rate among infectious and susceptible individuals within a population, a parameter contacts rate dilution factor (ϱ) was introduced in the model as presented in Table 3.2. The term ϱ was varied between 0 -1 depending on lockdown stringency. If ϱ =1, then there was high contact rate (no lock down), whereas ϱ=0 represented complete lockdown (no contact).

For contact tracing, the rates were varied from the lowest to the highest (meaning the contact tracing rate c varied between 0.05−0.25 to assess effect of slow and fast efficient contact tracing).

Intervention scenarios were analyzed based on their impact on total cumulative confirmed cases. The proposed model in Figure 3.2 was simulated under two scenarios given below and the total number of cumulative confirmed cases were estimated under each scenario. The study summarized the scenarios analyzed by comparing them to the worst-case scenario (baseline) of no lockdown and also calculated the percentage change.

Scenario 1: To determine the effect of lockdown on COVID-19 transmissions, this scenario analyzed different lockdown levels while keeping the value of contact tracing rate (0.05) at minimal and all other parameter values the same as in Table 1 over a period of 60 days. The contact tracing was maintained low because even-though lockdown was lifted, symptomatic individuals and their immediate contacts were tested and isolated as per requirement by MoHW, Botswana. For the purpose of this study, twenty, forty, fifty, sixty, eighty and ninety percent lockdowns which represented the rate of home-confinement were simulated. Ninety percent was considered full lockdown while 20%,40%,50%,60%,80% were assumed as partial lockdowns whereas 0% which was considered as no lockdown was used in baseline simulation to demonstrate the worst-case scenario. We did not consider the scenario in which 100% of the population was locked down because frontline workers were not home confined hence remained as susceptible population.

Scenario 2: In this scenario, lockdown and contact tracing measures were assumed to be implemented simultaneously. Thus, the model was used to examine the positive synergistic combination of contact tracing in the presence of various lockdown levels. To determine the efficacy these interventions; different lockdown levels were paired with varying contact tracing levels. For instance, pairing various lockdown levels with increasing levels of contact tracing (medium (0.125) and high (0.25).

3.3.1.3 Estimating the impact of lockdown on effective reproduction number

For any emerging infectious disease, the scale of its public health impact is determined by its basic reproduction number, *'Ro'*, defined as the number of secondary infections resulting from an infectious individual when introduced in a wholly susceptible population during the entire infectious period (Bugalia *et al.*, 2020; Dwomoh *et al.*, 2021).This quantity determines the potential of an infectious agent to cause an outbreak and the extent of spread if no control measures are implemented (Bugalia *et al.*, 2020; Dwomoh *et al.*, 2021). *Ro* is used when there is no immunity from past exposures, vaccination or interventions(Mugisha *et al.*, 2021). When intervention measures are taken into consideration, the effective reproductive number, denoted '*Re*' is used, which quantifies the average number of secondary cases per infectious case in a population made up of susceptible and non-susceptible individuals (Gupta *et al.*, 2021). Since *Re* estimates can be used to tracks or reflect the subsequent virus transmission dynamics, it can also be used to monitor the efficiency of public health interventions and adjust them accordingly (Gupta *et al.*, 2021) . If $Re > 1$, the number of infectious will increase. When $Re = 1$ the disease is endemic and if $Re < 1$, the disease will gradually die out (Bugalia *et al.*, 2020).

In the current study, the models depicted in Figure 3.1 (without interventions) and Figure 3.2 (with interventions (lockdowns only)) were used to estimate *Ro* and *Re* respectively for the COVID-19 transmission dynamics in Botswana.To evaluate the progressive transmission dynamics, *Ro* and

Re estimates were computed for each lockdown level implemented. The following formulas were used.

$Ro = ßD$

$Re = ϱßD$

Where ß is number of effective contacts between susceptible and infectious individuals per unit time, ϱ is the contact rate reduction factor between infectious and susceptible individuals due to lockdown measures and D is the mean duration of infectiousness.

3.4 Ethical consideration

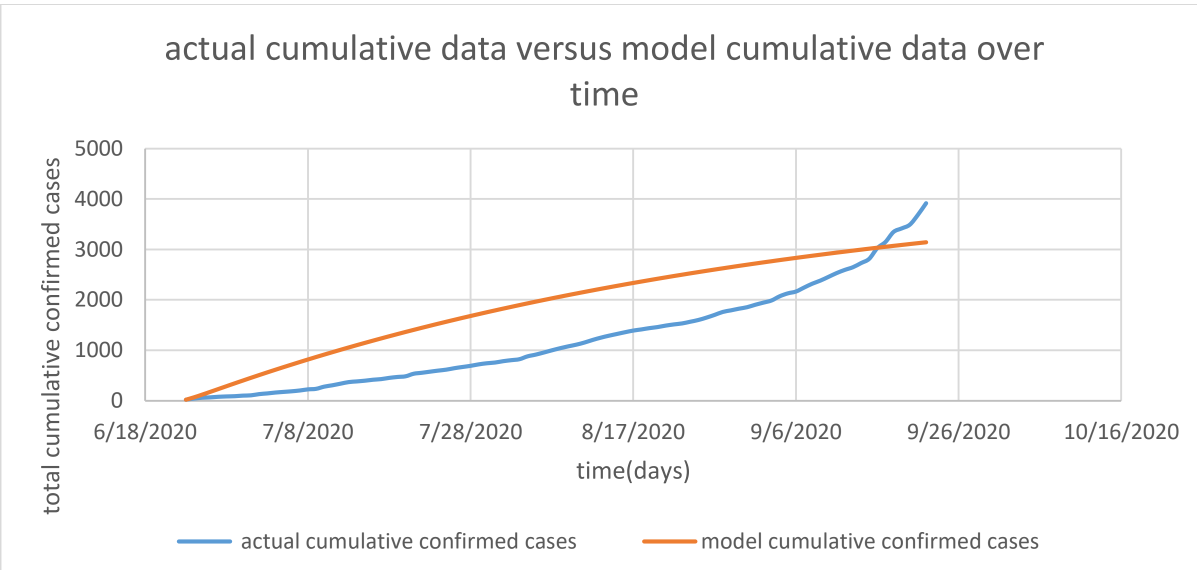
Only publicly available data reported by MoHW was used hence this study did not require ethical clearance.

CHAPTER FOUR

4.0 RESULTS

4.1 Model fit to the data.

The null transmission model had a significant fit to the reported COVID-19 confirmed cumulative cases from 23rd June 2020 to 22nd September 2020 as shown in Figure 4.1, under all the assessed conditions that could be used to mimic the evolution of the disease in Botswana.



Model fit: Pearson correlation coefficient: $r = 0.970$, $p < 0.001$ Chi-square goodness of fit: $p = 0.239$

Figure 4.1: Cumulative confirmed cases of Covid-19 in Botswana for the period 23rd June to 22nd September 2020. The blue line indicates the actual outbreak data while the orange line denotes the model simulated data.

4.2 Epidemic projections without intervention (lockdown and contact tracing)

Simulation of unmitigated epidemic in Botswana projected up to 4362 total confirmed cumulative cases being reported in Botswana from 23rd June 2020 until 23rd June 2021. Figure 4.2 shows that total number of confirmed cumulative cases will increase sharply, then at a steady rate and eventually later on reaches a plateau as more recoveries are recorded and a large proportion of the population reaches herd immunity.

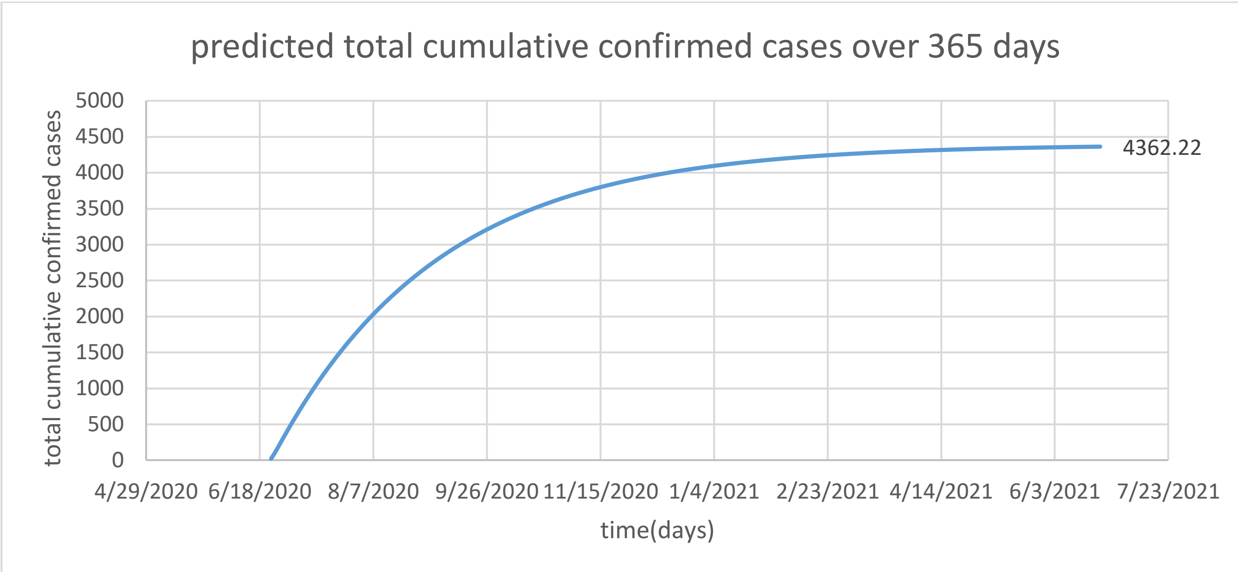
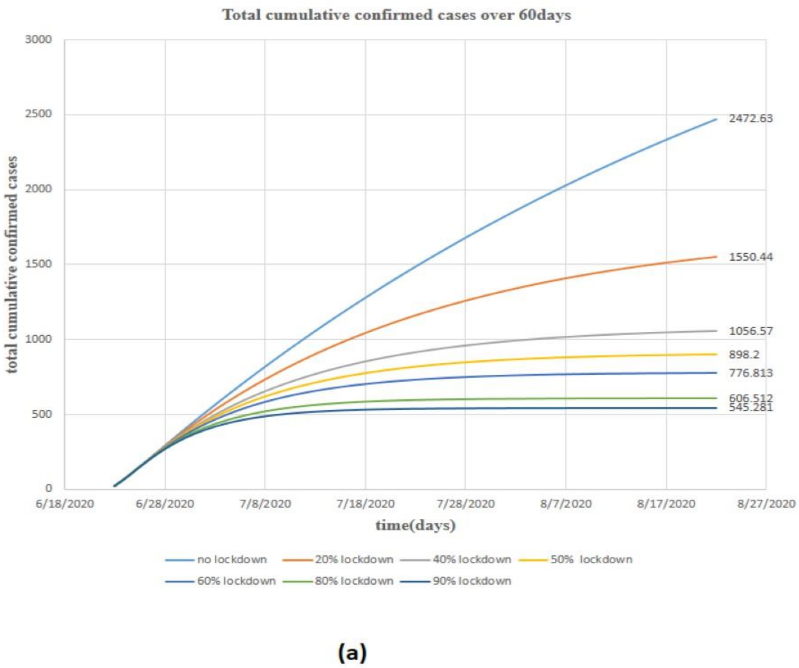


Figure 4.2: Simulation of forecasted total confirmed cumulative confirmed cases over a period of 365days without intervention.

4.3 Impact of intervention measures (lockdown and contact tracing)

Scenario 1: The model (Figure 4.3 (a)) showed that implementing lockdowns would significantly curtail the spread and burden of COVID-19. It presented that when compared to the baseline scenario (no lockdown), 2472 total confirmed cumulative cases could have been recorded if there was no lockdown for the period of 60 days from 23rd June 2020 to 22nd August 2020 in the country. The model also estimated that implementation of 20%, 40%, 50%,60%,80% and 90% lockdowns would have averted cumulative number of cases to 1580, 1056,898, 776, 606 and 545, respectively during this period. This can be translated to a percentage reduction of total cumulative number of confirmed cases to 37.28%, 57.26%, 63.67%, 63.57%, 75.47% and 77.94% as illustrated in Figure 4.3 (b). Thus, these simulation results demonstrate that adoption of lockdown policy by Botswana government had a significant community-wide impact in reducing the transmission of COVID-19. This implies that because of lockdowns, healthcare system would not be overwhelmed, and the country could manage infectious cases adequately. Nonetheless, based on this simulation results, complete lockdown is the only level that can effectively reduce the number of cases.

Scenario 2: Under this scenario, the model was used to explore multiple strategies where lockdown was supplemented with other interventions. Figures 4.4 and 4.5 summarized the outcome of these strategies by comparing them to the baseline scenario (no interventions). The results show that the non-pharmaceutical interventions (lockdown and contact tracing (medium and high rates)) from 23rd June 2020 to 22nd August 2020 had a significant impact on reducing the number of cases. When different lockdown levels were paired with a medium contact tracing rate (0.125), the model predicted that 1418, 1114,1004,913,772 and 717 cases would result from 20%,40%,50%,60%,80%, and 90% lockdown levels, respectively, (Figure 4.4(a). Figure 4.4 (b) shows that the above stated total number of confirmed cumulative cases would have decreased by 42.62%,54.93%,59.38%,63.06%,68.75 and 70.99%, when compared to the no intervention scenario. In contrast, when a combination of various lockdown scenarios was simulated with high contact tracing rate (0.25), the model estimated that varying lockout levels of 20%,40%,50%,60%,80%, and 90% would lead to 1302, 1130, 1060, 999, 895 and 851 total confirmed cumulative case, respectively (Figure 4.5(a)). Figure 4.5(b) illustrates how lockdowns and high contact tracing reduced the number of cases when compared to the no control scenario. The observed percentage reductions were 47.33%, 54.26%, 57.09%, 59.58%, 63.76%, and 65.55%, respectively. From the simulations, the study infers the influence of medium contact tracing to be more effective than high contact tracing. Nonetheless, in reference to the above scenarios, the study deduced that NPIs instituted aided in containment of the epidemic spread resulting in fewer confirmed cases as compared to the unmitigated scenario. However, the study findings also exhibit that partial lockdowns and use of contact tracing are insufficient to stop COVID-19 hence the disease would continue to spread in the population.



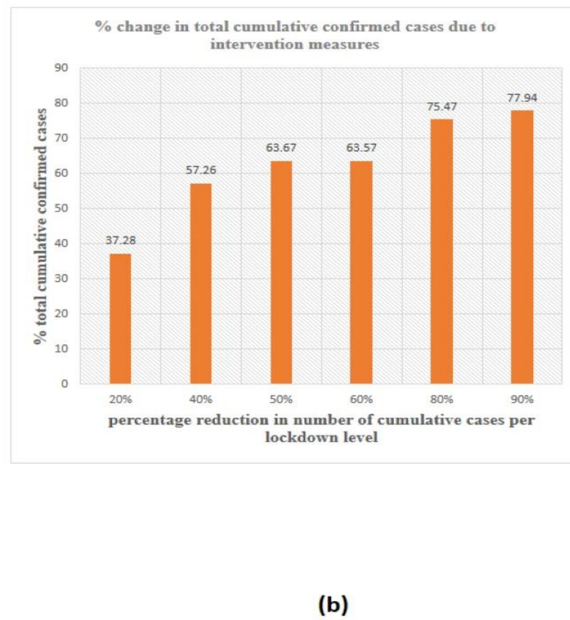
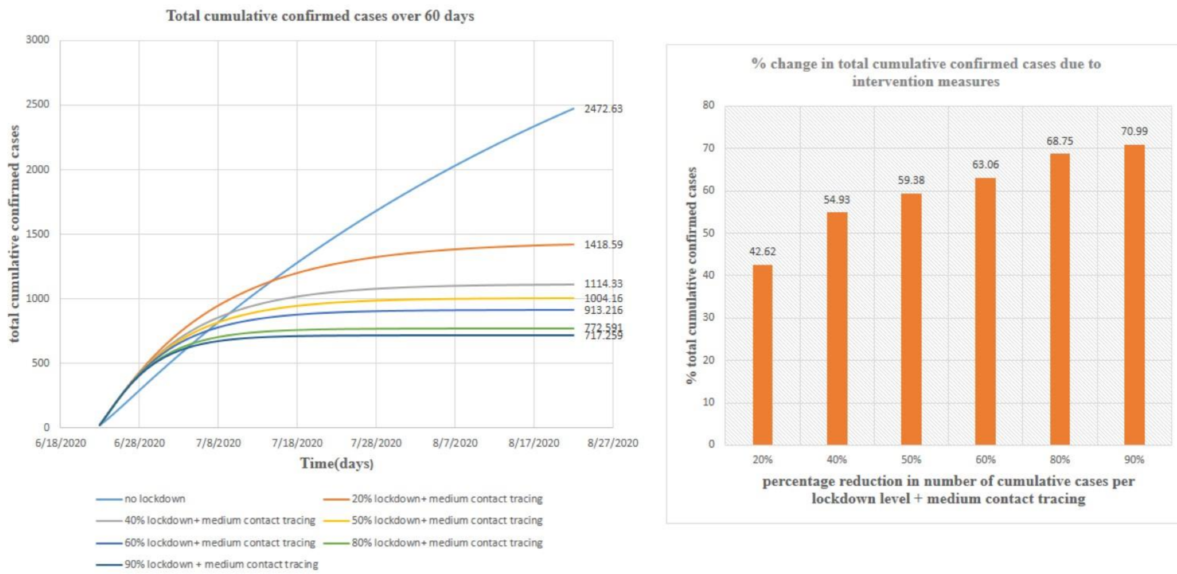
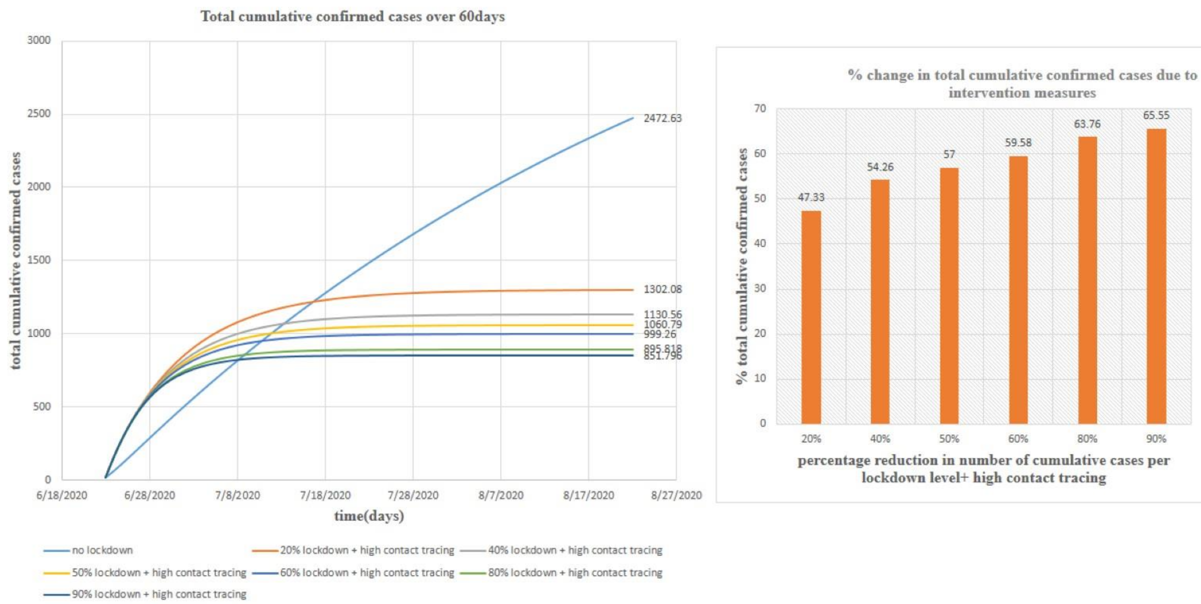


Figure 4.3: Impact of lockdown scenarios on confirmed cumulative cases (a) and associated percentage reduction in total number of cumulative confirmed cases after 60 days (b)



(a) (b)

Figure 4.4: Impact of lockdown scenarios and medium contact tracing on confirmed cumulative cases (a) its and associated percentage reduction in total number of cumulative confirmed cases (b) after 60 days.



(a) (b)

Figure 4.5: Impact of lockdown scenarios and high contact tracing on total number of confirmed cumulative cases (a) and its associated percentage reduction in total cumulative confirmed cases (b) after 60 days.

4.4 Impact of lockdown on reproduction effective number:

Table 4.1 shows the results of how increasing lockdown levels affected the reproduction numbers. When simulating the null model using parameter values listed in Table 1, the study predicted a basic reproduction number of *Ro* =3.9 at the early stage of the epidemic when lockdown was not in place. The estimated *Ro* =3.9 is greater than the threshold value of 1, thus implying that each infectious individual was able to transmit the COVID-19 infection to more than three people. Also, with Ro>1 it shows that the epidemic was still growing. After implementation of various lockdown levels (20%,40%,50%,60%,80% and 90%), a steady decrease in *Re* was observed; 3.1, 2.3,1.9,1.6,0.8 and 0.4, respectively. This indicates that the lockdown policies implemented were quite efficient in decreasing the contact rate and lower likelihood of transmission. A reduction in *Re* implies that fewer individuals were being infected, thus the disease spread was slowed down. This is a clear indication that if lockdown recommendations were observed, the threat of COVID-19 could be subdued in a short period.

Table 4.1: Estimating impact of lockdowns on R*o* and Re

Lockdown level (%)	*Ro*	*Re*
0	3.9	-
20		3.1
40		2.3
50		1.9
60		1.6
80		0.8
90		0.4

CHAPTER FIVE

5.0 DISCUSSION

Considering the exponential spread of COVID-19 and limited medical facilities in low- and middle-income countries, the analysis of COVID-19 progression and its subsequent trajectory is crucial. Henceforth, this current study attempted to predict how the COVID19 epidemic would have developed in the early months of the outbreak in Botswana in the absence of interventions and assessed the effectiveness of various interventions in curtailing the spread of COVID-19 in a population using a deterministic compartmental mathematical model. The choice of using deterministic SEIR model was deemed appropriate for this research because it is simple to use and also the Botswana population was considered large enough hence stochastic effects were negligible (Sichone *et al.*, 2021). Moreover, Ong'ala *et al.* (2020) further suggested that deterministic model is the most suitable tool to be used when modeling a new problem with few data. This was supported by Mwale *et al.* (2022) who indicated that modeling is useful in decision making especially in situations when there is absence of high quality and detailed disease data. In this study publicly available data on daily COVID-19 cases provided by MoHW from 30th March 2020 to 31st December 2021 was used to optimize the model. However, it was the data from the initial exponential growth of the epidemic until the first peak (from 22nd June 2020 to 23rd September 2020) that was used to calibrate the model. This period was considered because no or minimal lockdowns and contact tracing interventions were implemented and there was no compliance hence for this reason the period was assumed to be equivalent to the before/without intervention phase in Botswana. The simulation period of 60 days used in this study was deemed reasonable because Botswana was under lockdown for 48 days and due to a weak economy, the government could not sustain a lockdown of longer duration.

Future prediction of COVID-19 disease progress in a population has become of utmost importance for healthcare arrangements and disease control especially during the early stages of the pandemic when there was no vaccine. According to the model predictions, if Batswana ignored the MoHW guidelines and were not compliant to public health measures, 4362 total confirmed cumulative cases would have been reported from 22nd June 2020 until 22nd June 2021. This is consistent with earlier reports that although African continent was predicted to have high COVID burden, in reality Africa reported low cases; which was assumed to be due to younger population, climatic conditions and underreporting (Frost *et al.*, 2021, Bwire *et.al*.,2022; Pearson *et al.*, 2020).This lower projections was also plausible due to the fact that just like other African countries, Botswana was on highly alert as the situation unfolded in other countries and implemented lockdown early which significantly averted COVID-19 cases and slowed down the pandemic(Siamisang *et al.*, 2022). The lower predictions reported in this study could also have been a result of not taking the effect of seasonality and the SARS-CoV-2 variants of concern which were circulating in the population into consideration during the modeling period when simulation which also have affected the study's outcome.

In this study, model simulations were performed to examine the effects of lockdowns alone or in combination with contact tracing on COVID-19 transmission in Botswana. Given the NPIs' enormous societal and financial implications, it is important to know whether these control measure have had the desired impact of containing the pandemic and to determine which ones are necessary to keep the pandemic under control (Flaxman *et al.*, 2020). In addition, for public health and governmental planning purposes, it is crucial to comprehend how lockdowns and other interventions affected the spread of COVID-19 and the intensity of the measures needed to do so (Mangal *et al.*, 2020). In this study the effect of lockdown measures was assessed based on reduction in overall confirmed cumulative number of cases. Findings from various scenario analysis showed that the aggressive lockdown interventions implemented appeared to have achieved the interruption of transmission and the abatement of the pandemic as quickly as less than 60 days. In particular, simulation results indicated that lockdowns significantly reduced cumulative number of confirmed cases by a range of 37% to 78%.These results are consisted with findings by Roques *et al* (2020), who reported that lockdowns were able to minimize the transmission of COVID-19 by 84% in France. Ayoub Meo (2020) also reported that compared to the unmitigated scenario, lockdown prevented about 44%-81% of new cases. However, it was also observed from this study's simulation results that optimal outcomes were obtained when lockdowns are implemented and adhered to a maximum level of 90%. This observation was in line with other studies done in China highlighting that extensive lockdowns had a much larger influence in controlling the COVID-19 outbreak size(Yang *et al.*, 2020). Likewise, Bhadauria *et.al* (2021) and Mugisha *et al.* (2021) concluded that COVID-19 disease can only be eradicated from the system by imposing total lockdowns. Although this aggressive measure appears to be successful in reducing the number of COVID-19 cumulative cases, researchers have found out that it slows down the acquisition of herd immunity by the community hence when interventions are relaxed, transmission will rise again (Flaxman , 2020; Aleta *et al.*, 2020).Although intensified physical distancing measures have been proven effective in flattening the epidemic curve, other studies have indicated that extreme full lockdowns are not the ultimate solution especially in developing countries if implemented for a long tenure due to socioeconomic factors including high population density, poverty and weak healthcare system (Wangari *et al.*, 2020; Bhadauria *et al.*, 2020; Huang *et al.*, 2020).

The findings of this research further agrees with the claim made by previous researchers that prompt and sustainable implementation of intervention measures successfully prevented many subsequent cases, thereby reducing the disease burden in most nations including Botswana (Mugisha *et al.*, 2021; Jemal and Alemu , 2022; Huang *et al.*, 2020; Motlhatlhedi *et al.*, 2020). Early implementation of lockdown resulted in slower increase in confirmed number of cases reported in Botswana. The authors in Huang *et al* (2021) affirmed this study findings by suggesting that those countries which implemented lockdown prior to infection point (7days before the date on which at least 5 cumulative number of cases were reported) experienced a slower rise in COVID-19 over the first 50 days.

To cushion the financial and social crisis endured by implementation of full lockdowns while at the same time bearing in mind the public health consequences of the epidemic, gradual lifting of nation-wide complete lockdown was opted for and combined with other NPIs to reduce SARS-CoV-2 transmissibility. In this study, various levels and intensities of combined lockdown and contact tracing were suggested to contain the outbreak. This gave information on the best synergies of interventions that would manage the epidemic in the best way possible while having the least negative impact on socioeconomic needs. Based on the simulation results of this study, coupling lockdowns and contact tracing has shown to be effective as number of COVID-19 confirmed cumulative cases were significantly decreased after implementation. Lockdowns combined with medium contact tracing decreased the total number of cumulative cases by 42.62% to 70.99%. However, it reduced number of cumulative cases by 47.33% to 65.55% when combined with high contact tracing. According to the above-mentioned simulation results, lockdowns paired with moderate contact tracing appeared too more effective. This is probably because physical distancing measures such as lockdowns does not only reduce transmission, but also lessen number of unidentified contacts who can be harder to trace, thus making contact tracing more effective even at lower rates (Kucharski *et al.*, 2020). Although lockdowns combined with high contact tracing was expected to avert more cumulative number of cases, the results of this study showed the least percentage reduction, which was not as expected. This can be attributed to 'pandemic fatigue' or 'intervention fatigue' experienced by the community due to early and prolonged implementation of rigid control measures since the start of the pandemic, which might bring challenges in maintaining high levels of intervention measures like nationwide lockdown and contact tracing (Stuart *et al.*, 2021). In addition, Mugisha *et al.* (2021) highlighted that the effectiveness of contact tracing can be compromised by high proportion of asymptomatic and latently infected individuals in the population that may pass as false negatives. This was emphasized by the findings of this study whereby the baseline proportion of asymptomatic infected individuals was high (60%) which could have hindered the efficacy and contribution of contact tracing. Jarvis *et al.* (2021) have also suggested that the relatively small size impact of the control measure maybe indicative that restrictions were already implemented at the point where individuals had lowered their interactions, as opposed to an indication that the intervention had no effect.

Even though prior research works by other scholars (Zhang *et al.*, 2022; Flaxman *et al.*, 2020; Mugisha *et al.*, 2021; Huang *et al.*, 2020) have proven that combination of the two control measures were more effective and can synergistically suppress an outbreak when compare to implementation of a single intervention, in contrast based on this study findings lockdown is more effective alone than when paired with contact tracing. This is consistent with Browne *et al.* (2021) findings that lockdown was responsible for bringing down the growing COVID-19 cases in China as compared to contact tracing which was less influential in suppressing the epidemic. Also, Davis *et al.* (2021) highlighted that contact tracing has a significantly less impact on final outbreak size, but can lead to peak size reduction.

The effect of implemented lockdowns intervention on SARS-CoV-2 transmissibility in Botswana was also measured in terms of basic reproduction number *(Ro)* and net reproduction number *(Re)*. The *Ro* was estimated as *Ro*= 3.9 which is indicative of a still growing epidemic. This findings are within the range of COVID-19 outbreak estimates of basic reproduction number obtained in Africa and globally which takes values between 1.9 to 6.5 (Aronna et *et al.*, 2020; Giordano *et* *al.*, 2020; Jemal and Alemu, 2022; Huang *et al.*, 2020). The variation in the estimated basic reproduction number across countries is influenced by demographic, geographical and socio-economic factors as well as the type of intervention strategies adopted (Frost *et al.*, 2021) . According to Jemal and Alemu (2022) similar results to this study were obtained in Cameroon (*Ro*=3.7), Kenya (3.77), Morocco (*Ro*=3.9), and Algeria (*Ro*=3.31). Nonetheless the model's estimated R_0 was slightly higher compared to that of other Southern African countries like Malawi (*Ro*=2.16), Namibia (*Ro*=2.37) and Zambia (*Ro*=2.59) but less than South Africa's estimated *Ro*= 7.0 (Jemal and Alemu, 2022) reported during the early phase of the pandemic. The slightly high R_0 result (3.9) obtained in this study might be a result of using fixed parameter values (effective contact rate (ß) and duration of infectiousness (Ia)) throughout the entire modelling period which might have contributed to overestimation (Aronna et *et al.*, 2020; Giordano *et al.*, 2020). In actual fact these given parameters are uncertain and can vary over time due to several factors such as population density, environmental conditions, age distribution of the population and the measures imposed by the government (Aronna et *et al.*, 2020; Giordano *et al.*, 2020; Edholm *et al.*, 2020). Additionally, the value of R_0 was overestimated probably because of uncertainties associated with estimating R_0 using parameters from different literatures (Sichone *et al.*, 2020). The literature from which these parameter values were derived from relied on data from high- and low-income countries which may not be directly transferrable to Botswana. Several scholars have however emphasized that R_0 estimation is challenging. For instance, for precise estimation of R_0, certain conditions must be met like precise detection of cases in the early stage of the epidemic, restricting the calculation to a small time frame and choosing the appropriate estimation method (Charman, 2020).

It is worth noting that this research assumes that changes in Re was only due to an immediate response to lockdown interventions rather than perhaps gradual change in human behavior or other interventions which were instituted concurrently to curb SARS-CoV-2 spread. After applying different levels of lockdowns, it was found that the estimate values of Re with respect to strictness degree varied between 0.4 to 3.1. Hence according to this study's findings, these lockdown intervention measures appeared to be very efficient in lowering Re, with the greatest reduction being attained when the national lockdown was fully operational and strictly enforced at maximum lockdown levels of 80% and 90%; Re=0.8 and 0.4, respectively, which were significantly below the threshold one. This findings are in line with Browne *et al.* (2021), who report that the effectiveness of lockdown was proven in China where it reduced the basic reproduction number to Ro=0.3 and 0.5 in Wuhan and other provinces, respectively. In this study, it was shown that reproduction number subsequently increased up to Re=3.1 following the gradual lifting of lockdown which allowed for a larger proportion of population to interact and possibly even promoted "super-spreading events" that resulted in escalation in number of confirmed cases. Hence indicating that caution must be exercised when the government decides to open the economy by lifting lockdown policy. This observation was also made in another study in India where the trend of Re suggested that if lockdown was to be removed completely, a high spike of notified cases would be registered in some regions (Sardar et.al,2020). Henceforth, these findings agree with those of other researchers, who found that the disease can only be controlled if R_0 is less than unity. As a result, policymakers must strive to lower the reproduction number to below one to lessen the disease burden in the population. Nonetheless Lipsitch et.al (2003) affirmed that prevention of transmission need not be 100% effective because basic reproduction number simply needs to be reduced and maintained below one to bring the epidemic under control.

CHAPTER SIX

6.0 CONCLUSION, LIMITATIONS AND RECOMMENDATION

6.1 Conclusions

This study analyzed the transmission dynamics of COVID-19 in Botswana and assessed the impact of implemented NPI during the early stages of the pandemic using a mathematical model approach. Through the analysis of data, the model predicted that 4362 total cumulative confirmed cases would be reported within a year if intervention were not put in place. The effects of lockdown were estimated by comparing values of R*o* and R*e* or the trends of cumulative cases before introducing the intervention to that after introducing the intervention. Findings of this study envisages that lockdown measures instigated by the government of Botswana was effective in averting thousands of cases that would have overstretched the healthcare system and compromised quality of health care. However, this would come at a high cost because strict interventions seem to be more effective in reducing disease burden. The model estimated the basic reproduction number of R_0=3.9 at the beginning of the pandemic which was above unity thus indicating that COVID-19 outbreak was still growing. After implementation of lockdowns, effective reproduction number (Re) decreased from 3.1 to 0.4, thus further showing that contribution of lockdown was significant in shaping the overall disease dynamics.

6.2 Limitations

The study did not consider the potential changes to viral transmissibility due to environmental factors (seasonality) and variants of concern which could have led to biased estimates. Cold weather conditions and mutant virus strains have been linked to increased number of cases, thus ignoring their impact would lead to prediction of less disease burden. Furthermore, this study used constant effective contact rate ß which could also lead to biased estimation of time varying effective reproduction number *Re*. The usage of constant ß is associated with predicting a much higher peak and even overestimate the epidemic severity. Moreover, this study did not consider the effect of immigration (truck drivers) although it fueled increase in number of cases during the first month of the pandemic. The study also acknowledges the limited testing resources at the beginning of the outbreak in Botswana, with minimal testing capacity it is difficult to estimate the burden of the disease in the country probably resulting in underestimation.

6.3 Recommendation

1. A serological surveillance study should be conducted to estimate the true prevalence of SARS-CoV-2 in Botswana population. Seroprevalence studies can be used to explore the actual impact of the epidemic. On a population level, serological testing is important to follow the outbreak and population immunity level which could provide support for the scaling down of nationwide control measure.
2. More mathematical model studies together with cost-effectiveness studies should be done in Botswana to help policy makers in making informed decision by choosing the appropriate cost-effective intervention strategy at the right scale and at the right time.

7.0 REFERENCE

Al-Harbi, S.K. and Al-Tuwairqi, S.M. (2022) *Modeling the effect of lockdown and social distancing on the spread of COVID-19 in Saudi Arabia, PLoS ONE*. doi:10.1371/journal.pone.0265779.

Altahir, A. *et al.* (2020) 'Modeling the Impact of Lock-down on COVID-19 Spread in Malaysia', (May), pp. 1–20. doi:10.1101/2020.07.17.208371.

Ambikapathy, B. and Krishnamurthy, K. (2020) 'Mathematical modelling to assess the impact of lockdown on COVID-19 transmission in India: Model development and validation', *JMIR Public Health and Surveillance*, 6(2), pp. 1–8. doi:10.2196/19368.

Amouzouvi, K. *et al.* (2021) 'A model of COVID-19 pandemic evolution in African countries', *Scientific African*, 14, p. e00987. doi:10.1016/j.sciaf.2021.e00987.

Baba, I.A. *et al.* (2021) 'Mathematical model to assess the imposition of lockdown during COVID-19 pandemic', *Results in Physics*, 20, p. 103716. doi:10.1016/j.rinp.2020.103716.

Bagal, D.K. *et al.* (2020) 'Estimating the parameters of susceptible-infected-recovered model of COVID-19 cases in India during lockdown periods', *Chaos, Solitons and Fractals*, 140, p. 110154. doi:10.1016/j.chaos.2020.110154.

Bhadauria, A.S., Pathak, R. and Chaudhary, M. (2021) 'A SIQ mathematical model on COVID-19 investigating the lockdown effect', *Infectious Disease Modelling*, 6, pp. 244–257. doi:10.1016/j.idm.2020.12.010.

Browne CJ, Gulbudak H, Macdonald JC. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information . 2020;(January).

Bugalia, S. *et al.* (2020) 'Mathematical modeling of COVID-19 transmission: The roles of intervention strategies and lockdown', *Mathematical Biosciences and Engineering*, 17(5), pp. 5961–5986. doi:10.3934/MBE.2020318.

Chintalapudi, N. *et al.* (2020) 'COVID-19 outbreak reproduction number estimations and forecasting in Marche, Italy', *International Journal of Infectious Diseases*, 96, pp. 327–333. doi:10.1016/j.ijid.2020.05.029.

Daniel Deborah, O. (2020) 'Mathematical Model for the Transmission of Covid-19 with Nonlinear Forces of Infection and the Need for Prevention Measure in Nigeria', *Journal of Infectious Diseases and Epidemiology*, 6(5). doi:10.23937/2474-3658/1510158.

Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. eClinicalMedicine. 2021;38.

Diop BZ, Ngom M, Biyong CP, Biyong JN. The relatively young and rural population may limit the spread and severity of Covid-19 in Africa: a modelling study. BMJ Glob Health. 2020 May 1; 5(5):e002699. https://doi.org/10.1136/bmjgh-2020-002699 PMID: 32451367

Djaoue, S. *et al.* (2020) 'Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information ', (January).

Dwomoh, D. *et al.* (2021) 'Mathematical modeling of COVID-19 infection dynamics in Ghana: Impact evaluation of integrated government and individual level interventions', *Infectious Disease Modelling*, 6, pp. 381–397. doi:10.1016/j.idm.2021.01.008.

Dzobo, M., Chitungo, I. and Dzinamarira, T. (2020) 'COVID-19: a perspective for lifting lockdown in Zimbabwe', *The Pan African medical journal*, 35(Supp 2), p. 13. doi:10.11604/pamj.2020.35.2.23059.

Edholm CJ, Levy B, Spence L, Agusto FB, Chirove F, Chukwu CW, et al. A vaccination model for COVID-19 in Gauteng , South Africa. Infect Dis Model [Internet]. 2022;7(3):333–45. Available from: https://doi.org/10.1016/j.idm.2022.06.002

Frost, I. *et al.* (2021a) 'Modelling COVID-19 transmission in Africa: Countrywise projections of total and severe infections under different lockdown scenarios', *BMJ Open*, 11(3), pp. 1–10. doi:10.1136/bmjopen-2020-044149.

Garba, S.M., Lubuma, J.M. and Tsanou, B. (2020) 'Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information', *Mathematical Biosciences*, 328(2020), pp. 1–14.

Goscé, L. *et al.* (2020) 'Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information ', (January).

Guan, J. *et al.* (2022) 'Transmission dynamics model and the coronavirus disease 2019 epidemic : applications and challenges'.

Gupta, M. *et al.* (2021) 'Transmission dynamics of the COVID-19 epidemic in India and modeling optimal lockdown exit strategies', *International Journal of Infectious Diseases*, 103, pp. 579–589. doi:10.1016/j.ijid.2020.11.206.

Guzzetta G, Riccardo F, Marziano V, Poletti P, Trentini F, Bella A, et al. Impact of a nationwide lockdown on SARS-CoV-2 transmissibility, Italy. Emerg Infect Dis. 2021;27(1):267–70.

Haider, N. *et al.* (2020) 'Lockdown measures in response to COVID-19 in nine sub-Saharan African countries', *BMJ Global Health*, 5(10), pp. 1–10. doi:10.1136/bmjgh-2020-003319.

Ivorra, B. *et al.* (2020) 'Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information ', (January).

Jarvis CI, Gimma A, van Zandvoort K, Wong KLM, Abbas K, Villabona-Arenas CJ, et al. The impact of local and national restrictions in response to COVID-19 on social contacts in England: a longitudinal natural experiment. BMC Med. 2021;19(1):1–12.

Jemal SS, Alemu BD. Modeling the Transmission Dynamics of COVID-19 Among Five High Burden African Countries. Clin Epidemiol. 2022;14(August):1013–29.

Kifle, Z.S. and Obsu, L.L. (2022) 'Mathematical modeling for COVID-19 transmission dynamics: A case study in Ethiopia', *Results in Physics*, 34, p. 105191.

doi:10.1016/j.rinp.2022.105191.

Kim, B.N. *et al.* (2020) 'Mathematical model of covid-19 transmission dynamics in South Korea: The impacts of travel restrictions, social distancing, and early detection', *Processes*, 8(10), pp. 1–18. doi:10.3390/pr8101304.

MOHW (2020) 'Botswana COVID-19 Guideline 5 : Quarantine and Isolation', (May).

Motlhatlhedi, K. *et al.* (2020) 'Coronavirus disease 2019 in Botswana: Contributions from family physicians', *African Journal of Primary Health Care and Family Medicine*, 12(12), pp. 1–3. doi:10.4102/PHCFM.V12I1.2497.

Mugisha, J.Y.T. *et al.* (2021) 'Mathematical modeling of COVID-19 transmission dynamics in Uganda: Implications of complacency and early easing of lockdown', *PLoS ONE*, 16(2 February), pp. 1–16. doi:10.1371/journal.pone.0247456.

Nadim, S.S. and Chattopadhyay, J. (2020) 'Occurrence of backward bifurcation and prediction of disease transmission with imperfect lockdown: A case study on COVID-19', *Chaos, Solitons and Fractals*, 140(January), p. 110163. doi:10.1016/j.chaos.2020.110163.

Ndaïrou, F. *et al.* (2020) 'Mathematical modeling of COVID-19 transmission dynamics with a case study of Wuhan', *Chaos, Solitons and Fractals*, 135(January). doi:10.1016/j.chaos.2020.109846.

Nyabadza, F. *et al.* (2020) 'Modelling the potential impact of social distancing on the Covid-19 epidemic in South Africa', *Computational and Mathematical Methods in Medicine*, 2020. doi:10.1155/2020/5379278.

Oraby, T. *et al.* (2021) 'Modeling the effect of lockdown timing as a COVID-19 control measure in countries with differing social contacts', *Scientific Reports*, 11(1), pp. 1–13. doi:10.1038/s41598-021-82873-2.

Patel P, Athotra A, Vaisakh TP, Dikid T, Jain SK. Impact of nonpharmacological interventions on COVID-19 transmission dynamics in India. Indian J Public Health. 2020;64:S142–6.

Pearson CA, Van Schalkwyk C, Foss AM, O'Reilly KM, Pulliam JR, CMMID COVID-19 working group. Projected early spread of COVID-19 in Africa through 1 June 2020. Euro

Surveill. 2020 May 7; 25 (18):2000543.
https://doi.org/10.2807/15607917.ES.2020.25.18.2000543 PMID: 32400361

Rahman, A. *et al.* (2021) 'A review of covid-19 modelling strategies in three countries to develop a research framework for regional areas', *Viruses*, 13(11), pp. 1–23. doi:10.3390/v13112185.

Rawson, T. *et al.* (2020) 'How and When to End the COVID-19 Lockdown: An Optimization Approach', *Frontiers in Public Health*, 8(June). doi:10.3389/fpubh.2020.00262.

Roche, B., Garchitorena, A. and Roiz, D. (2020) 'The impact of lockdown strategies targeting age groups on the burden of COVID-19 in France', *Epidemics*, 33, p. 100424. doi:10.1016/j.epidem.2020.100424.

Roques, L. *et al.* (2020) 'Impact of Lockdown on the Epidemic Dynamics of COVID-19 in France', *Frontiers in Medicine*, 7(June), pp. 1–7. doi:10.3389/fmed.2020.00274.

Sardar, T. *et al.* (2020) 'Assessment of lockdown effect in some states and overall India: A predictive mathematical study on COVID-19 outbreak', *Chaos, Solitons and Fractals*, 139, p. 110078. doi:10.1016/j.chaos.2020.110078.

Siamisang, K., Kebadiretse, D. and Masupe, T. (2021) 'University of botswana public health medicine unit contributions to the national covid-19 response', *Pan African Medical Journal*, 39. doi:10.11604/pamj.2021.39.82.28314.

Sichone, J. *et al.* (2021) 'Assessing required SARS-CoV-2 blanket testing rates for possible control of the outbreak in the epicentre Lusaka province of Zambia with consideration for asymptomatic individuals: A simple mathematical modelling study', *PLoS ONE*, 16(4 April), pp. 1–18. doi:10.1371/journal.pone.0249479.

Sichone J, Simuunza MC, Hang'ombe BM, Kikonko M. Estimating the basic reproduction number for the 2015 bubonic plague outbreak in Nyimba district of Eastern Zambia. PLoS Negl Trop Dis [Internet]. 2020;14(11):e0008811. Available from: http://dx.doi.org/10.1371/journal.pntd.0008811

Singh, B.P. (2021) *Modeling and forecasting the spread of COVID-19 pandemic in India and significance of lockdown: A mathematical outlook*. 1st edn, *Handbook of Statistics*. 1st edn.

Elsevier B.V. doi:10.1016/bs.host.2020.10.005.

Stuart RM, Abeysuriya RG, Kerr CC, Mistry D, Klein DJ, Gray RT, et al. Role of masks, testing and contact tracing in preventing COVID-19 resurgences: A case study from New South Wales, Australia. BMJ Open. 2021;11(4):1–10.

Talmoudi, K. *et al.* (2020) 'Estimating transmission dynamics and serial interval of the first wave of COVID-19 infections under different control measures: a statistical analysis in Tunisia from February 29 to May 5, 2020', *BMC Infectious Diseases*, 20(1), pp. 1–8. doi:10.1186/s12879-020-05577-4.

Tiwari, V., Deyal, N. and Bisht, N.S. (2020) 'Mathematical Modeling Based Study and Prediction of COVID-19 Epidemic Dissemination Under the Impact of Lockdown in India', *Frontiers in Physics*, 8(November), pp. 1–8. doi:10.3389/fphy.2020.586899.

Wangari, I.M. *et al.* (2021) 'Mathematical Modelling of COVID-19 Transmission in Kenya: A Model with Reinfection Transmission Mechanism', *Computational and Mathematical Methods in Medicine*, 2021. doi:10.1155/2021/5384481.

Yang, H.M. *et al.* (2021) 'Mathematical modeling of the transmission of SARS-CoV-2—Evaluating the impact of isolation in São Paulo State (Brazil) and lockdown in Spain associated with protective measures on the epidemic of CoViD-19', *PLoS ONE*, 16(6 June), pp. 1–24. doi:10.1371/journal.pone.0252271.

Yang, Z. *et al.* (2020) 'Modified SEIR and AI prediction of the epidemics trend of COVID-19 in China under public health interventions', *Journal of Thoracic Disease*, 12(3), pp. 165–174. doi:10.21037/jtd.2020.02.64.

Zhao, S. and Chen, H. (2020) 'Modeling the epidemic dynamics and control of COVID-19 outbreak in China', *Quantitative Biology*, 8(1), pp. 11–19. doi:10.1007/s40484-020-0199-0.